Abstracts

International Academy of Cardiology
18th World Congress on Heart Disease
Annual Scientific Sessions 2013

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Asher Kimchi, Los Angeles, Calif., USA
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DISEASE MECHANISMS LEADING TO CARDIOMYOPATHY AND HEART FAILURE

001
ADVANCES IN PATHOPHYSIOLOGY AND MANAGEMENT OF DIASTOLIC HEART FAILURE
K. Chatterjee
The Carver College of Medicine, University of Iowa, Iowa City, IA, USA

Diastolic heart failure is defined as a syndrome of heart failure with preserved ejection fraction (HFPREF). In diastolic heart failure, left ventricular wall thickness and mass is increased and the cavity size is normal. The mass/cavity ratio is increased. There is also a decrease in wall stress which contributes to maintain ejection fraction. The diastolic pressure volume relation curve shifts upwards and to the left. This causes a disproportionate increase in left ventricular diastolic pressure. With a marked upward and leftward shift of the diastolic pressure volume curve, left ventricular filling is compromised and stroke volume and cardiac output declines. The left ventricular wall architecture is disorganised and characterised by marked increase in fibrosis which makes the left ventricle stiffer. The myocyte diameter is increased without a change in its length. There is also increased protein synthesis. Diuretic treatment is necessary to relieve congestion. Spironolactone has the potential to reduce fibrosis. Sildenafil (PDE5 inhibitor) may improve symptoms, exercise tolerance. It also decreases pulmonary capillary wedge pressure and pulmonary artery pressure.
REVERSAL OF CARDIAC REMODELING IN HEART FAILURE BY ALPHA- ADRENOCEPTOR BLOCKADE
N.S. Dhalla
Institute of Cardiovascular Sciences, St. Boniface Hospital Research, Faculty of Medicine, University of Manitoba, Winnipeg, MB, Canada

In view of the role of elevated levels of circulating catecholamines, the activation of both alpha-adrenoceptor (AR) and beta-AR is considered to play a critical role in the pathogenesis of heart failure. Previous studies have shown the beneficial effects of beta-AR blockade in the failing heart; however, very little information on the action of alpha-AR blockade is available. In this study, heart failure in rats was induced by occluding the coronary artery for 12 weeks and then treated with or without prazosin (10 mg/kg/day) for 8 weeks. Depressed left ventricular (LV) systolic pressure, cardiac output and ejection fraction as well as LV diastolic pressure in 20 weeks infarcted animals were corrected partially by prazosin treatment. Cardiac hypertrophy and cardiac remodeling including increased LV posterior wall thickness in the failing hearts were also partially reversed by prazosin. The elevated levels of plasma norepinephrine and depressed sarcoplasmic reticular (SR) calcium pump activities were partially reversed whereas depressed SR calcium release and myofibrillar ATPase activities in heart failure were not affected by prazosin. The results suggest that partial reversal of cardiac remodeling and cardiac performance in heart failure by alpha-AR blockade was associated with partial reversal of SR calcium pump activity. (Supported by a grant from the Canadian Institutes of Health Research)
AGING AND HEART FAILURE. UPDATE
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The population of older patients with heart failure is increasing worldwide. Apart from the role of cardiovascular aging in HF among older patients, impaired healing after myocardial infarction (MI) may be a major culprit. Cumulative evidence has established that acute MI triggers the healing process, and optimal healing is needed for survival with a favorable outcome. It is known that healing involves a well-orchestrated sequence of inflammation and remodeling of the myocardium and extracellular matrix over weeks to months, depending on the species and infarct characteristics. In humans, small infarcts heal within weeks while large infarcts may take months to heal. Importantly, profound remodeling at structural, cellular, molecular and biochemical levels occurs during the healing process. While improved therapies after acute MI have improved survival, current therapies do not target post-infarct healing. While early reperfusion therapy reduces infarct size, impaired healing appears to a major factor that contributes to adverse remodeling and HF in older survivors. Progressive left ventricular remodeling and progression to HF are persistent problems, both in older adults and elderly patients. Additionally, several recommended therapies after MI can impact early and late phases of healing in positive or negative directions. Preclinical studies have suggested that several pathways during early and late phases of the healing process can be potentially targeted to prevent HF. Translational research protocols that address the different phases of post-MI healing as well as aging may bring us closer to therapy for optimizing post-infarct healing and outcome.
MITOCHONDRIAL FISSION AND FUSION IN HEART FAILURE
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Mitochondrial fusion and fission are essential processes for preservation of normal mitochondrial function. OPA1, a mitochondrial fusion protein, is decreased in both human and rat failing hearts. A number of inherited neuropathies are associated with mutation of fission/fusion proteins, including Charcot-Marie-Tooth (CMT) disease. We hypothesized that mutation of OPA1, one cause of CMT type 2, would lead to cardiac dysfunction via impaired mitochondrial function in the mouse heart. The homozygote mutation B6;C3-Opa1(Q285STOP) mouse, which models autosomal dominant optic atrophy, is embryonic lethal. The heterozygote has a 50% reduction in OPA1 transcript and protein in the heart and was used for our studies. Reduced mtDNA copy number and decreased expression of nuclear antioxidant genes at 3-4 months occurred at 3 months. Although initial cardiac function was normal, at 12 months the OPA1+/- mouse hearts had decreased fractional shortening, cardiac output and myocyte contraction. This coincided with the onset of blindness. Besides small fragmented mitochondria, aged OPA1+/- mouse had impaired cardiac mitochondrial function compared to wild type littermates. In conclusion, OPA1 mutation leads to deficiency in antioxidant transcripts, increased ROS, mitochondrial dysfunction and late onset cardiomyopathy. This has implications for the clinical care of patients with inherited optic neuropathies and raises possibility of OPA1 mutation as cause of idiopathic dilated cardiomyopathy.
Clinical genetic testing is becoming more mainstream in inherited disorders, such as cardiomyopathies. At the same time, newer DNA sequencing technology can now complete the sequencing of an entire human genome several times over in a matter of days, in an efficient and cost effective manner. However, the extent of remarkable genetic variation is increasingly being appreciated and this undoubtedly adds new challenges to the difficulty of distinguishing true pathogenetic variants from benign variants in diagnostic genetics and in the research setting. In dilated cardiomyopathy (DCM), the recent discovery of high frequency of titin gene mutations will make genetic testing more efficient and clinically useful in this disease. Furthermore, better understanding of genotype-phenotype associations, in particular concerning genes associated with poor prognosis and arrhythmogenic traits, will assist the clinician in identifying early stages of disease and providing more appropriate treatments. This high level of complexity requires an expert genetic team for counseling, manage, deliver and follow-up over time the results of genetic testing, which is particularly important for screening of family members potentially at risk. In DCM, genetic testing may be useful for the identification of non-carriers and asymptomatic carriers, as well as for prevention strategies, sport recommendations, defibrillator implantation and to guide reproductive decision-making including utilization of pre-implantation genetic diagnostic strategies.
GENETIC EPIDEMIOLOGY OF LEFT VENTRICULAR HYPERTROPHY

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Left ventricular (LV) hypertrophy is a strong independent predictor of increased cardiovascular morbidity and mortality in clinical and population-based samples. Several studies have indicated that LV mass is influenced by genetic factors. The substantial heritability (h²) for LV mass in population-based samples of varying ethnicity indicates robust genetic influences on LV hypertrophy. Genome-wide linkage and association studies in diverse populations have been performed to identify genes influencing LV mass, and although several chromosomal regions have been found to be significantly associated with LV mass, the specific genes and functional variants contained in these chromosomal regions have yet to be identified. In addition, multiple studies have tried to link single-nucleotide polymorphisms (SNPs) in regulatory and pathway genes with common forms of LV hypertrophy, but there is little evidence that these genetic variations are functional. Up to this point in time, the results obtained in genetic studies are of limited clinical value. Much of the heritability remains unexplained, the identity of the underlying gene pathways, genes, and functional variants remains unknown, and the promise of genetically-based risk prediction and personalized medicine remain unfulfilled. However, molecular biological technologies continue to improve rapidly, and the long-term potential of sophisticated genetic investigations using these modern genomic technologies, coupled with smart study designs, remains intact. Ultimately, genetic investigations offer much promise for future prevention, early intervention and treatment of this major public health issue.
BLUNTED RESPONSES OF RENAL SYMPATHETIC NERVE ACTIVITY TO C-TYPE NATRIURETIC PEPTIDE IN THE PVN OF RATS WITH HEART FAILURE

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Volume expansion produces a reflex decrease in renal sympathetic nerve activity (RSNA) that is mediated by the PVN. C-type natriuretic peptide (CNP) has the attributes to be a potential candidate as a mediator of this sympathoinhibition in the PVN. First, we determined the presence of CNP receptors (NPR-C) on PVN neurones that projected to RVLM. The retrogradely transported tracers, green fluorescent latex microspheres, were microinjected into the RVLM and found primarily colocalized with NPR-C in parvocellular neurons in the PVN. Second, of the 19 spontaneously active neurons recorded in the PVN in normal rats with extracellular single-unit recording in vivo, 6 units were antidromically activated from the rostral ventrolateral medulla (RVLM). Picoinjection of CNP significantly decreased the basal discharge in 5/6 PVN-RVLM neurons, and in 6/13 neurons that weren’t antidromically activated from the RVLM. There were no significant changes after picoinjection of artificial cerebrospinal fluid. Third, microinjection of CNP into the PVN significantly decreased RSNA, means arterial pressure (MAP) and heart rate (HR). Fourth, microinjection of CNP into PVN produced significantly attenuated responses (in RSNA 56%, MAP 69%, HR 75% of sham rats) in rats with CHF. Consistent with these observations, the expressions of NPR-C in the PVN were decreased in CHF rats. These results suggest an altered inhibitory role for CNP in the PVN of rats with CHF.

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TRANSCRIPTIONAL MECHANISMS LEADING TO DILATED CARDIOMYOPATHY IN THE ABSENCE OF HYPERTROPHY

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The E2F/Rb pathway is comprised of at least a dozen distinct proteins which are expressed in a cell/tissue specific context to regulate genes involved in proliferation, differentiation, and death. Perturbation of the E2F/Rb pathway through modulation of its members induces changes in the cell cycle which could potentially be targeted in cell growth and death. However, the constellation of E2Fs and Rb family members and their exact role in cardiac growth and development remains to be fully explored. In order to modulate the E2F pathway in vivo in mouse myocardium, we expressed E2F6 (a transcriptional repressor of E2F responsive genes) under the control of the alpha myosin heavy chain promoter. The transgenic (tg) mice exhibited dilated cardiomyopathy (DCM). Microarray, microRNA array and protein expression profiling was utilized to identify targets which were sensitive to E2F6 levels in tg hearts. E2F responsive transcripts involved in cell cycle regulation including E2F1 and E2F3 were up regulated in tg hearts, but did not induce changes in cardiomyocyte size or number. Several critical proteins were down-regulated and microRNA array detected the induction of non-cardiac microRNAs which were linked to the protein loss at the post-transcriptional level. Specific activation of the Extracellular Receptor Kinases (ERK) which has been linked to loss of transcriptional control and DCM was apparent in E2F6 tg mice. Thus precise transcriptional control via the E2F/Rb pathway and cross talk with ERK is critical for normal gene expression, growth and function of myocardium.

Funded by CIHR.
Objective: To investigate the effect of Carnitine palmitoyltransferase 1b (CPT1b) deficiency on pressure overload-induced cardiac hypertrophy.

Background: CPT1 is a rate-limiting step of mitochondrial β-oxidation by controlling the mitochondrial uptake of long-chain acyl-CoAs. The muscle isoform, CPT1b, is the predominant isoform expressed in the heart. CPT-1 inhibitors have been shown to be protective against cardiac hypertrophy and heart failure. However, clinical and animal studies have shown mixed results, thereby posting concerns on the safety of this class of drugs. Preclinical studies using genetically modified animals should provide a better understanding of targeting CPT1 to evaluate it as a safe and effective therapeutic approach.

Methods: Heterozygous CPT1b knockout mice (CPT1b+/-) were subjected to transverse aorta constriction (TAC)-induced pressure-overload.

Results: These mice showed overtly normal cardiac structure/function under the basal condition. Under a severe pressure-overload condition induced by two weeks of transverse aorta constriction (TAC), CPT1b+/- mice were susceptible to premature death with congestive heart failure. Under a milder pressure-overload condition, CPT1b+/- mice exhibited exacerbated cardiac hypertrophy and remodeling compared with that in wild-type littersmates. There were more pronounced impairments of cardiac contraction with greater eccentric cardiac hypertrophy in CPT1b+/- than in controlled mice. Moreover, the CPT1b+/- heart exhibited exacerbated mitochondrial abnormalities and myocardial lipid accumulation with elevated triglycerides and ceramide content, leading to greater cardiomyocytes apoptosis.

Conclusion: We conclude that CPT1b deficiency can cause lipotoxicity in the heart under pathological stress, leading to exacerbation of cardiac pathology. Therefore, caution should be applied in the clinical use of CPT-1 inhibitors.
DELETION OF THE TRANSLATIONAL REPRESSORS EUKARYOTIC TRANSLATION INITIATION FACTOR 4E BINDING PROTEINS 1 AND 2 PROTECTS AGAINST PRESSURE OVERLOAD INDUCED HEART FAILURE

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Assembly of the translation initiation machinery is negatively regulated by the eukaryotic translation initiation factor 4E binding proteins, which sequester the mRNA cap-binding protein eIF4E, thus preventing assembly of an intact initiation complex. However, the role of translational control on the development of congestive heart failure (CHF) has not been systematically examined. Here we perturbed translational control in mice by knockout of both 4E binding protein 1 (Eif4ebp1) and 2 (Eif4ebp2) (designated as Eif4ebp1/2 double knockout) to study its impact on left ventricular hypertrophy and CHF resulting from transverse aortic constriction. Eif4ebp1/2 double knockout caused a modest increase in left ventricular mass under basal conditions. However, following transverse aortic constriction, Eif4ebp1/2 double knockout profoundly attenuated the development of CHF and its attendant mortality. Examination of candidate genes involved in the mechanism revealed increased expression of transcription factors for genes governing energy metabolism and mitochondrial biogenesis with corresponding increases in the expression of their target genes. Our data indicate that removing physiological restraints on translation initiation exerts a profound cardiac protective effect against pressure overload induced CHF, suggesting that method(s) to disrupt the function of the 4E binding proteins may be a novel therapeutic approach for preventing or treating CHF.
RESIDUAL MYOCARDIAL INJURY AND ATTENUATED PRODUCTION OF VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) IN PATIENTS WITH RECOVERED PERIPARTUM CARDIOMYOPATHY (PPCM)

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Background: PPCM is a rare disease and pathophysiology of this disease is still under investigation. We proposed that altered endothelial function during oxidative stress in pregnancy may contribute to the development of PPCM. In addition, we attempted to evaluate whether residual myocardial injury may be detected by comprehensive echo techniques such as tissue Doppler (TDI) and 2D Strain (2DS) imaging in post PPCM.

Methods: We evaluated 13 women (mean age 36±6 years) and 11 of them with complete LVEF recovery comprised this study. Both LV and RV function assessment using standard echo, tissue Doppler imaging (TDI) and 2D strain techniques were evaluated. The number of circulating EPCs (CD34 and CD34/KDR), VEGF, hsCRP, IL 6, Ox-LDL serum levels were quantified. All measures were compared to matched controls.

Results: The mean LVEF at presentation of PPCM was 32.5±8.8%, at follow-up (6.2±20 months) was 58.6±3.5%. When compared to controls, patients with PPCM had a trend for lower systolic velocities (S’) on TDI (lateral 7.9±2.0 vs. 9.5±1.9, p=0.07, septal 10.1±11.2±2.2 ms, p=0.08) and decreased global longitudinal strain (-20.5±2.3% vs. 22.8±2.2%, p=0.07). VEGF levels were significantly lower in PPCM group (1.41±0.06 vs.1.47±0.03 pg/ml, p=0.008) with no significant differences in EPCs, IL 6 and Ox-LDL.

Conclusions: In this pilot study TDI and 2D strain were able to identify some residual myocardial injury in patients post PPCM. Attenuated production of VEGF even after the initial insult may suggest the contribution of endothelial dysfunction in the acute setting.
Routine evaluation of LV function includes assessment of inward and longitudinal motion by echocardiographic techniques. However, it is well known that the LV also rotates and twists and untwists during the cycle because of the different orientation of different layers of muscle bundles present in the LV. One way to understand this is to conceptualize the LV as a long piece of muscle which has been twisted on itself. This concept, facilitates understanding of the role of different muscle layers in assessing cardiac function. Speckle tracking using three-dimensional transthoracic echocardiography (3D TTE) is more accurate than two-dimensional imaging to assess rotation, twist and torsion findings. This is because with the two-dimensional technique, a speckle can easily move out of the thin two-dimensional sector plane during cardiac motion resulting in inaccuracies. On the other hand, the 3D dataset volume is much larger, therefore, and the same speckle is more likely to be tracked throughout the cardiac cycle. Using 3D TTE, radial, transversal (lateral), longitudinal and circumferential strain and strain rate can be easily calculated. Both basal and apical rotation can be measured in degrees and the twist calculated as the difference between basal and apical rotations. Decrease in the rate of untwisting of the LV is considered to be the earliest sign of LV diastolic dysfunction. Torsion can be calculated by 3DTTE by dividing the twist with the distance of the short axis cross-sectional planes.
Flurpiridaz F-18, a new PET tracer for myocardial perfusion imaging has recently been studied in a Phase II trial. In pre-clinical and phase-I studies, flurpiridaz F-18 has shown essentially linear myocardial uptake throughout the range of flow. It does not require an on-site cyclotron. Unlike rubidium-82, flurpiridaz F-18 is retained in the myocardium and can be used with exercise. Various characteristics suggest flurpiridaz F-18 might an ideal myocardial perfusion tracer. In the Phase II clinical trial (Berman, et al: JACC 2013), we studied 143 patients with rest-stress PET and Tc-99m SPECT MPI. A higher percentage of PET images were rated as excellent/good at stress (99.2% vs. 88.5%, p < 0.01) and rest (96.9% vs. 66.4, p< 0.01). Diagnostic certainty (percentage definitely abnormal/normal) was higher for PET (90.8% vs. 70.9%, p<0.01). In 86 patients who underwent ICA, PET sensitivity was higher (78.8% vs. 61.5%, respectively, p=0.02). Specificity was not significantly different (PET: 76.5% vs. SPECT: 73.5%). Receiver-operating characteristic curve area was 0.82± 0.05 for PET and 0.70± 0.06 for SPECT (p=0.04). Normalcy rate was 89.7% with PET and 97.4% with SPECT (p=NS). In patients with CAD, reversible defect magnitude was greater with PET than SPECT (p=0.008). Thus, PET MPI with flurpiridaz F-18 was superior to SPECT MPI for image quality, interpretative, certainty, and overall CAD diagnosis. This new tracer might significantly improve the assessment of patients with radionuclide MPI compared with the standard SPECT MPI methods and could provide a major advance in noninvasive assessment of CAD.
USEFULNESS OF OPTICAL COHERENCE TOMOGRAPHY IN DAILY CLINICAL PRACTICE

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Recently developed frequency-domain optical coherence tomography (FD-OCT) allow us to obtain 75mm length of high resolution intravascular image (10-20 micrometer) within 3 sec during contrast injection through a guiding catheter. This FD-OCT demonstrates the pathophysiology of the coronary atherosclerosis including vulnerable plaques with thin cap fibroatheroma (TCFA) in vivo before percutaneous intervention (PCI). Using this, plaque rupture, erosion and thrombus were observed more frequently (73%, 23% and 100%, respectively) compared with intravascular ultrasound or angioscopy (p<0.01) at the culprit site in acute myocardial infarction. During PCI, it is quite easy to measure the minimum and reference lumen area (MLA and RLA) at the lesion and the length between the proximal and distal references can be demonstrated automatically by FD-OCT, and the decision of the stent size and length becomes very easy and accurate in the daily clinical practice. Three dimensional reconstruction (3D-OCT) may allow us to identify the position of guidewire across the stent struts at the site of bifurcation lesion and to perform the procedure of PCI more effectively. Furthermore, FD-OCT can demonstrate the results of PCI including malaposition and incomplete stent apposition, tissue and thrombus protrusion and edge dissection more clearly than IVUS (p<0.01) soon after PCI and the degree of neointima coverage and the presence of malaposition more precisely than IVUS (p<0.01) long after PCI. Thus, FD-OCT may allow us to improve the results of PCI and the mechanism of the primary and secondary prevention could be revealed in the near future by FD-OCT.
MYOCARDIAL STRAIN FOR THE ASSESSMENT OF LV FUNCTION
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It is now possible to measure myocardial deformation by tissue Doppler imaging and speckle tracking echocardiography. A number of studies have validated the accuracy of echocardiography derived measurements against sonomicrometry and cardiac MR. Furthermore, experimental and human studies have evaluated the hemodynamic determinants of strain and systolic and diastolic strain rate. There are several clinical applications for strain measurements including evaluation of myocardial ischemia and viability, congenital heart disease, as well as cardiac function in patients with systolic and diastolic heart failure. There is also increasing interest in the application of strain to evaluate patients with cardiomyopathic disorders and to differentiate pericardial constriction from restrictive cardiomyopathy. Finally, there are promising studies highlighting its potential utility in patients receiving chemotherapy.
SCREENING FOR ASYMPTOMATIC CORONARY ARTERY DISEASE: SEEKING VALUE IN A MULTI-MODALITY WORLD

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There are multiple potential candidate testing modalities for evaluating patients at risk for coronary artery disease (CAD) which include stress ECG testing; stress echocardiography and myocardial perfusion imaging (MPI); and cardiac computed tomography (CT). Stress echocardiography and MPI are considered inappropriate in low and intermediate risk patients but may have value in patients at high CAD risk. Stress ECG is inappropriate as a routine screening test but may have value in high risk patients who plan to start vigorous exercise. CT coronary angiography is considered inappropriate in any asymptomatic patient but non-contrast CT for determining the coronary artery calcium score (CACS) is appropriate in low risk patients with a strong family history of CAD and in those who are at intermediate risk. CACS has gained favor since it is a rapid, simple, inexpensive 10-second test that requires no patient preparation, has no contraindications, has very low radiation exposure, and is the only test to detect early atherosclerosis. CACS prognostic value has been demonstrated in multiple large clinical trials and in conjunction with stress MPI. Early CAD detection may significantly reduce cardiac morbidity following the initiation of statin therapy and CACS may also identify which asymptomatic patients require aggressive treatment. CACS may therefore provide the best value of current testing modalities in asymptomatic patients who are at risk for CAD.
Chronic symptomatic ischemic heart failure remains a major cause of morbidity and mortality in the adult. Coronary revascularization was recognized as an important strategy for patients with symptomatic chronic ischemic heart failure for several decades. Recently, the utility of coronary revascularization in early management of patients with stable ischemic heart failure has come into question by several randomized clinical trials. Some of these studies have also challenged the notion that the determination of the predominant state of the dysfunctional left ventricular myocardium (viable or scarred) may facilitate identification of patients who would benefit the most from revascularization. These prospective, randomized, multi-center trials have also exposed many of the practical impediments to conducting an ideal clinical investigation particularly in the context of increasingly recognized need for goal-directed and personalized approaches to management of ischemic heart disease. This presentation reviews the recent developments in diagnostic imaging for myocardial viability in chronic ischemic heart failure and summarizes the present evidence for an ischemia-guided approach to evaluation and treatment of patients with chronic ischemic heart disease with left ventricular systolic dysfunction.
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NOVEL USES OF CARDIAC MRI FOR NON-ISCHEMIC HEART DISEASE
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While the evaluation of ischemic cardiomyopathy (ICMX) has been well defined via Cardiovascular MRI (CMR), less is understood how the application of similar approaches can be incorporated for the identification non-ischemic cardiomyopathy (NICMX), often defining many obscure diagnoses. The utility for accurate, rapid, inexpensive and robust technique not requiring biopsy confirmation has particular value in the armamentarium of informed clinicians. Herein we shall define the current role of non-invasive CMR to diagnose NICMX patients. Examples include: cardiac sarcoid, hemochromatosis, hypertrophic cardiomyopathy, viral cardiomyopathy, neuro-muscular disease, thalassemia’s and ARVD will be presented along with relevant evidence-based medicine supporting CMR’s early promise. Additionally, considerations for cost-effective strategies, discussion of CMR’s additive value as well as risk-stratification and prognostication will be examined. We will propose that, similar to CMR’s role as the ‘gold-standard’ for ICMX, this path may well be in establishment for NICMX.
NON-INVASIVE CARDIOVASCULAR IMAGING FOR EVALUATION OF CORONARY ARTERY BYPASS GRAFT DISEASE
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Coronary artery bypass graft (CABG) surgery is a widely used method of revascularization in patients with severe coronary artery disease (CAD). Various studies have shown improvement of survival and cardiac symptoms after CABG, particularly in patients with low ejection fraction and multivessel CAD. Myocardial perfusion can be compromised after CABG due to graft disease, progression of CAD distal to the graft or in remote CAD distribution. Although abnormalities can be silent, these can lead to adverse outcome with subsequent left ventricular dysfunction, myocardial infarction and death. Various non-invasive methods are available for evaluation of patients after CABG. Stress echocardiography is an effective method for evaluation of CAD after CABG. Advantages include wide availability, lack of irradiation and incremental prognostic information. Sensitivity is modest, particularly with submaximal heart rate. The addition of myocardial contrast allows evaluation of perfusion and enhances sensitivity. SPECT imaging is widely used and provides excellent tomographic evaluation of ischemia. Both stress echocardiography and SPECT predict prognosis. Patients with normal studies have excellent outcome, whereas the extent of stress abnormalities is associated with higher incidence of cardiac events. Stress imaging techniques cannot differentiate graft disease from stenosis distal to graft. In general, stress testing is not routinely indicated in asymptomatic patients within 5 years after CABG. Functional imaging with CT angiography and MRI allows visualization of bypass grafts with excellent accuracy to detect graft occlusion. High density artifacts caused by metal clips during CABG may locally disrupt graft assessment. Average sensitivity and specificity of cardiac CT are 96% and 97% respectively. MR angiography has a high sensitivity and specificity for diagnosis of CABG disease. MRI enables anatomic and functional analysis in a single acquisition without ionizing irradiation. In addition, both CT and MRI can evaluate perfusion. Disadvantages of MRI are exclusion of patients with defibrillators and pacemakers. Metallic clips may result in image degradation due to radiofrequency shielding. It is concluded that several non-invasive modalities provide good accuracy for evaluation of bypass grafts and native CAD after CABG and can predict prognosis. Understating the merits and limitations of each technique is a key for proper selection of the appropriate imaging modality in a given patient.
PROGNOSTIC VALUE OF STRESS ECHOCARDIOGRAPHY IN PATIENTS WITH CORONARY ARTERY DISEASE

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Background: Negative test of stress echocardiography (SE) is associated with an annual event rate of major cardiac events less than 1%. Global ejection fraction (EF) and index of wall motion abnormalities (WMA) remains important predictor of cardiac events. Methods: 4500 patients underwent SE (mean age: 53.4±0.4; 84% males). We have used a 22-segmental scoring scheme and 7-point scale grading the degree of hypokinesia (mild-, moderate and severe).

Results: In assessing global and regional contractility in patients with CAD with a lot of coronary lesions and the risk of a major cardiac events to detect complex thresholds of global and regional contractility that identify high-risk patients we used the method of “classification trees”. We obtained the threshold levels of global and regional contractility and defined their importance and priority. From the set of parameters were identified three leading indicators: 1. Index of WMA 7 ranges from 1.78 to 2.71. 2. Dynamics of EF of LV after exercise. The threshold value increase in EF after exercise is 4.5%. 3. Ischemic EKG changes during exercise test. Occurrence of ST segment depression on EKG during stress test may also certify that the patient's extensive coronary lesions, provided at the height of the load disturbances of regional myocardial high index of WMA 7 and decreased EF of LV at the height of physical activity.

Conclusion: Positive indicators of severity of CAD are exercise induced regional WMA, dynamics of EF of LV after exercise and ischemic EKG changes during exercise test.
OPTICAL COHERENCE TOMOGRAPHY (OCT): WHAT YOU NEED TO KNOW

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Objectives: Understanding the technical aspects of Optical Coherence Tomography (OCT) as they apply to daily clinical practice and comparing OCT images and acquisitions to intra-vascular ultrasound (IVUS).

Background: OCT is an imaging technology that provides high resolution (10x) cross-sectional images in many fields of medicine. It uses light as opposed to the widely used intra-vascular ultrasound imaging. Traditional intravascular ultrasound images are different than those obtained by OCT.

Methods: Semi-automated high-resolution analysis of light derived OCT images allows for improved evaluation of mechanical complications of interventions, stent apposition, stent strut behavior, overlap, and neointimal hyperplasia.

Conclusions: This review will focus on the image acquisition, technical aspects, advantages and disadvantages of coronary OCT. It will compare OCT to IVUS and discuss future directions of OCT.
VP-PM was first described in 1978 by Rahimtoola. From that time to 2011, aortic VP-PM has received a great deal of attention but studies have come to varying conclusions especially with regard to its effect on mortality. This is because prosthetic heart valve (PHV) area [effective orifice area index (EOAi)] has been predicted rather than measured. To better assess the outcomes of VP-PM, EOAi should be measured at hospital discharge which provides information of actual PHV after insertion into the patient. It should also be measured at 6-12 months of follow-up at which time the 4 phases of physiological healing and morphological changes are complete; EOAi at this time determines the long-term impact of VP-PM on patients’ outcomes. Mild, severe and critical VP-PM should be defined as EOAi of > 0.9 cm²/m², ≤ 0.6 cm²/m² and ≤ 0.4 cm²/m². One needs to focus especially on severe/critical degrees of VP-PM and determine if death was actually due to VP-PM and/or was VP-PM an important determinant of cardiac related cause of death by multivariate analysis?
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COMPARISON OF DIFFERENT SURGICAL APPROACHES IN PATIENTS WITH TRANSPOSITION OF THE GREAT ARTERIES
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Two decades after surgery for transposition of the great arteries (TGA), the clinical status, cardiac function, cardiorespiratory performance and neurohormonal activity of patients who underwent either atrial switch (Mustard) or arterial switch operation (ASO) were compared. Sixty-two patients with simple TGA, who underwent either Mustard (n=34) or ASO (n=28) procedure, have been included in this cross sectional study. Following the same study protocol, a clinical work up including echocardiography, stress test and blood work was completed for all patients. Mean age in both groups was comparable: ASO vs. Mustard [20.6 (SD=2.1) vs. 20.6 (SD=3.4) years]. All ASO patients were in NYHA class I, whereas 59% of Mustard patients were in NYHA class II or III. Peak oxygen uptake was higher in ASO patients (% of predicted 80 vs. 69, p<0.01). Compared to healthy individuals, the mean Tei index for systemic ventricle was high in both groups, but this parameter was significantly higher in Mustard than ASO patients [0.60 (SD=0.16) vs. 0.47 (SD=0.14), p<0.01]. The median plasma N-terminal pro brain natriuretic peptide in ASO patients was within the normal range but the Mustard group had significantly higher levels [42 (18 – 323) vs. 172 (26 – 1018), p < 0.0001]. In conclusion, our cross sectional assessment two decades after surgery reveals better clinical status of patients who underwent ASO compared to Mustard patients. This holds in terms of cardiac function, cardiorespiratory performance and neurohormonal activity.
DETERMINATION OF RECURRENT TACHYCARDIA FOLLOWING SUCCESSFUL ABLATION IN SUBJECTIVELY SYMPTOMATIC CHILDREN

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Introduction: Sensed tachycardia (ST) can be a common complaint in children following successful acute supraventricular (SVT) ablation requiring objective differentiation of true recurrences from subjective complaints. The purpose of this study was to evaluate diagnostic efficacy of clinical studies to differentiate true from perceived arrhythmias.

Methods: Patient (pt) records between 2002 and 2012 were reviewed. Post ablation clinical testing included detailed history, ECG at 1 week, ECG/exercise testing (ET) at 1 month, and a recommended clinical visit at 1 year. Pts with ST were re-evaluated anytime. Additional testing included ECG, exercise, or 30-day ambulatory event monitoring (AEM) as required.

Results: On post ablation follow-up, 119/205 pts (58%) reported ST. However true SVT recurrence was found in only 67 of these (56%). Age at ablation (11.2y vs 13.3y, p=0.02) was significant but mean duration of follow up (7.2 y vs 6.4 y) was similar (p=NS) between pts with and without recurrences. Median time to SVT recurrence following ablation was 14.2 months. Of all the clinical studies, AEM was the most sensitive test for diagnosing SVT recurrence (100% specificity; 77% specificity; PPV 100%; NPV 84%). History, ET and ECG showed limited diagnostic efficacy.

Conclusions: Subjective tachycardia complaints are common in children post ablation, however not always reflecting true recurrences. Younger pts experience more true recurrences. While 30 day ambulatory event monitors are the most sensitive diagnostic tool for determining true recurrence, the diagnosis can still be missed in a significant number of patients. Serial clinical monitoring following even “successful” ablation is required.
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RELATION OF ECHOCARDIOGRAPHIC AORTIC VALVE SCLEROSIS TO VALVULAR CALCIFICATION ON MULTISLICE COMPUTED TOMOGRAPHY

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Background: Aortic valve sclerosis (AVS) on transthoracic echocardiogram (TTE) is associated with cardiovascular adverse events and mortality. Focal calcification is often detected as part of pathology of AVS. We aimed to investigate relation of TTE AVS to aortic valve calcification (AVC) on multi (64)-slice computed tomography (MSCT).

Methods: AVS [focal hyperechoic areas without stenosis (0=absent, 1=mild, and 2=moderate to severe)] was present in 51 (16%) of 325 patients (age 56±12 years, 52% women) who underwent TTE and MSCT.

Results: Mean coronary artery calcium score correlated directly with presence and severity of TTE AVS [p<0.0001 (Jonckheere-Terpstra Test)]. AVC was present in 34 (67%) with and in 39 (14%) of patients with and without TTE AVS, respectively. Compared to those with both AVS on TTE and AVC on MSCT, patients with AVS on TTE but no AVC on MSCT were younger (age 58±10- vs 69±11 years, p=0.0019) [Table] but were as likely to have hypercholesterolemia, diabetes, hypertension, or be active smokers (all p=NS).

Conclusions: AVS on TTE is associated with AVC on MSCT and correlates directly with CAC score, a marker of coronary atherosclerosis. Age appears to be an important determinant of calcification in AVS.

Table. Impact of age on development of calcification within sclerotic aortic valve cusps.

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<thead>
<tr>
<th>TTE AVS</th>
<th>Age (years)</th>
<th>AVC -</th>
<th>AVC +</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 60</td>
<td>75%</td>
<td>25%</td>
<td>&lt;0.001</td>
<td></td>
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<tr>
<td>&gt; 61</td>
<td>26%</td>
<td>74%</td>
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026
ACQUIRED VON-WILLEBRAND DISEASE SECONDARY TO MITRAL AND AORTIC REGURGITATION
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Objectives/Background: While the association between aortic stenosis and acquired von Willebrand disease (aVWD) has been well described, the connection between regurgitant lesions and aVWD is not as clearly defined.

Description: We describe the case of a 61-year-old man with long-standing mitral regurgitation who presented for cardiovascular surgery for a torn left coronary cusp causing severe aortic regurgitation due to infective endocarditis. Due to a history of recurrent bleeding following a prior prostate surgery, a thorough pre-operative work-up was performed, which demonstrated a normal platelet count and VWF antigen and activity. Platelet function assay (PFA) closure time was prolonged. A trial of intravenous desmopressin caused transient normalization of PFA closure times at 6 hours which were once again prolonged after 12 hours. Multimer analysis demonstrated loss of high molecular weight multimers of VWF, consistent with the diagnosis of aVWD.

Results/Discussion: Acquired VWD occurs from the selective loss of the largest multimers of VWF due to high shear forces in the circulation. Desmopressin leads to the release of large VWF multimers from the subendothelium, leading to transiently improved levels prior to its destruction from shear forces in the circulation. This phenomenon explains the transient shortening of prolonged PFA with epinephrine and ADP in our patient.

Conclusion: Our patient’s bleeding propensity was due to aVWD caused by severe aortic insufficiency superimposed on long-standing severe mitral regurgitation. Further research is required to interrogate the connection between aortic and mitral regurgitant lesions and aVWD.
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EFFECTS OF SODIUM BICARBONATE ON HEMODYNAMIC RECOVERY IN HYPOXIC NEWBORN PIGLETS RESUSCITATED WITH ROOM AIR
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Background: The effectiveness of sodium bicarbonate (SB) has been questioned although it is often used to correct metabolic acidosis of asphyxiated neonates. We aimed to examine its effects on hemodynamic changes, myocardial oxidative stress and oxygen balance in the resuscitation of hypoxic newborn animals with severe acidosis.

Methods: Newborn piglets were anesthetized, acutely instrumented and block-randomized into a sham-operated control group without hypoxia (n=6) and two hypoxia-reoxygenation (H-R) groups (2h normocapnic alveolar hypoxia followed by 4h normoxic reoxygenation with room air, n=8/group). At 10 min after reoxygenation, piglets were given either i.v. SB (2 mEq/kg), or saline (H-R controls) in a blinded, randomized fashion. Hemodynamic data and blood gas were collected at specific time points throughout experimental period. Left ventricle was harvested after experiment and its myocardial content of glutathione and lactate were assayed.

Results: Two hours of normocapnic alveolar hypoxia caused cardiogenic shock with metabolic acidosis (pH: 6.99±0.07, HCO₃⁻: 8.5±1.6 mmol/L). SB administration significantly enhanced the recovery of both arterial pH and HCO₃⁻ within the first hour of reoxygenation in piglets. However, it did not cause any significant effect in the arterial acid-base state and myocardial GSSG/GSH ratio and lactate content at the end of reoxygenation. Further, treating the piglets with SB did not cause any significant effects on temporal hemodynamics during reoxygenation.

Conclusions: Despite enhancing the normalization of acid-base imbalance in asphyxiated piglets reoxygenated with room-air, SB administration during resuscitation did not improve hemodynamics, myocardial oxidative stress nor oxygen balance during recovery.
Electrocardiograms (ECGs) are a frequently used pediatric diagnostic tool. The purpose of this study was to capture how frequently lead placement errors occur in pediatric ECGs.

Methods: A single-center, IRB-approved, retrospective review was conducted of all ECGs performed from January 2011 through April 2011. Inclusion criteria: age <18 years and an ECG performed at or transmitted to our center. All ECGs were re-reviewed by a blinded pediatric electrophysiologist for evidence of lead placement errors.

Results: A total of 1234 ECGs were identified. The average age of was 10.4 years old. The ECGs were performed in an outpatient clinic (827; 67%) followed by the ED (218; 18%), and the hospital (189; 15%). Abnormal lead placement was identified in 34 (3%). The most common form was reversal of the left arm and leg leads (42%), followed by left arm and right arm leads (35%). Smear was identified in 12%. Overall, the most common site of lead placement errors was the outpatient clinic (62%). ECGs performed in the hospital are most likely to have errors. A number of the ECGs identified as abnormal were previously interpreted as normal (42%).

Conclusions: Lead placement abnormalities occur commonly and are routinely missed by the interpreting physician occurring in 3% of all ECGs. These errors result in delayed diagnosis and treatment. Further training and quality improvement initiatives are necessary to obtain accurate ECGs.
A SILENT PRESENTATION OF A SERIOUS ILLNESS: INFECTIVE ENDOCARDITIS

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Introduction Infective Endocarditis (IE) is often diagnosed based on physical exam, laboratory, and echocardiographic findings. Pathologic diagnosis can be used to confirm the diagnosis after valvular replacement or repair. Rarely, IE can be clinically silent and diagnosed based on pathology of valve removed for non-IE reasons. The management of this situation may not be straightforward.

The Case A 67-year-old male presented with acute onset dyspnea. He had history of asymptomatic mitral valve (MV) regurgitation for 20 years. A transthoracic echocardiogram showed myxomatous changes of MV leaflets and severe regurgitation. Surgical repair was deemed necessary. His physical exam revealed a 2/6 holosystolic murmur at the apex. Intraoperatively, he was found to have severe mitral regurgitation with torn anterior leaflet chordae. He underwent annuloplasty and new prosthetic chordae placement. He received perioperative cefazolin. Histopathologic examination of the valve tissue and chordae revealed active endocarditis, containing numerous pleomorphic organisms with variable Gram staining. He was diagnosed with definitive IE. Blood cultures were negative. He was initiated on a six-week course of ceftriaxone.

To identify the organism, molecular testing on valve tissue for 16S rRNA gene PCR was submitted. This later showed evidence of Streptococcus mitis.

Discussion This case highlights the fact that IE can be silent. The diagnosis in such case is not made clinically and is incidental on valvular tissue pathology. The management should be targeted towards organisms recovered on valve tissue. If no organisms are identified on the tissue, treatment as per culture negative infective endocarditis guidelines would be appropriate.
ANY DEGREE OF MITRAL REGURGITATION FOUND DURING INVASIVE VENTRICULOGRAPHY IS ASSOCIATED WITH ALL CAUSE MORTALITY

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Background: Using a large data base of patients who underwent coronary angiography for clinical reason, we evaluated association between reported degree of mitral regurgitation (MR) with all-cause mortality.

Method: Using retrospective angiographic data of 1661 patients between 1993 to 1997 from the VA Long Beach Health Care System with documented ventriculography, we evaluated any association between reported degree of MR and all-cause mortality. We performed uni- and multivariable analysis adjusting for age and ejection fraction.

Results: Any degree of MR was associated with all-cause mortality. Total mortality was 10.1% (132/1301) in patients with no MR vs. 17.8% in patients with mild MR (64/360), p<0.001. Similar to mild MR, any degree of MR was independently associated with all-cause mortality.

Conclusion: The presence of any MR documented on invasive ventriculography is associated with increased total mortality independent of age or ejection fraction. Our finding suggests that even mild MR has negative prognostic significant.
PREDICTORS OF CARDIAC RELATED MORTALITY AFTER AVR FOR DEGENERATIVE AS IN NORMAL EJECTION FRACTION

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Purpose: The purpose of this study was to evaluate the predictors of outcome after aortic valve replacement (AVR) in the patients with severe aortic stenosis (AS) and normal ejection fraction (EF).

Methods: We retrospectively studied 559 patients who underwent AVR for severe AS between January 1995 and December 2011. 59 patients who underwent coronary artery bypass graft (CABG) or diagnosed with previous myocardial infarction (MI), 48 patients with EF was lower than 40% were excluded. Remained patients was categorized two groups as the patients with EF was higher than 60% (Group 1, n=304) and the patients with EF was from 40% to 60% (Group 2, n=148). Early and late cardiac related mortality and risk factors was analyzed in this two groups.

Results: Early cardiac related mortality was 0% in both group. Late cardiac related mortality was significantly higher in the Group 1 than the Group 2. Univariate analysis of the Group 1 found six variables to be associated with late cardiac related mortality: Age, sex, hypertension (HTN), mitral regurgitation (MR) >= mild, tricuspid regurgitation (TR) >= mild and preoperative hemoglobin (p=0.015, 0.087, 0.011, 0.039, 0.002, 0.011). Multivariate analysis found two variables to be associated with late cardiac related mortality: HTN, TR >= mild (p=0.040, 0.048).

Conclusions: The patients with Severe AS with normal EF with risk factors could present higher mortality. The patients with HTN or TR >= mild should be closely followed up after AVR.
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FENOFIBRATE THERAPY IN PATIENTS WITH HYPERTRIGLYCERIDEMIA HAS SUBSTANTIAL BENEFITS OVER OMEGA-3 FATTY ACIDS

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Background: Omega-3 fatty acids (Omacor) and fenofibrate are both used to treat patients with hypertriglyceridemia. However, direct comparisons of lipoprotein and metabolic effects of these two drugs are not typically explored within the same study.

Methods: This was a randomized, single-blind, placebo-controlled, parallel study. Age, sex, and body mass index were matched among groups. All patients were recommended to maintain a low fat diet. Fifty patients in each group were given placebo, Omacor 2 g, or fenofibrate 160 mg, respectively daily for 2 months.

Results: Omacor therapy decreased triglycerides by 21%, triglycerides/HDL cholesterol, and improved flow-mediated dilation (P<0.01). However, fasting insulin, plasma adiponectin levels, and insulin sensitivity (determined by QUICKI) did not change significantly relative to baseline measurements. Fenofibrate therapy decreased total cholesterol, triglycerides by 29%, non-HDL cholesterol, apolipoprotein B, and triglycerides/HDL-cholesterol while increasing HDL cholesterol and apolipoprotein AI (all P<0.01). Moreover, fenofibrate improved flow-mediated dilation, lowered hsCRP, fibrinogen, fasting insulin, and glucose levels (all P<0.05), increased plasma adiponectin by 18% (P<0.001) and improved insulin sensitivity by 4% (P=0.003) when compared with baseline. When compared with placebo and Omacor, fenofibrate therapy decreased non-HDL cholesterol (P<0.001) and triglycerides/HDL cholesterol (P=0.016) while increasing HDL cholesterol (P<0.001) and apolipoprotein AI (P=0.001). Of note, when compared with Omacor, fenofibrate therapy decreased fasting insulin (P=0.023) and increased plasma adiponectin (P=0.002) and insulin sensitivity (P=0.015).

Conclusions: Omacor and fenofibrate therapy promoted similar changes in triglycerides and endothelium-dependent dilation. However, fenofibrate therapy had substantially better effects on lipoprotein and metabolic profiles in patients with hypertriglyceridemia.
Introduction: Despite recent improvements in anti-coagulation treatment and a decline in bleeding rates overall, women continue to be at higher risk of bleeding complications following a percutaneous coronary intervention (PCI). The purpose of this study was to evaluate the differential impact of bivalirudin and closure method on bleeding risk and gender in real world, current clinical registry data for all primary PCIs.

Methods: We analyzed 93,282 patients undergoing catheterization over a 3-year period from a large national clinical registry comprising ACC/NCDR variables. All consecutive patients undergoing PCI (n=58,862) between June 1, 2009 and June 30, 2012 were included in the analysis. Independent predictors of PCI complications was determined by multiple logistic regression with stepwise selection and significance at p<0.01.

Results: Among the 58,862 PCI’s 66.9% (39,379) were males and 91.2% (53,663) Caucasians. Average age was 64.45yr (12.0). Controlling for age, prior procedures, diabetes, and other differences, bivalirudin was associated with reduced bleeding complications (p<0.01). Bleeding risk was four times greater in females than males for compression and heparin (4.4% Vs 1.9%, p<0.0001). However, closure by device and bivalirudin use reduced the risk to 1% and eliminated the female disadvantage (1% males vs 1% females, p=1.0).

Conclusion: These findings represent the most recent data currently for bleeding risk reduction in PCI. Closure by device and use of bivalirudin results in the best outcome for patients overall. However, women benefit significantly more than men, closing the gender gap, with differences in complication risks equalized when bivalirudin is used.
ADVANCED LIPID TESTING PREDICTS SUBCLINICAL ATHEROSCLEROSIS IN LOW RISK POPULATION BEYOND TRADITIONAL RISK FACTORS
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Objectives: To compare the association of lipid particle size and number with subclinical atherosclerosis measured by coronary artery calcification (CAC) in low and high risk population for cardiovascular disease (CVD).

Background: There is emerging data that lipid particle size and number measured by nuclear magnetic resonance (NMR) predicts CVD outcomes. However, their role in CVD risk assessment in low and high risk population is not well understood.

Methods: A sample of diabetic (DM) and non diabetic (nonDM) participants with family history of CVD were recruited (n=268). We collected CVD risk factors, calculated Framingham Risk Score (FRS), measured fasting lipids, apolipoprotein A1 (Hitachi) and lipoprotein concentration and size by NMR (LipoScience). Global CAC (Imatron) scores were quantified by the method of Agatston. Multivariable linear regression adjusting for CVD risk factors was performed.

Results: The participants were mostly male (70%) and 42% DM. As expected, FRS was low in nonDM compared to DM (5 (3-7) vs 14 (9-18), p<0.001) with similar patterns for CAC scores (2 (0-56) vs 157 (36-610), p<0.001). Large VLDL (beta coefficient 0.09, p=0.047), medium VLDL (0.02, p=0.032), small LDL (0.0009, p=0.047) and very small LDL (0.001,p=0.041) particles demonstrated relationship with CAC in nonDM after adjusting for demographics, traditional risk factors and apolipoprotein a1 which was not observed in DM.

Conclusion: Lipid particle number and composition was associated with CAC beyond traditional risk factors only in nonDM patients. These findings suggest NMR-based measures capture risk beyond standard lipids in low risk group compared to high risk warranting further study.
IMPACT OF CONTINUOUS POSITIVE AIRWAY PRESSURE THERAPY ON NON-HDL AND TOTAL CHOLESTEROL IN OSA PATIENTS

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Background: Non-HDL cholesterol is an important predictor for cardiovascular morbidity. The aim of our study is to investigate the impact of continuous positive airway pressure (CPAP) therapy for obstructive sleep apnea (OSA) on non-HDL and total cholesterol.

Methodology: This is a retrospective study of 2 groups of patients; G1 included 50 patients with moderate to severe OSA on CPAP, randomly selected from the sleep lab database (21 male and 29 female with mean age of 67 ± 10.8 years). G2 included 50 patients randomly selected from the normal sleep studies database (19 male and 31 females with mean age of 65.9 ± 13.5 years). Non-HDL and total cholesterol levels were averaged over 12 months prior to the diagnostic study in both groups and then over 6-12 months post CPAP therapy in G1.

Results: Mean Non-HDL cholesterol in G1 has dropped from 139.0 ± 6.2 (CI 126.5 - 151.62) prior to CPAP therapy to 123.1 ± 4.5 (CI 114.1 - 132.1) within 16 months after CPAP therapy which was statistically significant, p = 0.04. When comparing Non-HDL between G1 and G2, there was no statistically significant difference; the mean non-HDL in the control group was 134.9 ± 25.6 (CI 83.4 - 186.5) when compared to the OSA group before CPAP, p = 0.865. The same pattern was noticed when the mean total cholesterol levels were analyzed.

Conclusion: The study showed a statistically significant reduction in the non-HDL and total cholesterol in patient with OSA after CPAP treatment.
PHYSICIAN-PROVIDED LIFESTYLE MODIFICATION COUNSELING FOR HYPERLIPIDEMIA – DOES IT HELP?

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Objectives: To assess whether brief physician-provided counseling for diet and physical activity in patients with hyperlipidemia leads to a better lipid profile.

Background: Lifestyle modification counseling rates for hyperlipidemic patients still remain well below expectations.

Methods: This study evaluated the effect of lifestyle modification counseling trends by utilizing 12 year data from National Health And Nutrition Examination Survey (NHANES) from year 1999 to 2010. All patients who reported being diagnosed with hyperlipidemia were included in the analysis and were asked 3 questions whether they were told to: 1) reduce fat intake 2) reduce weight 3) exercise more. Individuals were divided into 4 groups based on the whether they were counseled for none, one, two, or all three factors (scores 0-3). The mean total cholesterol and low density lipoprotein (LDL) cholesterol levels were then calculated for each group.

Results: More than 9000 patients were analyzed across 12 years. As the counseling score increased from 0-3, there were significant decreases in mean total cholesterol levels (score 0: mean±SD total cholesterol 212.7±45.1; score 1: mean±SD total cholesterol 215.6±48.1; score 2: mean±SD total cholesterol 213.6±48.4; score 3: mean±SD total cholesterol 208.1±47.3, p < 0.001). Similarly, LDL levels also decreased significantly as the counseling score increased (score 0: mean±SD LDL 128.9±38.6; score 1: mean±SD LDL 130.8±40.6; score 2: mean±SD LDL 126.8±39.3; score 3: mean±SD LDL 122.0±39.5, p < 0.001).

Conclusion: Brief physician-provided lifestyle modification counseling for hyperlipidemic patients was associated with lower total cholesterol and LDL levels although the net effect was small.
UTILITY OF AMBULATORY BP MONITORING IN A CARDIAC PREVENTION AND REHABILITATION PROGRAMME

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Background: Although 24 hour ambulatory BP monitoring (ABPM) can provide a better estimate of true or mean BP and variability, clinic BP measurement is rapid, convenient and inexpensive.

Aims/Objectives: Our aim was to determine how well clinic BP measurements assessed achievement of BP target, compared to ABPM, in patients attending a cardiac prevention and rehabilitation programme (CPRP).

Methods: This cross sectional study was performed involving consecutive patients with coronary heart disease attending Charing Cross Hospital, London, from June to August, 2010. Clinic BP was measured twice 5 minutes apart using the Omron M5-1 Intellisense device. That same day, a 24 hour ABPM (DIASYS Integra Novacor) device was fitted to each patient. The means of the clinic and daytime ABPM readings were calculated and analysed by paired t test. Using clinic target of $\leq 130/80$ mm Hg and ABPM target of $\leq 120/75$ mm Hg, the proportions achieving target were determined for both methods.

Results: 40 patients were rescreened with 11 patients recruited for this study (response rate 25.5%). The mean clinic SBP ($\pm$ SD) was 129 $\pm$ 13.7 mm Hg and the mean ambulatory daytime SBP ($\pm$ SD) was 119 $\pm$ 12.3 mm Hg. On the other hand the clinic mean DBP ($\pm$ SD) was 77.1 $\pm$ 8.2 mm Hg and the mean ambulatory DBP ($\pm$ SD) was 73.2 $\pm$ 5.4 mm Hg. The mean difference of SBP between these 2 methods is 10 mm Hg (95% confidence interval, 4.2 to 15.8); ($p = 0.003$) and DBP 3.9 mm Hg (95% confidence interval, 0.2 to 7.7); ($p = 0.043$). The BP target for coronary patients is $\leq 130/80$ mm Hg. Using mean clinic BP 4 out of 11 (36.3%) patients achieved the BP target. On the other hand using target of ABPM as $120/75$ mm Hg, 5 out of 11 (45.4%) patients reached the BP target as obtained by mean daytime ABPM. Considering the ABPM as gold standard measurement in achieving targets, the sensitivity of mean clinic BP is 80% (4/5). With a difference of SD of 8.5, the power of this sample size (n=11) is 97%.

Conclusion: Mean clinic BP is a reliable measure of BP target achievement in coronary patients in a CPRP though a larger sample would assist validation of this.
ARTIFICIAL INTELLIGENCE MODEL OF CARDIOVASCULAR RISK IN RENAL DISEASE OUTLINES CAROTID MARKERS

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Prevention strategies to reduce cardiovascular (CV) complications in patients with renal disease may benefit from noninvasive vascular testing and risk models evaluations. We have studied common carotid intima media thickness (CIMT), plaque and stenosis and tested endothelial function by brachial flow mediated dilatation in chronic kidney disease and end stage renal disease (ESRD) patients. After one year we evaluated the value of CV risk factors for predicting end point events (EP), and after five years we aim to see the impact of noninvasive markers on the mortality prediction and CV model performance.

Ultrasound examinations were performed on 67 renal disease patients and 26 healthy matched subjects. EP prediction was evaluated with an original artificial neural networks model (NN). This used all 93 subjects' data as input: 24 risk factors including traditional and noninvasive markers (P1) and repeated without carotid plaque/stenosis features (P2) or without carotid markers and diabetes (P3) by retraining only the elements contributing more than 0.0001. We observed EP on subjects with carotid stenosis, plaque, or CIMT over 75 percentile. Success rate prediction was significantly greater utilizing carotid structural markers: P1=0.81, versus P2=0.5 and P3=0.62. Mortality after five years was found on about 50% from the ESRD patients and can be computed continuously into the NN model.

In conclusion, carotid markers highly increase a NN model performance to CV risk in renal disease. The model can be retrained on a larger scale and may be used for risk stratification and selective treatment aimed at reducing unfavorable CV outcome.
PLANT STEROLS AND CARDIOVASCULAR DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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The impact of increased serum concentrations of plant sterols on cardiovascular risk is unclear. We conducted a systematic review and meta-analysis aimed to investigate whether there is an association between serum concentrations of two common plant sterols (sitosterol, campesterol) and cardiovascular disease (CVD). We systematically searched the databases MEDLINE, EMBASE, and COCHRANE for studies published between January 1950 and April 2010 that reported either risk ratios (RR) of CVD in relation to serum sterol concentrations (either absolute or expressed as ratios relative to total cholesterol) or serum sterol concentrations in CVD cases and controls separately. We conducted two meta-analyses, one based on RR of CVD contrasting the upper vs. the lower third of the sterol distribution, and another based on standardized mean differences between CVD cases and controls. Summary estimates were derived by fixed and random effects meta-analysis techniques. We identified 17 studies using different designs (four case–control, five nested case–control, three cohort, five cross-sectional) involving 11,182 participants. Eight studies reported RR of CVD and 15 studies reported serum concentrations in CVD cases and controls. Funnel plots showed evidence for publication bias indicating small unpublished studies with non-significant findings. Neither of our meta-analyses suggested any relationship between serum concentrations of sitosterol and campesterol (both absolute concentrations and ratios to cholesterol) and risk of CVD. Our systematic review and meta-analysis did not reveal any evidence of an association between serum concentrations of plant sterols and risk of CVD.
OBJECTIVES: We studied the clinical characteristics and mortality in patients with LBBB and compared it with overall in-hospital mortality.

Method: Retrospective analysis of the 20-year registry data of cardiac patients hospitalized at Hamad General Hospital.

Results: Of the 41438 patients admitted under cardiology department, 582 patients had LBBB (1.4%). Compared to patients without LBBB, LBBB patients were older (63±12 vs. 54±12 years, P=0.001), have higher incidence of hypertension (56 vs. 40%, P=0.001), diabetes mellitus (52% vs. 39%, P=0.004) and chronic renal failure (11% vs. 4%, p=0.001). Congestive heart failure was the most common cause of admission in LBBB (40% vs. 17% P=0.001), followed by unstable angina (35 vs. 40%, P=0.03) and myocardial infarction (9.3 vs. 23%, p=0.001). LBBB patients had lower LV function (mean EF% 30±13 vs 43±13, p=0.001), more coronary artery bypass surgery (10% vs 5.5%, p=0.001), but less percutaneous coronary angioplasty (2.6% vs 4.3%, p=0.04). In-hospital mortality was higher in LBBB patients compared to non-LBBB patients (7.9% vs 4.7%, p=0.001) which is similar to overall in-hospital mortality of STEMI (8.8%). Moreover, in-hospital mortality in patients with LBBB triples when associated with STEMI (23.1% vs 8.8%, p=0.01), NSTEMI (16.1% vs 5.2%, p=0.001) or unstable angina (2% vs 0.7%, p=0.31).

Conclusions: Patients with LBBB were older, more likely to have cardiovascular risk factors. They were more likely to have left ventricular dysfunction and surgical revascularization. Moreover LBBB is associated with a 2-fold increase in mortality as compared to those without LBBB and of 3-fold increase in the setting of acute coronary syndrome.
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BRAIN NATRIURETIC PEPTIDE AS A PREDICTOR OF ADVERSE CARDIAC EVENTS AFTER SUCCESSFUL PERCUTANEOUS CORONARY INTERVENTIONS IN PATIENTS WITH ACUTE CORONARY SYNDROME

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Background: Value of brain natriuretic peptide (BNP) as a prognostic marker after successful PCI, to our knowledge, has not been studied before.

Purpose: We aimed to assess whether BNP level immediately after successful PCI was associated with major adverse cardiac events (MACE) during hospitalization and at 3 months.

Methods: We studied 88 consecutive patients hospitalized for ACS who underwent successful PCI. Patients with heart failure on admission were excluded. Plasma BNP levels were measured immediately after PCI. In-Hospital MACE & MACE at 3 months were recorded.

Results: Mean age of the study group was 54.28±9.35 years. There was significant correlation between BNP level and age (p=0.014), diabetes mellitus (p=0.011), hypertension (p=0.013), and serum creatinine (p=0.012). Patients were divided into 2 groups according to occurrence of MACE. Plasma BNP level in MACE group was significantly higher, [1330 ± 167 vs. 1176 ± 273 pg/ml ; p=0.01]. BNP level was significantly associated with the occurrence of heart failure (p=0.019), composite end point of in hospital MACE ( p=0.029) and composite end point of MACE at follow-up (p=0.009). Multiple logistic regression analysis identified BNP level (OR 1.003, 95% CI 1.000-1.005, p = 0.045) as an independent predictor of MACE at 3 months follow up.

Conclusion: Plasma BNP level immediately after successful PCI in patients with ACS is associated significantly with MACE during hospitalization and at 3 months follow up.
USING CHADS2 SCORE TO IDENTIFY ELDERLY PATIENTS WITH ATRIAL FIBRILLATION
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Objectives: (i) To determine if CHADS2 score can be used to identify patients with atrial fibrillation (AF) in elderly. (ii) To identify the number of new and pre-existing patients with AF in acute admissions.

Background: CHADS2 score was originally derived to enable risk stratification of stroke for AF patients. However, each of its components including congestive heart failure, hypertension, aged >75, diabetes and previous stroke or Transient Ischaemic Attack can be risk factors for AF.

Methods: A prospective cohort study of 500 acute admissions aged >65 was conducted. Electrocardiogram (ECG) was done on most of the patients to identify whether they had AF. CHADS2 score was calculated for everyone and compared between patients who had AF and those who did not.

Results: 480 patients of the 500 acute admissions had an ECG performed. 25% had AF with 88.8% of AF patients scoring ≥ 2 on CHADS2, and 11.2% of patients scoring 1 or 0. The mean CHADS2 score for AF and those without AF were 2.84 and 1.75 respectively. The difference in mean was 1.085 between these 2 groups of patients, which was statistically significant with p value <0.05. During this acute admission, 19.2% of AF patients were newly identified, while 80.8% were patients with pre-existing AF.

Conclusion: Our findings highlighted that AF in elderly was related to a high CHADS2 score. CHADS2 score can be performed on all patients for risk stratification purposes prior to an ECG. Early treatment of AF can prevent certain morbidities in the future.
043
TRENDS IN CARDIOVASCULAR DISEASE IN ETHIOPIA: A 30-YEAR RETROSPECTIVE ANALYSIS OF MEDICAL-ICU ADMISSIONS
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Introduction: Non-communicable diseases, including cardiovascular diseases, are the leading cause of death globally, and the burden of disease is rising fastest among lower-income countries. Scarce epidemiological data exists on the impact of cardiovascular diseases in Ethiopia. We sought to evaluate trends in medical intensive care unit (MICU) admissions over a 30-year period in Addis Ababa, Ethiopia.

Methods: The study took place in the MICU at Black Lion Hospital, Addis Ababa, the national tertiary care center. A retrospective registry review was used to conduct a 30-year analysis of trends in MICU admissions. Data was collected regarding age, sex, admission diagnosis, and mortality within seven one-year cohorts of patients, each separated by five years from 1982 – 2012. Admission diagnosis was categorized into three groups for analysis: (1) cardiovascular diseases, (2) communicable, maternal, perinatal, and nutritional conditions, and (3) other non-infectious diseases.

Results: A total of 1,932 patients were included in the study. The mean age of the study population was 38.4 years (CI 37.6 – 39.2) with 58% of the cohort being male. Cardiovascular diseases increased from 18% to 46% of all MICU admissions over the study period. The percentage of admissions from both infectious diseases and other non-infectious diseases decreased proportionately.

Conclusions: This retrospective analysis of MICU admissions suggests that the burden of cardiovascular diseases has increased greatly in Ethiopia over the last 30 years. Epidemiologic study at the population level is required to confirm the generalizability of these findings.
044
SYSTEMIC INVOLVEMENT OF CONNECTIVE TISSUE AS PREDICTOR OF CARDIOMYOPATHY IN MITRAL VALVE PROLAPSE AND MARFANOID HABITUS
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2. Almazov Federal Heart, Blood and Endocrinology Centre, Laboratory of Inherited Connective Tissue Disorders, St. Petersburg, Russia

Ghent nosology (2010) propose the score of connective tissue systemic involvement (SI) which is represented by the skeletal features. We suppose, that the high score of SI typical for marfanoid habitus (MH) and mitral valve prolapse (MVP) could be the cause of the cardiomyopathy (CMP). Objective was to evaluate the interrelation between the SI score and left ventricular (LV) function in young with primary MVP and MH. Materials. 78 asymptomatic subjects were studied with MVP and 17 subjects with MH and high SI score in comparison with 80 sex- and age-matched control group (CG). Transthoracic echocardiography extended with speckle-tracking technique was performed in all subjects (Vivid 7 Dimension, EchoPAC’08).

Results. During the k-means clustering two clusters of subjects with MVP were identified. In 1st cluster (17 subjects) a significant reduction of global systolic strain was observed compared with the control group (-15.5±2.9% vs. -19.6±3.4%; p=0.00001) and the 2nd cluster (61 subjects) (-15.5±2.9% vs. -20.6±3.8%; p=0.00001). These low strain in the 1st cluster was coupled with the highest SI score in comparison to the 2nd cluster and CG (5.4±1.5; 3.7±1.6; 2.6±14; δ<0,0002). The MH subjects with high SI score displayed a statistically reliable reduction of ejection fraction (55.7±4.3 vs 62.3±5.2; p<0,0002) against the CG, increase of the end-diastolic dimension (49,4±3,7 vs 45,2±4,0; p<0,003), as the aorta route diameter (31.5 ±2,0 vs 26,9±2,0; p<0,0001).

Conclusions. High score of the SI in subjects with the MVP and MH could be regarded as a predictor of violation of LV systolic function and development of the CMP.
045
SCREENING AND IDENTIFICATION OF NOVEL BIOMARKERS FOR EARLY DIAGNOSIS OF ACUTE CORONARY
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2. Department of Emergency, 306 Hospital of PLA, Beijing, China

Objective: Magnetic bead-weak cation exchange (MB-WCX) combined matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS) was used to explore biomarkers for early diagnosis of acute coronary syndrome (ACS). Method: A total of 31 samples of serum obtained from patients within 4 h after ACS symptoms emerged, including 12 patients with unstable angina (UA), 5 with non-ST-segment elevation acute myocardial infarctions (NSTEMI) and 14 with ST-segment elevation acute myocardial infarctions (STEMI). Levels of myocardial creatine kinase isoenzyme MB (CKMB) activity, cardiac troponin I (cTnI), Heart type fatty acid binding protein (H-FABP) and myeloperoxidase (MPO) were measured with commercial kits. Another 30 serum samples obtained from gender, age, past history matched volunteers as control group. The serum proteins were processed by magnetic bead separation technique and detected by MALDI-TOF-MS. The performance of candidate biomarkers was assessed by ROC curve with SPSS13.0 software. Protein markers were separated by high performance liquid chromatography (HPLC) and identified by peptide mass fingerprint (PMF) technique.

Results: Twelve peaks with different abundance in two groups were found. Three peaks with m/z 3167 Da, 4183 Da and 4292 Da had the larger area under receiver operating characteristics (ROC) curve in diagnosis of ACS compared with H-FABP and MPO. 4183 Da peak isolated and identified as dermcidin had high sensitivity and specificity for UA.

Conclusions: Three differential proteins might be novel biomarkers for the diagnosis of ACS at the early stage. Dermcidin may contribute to the differential diagnosis UA from ACS.
046
MATRIX METALLOPROTEASES, CHITOTRIOSIDASE AND CYSTATIN C IN LONG-TERM STUDY OF PATIENTS AFTER CARDIOSURGERY

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2. Regional Unit of Cardiology, Novosibirsk, Russia

Objectives: 107 persons, male were enrolled: 1) low ischemic heart disease (IHD) risk group, 25 donors, aged 31.4±6.5; 2) high IHD risk group, 50 patients with hypertension, aged 56.8±2.9, treated (25) by simvastatin, 20-40 mg/kg; 3) 32 patients with IHD (56.5±6.9), underwent coronary bypass surgery (1 month, 1, 2 and 3 years after surgery). Patients with diabetes mellitus, kidney insufficiency were excluded from this study. Background: New inflammatory biomarkers may be helpful in revealing of cardiovascular complications and atherosclerosis development after cardiosurgery. The aim: to evaluate the prognostic value of matrix metalloproteases (MMP), chitotriosidase, and cystatin C in patients with IHD after coronary bypass surgery.

Methods and Results: MMP (Knight et al., 1992) and chitotriosidase (Guo et al., 1995) activity was assayed by fluorescent methods, cystatin C - by ELISA kit (BioVendor, Czechia), high sensitivity C-reactive protein (hs-CRP) by BioScience (Spain) kits. Baseline level of MMP, chitotriosidase and cystatin C increased in patients of high risk of IHD and especially, in IHD group before operation. Simvastatin treatment significantly decreased serum MMP, hs-CRP, total cholesterol and non-HDL-cholesterol 1, 2 and 3 years after cardiosurgery. However, simvastatin treatment had no effect on increased chitotriosidase activity at all periods studied after surgery.

Conclusion: Patients with IHD circulating MMP activity appear to have an increased cardiovascular risk profile. Hypolipidemic effect of simvastatin in IHD patients after cardiosurgery was shown to correlate both with decreased hs-CRP level and decreased MMP activity, involved into pleiotropic effects of statin.
CORRELATION BETWEEN ADIPONECTIN PLASMA LEVELS AND CORONARY ARTERY DISEASE

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Introduction: Adipose tissue is not only an energy store but also an endocrine organ which secretes cytokines and hormones such as adiponectin. Adiponectin has antiatheromatic and antiinflammatory effects reducing the endothelial cell adhesion molecule expression and ejets the lipid removal.

Objective: Correlation of adiponectin plasma levels with the severity of coronary artery disease on angiography.

Design – Methods: We studied 60 patients (47 male, 13 female) (mean age 64.5 ± 10.8 years) with chest pain who submitted for coronary angiography. Patients characteristics: 23 abdominal obesity, 37 arterial hypertension, 27 smokers, 29 dislipidaemia, 17 cardiovascular history and 10 positive family history for coronary artery disease (CAD). Patients divided into four groups. Group A: coronary arteries without significant obstruction, Group B: 1 vessel disease, Group C: 2 vessel disease and Group D: 3 vessel disease

Results: Adiponectin plasma levels were 38.52 ± 9.06 for Group A, 17.98 ± 10.53 for Group B, 14.31 ± 8.61 for Group C and 13.92 ± 6.92 for Group D. Also adiponectin plasma levels were 19.3 ± 13.1 for patients with abdominal obesity and 27.1 ± 21.9 for those without. Finally, patients with dislipidaemia had adiponectin levels 22.4 ± 18.7 vs patient without dislipidaemia who had adiponectin levels 24.4 ± 18.1

Conclusion: There was a statistical significant difference of adiponectin plasma levels among the 4 groups. Patients with 1, 2 or 3 vessel CAD had significant lower adiponectin plasma levels vs patients without CAD. There was no statistical significant difference between the patients with and without abdominal obesity and dislipidaemia.
048
RELATION OF SERUM CALCIUM LEVEL WITH METABOLIC RISK FACTORS AND CORONARY ARTERY DISEASE IN AFRICAN AMERICANS
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Background: Calcium has been shown to play an important role in the pathogenesis of atherosclerotic disease; either as an independent risk factor or as a possible component of metabolic syndrome. We propose to study the relationship between serum calcium, coronary artery disease (CAD) and metabolic risk factors (MRF) in the African American (AA) population which has not been studied extensively.

Methods: This study was a retrospective review of the medical records of all AA patients discharged with CAD during a one year period. A total of 325 charts were reviewed and following variables were tabulated: age, gender, ethnicity, MRF Fasting blood sugar, HDL, triglycerides, BP, BMI, albumin corrected serum calcium (ACC), and CAD identified via cardiac catheterization. Patients were included in the MRF group according to parameters that define metabolic syndrome. The criteria for CAD was to have 30% or more stenosis of any major coronary artery on catheterization.

Results: Out of 229 AA subjects, majority were between 56 to 65 years with no relevant differences between the genders. 190 patients were diagnosed with CAD and 143 patients had MRF. In our study population, no statistical difference in ACC was noted between cases with or without MRF (p<0.05). Also of note, no other statistically significant association was found between abnormal ACC with CAD in African Americans.

Conclusion: For the African American population, serum calcium level has no correlation with CAD or MRF. Our study differed from the CoLaus study which found strong association between serum calcium and MRF in Caucasian population.
Background: The geriatric syndrome of frailty is prevalent in older adults with coronary artery disease (CAD); however, its association with angiographic and echocardiographic characteristics, as compared to those without frailty, has not been well described.

Methods: We assessed for frailty using the validated Fried frailty index in patients ≥65 years old who underwent percutaneous coronary intervention (PCI) at Mayo Clinic Health System (Rochester, MN and La Crosse, WI). Frailty was determined based on deficits of weight loss, exhaustion, physical activity, gait speed, and grip strength (3 features or greater = frail; 2 features or less = not frail). We used logistic regression models to estimate the association of frailty with clinical, angiographic, and echocardiographic characteristics.

Results: Of 448 patients studied, 92 (20.5%) were frail. Frailty was associated with older age, female sex, and more comorbidities. Frailty was associated with higher rates of left main and bifurcation CAD. Echocardiographically, frail adults had more wall motion abnormalities and greater degrees of mitral and tricuspid valve regurgitation as compared to non-frail patients. After adjustment, left main CAD, presence of bifurcation CAD, and moderate-severe tricuspid valve regurgitation were independently associated with frailty (Table). Conclusions: One-fifth of older adults undergoing PCI have frailty, and frail status was associated with greater burden of CAD and valvular heart disease.

<table>
<thead>
<tr>
<th>Variable (%)</th>
<th>Frail (n=92)</th>
<th>Not Frail (n=356)</th>
<th>p</th>
</tr>
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<tbody>
<tr>
<td>Univariate</td>
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<td></td>
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<tr>
<td>Age, y (mean ± SD)</td>
<td>77.7±7.1</td>
<td>74.0±5.8</td>
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<td>Female</td>
<td>43.0</td>
<td>26</td>
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<td>Hypertension</td>
<td>87.0</td>
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<td>Chronic kidney disease</td>
<td>25.0</td>
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<tr>
<td>Peripheral Arterial Disease</td>
<td>25.0</td>
<td>10.0</td>
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<tr>
<td>Congestive Heart Failure</td>
<td>30.0</td>
<td>15.0</td>
<td>0.002</td>
</tr>
<tr>
<td>Left Main 70% stenosis</td>
<td>18.0</td>
<td>9.0</td>
<td>0.02</td>
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<tr>
<td>Bifurcation disease</td>
<td>28.0</td>
<td>17.0</td>
<td>0.03</td>
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<tr>
<td>Ejection Fraction, mean</td>
<td>53.1</td>
<td>55.7</td>
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<td>Wall motion score index, mean</td>
<td>1.7</td>
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<td>Mitral regurgitation</td>
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<td>Mild to Mild-moderate</td>
<td>49.5</td>
<td>33.5</td>
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<tr>
<td>Moderate to Severe</td>
<td>7.7</td>
<td>3.7</td>
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<td>Tricuspid regurgitation</td>
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<tr>
<td>Mild to Mild-moderate</td>
<td>42.4</td>
<td>32.4</td>
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<tr>
<td>Moderate to Severe</td>
<td>9.8</td>
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<tr>
<td>Multivariate</td>
<td>Hazard ratio (95% CI)</td>
<td>2.29 (1.09-4.79)</td>
<td>0.03</td>
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<tr>
<td>Left Main 70% stenosis</td>
<td>2.59 (1.40-4.79)</td>
<td>0.003</td>
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<tr>
<td>Bifurcation disease</td>
<td>4.35 (1.27-14.92)</td>
<td>0.02</td>
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</table>
Background: Stress induced cardiomyopathy (SIC) is characterized by left ventricular apical ballooning and manifests as acute coronary syndrome. A psychosomatic mechanism is hypothesized that emotional stress can compromise coronary circulation, but the role of coronary artery disease has not been well characterized.

Method: 34 patients (26F, 8M) diagnosed with SIC were divided into two groups by absence or presence of coronary atherosclerosis (CA) and were examined for risk factor profiles.

Results: 14 patients without CA (Group A) with mean age of 49+/-9.7 years were younger than 20 patients with CA (Group B) with mean age of 64+/-14 years (p= 0.0015), with CA of LAD (35+/-5%), LCX (45+/-38%), and RCA (50+/-23%). Group A had fewer patients with HTN than Group B (4/14 vs. 15/20) (P: 0.0073). CK of 247+/-300ng/dL vs. 180+/-150ng/dL, CK-MB of 24.0+/-50.5ng/dL vs. 13.2+/-10.9ng/dL, Trop of 3.11+/-4.70ng/dL vs. 6.28+/-6.93ng/dL, TG of 169+/-165mg/dL vs. 136+/-70.2mg/dL, HDL of 39+/-18mg/dL vs. 48+/-17mg/dL, and LDL of 81+/-35mg/dL vs. 86+/-37mg/dL were not different between the two groups (P:NS). T wave abnormality (5/14 vs. 13/20), ST abnormality (4/14 vs. 4/20), prolonged QT (2/14 vs. 5/20), transmural infarct (4/14 vs. 7/20), acute MI (3/14 vs. 2/20), and ejection fraction of 48+/-14.3% vs. 43.5+/-11.8% were not different between the two groups (P:NS).

Discussion: There was no significant difference in risk factor profile between the two groups except for age and incidence of hypertension. More than half of patients had coronary artery disease, albeit hemodynamically insignificant, suggesting many patients with SIC have ongoing atherosclerosis.
051
TYPES OF MENTAL STRESS IN STRESS INDUCED CARDIOMYOPATHY
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Background: Stress induced cardiomyopathy (SIC) is characterized by left ventricular apical ballooning and manifests as acute coronary syndrome. A psychosomatic mechanism is hypothesized that mental stress (MS) can compromise coronary circulation, but different forms of MS have not been categorized.
Method: 34 patients (26F, 8M) diagnosed with SIC were divided into two groups by absence or presence of MS and were classified as follows:
Results: 10 patients with mean age of 53+/-12 years reported not having MS (Group A), and 24 patients with mean age of 60+/-15 years reported having some form of ES (Group B). Group A reported more alcohol use than Group B (8/10 vs. 8/24) (P: 0.013); however, smoking was not different between the two groups (8/10 vs. 8/24) (P:NS). Group B had incidence of perioperative stress (8/24), depression (6/24), acute situational stress (5/24), mental disorder (5/24), and drug abuse (2/24). Analysis of comorbidities revealed incidence of coronary artery stenosis (5/10 vs. 9/24), chronic pain (2/10 vs. 11/24), cancer (3/10 vs. 3/24), and lung disease (1/10 vs. 7/24) (P:NS). Patients were also taking psychotropic drugs such as hypnotics, anti-psychotics, anti-depressants, and anti-convulsants (3/10 vs. 12/24) (P:NS).
Discussion: Nearly a third of patients with SIC reported no incidence of MS, except alcohol use. Most cases of SIC with MS stemmed from perioperative stress and associated comorbidities. Stress levels in patients with SIC have a wide spectrum of variety including patients who had no MS, suggesting existing pathology may play a role in inducing SIC.
MYOCARDIAL STUNNING IN HEMODIALYSIS PATIENTS: “A SILENT OVERLOOKED INSULT”

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2. NYU School of Medicine
3. Brookdale University Hospital and Medical Center - Nephrology Division
4. SUNY Downstate School of Medicine

Background: Hemodialysis (HD) is capable of inducing left ventricular dysfunction, which may persist even after hemodynamic or clinical status has returned to normal. Repeated episodes of myocardial depression result in myocardial hibernation, remodeling, and some degree of irreversible loss of contractile function.

Objectives: Our goal is to highlight the impact of this phenomenon, sometimes not considered an important risk factor for cardiovascular morbidity.

Methods: Review of literature, identifying predisposing factors, diagnostic approaches and therapeutic options.

Discussion: Predisposing factors include dialysis-related, cardiac and medical. The most important are:
- Large volume of fluid removal.
- Hemodialysis-related hypotension.
- Small cardiac chamber size or chamber hypertrophy.
- Microvascular endothelial dysfunction.
- Overmedication with antihypertensive agents
- Reduced fluid intake or volume loss.

Symptoms occur during HD and include chest discomfort, palpitations, and general fatigue as well as ECG changes. Echocardiography is ideally suited to diagnose transient reversible regional wall motion abnormalities (RWMA) that are hallmark to this condition. Increase in troponin T levels is also related with presence and severity of myocardial dysfunction. The therapeutic approach is aimed to reduce the episodes of intradialytic hypotension and avoid large UF volumes. Biofeedback dialysis, reduced dialysate temperatures, frequent dialysis sessions, switch peritoneal dialysis and use of beta-blockers are some options.

Conclusions: Cardiac dysfunction occurs in two-thirds of HD patients and predicts a substantial increase in mortality. As shown, HD-related myocardial ischemia with recurrent ischemic insults leads to structural and functional changes resulting in systolic dysfunction. Preliminary evidence has shown that modifications of dialysis technique may reduce the myocardial perturbation.
053
PATTERN OF ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION IN CHRONIC QAT CHEWERS IN YEMEN
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2. Sana'a University, Faculty of Medicine and Health Sciences, Sana'a, Yemen

Background: Qat chewing is a common practice in Yemeni population and its harmful effects on health have been established in many studies. Its effect on the cardiovascular system remains, however, less clear.

Purpose: We aimed to study the clinical characteristics, presentation, outcomes of acute ST segment elevation myocardial infarction (STEMI) in chronic qat chewers in comparison to non qat chewers yemeni patients.

Methods: 70 consecutive patients with confirmed acute STEMI were divided into two groups, chronic qat chewers: 50 patients, and non qat chewers:20 patients.

Result: Qat chewers were younger (51.4±11 vs 63.6±10, p=0.001). Non qat chewers were more likely to have diabetes mellitus (55 vs 18 percent, p=0.003), hypertension (60 vs 11 percent, p=0.003), and dyslipidemia (40 vs 16 percent, p=0.03). Cigarette smoking was more prevalent in qat chewers (50 vs 25 percent, p=0.05). On admission, qat chewers had poor response to fibrinolytic therapy with a trend to failure of reperfusion (69.6 vs 29.6 percent, p=0.05), more likely to have heart failure Killip class III and IV on admission (12 vs 0 percent, p<0.03) but no difference regarding in hospital mortality. Regional wall motion score in echocardiography was significantly higher in chronic qat chewers (23.9±4.5 vs 21.5±2.5, p<0.03).

Conclusion: Acute myocardial infarction in chronic Qat chewers has special pattern at presentation that has to be considered in the line of management.
THE EFFECT OF THE LUNAR CYCLE ON ADMISSIONS FOR ACUTE CORONARY SYNDROMES TO A TERTIARY HEART HOSPITAL

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2. Stony Brook University, Stony Brook, NY, USA

Objective: Determine if a relationship exists between the lunar cycle (LC) and admissions for acute coronary syndromes (ACS).

Background: The triggers of ACS are of great interest. An effect of the lunar cycle (LC) on seizures & psychiatric disturbances has been documented. While circadian variations in the incidence of ACS are well known, little has been reported on the relationship between LC and ACS.

Methods: We retrospectively reviewed admissions to St. Francis Hospital with a diagnosis-related group suggesting ACS between January 2006 & December 2010. The LC & fraction of the moon illuminated (FMI) was obtained using US Naval Observatory tables. The daily ACS was correlated with the LC. We defined thresholds of ‘fullness’ (e.g., 90%) & compared the admissions on days above the threshold to days below the threshold using ANOVA. Pearson correlation coefficients (r) with a p-value <0.05 was deemed statistically significant & a 95% confidence interval (CI) was used to measure precision of the estimates. (SAS 9.3, SAS Institute).

Results: There were 12,098 ACS over the 5 year study. The daily mean was 6.6 with a standard deviation of 3.0 [Range 0-19]. The r between FMI & ACS was 0.005 (95% CI: -0.05, 0.04). Comparing the mean ACS on days when FMI exceeded thresholds of 0.8, 0.9 and 0.95 to days below the threshold showed no statistically significant differences. Conclusion: No statistically significant relationship between the number of ACS admissions & the LC could be demonstrated in a large sample drawn from a busy tertiary cardiac hospital.
REVIEW OF TROPONINS ORDERS, EVIDENCE OF TYPE I MYOCARDIAL INFARCTION AND CARDIOLOGY CONSULTS IN A US COMMUNITY HOSPITAL

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2. Johns Hopkins Hospital, Baltimore, MD, USA

Objectives: To study the relationship between troponin elevations, proof of type I vs. type II myocardial infarction (MI), and impact in management from cardiologist consults. Background: There is no sufficient information regarding the proportion of type I vs. type II MI among patients with elevated troponins in a community setting. It is also unknown about the change in management from cardiologist consults especially for type II MI. Methods: 2 year database from 2010-2012 AD was accessed comprising 14,556 patients who underwent high sensitivity troponins testing in a sub-urban hospital. Among those with elevated troponins, type I vs. type II MI was identified using criteria for Universal definition of MI based on available patients’ data. Among type II population, patient notes were accessed to find out any management change based on cardiologist’s recommendations.

Results: 2232 patients had elevated troponins. Only 22 patients had type I MI. 2210 had type II MI who mostly had acute or chronic renal failure (1561). Cardiologists were consulted for 1004 type II patients. There was change in management recommendations (addition or alteration of the diagnostic work-up, treatments or referrals) only in 64 patients.

Conclusion: Based on data from a typical community hospital in the US, the vast majority of troponemia is related to type II MI. If established guidelines are followed for managing these patients by primary team, the overwhelming number of cardiology consults can be utilized for more complex situations with optimization of specialist resources in rural areas.
DIFFERENT CLINICAL MEANINGS OF PRE AND POST-PROCEDURAL TIMI FLOW IN PATIENTS WITH NON-ST SEGMENT ELEVATION MYOCARDIAL INFARCTION UNDERGOING PERCUTANEOUS CORONARY INTERVENTION

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The aim of the study was to evaluate the clinical prognostic meanings of pre-and post-procedural Thrombolysis in Myocardial Infarction (TIMI) flow in patients with non ST-segment elevation (non-STEMI) undergoing percutaneous coronary intervention (PCI). Reduced pre-and post-procedural TIMI flow in patients with STEMI has been associated with mortality. However the difference of clinically implication between low baseline and post-procedural TIMI flow in patients with non-STEMI has not been clear. A total of 3065 patients with non-STEMI undergoing PCI were enrolled in a nationwide Korea Acute Myocardial Infarction Registry (KAMIR). Patients were divided in each 2 groups according to pre-and post-procedural culprit vessel TIMI flow (TIMI0/1, TIMI 2/3 flows). Baseline culprit vessel flow was low (TIMI 0/1) in 880 patients (28.7%) and high (TIMI 2/3) in 2185 patients (71.3%). Post-PCI TIMI 2/3 flow was achieved in 98.3%, low post-PCI TIMI was 1.7%. At 1 month, cardiac mortality (including in-hospital mortality) occurred in 0.6% and 0.3% of patients with baseline TIMI 0/1 and 2/3 flows, respectively (P=0.377). However, the post-PCI TIMI 0/1 group had a higher incidence of cardiac death (3.8% vs. 0.4%; P=0.001) at 1 month. By multivariable analysis, post-PCI flow 0/1 was an independent predictor of 1-year mortality (HR, 2.8; 95% CI, 1.08-7.31; P=0.034). Reduced pre-procedural TIMI flow in patients with non-STEMI was in contradistinction to that seen in the patients with STEMI. However making it into TIMI2/3 in non-STEMI is equally important with that in ST-segment elevation myocardial infarction.
DIAGNOSTIC YIELD OF RIGHT AND POSTERIOR ELECTROCARDIOGRAPHIC
LEADS IN EGYPTIANS WITH ACUTE CORONARY SYNDROME

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Background: Twelve-lead electrocardiogram (ECG) has limited sensitivity in identifying myocardial ischemia in patients with acute coronary syndrome (ACS). The use of right ventricular (RV) (V4R-V6R) and posterior chest extra-leads (V7-V9) may add important information.

Objective: Our aim was to determine the prevalence of ST segment changes in right precordial and posterior electocardiographic leads in Egyptian patients presenting with ACS.

Methods and Results: We studied 101 patients presenting with chest pain suggestive of ACS. Mean age was (56.4±9 years) with 77 males. ST elevation myocardial infarction (STEMI) was the commonest mode of presentation (67.3%). Thirty two (31.7%) patients showed ST segment changes in the extra-leads. The RV leads showed ST elevation (STE) in 14 patients, while ST segment depression was present in 3. The posterior chest leads showed 2 isolated posterior STE, 7 STE in the setting of infero-posterior and right STEMI, and 10 STE in infero-posterior STEMI. Three patients had posterior ST segment depression. Patients with ST segment changes in the extra-leads had a higher prevalence of segmental wall motion abnormalities (p=0.002), significant mitral regurgitation (p=0.001), and increased RV dimensions (p=0.003). The RCA was the culprit vessel in most patients with inferior MI with or without RV involvement (71% and 66%) respectively, while the circumflex artery was the culprit vessel in those with infero-posterior MI with or without RV involvement (100% and 90%) respectively.

Conclusions: The use of posterior and right ventricular electocardiographic leads yields important diagnostic and prognostic information in patients with acute coronary syndrome.
ST ELEVATION IN LEAD AVR AS AN INDICATOR OF EARLY ADVERSE EVENTS IN PATIENTS WITH ST ELEVATION MYOCARDIAL INFARCTION

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Objectives: ST segment elevation in lead aVR may provide useful short term and long term prognostic information in patient with ST segment elevation myocardial infarction (STEMI).

Methods: Patients with documented STEMI were categorized in aVR (+) group if there was > 0.05 mv ST elevation in lead aVR; otherwise they were categorized in aVR (-) group. Excluded patients were those with left bundle branch block, pace maker rhythm and left ventricular hypertrophy. Patients were followed up during admission and 6 months thereafter.

Results: Totally 334 patients [49 in aVR (+) group and 285 in aVR (-) group] were included in the study. Mean age of the study group was 59.6 ± 13 years and 75.4% were male. Composite end point of "death, overt heart failure, recurrent chest pain with ST, T change during admission and recurrent STEMI during admission" was seen more in aVR (+) group [19 (38.8%) in aVR (+) group versus 72 (25.3%) in aVR (-) group, P = 0.05]. This difference was primarily due to overt heart failure [7 patient (14.3%) of aVR (+) group versus 12 (4.2%) of aVR (-) group, P = 0.01]. During 6 months follow up this composite end point tended to be higher in aVR (+) group [19 patient (49.7%) of aVR (+) group versus 74 (34.3%) of aVR (-) group, P = 0.08].

Conclusion: ST elevation in lead aVR might be considered as a useful and inexpensive indicator for early adverse events of patients with STEMI.
CHARACTERISTICS OF ACUTE MYOCARDIAL INFARCTION WITH MILD CAROTID ARTERIOSCLEROSIS

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Acute myocardial infarction (AMI) may occur without generalized arteriosclerosis. Then, we evaluated clinical characteristics of the patients with AMI without prominent carotid arteriosclerosis in reference to cardiovascular risk factors (RF).

Methods: Fifty one AMI cases with no or mild carotid arteriosclerosis was evaluated and compared with 31 cases with stable angina pectoris (SAP). Plaque score (PS: summation of max plaque thickness) was calculated by ultrasonography and PS of less than 5 was mild arteriosclerosis.

Results: In 15 AMI cases without plaque (mean age 57.6), there were only 1 case with 3-vessel disease (VD) and 2 with 2 VD, and the mean number of diseased vessel (DV) was 1.33 ± 0.62. In 36 AMI cases with mild arteriosclerosis (mean age 63.03), there were 2 cases with 3-VD and 12 with 2-VD, and the mean number of diseased vessel was 1.31 ± 0.49. The mean PS was 3.67 ± 1.27.

In 31 cases with SAP cases with mild carotid arteriosclerosis, mean age was 69.7 years old and higher than that in AMI cases (P < 0.05). The mean number of DV was 1.63 ± 0.68. The mean number of DV in cases with moderate or marked arteriosclerosis (PS of more than 5) was 2.36 ± 0.74 and was greater than that in cases with non or mild arteriosclerosis (P < 0.01).

Conclusions: AMI may occur without prominent carotid arteriosclerosis. PS was significantly associated with number of DV. Mean age of AMI patients was lower than that of SAP.
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EARLY DIASTOLIC AND SYSTOLIC ABNORMALITIES IN PATIENTS WITH DIABETES MELLITUS AND NORMAL EJECTION FRACTION: A 2D STRAIN ECHOCARDIOGRAPHY STUDY

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Background: In diabetes previous data usually show an early diastolic impairment of left ventricular (LV) function in the presence of a normal ejection fraction (EF). Objective Aim of this study was to evaluate the effect of diabetes on LV systolic and diastolic function.

Methods: Seventy diabetic patients (D) (mean age: 60 +/- 8.1 yrs; 40% F; HB1Ac: 7.2 +/- 0.9; duration DM: 10 +/- 9 yrs) and 23 healthy controls (N) (41% F; mean age: 59.4 +/- 9 yrs) were evaluated. All patients performed conventional 2D echocardiography. Global longitudinal strain (GLS) was obtained by Speckle tracking imaging method.

Results: D and N showed similar EF values and Left atrial volume. LVMass indexed for height was significantly higher in diabetics (N: 40,4 +/- 6 vs D: 45,3 +/- 10 g/m2.7; p<0.02). In diabetics patients mitral inflow velocities showed a pattern of impaired relaxation (N: E/A 1,09 +/- 0.2; D: 0.8 +/- 0.1; p < 0.0001; decTime N: 197 +/- 31; D: 218 +/- 0.9 msec p<0.02) and reduced PW-TDI mitral annulus proto-diastolic velocities (E’lat N: 11,8 +/- 3 ; D: 9,1 +/- 2; p<0,0001). E/E’ was significantly lower in controls (N: 6,24 +/- 1.3 vs D: 8,64 +/- 3.5; p<0.002). Radial and circumferential strain was lower in diabetics patients but only GLS reached statistical significance (N: -20,86 +/- 1.4%; D: -18,6 +/- 2%; p<0,01).

Conclusions: In diabetics patients an early LV diastolic dysfunction was present. By Speckle Tracking analysis, it is possible to unmask a parallel LV systolic dysfunction, mainly involving sub-endocardial longitudinal fibers. In this group of patients an early impairment of systolic and diastolic dysfunction coexist.
THE EFFECT OF SITAGLIPTIN THERAPY COMPARED WITH PIOGLITAZONE IN HEART FAILURE PATIENTS WITH TYPE 2 DIABETES

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Background: Recent studies have suggested that pioglitazone reduce the composite of all-cause mortality, non-fatal myocardial infarction, and stroke in patients with type 2 diabetes who have a high risk of macrovascular events. But, previous studies have suggested an increased risk of bladder cancer with pioglitazone exposure. Dipeptidyl-peptidase-4 (DPP-4) inhibitors have recently been introduced as anti-diabetic agents. However, it is unknown whether oral DPP-4 inhibitors have cardioprotective effects.

Purpose: To evaluate the efficacy and safety of initial therapy with sitagliptin, DPP-4 inhibitors, compared with pioglitazone in heart failure patients with type 2 diabetes.

Methods: A total of 11 type 2 diabetes patients with heart failure received 15mg a day of pioglitazone. All patients were switched to sitagliptin from daily pioglitazone. Treatments were then continued for an additional 26 weeks. Subjective symptoms, body weight, peripheral edema, glycaemic control and cardiac function were evaluated before and 26 weeks after taking sitagliptin.

Results: Patients who switched to sitagliptin from daily pioglitazone had improved or sustained glycaemic control. Compared with pioglitazone, sitagliptin treatment resulted in greater reductions in fasting plasma glucose and in HbA1c at week 26. Worsening of cardiac function was not observed.

Conclusions: Compared with pioglitazone, initial therapy of sitagliptin led to significantly greater improvement in glycaemic control and did not impair cardiac function.
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THE OBESITY PARADOX IN PATIENTS WITH ACUTE CORONARY SYNDROME: RESULTS FROM THE GULF RACE-2 STUDY
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We explored the relationship between mortality (in-hospital or peri-hospital) and patterns of body adiposity defined by body mass index (BMI) and waist circumference (WC). We used data from Gulf RACE-2, a prospective multicentre registry of ACS in Gulf Arab countries. We performed regression analysis of mortality as an independent variable, with dependent variables: measures of obesity, age, gender, diagnosis of STEMI/MI, history of heart failure, smoking, diabetes, stroke, dyslipidaemia, and hypertension. Increased WC in normal weight patients was associated with the highest in-hospital mortality, though not significantly. Peri-hospital mortality was significantly associated with BMI class. Adjusted, no association was observed between BMI and WC with morality. The risk of in-hospital death increased with age by 5% (OR = 1.051; 95% CI: 1.042-1.060), and decreased with male gender by 32% (0.578; 95% CI: 0.454-0.737). The risk of death increased 3.7 fold (2.742; 95% CI: 2.922-4.793) with diagnoses of STEMI/MI, and 3 fold (3.06; 95% CI: 2.149-4.358) with history of HF. Dyslipidaemia reduced the risk by 33% (0.665; 95% CI: 0.512-0.865). The odds of peri-hospital death increased by 4% per year of age (1.045; 95% CI: 1.038-1.052), and decreased by 30% for males than females (OR = 0.694; 95% CI: 0.567-0.848). The risk of death increased 2.8 fold (2.809; 95% CI: 2.325-3.394) with diagnoses of STEMI/MI and 2.4 fold (2.391; 95% CI: 1.794-3.187) and HF. In- and peri-hospital mortality in ACS is significantly associated with age, gender, STEMI/MI, HF, and history of dyslipidaemia, but not with measures of obesity.
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ULTRASOUND STUDY OF ARTERIES OF LOWER LIMBS IN PATIENTS WITH TYPE 2 DIABETES
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The purpose of research was to study of structure and frequency of atherosclerotic changes of arteries of the lower extremities in patients with type 2 diabetes.

Materials and methods. 57 patients (53% men and 47% women) with type 2 diabetes mellitus at the age from 45 to 79 years (average age 63, 8 +/- 6 years) were examined. Duplex scanning of arteries of lower limbs was provided on ultrasonic scanner Voluson 530 DMT (Austria) with linear probe 5, 5- 7, 0 MHz. The intima-media thickness of common femoral artery was determined in 2 cm distal from the bifurcation of the artery. Take into account the hemodynamic significance of arterial stenoses. In this case, hemodynamic changes were assessed in the area of stenosis, proximal and distal to the stenosis. Quantitative and qualitative assessment of the arterial wall and atherosclerotic plaques was conducted.

Results. 17% of the patients showed signs of arterial insufficiency of the lower limbs. The intima-media thickness of common femoral artery ranged from 0, 9 to 2, 1 mm (average of 1,4 +/- 0, 39 mm). Changes in the arterial walls regarded as plaques identified 63, 4% of cases. Plaques were mainly heterogeneous structure, with calcifications. According to characteristics hard calcified plaques (58%) were prevailed less frequently- dense, heterogeneous (19%), and dense, homogeneous (8%). The average degree of stenosis of common femoral artery was 28, 7 +/- 16, 8%.

Conclusion. Most patients with type 2 diabetes have symptoms of atherosclerosis of the arteries lower limbs. Atherosclerotic plaques were mostly heterogeneous with calcifications.
A COMPARISON OF THE PREVALENCE OF THE MS AND ITS COMPLICATIONS USING THREE PROPOSED DEFINITIONS IN KOREAN SUBJECTS

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To compare the prevalence of the metabolic syndrome (MS) using 3 definitions (World Health Organization [WHO], Adult Treatment Panel [ATP III], and International Diabetes Foundation [IDF]) in Korean subjects, we reviewed 6,196 participants (3,436 men and 2,760 women; mean age 51 +/- 11 and 49 +/- 12 years) who underwent a general health status evaluation and had findings of MS components, including serum insulin and microalbuminuria. The prevalence of the MS according to the WHO, ATP III, and IDF definitions (male and female) was 17.1% and 10.3%, 26% and 19.3%, and 22% and 25.4%, respectively. The degrees of agreement according to the k statistics (WHO and IDF, WHO and ATP III, and IDF and ATP III) were modest in both genders. The diagnosis of the MS was associated with a high odds ratio for nonalcoholic fatty liver disease but with a significantly varying prevalence of a Framingham risk score of >10%. The MS was seen in 10% to 30% of otherwise healthy middle-age Korean subjects presenting for health screening and the prevalence varied widely according to the criteria of its definition. The effect of the diagnosis of the MS in terms of cardiovascular risk varies significantly according to the criteria used. In conclusion, a universally accepted definition of the MS is needed for clinical and population-based studies.
065 A NOVEL CRYOMAPPING TECHNIQUE FOR AVNRT HAS A BETTER RECURRENCE AND SAFETY PROFILE THAN RFA

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Objectives: The objective was to introduce a new cryomapping technique for AVNRT ablation, “time to terminate” (TTT), to rival the outcomes of radiofrequency ablation (RFA), without its 0.7-1.3% risk of permanent AV block.

Background: Cryothermal ablation (CTA) is safe, but not broadly used for AVNRT since the early experience showed a high late recurrence rate (LRR) compared to RFA. Seeking improved LRR, we compared TTT with conventional cryomapping and previous CTA and RFA trials.

Methods: This was a retrospective study with 128 consecutive AVNRT cryoablations, divided into 2 groups: TTT (88) and conventional cryomapping (40). In TTT, CTA target sites were identified by the ability to promptly terminate AVNRT. The CTA catheter was placed during sinus rhythm at the posteroseptal tricuspid annulus, where the A-V ratio was <1:3. Sustained AVNRT was then induced. If AVNRT was promptly terminated, CTA was continued for 4 minutes, followed by placement of adjacent consolidative lesions. Success was defined as no inducible AVNRT and < double echoes.

Results: Sample size, mean follow up and immediate procedural success were similar to prior studies. CTA for AVNRT was not associated with permanent AV block. TTT had a lower LRR than conventional cryomapping (3.4% x 10%, p 0.12), which rivals previously reported outcomes for RFA (5-7.6%) and CTA (5.8-17%).

Conclusions: CTA with TTT for AV nodal modification is safer and provides equivalent short and long term efficacy when compared to RFA. Larger studies should confirm if TTT is the optimal ablation strategy for AVNRT.
INITIAL EXPERIENCE WITH THREE-DIMENSIONAL ANATOMICAL MAPPING DURING CARDIAC PACING LEAD EXTRACTION

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Objectives: We assessed the feasibility of CartoSound\textsuperscript{\textregistered} technology (Biosense Webster Inc, Diamond Bar, CA) to image the three-dimensional (3D) relationships of fibrotic binding sites between leads and the cardiovascular system during lead extraction. Background: Fibrous adherences are the principal cause of permanent cardiac pacing lead failed removal and complications, and are not directly visualized by standard approach. Methods and Results: Segments of real-time 2D ultrasound images were acquired using a 10-Fr 3D SoundStar\textsuperscript{\textregistered} catheter and integrated into the Carto mapping system to obtain 3D CartoSound anatomical maps of the superior vena cava, right atrium (RA), coronary sinus, right ventricle (RV), pacing leads, and fibrous tissue during lead removal. Lead extraction procedure was performed on 46 patients (38 men; mean age 73.7±10.5 years), and 90 leads (1.96 leads/patient) with a mean time from implant of 62.7±51.8 months. CartoSound was able to detect more binding sites in RA (17.4\% vs. 4.3\%, \textit{p}=.04), and RV (43.5\% vs. 21.7\%, \textit{p}=.04) compared to fluoroscopy. Mean fibrosis volume (mean 2.0±1.6 cm\textsuperscript{3}) correlated positively with time from implant (\textit{r}=.38, \textit{p}<.05), and powered-sheaths use (\textit{r}=.39, \textit{p}<.05), and negatively with procedural success (\textit{r}=-.37, \textit{p}<.05). Mean CartoSound evaluation time was 4.9±2.3 min. When compared to standard approach, the CartoSound use was characterized by a significantly lower mean procedure time (99±35.5 min vs. 30.1±23.2 min, \textit{p}=.001), and major complications (1.7\% vs. 0\%, \textit{p}=.03).

Conclusions: Real-time 3D fibrosis assessment using CartoSound anatomical mapping is feasible during lead extraction. Its role as a complementary surveillance tool to improve procedural outcomes requires extensive validation.
OUTCOME OF RIGHT ATRIAL FLUTTER ABLATION IN PATIENTS WITH CARDIAC RESYNCHRONIZATION DEVICES

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Objective: To determine the rate of atrial fibrillation (AF) development in patients with biventricular (BiV) pacing devices following radiofrequency ablation of typical atrial flutter.

Background: Freedom from atrial arrhythmias is beneficial in patients with BiV pacing devices. Atrial flutter is a risk factor for subsequent development of AF in patients without devices.

Methods: We analyzed BiV device data (91% BiV implantable cardioverter-defibrillator) one year before and one year after isthmus-dependent right atrial flutter ablation in 22 consecutive patients (mean age 71±10.8 years) from June 2006 to December 2009. Arrhythmias following ablation procedure were identified by device interrogation at clinical follow-up.

Results: No patients had evidence of AF on device interrogation in the year prior to flutter ablation, and all had successful ablation of their atrial flutter. During the one-year follow-up period, seven patients (32%) developed AF. Two other patients (9%) had atrial flutter recurrence without documented AF.

Conclusions: In patients with BiV pacing devices, the incidence of atrial fibrillation is high after successful ablation of isthmus-dependent right atrial flutter. This suggests that further strategies to control atrial arrhythmias to maximize BiV pacing are needed in certain patients.
Objective: Comparing conscious sedation versus general anesthesia (GA) complication rates in patients undergoing percutaneous epicardial access.

Background: Percutaneous epicardial access and ablation, increasingly performed in the treatment of ventricular tachyarrhythmias, potentially increases complication risk with patient motion as the access needle passes in close proximity to the abdomen and thorax. Methods/results: We retrospectively analyzed planned epicardial access ablation procedures between 1/2004 and 12/2011, and classified patients into conscious sedation vs. GA at the time of access. Complications were defined as any event resulting in prolonged disability or harm, or requiring a separate invasive procedure. There were 116 epicardial access attempts in 107 patients (94.4% successful). 71 (66.4%) were male with a mean age of 51.0 years. Access was obtained under conscious sedation in 71 (66.4%) patients. Those in the sedation group were younger (48.6 vs. 55.7 years) with less sleep apnea (12.9 vs. 31.4%) (P=0.02 for both). Otherwise, there was no difference in baseline characteristics including gender, BMI, comorbid conditions, previous cardiac surgery and route of access (anterior vs. inferior). Overall complication rates (13.1%) were similar, with 5 vs. 4 cases of pericardial effusion requiring repeat access, 2 vs. 0 recurrent pericarditis (1 requiring pericardiectomy), 1 vs. 0 pleural injury, 0 vs. 1 phrenic nerve injury and 2 vs. 0 intra-abdominal bleeding in the sedation group compared to the GA group, respectively. There were no procedural-related deaths.

Conclusion: Percutaneous epicardial access can be performed safely in patients under conscious sedation. Excluding postoperative pericardial effusion, complications were infrequent (5%).
AN UNUSUAL ABLATION LOCATION FOR OBTAINING COMPLETE HEART BLOCK IN A PATIENT WITH DRUG REFRACTORY ATRIAL TACHYARRHYTHMIA AND BASELINE BIFASCULAR BLOCK

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Introduction: AV node ablation in conjunction with a pacemaker or ICD is an effective rate control strategy in patients with drug refractory atrial tachyarrhythmia. At times, obtaining lasting AV block can be challenging.

Methods: N/A

Results: We report a 51 year old man with non-ischemic cardiomyopathy and a biventricular ICD who continued to have symptomatic atrial tachyarrhythmias despite aggressive rate and rhythm control therapy. We elected to pursue AV nodal ablation. Despite right ventricular ablation at the compact AV node and along the left ventricular (LV) septum below the aortic valve, AV block could not be obtained. As the patient had a known right bundle branch block (RBBB) with left posterior fascicular block (LPFB), we mapped the remaining area of conduction in the lateral LV looking for a left anterior fascicular potential. Using the EnSite NavX system, we created a 3D electro-anatomic map of the LV cavity. Once the fascicular potential was identified, ablation was performed at the lateral LV site resulting in immediate AV block (figure, arrows). Using the 3D map, additional ablation was performed extending from the area of the fascicular potential proximally along the presumed course of the anterior fascicle toward the septum. Complete AV block persisted and was observed in follow up two weeks later. Conclusion: The left anterior fascicle can provide a lateral LV target for obtaining complete heart block in patients with known bifascicular block when ablation of the ventricular septum is unsuccessful.
SUBCLINICAL UNEXPECTED CENTRAL VENOUS OCCLUSION IN THE ELECTROPHYSIOLOGY LABORATORY: CASE SERIES

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Objectives: describe a case series of unexpected central venous occlusion (CVO) in the electrophysiology (EP) laboratory.

Background: cardiac rhythm management devices (CRM) and catheter based EP procedures require access to the heart through the central venous system. Subclinical CVO is rare, but may prevent access to the heart.

Methods and results: we reviewed 258 consecutive EP procedures (102 ablations and EP studies and 158 CRM implants). Subclinical unexpected CVO was encountered in 4 patients (2.5%), all woman, age 63±15. Two scheduled for CRM implant, prior history of breast cancer, mastectomy in the contralateral site and no superficial venous collaterals. In one, venography showed subclavian vein patency in the surgical side. After axillary access in both cases, CVO at the proximal superior vena cava was encountered and confirmed with a repeat venogram. One patient received a subcutaneous defibrillator and the other, an epicardial pacemaker. Two patients planned for ablation of supraventricular tachycardia and atrial flutter had no known lower extremity thrombus or edema. One had history of failed kidney transplant and the other, ventricular septal defect with corrective surgical interventions at childhood. CVO at the level of the proximal IVC was encountered advancing the catheters and confirmed with venography. Both ablations were successfully performed through superior access using the internal jugular and subclavian veins with 2-3 catheters plus a three dimensional mapping system. Conclusions: CVO is rare, should be suspected in patients with history of breast cancer and selected surgeries. Ablation procedures are feasible with a superior vascular approach.
AV NODE ABLATION AND CARDIAC RESYNCHRONIZATION THERAPY IN PATIENTS WITH PERMANENT ATRIAL FIBRILLATION

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Objective: The aims of this study were: 1-assessing the clinical benefit of cardiac resynchronization therapy (CRT) in patients with atrial fibrillation (AF), 2-evaluating the impact of AV-Node (AV-N) ablation in outcome of AF patients undergoing CRT.

Background: Heart failure (HF) predispose AF and AF can worsen HF , CRT is an important advance in treatment of end stage HF

Method: A total of 68 permanent AF patients were included in this prospective study. 34 patients received optimized medical treatment controlling ventricular rate, and 34 patients underwent AV-N ablation and Biv pacing. Mean age was: 58.3±18 year and NYHA class: II,III,IV : 29/51/18.Duration of follow up was 21±11 months.

Result: Clinical and echocardigraphic parameters were compared at baseline and 1 and every 6 month then after. Patients were evaluated for the occurrence of cardiac death, hospitalization for HF , and CRT responsiveness. LVEF and NYHA class was improved significantly in AV-N ablation group rather than in medical treatment group. Also cardiac death and hospitalization rate decreased in the first group.

Conclusion: AF can worsen HF and vice versa. AV-N ablation and CRT in these patients who are non-responsive to medical treatment and are poor candidate for AF ablation is an acceptable treatment. Also by AV-N ablation Atrio Ventricular dysynchrony in AF is disappeared.
Obesity predicts left ventricular diastolic dysfunction in healthy middle age adults with no cardiovascular risk factors

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Introduction: Previous studies have demonstrated that increased BMI (Body mass index) is associated with left ventricular diastolic dysfunction in elderly patients and patients with traditional cardiovascular risk factors such as hypertension, diabetes, and coronary artery disease.

Objective: To assess the effect of BMI on left ventricular diastolic dysfunction in young patients with no traditional cardiovascular risk factors such as hypertension, coronary artery disease, and diabetes.

Methods: Echocardiography data of 337 patients with age < 65 years, no history of diabetes, hypertension, and coronary artery disease with normal ejection fraction (EF) was divided into three groups: normal weight (BMI < 25 kg/m\textsuperscript{2}), overweight (25-29.9 kg/m\textsuperscript{2}) and obese (>=30 kg/m\textsuperscript{2}) and analyzed. Peak early transmitral diastolic flow velocity (E), late transmitral diastolic flow velocity (A), and early diastolic mitral annulus velocity (e') were measured, and E/A and E/e' were calculated and compared.

Results: The mean age in normal weight, overweight and obese groups were 45 ± 13 yrs, 48 ± 11 yrs and 49 ± 11 yrs respectively (p < 0.03). Patients with overweight and obesity had lower e' (0.08± 0.03 m/sec vs 0.1± 0.02 m/sec, P < 0.001) and higher E/e' (9.4 ±0.28 vs 8.5 ± 0.26, P < 0.017). After adjusting for age and gender, the risk of abnormal diastolic dysfunction was higher in BMI >= 30 kg/m\textsuperscript{2} (odds ratio 2.2, 95\% Confidence Interval: 1.04-4.63).

Conclusion: Obesity predicts abnormal diastolic dysfunction in healthy adults with no traditional cardiovascular risk factors such as hypertension, diabetes and coronary artery disease.
Value of Statins in Congestive Heart Failure Patients with Elevated High Sensitivity C-Reactive Protein

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Background: Elevated levels of high sensitivity C-reactive protein (hs-CRP) have been observed in patients with congestive heart failure (CHF) and activation of the immune response may play a role in heart failure progression. Statins have pleiotropic effects and may have a role in this subset of patients.

Objective: The study addresses the possible therapeutic role of statins in CHF patients with elevated hs-CRP.

Methods and Results: The study included 45 patients with CHF who were given atorvastatin 20mg/day, and followed up for 6 months. Their mean age was 52.7±8.6 years (71% males). Patients were divided into two groups; group 1 (G1), 15 cases with hs-CRP level less or equal to 1 g/L, and group 2 (G2), 30 cases with hs-CRP level more than 1 g/L. Group 2 patients had worse New York Heart Classification (NYHA) functional class (p<0.001), and lower left ventricular ejection fraction (LVEF) (P<0.03). On follow-up, G2 patients had a significant decrease of hs-CRP level (p<0.001), and significant improvement in their NYHA classification (p<0.001), and LVEF (p<0.03), while the changes in G1 patients were not significant (p=NS). Compared to G1, G2 patients had a higher need for treatment intensification (p<0.008), however the difference in hospital admission, was not significant (p=0.2). Subgroup analysis of G2 patients showed that those in whom hs-CRP did not decrease had more hospital admissions (p<0.001).

Conclusions: CHF patients with elevated hs-CRP had worse prognosis. The use of statins significantly reduced hs-CRP and improved clinical outcomes.
THE RELATIONSHIP OF PLATELET COUNTS AND PLATELET INDICES TO CLINICAL OUTCOMES IN PATIENTS WITH CHRONIC HEART FAILURE

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Background: Acute decompensated heart failure is known to be associated with increased platelet activation and abnormal platelet counts. We sought to determine the prognostic impact of platelet counts and trends in platelet count in patients with chronic heart failure. Methods: Consecutive patients enrolled in the Creighton University Cardiac Center Heart Failure clinic between January 2000 and June 2012 were included in this retrospective study. The key outcome assessed was a composite of all-cause mortality and CHF hospitalization. Patients were classified into those with low platelet count (150,000/μl) and normal platelet count (150,000-600,000/μl). Results: A total of 149 patients fulfilling the inclusion criteria were included in the current study. Mean age of 63.7 years and 60.4% were males; Mean index platelet count was 232.7 x10^3 per microliter. Twenty one patients (14%) had a low platelet count at the time of enrollment. Of these, 11 (52%) had improvement in platelet count to >150,000 /μl during 3-6 month follow up. A total of 91 patients (61.1%) had primary outcome during a mean follow up of 39.6 months including 37 deaths (24.8%). Baseline platelet count, platelet volume and changes in platelet count during follow up did not predict the composite outcome measure. Low platelet count at the time of enrollment was a predictor of all-cause mortality on univariate analysis but age was the only independent predictor. Conclusion: Platelet counts, platelet volume at the time of enrollment and trends in platelet count during follow up did not predict mortality or CHF hospitalization.
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SELF-CARE AND ASSOCIATED FACTORS IN PATIENTS WITH CHRONIC HEART FAILURE IN KERMANSHAH, IRAN

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Objective: We sought to determine the extent of self-care and associated factors in patients with CHF living in Kermanshah, Iran.

Background: Chronic heart failure (CHF) is common and poor outcome health problem worldwide. Effective self-care can improve quality of life, reduce hospitalization and rate of mortality. Health interventions related to self-care in patients with CHF need baseline information of self-care and the associated factors.

Methods and results: Having approval from ethics committees and signed consent form participants, 231 patients average between 29 and 90 years (mean= 66 ± 13.03, 51.5% Female), diagnosed with HF admitted May 2010 to June 2012 in Kermanshah, Iran were interviewed. The Persian version of self-care heart failure index (pSCHFI) was used to evaluate self-care maintenance, self-care management and self-care confidence. Information about age, sex, level of education, social isolation, marital status, occupation, smoking, treated hypertension, diabetes mellitus and duration of heart disease collected to assess their regression with level of self-care. Data was analyzed using descriptive statistic and regression. In the current study, according scoring of SCHFI from Riegel et al.(2004), the mean of self-care subscales were 33.7 ± 10.64, 37.2 ± 12.04 and 43.9 ± 15.60 for self-care maintenance, self-care management and self-care confidence respectively.

Conclusion: Patients with CHF in Kermanshah do not have acceptable levels of self-care that might explain many unplanned hospital admissions. These results underscore the need to revise methods of providing education and developing campaigns to improve self-care.
BARRIERS AND FACILITATORS TO SELF-CARE IN PATIENTS WITH CHRONIC HEART FAILURE: A REVIEW OF QUALITATIVE STUDIES
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Objectives: To explore affecting factors on self-care in patients with chronic heart failure (CHF) and address the research question, “What are the barriers and facilitators to an effective self-care?”

Background: CHF is a common and costly condition globally that places large demands on self-care. Failure to adhere with self-care recommendations is common. Understanding the factors that enable or inhibit self-care is essential in developing effective health care interventions to improve patients’ outcome.

Methods: Medline, Embase, CINAHL, Web of Science, Scopus and Google scholar were searched. A combination of Mesh terms and text words were used with the key words related to “facilitators” or “barriers”. Articles were included if they were peer reviewed (1995 to 2012), in the English language and investigated at least one contextual or individual factor impacting on self-care in CHF patients > 18 years.

Results: Among 1105 articles, 23 titles met the inclusion criteria. Factors impacting on self-care such as environmental factors; factor related to processes of self-care and the health care system etc were discussed in this review. Also, we explained our finding regarding factors such as socioeconomic situation and education level which not been explored extensively by researchers.

Conclusion: Self-care in patients with HF is complex and challenging. This study shows although there is an emerging literature, further research is required to address the barriers and facilitators of self-care in patients with heart failure in detail to provide sustain applicable health policy strategies.
DESCRIPTIVE PROFILE OF RESOURCES UTILIZATION AMONG HEART FAILURE PATIENTS AT KAH, EASTERN PROVINCE, SAUDI ARABIA
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The primary purpose of this study is to describe the sample characteristics profile of admitted HF patients. These characteristics include: contextual factors [age, gender, individual characteristics and Body Mass Index (BMI)], disease characteristics of severity of illness [Ejection Fraction (EF) and blood pressure stability (BP)], treatment and lab characteristics (Na, Serum Cholesterol, Serum Triglyceride, creatinine, hemoglobin (Hgb) and international normalized ratio (INR)]. The outcome was measured by length of hospitalization after admission as well as the number of re-admission during the first and second year.

Design: A Retrospective Electronic Data Base Analysis with a descriptive design. Sample: Convenient sample of 236 HF patients were used.

Results: The results revealed that the contextual factors including ([age (M=69.012±11.92), gender [male (42.5%), individual characteristics [Smokers (7.2%), BMI (M=34.0±8.7)], and EF (M=41.24±15.7), BP (Systolic M=135.99±24.8, Diastolic M=70.54±13.6)]. The patient were on medication regime of HF (Co-morbidities of: HTN (92.8%), COPD (31.4%) ) Pulmonary hypertension (11.9%), DM (81.4 %), AFib (23.7%), CABG (16.1%) and Renal disease (45.8%). Laboratory characteristics indicating: Na+ (M=137.75±4.65), Cholesterol (M=3.85±1.034), Triglyceride (M=1.30±0.76), Creatinine (M=116±73.11), Hgb (M=11.98±2.02), TSH (M=3.686±15.697) and INR (M=1.252±0.66). The median length of hospitalization was 10 and 13 days for the first year and the second year, respectively. The number of re-admission during the first year was (M=2±1.15) and the second year was (M=2±1.3).

Conclusion: These preliminary results highlighted the main sample characteristics of HF patients at our center are in keeping with the international registries published.
CHARACTERISTICS OF RESOURCES UTILIZATION AMONG MALE AND FEMALE HEART FAILURE PATIENTS AT KAH, EASTERN PROVINCE, SAUDI ARABIA

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Design: A Retrospective Electronic Data Base Analysis with a descriptive design were used.

Sample: A sample of 236 HF patients.

Results: Gender based differences in HF population in Saudi Arabia are not well studied. We analyzed data from 236 patients with HF who were admitted to King Abdulaziz hospital in eastern region. Differences in their clinical and demographic characteristics, co-morbidities, lab investigations, and re-admissions were analyzed. Female patients were 57.5% of the sample. Female patients were slightly younger ((M=68.02±10.72 vs M=70.42±13.29) with higher BMI (M=35.3 ±9.2 vs M=31.374±7.57829). BP control was similar (SBP M=138.31±; 25.418, DBP M=69.09±14.015) vs (SBP M=133.24±; 23.63, DPB M=72.82±12.75). Female patients had better EF (M=45.08±14.47 vs M=36.52±16.01). A trend of higher prevalence of systemic HTN (94.8% vs 89.9%), pulmonary hypertension (14.2% vs 9.1%), DM (82.1% vs 79.8%), and AF (26.9% vs 18.2%) were in females. However, IHD burden (18.2% vs 12.7%) and CKD (49.5% vs 44%) were more prevalent in male. With view to lab characteristics Na, Hb and lipid profiles were similar in both groups. There was a significantly higher creatinine level in male. The median lengths of hospitalization for first and second year for female were 11 and 14 days and for male were10 and 12 days. The number of re-admission during first and second year for female were (M=2±1.17; M=1.9±1.3) and for male were (M=1.9±1.15; M=2.07±1.3).

Conclusion: The Mann–Whitney U test results indicated that a significant differences between male and female for the following:(Age, BMI, EF, Systolic BP, Creatinine; P value=0.033,0.027,0.002,0.024,0.002 respectively).
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SEX DIFFERENCES IN CARDIOVASCULAR DISEASE
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Sex differences affect the presentation, treatment results, and outcomes of cardiovascular diseases. Men suffer at younger ages than women from coronary artery disease and hypertension and more commonly develop systolic heart failure or aortic aneurysms. Women are more frequently affected by heart failure with preserved ejection fraction, long QT-syndromes and Takotsubo cardiomyopathy. They exhibit a more favorable remodeling under pressure overload and a better survival with heart failure. Even within the same clinical syndromes of myocardial infarction, hypertension, or heart failure, sex differences exist in pathophysiological mechanisms, in the development of myocardial hypertrophy, fibrosis, inflammation, and vascular remodeling. As a result, male or female sex is characterized by specific manifestations of organ damage. In several animal models of myocardial infarction, vascular disease, myocardial hypertrophy, or heart failure, females have better outcomes than males. Sex differences arise at the molecular and cellular level from the control of gene transcription, intracellular signaling, organelle function, and crosstalk between heart, skeletal muscle, adipose tissue, and the immune system. A better understanding of sex differences in cardiovascular pathophysiology will facilitate identifying targets that respond to specific therapies and subsequently could lead towards a more individualized medicine. At present, the development of new cardiovascular drugs has reached a plateau after years of continuous progress. An improved understanding of sex-specific disease mechanisms, therapeutic targets, and target groups will ameliorate this situation towards more efficient treatments of both women and men.
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THE ASSOCIATION BETWEEN DEPRESSION AND DIABETES
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Depression increases the risk of mortality, shown in a 12-year follow-up of 10,025 U.S. NHANES adults (Egede LE, Diabetes Care, 2005). Because both diabetes and depression are common, there is considerable overlap by chance alone; a diagnosis of both is most likely to be made in hospitalized patients (Berkson’s bias). Research is complicated by disagreements about the diagnostic criteria and treatment for diabetes and depression. In the community, depressed mood is usually defined using self-administered questionnaires like the CES-D (maximum 60 Points) or the BDI (maximum 21 points). The PHQ (Physician’s Health Questionnaire) has been used to screen for major depression in the community while HADS is used in the hospital. Both the Hamilton rating scale and the DSM diagnostic require an interview. These are research tools. Most physicians use nonstandard queries driven by clinical insight (e.g., Are you feeling depressed? Can you tell me why?), but doctors admit that they do not often ask these questions in part because they do not have enough time to make important additional queries (e.g., about suicidal ideation) and follow-up referrals.

A meta-analysis of 20 studies (Mezuk B, Diabetes Care, 2008) showed a bi-directional association of diabetes with depression. Both diabetes medications and antidepressants increase obesity, stacking the deck against patient success with weight control. There is a difference of opinion whether the marginal effectiveness of antidepressants is sufficient to recommend screening for depression. Cognitive behavior therapy is more effective than antidepressants in most patients without severe depression (Fournier JC, JAMA, 2010).

Depressed patients usually eat more and are less likely to sustain diabetes or cardiovascular interventions. Diabetes nurse educators improve patient self-management because they have the time and training to provide positive problem-solving messages about sustaining a healthy diet and physical activity.
ALDOSTERONE - A BRIDGE BETWEEN CARDIOVASCULAR AND MOOD DISORDERS?

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Aldosterone is the main mineralocorticoid hormone involved in the control of blood volume. Its effects on water-electrolyte homeostasis have impact on the control of blood pressure and cardiovascular functions. It is well known that the comorbidity of cardiovascular and mental disorder is high, however, aldosterone has not been implicated in the psychopathology so far. Aldosterone is acting via mineralocorticoid receptors, which are thought to be fully occupied by glucocorticoids in the brain. We have recently provided new evidence on anxiogenic effects of chronic treatment with aldosterone in an animal model. Hyperaldosteronism was associated also with increased depression-like behaviour which was concomitant with gene expression changes in the hippocampus relevant to major depression (Hlavacova and Jezova, Horm. Behav. 2008; Hlavacova et al. Int.J.Neuropsychopharmacol. 2012). To challenge possible immediate therapeutic impact of these findings we evaluated the effects of a well established drug in the treatment of cardiovascular disorders, the aldosterone antagonist eplerenone. Indeed, both single and repeated treatment of rats with eplerenone decreased anxiety and induced neuroendocrine changes consistent with anxiolytic outcome. Moreover, we have demonstrated significant correlations between salivary aldosterone concentrations and trait anxiety in healthy humans, which were dependent on the gender and on the phase of the menstrual cycle in women. These finding may support a role for aldosterone in the development and course of depression or at least in some subtypes such as those linked to cardiovascular disease.

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HDL AND ATHEROSCLEROSIS - MYTH OR REALITY
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Low HDL cholesterol (HDL-C) is an established biomarker for the future development of atherosclerosis and atherosclerotic cardiovascular disease (CVD) events in population-based observational studies and clinical trials of cholesterol-lowering therapies and this includes coronary heart disease (CHD) patients with low levels of LDL cholesterol (LDL-C) on statin therapy. Because multiple clinical trials designed to increase HDL-C and reduce CVD risk have not demonstrated efficacy and instead have shown potential harm, there has been widespread confusion regarding the importance of HDL as a biomarker of risk and as a potential target for therapeutic intervention. Confusion concerning the importance of HDL in atheroprotection has been magnified by a Mendelian randomization study that utilized HDL-C as an intermediary biomarker of CVD risk. In contrast to studies that utilized HDL-C as a surrogate measure of HDL, a genome wide association study (GWAS) that evaluated the associations between phospholipid transfer protein polymorphisms and CVD risk reported that high concentrations of small HDL particles and total HDL particles were associated with lower CVD risk. Based on the limitations of HDL-C as a biomarker of risk, and misguided attempts to reduce atherosclerosis through effectuating changes in the cholesterol content of HDL particles, future trials that investigate HDL-modifying therapies should assess HDL particle number, and structure function relationships of the HDL proteome and lipidome that are associated with atheroprotective functional measures.
OMEGA-3 SUPPLEMENTATION IMPROVES ARTERIAL STIFFNESS AND BIOMARKERS OF CV RISK IN LATINO AND WHITE PATIENTS WITH HYPERTENSION SERVED BY A SAFETY-NET HEALTHCARE SYSTEM

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We previously reported on a cross sectional study of Latino and White hypertension patients in a safety-net healthcare system in which Framingham risk factors, markers of inflammation (hsCRP, LPpLA2), arterial stiffness (Pulse wave velocity, augmentation index, and central aortic pressure), and endothelial function (brachial artery flow-mediated dilatation) were measured (BMC Cardiovasc Disord. 2011; 11: 15). Univariate and multivariable associations between these parameters using carotid intima media thickness (cIMT) as a “gold-standard” for the presence of atherosclerosis we found that PWV, a measure of arterial stiffness, was associated with preclinical carotid atherosclerosis independent of Framingham risk factors. This is the first study to demonstrate that PWV is associated with preclinical atherosclerosis in an underserved population and suggests that measures of arterial stiffness could play a role in CVD risk stratification within the growing US safety-net population. In a follow-up to this work we conducted a randomized, placebo-controlled trial of the effect of omega-3 fatty acid supplementation on vascular function as measured by PWV and on circulating inflammatory markers. Results of this trial and its implications on CVD risk stratification in underserved populations will be discussed.
USE OF NMR LDL LIPOPROTEIN PARTICLE ANALYSIS IN CARDIOVASCULAR DISEASE PREVENTION

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Low density lipoprotein particle counts, assessed by NMR technology, is available and is a valuable adjunct to the standard lipid profile normally used in lipid management. This technology is most useful in the following 3 settings:
1. Management of lipids in a patient on therapy who is near goal
2. Recurrent cardiovascular events despite apparent proper management of LDL goal
3. Occurrence of early atherosclerotic events in patient with seemingly minimal risk factors
These 3 medical situations will be discussed with appropriate case examples.
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IMPACT OF RENAL SYMPATHETIC DENERVATION IN PATIENTS WITH DRUG RESISTANT HYPERTENSION
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As much as one third of patients with hypertension are treatment refractory as they do not reach sufficient blood pressure control despite antihypertensive combination therapy of significant duration. In patients with therapy-resistant hypertension, the kidneys play a central role as activator of the sympathetic nervous system. Therefore, alternative treatment strategies have been explored. Most recently, attention has been redirected to the sympathetic nervous system in the pathogenesis of hypertension. In addition, interruption of the renal sympathetic nervous system in humans with resistant hypertension has been studied with promising results. Recent studies showed a significant and continuous reduction of blood pressure of 25-30 mmHg systolic and 10-15 mmHg diastolic for at least 2 years. This presentation provides an overview of the results of therapeutic renal sympathetic denervation in patients with drug refractory hypertension.
HOW MUCH OF THE CVD RISK IS ATTRIBUTED TO DIET?
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Risk prediction scores have received much attention the past few years, especially in the primary prevention of cardiovascular disease (CVD). Although diet has been independently associated with CVD risk, its role in the accuracy of the developed models has rarely been studied. Thus, in this review, the role of dietary patterns' assessment on the predictive ability of CVD risk scores was critically discussed. A computer-assisted literature search retrieved 15 prospective studies, but only one out of the 15 studies evaluated the role of dietary patterns' on the accuracy of the developed models and the inclusion of dietary habits improved the accuracy by 37%. The remaining studies suggested an independent protective effect of healthy dietary habits on CVD risk, with an attributable risk varying from 9% to 37%. There is a need for separately evaluating the role of diet in the accuracy of CVD risk prediction scores.
BEYOND HDL CHOLESTEROL: WHAT CAN WE LEARN FROM PARTICLE NUMBER AND SIZE?
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Given the consistent inverse association of HDL cholesterol (HDL-C) with cardiovascular disease (CVD), there is immense interest in developing therapies that raise HDL-C. But HDL-C, the cholesterol carried by HDL particles, may not fully capture HDL-related cardioprotection. HDL-C is carried within HDL lipoprotein particles that are heterogeneous in size, density, charge, core lipid composition, specific apolipoproteins, and function. Recent failures of drugs targeting HDL-C have fueled interest in other metrics of HDL, including HDL particle number (HDL-P), size, and function. We hypothesized that HDL-C cardioprotection may at least partly be influenced by metabolic correlations with other lipoproteins, particularly atherogenic particles, but that HDL-P may be less affected. Using data from 5,598 individuals (ages 45-84 years) from the prospective Multi-Ethnic Study of Atherosclerosis (MESA), we compared the association of chemically-assayed HDL-C and NMR-spectroscopy-measured HDL-P with subclinical atherosclerosis and incident CVD before and after accounting for atherogenic lipoproteins. HDL-C was correlated with HDL-P (r = 0.73). Notably, HDL-C associations with atherosclerosis and incident CVD were substantially attenuated and became non-significant after adjusting for atherogenic lipoproteins. In contrast, HDL-P associations with atherosclerosis and incident events were relatively unaffected. In addition, a very high HDL-C also conferred increased risk (HR 2.59, 95% CI 1.11-6.02) after adjusting for HDL-P, while very high HDL-P remained inversely related to risk (HR 0.50, 95% CI 0.19-1.35). These results may have implications both for risk assessment and evaluating therapeutic interventions, particularly pharmacologic interventions which may differentially affect several lipid and lipoprotein parameters concurrently.
The annual incidence of sudden cardiac death in the United States is between 184,000 and 462,000, with estimates that 50% to 70% of the deaths are due to VT or VF. Availability of therapies shown to reduce death in various at-risk groups, including beta-blockers, ACE-inhibitors, statins, aldosterone blockers, and the implantable cardiac defibrillator (ICD), underscore the need to accurately identify patients who will develop VT/VF and exclude those who will not. Multiple tests have been evaluated, but currently no optimal strategy for risk stratification exists. Left ventricular (LV) ejection fraction (EF) remains the single best predictor of benefit from an ICD. New evidence suggests myocardial sympathetic denervation may identify high-risk independently of EF. Positron emission tomography is being used to quantify myocardial sympathetic denervation (11C-meta-hydroxyephedrine, 11C-HED), perfusion (13N-ammonia, 13NH3) and viability (insulin-stimulated 18F-2-deoxyglucose, 18FDG) in patients with ischemic cardiomyopathy eligible for a primary prevention ICD. The primary outcome is sudden cardiac arrest or equivalent (SCAE) defined as arrhythmic death or ICD discharge for VT/VF >240 bpm. Based on data acquired so far, volumes of total denervated (p=0.001) and viable denervated myocardium (11C-HED-18FDG mismatch, p=0.03) predict SCAE, while hibernating (13NH3-18FDG mismatch) and infarcted myocardium do not. Denervated myocardium had a hazard ratio of 3.5 for SCAE (10.3%/year vs. 3.0%/year, p=0.001). Denervated myocardium quantified using 11C-HED PET strongly predicts risk of SCAE, and is independent of EF, infarct volume and other clinical variables. Thus, molecular imaging may improve risk stratification for current ICD candidates.
CATHETER ABLATION IN PATIENTS WITH ELECTRICAL STORM – BENEFIT OF A CLINICAL NETWORK

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Introduction: Electrical storm (ES) – defined as ≥ 3 sustained distinct episodes of ventricular arrhythmia needing cardioversion/anti-tachy-pacing within 24 hours – may occur in up to 20% of patients with implanted ICD. Only 50% of these patients survive a 2-year follow-up period. Can early invasive therapy and a structured algorithm for in-hospital treatment increase outcome and rhythm stability?

Methods: In between October 2011 and October 2012 29 patients with electrical storm were included and treated based on a prespecified algorithm including catheter ablation during the initial hospitalization phase.

Results: Patients were recruited within 13 cardiology departments and sent to the invasive electrophysiology center within the first days after occurrence. Out of the 29 patients 3 were not transiently rhythm stabilized and underwent early invasive treatment. Mean age of 69 years, mean ejection fraction 32%. 19 (66%) of ES-patients had ischemic, 9 non-ischemic (31%) and 1 arrhythmogenic right ventricular cardiomyopathy. The clinical arrhythmia of ES was monomorphic ventricular tachycardia in 28 (97%) and only 1 patient had episodes of ventricular fibrillation (3%).

Effective ablation of the clinical ventricular arrhythmia was achieved in all patients after a mean of 1.2 ablation sessions. Overall 7 patients (out of the 9 patients with non-ischemic cardiomyopathy) underwent an epicardial ablation in addition to endocardial evaluation (3 within the acute setting and 4 after recurrence of ES). Overall after a mean 9-month-follow-up period 8 patients (28%) had recurrent ventricular arrhythmia including 4 with recurrent ES (all of these 4 patients underwent effective epicardial ventricular tachycardia ablation and were free of any arrhythmia during further follow-up).

2 patients (6%) died during follow-up due to worsening of heart failure.

Conclusions: Early catheter ablation of ventricular arrhythmias occurring during ES is feasible and may have beneficial outcome and rhythm stability during follow-up. Early access to invasive electrophysiology may be achieved in a clinical network of cardiology departments working close together with an invasive center with eligibility of ES ablation (including epicardial ablations).
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THE ROLE OF ELECTROPHYSIOLOGIC TESTING ON OUTCOME IN PATIENTS WITH ARVC
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Introduction: The role of electrophysiological (EP) study for risk stratification in patients with arrhythmogenic right ventricular cardiomyopathy (ARVC) is controversial. Our aim was to test the predictive role of inducible sustained monomorphic ventricular tachycardia (SMVT) for an adverse clinical outcome.

Methods: From 101 patients who fulfilled the 2010 Revised Task Force Criteria for ARVC at the University Hospital of Zurich, the clinical outcome of 62 patients who underwent EP study was analyzed.

Results: During a median follow-up of 9.8 years, 30 patients (48.4%) experienced an adverse outcome (cardiac death, heart transplant, sudden cardiac arrest, ventricular fibrillation, VT with hemodynamic compromise or syncope). EP study demonstrated SMVT in 34 patients (54.8%). Of those, 22 (64.7%) had an adverse outcome. Conversely, in 28 patients without inducible SMVT, 8 (28.6%) had an adverse outcome. Kaplan-Meier analysis showed a significant event-free survival benefit for patients without inducible SMVT (log-rank p=0.008) with a cumulative survival free of adverse events of 76% [95% CI 61-95%] and 72% [95% CI 56-92%] in the group without inducible SMVT as compared to 42% [95% CI 28-64%] and 26% [95% CI 14-50%] in the other group after 5 and 10 years, respectively. Inducibility of SMVT (HR 2.34; 95% CI 1.02-5.37) was a significant predictor on multivariate analysis.

Conclusion: This long-term observational data suggests that SMVT inducibility during EP study may predict an adverse outcome of patients with ARVC.
ROBOTICS IN THE EP LABORATORY: PROMISE, REALITY AND FUTURE DIRECTIONS

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Robotics, the concept that automated machines can operate in place of humans in delicate or dangerous environments or in manufacturing processes, has in recent years been extended to many branches of medicine. Various attempts at incorporating machine technology to the clinical electrophysiology (EP) laboratory in recent years have not yet gained traction in routine clinical practice. Potential advantages and drawbacks of existing systems will be reviewed. Determinants of successful ablation procedures such as catheter tip force as well as accuracy and stability of catheter travel will be reviewed. We have developed a system (CGCI, Magnetecs, USA) utilizing eight rapid electromagnets that provide real-time automated navigation of magnetic tipped EP catheters within the human heart. In vivo animal validation was performed and clinical trials in Europe have confirmed excellent target acquisition using both a “manual” robotic (joystick driven) as well as “automated” robotic (automatic travel of the catheter to designated sites) modes. More recently, the system has been utilized in creating excellent 3-D depictions of cardiac chambers, devoid of distortions commonly seen with conventional manual mapping techniques. As well, RF lesion sets were created at sites of arrhythmia circuits or foci and a high success rate has been obtained with automated RF application along the pre-designed lesion sets. A group of 11 patients with left atrial flutter underwent mapping and ablation using the CGCI magnetic navigation technology. In all 11 patients, the responsible circuits or foci were identified and successfully ablated.

Conclusions: Robotic (remote) navigation holds great promise in improving efficiency, safety and procedure results in the EP laboratory. However, the burden of proof is upon the various robotic technologies to provide convincing data that will encourage tomorrow’s clinicians to perform ablations in a robotic environment.
BIVENTRICULAR PACING FOR ATRIOVENTRICULAR BLOCK AND SYSTOLIC DYSFUNCTION


Background: Right ventricular pacing restores an adequate heart rate in patients with atrioventricular block, but high percentages of right ventricular apical pacing may promote left ventricular systolic dysfunction. We evaluated whether biventricular pacing might reduce mortality, morbidity, and adverse left ventricular remodeling in such patients.

Methods: We enrolled patients who had indications for pacing with atrioventricular block; New York Heart Association (NYHA) class I, II, or III heart failure; and a left ventricular ejection fraction of 50% or less. Patients received a cardiac-resynchronization pacemaker or implantable cardioverter–defibrillator (ICD) (the latter if the patient had an indication for defibrillation therapy) and were randomly assigned to standard right ventricular pacing or biventricular pacing. The primary outcome was the time to death from any cause, an urgent care visit for heart failure that required intravenous therapy, or a 15% or more increase in the left ventricular end-systolic volume index.

Results: Of 918 patients enrolled, 691 underwent randomization and were followed for an average of 37 months. The primary outcome occurred in 190 of 342 patients (55.6%) in the right-ventricular-pacing group, as compared with 160 of 349 (45.8%) in the biventricular-pacing group. Patients randomly assigned to biventricular pacing had a significantly lower incidence of the primary outcome over time than did those assigned to right ventricular pacing (hazard ratio, 0.74; 95% credible interval, 0.60 to 0.90); results were similar in the pacemaker and ICD groups. Left ventricular lead–related complications occurred in 6.4% of patients.

Conclusions: Biventricular pacing is superior to conventional right ventricular pacing in patients with atrioventricular block and mild-to-moderate left ventricular systolic dysfunction with NYHA class I, II, or III heart failure.
LIMITATIONS OF RESYNCHRONIZATION THERAPY IN PATIENTS WITH NARROW QRS: INSIGHTS FROM THE EARTH TRIAL

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Although the benefits of cardiac resynchronization therapy (CRT) are well established in selected patients with heart failure (HF) and prolonged QRS duration, salutary effects in patients with narrow QRS complexes remain to be demonstrated. The EvaluAtion of Resynchronization Therapy (LESSER-EARTH) trial compared the effects of active and inactive CRT in patients with severe HF and QRS < 120 ms. The trial was interrupted prematurely by the DSMB because of futility and safety concerns. Changes in exercise duration after 12 months were not different in patients with and without CRT. Similarly, no significant differences were observed in LV ejection fraction and LVES volume by echocardiography. On the opposite, CRT was associated with a significant reduction in the 6-minute walk distance and a non significant trend toward an increase in HF-related hospitalizations.

Conclusion: In HF patients with QRS <120 ms, CRT did not improve clinical outcomes of left ventricular function and was even associated with potential harm.
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IN THE OR V. THE EP LAB--WHERE IS THE BEST LOCATION FOR LEAD EXTRACTION?
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Pacemaker and defibrillator lead extraction is a highly specialized procedure done chiefly in referral centers. The operators are predominantly electrophysiologists, but cardiac surgeons, cardiac interventionalists, and other surgeons sometimes perform the procedure. The risks of lead extraction are typically a 1-2% risk of vascular or cardiac tear and subsequent intrapericardial or intrapleural bleed. If the operator is not a cardiac surgeon, then it is recommended that one be immediately available for sternotomy in case of complication. The location for the procedure is highly variable—sometimes done in the EP lab, sometimes done in the cardiac OR or hybrid suite. There are risks and benefits to each location, but there has been a general trend towards moving this procedure to the operating room, for more prompt and satisfactory treatment of complications. The downsides of the OR are generally inferior fluoroscopy, personnel who are less familiar with device procedures, and time delays in getting supplies from the EP lab. Overall, the decision on where to base lead extraction procedures needs to be individualized according to the strengths and weaknesses of the individual hospital.
CATECHOLAMINERGIC POLYMORPHIC VENTRICULAR TACHYCARDIA: THE CLINICIAN’S PERSPECTIVE
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Catecholaminergic polymorphic polymorphic ventricular tachycardia (CPVT) is a potentially lethal, genetic channelopathy syndrome characterized by ventricular arrhythmias occurring primarily during exercise. Patients typically present with syncope or seizures and initial misdiagnosis is common because baseline cardiac testing is normal. Untreated CPVT imposes a 30-50% mortality risk by age 30. The past decade has seen important advances in the genetic diagnosis and treatment of this disease which can significantly decrease the risk of sudden death. This presentation will focus on the recognition and accurate diagnosis of CPVT in addition to the pathophysiology and appropriate treatment.
GENETIC BACKGROUND, CLINICAL CHARACTERISTICS, AND TREATMENT OF EARLY REPOLARIZATION SYNDROME

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Early repolarization is a common electrocardiographic finding that occurs in 1% to 10% of healthy persons, and it has been generally considered benign for decades. However, there is increasing evidence showing that early repolarization is associated with an increased risk of ventricular fibrillation and sudden cardiac death. Idiopathic ventricular fibrillation associated with early repolarization, the so-called early repolarization syndrome, started receiving increasing attention. The age at diagnosis is around 40 years and 70% to 80% of patients are men. A family history of unexplained sudden death is present in 10% to 20% of patients. Similar to other arrhythmia syndromes, early repolarization syndrome is an inherited disease, and 5 causative genes including KCNJ8, CACNA1C, CACNB2b, CACNA2D1, and SCN5A have been identified. Cardiac arrest occurs during sleep in 19% to 26% of patients while it also occurs during physical effort in 9% to 19% of patients. The frequency of arrhythmia recurrences in survivors of ventricular fibrillation is 6% to 7% per year. Atrial fibrillation can also occur in about 20% of patients. Although early repolarization in the inferolateral leads has initially associated with idiopathic ventricular fibrillation, early repolarization in the right precordial leads can be also found in up to ~20% of patients. The amplitude and the existence of early repolarization can dramatically vary, and early repolarization becomes most prominent just before the development of ventricular fibrillation. Implantable cardioverter defibrillator is the only proven effective treatment to prevent sudden cardiac death. Isoproterenol and quinidine have been effective in arrhythmia recurrences.
THE EVOLUTION OF THE PACING SITE: PAST, PRESENT AND FUTURE
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As cardiac pacing system for bradyarrhythmias has been developed in clinical practice over half century, the preferential pacing site has been also evolved. [PAST] In the early stage, the object of the pacing was only maintenance of heart rate and pacing lead has been implanted to right atrial appendage and/or right ventricular apex for easiness in terms of implantation and the stability even using conventional passive fixation lead. [PRESENT] Since recent studies elucidated that pacing from those conventional sites result in deterioration of cardiac function and increasing co-morbidity, non-appendage or non-apical pacing has been chosen as alternative pacing sites to achieve more physiological cardiac activation. In addition, the cardiac resynchronization therapy (CRT) system using epicardial coronary sinus pacing lead is established for the heart failure patients with dyssynchrony of cardiac contraction. Although the variation of cardiac pacing site has been increased, it has not been elucidated which site is most effective for each patients. In this lecture, I would like to review the footsteps and importance of pacing site as well as expected pacing site enabled by promising new technologies for the [FUTURE].
A BLOOD TEST TO PREDICT ARRHYTHMIC RISK


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Objectives: The aim of this study was to measure SCN5A cardiac sodium channel mRNA splicing variants in white blood cells (WBCs) from three heart failure (HF) groups and correlate levels with arrhythmic risk.

Background: HF is associated with upregulation of two cardiac SCN5A mRNA splicing variants and a concomitant decrease in the full-length transcript. These mRNA variants encode prematurely truncated, nonfunctional Na+ channels, which increase arrhythmic risk. WBCs show similar SCN5A mRNA splicing.

Methods: Simultaneously obtained left ventricular assist device myocardial core samples and WBCs were compared for levels of SCN5A variants C (VC) and D (VD). Variant levels were compared between HF patients divided into three groups: HF (n=45), HF with an implantable cardioverter-defibrillator (ICD) without appropriate intervention (n=42) and HF with an ICD with appropriate intervention within 1 year of blood sample acquisition (n=23).

Results: SCN5A variant expression levels correlated between paired ventricular and WBC samples. The correlation coefficient, r, was 0.78 and 0.75 for VC and VD, respectively. The expression of SCN5A variants in WBCs was graded with arrhythmic risk between the groups. Controlling for covariates, HF patients who had received an appropriate ICD intervention had higher levels of SCN5A variants compared to those who had not, OR= 3.25 (95% CI 1.64-6.45; p=0.001). The area under the receiver operating characteristic (ROC) curve for determination of appropriate ICD intervention using blood SCN5A variants levels was > 0.97.

Conclusions: Blood and myocardial levels of SCN5A variants correlated. Blood variant levels were correlative with arrhythmic risk.
Introduction: Left ventricular assist devices (LVAD) have become increasingly common therapy for advanced heart failure. It is thought that hospitalizations after LVAD implantation are frequent. The aim of this study is to examine the frequency and causes of first time versus incident rehospitalization after LVAD implantation.

Methods: This was a single center, retrospective review of post-LVAD hospitalizations in 190 consecutive outpatients living with a continuous flow LVAD between 2005-2013, either HeartMate II (173 patients) or HeartWare (17 patients). Reasons for admissions were reviewed and classified.

Results: There were 660 total admissions in 190 LVAD recipients. The most common causes for first time readmission (n=190) were anemia (24%), infection (21%), heart failure (13%), and device complications (12%). The most common causes for incident readmission (n=470) were also anemia (24%), infection (19%), heart failure (10%), and device complications (8%). Time to readmission after implant ranged from 10-1351 days, median = 88 days; mean = 174 ± 235 days.

Conclusions: Hospitalizations in patients living with continuous flow LVADs remain frequent. Bleeding and infection seem to be the most common reasons for both first time and incident readmissions, suggesting current treatment strategies for these complications may be ineffective at preventing recurrence. Further studies are needed to identify effective therapies to prevent readmission.
Background: The use of left internal mammary artery (LIMA) in multivessel coronary artery disease (MVCAD) improves survival following coronary artery bypass graft surgery (CABG); however, survival benefit of multiple arterial (MultArt) grafts is debated.

Methods and Results: We reviewed 8,622 Mayo Clinic patients who had isolated primary CABG for MVCAD from 1993 to 2009. Patients were stratified by number of arterial grafts: LIMA plus saphenous veins (LIMA/SV) group (n=7,435), and MultArt group (n=1,187). Propensity score analysis matched 1,153 patients. Operative mortality was 0.8% (n=10) in MultArt and 2.1% (n=154) in LIMA/SV (P=0.005), but not statistically different (P=0.996) in multivariate analysis, or in matched groups (P=0.818). Late survival was greater for MultArt versus LIMA/SV (5-, 10-, and 15-year survival (y/s) were 95%, 84%, and 71% vs 85%, 61%, and 36%, respectively [P<0.001] in unmatched groups, and 96%, 83% and 70%, vs 93%, 80% and 60%, respectively [P=0.0025] in propensity matched groups). MultArt subgroups, with bilateral internal mammary artery (BIMA)/SV (n=589) and BIMA only (n=271), had improved 15-y/s (97%, 86%, 76%, and 94%, 82%, 75% at 5-, 10-, and 15-years, [P<0.001]), and BIMA/radial artery(RA) (n=147) and LIMA/RA (n=169), had greater 10-y/s (95%, 84% and 93%, 78% at 5- and 10-years, [P<0.001]) versus LIMA/SV. In multivariate analysis, MultArt grafts remained a strong independent predictor of survival (HR= 0.79, 95 % CI, 0.66-0.94, [P=0.007]).

Conclusions: In patients with MVCAD undergoing isolated CABG with LIMA to left anterior descending (LAD) artery, arterial grafting of the non-LAD vessels, conferred 15-year survival advantage compared with SV grafting.
We aimed to evaluate the predictors of acute cellular rejection (ACR) within 12 months after cardiac transplantation and the association between ACR episodes and risk of cardiac allograft vasculopathy (CAV) among heart transplant recipients. All patients who underwent heart transplant at a single tertiary care academic center between 2003 to 2011 were studied retrospectively. Demographic, clinical and laboratory variables were obtained, including cytomegalovirus and Epstein Barr virus serology. The primary outcome was ACR episodes within 12 months from the day of transplantation. This was categorized as grade I (mild rejection) or II-III (moderate to severe rejection), based on the cytopathology report of the endomyocardial biopsy. Using linear regression analysis the potential correlates of ACR grade I or II (and above) were examined at univariate and multivariate analysis. We analyzed 85 recipients: mean age 46; male 75%. Younger age (regression coefficient: -0.07, 95%CI: -0.12, -0.02, p=0.006) and female gender (mean ACR episodes 5.7 versus 3.7 in males, p=0.0085) were associated with higher frequency of grade I ACR. Body mass index, smoking, diabetes, hypertension, dyslipidemia, chronic kidney disease and cytomegalovirus/Epstein Barr virus serology were not associated. There were no associations between any recipients or donor risk factors with grade II or III ACR. Of note, there was a significant association between grade I ACR and the incidence of CAV (regression coefficient:1.4, 95%CI: 0.1, 2.8, p=0.037). Younger female patients were at higher risk of grade I ACR in our population. Moreover, higher frequency of grade I ACR episodes were strongly associated with increased risk of CAV.
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REDUCTION IN LV SIZE AFTER LVAD IMPLANTATION IS ASSOCIATED WITH REDUCTION IN QRS VOLTAGE AND DURATION
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Introduction: Previous reports have shown that the QRS duration shortens after placement of a Left ventricular assist device (LVAD). The purpose of this study was to determine electro- and vectocardiographic changes in ventricular activation pattern and LV size after mechanical unloading following LVAD placement.

Methods: Twelve lead electrocardiograms and vectorcardiograms were analyzed immediately before and 1 week after the implantation of a LVAD in 46 consecutive patients with a mean age of 57±12 years (38 males) who received a HeartMate II.

Results: Twenty-two patients (age=54±13; 18 males) were in sinus rhythm (n=18) or in atrial fibrillation (n=4) with preserved A-V conduction. A reduction in the QRS amplitude (SV1 plus RV6) and duration was observed in these patients (13±9 vs 7±5 mV and 105±18 vs 90±16 ms respectively; p<0.01 and p<0.001; Figure). Similarly, the QRS area in the horizontal plane of the vectocardiogram was reduced (50±66 vs 15±15 mm²; p=0.02). Left ventricular diastolic diameter was significantly reduced (61±1 vs 45±9.7 mm; p<0.001). Twenty-four patients were ventricularly paced (age=59±1; 21 males). A reduction in QRS duration was also observed in these patients (174±19 vs 139±27 ms and; p<0.0001).

Conclusions: One week after LVAD implantation, there is a significant reduction in QRS voltage and duration. This rapid reduction in QRS voltage cannot be explained by a reduced LV mass. A smaller LV cavity, as observed in this study, appears to explain the reduction in QRS voltage by the Brody effect and QRS duration by shortening ventricular activation time.
MORTALITY REDUCTION WITH IABP PRIOR TO CABG IN EMERGENCY PATIENTS WITH SHOCK
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Objectives: Patients with cardiogenic shock undergoing CABG surgery are recommended to be supported by IABP therapy. The optimal beginning of the IABP therapy, before or after surgical revascularization, remains questionable.

Methods: In a retrospective study in one center consecutive patients with cardiogenic shock undergoing emergency CABG in 2009 and 2010 were supported by IABP therapy either beginning before (“IABP-before” group) or after (“IABP-after” group) revascularization, with 100 patients in each group. The IABP support started in the IABP-before group before or at the beginning of the CABG operation, in the IABP-after group at the end of the CABG operation.
All patients received the best available therapy with the aim of early CABG. After CABG, the duration of IABP support in the IABP-before group was 4.1±2.0 and in the IABP-after group 5.6±4.4 days.

Results: At 30 days after CABG, the all-cause mortality was slightly lower in the IABP-after group, without significance, than in the IABP-before group (34% vs. 38%). Conversely, after 1 year the IABP-before group showed a significantly lower all-cause mortality rate than the IABP-after group (40% vs. 50%). Complications as major bleeding, peripheral or intestinal ischemia, sepsis and stroke did not differ significantly between the two groups.

Conclusion: IABP support initiated before surgical revascularization markedly reduced the 1 year mortality in patients with cardiogenic shock undergoing early CABG revascularization in contrast to IABP therapy beginning after surgical revascularization. These beneficial effects were not obvious at 30 days. The onset of IABP therapy before CABG did not cause an increase in IABP related complications.
CUSTODIOL-N VERSUS CUSTODIOL: A PROSPECTIVE RANDOMIZED DOUBLE BLIND MULTICENTER PHASE III TRIAL

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Objectives: HTK-Solution (Custodiol) is a well established cardioplegic and organ preservation solution. We currently developed a novel HTK based solution Custodiol-N which includes iron chelators to reduce oxidative injury as well as L-arginine, to improve endothelial function. In the present first-in-human study, Custodiol-N was compared with Custodiol in patients undergoing elective coronary bypass surgery.

Methods: The study was designed as prospective randomized double blind non-inferiority trial. Primary end-point was area under the curve (AUC) of creatine kinase MB (CKMB) within the first 24 hours after surgery. Secondary endpoints included, peak CKMB and troponin-T and AUC of troponin-T release, cardiac index, cumulative catecholamine dose, ICU-stay and mortality. All values are given as mean±SD, p<0.05 was considered as statistically significant.

Results: 101 Patients were included into the trial. Patient characteristics, medical history, operation and crossclamp times did not differ between the groups. CKMB AUC (878±549 vs. 778±439 h*U/l, non-inferiority p<0.001) and Troponin-T AUC (12990±8347 vs. 13498±6513 h*pg/ml, non-inferiority p<0.001) was similar in both groups. While peak Troponin-T (888±554 vs. 847±380 pg/ml) did not differ between the groups, peak CKMB (52±40 vs. 41±30 U/l, superiority p<0.002) was significantly lower in the Custodiol-N group. Cardiac index, catecholamines ICU-stay and mortality (1 death in the control group) was similar in both groups.

Conclusions: This study shows that Custodiol-N is safe and provides similar cardiac protection as the established HTK-Custodiol solution. The significantly reduced peak CKMB levels in the Custodiol-N group may implicate a beneficial effect on ischemia/reperfusion injury in the setting of coronary bypass surgery.
LOW INCOME IS AN INDEPENDENT PREDICTOR OF IN-HOSPITAL MORTALITY AMONG HEART TRANSPLANT RECIPIENTS: A NATIONWIDE INPATIENT SAMPLE STUDY

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Background: Lower socio-economic condition has been shown to have greater risk of rejection and graft loss among heart transplant recipients who survive the transplant hospitalization. However, the association of income status and in-hospital outcomes among heart transplant recipients have not been studied from a national database.

Methods: Hospitalized patients (N=3418) with elective heart transplant procedure (ICD-9 procedure code 37.51) in the nationwide inpatient sample (NIS) 2003 through 2010 databases were identified. Socio-economic status of a patient was determined by median household income (MHI) for patient's ZIP Code (based on respective year) and were categorized by MHI quartile 1, 2, 3 and 4. Discharge weights were used to create nationwide estimates. Multivariable logistic regression models were used to determine the associations of MHI and inpatient mortality, length of stay and total cost among these patients.

Results: Patients had a mean age of 49(±17) years, 27% women, 36% non-whites. The risk of in-hospital mortality in the MHI quartile 2 and 3 were similar to that of the highest income group (adj.ORs, 95%CIs were 1.30; 0.82–2.09; p=0.268 and 0.77; 0.47–1.27; p=0.309, respectively); however, MHI quartile 1 had higher risk of in-hospital mortality (adj.OR, 1.73; 95%CI, 1.03–2.90; p=0.039). Income status had no association with length of hospital stay and total cost.

Conclusion: In this large national database, lowest quartile of MHI was an independent predictor of in-hospital mortality among heart transplant recipients. Further prospective studies with more complete and direct measurement of socioeconomic status may be needed to evaluate this association.
IMPACT OF POSTTRANSPLANT WEIGHT GAIN ON CARDIAC ALLOGRAFT VASCULOPATHY

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Background: Excessive weight gain and obesity are commonly reported after heart transplantation (HTx). Currently, it is not clear whether weight gain is a risk factor of cardiac allograft vasculopathy (CAV) in heart transplant recipients.

Methods: We studied all patients (n = 95; mean age 49.9 ± 13.1 years) who underwent orthotopic cardiac transplantation at the Swiss Cardiovascular Centre Berne since 1994 and survived for ≥1 year. Vascular risk factors were registered before transplantation and at regular follow-up visits. Coronary angiography was performed yearly for the evaluation of CAV. The follow-up period was 5.7 ± 3.1 years.

Results: Baseline body mass index (BMI) was 23.8 ± 3.4 kg/m² and increased to 28.2 ± 4.2 kg/m² at follow-up year 10 (+4.4; p<0.001). Weight gain proofed inversely associated with incident CAV (hazard ratio 0.78, 95% confidence interval (CI) 0.64 – 0.94; p=0.01) in Cox regression analysis adjusting for type 2 diabetes, BMI preHTx, hypertension, recipient ischemic heart disease preHTx, number of cardiac allograft rejection episodes, lipids, statin use, recipient age and gender. In contrast, recipient preHTx ischemic heart disease was positively predictive of the incidence of CAV (hazard ratio 7.22; 95% CI 1.704 – 30.61; p<0.01). No significant associations between hypertension, lipid parameters, gender, type 2 diabetes and recipient age at the time of HTx with CAV were observed.

Conclusions: Weight gain after heart transplantation is common but does not necessarily reflect a risk factor for CAV in heart transplant recipients. Recipient preHTx ischemic heart disease is positively predictive of the incidence of CAV.
SUCCESSFUL USE OF IMPPELLA 2.5 DEVICE IN CARDIAC ARREST DUE TO LEFT MAIN STENOSIS

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Introduction: Cardiac arrest due to left main occlusion immediately after diagnostic coronary angiography is usually treated with balloon angioplasty. We describe a case series of two patients who underwent implantation of Impella assist device prior to the emergent PTCA.

Case 1: 57Y/o male with NSTEMI was found to have 95% mid left main stenosis. Immediately after the procedure, he complained of chest pain and went into asystole. CPR was initiated. Left sided access was obtained and Impella 2.5 Device was inserted and turned on. Temporary pacemaker was also placed. PTCA and stent placement was performed to the left main. Impella was removed the next day. Patient was discharged home without sequelae. Angiogram 3 months later showed widely patent stent.

Case 2: 76Y/o male with exertional dyspnea was found to have 99% distal left main stenosis. Immediately after the angiogram, blood pressure and heart rate started dropping. He became asystolic and ACLS protocol was started. Impella 2.5 device was inserted through the pre existing right groin access and turned on. Left groin access was then obtained and PTCA of left main was done improving flow from TIMI 1 to TIMI 3. Patient underwent emergent CABG with an uneventful recovery.

Discussion: Left main occlusion can occur in patients with severe left main stenosis after diagnostic angiography. If the patient has already gone into cardiac arrest, there is sometimes a lag in LV contractility and improvement in flow in the coronaries despite PTCA. Both our patients had Impella placement prior to PTCA with excellent outcomes.
THE ROLE OF GALECTIN-3 AND CONNECTIVE TISSUE GROWTH FACTORS IN HYPERTENSIVE PATIENTS WITH DIASTOLIC HEART FAILURE: LINK OF CLINICAL AND BASIC STUDIES

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Background: Galectin-3 (Gal-3), a beta-galactoside binding lectin is a novel marker of heart failure. Connective tissue growth factor (CTGF), a matrixcellular protein, plays a pathogenic role in cardiac fibrosis. We investigated the role of gal-3 and CTGF in diastolic dysfunction.

Material and Method: A total of 125 hypertensive patients, recruited from Taiwan diastolic heart failure (DHF) registry received echocardiography, cardiac MRI, and ELISA. Basic experiments included mice with aortic banding, immunohistochemistry, RT-PCR, Western blot, cell culture, co-immunoprecipitation, confocal microscopy, MTT assay and Brdu incorporation.

Results: Gal-3 and CTGF plasma levels were more significantly elevated in severe DHF patients (E/e’>15, n=29), compared with mild DHF patients (n=96)(19.4±12.4 vs. 6.85±5.3 ng/mL, p<0.001; 73.8±31.1 vs.30.1±30.4 pg/mL, respectively). Linear regression analysis revealed that gal-3 and CTGF plasma levels closely correlated with E/e’ (r=0.69; 0.80, respectively, p<0.001). CTGF level is also associated with myocardial fibrosis by cardiac MRI (r=0.70, p<0.001).

Gal-3 null mice with aortic banding revealed significant suppression of myofibroblast activation, and interstitial fibrosis but not CTGF expression compared with wild type mice. Mechanical stretch significantly increased CTGF secretion in cultured cardiomyocytes. In cultured cardiac fibroblasts, exogenous addition of gal-3 induced phosphorylation of EGFR and ERK1/2, and fibroblast proliferation. Co-immunoprecipitation assay revealed interaction between gal-3 and EGFR.

Conclusion: We demonstrated that macrophage-secreted gal-3 and cardiomyocyte-derived CTGF separately contributed to cardiac fibrosis in pressure overload-induced DHF and gal-3 can bind to its glycoconjugate, EGFR inducing its autophosphorylation via receptor clustering, and activation of subsequent mitogenic pathway. Our findings may provide novel therapeutic targets for DHF.
CARDIOMYOCYTE-CARDIAC FIBROBLAST INTERACTION IN THE PATHOGENESIS OF DIABETIC CARDIOMYOPATHY - ROLE OF HMGB1/TLR4/IL-33 AXIS

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Cardiac fibroblasts (CFs) play a key role in pathogenesis of diabetic cardiomyopathy (DiCM) by producing extracellular matrix protein (e.g., collagen). Whether cardiomyocytes could interact with the CFs and promote collagen production is not clear. HMGB1 is a cytokine which is produced by stressed cardiomyocytes. IL-33 is another cytokine expressed in fibroblasts which has anti-fibrotic effect. The objective of the study is to demonstrate whether the HMGB1 could mediate cardiomyocyte-fibroblast interaction thereby represses fibroblast IL-33 expression and promotes myocardial fibrosis in diabetes.

Methods and Results: Streptozotocin (STZ)-induced mouse model of diabetes and cardiomyocyte/fibroblast co-cultures treated with high glucose (HG) was used in the study. In diabetic mice, myocardial HMGB1 expression was elevated while interleukin (IL)-33 expression was decreased. Further, treatment of diabetic mice with either A-box or exogenous IL-33 prevented the myocardial collagen deposition and dysfunction. In vitro experiments showed that HG treatment increased cardiomyocyte HMGB1 production. Further, challenge myocyte/fibroblast co-cultures with HG revealed that myocytes dramatically potentiated HG-induced decrease in IL-33 and increase in collagen (I and IV) in the CFs by HMGB1. Over-expression of IL-33 in fibroblasts attenuated the HG- or HG/HMGB1-induced collagen production. When toll-like receptor 4 deficient (TLR4-/-) fibroblasts were co-cultured with wild-type myocytes, the potentiating effects was prevented. Finally, compared to wild type mice, TLR4-/- mice with diabetes incurred less collagen deposition with improved cardiac function.

Conclusions: We have demonstrated a novel mechanism of the pathogenesis of DiCM. Specifically, myocyte-derived HMGB1 represses fibroblast IL-33 expression, thereby potentiating their ability to induce fibrosis and cardiomyopathy.
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DOXORUBICIN-INDUCED CARDIOTOXICITY IN MICE IS PREVENTED BY LATE INA INHIBITION WITH RANOLAZINE, WITH IMPROVEMENT IN HEART FUNCTION, FIBROSIS AND APOPTOSIS
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Background. Doxorubicin (D) produces a cardiomyopathy through multiple mechanisms. D generates Reactive Oxigen and Nitrogen Species, setting the stage for metabolic ischemia that activates late INa, target of ranolazine (RAN). Objectives. We aim at assessing whether RAN prevents D cardiotoxicity.

Methods. We measured left ventricular (LV) fractional shortening (FS) and radial strain (RS) in C57BL/6 mice, pretreated with RAN for 3 days. RAN was then administered for 7 days, alone and with D. In excised hearts, we evaluated mRNA expression, interstitial fibrosis and apoptotic pathway.

Results. After 7 days with D, FS decreased to 50±2%, p=.002 vs 60±1% (sham). RAN alone did not change FS (59±2%). In mice treated with RAN+D, the reduction in FS was milder: 57±1%, p=.01 vs D. D-cardiotoxicity was accompanied by elevations in ANP, BNP, CTGF and MMP2 mRNAs, while co-treatment with RAN significantly lowered these same genes compared to D. The alterations in extracellular matrix remodeling were confirmed by an increase of interstitial collagen with D, which was normal in hearts co-treated with RAN. PARP and pro-Caspase 3 levels were decreased with D, with a parallel increase in cleaved caspase 3, but not with RAN+D. About the assessment of LV function, after 2 days, FS is decreased significantly and this data is accompanied by a reduction of RS (34±3%), p=.0003 vs sham (64±4%). This pattern is not observed in RAN+D-treated mice (49±3%, p=.01 vs D).

Conclusions. In mice, D produces LV dysfunction which can be diagnosed by FS and RS and prevented by RAN.
Background and objectives: The survival ratio of implanted mesenchymal stem cells (MSCs) in the infarcted myocardium is low. Autophagy is a complex “self-eating” process and could be utilized for cell survival. We have found that atorvastatin (ATV) could effectively activate autophagy to enhance MSCs survival during hypoxia and serum deprivation (H/SD). Moreover, MEK/ERK pathway is a non-canonical autophagy pathway. Therefore, we hypothesized that MEK/ERK pathway participates in ATV-induced autophagy of MSCs under H/SD.

Methods: MSCs were pretreated with ATV (0.01-10 μM) for 3 h under H/SD. For inhibitor studies, the cells were pre-incubated with MEK1/2 inhibitor U0126. Cell autophagy was assessed by acridine orange (AO)-positive cells using flow cytometry, autophagy related protein using western blotting and autophagosome using transmission electron microscopy.

Results: Autophagy was elevated in the H/SD group compared with the normal group. ATV further enhanced the autophagic activity as well as upregulated phosphorylation of ERK1/2. And treatment with U0126 downregulated phosphorylation of ERK1/2 and attenuated ATV-induced autophagy.

Conclusions: MEK/ERK pathway participated in ATV-induced autophagy in MSCs under H/SD, and modulation of the pathway could be a novel strategy to improve MSCs survival.
EXCITABILITY OF DIRECT REPROGRAMMED MURINE TAIL FIBROBLASTS: BETWEEN WILD-TYPE FIBROBLASTS AND CARDIOMYOCYTES

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Introduction: Limited regenerative capacity of postnatal cardiomyocytes (CM) creates a need for alternative regenerative approaches. Cellular rejection, low efficiency differentiation, and tumor formation have presented hurdles for stem cell based approaches. Direct reprogramming of fibroblasts into CM using Gata4, Mef2c, Tbx5 (GMT) was recently described to circumvent some of these challenges. We investigated the electrophysiological (EP) changes induced by overexpression of GMT in murine tail fibroblasts (TF).

Methods: Lentiviral overexpression of GMT was induced in TF from multiple lines of transgenic mice carrying different CM lineage reporters. Infected TF expressed a subset of CM specific genes and protein profiles. Whole cell current and voltage clamp studies of wild-type (WT) TF (n=30), GMT infected TF (n=32) and control CM (n=26) were performed.

Results: All isolated CM showed a spontaneous repetitive action potential (AP) activity which did not appear in any of the WT or GMT infected TF. Pacing of CM with variable amplitudes elicited an “all or none” AP response (Fig 1A), while all WT and majority (78%) of GMT infected TF showed a passive decay of membrane potential according to the cell’s time constant (Fig 1B). Nevertheless, a minority (22%) of GMT infected TF demonstrated a stimulus dependent response consisting of rapid up-sloping nifedipine-sensitive potential followed by a variable duration (50-500 ms) plateau, suggestive of Ca-dependent Chloride current (Fig 1C). Voltage clamp recordings revealed a voltage gated calcium current in GMT infected TF but in contrast to CM, no voltage gated sodium current could be detected.

Conclusion: GMT overexpression in fibroblasts results in induction of voltage dependent Ca and Ca-dependent chloride currents. These currents are responsible for some excitable features in the reprogrammed cells. However, these changes fall short of the essential characteristic EP properties of functional CMs.

![Graph showing AP activity in myocytes, control TF, and infected TF.](chart.png)
IMPORTANCE OF SLMAP IN CARDIOMYOCYTE VIABILITY AND MEMBRANE FUNCTION

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Sarcolemmal membrane-associated proteins (SLMAPs) are tail-anchored membrane proteins found in the cell membrane, reticulum/endoplasmic reticulum (SR/ER), and mitochondria. SLMAP regulate cardiac function and is involved in excitation-contraction (E-C) coupling. Transgenic (Tg) mice that overexpress SLMAP in myocardium exhibit changes in ER/SR morphology accompanied by electrophysiological abnormalities. In order to further access the role of SLMAP, we isolated neonatal cardiomyocytes and fibroblasts to examine the ability of these cells to respond to known cardiac stressors. Cell viability assay using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) indicated that Tg cardiomyocytes are ~20% less viable as compared with wild-type cardiomyocytes. Further, the viability of Tg cardiomyocytes was markedly decreased (~90%) to treatments with thapsigargin or palmitate, compared with Wt cardiomyocytes. ER stress sensors such as binding immunoglobulin protein (BIP), Protein disulfide-isomerase (PDI), and autophagy marker Light Chain 3 (LC3) were found to be upregulated in Tg- cardiomyocytes. These markers were further increased upon treatment with thapsigargin and palmitate. Interestingly, BiP and PDI were downregulated in the fibroblasts from transgenic hearts. The increase in expression of Bip, PDI, and LC3 was more remarkable in Wt cardiomyocytes upon palmitate treatment. The apoptosis marker caspase-3 was markedly upregulated in Tg cardiomyocytes. These data suggests that normal SLMAP levels are important for viability and proper membrane biology in cardiomyocytes.
GLIVEC (IMATINIB MESYLATE) INDUCES AUTOPHAGIC SIGNALLING IN CARDIAC MYOCYTES

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Glivec, targeting the Bcr-abl oncogene, is used in treatment of a variety of cancers. A syndrome of CHF has been observed in an increasing number of glivec treated patients. To evaluate the mechanisms of toxicity we exposed neonatal rat ventricular myocytes (NRVM) to glivec at a median therapeutic dose of 5 micrograms. Cellular stress was evidenced by a rapid decline in cellular ATP and loss of mitochondrial delta psi. Exposure to glivec also resulted in translocation of c-abl to the mitochondria and Sarcoplasmic reticulum. C-abl localization to the SR was followed by BAX cross-linking and translocation to the SR in a time dependent manner. There was also biochemical and immunohistochemical evidence of increasing levels of proautophagy beclin1/PI3KIII and declining levels of anti-autophagy beclin1/bcl2 complexes. In contrast pathways classically implicated in apoptosis were modestly affected with minimal cleavage of caspase 9 and 3 and slightly increased caspase 3/7 activity. Pathologic findings in patients with presumed imatinib induced cardiac dysfunction and experimental mouse models were also consistent with autophagy and consisted of cytoplasmic vacuolization, abnormal accumulation of membrane whorls in vacuoles and enhanced propidium iodide uptake in the absence of the nuclear fragmentation of apoptosis. Taken in total these findings suggest induction of autophagy rather than necrosis or apoptosis as the primary cardiac response to glivec exposure. We hypothesize that autophagy in this setting may represent an adaptative response that contributes to the frequently self-limited and reversible nature of glivec-associated cardiac dysfunction.
CARDIOMYOCYTE-SECRETED ACETYLCHOLINE IS REQUIRED FOR MAINTENANCE OF HOMEOSTASIS IN THE HEART


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The parasympathetic nervous system plays an important role in regulating cardiac function. Genetically modified mice with globally reduced expression of the vesicular acetylcholine transporter (VAChT), the protein responsible for packaging acetylcholine (ACh), develop significant ventricular dysfunction despite the fact that parasympathetic innervation of ventricles is sparse. Recently, it has been proposed that rat cardiomyocytes are able to synthesize and release ACh. Ventricular cardiomyocytes express prototypical markers of the neuronal cholinergic system. Furthermore, cardiomyocyte-derived ACh is secreted in a VAChT-dependent manner and protects isolated cardiomyocytes from the hypertrophic response induced through hyperadrenergic stimulation. To test for the physiological role of cardiomyocyte-derived ACh we used the Cre/loxP system to genetically eliminate VAChT only in cardiomyocytes (cVAChT). Control experiments indicate that parasympathetic nerves are spared of Cre-mediated recombination, while cardiomyocytes in cVAChT mice show deletion of VAChT. Interestingly, 3 month-old cVAChT mice present cardiomyocyte and cardiac hypertrophy. Additionally, these mice display several signs of cellular stress as well as altered calcium handling. Furthermore, an increase in heart rate under restraint is observed. Importantly, heart rate recovery following acute exercise, a process dependent on cholinergic parasympathetic activity, is delayed in cVAChT mice. These data suggest a novel mechanism for regulation of heart rate wherein cardiomyocyte-derived ACh is involved in amplifying neuronal parasympathetic signalling with functional consequences for the control of heart rate and cardiac remodelling in vivo.

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UTILITY OF 2D-SPECKLE TRACKING ECHOCARDIOGRAPHY IN DIAGNOSIS OF LEFT VENTRICULAR DYSFUNCTION IN ANTI-ERBB2 THERAPY
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Background: ErbB2 is overexpressed in 25% of breast cancers; in the heart, it modulates myocardial development and function. Trastuzumab (T), an anti-ErbB2 inhibitor, has improved the prognosis of patients with breast cancer, but is related to an increased risk of left ventricular (LV) dysfunction. Fractional shortening (FS) and ejection fraction (FE) are insensitive in detecting early cardiomyopathy. Objectives: We aim at assessing whether myocardial strain by 2D-speckle tracking (ST) is able to identify early LV dysfunction in mice treated with doxorubicin (D), T and D+T and to relate data of cardiac function with tissue alterations.

Methods: Cardiac function was measured with FS, and with radial strain in sedated C57BL/6 mice at time 0, 2 and 6 days of daily administration of D, T, D+T and in sham. In excised hearts, we evaluated TNF alpha, CD68 and interstitial fibrosis.

Results: FS was reduced in group D and D+T at 2 days (52+0.2% and 49+2%), both p<0.001 vs 60+0.4% (sham), while in group T it decreased only at 6 days (49+1.5% vs 60+0.5%, p=.002). In contrast, after 2 days, myocardial strain was already reduced not only in D and D+T, but also in T: 43+3%, 49+1%, and 44+7%, all p<0.05 vs sham (66+0.6%). Cardiotoxicity was associated with alterations in extracellular matrix remodeling as confirmed by an increase of interstitial collagen and cardiac inflammation with D, T and D+T.

Conclusions: Myocardial strain identifies LV systolic dysfunction earlier than conventional echocardiography in group T and can be a useful tool to predict cardiotoxicity.
Objective: To evaluate the effect of hydrophilic and lipophilic HMG-CoA reductase inhibitors (statin) on bone marrow-derived mesenchymal stem cell (MSC) viability, NF-κB and mevalonate signaling.

Background: Circulating progenitor cells of bone marrow origin have been implicated in transplant cardiac allograft vasculopathy (CAV) and cardiac fibrosis. Statins have been shown to impair the progression of CAV and improve patient survival. We examined the in vitro effects of two lipophilic statins (atorvastatin and simvastatin) and one hydrophilic statin (pravastatin) on the viability of MSCs and expression of NF-κB.

Methods: MSCs were isolated from the sternum of patients undergoing open heart surgery and cultured in standard DMEM/F12 with 20% FBS. MSCs were treated with atorvastatin, simvastatin, and pravastatin at 0.1, 1.0 or 10 μM ± mevalonate. Cell viability was assessed using an MTT assay. NF-κB p65 expression was assessed by western blot. Activation of the NF-κB pathway was achieved through adenoviral overexpression of Ikk-β.

Results: MSC treatment with 1 and 10 μM simvastatin or atorvastatin resulted in progressively reduced cell viability to about 50%, corresponding with a NF-κB p65 decline to 70 and 50% respectively. Viability was rescued by co-incubation with mevalonate or by pretreatment with Ikk-β. Pravastatin did not affect MSC viability or NF-κB expression.

Conclusions: Mevalonate depletion through HMG-CoA reductase inhibition impairs the viability of primary human MSC through down-regulating NF-κB. This represents another pleiotropic effect of statins and may explain a lipid-independent beneficial effect of this therapy. The differential effect of lipophilic versus hydrophilic compounds requires further investigation.
TETRAHYDROBIOPTERIN DEFICIENCY INDUCED HEART FAILURE VIA DYSREGULATION OF MITOCHONDRIAL BIOGENESIS, OXIDATIVE PHOSPHORYLATION AND ANTIOXIDANT SYSTEM

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Objectives: The aim of this study was to investigate the role of tetrahydrobiopterin (BH₄) in the regulation of heart and cardiac mitochondrial function.

Background: The multifunctional cofactor tetrahydrobiopterin (BH₄) has antioxidant effects, and lower BH₄ concentration have been found in various cardiovascular diseases. However, the putative role of BH₄ in heart and mitochondria was unknown.

Methods and Results: We investigated the role of BH₄ in the regulation of heart and cardiac mitochondrial function using sepiapterin reductase knockout (Spr-) mice as a model of BH₄ deficiency. BH₄ deficiency induced cardiac damage and systolic dysfunction that resulted in shortened life span. BH₄ deficiency resulted in significant oxidative phosphorylation remodeling at the protein level. BH₄ deficiency reduced mitochondrial number, impaired mitochondrial inner membrane integrity and oxidative phosphorylation, and increased reactive oxygen species generation and oxidative stress on mitochondrial DNA. BH₄ deficiency also reduced mRNA and protein expression of major regulators of mitochondrial biogenesis and respiration, such as peroxisome proliferator-activated receptor γ coactivator-1 α and mitochondrial transcription factor A. Major mitochondrial antioxidant proteins, peroxiredoxin 3 and super oxide dismutase 2 were also decreased in Spr- heart. In vitro knock down spr gene in HL-1 cell by lentiviral transduction show similar mitochondrial dysfunction as mice model. Importantly, exogenous BH₄ supplementation rescued mitochondrial and cardiac dysfunction in Spr- mice and in vitro model.

Conclusion: Collectively, these results indicate that BH₄ is essential for mitochondria-mediated heart energy metabolism.
PL05  Plenary Session
INFLAMMATION / INNATE AND ADOPTIVE IMMUNITY AND CARDIOVASCULAR DISEASES

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INFLAMMATION - THE NEW TARGET FOR PREVENTION OF CORONARY ARTERY DISEASE
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New Technology that evolved in 2005 made it possible to genotype the whole human genome sequence utilizing a million DNA markers in the form of single nucleotide polymorphisms (SNPs). This led to the first genome-wide association study (GWAS) in pursuit of the genes for coronary artery disease (CAD). Since that time, the technology has evolved and with the information from the HapMap and 1000 Genomes Projects, it is possible now to genotype with over 12 million SNPs. Utilizing this technology, we first identified 9p21 risk allele for CAD, and in a collaboration with UK, USA and Germany, we have genotyped nearly 2,000 individuals. The total number of genes predisposing to CAD that have been confirmed in independent populations is 50. Analysis of the data utilizing computerized metabolic pathways indicate that a major number of these genes mediate their risk through inflammation. This analysis also shows that pathways related to inflammation and those related to cholesterol interact in the pathogenesis of atherosclerosis. Comprehensive prevention of CAD will have to incorporate therapy to inhibit those selected aspects of inflammation related to the pathogenesis of CAD. Interestingly, of the 50 genes associated with increased risk for CAD, 15 are acting through known conventional risk factors and only one is directly related to myocardial infarction, the ABO locus. It is crucially important to recognize that 35 of these genes act through unknown mechanism, indicating that cholesterol is only one of many factors involved in the pathogenesis of CAD.
SEPSIS AND THE CARDIOVASCULAR SYSTEM: GOING TO THE HEART OF THE MATTER

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Sepsis, a major cause of morbidity/mortality in ICU worldwide, is commonly associated with cardiac dysfunction, which worsens the prognosis dramatically for patients. Although in recent years the concept of septic cardiomyopathy has evolved, the importance of myocardial structural alterations in sepsis has been put aside. This study offers novel and mechanistic data to clarify events that occur in the pathogenesis of cardiac dysfunction in severe sepsis. Cultured neonatal mice cardiomyocytes subjected to serum obtained from mice with severe sepsis presented striking increment of [Ca2+]i and calpain-1 levels associated with decreased expression of dystrophin and disruption and derangement of F-actin filaments and cytoplasmic bleb formation. Severe sepsis induced in mice led to an increased expression of calpain-1 in cardiomyocytes. Moreover, decreased myocardial amounts of dystrophin, sarcomeric actin, and myosin heavy chain were observed in septic hearts associated with depressed cardiac contractile dysfunction and a very low survival rate. Actin and myosin from the sarcomere are first disassembled by calpain and then ubiquitinated and degraded by proteasome or sequestered inside specialized vacuoles called autophagosomes, delivered to the lysosome for degradation forming autophagolysosomes. Verapamil and dantrolene prevented the increase of calpain-1 levels and prevented dystrophin, actin, and myosin loss/reduction as well cardiac contractile dysfunction associated with strikingly improved survival rate. These abnormal parameters emerge as therapeutics targets, which modulation may provide beneficial effects on future vascular outcomes and mortality in sepsis. Further studies are needed to shed light on this mechanism, mainly regarding specific calpain inhibitors. Supported by grants from FAPESP and CNPq.
NEUTROPHILS IN ACUTE CORONARY ARTERY DISEASE
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Neutrophil granulocytes are present in atherosclerotic lesions and contribute to inflammatory tissue injury underlying all phases of atherosclerosis from nascent lesions to culmination in acute coronary artery disease (CAD). Acute CAD is characterized by widespread neutrophil accumulation, neutrophil infiltration of culprit lesions and prolonged neutrophil lifespan. Elevated plasma levels of the neutrophil granule component myeloperoxidase (MPO) predict adverse cardiac outcomes in patients with CAD. MPO-derived oxidants are important mediators of neutrophil-mediated tissue injury. MPO also binds to the beta-2 integrin Mac-1 and generates survival cues for neutrophils by preserving expression of the anti-apoptotic protein Mcl-1. Emigrated neutrophils die via apoptosis, which is critical for timely resolution of inflammation and minimizing tissue damage. Treatment of human neutrophils with the pro-resolving lipid mediators aspirin-triggered 15-epi-lipoxin A4 or the omega-3 fatty acid eicosapentaenoic acid-derived resolvin E1 acting through formyl-peptide receptor FPR2 or the leukotriene B4 receptor BLT1, respectively, effectively countered the powerful anti-apoptosis signal from MPO and redirect neutrophils to apoptosis. These lipid mediators also promoted resolution of MPO-dependent inflammation in mice parallel with enhancing neutrophil apoptosis. Pharmacological inhibition of caspase activation prevented neutrophil death and aggravated tissue injury. Our results provide a potential link between MPO, neutrophil survival and acute CAD. These data also suggest that therapeutic induction of neutrophil apoptosis by pro-resolving lipid mediators may represent a novel approach for reducing neutrophil-mediated tissue injury and/or promoting the resolution of inflammation underlying acute CAD. (Grant support: CIHR).
INTERACTION OF GENE AND SALT DIETS ON CARDIAC ANGIOTENSIN II, ALDOSTERONE, AND CYTOKINES IN HYPERTROPHIED HEART

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The objective of the present study was to elucidate the interactive roles of guanylyl cyclase/natriuretic peptide receptor-A (GC-A/NPRA) gene (Npr1) and salt diets on cardiac angiotensin II (ANG II), aldosterone (ALDO), and pro-inflammatory cytokines in hypertrophied hearts. Npr1 genotypes included gene-disrupted heterozygous (+/-; 1-copy), wild-type (+/+; 2-copy), gene-duplicated heterozygous (++/+; 3-copy), and gene-duplicated homozygous (++/++; 4-copy) mice. Animals were fed with low, normal, and high salt-diets. Cardiac and plasma ANG II, ALDO, and pro-inflammatory cytokines were determined. The results showed that cardiac ANG II and ALDO levels were greatly increased in Npr1 gene-disrupted 1-copy mice having hypertrophied hearts, however, greatly reduced in Npr1 gene-duplicated 3-copy and 4-copy mice. High salt-diet showed a significant baseline elevation of pro-inflammatory cytokines in 1-copy mice but the magnitude of elevation were only minimal in 3-copy and 4-copy mice compare with 2-copy wild-type control mice. The results showed that high salt-diet greatly elevated ANG II, ALDO, and pro-inflammatory cytokines in 1-copy mice, however, gene-duplicated mice did not render such elevated effect indicating the potential role of Npr1 gene against salt loading. The present results suggest that ANP/NPRA/cGMP signaling decreases cardiac ANG II, ALDO, and pro-inflammatory cytokines levels and protects heart from salt loading and cardiac remodeling process in the disease states.
MICROBIOTA, SYSTEMIC INFLAMMATION AND CARDIOVASCULAR FUNCTION


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Inflammation contributes to different degrees to most if not all pathological conditions. The GI system including small intestine plays a major role in systemic inflammation and thus cardiovascular well being. We have reported that anti inflammatory peptides that do not get absorb significantly and are not present in high concentrations in circulation reduce inflammation due to high fat-high cholesterol diet (Western Diet) in preclinical studies. This was paralleled by reduction in atherosclerotic lesion formation. Therefore the site of action of the peptides is likely the intestine. We have observed that small intestine appears to be a major site for this effect. One mechanism of action seems to be the action of the lysophosphatidic acid, a powerful growth promoter that has an extremely high affinity for toxic oxidized fatty acids and phospholipids. Reduction in these toxic oxidized lipids was shown to correlate with liver SAA and circulation SAA. The fascinating phenomenon for which a hypothesis is gaining strength is the effect on the intestinal microbiota. The high fat-high cholesterol diet (Western Diet) results in changes in the micro flora of the small intestine. It would be important to show the effect of the anti inflammatory peptides on reversal of eth Western diet, on systemic inflammation and on cardiovascular physiology and pathology.
ROLE OF COPPER TRANSPORTERS IN VASCULAR REMODELING AND INFLAMMATION

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Copper, essential micronutrient, has been implicated in vascular remodeling, atherosclerosis, and inflammation by unknown mechanisms. Because excess copper is toxic, bioavailability of copper is tightly controlled by the copper transporter ATP7A and the copper chaperone/transcription factor Antioxidant-1 (Atox1). Copper is required for the catalytic activity of copper enzymes such as lysyl oxidase (LOX). However, the role of ATP7A and Atox1 in vascular remodeling and inflammatory responses linked to atherosclerosis remain unknown. Our recent studies indicate that in atherosclerotic vessels, Atox1 is highly expressed at neointimal lesion, including at highly proliferating nucleus. At neointimal lesions in mouse wire injury model, ATP7A as well as Atox1 expression are markedly increased and copper accumulation is observed, while ATP7A mutant and Atox1-deficient mice show reduced neointimal formation. Mechanistically, Atox1 is involved in copper-dependent PDGF-stimulated VSMC migration via recruiting ATP7A and Rac1 to lipid rafts at the leading edge, as well as regulating LOX activity, which may contribute to neointimal formation after vascular injury. Moreover, we found that depletion of Atox1 in cultured endothelial cells (ECs) inhibits monocyte adhesion to ECs, which are associated with decreased inflammatory cell recruitment as measured by intravital microscopy ex vivo. These findings provide novel insights into copper chaperone and transporters as novel therapeutic targets for inflammation-dependent various vascular diseases, and implicate the importance of copper homeostasis in vascular biology and pathophysiology.
The Complex Cardiovascular Effects of Leptin

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Leptin is a cytokine released primarily from adipose tissue and that has central nervous system, as well as peripheral tissue, effects. This presentation will summarize findings from three studies embedded in the Multi-Ethnic Study of Atherosclerosis that have examined the associations of leptin with blood pressure, the renin-angiotensin-aldosterone system (RAAS) and left ventricular structure and function. The concept of selective leptin resistance will be discussed.
HUMAN ENTEROVIRUS PERSISTENCE: POTENTIAL FOR EXACERBATION OF MYOCARDITIS

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Human enteroviruses like the group B coxsackieviruses (CVB) are known to cause human inflammatory cardiomyopathies but until recently, the CVB were thought to be acute infections, rapidly cleared by the host’s immune system. We discovered that CVB can persist for weeks to months following either experimental inoculation (in cell cultures or mice) or natural infection (humans) through a mechanism that involves the loss of the 5' terminal genomic sequence. These 5' terminally deleted (TD) viruses replicate very slowly because the deleted region is key to efficient viral genome replication. Although isolation of CVB-TD from experimentally inoculated mouse hearts revealed a strain with a 49 nucleotide deletion, containing nearly all the domain I structure at the 5' end, we have now deleted the remainder of domain I with a 77 nucleotide deletion. This viable CVB3 strain shows that domain I, previously thought required for virus replication, can be entirely deleted. Slow persistent replication of an enterovirus in heart muscle has been proposed as one mechanism by which heart function can be progressively and deleteriously impacted following an enterovirus infection. The discovery of naturally occurring enteroviral terminal deletions provides a mechanism by which the virus can persist in the host cardiomyocyte, producing viral proteases which can cleave host proteins.
VIRAL ANTI-ATHEROGENIC PROTEINS ALTER MONOCYTE AND NEUTROPHIL INVASION IN MICE WITH ALTERED BAG3 GENE EXPRESSION

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Objectives and Background: Atherosclerosis is characterized by chronic inflammation and apoptosis. Serine protease inhibitors, serpins, regulate inflammation, thrombosis and apoptosis. Myxomavirus-derived Serp-2 reduces plaque, inflammation and apoptosis in animal models, but CrmA does not. Both serpins target Caspase 1 and Granzyme B, indicating differing target pathways in vivo. Serp-2 alters expression of 48 apoptosis-related genes in human monocytes. We assessed specific apoptotic gene expression changes with Serp-2 and CrmA in a mouse inflammation model.

Methods: Granzyme B (GzmB, N=13) and Caspase 1 (Casp1, N=15) deficient mouse mononuclear cells were compared to background mice (C57Bl/6 and Nod, N=15 each) 18 hours after treatment with PMA and either Serp-2 or CrmA. RNA was analyzed by RT-PCR.

Results: Compared to human monocytes, mouse peritoneal exudates from knockout mice displayed differential expression of BCL2-associated athanogene 3 (BAG3) after treatment with Serp-2 or CrmA. Serp-2 reduced expression compared to CrmA treatment in GzmB (p=0.0267) and C57Bl/6 mice (p=0.0280). Casp1-/+ mice treated with Serp-2 downregulate BAG3, expressing 9.7-fold less than Nod mice (p=0.0006), but CrmA had no significant effect in either strain. An associated differential migration of Ly6Chi and Ly6Ghi cells was also discovered.

Conclusions: Anti-inflammatory myxomaviral protein, Serp-2 reduces vascular inflammation and plaque growth, whereas CrmA does not. Both proteins block apoptotic and inflammasome pathways, but Serp-2 alone reduces BAG3 in human monocytes and mouse peritoneal exudates. BAG3 alters cell migration and apoptosis, important to atherogenesis, underscoring a potential role as a central mediator and therapeutic target in inflammatory and apoptotic pathways.
Stroke is the third leading cause of death and leading cause of disability in western countries. Though progress has been made in acute stroke intervention with the use of intravenous thrombolytic therapy, a large number of patients remain significantly disabled despite thrombolysis. Importantly, the most disabling strokes, those related to the M1 segment occlusion of the middle cerebral artery, to thrombus or embolus lodged at the internal carotid bifurcation and basilar artery occlusions do not respond well to intravenous thrombolytic therapy. Moreover, intravenous thrombolysis can only be used in a short time interval and provided there are no contraindications. Hence, only a small number of patients are eligible for intravenous thrombolytic therapy. Therefore, alternative treatment strategies are needed. Attention has been directed in the last two decades to intra-arterial thrombolysis and percutaneous removal of thromboembolic material. In this context, several concepts have been studied including intracranial balloon angioplasty and stenting with variable results. Most recently, a concept has been explored with promising results, removal of thromboembolic material with stentriever, self-expanding stents that are deployed at the site of thromboembolic material. The thrombus/embolus is captured within the stent and the stent removed together with the captured material into a balloon-tipped guide catheter while the balloon remains inflated minimizing the risk of embolization during stent removal. The presentation is an overview of interventional concepts of acute stroke therapy including a review of recent data using the concept of stentriever.
Objectives: To inform the transplant community of potential modifications in the heart allocation system.

Background: Efforts to increase transplantation rates for candidates with highest waiting mortality and offer the greatest survival benefit due to transplantation remains the goal of our current systems. Modifications occurred in both the Eurotransplant system and the Organ Procurement and Transplant Network (OPTN) in 2005-6. Increases in recipients but not in available donors, continued elevated waiting list (WL) mortality in high acuity patients, and changing landscape of the WL with increased utilization of VADs, a call for a reassessment of the current allocation scheme was made. The OPTN Thoracic Committee was charged with the development a new allocation system and is considering an expanded multi-tiered scheme could potentially provide more definition of risk and disease severity.

Methods: Status IA patients over a recent 2-year period with the different criteria were analyzed, assessing WL mortality and post-transplant (PT) survival.

Results: Highest WL mortality included patients with IABP, ECMO, retransplantation, and those on mechanical ventilation. PT mortality was highest in the ECMO, TAH, retransplantation, and congenital heart disease patients, and those with ventricular arrhythmias. Many groups were small, making statistical comparison challenging. WL and PT mortality was lowest in patients on IV inotropes and invasive monitoring, and LVADs without complications.

Conclusions: Modification of the current system must encompass considerations in addition to the WL and PT mortality. LVAD utilization, presence of sensitization, and geographic variations in organ allocation will all interact to develop an effective and equitable system.
ASSIST DEVICES IN THE ELDERLY

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Aims: During recent years non-pulsatile assist devices have been increasingly used for long-term support. Now, the question arises whether pulsatile or non-pulsatile systems can ensure a comparable low rate of complications for extended time periods in elderly patients.

Methods: Of 420 patients older than 60 years, 135 had pulsatile (91 Berlin-Heart Excor, 18 Novacor, 4 LionHeart, 3 HeartMate I, 19 CardioWest TAH) and 285 non-pulsatile assist devices (79 Berlin-Heart Incor, 19 DeBakey, 58 HeartMate II, 7 DuraHeart, 6 Jarvik 2000, 116 HVAD HeartWare) implanted between 06/1991 and 03/2013 (age: 60-82 years). The last pulsatile device was implanted 6/2011.

Results: In the pulsatile group mean support time was 158±318 (1-1836) days, in the non-pulsatile group 386±459 (1-2510) days. In the first group 8 patients (6%) were supported for >6 months, 8 (6%) for >1 year, 6 (4%) for >2 years and 4(3%) for > 3 years; 12 patients received heart transplantation, 4 were weaned and 1 still has the device. In the second group 40 patients (14%) were supported for >6 months, 50 (18%) for >1 year, 29 (10%) for >2 years, 18 (6%) for >3 years, 5 (2%) for >4 years: 17 are still on support, 9 received transplantation and 3 were weaned.

Conclusion: Although both types of devices have proven to be suitable for extended periods of time, today’s non-pulsatile systems with significantly higher survival rate and time have largely replaced the pulsatile devices. They allow elderly patients additional years of life at home with an improved quality of life.
Only around 70 heart-kidney transplants are performed worldwide annually, representing 2-3% of heart transplants and 0.5% of kidney transplants. However, due to the shortage of donor kidneys (in the United States over 95,000 people are waiting for a donor kidney and only 11,000 deceased donor kidney transplants are performed annually) it is important that all candidates receiving a heart-kidney transplant truly need the kidney. A creatinine > 1.5 increases the risk of 1-year mortality following heart transplantation and heart transplant recipients who require dialysis during the transplant hospitalization have a hospital mortality as high as 40% and a 1-year survival of <75%. Heart-kidney transplant recipients have similar survival, less rejection and less cardiac allograft vasculopathy compared to heart only transplant recipients. Of note, heart transplant recipients requiring dialysis pre-transplant have a 1-year survival following heart transplant alone of only 50%, so heart transplant alone should generally not be performed in this patient group. Available data suggest that combined heart-kidney transplantation should be considered for heart transplant candidates: 1) on pre-transplant dialysis or with a creatinine clearance < 30 or creatinine > 2.5; 2) with a longer duration of renal insufficiency; or, 3) with comorbid diseases known to cause renal disease such as hypertension and diabetes mellitus. However, due to poor outcomes, heart-kidney transplant should not be performed in recipients >60 years or with peripheral vascular disease or a peak reactive antibody level > 30%.
UPDATE IN THE TREATMENT OF LEFT MAIN DISEASE
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Percutaneous coronary intervention (PCI) with drug eluting stents (DES) has emerged as a treatment alternative with left main (LM) disease. Three randomized clinical trials (RCT) compared DES to coronary artery bypass surgery (CABG). Certain conclusions are forthcoming: at 4 year follow-up, PCI and CABG are comparable for the combined outcome of death, MI, and stroke. Target vessel revascularization is required more frequently with PCI. There are several areas of uncertainty. With 4-year follow-up, the low/intermediate Syntax terciles showed similar outcomes. In the highest tercile, however, PCI showed a trend to worsened survival. Whether this trend relates to PCI itself or less complete revascularization with PCI is uncertain. There is agreement—though no RCT—that IVUS should be used for stent optimization. Fractional flow reserve, particularly in isolated LM disease, and probably IVUS may be helpful to differentiate patients who can be safely deferred from revascularization. LM bifurcation stenting has a higher restenosis risk (vs ostial/shaft lesions) without increased risk of death/MI. The preferred treatment method is one stent when possible. Whether it is safe to observe or proactively perform angiography for LM restenosis is unsettled but current data suggest that surveillance angiography may be unnecessary. Finally, current RCT are confined to stable CAD patients with relatively preserved ventricular function. LM ACS patients with cardiogenic shock have a high mortality whether treated with PCI or CABG. If the PCI pt survives the in-hospital period, long-term outcome is relatively good, with 50-70% alive at one year.
Introduction: In California (CA), 141 hospitals perform percutaneous coronary intervention (PCI) with 122 hospitals reporting to the NCDR® CathPCI registry.

Objective: To evaluate the PCI volume and composite event outcomes in hospitals with surgery On-site versus hospitals with surgery Off-site in CA.

Methods: We examined consecutive NCDR® records for PCI in CA from July 2010 to July 2012. Clinical data from 200 fields obtained from 6 pilot hospitals participating in the PCI-CA Audit-Monitored-Pilot-Off-site-Surgery (PCI-CAMPOS) program were compared with NCDR® de-identified clinical data from 116 CA hospitals with surgery On-site. Observed composite events (in-hospital death and emergent CABG), mortality, MI biomarkers, cardiogenic shock, heart failure, stroke, tamponade, dialysis, other vascular complications, transfusion and bleeding were obtained from both groups. Risk models were developed using bivariate and multivariate logistic regression.

Results: A total of 101,933 PCIs were performed (99,332 On-site including 17,577 STEMI cases and 2,601 Off-site including 837 STEMI cases). Bivariate analysis identified 22 significant variables. The Multivariate Logistic Regression Model demonstrated excellent prediction with a C-statistic of 0.902-0.903. The risk-adjusted composite event rate was 2.11% (On-site) and 1.58% (Off-site) for all cases and 1.16% (On-site) and 1.15% (Off-site) for STEMI excluded cases. On-site hospitals risk-adjusted composite events were as expected (105) with 4 better and 7 worse outliers. Off-site hospitals risk-adjusted composite events were as expected (5) with 1 better outlier.

Conclusion: PCI risk-adjusted composite event rates for 6 hospitals in the PCI-CAMPOS pilot program were similar to the composite event rates of 116 CA hospitals with On-site surgery.
UPDATE ON THE USE OF IMPELLA ASSIST DEVICE FOR HIGH RISK PATIENTS

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The use of impella has gained increasing popularity. In patients presenting with severe cardiogenic shock, impella can be lifesaving. In many cases of severe cardiogenic shock in the setting of myocardial infarction, the use of intraaortic balloon pump may not be sufficient enough to maintain adequate blood pressure. In these patients, the use of impella will stabilize hemodynamic condition in order to perform percutaneous coronary intervention. Furthermore, high risk patients undergoing percutaneous coronary intervention, the use of impella before the procedure can prevent the occurrence of cardiogenic shock during the procedure. Finally, immediate insertion of an impella device during percutaneous intervention that has led to cardiogenic shock can normalize hemodynamic and be lifesaving. In a small study of 26 patients, the use of impella in comparison to intraaortic balloon pump has been found to give superior hemodynamic support. Largest trial comparing impella to intraaortic pump in patients undergoing high risk percutaneous intervention in PROTECT II, impella improved outcome in patients who followed the specified study protocol. Based on our experience and small available trials, the use of impella is in selected high risk patients undergoing percutaneous coronary intervention should be encouraged.
Device closure of ASD is now standard of treatment for suitable defects. There are however concerns over long-term outcome of device closure with special reference to complications mainly erosions and aortic regurgitation. The long term data is now available. Kutty et al reported the results of a retrospective observational outcomes study (AJC 2012), comparing long-term results of transcatheter and surgical ASD closure. This study represents the longest reported duration of follow-up after transcatheter closure with a mean follow up of 10 years. All cause mortality rates following transcatheter ASD closure compare favorably to surgical closure. We have reported on 205 patients with secundum ASD (CTY 2012). Device closure was successful in 200/205 (98%) patients. Early complications included embolization (4 pts), pericardial effusion, 2:1 heart block and infective endocarditis (1 patient each). Eight patients reported migraine (3.9%). At median follow up of 5.8 (0.6-10.3) years, complete closure occurred in 197/200 patients. Two patients developed mild AR (1%). There were no erosions, late embolisation or thrombo-embolism. Atrial fibrillation occurred in 3 adults (1.5%). Between December 2001 and March 15, 2012, 97 worldwide cases of erosion have been identified in association with the on label use of the ASO device, representing an overall risk of erosion of 0.043%. Device closure of secundum atrial septal defects using Amplatzer septal occluder is safe and effective in long-term. The risk of developing aortic regurgitation is low. Erosions do occur but risk is extremely low and can be minimized further by taking precautions in case and device selection.
WHERE IS THE FINE BALANCE BETWEEN IMMUNOSUPPRESSION AND MALIGNANCY IN CARDIAC TRANSPLANTATION?

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Cardiac transplantation continues to remain the gold standard in the treatment of end stage heart failure. Advances in transplantation research such as immunosuppression and effective prophylaxis for infection control have improved the survival in the post heart transplantation population. However the long-term survival of patients is still limited by cardiac allograft vasculopathy and malignancy. This review addresses briefly the types of common malignancies in the immunosuppressed population, their etiologies and the role of immunomodulation in management. The fine balance between adequate immune suppression and the prevention of cancer would rest in the delicate art of immunomodulation.
MANAGEMENT STRATEGIES OF COMBINED SEVERE SYMPTOMATIC CAROTID AND CORONARY ARTERY DISEASE
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In patients who require coronary artery bypass grafting (CABG), the risk of perioperative stroke is close to 2%. Several studies reported that the risk of stroke associated with CABG is < 2% in patients with no significant carotid disease and 3% in patients with asymptomatic severe carotid stenosis. The risk increases to 5% in patients with bilateral carotid stenosis or a history of stroke or transient ischemic attack (TIA) and to 7% to 11% in patients with carotid occlusion. Combined carotid and cardiac surgical procedures are performed frequently in an effort to reduce the incidence of postoperative stroke. The timing and sequence of revascularization are controversial and influenced by the respective symptom severity of the coronary and carotid disease. Treatment options include combined CABG and carotid endarterectomy (CEA), staged CEA followed by CABG or CABG followed by CEA. Another emerging treatment plan include carotid angioplasty and stenting (CAS) with cerebral protection followed by CABG. In the absence of randomized trials comparing these treatment options or no revascularization before CABG, management needs to be individualized using the generally agreed upon concepts.
THE NO-TOUCH SAPHENOUS VEIN AS THE PREFERRED SECOND CONDUIT FOR CORONARY ARTERY BYPASS SURGERY

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Background: Injury incurred during saphenous vein harvesting results in poor graft patency and impairs the results of coronary artery bypass grafting surgery. A novel harvest method, the No-touch technique, has shown improved long-term saphenous vein graft patency.

Methods: This randomized trial included 108 patients undergoing coronary artery bypass grafting and compared the patency for No-touch saphenous vein with radial artery grafts. Each patient was assigned to receive one No-touch saphenous vein and one radial artery graft either to the left or right coronary territory to complement the left internal thoracic artery.

Results: Angiography was performed in 99 patients (92%) at mean 36 months postoperatively. Graft and grafted coronary artery patency was evaluated. Patent grafts for No-touch saphenous vein and radial artery was 94 % versus 82 % (p=0.01) respectively. Patent coronary arteries grafted with No-touch saphenous vein and radial artery grafts was 95 % versus 84 % (p=0.005) respectively. Eighty nine of 96 (93%) left internal thoracic artery grafts were patent.

Conclusions: No-touch saphenous vein grafts showed a significantly higher patency rate than the radial artery grafts and was comparable to the patency for left internal thoracic artery grafts. This highlights the improvement in saphenous vein graft quality with No-touch technique and increases the number of situations where saphenous veins may be preferable to radial artery grafts as conduits in coronary artery bypass grafting.
INGESTION-TIME-DEPENDENT EFFECTS OF HYPERTENSION TREATMENT ON AMBULATORY BLOOD PRESSURE IN PATIENTS WITH CHRONIC KIDNEY DISEASE: THE HYGIA PROJECT

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Objectives: Many published trials have reported clinically meaningful morning-evening, treatment-time differences in the blood pressure (BP)-lowering efficacy, duration of action, and safety of most classes of hypertension medications. Here, we investigated the effects of hypertension treatment-time on the 24h BP pattern of patients at different stages of chronic kidney disease (CKD) enrolled in the Hygia Project, designed to evaluate prospectively cardiovascular risk by 48h ambulatory BP monitoring (ABPM) in primary care centers of Northwest Spain.

Methods: We evaluated 4523 treated hypertensive patients with CKD, 2635 men/1888 women, 66.3±12.9 years of age. Among the participants, 2275 were ingesting all BP-lowering medications upon awakening, while 2248 patients were ingesting at least one medication at bedtime. BP was measured every 20-min from 07:00 to 23:00h and every 30-min at night for 48h.

Results: The sleep-time relative BP decline was attenuated (P<0.001) and the prevalence of non-dipping was significantly higher when all medications were ingested upon awakening (66.1%) than when some of them were ingested at bedtime (55.3%; P<0.001), and even further attenuated (46.5%; P<0.001) when all medications were ingested at bedtime. The prevalence of a riser BP pattern was much greater (20.1%) among patients ingesting all medications upon awakening, compared to those ingesting some (16.1%) or all medications at bedtime (11.0%; P<0.001), independent of CKD severity.

Conclusions: Our findings demonstrate significantly attenuated prevalence of non-dipping/rising in patients with CKD, at all stages of disease severity, ingesting hypertension medications at bedtime. These findings indicate bedtime treatment should be the preferred therapeutic scheme for CKD.
RENAL SYMPATHETIC DENERVATION FOR RESISTANT HYPERTENSION IN THE REAL WORLD CLINICAL PRACTICE: PRELIMINARY RESULTS OF THE SYMPLICITY VENEZUELA REGISTRY

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Background: Catheter-based renal denervation (RDN) had shown to be an effective treatment to control blood pressure (BP) in patients with resistant hypertension. In the Symplicity HTA-2 trial, RDN lowered systolic blood pressure by 32 ± 23 mmHg. In addition, radiofrequency (RF) ablation of renal arteries reduces sympathetic activity reducing left ventricular mass. However, the efficacy of this novel procedure in the real world clinical practice is still unknown.

Methods: Prospective, multicenter, observational registry of all consecutive patients submitted to RDN at 14 centers in Venezuela between February and September 2012. We included patients with resistant hypertension: systolic BP > 160 mmHg despite taking three or more antihypertensive drugs (including a diuretic) with normal renal function (eGFR > 45 ml/min/1.73 mts²). The primary end-point was reduction in systolic BP at 1 and 6 months follow-up, the secondary end-point was any adverse event after the procedure.

Results: Sixty patients were included for this analysis; mean age 56.1 ± 10, 42% were females, 38% caucasians and 32% diabetics. Pre-procedural office BP was 178/101 mmHg (SD 20/15), the mean number of anti-hypertensive medications was 4.4. Regarding procedural characteristics 9.9 ± 1.6 RF ablations were done per patient, with a mean impedance reduction of -14%. At 30 days office BP reduction was −39/18 mmHg (SD 18/14, p=0.002) and at 6 months (n=15) −34/19 mmHg (SD 11/6, p=0.004). One intraprocedural renal artery dissection occurred before RF delivery that required no additional treatment.

Conclusions: Catheter-based RDN effectively reduces BP in the real world scenario; in this preliminary experience, no major complications were observed.
PREVALENCE OF HYPERTENSION IS HIGHER IN WOMEN WITH AN EXPERIENCE OF PRE-ECLAMPSIA

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Background: Patients with pre-eclampsia have shown increased frequency of endothelial dysfunction, insulin resistance and thrombophilia. The aim of this study was to investigate the relationship between pre-eclampsia and risk factors of cardiovascular disease.

Methods: Current cardiovascular health status including body mass index, hypertension, diabetes mellitus, ischemic heart disease and stroke, and history of pregnancy and pregnancy-related complications were ascertained through internet questionnaire survey to 3895 women nurses who have an experience of pregnancy. Among 3895 subjects, 160 (4.1%) women had experienced pre-eclampsia and 3735 (95.9%) women had not experienced pre-eclampsia.

Results: The rate of hypertension in women nurses who had experienced pre-eclampsia was higher than in those without pre-eclampsia (8.1% vs. 4.4%, P=0.029). After adjustment for known risk factors for hypertension, the adjusted odds ratio of a later onset hypertension in women after preeclampsia was 1.834 (95% confidence interval 1.006 to 3.344, P=0.048) compared with women who did not experience pre-eclampsia. In addition, the body mass index of women with pre-eclampsia was higher than those of women without pre-eclampsia (22.4 kg/cm² vs. 21.9 kg/cm², P=0.005). However there were no significant differences in the prevalence of diabetes mellitus, ischemic heart disease and stroke between women with preeclampsia and women without pre-eclampsia.

Conclusions: Pre-eclampsia seems to be associated with later onset of hypertension. Greater awareness of this association can lead the way to earlier diagnosis and improved management of hypertension and it may be helpful to reduce a proportion of the morbidity and mortality from hypertension.
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PROGNOSTIC VALUE FOR CARDIOVASCULAR RISK OF CLINIC AND AMBULATORY BLOOD PRESSURE IN CHRONIC KIDNEY DISEASE

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Objectives: We evaluated in patients with chronic kidney disease (CKD) the comparative prognostic value of clinic systolic (SBP) and diastolic (DBP) blood pressure (BP) and multiple ambulatory BP (ABPM)-derived characteristics, including asleep/awake BP means, morning surge, ambulatory arterial stiffness index (AASI), and indices of BP variability.

Methods: A total of 793 patients with CKD, 469 men/324 women, 57.9 +/- 13.9 years of age, were prospectively studied throughout a 5.4-year median follow-up. At baseline and annually thereafter, ambulatory BP was monitored for 48h.

Results: The asleep SBP mean was the most significant predictor of cardiovascular (CVD) events in a Cox proportional-hazard model adjusted for the significant confounding variables of patient’s sex and age, diabetes, and albuminuria (hazard ratio 1.23, 95%CI [1.15-1.32] for each 10 mmHg elevation in asleep SBP mean, P<0.001). A greater morning BP surge was significantly associated with lower, not higher, CVD risk, in agreement with the significant association between increased dipping and reduced CVD risk. Moreover, when the asleep BP mean was adjusted by the awake mean, only the former was a significant independent predictor of outcome. Clinic SBP/DBP and other ABPM variables, including 24h BP mean, AASI, and standard deviation, were not statistically significant when the asleep SBP mean was simultaneously used as a predicting variable.

Conclusions: Sleep-time SBP mean is the most significant independent prognostic marker of CVD events in CKD. These findings indicate CKD must be included among the clinical conditions for which ABPM is recommended for the accurate diagnosis of hypertension and assessment of CVD risk.
PREVALENCE OF HYPERTENSION AND ITS ASSOCIATION WITH METABOLIC RISK FACTORS IN TYPE 2 DIABETIC PUNJABI POPULATION

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Aim: To study the Prevalence of hypertension and its association with metabolic risk factors in Type 2 Diabetic (T2D) Punjabi population.

Method: 8000 (5041 M, 2959 F) T2D subjects, aged between 31-79 yrs were screened for the presence of hypertension according to JNC VII criteria. Waist Hip Ratio (WHR), Body Mass Index (BMI), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Fasting blood sugar (FBS), Lipid Profile (Total Cholesterol, Triglycerides, HDL, LDL) and HbA1c of the subjects were analyzed.

Results: SBP was found to be elevated in 68.29% subjects whereas DBP was elevated among 23.34% subjects. Out of all the subjects, 52.83% were overweight and 35.39% obese. Obese subjects were found to be more hypertensive than non-obese subjects (r=0.38). SBP had strong correlation with age (r=0.126), BMI(r=0.15), WHR(r=0.09), FBS(r=0.10), Cholesterol(r=0.11) and LDL(r=0.13) whereas DBP was found to be strongly correlated with same parameters and Triglycerides (r=0.08) also. No significant correlation was found with HbA1c levels and HDL-cholesterol.

Conclusion: Hypertension was found to be more prevalent in males as compared to females in the diabetic population. There was an increased prevalence of overweight in male patients, whereas women had increased prevalence of obesity (Grade II and III). Hypertensive diabetic subjects with other metabolic risk factors are more prone to microvascular and macrovascular complications.
CARDIORESPIRATORY RESPONSE TO EXERCISE AFTER RENAL SYMPATHETIC DENERVATION IN RESISTANT HYPERTENSION

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Background: Renal sympathetic denervation (RD) reduces blood pressure at rest in patients with resistant hypertension. The effects on cardiorespiratory response to exercise are unknown.

Methods: We enrolled 46 patients with therapy resistant hypertension as extended investigation of the Symplicity HTN-2 Trial (ClinicalTrials.gov NCT00888433). Thirty-seven patients underwent bilateral RD and 9 patients were assigned to the control group. Cardiopulmonary exercise test were performed at baseline and 3 months follow-up. Results: In the RD group compared to baseline examination, blood pressure at rest and at maximum exercise after 3 months was significantly reduced by 31 ± 13/9 ± 13 mmHg (p<0.0001) and by 21 ± 20/5 ± 14 mmHg (p<0.0001), respectively. Achieved work rate increased by 5 ± 13 Watt (p=0.029) while peak oxygen uptake remained unchanged. Blood pressure 2 minutes after exercise was significantly reduced by 29 ± 17/8 ± 15 mm Hg (p<0.001 for SBP; p=0.002 for DBP). Heart rate at rest decreased after RD (4 ± 11 beats per minute (bpm); p=0.028), whereas maximum heart rate and heart rate increase during exercise were not different. Heart rate recovery improved significantly by 4 ± 7 bpm after renal denervation (p=0.009). In the control group, there were no significant changes in blood pressure, heart rate, maximum work rate or ventilatory parameters after 3 months.

Conclusions: RD reduces blood pressure during exercise without compromising chronotropic competence in patients with resistant hypertension. Heart rate at rest decreased and heart rate recovery improved after the procedure.
CORRELATION BETWEEN LVEDP AND PCWP IN PATIENTS WITH PULMONARY HYPERTENSION

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Background: Right heart catheterization (RHC) is frequently performed to confirm and differentiate pulmonary hypertension (PHT). The pulmonary capillary wedge pressure (PCWP) is used as a surrogate for left atrial pressure and is usually used to differentiate between PHT entities. Sometimes a damped pulmonary arterial pressure could be mistaken for PCWP. Obtaining O2 saturation on assumed wedged pulmonary artery sample is one way of differentiating a true PCWP form a damped PA pressure. Elevated PCWP should be associated with elevated left ventricular end diastolic pressure (LVEDP), unless in a setting of mitral stenosis. We aimed to study the correlation between LVEDP and PCWP in patients with PHT.

Methods: Retrospective analysis of invasive hemodynamic data from patients referred to our catheterization lab in the last year for concomitant left and RHC.

Results: A total of 58 patients did meet the inclusion criteria. The average mean PAP was 31.3 mmHg. Overall, the mean LVEDP correlated well with the mean PCWP (20.9 vs 20.8 mmHg, R=0.7). In patients with PHT (n=35) the correlation between the LVEDP and PCWP was good (R=0.6). The Correlation coefficient (R) was highest with mild–moderate hypertension (n=26, R=0.55), and lowest with severe pulmonary hypertension (n=9, LVEDP 31 vs PCWP 36 mmHg, R=0.2).

Conclusion: PCWP correlated poorly with LVEDP in patients with severe PHT, and modestly in patients with mild to moderate PHT. When PWCP is discordant with LVEDP, PCWP O2 saturation should be performed to prevent a damped PA pressure mistaken for a true PCWP.
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PREDICTORS OF PULMONARY HYPERTENSION IN PATIENTS WITH DIASTOLIC DYSFUNCTION
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Background: Pulmonary Hypertension (PH) is a frequent complication of left heart disease. The development of PH in patients with left heart disease is associated with poor prognosis.

Objective: To investigate predictive factors for PH in patients with diastolic dysfunction (DD).

Methods: We retrospectively analyzed echocardiograms of 2,681 patients performed at a University hospital. Due to missing data, 842 patients were excluded from analysis. Patients were classified into normal (n=842, 31.4%) & those with DD (n=1,839, 68.6%), including Impaired Relaxation (IR, n=1,530, 57.1%), Pseudonormal (PN, n=234, 8.7%), & Restrictive pattern (Res, n=75, 2.8%).

Results: In patients with DD, we found 28.1% with PH vs 71.9% with no PH p<0.0001. The presence of PH is more frequent in IR (55.8%) vs control (24.9%), but not for the two higher levels of DD (15.4% & 4.0%, respectively). GFR<60 were more frequent in patients with different stages of DD (30.4% vs 31.5% vs 79.1%) compared with controls(17.3%), p<0.0001. Gender wasn’t predictor of PH (p=0.2127). Data for pro BNP in 722 individuals with values >100, >100-400, >400-900, & >900 in stages of DD (37.5% IR, 32.9% PN, 50.0% RR vs 32.5% in controls. It was statistically significant difference in this comparison (p=0.0291).

Conclusions: There is increased prevalence of PH in patients with DD. GFR <60 and higher levels of pro-BNP are strong predictors of PH in patients with DD.
P201 PROGRESS IN ECHOCARDIOGRAPHY

147 ASSESSMENT OF MYOCARDIAL SCAR BY OPTISON ENHANCED ECHOCARDIOGRAPHY
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Objectives: Investigate the potential for visualization of myocardial scar by contrast echocardiography.
Background: Late gadolinium enhancement (LGE) cardiac magnetic resonance imaging (CMR) is a gold-standard technique for assessment of myocardial scar in patients with coronary artery disease (CAD). The purpose of this study was to compare LGE-CMR with Optison enhanced (OE) transthoracic echocardiogram (TTE) for assessment of myocardial scar in patients with CAD.

Methods: 14 patients presenting with either acute coronary syndrome or symptomatic coronary artery disease (CAD) underwent a LGE-CMR and OE-TTE. LGE-CMR was acquired and evaluated using standard protocols. 2D-echo images were acquired with and without Optison contrast in all standard views using bolus injections and left ventricle enhancement mode. Myocardial enhancement was visually assessed as a percentile (0%, <50%, ≥50%) of myocardial thickness for each segment of the standard 17 segment model. Clinically significant scar was considered to be myocardial enhancement ≥50%. Scar presence and location in a coronary territory was defined as presence in two or more contiguous segments within a single coronary anatomic distribution in short or long axis views with at least one segment demonstrating ≥50% enhancement.

Results: Mean age was 56 ± 6.5 yrs. There were 11 males, 14 Hispanics, 79% had diabetes mellitus, and 86% had hyperlipidemia and hypertension. The concordance between both techniques for the assessment of scar by regional coronary distribution was 79%. Single segment concordance as shown in Table 1 was 60% (p<0.05 using chi square analysis for both).

Conclusions: OE-TTE may be a promising new technique for the detection of myocardial scar in patients with CAD.

Table 1. Presence of Scar by 17 Segment Model Using LGE-CMR and OE-TTE

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<th>LGE-CMR</th>
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<td>0</td>
<td>0-50%</td>
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<tr>
<td>0</td>
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<td>&gt;50%</td>
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<td>11</td>
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<td>Total</td>
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Background: A correlation between the clinical outcome and the dose of dobutamine and additional atropine used to achieve target heart rate (THR) in patients undergoing DSE is not well established.

Methods: We analyzed the records of patients from our institution from September 2007 to January 2008 who underwent DSE. Baseline clinical and DSE variables were obtained through chart review. Logistic regression analysis was used to identify factors significantly associated with the composite endpoint of death, stroke or acute coronary syndrome (ACS) at the end of the follow-up period.

Results: In the specified time period, 219 consecutive patients were identified. During a mean follow-up of 3.1±1.0 years, 31 (14%) patients had an event. The dose of dobutamine required to achieve THR was inversely associated with the composite outcome by univariate analysis (odds ratio [OR] 0.59, 95% confidence interval [CI] 0.37-0.94; p=0.025). However, the significance was lost in multivariate analysis. Multivariate analysis revealed independent predictors for the composite outcome to be, an indication for DSE (acute coronary syndrome versus routine screening for CAD [OR 11.28; 95% CI 3.52 – 36.13; p<0.0001]), male gender (OR 4.21; 95% CI 1.17 – 15.13; p = 0.028) and use of clopidogrel (OR 4.69; 95% CI 1.50-14.68; p = 0.008).

Conclusion: In patients undergoing DSE, a lower dose of dobutamine required to achieve THR was associated with worse cardiovascular outcome; but this relationship was not apparent in multivariate analysis which showed that age, male gender and indication of DSE were determinants of adverse outcome.
Background: It is well established that diabetes adversely affects on myocardial function. This impairment is mainly responsible for 50% to 80% of death in diabetic patients. The aim of this study was comparison of TDI parameters on LV basal segments between diabetic and nondiabetic patients to evaluate the cardiovascular change in these patients sooner.

Methods: Using tissue Doppler imaging (TDI), systolic (S’), early diastolic (E’) and atrial (A’) tissue velocities of thirty diabetic patients (with the history of more than 5 years of diabetes) and without CAD (all of them had normal angiography or CT angiography), were measured in basal segments of anterior, posterior, lateral, anteroseptal, septal, and inferior walls of left ventricular in apical 2 chambers, 3 chambers, and 4 chambers views and then compared to sixty matched healthy normal controls.

Results: Mean of total S’ and E’ and also S’ and E’ in each segments were significantly lower in patients with DM, compared to controls. Mean A, and A’ were higher in diabetic patients, compared to healthy normal control group.

Conclusions: Our findings are suggestive that TDI may detect diastolic and systolic dysfunction in diabetic patients sooner.
Background: Patients undergoing primary percutaneous coronary intervention (PCI) for acute myocardial infarction (AMI) are at a higher risk for Contrast-induced nephropathy (CIN). Especially, the occurrence of CIN is strongly related to the presence of diabetes mellitus primary PCI are not well characterized.

Objectives: The aim of this study was to determine the clinical predictors of CIN in patients with DM undergoing primary PCI for AMI.

Methods and Results: 367 consecutive AMI patients undergoing primary PCI were enrolled in this study. Overall, CIN occurred in 107 (29.2%) patients. Of the 111 patients with DM, 47 (42.3%) developed CIN. Regarding DM patients, the incidence of higher age (>70), Killip classification >=2, contrast agent volume >130ml and slow/no reflow during the procedure were significantly higher in patients with CIN. And the maximum creatine phosphokinase (CPK) was higher in patients with CIN. In multivariate analysis, contrast agent volume > 130ml (OR 4.56, 95% CI 1.53-13.55 ; p=0.006) and age > 70 (OR 3.50, 95%CI 1.20-10.23 ; p=0.022) were independent predictor of CIN.

Conclusion: CIN frequently occurs in patients with DM undergoing primary PCI for AMI. Restricted volume of the contrast medium is needed to prevent for CIN in these patients, especially with higher age. And also, hemodynamic instability such as slow/no reflow or elevated CPK might have some influences on CIN.
CULPRIT VESSEL VERSUS COMPLETE MULTIVESSEL REVASCULARIZATION IN PATIENTS PRESENTING WITH ST-SEGMENT MYOCARDIAL INFARCTION: A SINGLE CENTER RETROSPECTIVE ANALYSIS

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Objective: We investigated whether complete versus culprit only revascularization in patients presenting with STEMI influences success during PCI in pts with obstructive multivessel disease.

Background: Whether performing multivessel revascularization during STEMI adds to the complexity of procedural success and outcomes is unknown. Previous retrospective, non-randomized trials have shown that patients with STEMI who have undergone multivessel PCI have increased rates of reinfarction, need for revascularization and stroke but contemporary studies have produced controversial results.

Methods: A retrospective analysis of 350 patients with STEMI from 2004-2012. Pts were categorized if culprit vessel only PCI or multivessel (MV) PCI was performed during primary PCI. Primary end point was a composite of angiographic success, procedural success and clinical success.

Results: 350 STEMI pts, 276 underwent primary PCI. 90.6% (n=250) underwent culprit vessel PCI and 9.4% (n=26) underwent MV revascularization (MVR). Pts undergoing MVR 46.1% (n=12) during primary PCI compared with those undergoing staged PCI 53.9% (n=14) had improved procedural success TIMI flow 2.5 + 0.52 vs 2.85 + 0.36 (p=0.05). In the absence of cardiogenic shock, MVR during primary compared with staged was associated with a non-significant trend in TIMI flow, 2.5 + 0.71 vs 2.85 + 0.36 (p=0.26). No significant difference in primary outcome was found among pts with MVR during index hospitalization compared with staged PCI 3-6 months following index STEMI 2.75 + 0.46 vs 2.67 + 0.51 (p=0.75).

Conclusions: The results of our study suggest that in STEMI pts with MVD presenting with cardiogenic shock, MVR may improve procedural outcomes.
ACCESS TO HEALTH CARE IN PATIENTS WITH ST-ELEVATION MYOCARDIAL INFARCTION IN SOUTHERN FLORIDA

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Introduction: Race and legal status may influence hospital outcomes in patients with ST-Elevation myocardial infarction (STEMI). The aim of this study was to examine the relationship between patients access to health care and clinical outcomes by racial and immigration status.

Methods: This is a single-center retrospective review of all patients admitted with STEMI from January, 2006 to December, 2012. STEMI was defined as ST segment elevation >2 mm in 2 contiguous precordial leads or >1mm in other leads.

Results: A total of 820 patients were admitted with STEMI over the specified period. There were 23% White, 49.5% Latinos, and 27% Blacks. Of those 3 subgroups, the median [IQR] age was 63 [54.5, 72], 60 [52, 70], and 55 [44, 62], respectively (p=<0.001). Male gender was 79%, 78%, and 72%, respectively (p=0.182). The median time (min) of chest pain-to-door was 120, 100.5, and 120, respectively (p=0.085). The median time (min) of door-to-balloon was 67, 62 and 67, respectively. (p=0.345). The median length of stay (days) was similar in all groups (3 days, p=0.392). All-cause mortality was 6%, 3.2%, and 6% (p=0.009). Among all groups, there were 93% documented and 7% undocumented immigrants. There is no difference in chest pain-to-door, door-to-balloon, and hospital length of stay between the two groups.

Conclusions: In this cohort of patients with STEMI, Latinos have a shorter chest pain-to-door time, similar door-to-balloon time, and lower mortality compared to other ethnicities. Immigration status did not appear to influence access to care or clinical outcomes.
IMPACTS OF PCI IN-HOSPITAL OUTCOMES AND LIFE EXPECTANCY IN PATIENTS AFTER ACUTE MYOCARDIAL INFARCTION

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Background: Acute myocardial infarction is the leading cause of death worldwide for several decades. To clarify the association between percutaneous coronary intervention and in-hospital outcome in both elderly and non-elderly, and life expectancy, we conducted a population-based study in Taiwan using the National Health Insurance Research Database.

Methods and Materials: This study was conducted in a retrospective cohort of Chinese population in Taiwan. In-patients from 2004 through 2010, with age greater than 18-year-old, had their first AMI with ICD-9-CM code of 410.xx were recruited. In-hospital outcome was analyzed by multivariate logistic regression, and the estimated survival time was analyzed by Monte Carlo method. The statistical significance was defined when the P less than 0.05.

Results: In total of 3,352 enrolled patients, the multivariate logistic regression revealed elderly, chronic kidney disease, prior infarction stroke, cardiogenic shock etc. are independent determinants of in-hospital mortality. Impact of PCI in reducing in-hospital mortality was significantly in both non-elderly and elderly. Impact of PCI in prolongation of survival time and life expectancy of patients after AMI revealed significantly.

Conclusion: Utilization of PCI was not high enough, especially in the elderly. The association was observed to produce a negative impact on outcome. Our study clearly reveals that the PCI improved in-hospital outcome in elderly in a longitudinal investigation is consistently better in comparison with non-elderly. The impact of PCI could offer significant survival time and increase life expectancy.
PERI-PROCEDURAL HEMOGLOBIN DROP AND CREATININE CHANGE IN PATIENTS UNDERGOING SINGLE VESSEL PCI, A COMPARISON BETWEEN TRANSRADIAL AND TRANSFEMORAL APPROACHES

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Background: Tran-radial (TR) approach is being more frequently used for percutaneous cardiac interventions (PCI). However, the amount of peri-procedural Hemoglobin (Hb) drop or Creatinine (Cr) change has not been readily reported in the literature compared with the trans-femoral (TF) approach.

Objective: To compare serum Hb drop and Cr change in patients who underwent TR vs. TF single vessel PCI.

Methods: In a retrospective cohort, we reviewed our academic tertiary care center catheterization lab data from January 2010 till March 2013 and randomly selected 61 patients who had single vessel PCI through the TR approach (Group 1) and another 98 patients with the TF approach (Group 2) by Single Operator. We recorded serum Hb (for all patients) and Cr (for all patients in group 1 and 95 patients in group 2) before and 48-72 hours after the procedure.

Results: The mean post-procedural Hb drop was 0.96 mg/dl in group 1 and 1.23 mg/dl in group 2 with a mean difference of 0.27 mg/dl (P=0.097). The mean post-procedural Cr change was -0.076 mg/dl in group 1 and 0.019 mg/dl in group 2 with a mean difference of 0.09 mg/dl that was not statistically significant (P= 0.394).

Conclusion: Among patients who underwent single vessel PCI, TR approach was associated with less hemoglobin drop and with no increase in creatinine compared to TF approach.
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CHRONIC KIDNEY DISEASE: AMBULATORY BLOOD PRESSURE DIAGNOSTIC THRESHOLDS OF HYPERTENSION IN BASED ON CARDIOVASCULAR OUTCOMES

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Objectives: Currently proposed ambulatory (ABPM) blood pressure (BP) thresholds for diagnosis of hypertension do not differentiate uncomplicated persons from those at higher risk, e.g., patients with chronic kidney disease (CKD). We aimed to derive diagnostic thresholds for the awake and asleep BP means in terms of cardiovascular (CVD) outcome for patients with as well as without CKD.

Methods: A total of 3344 subjects (1718 men/1626 women; 793 with CKD), 52.6+/-14.5 years of age, were prospectively studied throughout a 5.6-year median follow-up. At baseline and annually thereafter, ambulatory BP was monitored for 48h. Cox regression analysis was used to derive outcome-based reference thresholds for ABPM in subjects with and without CKD.

Results: CVD risk was consistently and significantly greater in patients with than without CKD for awake systolic/diastolic (SBP/DBP) BP means >125/75 mmHg and asleep SBP/DBP means >110/60 mmHg. The outcome-based reference thresholds for uncomplicated persons were 135/85 mmHg for the awake and 120/70 mmHg for the asleep SBP/DBP means. The equivalent, in terms of CVD risk, cutoff values for patients with CKD were 120/75 mmHg for the awake and 105/60 mmHg for the asleep SBP/DBP means, respectively.

Conclusions: The proposed ABPM reference thresholds are 15/10 mmHg lower for ambulatory SBP/DBP in patients with than without CKD, reflecting also the significantly increased ambulatory pulse pressure in CKD. This marked difference indicates the need for revision of current guidelines that propose diagnostic thresholds for ABPM without differentiating between presence/absence of CKD.
DISTANCE GUIDANCE REINFORCEMENT PROGRAM AND ADHERENCE OF THE TREATMENT OF DYSLIPIDEMIA IN PRIMARY CARE THE PRECAVER STUDY

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Objectives: To evaluate treatment compliance, by reduction of LDL-C in the group of patients that have received a program of guidance reinforcement, addressed to patients eligible for treatment with rosuvastatin compared to a control group.

Material and Methods: 600 patients with dyslipidemia that required treatment with rosuvastatin were screened from 60 primary care offices. The study was open, prospective, observational, with 2 (two) arms: Intervention through the Distance Program of guidance and awareness vs. non-intervention (control group). Patients receiving rosuvastatin were randomized either or not to receive a distance reinforcement program with learning addressed to the treatment. The control group received the usual information by the physician, while the patients taking part in the program, in addition to that information, received support through shipment of instructional materials and had access to an electronic site with restricted access.

Results: Both groups had similar treatment results in terms of LDL-C reduction, with no statistical difference between them (p=0.8196). Those patients presenting with comorbidities had a more significant lowering of LDL-C, either in the active or in the control group (p<0.0001) but there was no influence on being in the active or control group for the final results.

Conclusions: Distance reinforcement program haven’t seemed to influence significantly in the results, since the LDL-C levels were statistically lowered across all groups. Additional information outside the medical office has not added any benefit to treatment success. Advice and explanations in the medical office were sufficient for adequate awareness and adherence.
Background: Patients undergoing abdomino-pelvic surgeries may have postoperative cardiac events. In patients above age of 40, ECG is frequently performed preoperatively to screen for asymptomatic coronary artery disease. Many perioperative factors may play role in precipitating silent myocardial ischemia that's only presented by postoperative ECG changes.

Objectives: To evaluate the association between different perioperative factors and postoperative ECG changes suggestive of silent myocardial ischemia.

Patients and Methods: The study included 200 non-cardiac patients, above the age of 40, with a normal preoperative ECG, who underwent major elective non-vascular abdomino-pelvic or laparoscopic surgeries. A twelve-lead ECG was performed pre-, immediately post- and 3 days postoperative. Patients, who showed any postoperative ECG changes, were tested for their CK-MB, Na, K, Mg and ionized Calcium serum level.

Results: Six patients (3%) showed postoperative T-wave inversion, none of them experienced cardiac symptoms, elevation of CM-MB, or abnormal electrolyte level. Three patients (50%) underwent abdominal, 2 (33.3%) laparoscopic and 1 (16.7%) pelvic surgery. Two patients (33.3%) experienced intraoperative hypotension. ECG changes were significantly related to the mean duration of surgery (5.0 ± 2.5 Vs 3.6 ±1.5 hours, p=0.02) but were not related to patients' age (p= 0.6), preoperative heart rate (p= 0.2), preoperative systolic (p= 0.7) or diastolic blood pressures (p= 0.6).

Conclusion: The long duration of major non-vascular abdomino-pelvic surgeries may cause serious cardiovascular hemodynamic effects leading to silent myocardial ischemia. Postoperative ECG changes may be the only tool to detect postoperative silent myocardial ischemia.
PREVALENCE OF POSTOPERATIVE ECG CHANGES IN NON-CARDIAC PATIENTS UNDERGOING MAJOR ABDOMINO-PELVIC SURGERIES
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Background: Patients undergoing abdomino-pelvic surgeries may have postoperative cardiac events. In patients above age of 40, ECG is frequently performed preoperatively to screen for asymptomatic coronary artery disease. Even with normal preoperative ECG, new postoperative ECG changes may develop.

Objectives: To estimate the prevalence of postoperative ECG changes following major elective abdomino-pelvic and laparoscopic surgeries in non-cardiac patients.

Patients and Methods: The study included 200 non-cardiac patients, above the age of 40, with a normal preoperative ECG, who underwent major elective abdomino-pelvic or laparoscopic surgeries. Abdominal vascular surgeries were excluded. A twelve-lead ECG was performed pre-, immediately post- and 3 days postoperative. Patients who showed any postoperative ECG changes, were tested for their CK-MB, Na, K, Mg and ionized Calcium serum level.

Results: Six patients (3%) showed postoperative T-wave inversion. None of the 6 patients experienced cardiac symptoms, concomitant elevation of CM-MB, or abnormal electrolyte level. The mean age was 55.8 ± 9.7 years. Four of these patients (67.6%) were males, 2 (33.3%) were hypertensive, 1 (16.7%) was diabetic and 3 (50%) were current smokers. Three patients (50%) underwent abdominal, 2 (33.3%) laparoscopic and 1 (16.7%) pelvic surgery. Two patients (33.3%) experienced intraoperative hypotension. The mean duration of surgery was 5.0 ± 2.5 hours.

Conclusion: Postoperative ECG changes, was infrequent in patients undergoing major elective abdomino-pelvic and laparoscopic surgeries. Despite the T wave inversion suggestive of silent ischemia, there were no cardiac enzyme elevation, no symptoms of ischemia and no electrolyte disturbance.
ISOLATED CHRONIC TOTAL OCCLUSION OF LEFT ANTERIOR DESCENDING ARTERY: FOLLOW-UP PATIENTS FOR 8 YEARS

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Background: There is no agreement regarding the revascularization of patients with chronic total occlusions (CTO) and signs of ischemia. Controlled randomized trials did not show prognostic benefit of revascularization. But supposed consequences of «closed» artery are dilatation of left ventricle (LV) and deterioration of LV systolic function.

Methods: 15 patients with isolated CTO of left anterior descending artery (LAD) were included. All patients had positive exercise stress echocardiography (SE) with ischemia in LAD zone. 36% patients met high risk criteria of SE (decrease of LV ejection fraction (EF)). All patients had medical treatment and did not get any revascularization. Mean follow-up period was 8.8 years. Diastolic diameter, diastolic volume, systolic volume of LV were assessed. Exercise SE was performed, EF and wall motion score index (WMSI) were estimated before and after the test.

Results: Diastolic diameter, diastolic volume reduction and systolic volume reduction were observed among patients without revascularization (p<0.05). EF and WMSI did not change significantly, but ΔWMSI significantly decreased (p<0.05). We did not find any high risk criteria of SE among CTO patients on the second visit.

Conclusion: Patients with isolated CTO of LAD demonstrate improvement of LV parameters and reduction of ischemia level despite absence of revascularization.
P204 INSIGHTS INTO MECHANISM AND MANAGEMENT OF ATRIAL FIBRILLATION

160 POSTOPERATIVE ATRIAL FIBRILLATION IS ASSOCIATED WITH HIGHER EUROSCORE, BUT NOT WITH HOSPITAL MORTALITY AFTER CORONARY ARTERY BYPASS GRAFT SURGERY
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Background: Postoperative atrial fibrillation (POAF) is the most common arrhythmia after coronary artery bypass surgery (CABG) and is associated with an increased morbidity. Recently, it has been suggested that POAF is also associated with increased postoperative mortality. Hence, we investigated whether POAF after isolated CABG was associated with a higher EuroSCORE, indicating greater in-hospital mortality risk.

Methods: We reviewed data from our prospective cardiac surgery database of all patients (n=2791) undergoing isolated CABG from January 2003 through December 2006 at a large university medical center.

Results: The mean age was 68 ± 9.1yrs, and mean EuroSCORE was 6.91 ± 3.18. The overall incidence of POAF was 32.3%. The POAF group was older (70.5 ± 7.8 vs. 66.8 ± 9.5yrs non-POAF: p<0.0001), but there was no significant difference in ejection fraction (EF) between the two groups (p=0.13). There was a significant difference in the mean EuroSCORE (POAF, 7.6 ± 3.2 vs non-POAF, 6.6 ± 3.1, p<0.0001), indicating that the POAF group was at greater risk for postoperative mortality. Although, there was a significant association between EuroSCORE and POAF (p<0.0001), there was no significant difference in hospital mortality between the POAF and non-POAF groups. The overall hospital mortality was 1.9%, with no difference between the two groups (p=0.91). Furthermore, POAF was not predictive of hospital mortality after CABG.

Conclusion: POAF is associated with a higher EuroSCORE, but it is neither associated with, nor predictive of increased hospital mortality after CABG.
Background: Atrial fibrillation (AF) is the most common sustained arrhythmia affecting humans. Antiarrhythmic agents have variable effectiveness in restoring sinus rhythm, and the choice of a drug may have significant implications. Objective: To compare the efficacy and rapidity of conversion of recent onset AF by oral propafenone and intravenous infusion (IVI) of amiodarone.

Methods and Results: Fifty patients with a mean age of 52.58 ± 4.99 years (64% males), and a diagnosis of recent onset AF of less than 48 hours were randomly assigned to two equal groups; Group 1 (G1) in which IVI of amiodarone was administrated, and group 2 (G2) for whom oral propafenone was administrated. There was no significant difference between both groups as regards age, gender, the presence of hypertension or diabetes, the presence of underlying structural heart disease, the mean left atrial diameter, and the left ventricular ejection fraction. In 72% of either group AF was the first attack. Eighty eight percent of G1 patients had successful conversion into sinus rhythm compared to 84% of patients in G2 which was statistically insignificant (p=0.076). The time elapsed from drug administration till conversion to sinus rhythm in G1 was 9:07 ± 5:04 hours, while that in G2 was 3:9 ± 1:54 hours, a difference that was statistically highly significant (p<0.001). Drug related complications were rare, with no significant difference between both groups.

Conclusions: Oral propafenone was as effective as IVI of amiodarone in conversion of recent onset AF into sinus rhythm and needed a significantly shorter duration.
THE VALUE OF LAVI AND CHADSVASC AS PREDICTORS OF STROKE RECURRENT IN PATIENTS WITH NO PRIOR AF: A SAUDI EXPERIENCE

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Background: The relationship between ischemic strokes and silent paroxysmal atrial fibrillation (AF) has been of growing interest. The aim of this study is to try to identify whether parameters like the CHADS-VASc score or the left atrial volume index (LAVI) are correlated with recurrence of stroke in a population where AF burden has not been detected.

Methods: This is a retrospective observational study looking at consecutive patients with a primary diagnosis of ischemic stroke/TIA admitted in a single center at the Eastern Province in Saudi Arabia. The patients’ characteristics and echocardiographic findings were documented.

Results: 159 patients were admitted with a diagnosis of ischemic stroke/TIA. The mean age was 64.5±7.2 years. 61% of the patients were male, 78% were diabetic, 65% were hypertensive, 6.1% had prior heart failure, and 40.8% had ischemic heart disease. Three of the patients had documented AF on their ECG on admission. Ten others had documented AF on holter monitor. 17 of the patients with no documented AF had re-admission with another stroke over the 2 years studied. Out of the 17 patients, 16 of them had moderately increased LAVI, and a mean CHADS-VASc score of 4.2. The two points allocated for prior stroke/TIA were excluded when the latter score was calculated.

Conclusion: The presence of moderately increased LAVI coupled with a high CHADSVASc score in spite of the absence of overt AF are associated with a higher risk of recurrence of stroke. This could be due to the presence of “silent” or undetected atrial fibrillation.
Background: Systolic heart failure is one of the conventional risk factors of stroke in patients with atrial fibrillation (AF).

Objectives: Whether diastolic dysfunction (DD) is a predictor for stroke in patients with AF.

Methods: We retrospectively analyzed echocardiograms of 1658 patients performed at University hospital. The patients were divided to normal (n=702, 42%) & DD (n=956, 58%). We analyzed in total 1658 patients, 197 with atrial fibrillation, & 19 with stroke. Results: We found a mild association between stroke and AF in patients with DD with a frequency of 10.7% vs. 7.2% in control (p=0.078). GFR has a mild association as a predictor of stroke with p=0.079. In the Logistic regression analysis, for every 30 units of increasing levels of GFR the risk of stroke decreased by 17% (OR:0.83, 95%CI 2.5-29.2, p=0.023). Also patients without diabetes for every 30 units of increased GFR the risk of stroke decreased by 22% (OR:0.78, 95%CI: 0.66-0.93, p=0.006). Hypertension & age were also significant in patients with DD, for every 5 years more the risk of stroke increased 9% (OR:1.09, 95%CI:1.02-1.17 p=0.012).

Conclusions: In patients with DD and atrial fibrillation worsening renal function is associated with increased risk of stroke. HTN and age are risk factors for stroke in patients with DD with & without atrial fibrillation.
ATRIAL ELECTROMECHANICAL INTERVAL IN THE PREDICTION OF RECURRANCE OF ATRIAL FIBRILLATION IN PATIENTS UNDERGOING SUCCESSFUL ELECTRICAL CARDIOVERSION TO SINUS RHYTHM

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Background: Atrial fibrillation (AF) is the most common sustained arrhythmia. Electrical cardioversion is used in patients in whom a rhythm control strategy is selected. However, only a minority of patients successfully cardioverted maintain sinus rhythm long-term. The ability to identify individuals where AF is likely to recur may assist decision making regarding the use of antiarrhythmic therapy. Recently, atrial electromechanical interval (AEMI) has been shown to be useful for predicting post-operative AF. This prospective study aimed to evaluate the utility of AEMI for predicting AF among patients who underwent successful direct current cardioversion.

Methods: Inclusion criteria: age ≥ 19, AF with planned cardioversion, and informed consent. Following successful cardioversion, a 12-lead electrocardiogram and echocardiogram were immediately performed to assess AEMI using the transmural velocities, tissue doppler velocities, electrocardiogram. AEMI was measured from the beginning of the P-wave to the beginning of the A’ of the lateral and septal mitral annulus, A’ of the lateral tricuspid annulus, or A wave of mitral inflow, respectively. The patients were followed for 6 months with electrocardiograms to assess their rhythm. The primary endpoint was recurrence of AF by 6 months. Analysis was performed by logistic regression to determine if AEMI was predictive of recurrence.

Results: 55 patients (mean age 66, ± 11.7; 68% male) completed follow-up. AEMI of the lateral mitral annulus, septal mitral annulus, tricuspid annulus, and mitral inflow showed no correlation with recurrence (p=0.108, 0.061, 0.278, 0.114, respectively).

Conclusion: In this study AEMI was not predictive of AF recurrence following successful cardioversion.
SUCCESS RATES FOR MAINTENANCE OF SINUS RHYTHM WITH DIRECT CURRENT CARDIOVERSION AND AGGRESSIVE ANTI-ARRHYTHMIC THERAPY IN PATIENTS WITH ATRIAL FIBRILLATION

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Direct current cardioversion (DCCV) has been used extensively for rhythm control in AF patients, without significant data to support. The aim of this study was to look at clinical predictors of failed DCCV.

Methods: Patients who underwent DCCV for AF from 2009-2012 were identified and clinical data (including medication and ECHO) was reviewed. SPSS 21.0 was used for statistical analysis.

Results: A total of 176 patients received DCCV for AF during this period. The mean age of the patients was 63 ±14 (mean ± SD), mean LVEF 49 ± 12 % (mean ± SD) and LA size 4.2 ± 0.8 cm (mean ± SD). Paroxysmal AF was found in 63 (34.7%), 93 (52.8%) had persistent AF and 20 (11.4%) had permanent AF. During the follow up, maintenance of sinus rhythm at 1, 6, 12 and 24 month was observed in 67%, 41%, 29% and 14% of the patients, respectively. Age, sex, BMI, DM, HTN, CAD, Creatinine, use of ace inhibitors, ARBs and statins, LA size and EF were not associated with outcome of DCCV. Type of AF was significantly linked to DCCV outcome at 1, 6 and 12 months after adjusting for LA size, EF and use of AADs. Use of AAD pre-procedure significantly predicted the success at 1 month (p-value 0.013) but not thereafter. Conclusion: Following DCCV, patients revert back to AF cumulatively with time. Type of AF was the only short term and long term clinical predictor of failure.
ATRIAL FIBRILLATION ADDS TO THE BURDEN OF ISCHAEMIC STROKES IN A MULTI-ETHNIC SOUTHEAST ASIAN POPULATION

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Background: Atrial fibrillation (AF) is associated with an increased risk for ischaemic strokes. AF-related strokes have poorer outcomes with such data mostly from Western or Far East populations. This study aims to review the impact of AF-related strokes in a single center multi-ethnic Southeast Asian population.

Methods: This is a retrospective cohort study of 243 consecutive patients with ischaemic strokes admitted between January and June 2009. Follow up information up to 3 years was also collected. Data was analyzed using SPSS 19.

Results: Mean age of the study population was 64.0 years. Majority of patients were male (63.4%). There were 47 patients (19.3%) with known or newly diagnosed AF. Patients with AF were older (p<0.001), had a higher prevalence of hypertension (p=0.015) and hyperlipidemia (p=0.009). There were no differences in terms of gender (p=0.738), diabetes mellitus (p=0.069), ischaemic heart disease (p=0.841) and congestive heart failure (p=0.127). Of the 29 patients with prior AF, only 3 were on anticoagulation. Patients with AF had a longer length of stay (p=0.016), and higher in-hospital costs (p=0.003). At 3 years, there was a higher rate of recurrent stroke, myocardial infarction and death (p=0.003). Mixed model analysis showed that AF was an independent predictor of cardiovascular outcomes (p=0.020).

Conclusion: AF is prevalent in Southeast Asian patients presenting with ischaemic strokes with many not receiving anticoagulation. The consequent burden of AF-related strokes is higher in terms of monetary costs and cardiovascular outcomes with real costs probably even greater considering the loss of productivity and psychosocial impact.
USEFULNESS OF DABIGATRAN IN THE PATIENTS WITH NON VALVULAR ATRIAL FIBRILLATION

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Anticoagulant effect and bleeding risk of a direct thrombin inhibitor Dabigatran (D) have not been fully elucidated in Japan. Methods: In 62 patients with non valvular Atrial Fibrillation (AF), 220mg of D was administered and anticoagulant effects were evaluated using Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT). Results: Four patients stopped D due to gastric manifestation, and 58 patients were studied. Mean age was 70.85 years old. APTT was prolonged to 41.9 seconds (sec) (mean± SD) and ranged from 32 sec to 70 sec (APTT control 29sec). Mean APTT was 50.48±6.49 sec at peak and 40.99±3.33 sec at trough (P<0.001 vs peak). PT-INR (International Normalized Ratio) increased from 0.94±0.05 to 1.08±0.13 (P<0.005). APTT was associated with eGFR, but not with creatinine level. No thromboembolic events occurred within 1 year follow-up. Major bleeding occurred only in 1 patient, and minor bleeding occurred in 7 patients. HAS-BLED score ranged from 2 to 4. There was not clear association between bleeding and HAS-BLED or CHADS2 score.

Conclusions: Dabigatran is a safe and effective drug for the patients with AF including the aged patients, and its anticoagulant effect is stable. However, minor bleeding may occur without marked prolongation of APTT.
SAFETY OF CLASS-1C ANTIARRHYTHMIC DRUG TREATMENT IN PATIENTS WITH ATRIAL FIBRILLATION AFTER EXCLUSION OF CORONARY CALCIFICATIONS BY CT - LONG TERM RESULTS

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Medical Department I, Klinikum Grosshadern, University of Munich

Introduction: Drug treatment is still 1st line therapy for treating atrial fibrillation (AF). However, the use of class-1c antiarrhythmic agents has to be done with caution. In this study we investigated the use and safety of non-invasive assessment of coronary calcification (CC) burden by computed tomography (CT) to rule out a significant coronary artery disease prior initiation of class-1c therapy. Objective was to evaluate the suitability of the method and safety in a daily routine.

Methods: A total of 457 patients (pts) with paroxysmal AF were screened in our outpatient clinic. Routine ECG, echo and ultrafast CT for CC burden assessment was performed. If no CC was present and no other pathological findings in ECG and echo occurred class-1c therapy was initiated. Follow ups (FU) were performed at 3, 9 and 18 months.

Results: Based on the inclusion criteria 81% (369/457) of the pts were included. In 45% of pts (166/369) CC could be excluded, which were then assigned to a class-1c therapy. Adverse events occurred as follows: syncope (3%), non-sustained-VT (4%), QTc-prolongation (1%), bradycardia (4%) transient sinus arrest (1,8%), no case of Torsades-d-P/sustained VT/VF were documented.

Conclusions: Our results suggest that non invasive assessment of CC burden by CT prior to class-1c therapy initiation is a suitable and useful tool to determine safety of this therapy.
IN HOSPITAL REGISTRY OF ATRIAL FIBRILLATION AND MULTIVARIANT ANALYSIS

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Sri Ramachandra University, Nagarjuna Hospitals, Chennai, Indai

Aim: To study the role of risk factors in the genesis of atrial fibrillation and its association with valvular and non valvular heart diseases and incidence of complications.

Methods & Results: In a large single centre study, 1506 hospitalized patients with ECG-documented AF between Jan 2007 to 31st Dec 2012 were enrolled. The clinical type of AF was grouped as chronic (n=614), paroxysmal (n=586) and first detected (n=306). Classified them into valvular (30.6%) and non valvular(69.33%). Among valvular 70.33% are of rheumatic in nature. Among the non valvular causes large number of patients had hypertension (59.8%).11.2% had lone AF.6.9% had thromboembolic complications. Heart failure was noted in 27%. Antithrombotic measures for stroke prevention was given to 41.2% of eligible patients, among them antiplatelets (73.5%) are preferred. No direct relation between LA size and LVEDD and LV mass index was noted, but LA enlargement more than 4.0 cm seen in 78.6% patients.

Conclusion: Rheumatic valvular heart disease is still a considerable burden in the developing world. Systemic hypertension is becoming a prevalent, anti-thrombotic measures are still inadequate in atrial fibrillation. LA size can be a single most reliable factor in the genesis and propagation of atrial fibrillation.
Background: The Role of LV Diastolic Dysfunction (DD) in predicting atrial fibrillation (AF) is known.

Objectives: To investigate the correlation with renal Dysfunction and levels of pro-bnp in patients with DD and AF.

Methods: We retrospectively analyzed echocardiograms of 2670 patients performed at University hospital. Due to missing data, 1752 patients were excluded from analysis. The patients were divided in three groups according to GFR. Patients were classified to GFR>60 (control, n=618, 70%), GFR 30-60 (n=208, 23%), and GFR <30 (n=92, 7%). We analyzed in total 114 patients with atrial fibrillation and 774 without atrial fibrillation.

Results: When divided in groups according GFR <30, 30-60 and >60; we found that patients with GFR<30 have twice risk to develop AF than the control (OR=2.03, 95%CI 1.27-3.24, p=0.003) and patients with GFR 30-60 have 1.7 more risk than the control to have AF (OR:1.74, 95%CI 1.2-2.52, p=0.003). We found that there is an inverse relationship between pro-bnp and GFR, lower levels of pro-bnp are associated with higher levels of GFR with r=-0.18, p<0.001).

Conclusions: Renal dysfunction is associated with onset of AF in patients with DD. There is an inverse relationship between pro-bnp and GFR.
RELATIONSHIP OF CARDIOVASCULAR MORTALITY & HOMOCYSTEINE LEVELS IN CHRONIC KIDNEY DISEASE

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Elevated homocysteine is an important risk factor for increased cardiovascular mortality. It is elevated in majority of patients of CKD and can be an important modifiable risk factor. The present study was undertaken to see homocysteine levels & cardiovascular mortality in CKD cases and evaluate the effect of folic acid and B12.

Methods: Patient of CKD having GFR <60ml/min were enrolled for the study. A randomized placebo controlled trial on 100 cases was carried out at tertiary care hospital for one year. Patients were randomly assigned into two groups. Control group was given placebo and interventional group was given folic acid and vitamin B12 supplementation. Homocysteine levels were estimated at base line and after 6 months and cardiovascular mortality was compared.

Results: Mean baseline homocysteine levels were 32.61 µmol/L in the interventional group and 29.48 µmol/L in the placebo group (p >0.05). The level decreased significantly to 19.69 µmol/L (p<0.001) in the interventional group and it increased to 34.41µmol/L (p>0.05) in the placebo group after 6 months. The homocysteine level had a negative co-relation with haemoglobin (r= -0.19), GFR (r= -0.16), folic acid (r= -0.19) and vitamin B12 (r= -0.35). There was no significant effect on total mortality, deaths due to cardiovascular events, total ischemic event, and hospitalisation due to unstable angina, heart failure or venous thrombotic events after 6 months of supplementation therapy.

Conclusion: Serum homocysteine is elevated in patients of CKD. Folic acid and vitamin B12 supplementation lowered homocysteine, but it did not reduce cardiovascular disease mortality.
Case: A 33-year-old woman with history of systemic lupus erythematosus (SLE) presented with chest pain. She was diagnosed 15 years ago with SLE via serologies, renal biopsy, joint pains, and malar rash, and has been on chronic immunosuppressive therapy. One week prior, the patient received a trans-septal mitral valvuloplasty complicated by cardiac tamponade. Pericardiocentesis removed >1000 mL bloody fluid, and pericardial drain was placed. On discharge, azathioprine, hydroxychloroquine, and prednisone were resumed. The patient returned with chest pain, dyspnea, and fever to 38.2°C. Chest x-ray demonstrated left pleural effusion, a TTE revealed small circumferential pericardial effusion, and CRP and ESR were significantly elevated. Laboratory studies demonstrated strongly positive ANA, elevated anti-DS-DNA, and low C4 complement. Colchicine was held due to acute kidney injury. Prednisone 80mg was initiated with plan for slow taper over several months. The patient’s chest pain improved.

Discussion: Hemorrhagic pericardial effusion and tamponade likely occurred secondary to microperforation that occurred during trans-septal mitral valvuloplasty. SLE flare results in systemic inflammation and may be precipitated by increased physiological stress and withholding of chronic suppressive therapy. Prompt diagnosis and treatment requires a high clinical suspicion coupled with appropriate serology. Pericarditis and pleural effusion are common systemic manifestations of SLE.

Conclusion: Pericarditis is a common manifestation of a lupus flare and requires a high level of suspicion for timely and accurate diagnosis.
Case Report: A 47-year-old woman with positive family history of hypertrophic obstructive cardiomyopathy (HOCM) presented with three days history of breathlessness, chest pressure, lightheadedness and palpitations. She demonstrated orthostatic symptoms, occurring more while she was upright. She had vomited one day prior. On examination she was found to have a blood pressure of 90/60mm of Hg and 3/6 holosystolic murmur over the left parasternal border with a parasternal heave. A bedside two-dimensional echocardiogram showed mild concentric left ventricular hypertrophy with severe systolic motion of the anterior mitral leaflet (SAM). There was a large left ventricular outflow tract (LVOT) gradient, with a peak of 258mm of Hg. After volume resuscitation with two liters of intravenous fluid the patient’s symptoms improved. Surprisingly, a repeat echocardiogram conducted two days later -- including transesophageal views -- showed no features of HOCM, LVOT gradient or SAM.

Discussion: If the echocardiogram had not been conducted in the acute setting of volume depletion, the transient features of HOCM would have gone unidentified, thereby leaving the patient at risk for sudden cardiac death. Current routine screening with an echocardiogram may not be sufficient to diagnose HOCM in people at risk for such life threatening condition. Different new techniques along with genetic testing are required. This can facilitate early treatment and prevent sudden cardiac deaths in patients with unidentified HOCM during routine evaluations.

Conclusion: Further studies are required to develop new methods for screening HOCM in genetically predisposed individuals to prevent sudden unwarranted deaths. This case underscores the need for further research in this area.
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REPEAT ECHOCARDIOGRAPHIC SCREENING IN SUBJECTS UNDERGOING SCREENING ECHOCARDIOGRAPHY FOR DETECTION OF HYPERTROPHIC CARDIOMYOPATHY

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2. CareMore, Tucson, Arizona, USA
3. Anthony Bates Foundation

Background: Diagnosis of Hypertrophic Cardiomyopathy (HCM) can be challenging. HCM can present later in life and the value of repeat echocardiogram to evaluate late presentation of HCM is not known. The goal of this study was to evaluate any changes in wall thickness occurring within 2 years using repeat screening echocardiography.

Method: A total of 206 subjects underwent baseline and repeat echocardiography within 2 years. We evaluated the prevalence of HCM before and after repeat echocardiography. Suspected HCM was defined as any wall thickness ≥ 15 mm.

Results: The total prevalence of suspected HCM, defined by a cut off value of 15 mm or more, were two from 206 (0.9%). Repeat echo within one year found one additional case of suspected HCM (wall thickness changed from 1.4 to 1.5 cm). However, the other two initial cases of suspected HCM showed regression of wall thickness to <1.5 not qualifying as HCM anymore as previously suspected after 2 years (one decreased wall thickness from 1.5 to 1.2 and the other one from 1.5 to 1.3 cm).

Conclusion: Based on this small study, repeat echocardiography is warranted in subjects with suspected HCM in order to prevent over diagnosis. Furthermore, further increases in the wall thickness can occur in subjects with borderline finding in short period of time. Larger studies are needed to evaluate best timing and frequency of screening echocardiography for detection and prevention of HCM.
EFFICACY AND SAFETY OF CITALOPRAM IN TREATMENT OF NEUROCARDIOGENIC SYNDROME: EARLY AND LATE FOLLOW UP

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3. The University of Jordan, Amman, Jordan

Introduction: Selective serotonin uptake inhibitors (SSRI) have been suggested a beneficial therapy of neurocardiogenic syndrome/syncope (NCS). We report our experience using citalopram in 273 patients having NCS.

Methods: Charts of 273 patients, with diagnosed NCS, with no cardiovascular co morbidities, and were treated with citalopram at a dose of 5-10 mgs, were reviewed. 87 patients (49 male, 38 female) had no follow up. The remaining 186 patients (73 male, mean age 32.71 and 113 female, mean age 33.94) had follow up for their response. HUTT was utilized to diagnose 151 /186 patients. The rest 35 patients were treated empirically. Derived Minnesota score (MS) was used to assess response for 186 early follow up patients (1m), and for 92 late follow up patients (>1-6m or more).

Results: 186 early follow up patients received 5-10 mgs of citalopram showed significant improvement in MS from 7.35 to 4.46 (p<0.001). Citalopram was well tolerated in 181 patients. Five patients stopped citalopram because of intolerance (Insomnia, anorgasmia, nausea, hot flushes, hair loss, and exacerbation of all NCS symptoms). Therapy benefits persisted in late follow up (92 patients) with a reduction in MS from 7.42 to 4.43 in the early follow up and to 4.29 in the late follow up (p<0.001). Only six patients developed late significant intolerance. One patient developed very late resistance to citalopram after 3 years.

Conclusions: Citalopram is highly effective and well tolerated in the treatment of NCS at a dose of 5-10 mg. This effectiveness persisted with time.
PREDICTORS OF DIASTOLIC DYSFUNCTION IN PATIENTS WITH PERIPHERAL ARTERIAL DISEASE

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2. Lima, Peru

Background: Peripheral arterial disease and heart failure share many risk factors. Objectives: To investigate the prevalence & characteristics of patients with PAD & Diastolic Dysfunction (DD).

Methods: We retrospectively analyzed echocardiograms of 1659 patients performed at University hospital. Due to missing data, 1046 patients were excluded from analysis. The patients were divided in two groups; normal (n=210, 34%) & those with DD (n=403, 66%), including Impaired Relaxation (IR, n=341, 56%), Pseudonormal (PN, n=52,8%), & Restrictive Pattern (RP, n=10, 2%). We analyzed 27 patients with PAD and 587 without PAD. PAD was defined as ABI<0.9%.

Results: In patients with PAD we found that DM is strongly associated with DD (OR:2.4, 95%CI 1.03-5.8, p=0.044). GFR less than 30 has 4 times more risk to develop DD vs normal controls (95%CI 1.3-12.47, p=0.015). GFR between 30 and 60 was found to have a risk of 2.33 more of DD vs. normal controls (95%CI 0.93-5.8, p=0.07). Logistic regression analysis indicated that for every 5 years the risk of DD increases in 19.6% (OR:1.195, 95%CI 1.03-1.38, p=0.015) in patients with PAD. Patients with HTN and PAD have 4.47 more risk to have DD vs control (95%CI 1.93-10.35, p<0.0001).

Conclusions: Diabetes and renal dysfunction are strong predictors for DD in patients with PAD. Age and HTN strongly associated with DD in patients with PAD.
ASSOCIATED MEDICAL CONDITIONS IN PATIENTS TREATED WITH THERAPEUTIC NORMOTHERMIA OR HYPOTHERMIA FOR CARDIOVASCULAR AND NEUROLOGICAL INDICATIONS

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Background: Baseline characteristics in cardiac (CV) or stroke (CNS) patients treated with therapeutic hypothermia or normothermia were compared.

Methods: Data in 89 consecutive CV or CNS patients treated with therapeutic hypothermia or normothermia at a single institution were reviewed.

Results: There were no statistically significant difference between CV and CNS patients with respect to their gender, admission weight, sodium, potassium, calcium, magnesium, glucose, hemoglobin, hematocrit, systolic blood pressure, and heart rate. The prevalence of diabetes mellitus and chronic kidney disease were similar in CV and CNS patients. When compared to patients with CNS event, CV patients were older (59+-15 vs. CNS 39+-23 years old, p<0.0001), had a higher prevalence of hypertension (63% vs. CNS 44%, p<0.077), hyperlipidemia (40% vs CNS 19%, p<0.037), and coronary artery disease (49% vs CNS 6%, p<0.0001). These differences remained significant, when patients younger than 25 years old were excluded from the analysis. CV patients were more acidotic (pH 7.2+-0.15 vs CNS pH 7.4+-0.08, p<0.0001), with higher creatinine (2+-2 vs CNS 1.1+-0.4, p<0.01), BUN (19.9+-12.9 vs CNS 13.3+-7.6, p<0.013), and osmolality (296+-8.7 vs CNS 292+-6.5, p<0.029). There was also a higher prevalence of moderate-severe left ventricular dysfunction (47% in CV vs. CNS 0%, p<0.001). Conclusions: Patients with CV or CNS indications are similar with respect to their baseline characteristics; however, vastly different hemodynamic and metabolic derangements in CV and CNS patients are likely driven by the affected vascular territory. These dissimilarities should be taken into account during implementation of the therapeutic temperature manipulation.
IGE ACTIVITIES ON CD4+ T CELLS ARE EQUALLY IMPORTANT TO THOSE ON MAST CELLS IN EXPERIMENTAL ABDOMINAL AORTIC ANEURYSMS

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2. Elitary Research Centre of Individualized Medicine in Arterial Diseases, Department of Cardiovascular and Thoracic Surgery, University Hospital of Odense, Odense, Denmark

Immunoglobulin E (IgE) is a major activator of mast cells (MCs), and recently has been implicated in the pathogenesis of atherosclerosis. Here, we demonstrate that CD4+ T cells also express cell surface high-affinity IgE receptor FcepsilonRI, much more than CD8+ T cells do. IgE induces CD4+ T-cell production of pro-inflammatory IL6 and IFN-gamma, but reduces their production of anti-inflammatory IL10. FcepsilonRI deficiency (Fcer1a−/−) protects apolipoprotein E-deficient (Apoe−/−) mice from angiotensin-II (Ang-II) infusion-induced abdominal aortic aneurysms (AAAs) and reduces plasma IL6 levels. Adoptive transfer of CD4+ T cells, but not CD8+ T cells, from Apoe−/− mice, but not those from Apoe−/−Fcer1a−/− mice, increases AAA sizes and plasma IL6 levels in Apoe−/−Fcer1a−/− recipient mice. Using the same cell adoptive transfer approach and in vitro differentiated bone-marrow mast cells (BMMCs), we demonstrate that IgE activities on BMMCs are equally important to those of CD4+ T cells. Adoptive transfer of BMMCs from Apoe−/− mice also fully reverse AAAs in Apoe−/−Fcer1a−/− recipient mice. In contrast, BMMCs from Apoe−/−Fcer1a−/− mice fail to reverse AAAs in Apoe−/−Fcer1a−/− recipient mice. These observations suggest that T cells and MCs, and probably other inflammatory cells, such as macrophages, are all essential targets of IgE during AAA growth. In Ang-II infusion-induced AAAs in mice, anti-IgE monoclonal antibody therapy effectively reduces AAAs to the levels in Apoe−/−Fcer1a−/− mice, likely by blocking the activities of these IgE-targeting inflammatory cells. Therefore, anti-IgE therapy may become an effective regimen for AAA patients.
LESSONS FROM ANIMAL MODELS OF ARTERIAL ANEURYSM

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Histopathologic studies of human abdominal aortic aneurysms (AAA) have been performed primarily on severely advanced aneurysms excised at autopsy or resected at surgery after exceeding 5-6 cm maximum anterior-posterior diameter. Such specimens, frequently complicated by mural thrombus, calcific deposits, intramural hemorrhage, and necrotic pultaceous debris, provide little information concerning the initial structural changes in the arterial wall at the beginning of aneurysm formation. In this presentation we identify those experimental animal models that have made significant contributions (and those that have not) to our understanding of the pathogenesis of aneurysm with implications for therapeutic regimens that target mechanisms of progression. Most experimental studies of aneurysm progression have been conducted in rodents and small mammals. These models do not permit evaluation of novel devices for the treatment of AAA where an aortic diameter similar to that of humans is necessary. The existing large animal models of aneurysm have serious limitations such as the necessity of clamping the aorta (e.g. elastase infusion) and the lack of similarity to the cellular physiology of the disease process (e.g. graft interposition). Consequently, although the current swine models of AAA may be useful for device procedural training, development of a more physiological large animal model of AAA is of particular importance for testing the effect of evolving technologies on the pathological changes associated with progressing aneurysms of relevance to the human interventional setting.
The discovery of the genetics of thoracic aortic aneurysm dates back to observations by Hippocrates in 400 BC. The contributions of Marfan, Ehler, and Danlos are well-appreciated. Another germinal advance was the recognition in 1981 by M. David Tilson at Yale that abdominal aortic aneurysm runs in families. In recent times, Loeys and Dietz have identified the syndrome that carries their names. Milewicz has identified specific mutations that account for about 1/5th of all familial thoracic aortic aneurysms.

Our work at Yale has indicated that 21% of patients with thoracic aortic aneurysm have at least one family member with a thoracic aortic aneurysm somewhere in the body. The majority show an autosomal dominant pattern of inheritance with incomplete penetrance. Probands with ascending aneurysms tend to have family members with ascending aneurysm, while probands with descending aneurysms tend to have family members with either descending or abdominal aortic aneurysms. Bicuspid aortic valve, being so common (2% of general population) produces orders of magnitude more aortic dissections than the better appreciated Marfan syndrome.

The Table summarizes the known mutations that can produce thoracic aortic aneurysm. Genetic testing is available for all of these conditions.

In addition to the tests in the Table, our RNA Signature test for thoracic aortic aneurysm, now replicated in a second population, show a greater than 80% accuracy in detecting thoracic aortic aneurysm from a simple blood test.

The genetic understanding of thoracic aortic aneurysm promises to enhance detection of this silent killer and to permit “personalized” decision-making in the near future.

### GENETICS OF THORACIC AORTIC ANEURYSM

<table>
<thead>
<tr>
<th>Classification</th>
<th>Chromosome</th>
<th>Gene</th>
<th>Protein</th>
<th>Location</th>
<th>Frequency</th>
<th>Inheritance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marfan</td>
<td>15q11.1</td>
<td>FBN1</td>
<td>Fibrillin 1</td>
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<td>1:5000-10,000</td>
<td>Dominant</td>
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<td>Loew-Dietz</td>
<td>3p24-25, 9q31-34</td>
<td>TGFBR2, TGFBR1</td>
<td>TGFβ-R2, TGFβ-R1</td>
<td>Cell surface</td>
<td>Rare</td>
<td>Dominant</td>
</tr>
<tr>
<td>Ehlers-Danlos</td>
<td>2q24.3-31</td>
<td>COL3A1</td>
<td>Type III collagen</td>
<td>ECM</td>
<td>1:10,000-25,000</td>
<td>Dominant</td>
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<td>ATS</td>
<td>20q13.1</td>
<td>SLC2A10</td>
<td>GLUT10</td>
<td>Intracellular</td>
<td>Rare</td>
<td>Recessive</td>
</tr>
<tr>
<td>ADS</td>
<td>15q12.2-24.3</td>
<td>Smad3</td>
<td>SMAD3</td>
<td>Intracellular</td>
<td>Rare</td>
<td>Dominant</td>
</tr>
<tr>
<td>TGFBR2</td>
<td>1q31.1</td>
<td>TGFBR2</td>
<td>TGFβ-R2</td>
<td>Intracellular</td>
<td>Rare</td>
<td>Dominant</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Classification</th>
<th>Chromosome</th>
<th>Gene</th>
<th>Protein</th>
<th>Location</th>
<th>Frequency</th>
<th>Inheritance</th>
</tr>
</thead>
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<tr>
<td>TAAD2</td>
<td>3p24-25</td>
<td>TGFBR2</td>
<td>TGFβ-R2</td>
<td>Cell surface</td>
<td>~3 % of TAA</td>
<td>Dominant</td>
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<tr>
<td>TAAD4</td>
<td>10q13-24</td>
<td>ACTA2</td>
<td>Actin</td>
<td>Intracellular</td>
<td>10-15% of TAA</td>
<td>Dominant</td>
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<tr>
<td>TAAD5</td>
<td>9q31-34</td>
<td>TGFBR1</td>
<td>TGFβ-R1</td>
<td>Cell surface</td>
<td>~2 % of TAA</td>
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<td>TAAD-PDA</td>
<td>16p12-13, 3q21.1</td>
<td>MYH11</td>
<td>β-MHC</td>
<td>Intracellular</td>
<td>1-2% of TAA</td>
<td>Dominant</td>
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International Academy of Cardiology

18th World Congress on Heart Disease

Annual Scientific Sessions 2013
UPDATE ON AHA GUIDELINES FOR MANAGEMENT OF THORACIC AORTIC DISEASE
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University of Utah, Salt Lake City, UT, USA

The AHA/ACC/AATS Guidelines on the Management of Thoracic Aortic Disease were published in 2010 as a consensus statement designed to assist cardiologists and cardiothoracic surgeons with clinical decision making when caring for patients with potentially lethal thoracic aortic diseases. This presentation will review the guidelines and related works as they pertain to “at risk” patients, namely those with familial aortic aneurysms, Marfan syndrome, and Turner syndrome. The current state of genetic testing for the various disorders will be reviewed.
We evaluated usefulness of ultrasonography (US) for diagnosis of polyvascular disease (PVD). US was as useful as CTA for final diagnosis except a few cases with iliac lesion. Progression of carotid arteriosclerosis was associated with peripheral artery disease (PAD) because mean plaque score (PS) was 12.8±6.8 (5.1 to 26) in PAD patients. Cardio-ankle vascular index (CAVI) derived from pulse wave velocity was also elevated to 10.23±1.16(mean 8.2 in control) in PAD patients. Ankle-Brachial Index (ABI) has been used for diagnosis of PAD, however, ABI was 0.97±0.13 in the patients with below knee lesions (anterior and/or posterior tibial artery), and it was 0.74±0.19 in the patients with ilio-femoral lesions (P<0.05 vs tibial lesions). After angioplasty and stenting, US revealed that in-stent restenosis was observed only in 3 case out of 24 iliac lesions and in 7 out of 24 femoral lesions. Plaque characteristics was not associated with restenosis. US can evaluate carotid, peripheral or coronary artery lesions in most cases with PVD. In conclusion, usefulness of ABI is limited for diagnosis of PAD, and non invasive US and CAVI test with evaluation of risk factors for arteriosclerosis may be useful for final diagnosis of PAD or PVD.
DRUG ELUTING BALLOONS AND STENTS FOR ENDOVASCULAR TREATMENT OF PERIPHERAL ARTERIAL DISEASE

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VA North Texas Health Care System, University of Texas Southwestern Medical Center Dallas, TX, USA

The issue of restenosis has long plagued attempts to treat atherosclerosis, with up to 50% of procedures experiencing this complication within the first year post-intervention. In recent times, drug-eluting stents (DES) have been the focus of technological innovation in preventing and treating restenosis. Whereas the coronary arteries have paved the way for DES research, their use in successfully treating peripheral arterial disease (PAD) has yet to be as ubiquitously accepted. This presentation will provide an overview of the development of DES for PAD and also highlights exciting new technologies that are currently under development. A summary of current drug eluting balloons and stents is provided in Tables 1 and 2. The first generation DES has not proven to be significantly effective than BMS in the SFA lesions and there is still a paucity of data to reach any conclusions about the second-generation of stents. However, the BTK results are promising and such a treatment could supplant PTA and BMS as the primary treatment for these lesions. The Zilver PTX has already been FDA approved for peripheral use as of November 2012. If history has proven anything, it is that endovascular peripheral treatment methods take their cues from interventional cardiology, and it is only a matter of time before localized drug application in the manner of stents or balloons becomes a clinically acceptable standard of care.

Table 1a: DES Trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Drug</th>
<th>Location</th>
<th>Enrollment</th>
<th>Stent</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zilver PTX10</td>
<td>Paclitaxel</td>
<td>SFA</td>
<td>479</td>
<td>Zilver PTX</td>
<td>PTA &amp; BMS</td>
</tr>
<tr>
<td>SIROCCO22</td>
<td>Sirolimus</td>
<td>SFA</td>
<td>93</td>
<td>Sirolimus + SMART</td>
<td>Bare SMART</td>
</tr>
<tr>
<td>1PARADISE17</td>
<td>Paclitaxel</td>
<td>BTK</td>
<td>106</td>
<td>83% Cypher, 17% Taxus</td>
<td>N/A</td>
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<tr>
<td>Yukon-BTK24</td>
<td>Sirolimus</td>
<td>BTK</td>
<td>161</td>
<td>Yukon</td>
<td>BMS</td>
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<tr>
<td>1STRIDES21</td>
<td>Everolimus</td>
<td>SFA</td>
<td>104</td>
<td>Dynalink</td>
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</table>

Table 1b: DES Trials Cont’d
<table>
<thead>
<tr>
<th>Trial</th>
<th>Dose (µg/cm²)</th>
<th>Lesion (mm)</th>
<th>Follow-Up (mo)</th>
<th>Restenosis*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zilver PTX¹⁰</td>
<td>300</td>
<td>65</td>
<td>24</td>
<td>19% vs. 37% (BMS)</td>
</tr>
<tr>
<td>SIROCCO²²</td>
<td>90</td>
<td>85</td>
<td>24</td>
<td>23% vs. 21%</td>
</tr>
<tr>
<td>†PARADISE¹⁷</td>
<td>140</td>
<td>60</td>
<td>27</td>
<td>12%</td>
</tr>
<tr>
<td>Yukon-BTK²⁴</td>
<td>31</td>
<td>24</td>
<td></td>
<td>19% vs. 44%**</td>
</tr>
<tr>
<td>†STRIDES²¹</td>
<td>225</td>
<td>90</td>
<td>12</td>
<td>32%</td>
</tr>
</tbody>
</table>

*Defined as >50% binary, **12 month results, †Not a randomized-control trial

Table 2a: DEB Trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Location</th>
<th>Enrollment</th>
<th>Balloon</th>
<th>Control</th>
<th>Lesion (mm)</th>
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</thead>
<tbody>
<tr>
<td>DEBATE-BTK³³</td>
<td>BTK</td>
<td>120</td>
<td>In.Pact AmphiRon</td>
<td>Plain Balloon</td>
<td>122</td>
</tr>
<tr>
<td>DEBELLUM³⁴</td>
<td>SFA, BTK</td>
<td>50</td>
<td>In.Pact Admiral and AmphiRon</td>
<td>Plain Balloon</td>
<td>75</td>
</tr>
<tr>
<td>FemPac³⁵</td>
<td>SFA</td>
<td>87</td>
<td>Paccocath</td>
<td>Plain Balloon</td>
<td>60</td>
</tr>
<tr>
<td>Katsanos³⁶</td>
<td>AV Fistula</td>
<td>40</td>
<td>In.Pact Pacific</td>
<td>Plain Balloon</td>
<td>58</td>
</tr>
<tr>
<td>LEVANT I³⁷</td>
<td>SFA</td>
<td>101</td>
<td>Moxy</td>
<td>Plain Balloon</td>
<td>81</td>
</tr>
<tr>
<td>PACIFIER³⁸</td>
<td>SFA</td>
<td>91</td>
<td>In.Pact Pacific</td>
<td>Plain Balloon</td>
<td>70</td>
</tr>
<tr>
<td>THUNDER³⁹</td>
<td>SFA</td>
<td>154</td>
<td>Paccocath</td>
<td>Plain Balloon</td>
<td>74</td>
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</table>

Table 2b: DEB Trials Cont’d
<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Event Rate 1</th>
<th>Event Rate 2</th>
<th>Mean Event Rate 1 ± SD 1</th>
<th>Mean Event Rate 2 ± SD 2</th>
<th>Comparison Rate 1 vs. Rate 2</th>
<th>Comparison Rate 2 vs. Rate 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>DEBATE-BTK</td>
<td>12</td>
<td>29% vs. 72%</td>
<td>N/A</td>
<td>6% vs. 24%</td>
<td>0.5±1.4 vs. 1.6±1.7</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>DEBELLUM</td>
<td>6</td>
<td>9% vs. 29%</td>
<td>6% vs. 24%</td>
<td>0.5±1.1 vs. 1.0±1.1</td>
<td>N/A</td>
<td>8% vs. 36%</td>
<td>N/A</td>
</tr>
<tr>
<td>FemPac</td>
<td>18</td>
<td>7% vs. 17%</td>
<td>7% vs. 33%</td>
<td>0.5±1.1 vs. 1.0±1.1</td>
<td>N/A</td>
<td>8% vs. 36%</td>
<td>N/A</td>
</tr>
<tr>
<td>Katsanos</td>
<td>6</td>
<td>25% vs. 70%</td>
<td>20% vs. 65%</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>LEVANT I</td>
<td>6</td>
<td>28% vs. 51%</td>
<td>13% vs. 22%</td>
<td>0.5±1.2 vs. 1.1±1.4</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>PACIFIER</td>
<td>12</td>
<td>10% vs. 31%</td>
<td>7% vs. 28%</td>
<td>0±1.2 vs. 0.7±1.4</td>
<td>N/A</td>
<td>7% vs. 35%</td>
<td>N/A</td>
</tr>
<tr>
<td>THUNDER</td>
<td>60</td>
<td>17% vs. 44%</td>
<td>4% vs. 37%</td>
<td>0.4±1.2 vs. 1.7±1.8</td>
<td>N/A</td>
<td>12% vs. 39%</td>
<td>N/A</td>
</tr>
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</table>
Background: Consensus is lacking about the clinical importance of aortic root dilatation in assessment of the risk of cardiovascular disease.

Objective: The aim of this study was to assess the aortic root dilatation in patients with Diastolic Dysfunction (DD)

Methods: We retrospectively reviewed 2,262 medical records of patients receiving Echocardiograms at a University hospital between 2008 year and 2012 year. The patients were divided in two groups according to presence or absence of diastolic dysfunction. Aortic root diameter was measured by M-mode echocardiography, and LV diastolic function was evaluated by measuring the peak velocity of early (E) and late (A) diastolic transmitral blood flow, peak early diastolic mitral annular velocity (E') by Tissue Doppler echocardiography, and pulmonary venous sampling. Aortic dilation was assessed by measurement of aortic root diameter <3.7mm vs. ≥3.7mm

Results: In this study, correlations between aortic root diameter and echocardiographic features of left ventricular (LV) diastolic function were investigated in 2,262 patients. Aortic dilation was present in 11.34% of patients with DD vs. 7.84% without DD (p= 0.0132). Logistic regression analysis indicated that aortic dilation, age and hypertension were associated with presence of DD, after adjustment for sex, obesity, and DM (Aortic dilation: OR: 2.488, 95%CI 1.06-5.86, p=0.0370; Age: OR:1.052, 95%CI 1.04-1.07, p<.0001; HTN: OR: 3.508, 95%CI 2.08-5.93, p<.0001).

Conclusions: Aortic root dilation is strongly associated with DD
Objectives: The feasibility of laparoscopic aortic surgery has been adequately demonstrated. Our clinical experience with robot-assisted aortoiliac reconstruction for occlusive diseases, aneurysms, endoleak II treatment and hybrid procedures performed using the da Vinci system is herein described.

Methods: Between November 2005 and April 2012, we performed 250 robot-assisted vascular procedures. 189 patients were prospectively evaluated for occlusive diseases, 48 patients for abdominal aortic aneurysm, two for a common iliac artery aneurysm, two for a splenic artery aneurysm, one for an internal mammary artery aneurysm four for hybrid procedures, and four for endoleak II treatment post EVAR. The robotic system was applied to construct the vascular anastomosis, for the thromboendarterectomy, for the aorto-iliac reconstruction with a closure patch, for dissection of the splenic artery, and for the posterior peritoneal suture. A combination of conventional laparoscopic surgeries and robotic surgeries were routinely included. A modified, fully-robotic approach without laparoscopic surgery was used in the last 80 cases in our series.

Results: 241 cases (96.4%) were successfully completed robotically, one patient's surgery was discontinued during laparoscopy due to heavy aortic calcification. In eight patients (3.2%) conversion was necessary. The thirty-day mortality rate was 0.4%, and non-lethal postoperative complications were observed in 13 patients (5.2%).

Conclusions: Our experience with robot-assisted laparoscopic surgery has demonstrated the feasibility of this technique for occlusive diseases, aneurysms, endoleak II treatment post EVAR and hybrid procedures. The da Vinci robotic system facilitated the creation of the aortic anastomosis, and shortened the aortic clamping time as compared to purely laparoscopic techniques.
ENDOVENOUS ABLATION THERAPY FOR TREATMENT OF VENOUS INSUFFICIENCY: COMPARATIVE STUDY EVALUATING EFFICACY BETWEEN LASER AND RADIO FREQUENCY IN SYMPTOMATIC VENOUS INSUFFICIENCY

Lorven Heart & Vascular Institute, Ocala, FL, USA

Objective: Evaluating efficacy and patient tolerance between Radiofrequency (RF) and LASER Endovenous Ablation in patients with symptomatic venous insufficiency. Background: Over 50 million people suffer from symptomatic venous insufficiency in US and as the population ages, these numbers are increasing (Bergan, 2007). The two most common treatments are Radiofrequency Ablation (RF) and Laser Ablation. Each of these options has its limitations. The efficacy of the two treatment options is unknown. Methods: Single center, comparative prospective study of 130 patients in each group (RF and LASER) between January 2013 to March 2013. Patient surveys were conducted at 72 hours and one month post procedure to answer five variables including: decreased leg pain, decreased leg swelling, improved walking distance, improved skin color, and improved quality of life (QOL). Data is tabulated and a P value obtained for each groups to compare the efficacy and statistical significance. Results: We found that Laser Endovenous ablation outperformed RF ablation in all treatment variable studied. Improvement was 96% vs. 91% (P=0.7) for decreased leg pain, 93% vs. 81% (P=0.7) for swelling, 89% vs. 81% (P=0.7) for walking distance, 73% vs. 56% skin color (P=0.03) improvement and 96% vs. 86 (P=0.5) for QOL. Conclusions: The study clearly demonstrates the benefit of Laser Ablation over RF in all study variables. Laser Fiber technology is fast advancing with newer 1610 fiber and have even better outcomes. Considering the low cost of laser to Medicare and patients and significant healthcare advantage this should be widely adapted to vascular clinical practice.
PL08  Plenary Session
VASCULAR BIOLOGY, IMMUNE MEDIATED SURVIVAL AND OXIDATIVE STRESS

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STATIN EFFECTS BEYOND LIPID LOWERING: ATORVASTATIN INHIBITION OF MYOCARDIN EXPRESSION IN VASCULAR SMOOTH MUSCLE
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Department of Biochemistry & Molecular Biology, University of Calgary, Calgary, Alberta, Canada

3-hydroxy-3-methylglutaryl (HMG)-coenzyme A (CoA) reductase inhibitors (statins) have lipid-lowering effects, contributing to significant reduction of morbidity and mortality of cardiovascular disease. However, many of these beneficial effects on cardiovascular disease could not be explained by its lipid-lowering effects. Inhibition of HMG-CoA reductase CoA reduces production of isoprenoid intermediates in the cholesterol biosynthetic pathway, which also decreases post-translational modifications of various signaling proteins, such as RhoA. This effect on peripheral tissues or cells may contribute to non-lipid-lowering effects by statins. It was previously reported that statins attenuate spontaneous contraction of smooth muscle (SM) through inhibiting the RhoA-ROCK pathway, and activation of this pathway increases the gene expression of myocardin, a coactivator of serum response factor (SRF). Myocardin stimulates the expression of SM contractile proteins. Importantly, atorvastatin (ATV) was reported to inhibit the expression of myocardin and SM alpha-actin in human fetal penile smooth muscle cells (SMCs). Therefore, we have investigated whether ATV reduces contractility of the blood vessel through inhibiting myocardin and its target genes. Our research has revealed that ATV indeed reduced the expression of myocardin and its target genes both in vivo and in vitro. Mevalonate and GGPP reversed ATV-induced inhibition of these gene expression. Activation of RhoA and its membrane translocation were also inhibited by ATV in human vascular SMCs. We conclude that ATV directly inhibits vascular contractility through reduction of myocardin gene expression in vascular SMCs.
CROSS-TALK BETWEEN NADPH OXIDASE AND MITOCHONDRIA FOR ROS-DEPENDENT VEGF SIGNALING AND ANGIOGENESIS

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University of Illinois at Chicago, Chicago, IL, USA

Angiogenesis is a key process involved in normal development and wound repair as well as in ischemic cardiovascular disease. Although excess amount of reactive oxygen species (ROS) have cytotoxic effects, ROS at proper levels function as signaling molecules to mediate VEGF-induced angiogenesis and post-ischemic neovascularization. However, underlying molecular mechanisms remain unknown. Here we demonstrate that the adaptor protein p66Shc, a key regulator of mitochondrial ROS (mtROS) production, mediates interaction between NADPH oxidase (Nox)-derived ROS and mtROS, thereby promoting VEGF receptor type2 (VEGFR2)-dependent signaling in endothelial cells (ECs) as well as postnatal angiogenesis in vivo. Mechanistically, VEGF stimulation of human cultured ECs rapidly increases phosphorylation of p66Shc on Ser36, which is prevented by Nox inhibitor or Nox2 siRNA. Adenovirus-mediated transfer of phosphorylation-defective mutant p66shc (S36A) or mitochondria-targeted catalase or p66Shc siRNA inhibits VEGF-stimulated mtROS production; VEGFR2 autophosphorylation (VEGFR2-pY); EC proliferation and migration; capillary-tube formation in 3D-collagen gels. Moreover, VEGF-induced p66shc (pS36)-mtROS axis induces activation of VEGFR2 through oxidative inactivation of PTP1B that dephosphorylates VEGFR2. In vivo, p66shc (pS36) is increased in a mouse hindlimb ischemia model, and adenovirus gene transfer of p66shc (S36A) inhibits blood flow recovery and capillary density in ischemic tissues after ischemic injury.

Conclusions: VEGF-induced pS36-p66Shc links Nox2-derived ROS and mtROS to promote VEGFR2 activation through PTP1B oxidation, leading to post-ischemic neovascularization.
The CCN family of proteins consists of six secreted extracellular matrix associated proteins. Each member contains four cysteine-rich modular domains that include insulin-like growth factor-binding domain, von Willebrand factor type C module, thrombospondin domain, and C-terminal cysteine knot-like domain. CCNs have a broad array of biological functions to oversee vascular integrity and survival. In particular, Wnt1 inducible signaling pathway protein 1 (WISP1), a member of the CCN family termed CCN4, has been shown to have increased expression during cardiac ischemia and in primary neurons during exposure to oxidative stress that may correlate with enhanced cellular survival. WISP1 fosters cellular survival through wingless mediated pathways, phosphatidylinositol-3-kinase (PI 3-K), and protein kinase B (Akt). These pathways can converge upon the mammalian target of rapamycin (mTOR) that has been shown to modulate inflammatory cell survival that is necessary to avert injuries such as amyloid toxicity and oxidative stress. One component that can regulate the activity of mTOR is the proline rich Akt substrate 40 kDa (PRAS40). We therefore investigated whether WISP1 could preserve inflammatory microglial cellular integrity that relied upon mTOR signaling and its regulatory component PRAS40. We show that WISP1 and the mTOR signaling pathways of p70 ribosomal S6 kinase (p70S6K), the eukaryotic initiation factor 4E-binding protein 1 (4EBP1), and PRAS40 are novel considerations for targeted therapies that can be relevant during degenerative cell injury.
CORONARY VASOMOTOR REGULATION BY ENDOTHELIN-1 AND OXIDATIVE STRESS

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Departments of Medical Physiology and Surgery, Texas A&M Health Science Center, Temple, TX, USA

Endothelin-1 (ET-1) is a potent vasoconstrictor implicated in the development of coronary heart diseases, but its signaling for coronary vasoconstriction remains elusive. Herein, we probed the role of voltage-gated Ca2+ channels (VGCCs), phospholipase C (PLC), myosin light chain kinase (MLCK), protein kinase C (PKC) and Rho kinase (ROCK) in the coronary arteriolar constriction to a pathologic concentration of ET-1 (0.1 nM). Porcine coronary arterioles (40-70 µm) were isolated, cannulated and pressurized for vasomotor assessment using videomicroscopic techniques. Coronary arterioles developed basal tone and constricted to ET-1 in a manner sensitive to ETA receptor blocker, zero-extraluminal Ca2+, and PLC inhibitor. Inhibiting VGCCs by nifedipine or MLCK by ML-9 abolished basal tone without affecting vascular response to ET-1. ROCK inhibitor H1152 blocked vasoconstriction to ET-1 but not to PKC activator PDBu. Additionally, the broad-spectrum PKC inhibitor bisindolylmaleimide XI blocked vasoconstriction to PDBu but not to ET-1. The PKC-activated CPI-17 protein was undetectable in coronary arterioles. Moreover, ET-1 elicited phosphorylation of myosin-binding subunit (MBS) in H1152-sensitive manner. Knockdown of ROCK2, but not ROCK1, expression by siRNA inhibited vasoconstriction to ET-1. Exposure of coronary arterioles to a subthreshold concentration of ET-1 (10 pM, 1 hr) promoted superoxide production in vascular wall and caused impaired endothelium-dependent, nitric oxide-mediated vasodilation. We conclude that the sequential activation of ETA receptors, PLC and the VGCC-independent Ca2+ entry leads to vasoconstriction to ET-1 via a pathway involved in ROCK2-associated MBS phosphorylation independent of PKC signaling. Moreover, the sub-vasomotor level of ET-1 leads to endothelial dysfunction due to oxidative stress.
IL-10 AND INNATE SIGNALING IN CARDIOMYOCYTE PROTECTION
A. Bagchi, A. Sharma, G. Akolkar, P.K. Singal
Institute of Cardiovascular Sciences, St. Boniface Hospital Research Centre, University of Manitoba, Winnipeg, Canada

Interleukin-10 (IL-10) has been shown to have anti-inflammatory properties. It is suggested to counterbalance many adverse effects of proinflammatory cytokine, tumor necrosis factor (TNFα). IL-10 suppresses the production of TNFα and many other proinflammatory cytokines. TNFα–induced oxidative stress as well as apoptosis are also known to be mitigated by IL-10. Moreover, improvement in cardiac function after treatment with various drugs is also shown to be associated with an increase in IL-10 content. We have recently obtained evidence that IL-10 can also activate the innate signaling in cardiomyocytes. Such signaling may also involve an activation of TLR4, its co-receptor CD14 and a downstream protein MyD88 in an intricate manner to control apoptosis as well as synthesis of some of the primary cytokines. IL-10 receptor blocker inhibits upregulation of TLR4 and its downstream effects suggesting a linkage between IL-10 and TLR4 activation. Based on these data, it is suggested that optimal levels of IL-10 may be a new therapeutic strategy towards a healthier heart. (Supported by CIHR)
THE ROLE OF NITRIC OXIDE/PEROXYNITRITE IMBALANCE IN THE ISCHEMIC HEART
H. Wang, T. Malinski
Ohio University, Athens, OH, USA

Background: The functional endothelial cells are the main source of nitric oxide (NO) in the heart. NO release in the beating heart is stimulated by mechanical forces during systole and diastole. NO release can be also stimulated in the heart by chemical pathways, i.e. epinephrine. The highest concentration of NO (1.5 to 2 micromoles/liter) is produced by endocardium. A concentration of peroxynitrite (ONOO-) in the beating heart is minimal (<30 nanomoles/liter). ONOO- is generated after the reaction of NO with superoxide (O2.-). In dysfunctional endothelium, a main source of O2.- is nitric oxide synthase and NAD(P)H.

Methods and Results: Nanosensors with diameter <300 nanometers were used to measure: NO, O2.-, and ONOO-. A module of catheter protected nanosensors was placed in the left ventricular wall of the heart of WKY rats. A rapid increase in NO was observed after 15 s of ischemia. The increase in NO was accompanied by the increase in O2.- and ONOO-. At about 9 min, NO reached a maximum concentration and decreased rapidly after that, to 30 to 50 nanomoles/litre after 15 min of ischemia. A decrease in the NO to ONOO- ratio correlated directly with an increase of myocardial infarction. After 15 min of ischemia, the cytoprotective effect of NO is diminished while the cytotoxic effect of ONOO- reached the maximum. ONOO- is the main product of nitroxidative stress. In the ischemic heart, a high concentration of ONOO- can trigger a chain of reactions leading to apoptosis, necrosis, and myocardial infarction.
It has become clear during the past decade that endothelial nitric oxide synthase (eNOS) can transform into a superoxide-generating/pro-oxidant enzyme, when its essential cofactor tetrahydrobiopterin (H4B) becomes deficient. This phenomenon is now referred to as eNOS uncoupling. During the past 7-8 years my laboratory has pioneered the discovery that endothelial dihydrofolate reductase (DHFR) is critical for physiological regulation of nitric oxide (NO) production; and that a DHFR deficiency mediates angiotensin II uncoupling of eNOS in cultured endothelial cells, (Proc Natl Acad Sci U S A. 2005), hypertensive mice (Journal of Molecular and Cellular Cardiology 2009), and animals with type I diabetes mellitus (Diabetes 2007). Our group has further shown that folic acid administration is highly effective in recoupling eNOS via restoration of DHFR function (Journal of Molecular and Cellular Cardiology 2009; Hypertension 2011). Our latest work has identified upstream signaling events leading to dysfunction of DHFR in pathological conditions that involve activation of NADPH oxidases. Follow-up studies from other independent groups confirming our observations on the key regulatory role of DHFR in cardiovascular pathophysiology will also be discussed.
HYPERCHOLESTEROLEMIA-INDUCED OXIDATIVE STRESS IN THE HEART

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Hypercholesterolemia increases the generation of reactive oxygen species which could induce oxidative stress in the heart. The objectives of this study were to determine if a) hypercholesterolemia induces oxidative stress in the heart, b) magnitude of oxidative stress is dependent upon duration of hypercholesterolemia, and c) vitamin E an antioxidant suppresses, regresses, and slows the progression of hypercholesterolemia-induced oxidative stress in the heart.

The studies were conducted in hypercholesterolemic rabbits. The serum levels of total cholesterol, and oxidative stress parameter malondialdehyde (MDA) and antioxidant reserve cardiac chemiluminescent (cardiac CL) activity of cardiac tissue were measured. Hypercholesterolemia induced by high cholesterol diet increased the MDA content and decreased the antioxidant reserve of cardiac tissue. The extent of oxidative stress in the heart was dependent upon the duration of hypercholesterolemia. Vitamin E reduced the MDA content and increased the antioxidant reserve of the heart in suppression study. Vitamin E reduced the MDA content and increased the antioxidant reserve of the cardiac tissue in slowing of progression study. In regression study Vitamin E did not reduce the MDA content but increased the antioxidant reserve of the heart.

In conclusion hypercholesterolemia induces oxidative stress in the heart, the extent of which is dependent upon the duration of hypercholesterolemia. Vitamin E suppresses, slows the progression but does not regress hypercholesterolemia – induced oxidative stress in the heart.
CD137 DEFICIENCY REDUCES THE DEVELOPMENT AND PLAQUE INSTABILITY OF ATHEROSCLEROSIS

G.T. Oh¹, I.H. Jung¹, J. Jin¹, D.Y. Kim²
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2. Seoul National University, Seoul, Korea

CD137 (4-1BB), a member of the TNFRSF family, has been reported to be expressed in human atherosclerotic plaques and promotes development of plaque inflammation. In mouse study, we found that CD137 exacerbates atherosclerosis via combined actions on immune and vascular cells. But limited information are available on the exact role of CD137 signaling in plaque stability of advanced atheroma. Thus, this study tries to elucidate the role of CD137 signaling in plaque stability. We established atherogenic ApoE−/− and ApoE−/-CD137−/- mice. These mice were fed with normal chow diet for 66 weeks. We confirmed CD137 expression on macrophages and smooth muscle cells in plaque. Then, we examined formation of atherosclerotic plaque with oil red-O staining. As a result, ApoE−/-CD137−/- mice had little plaque in aorta. In plaque of ApoE−/-mice, infiltrated macrophages and necrotic core size were increased. Also, collagen contents were decreased and migrated smooth muscle cells. In addition, MMP-9 expression on macrophages were increased in ApoE−/- mice and other membrane type MMP-14 expression was increased in aorta of ApoE−/- mice. Our results suggest that CD137 signaling induces unstable plaque in hyperlipidemic mice. As CD137 signaling increases more inflammation and formation of plaque lesion, CD137 signaling contributes to the formation of necrotic core. And CD137 up-regulates MMP-9, -14 expression on macrophage, which in turn can trigger collagen break down. Thus, blockade of CD137 signaling would alleviate plaque stability in atherosclerosis.
Background and Objectives: Echocardiographic contrast (EC) improves the diagnostic accuracy of suboptimal echocardiograms. In October 2007 the FDA placed a black box warning on the label of the perflutren based agents Definity and Optison, contraindicating their use in patients with pulmonary hypertension (PHT) and unstable cardiopulmonary status, after serious cardiopulmonary reactions occurred in temporal relation to EC administration. In 2008 and 2011 the FDA revised the black box warning, allowing their use in this same population. However, limited data exist regarding the safety profile of these agents in patients with PHT.

Methods: Consecutive hospitalized patients with PHT who were referred for echocardiographic evaluation (including stress echo) at the participating institutions, but required EC were included. All patients received the EC agent Definity. We evaluated these patients for serious adverse events (respiratory decompensation, hypotension, syncope, convulsions, arrhythmias, anaphylactic reactions, or death) occurring within 24 hours of EC administration.

Results: We included 1513 patients (69 ± 14 years, 55% males, BMI 33 ±9 kg/m²). Our patients were at high risk for cardiovascular and pulmonary events. 911 (60%) had mild PHT, 515 (34%) moderate PHT, and 87 (6%) severe PHT. The mean PASP in the respective groups were: 41 ± 4 mm Hg, 55 ± 5 mm Hg, and 78 ± 9 (range 70-122) mm Hg. No deaths or serious adverse events related to the use of the EC agent Definity were observed in our study population.

Conclusion: The use of the EC agent Definity is safe in hospitalized patients with PHT.
MDCT QUANTIFICATION OF EXTRACELLULAR VOLUMES IN ACUTE AND SCARRED MYOCARDIAL INJURIES

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University of California San Francisco, San Francisco, CA, USA

Objective: To use MDCT in quantifying extracellular volume (ECV) in patchy and homogeneous myocardial infarct.

Background: Patchy infarct is an increasingly recognized cardiac pathology resulted from coronary intervention and systemic thrombi. MDCT has not been used to quantify ECV in patchy infarct.

Methods and Results: Under X-ray guidance (n=8 pigs/group), 16mm³ or 32mm³ microemboli were delivered in the LAD coronary artery. In another groups LAD was occluded for 90min followed by 3 days or 5 weeks reperfusion. A 128-MDCT scanner was used to acquire images before and after (3,5,10, 15min) injecting Omnipaque. Signal attenuation (SA) were obtained from the myocardium (remote and site of damage) and blood. ECV was determined from $\frac{1 - \text{hematocrit}}{\text{the difference between pre and post myocardial SA/the difference between pre and post blood SA}}$. The ECV significantly and progressively increased with the severity of injury: infarct caused by 16mm³ < 32mm³< 90min LAD occlusion in acute and scar infarct (Table 1). At 5 weeks, remote myocardium showed reduction in ECV related to the compensatory hypertrophy. Microscopic examination confirmed the damage in interventional animals, but not controls.

Conclusions: ECV provides quantitative information in patchy and homogeneous infarct. The method may be useful in the clinical setting and particularly in patients suffer chest pain without visible infarct.

LONG-TERM FOLLOW-UP OF CORONARY COMPUTED TOMOGRAPHY IN PATIENTS WITH CHEST PAIN AT INTERMEDIATE RISK

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1. Fondazione IRCCS Cà Granda, Cardiology, Milan, Italy
2. Cardiothoracic Centre, Monaco, MC

Background: Data on the long-term outcome of 64-slice coronary computed tomography (CCT) in patients with first-time chest pain and intermediate risk of coronary artery disease (CAD) are still scarce. Objective: The aim of this study was to assess the long-term incremental value of CCT in a homogeneous patients group. An analysis based on plaque texture was performed. Methods: A total of 222 patients (136 men [61%], age 59±11 years) with chest pain at intermediate risk of CAD and no previous cardiac events underwent 64-slice CCT. Coronary lesions were considered obstructive or not based on a threshold of 50% luminal narrowing. Plaques were classified as calcified, non-calcified and mixed based on type. End-point during follow-up was major adverse cardiac events (non-fatal myocardial infarction, unstable angina requiring hospitalization, myocardial revascularization). Results: Coronary plaques were detected in 162 (73%) patients. Coronary artery stenosis was significant in 62 patients. Normal arteries were found in 59 patients (27%). During a mean follow-up of 4.8±0.8 year 30 cardiac events occurred. The annualized event rate was 0% in patients with normal coronary arteries, 1.2% in patients with non-significant obstructions and 4.2% in patients with significant obstructions (p<0.01). Predictors of cardiac events were the presence of significant stenosis, proximal stenosis and multivessel disease. Non-calcified and mixed plaques were carrying the worse prognosis (p<0.05) [see figure].

Conclusion: CCT provides long-term incremental value in patients at intermediate risk of CAD with first-time chest pain.
WHO IS YOUNG AT HEART AND WHEN? DATA FROM THE MIND YOUR HEART STUDY

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1. California Pacific Medical Center; San Francisco, CA, USA
2. University of California, San Francisco; San Francisco, CA, USA

Background. The age-sensitive ratio of mitral inflow E wave to A wave (E/A) velocity is often the initial parameter considered in the evaluation of diastolic function. To appropriately direct a comprehensive evaluation of diastolic function, we sought to improve the characterization of the influence of age on E/A ratio.

Methods. We analyzed echocardiographic data from the Mind Your Heart Study, a cohort of outpatients recruited from two San Francisco area Veterans Affairs medical centers designed to examine the effect of mental health on cardiovascular outcomes. Individuals with a history of heart disease or hypertension were excluded, leaving 319 veterans for these analyses. We examined E/A by five-year increments and performed linear and logistic regression analyses to predict trends in E/A and E dominance.

Results. Within the age ranges of the population (24 to 91 years), there is a steady gradual decline in absolute E/A ratio (beta coefficient/year -0.018, p<0.001) and the odds of E dominance similarly declines with age (OR/year= 0.89, p<0.001). Despite this decline, 90% of individuals below the age of 50 years maintain E dominance. Beyond age 50, 55% maintain E dominance, and beyond age 70, only 28% have E dominance.

Conclusions. This study examines the effect of age on diastolic function as represented by the mitral inflow signal E/A ratio and permits recognition of age appropriate changes. These data will refine the separation of normal alterations in the ratio from alterations due to pathologic influences.
OPTICAL COHERENCE TOMOGRAPHY FINDINGS OF LESION WITH VERY LATE RESTENOSIS AFTER BARE METAL STENT IMPLANTATION

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Background: Although in-stent restenosis (ISR) after bare-metal stent (BMS) implantation peaks in the early phase, very late ISR is occasionally observed beyond a few years after BMS implantation. To date, this mechanism has not been fully clarified.

Methods and Results: We compared the morphological characteristics of very late ISR (VL-ISR (n=43): later than 5 years, without restenosis within the first year) to those of early ISR (E-ISR (n=39): within first year) using optical coherence tomography (OCT). Qualitative restenotic tissue analysis included assessment of tissue structure (homogeneous or heterogeneous), presence of microvessel, disruption with cavity of intima, and intraluminal material, and was performed at every 1mm slice of the entire stent.

The mean ratio of cross sections with heterogeneous intima in the entire stent was significantly higher in VL-ISR group compared to E-ISR group (60.5\% vs 5.8\%, p<0.0001), with heterogeneous intima being more frequently observed at minimum lumen area (MLA) site in VL-ISR group (90.7\% vs 17.9\%, p<0.0001). Disrupted intima with cavity and intraluminal material were also more frequently observed in VL-ISR group in the entire stent (18.6\% vs 0\%; 20.9\% vs 2.6\%; p<0.03) as well as at MLA site (13.9\% vs 0\%;16.2\% vs 0\%; p<0.03).

Conclusions: The morphological characteristics of restenotic tissue with VL-ISR were different from those with E-ISR, which were similar to atherosclerotic plaque in native coronary artery. In BMS, progression of the atherosclerotic process within neointima after stent implantation may be associated with very late ISR.
CORONARY CHRONIC TOTAL OCCLUSIONS; EVALUATION AND PREDICTION OF PERCUTANEOUS INTERVENTION OUTCOME BY COMPUTED TOMOGRAPHY CORONARY ANGIOGRAPHY AS COMPARED TO CONVENTIONAL CORONARY ANGIOGRAPHY

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Aims: Determine the role of computed tomography coronary angiography (CTCA) and conventional coronary angiography (CCA) in evaluation of coronary chronic total occlusions (CTOs) and prediction of outcome of percutaneous coronary intervention (PCI) for coronary CTOs.

Methods and results: Thirty four CTO PCI attempts were performed in 31 coronary CTO lesions. CTCA was performed using 320-channel scanner. Median estimated CTO length by CTCA was 22.2 mm (range 7.7-89.4) and by CCA was 20.9 mm (range 6.1-80.7); p= 0.49. CTO calcification was detected by CTCA in 24 (77.4%) CTO lesions and by CCA in 14 (45.2%) CTO lesions; p=0.019. Severe calcification; >50% of cross sectional area (CSA) was detected by CTCA in 12 (38.7%) CTO lesions. Eighteen (52.9%) of the attempts utilized the antegrade approach, 3 (8.8%) utilized the retrograde approach alone and 13 (38.2%) of the attempts utilized a bidirectional approach. Overall success rate per CTO PCI attempt was 85.3%. Severe calcification by CTCA was the only predictor of failure of the antegrade approach; p=0.036. There were trends of longer estimated CTO duration and CTO length in the failed antegrade approaches (p=0.073, p=0.063 respectively). None of the CTCA or the CCA factors predicted the retrograde approach outcome. A trend of retrograde approach successful outcome was noted with higher Werner collateral channel grades (p=0.057).

Conclusions: CTCA provides better means of detection and assessment of calcification within the coronary CTO lesions than CCA. Severe calcification (>50% of CSA by CTCA) was the only statistically significant predictor of antegrade approach failure in CTO PCI.
UNVEILING RESTRICTIVE CARDIOMYOPATHIES WITH CARDIAC MAGNETIC RESONANCE

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Objectives: To evaluate the diagnostic role of cardiac magnetic resonance (CMR) imaging in patients with restrictive cardiomyopathies (RC).

Background: Owing to its superior temporal and spatial resolution and ability to characterize tissue, CMR is an ideal noninvasive imaging tool for patients with restrictive cardiomyopathy. However, data on the use of CMR is limited.

Methods and Results: Over the last 5 years, we identified patients with restrictive cardiomyopathy from the CMR database demonstrating characteristic CMR features of restrictive cardiomyopathy. Comprehensive CMR protocols including T1- and T2-weighted signals, cine, perfusion, and myocardial delayed enhancement (MDE) sequences were performed on a 1.5-Tesla scanner. Corresponding PET and echocardiographic images were included when available.

**FIGURE:** RV= right ventricle, LV= left ventricle, XX= myocardial delayed enhancement (MDE)

Iron cardiomyopathy is characterized by increased left ventricular mass, no MDE, and myocardial signal attenuation from iron deposition (dark myocardium) on CMR (panel A). Similarly, cardiac amyloidosis also has increased cardiac mass, but is associated with speckled appearance on echocardiography (panel C), and diffuse subendocardial MDE on CMR (panel D). Eosinophilic myocarditis is associated with diffuse subendocardial MDE, systolic dysfunction and thrombus formation (panel B). CMR features of sarcoidosis and Fabry’s disease are also presented.

Conclusions: Recognizing the distinct CMR findings in patients with restrictive cardiomyopathy has important diagnostic implications. CMR holds promise in differentiating between various restrictive cardiomyopathies including iron cardiomyopathy, amyloidosis, eosinophilic myocarditis, sarcoidosis, and Fabry’s disease, and may reduce the need for biopsy.
LOW RISK CHEST PAIN PATIENTS MIGHT NOT BENEFIT FROM IN PATIENT STRESS TESTING

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Background: Assessment of non-cardiac chest pain places a considerable burden on healthcare resources requiring serial cardiac enzymes, electrocardiograms and stress tests to detect suspected coronary artery disease (CAD).

Objective: The purpose of this study was to examine the utilization of stress tests and its impact on low risk chest pain admissions.

Methods: A retrospective observational chart review of patients admitted to Abington Memorial Hospital from January 2011 to April 2011 was conducted. Patients without prior history of CAD were included if they had atypical chest pain, normal initial EKG and first troponin.

Results: Out of 272 consecutive chest pain patients, 164 patients were included based on the inclusion criteria. Mean age was 60 yrs and 33.5\% were male. Risk factors included: hypertension (63\%), diabetes mellitus (23\%), smoking (20\%), dyslipidemia (49\%), and family history of CAD (38\%). Two patients had positive troponin (peak level 0.43 ng/ml) and subsequent negative stress tests. A stress test was performed in 48\% of the patients. None of the stress tests were true positive. 97.4\% were negative. 2.6\% (2/78) were initially read as positive and were followed by cardiac catheterizations which revealed normal coronary arteries. Inpatient stress test increased patient’s length of stay by 17 hours on average. There were no acute coronary syndromes, no deaths, and no 30 day re-hospitalizations due to cardiac events in patients who did or did not had an inpatient stress test.

Conclusion: Ordering stress tests in low risk chest pain patients is low yield with a high false positive rate and significantly increases the length of hospital stay.
NON-INVASIVE ASSESSMENT OF THE LEFT VENTRICULAR END-DIASTOLIC PRESSURE USING PORTABLE ULTRASOUND MEASUREMENTS OF THE RIGHT INTERNAL JUGULAR VEIN

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2. Virginia Tech Carilion School of Medicine
3. Virginia Tech
4. Carilion Roanoke Memorial Hospital

Objective: To determine whether quantitative ultrasound measurements of the right internal jugular vein (RIJV) correlate with the left ventricular end-diastolic pressure (LVEDP)

Background: Direct measurement of LVEDP is invasive, estimation by physical exam is inaccurate, and non-invasive techniques are technically challenging.

Methods: We performed a prospective, cohort study (n=45). All adult patients undergoing non-emergent diagnostic cardiac catheterization were eligible for inclusion. RIJV parameters including those indexed to body surface area (BSA) were measured. Receiver operator curves (ROC) and logistic regression were completed for each parameter to determine which best correlated with elevated LVEDP (> 18 mmHg).

Results: Four patients had no LVEDP measurements and were excluded. Mean age was 59 years, 60% were males, 67% had hypertension, 11% had heart failure, 38% were obese, and 4% had mild COPD. Twenty-nine percent had elevated LVEDP. Of the various static and dynamic RIJV parameters tested, the indexed change in cross-sectional area (∆CSA/BSA) and ∆CSA had the best ROC characteristics and were similar (Table 1). None of the RIJV parameters correlated well with normal LVEDP (5-12 mmHg).

Conclusion: The ∆CSA/BSA was the RIJV parameter that best correlated with elevated LVEDP. It slightly outperformed the ∆CSA although the latter is easier to apply clinically.

Table 1. Measures of accuracy of RIJV parameters that best correlated with elevated LVEDP

<table>
<thead>
<tr>
<th>RIJV parameter</th>
<th>AUC (95% CI)</th>
<th>p value</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Phi coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>∆CSA/BSA</td>
<td>0.79 (0.64,0.95)</td>
<td>0.0002</td>
<td>67%</td>
<td>86%</td>
<td>0.46</td>
</tr>
<tr>
<td>∆CSA</td>
<td>0.78 (0.62, 0.94)</td>
<td>0.0004</td>
<td>92%</td>
<td>62%</td>
<td>0.49</td>
</tr>
</tbody>
</table>
THE INFLUENCE OF EARLY TRAINING IN TRANS-RADIAL VERSUS TRANS-FEMORAL APPROACH DURING SELECTIVE CORONARY ANGIOGRAPHY

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Objectives: To evaluate the hypothesis that with early training fellows develop equitable competency in radial access (RA) versus femoral access (FA) in doing selective coronary angiography (SCA) and exposure to radiation and contrast should be comparable among these two approaches.

Background: RA in doing diagnostic SCA has been shown to be technically challenging and to result in higher level of radiation and contrast dose when compared to FA. Methods: We performed a descriptive review of RA versus FA in 358 patients who underwent selective diagnostic coronary angiography between January 2010 and March, 2012, among fellows of various levels of training supervised by a single cardiologist. We compared the mean radiation dose, fluoroscopy time, and contrast dose among the three groups of general cardiology fellows divided by their year of training.

Results: Among the total of 358 patients, 184 had trans-radial approach and 174 had trans-femoral approach. There was no significant difference between the two approaches in the use of fluoroscopy as measured by the fluoroscopy time and radiation dose among the three groups of fellows. However the first year fellows had used significantly higher amount of contrast during trans-radial approach than during trans-femoral approach (p=0.02). Such a difference was not observed among second and third year fellows. Conclusions: With early exposure in training RA will likely result in equitable exposure to radiation dose and contrast dose when compared to FA in doing SCA despite the significantly higher dose of contrast use during the earlier part of training.
Objective: The cardioprotective role of coronary collateralization is unknown in multiethnic patients with STEMI. The aim of our study was to examine the ethnic variations in collateralization and its cardioprotective role in multiethnic patients with STEMI who underwent successful revascularization.

Methods: STEMI patients who underwent successful PCI were included. The collateral flow was graded as per the Rentrop classification and patients were categorized as having either significant collateral flow or poor/absent collateral flow to the infarct-related artery.

Results: 337 patients from 5 ethnic groups: Caucasian 55%, Asian 19%, Hispanic 12%, South Asian 10%, African American 4% were included who had a TIMI flow grade ≤ 1 before PCI, and TIMI III flow afterwards. 50 patients had significant collateral flow (Group A), whereas 287 patients had either poor or absent collateral flow (Group B). Ethnic, gender and age distributions and prior CAD were similar between the groups. Initial serum CPK levels were significantly lower in Group A (676 +/- 1392 ng/ml vs 1293 +/- 1987 ng/ml, P=0.03). However, peak serum CPK levels were similar between the groups. Presenting LVEF and discharge LVEF were similar between the groups. Incidence of cardiogenic shock, hemodynamic instability requiring IABP support and arrhythmias were similar between the groups.

Conclusions: This data shows no significant variability in collateralization amongst STEMI patients between ethnic groups. Contrary to prior data, the presence of prior CAD did not affect collateralization. Moreover, the presence of a well-developed collateral network does not appear to limit infarct size or early left ventricular function recovery.
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MICROVASCULAR OBSTRUCTION LIMITS MYOCARDIAL INFARCT RESORPTION

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Objective: To use contrast enhanced cardiac MRI in quantifying the effects of microvascular obstruction (MVO) on infarct resorption in swine model with poor collateral flow.

Background: It has been recently proposed that MVO limits delivery and transit of cellular components required for phagocytosis of cellular debris and nutrients needed for optimal infarct healing1.

Methods and Results: Group I animals (n=8) were subjected to myocardial infarction by LAD coronary artery occlusion, while group II (n=8) were subjected to myocardial infarction (LAD occlusion) plus MVO by injecting microemboli. All infarcts were reperfused after 90min occlusion and imaged at 3 days and 5 weeks. Delayed contrast enhanced MRI (DE-MRI) was used to measure myocardial infarct and MVO using ±3SD threshold method. DE-MRI illustrated myocardial infarct as hyperenhanced region in all animals and MVO as hypoenhanced region. The studied animals have matching infarct size on DE-MRI at 3 days (Table 1), but group I animals had significantly smaller MVO (4/8) than group II (8/8). Five weeks later, occlusion/reperfusion animals showed greater infarct resorption and less compensatory LV hypertrophy than occlusion/reperfusion plus microembolization and no evidence of MVO on DE-MRI.

Conclusions: MVO limits infarct resorption (healing). MRI has the potential to monitor infarct evolution.


Table 1. Myocardial infarct and MVO measurements from delayed contrast enhanced MRI.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Infarct (% LV)</th>
<th>MVO</th>
<th>Infarct (% LV)</th>
<th>MVO</th>
</tr>
</thead>
<tbody>
<tr>
<td>I occlusion/reperfusion</td>
<td>15.9±0.7</td>
<td>2.1±1.1</td>
<td>10.6±0.4 (34%)*</td>
<td>None</td>
</tr>
<tr>
<td>II LAD occlusion/reperfusion plus microemboli</td>
<td>16.2 ±0.7</td>
<td>5.7±0.2</td>
<td>12.8±0.4 (21%)*+</td>
<td>None</td>
</tr>
</tbody>
</table>

* P<0.05 compared with 3 days of same cohort, + P<0.05 compared with group I.
ACUTE MYOCARDIAL INFARCTION AND MULTIVESSEL DISEASE: DIFFERENT PERCUTANEOUS REVASCULARIZATION STRATEGIES IN REAL WORLD


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Objectives. The purposes of this study were to examine the differences in cardiac outcomes for ST-segment elevation myocardial infarction (STEMI) patients and multivessel disease (MVD) undergoing culprit vessel primary percutaneous coronary intervention (PCI) or multivessel PCI, either during primary PCI or as a staged procedure.

Background. A significant percentage of STEMI patients without hemodynamic compromise have MVD. However, the best revascularization strategy for non-culprit vessel lesions is still unknown.

Methods and results. STEMI patients with MVD undergoing primary PCI and prospectively enrolled in the REAL Registry between July 2002 and December 2010, were considered. A total of 2061 patients were analyzed, treated with culprit-only primary PCI (706), multivessel PCI during the index procedure (367), or with a staged PCI within 60 days (988). Culprit-only primary PCI was associated with a higher risk of mortality as compared to a staged multivessel PCI [Hazard Ratio (HR): 2.81, 95% confidence interval (CI): 1.34-5.89, p=0.006 for 30-day mortality and HR: 1.96, 95% CI: 1.38-2.78, p=0.0002 for 2-year mortality, respectively). Acute multivessel PCI was associated with a higher short-term mortality risk as compared to a staged PCI (HR: 2.71, 95% CI: 1.07-6.84, p=0.03); such difference disappeared at 2-year follow-up (HR: 1.11, 95% CI: 0.65-1.90, p=0.69).

Conclusions. Our findings support the current guidelines recommendation that culprit-only primary PCI should be performed in STEMI patients with MVD without hemodynamic compromise, followed by a staged non-culprit PCI within 60 days after the index procedure.
INFLAMMATION/LIPID SCORE MAY OUTPERFORM TIMI SCORE FOR PREDICTION OF PCI-TREATED STEMI OUTCOMES

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Background. Novel inflammatory and neurohumoral markers are potential prognostic factors after acute coronary syndromes. The aim of the study was to reassess the prognostic model after the first myocardial infarction (MI) treated with primary PCI (pPCI).

Methods. 85 patients (20 females) aged 61±9 years admitted with first ST-elevation MI and treated with pPCI. Laboratory panel extended with IL-1, IL-10, MCP-1, sFASl, NT-proBNP, fibrinogen and CRP were sampled prior to intervention. Patients were followed-up with regard to the occurrence of death, MI or ventricular fibrillation during 12 months follow-up.

Results. 27% pts reached the composite endpoint. We defined univariate predictors of 1-year prognosis: IL-10 (p=0.0014), HDL-cholesterol (OR=7.5; 95% CI 1.9-30.1, p=0.0001), creatine kinase (CK, p=0.007)) and CK-MB (p=0.05), left ventricular ejection fraction (p=0.026), TIMI risk score (p=0.027) and white blood count/WBC (P=0.029). In multivariate logistic regression model (86% correct, p=0.001) the independent prognostic factors were: HDL-cholesterol; HR=0,89 (0.81-0.98), p=0,0001; IL-10; HR=1,392 (1.01-1.96), p=0,014, and WBC; HR=1,39 (1.03-1.88), p=0,038. A prognostic score based on 3 factors: HDL<31,2 mg/dl, IL-10>0.4pg/ml, WBC>10800/mm³ yielded Kaplan-Meier's HR=10.4 (p<0.0001) when 2 or 3 factors were present (event rate 0%, 17% and 80% for scores 0, 1 and 2 or 3, resp.). TIMI score at optimal ROC-defined threshold>3 offered low HR=2.37 (p=0.028).

Conclusions. A simple prognostic score including white cell count, HDL-cholesterol and interleukin-10 concentration enabled optimized risk stratification and outperformed TIMI risk score in this study. These variables may improve prognostication in patients reperfused with primary percutaneous intervention as compared to TIMI score.
OUTCOME OF PATIENTS WITH ACUTE CORONARY SYNDROME REQUIRING INTENSIVE CARE UNIT ADMISSION

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Introduction: Small number of patients with acute coronary syndrome (ACS) treated with percutaneous coronary intervention (PCI) require Intensive Care Unit (ICU) admission following cardiogenic shock or out of hospital cardiac arrest (OOHCA). Data on outcome of this group is sparse.

Aim: To assess and compare outcome after PCI between ACS with cardiogenic shock (Group A) and ACS with OOHCA (Group B)

Methods: Patient demographics and ICU data between April 2010 and August 2012 was retrospectively collected and analysed.

Results: During the study period, 2478 patients were admitted to our hospital with ACS. 61 patients (2.5%) required ICU admission following PCI. Results are summarised in table 1.

<table>
<thead>
<tr>
<th></th>
<th>Cardiogenic shock Group A, n=29</th>
<th>OOHCA Group B, n=32</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean/SD)</td>
<td>69±12</td>
<td>62±18</td>
<td>0.67</td>
</tr>
<tr>
<td>Sex (male%)</td>
<td>45</td>
<td>52.4</td>
<td>0.78</td>
</tr>
<tr>
<td>Ventilation (%)</td>
<td>82.8</td>
<td>96.8</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Inotropes (%)</td>
<td>79.3</td>
<td>65.6</td>
<td>0.18</td>
</tr>
<tr>
<td>IABP (%)</td>
<td>96.5</td>
<td>68.7</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>CRRT (%)</td>
<td>24.1</td>
<td>6.2</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>ICU stay(median/range)</td>
<td>2(0-12)</td>
<td>4(0-38)</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Hospital stay(median/range)</td>
<td>5(0-68)</td>
<td>8(0-39)</td>
<td>0.23</td>
</tr>
<tr>
<td>Neurological complications(%)</td>
<td>10.3</td>
<td>40.6</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Mortality in hospital(%)</td>
<td>62.1</td>
<td>43.7</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>1 year survival(%)</td>
<td>41.1</td>
<td>61.2</td>
<td>0.13</td>
</tr>
</tbody>
</table>

Patient demographics were comparable. Ventilation, renal replacement therapy and balloon pump requirements were significantly higher in group A (p<0.05). Inotrope requirement was comparable. ICU stay was significantly longer in group B (p<0.05), however the overall hospital stay was comparable (p=0.23). The incidence of neurological complications was significantly higher in group B (10.3% vs 40.6%, p<0.05), however, in-hospital mortality was significantly lower (62.1% vs 43.7%, p<0.05). One year survival was similar in both groups.

Conclusion: Following PCI for ACS, only 2.5% patients required ICU admission. OOHCA group had better survival rate but significantly poor neurological outcome as compared to cardiogenic shock.
STEMI AS COMMON AS WE THINK IN SYMPTOMATIC PATIENTS WITH LEFT BUNDLE BRANCH BLOCK?
Hamad Medical Corporation, Doha, Qatar

Purpose: We studied the demographics, common symptoms and final diagnosis of patients with LBBB hospitalized in the cardiology department.

Methods: Retrospective analysis of the 20-year registry data (Jan 1991 to Jun 2011) of cardiac patients hospitalized at the General Hospital and the Heart Hospital, Doha, Qatar. Results: Of the 41438 patients admitted under cardiology department, 582 patients had LBBB (1.4%). LBBB patients were older (63±12 vs. 54±12 years, P=0.001), have more hypertension (56 vs. 40%, P=0.001), Diabetes (52% vs. 39%, P=0.004) and chronic renal failure (11% vs.4%, p=0.001). Compared to patients without LBBB, SOB was the main clinical symptom (57.3 % vs. 40.5%, p=0.004), followed by chest pain (31.7% vs. 52.2%, p=0.001). Among all symptomatic patients with LBBB, STEMI was diagnosed only in (3.9%, p=0.001), NSTEMI in (5.7%, p=0.57) and 35.2 % as unstable angina with p=0.03. On analyses based on presenting symptoms, only 1.4% of those who presented with shortness of breath had final diagnosis of STEMI as compare to 10.8% in those who presented with chest pain with p value of 0.001.

Conclusions: Among all comers with symptomatic left bundle branch block, STEMI is less likely regardless of the presenting symptoms compare to patient without LBBB. This may require further review of the current guidelines in symptomatic patient with new or presumed new LBBB.
QT Dispersion and T Wave Peak to End Time Significantly Change After Primary Percutaneous Coronary Intervention in Patients with Acute ST Elevation

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2: CareMore, Arizona, USA
3: University of Arizona, USA

Background: Acute ST elevation myocardial Infarction (STEMI) is associated with significant arrhythmia and cardiac arrest. QT prolongation can occur in the setting of ischemia or acute STEMI as a risk factor for arrhythmia. The goal of this study was to investigate QTc, QT dispersion (QTd) and T wave peak to end (TPE) times in this patient population and evaluate the effect of primary percutaneous coronary intervention (PCI) in STEMI patients on these indices.

Method: This study was a clinical trial, whereby eligible patients presenting with acute STEMI who were appropriate candidates for primary PCI were enrolled. QTc, QTd and TPE indices were calculated before and after the procedure.

Result: 80 patients (60 male, 20 female) with a mean age of 58.8 were evaluated. We found significant reduction in QTd after PCI (mean of 5.8 ms before vs. 3.6 ms after PCI, p<0.001) and significant reduction in TPE after PCI (mean of 9.7 ms before vs. 7 ms after PCI, p<0.001). QTc did not show significant changes before or after PCI (44.9 vs. 43.7, p value=.057)

Conclusion: Our study showed that primary PCI was effective in reducing the degree of arrhythmogenic indices such as QTd and TPE. Our finding suggests that ischemia induced QTd and TPE are important arrhythmogenic parameters responding to successful primary PCI and may be used as markers for successful reperfusion.
MICROEMBOLI EFFECTS ON LEFT VENTRICULAR FUNCTION, NECROSIS BIOMARKERS AND HISTOPATHOLOGY IN PRE-EXISTING AMI
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Objective: To use invasive and noninvasive methods (biopsy, cardiac necrosis biomarkers and MRI) to assess the effects of coronary microemboli on LV structure and function in swine AMI.

Background: Dislodged microemboli during PCI became a clinical problem because it is silent, lack of proper filters and sensitive detection method.

Methods and Results: A 3F balloon catheter was used for occluding the LAD artery (single insult) for 90min, delivering 32mm3 microemboli or both insults (double). Cardiac necrosis biomarkers, MRI LV function and myocardial damage on histopathology were determined and compared. MRI illustrated the drop in ejection fraction and increase in end systolic volume in single insult compared with controls. Microemboli in AMI caused additional reduction in ejection fraction and increase in LV volumes compared with single insult. Cine MRI also showed regional hypokinesis and akinesis in LAD territory in single insult compared with controls, but dysfunction was greatest (paradoxical systolic wall thinning) in double insult. Furthermore, significant increases in creatine-kinase and troponin-I were observed at 18hr in experimental cohorts. Microscopically, myocardial damage was less in single than double insult (14±1% LV mass versus 18±2%, P<0.03). Troponin-I showed differential effect of microemboli in AMI. Microscopy revealed various degrees of cellular damage, edema, microvascular obstruction, hemorrhage and inflammation.

Conclusions: Cine MRI, but not creatine-kinase, differentiates LV dysfunction in AMI after microembolization. The difference in myocardial damage between single and double insult was disproportionately small compared with the accentuated LV dysfunction, suggesting that myocardial necrosis is not the only factor governs LV function.
ACUTE MYOCARDIAL INFARCTION IN HOSPITALIZED PATIENTS WITH THROMBOTIC THROMBOCYTOPENIC PURPURA


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Objective: To identify the predictors of acute myocardial infarction (AMI) in hospitalized patients with thrombotic thrombocytopenic purpura (TTP).

Background: Several cardiac manifestations have been known to be associated with TTP. AMI in TTP has been described. Little is known about the magnitude of this problem, its risk factors, and its influence on mortality in patients hospitalized with TTP.

Methods: We used the National Inpatient Sample (NIS) database for the years 2001 to 2010. Patients aged above 18 years with the diagnosis of TTP (ICD-9 code 446.6) who received therapeutic plasmapheresis (ICD-9 code 99.71) were analyzed. Patients with AMI were identified using the HCUP Clinical Classification Software code (100 for AMI).

Results: A total of 4032 patients (68% women) were identified as having TTP. Of these patients, 228 (5.6%) also had the discharge diagnosis of AMI. Compared to the non-AMI group, patients with AMI were older, men, had a higher prevalence of cardiac risk factors, congestive heart failure (CHF), acute renal failure, acute cerebrovascular disease (CVD), longer length of stay and higher in-hospital mortality. By logistic regression analysis, independent predictors of AMI in TTP were age (OR 1.026; 95% CI 1.016-1.037), acute renal failure (OR 1.917; 95% CI 1.374-2.674), prior coronary artery disease (CAD) (OR 2.130; 95% CI 1.344-3.735), CHF (OR 2.642; 95% CI 1.779-3.922) and acute CVD (OR 3.598; 95% CI 2.409-5.372).

Conclusion: AMI was diagnosed in 5.6% of patients with TTP. Significant independent predictors of AMI in TTP were age, acute renal failure, prior CAD, CHF and acute CVD.
ANALYSIS OF CURRENT TREATMENT AND OUTCOMES FOR ACUTE MYOCARDIAL INFARCTION IN ETHIOPIA
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Background: Limited literature evaluates the state of care provided for patients with acute coronary syndromes (ACS) in Sub-Saharan Africa. We explored the medical therapies provided and short-term outcomes of patients admitted to a government-funded tertiary care hospital in Addis Ababa, Ethiopia.

Methods: Charts of all patients admitted with the diagnosis of ST segment elevation myocardial infarction (STEMI) or non-STEMI with biomarker confirmation over a six-month period in 2012 were reviewed.

Results: A total of 21 patients were admitted during this period with STEMI (71%) or non-STEMI (29%). The mean age was 58 years and 76% were male. Patient risk factors were as follows: 48% had hypertension, 29% had diabetes mellitus, 43% had hypercholesterolemia and 43% had tobacco use. Median time to presentation was 48 hours, with 28% of patients in Killip class III or IV. Echocardiography showed moderate or severe systolic dysfunction in 33% of patients. In-hospital mortality was 14%. Mean length of stay was 14 days. No patients were administered thrombolytics or underwent primary percutaneous coronary intervention (PCI). For medical therapy, 100% received aspirin and clopidogrel; 81% were given heparin, 95% received a statin; 91% received a beta blocker, 91% received ACE inhibitors, 52% received morphine, 10% received nitrates, 57% received furosemide and 14% required dopamine.

Conclusions: In this single center study in Ethiopia, in-hospital therapy for acute myocardial infarction, with the exception of lack of thrombolysis or PCI, generally follows current guidelines. Cost-effective strategies for reperfusion should be assessed to improve mortality rates.
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ANTICOAGULATION AND HEART VALVE DISEASE: IS IT TIME TO RECONSIDER WHO AND HOW?
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Intra cardiac thrombosis and thromboembolism long have been associated with heart valve diseases (VHD). However, except when atrial fibrillation (AF) coincides with VHD, anticoagulation seldom is considered unless a valve has been replaced, particularly with a mechanical prosthesis. The recent availability of new oral anticoagulants (NOACs), more convenient to use than the long-available warfarin regimens, requires reconsideration if this issue. In fact, VHD is thrombogenic even without AF. VHD promotes (1) turbulent flow with shear stresses that cause platelet activation; (2) excess thrombin generation; (3) high platelet CD40L, promoting aggregation; (4) roughened platelet surfaces activating platelets; (5) high P-selectin, fibrinogen, von Willebrand factor and anticardiolipin antibody titres; (6) endothelial dysfunction; (7) residual rheumatic inflammation after rheumatic fever. Moreover, prosthetic valve material activates platelets, but, at least when the mitral valve is involved, mitral replacement/repair with normalization of hemodynamics reduces platelet activation. In summary, VHD and, especially, prostheses used to replace diseased valves, are thrombogenic and are sources of systemic emboli, even without AF. VHD, especially mitral, are risk factors for AF. Antithrombotic therapy is standard when VHD and AF coincide and when valve prostheses are implanted. It is now time to reconsider such therapy in certain settings of VHD alone; NOACs may improve the therapeutic to adverse relation of antithrombotic therapy associated with warfarin, and now must be further studied in this setting.
NEW INSIGHT INTO TREATMENT OF AORTIC STENOSIS: LIGHT AT THE END OF THE TUNNEL

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No medical therapy for fibro-calcific aortic valve stenosis (FCAVS) is effective. We have developed experimental models of severe FCAVS in mice, and are using these models to examine interventions that may be useful in slowing the development or progression of FCAVS.

First, we have examined effects on FCAVS of osteoprotegerin (OPG), an endogenous decoy receptor of receptor-activator of NFkB ligand (RANKL). OPG effectively suppresses calcification of the aortic valve, by both inhibition of the osteogenic pathway and reduction of apoptosis, and preserves aortic valve function. The mechanism of action of denosumab, which is used for treatment of osteoporosis and boney metastases, is similar to OPG. We speculate that inhibition of the RANKL/RANK mechanism might be useful in prevention or treatment of FCAVS.

Second, we have examined effects of pioglitazone (a PPARgamma ligand) on FCAVS. PPARG is antiinflammatory and antioxidant, and both effects may protect against FCAVS. Pioglitazone attenuated lipid deposition as well as calcification in the aortic valve.

Third, we have studied mice (Egfr knockdown-wave) with a 90 percent reduction in epidermal growth factor receptor, which modulates semilunar valvulogenesis. The aortic valve develops fibrosis and calcification. About 80 percent of the mice have moderate or severe aortic regurgitation. The mice also develop dilated cardiomyopathy. Thus, severe fibrocalcific disease of the aortic valve can produce aortic regurgitation with volume overload cardiomyopathy.
TRANSAPICAL TRANSCATHETER AORTIC VALVE REPLACEMENT IN THE PRESENCE OF A MITRAL PROSTHESIS

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Transcatheter aortic valve replacement (TAVR), using the Edwards Sapien balloon expandable valve (Edwards Lifesciences, Irvine, California, USA) has expanded our ability to treat patients with symptomatic severe aortic stenosis, and become the treatment of the choice in high-risk inoperable patients. Further inroads into its application in subgroup populations such as patients with functioning mitral valve prosthesis, has also been defined over recent years. With experience, these patients now need not be uniformly excluded. Our case series have demonstrated that the transapical TAVR of a balloon expandable valve is feasible and safe in patients with both mechanical and bioprosthetic mitral prostheses. Technical challenges however exist in patients with mitral bioprostheses. Various degree of balloon displacement occurs due to impingement on the housing cage and pivot guards of mechanical mitral valves, and on the bioprosthetic struts. The high-risk patients have either bioprosthetic mitral valves, or mechanical valve cages seated below the mitral annulus impinging onto the balloon during balloon aortic valvuloplasty. The understanding of the interaction between both prostheses at the anatomic aorto-mitral continuity is critical for patient selection, and procedural modification to ensure success. The transarterial approach should be avoided in these high-risk patients. The transapical approach with some technical modifications is safe, with good outcomes in patients with functioning mitral prostheses. However, TAVR in the presence of a mitral prosthesis should be reserved for experienced centers.
OXIDATIVE-MECHANICAL SIGNALING ACTIVATES Wnt3a-Lrp5 MEDIATED AORTIC VALVE OSTEOGENESIS IN BICUSPID AORTIC VALVE DISEASE
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Introduction: Calcific aortic valve disease (CAVD) is the most common indication for valve surgery in the USA. Cellular mechanisms are under intense investigation. This study hypothesizes that calcific aortic valve disease develops secondary to Wnt3a/Lrp5 activation via oxidative-mechanical stress via a tissue stem cell niche resident in the aortic valve.

Methods: eNOS−/− mice were tested with experimental diets including a control (n=20), cholesterol (n=20), cholesterol + Atorvastatin (n=20). After 23 weeks the mice were tested for the development of aortic stenosis by Echo, Histology, MicroCT and RTPCR for bone markers. In vitro studies measured Wnt3a secretion from aortic valve endothelial cells and confirmed oxidative stress via eNOS activity. Anion exchange chromatography was performed to isolate the mitogenic protein. Myofibroblast cells were tested to induce bone formation.

Results: Cholesterol treated eNOS mice develop severe stenosis with an increase in Wnt3a, Lrp5, Cbfa1, (3-fold increase (p<0.0001) in the bicuspid versus tricuspid aortic valves. Secretion of Wnt3a from aortic valve endothelium in the presence of abnormal oxidative stress was correlated with diminished eNOS enzymatic activity and tissue nitrite levels. Initial characterization of the architecture for a stem cell niche was determined by protein isolation using Anion-Exchange Chromatography and cell proliferation via thymidine incorporation. Osteoblastogenesis in the myofibroblast cell occurred via Lrp5 receptor upregulation in the presence of osteogenic media.

Conclusion: Targeting the Wnt3a/Lrp5 pathway in valve calcification and activation of osteogenesis is via an oxidative-mechanical stress in CAVD. These findings provide a foundation for treating this disease process by targeting the cross talk mechanism in a resident stem cell niche.
Tricuspid valve regurgitation (TR) is often considered a benign disease and therefore apathy for it. Most common causes of TR include left sided heart failure with pressure volume overload. This type of TR is functional in nature lends itself to conservative treatment including medical treatment and steps to correct left sided pathology. On the other hand, more than severe TR degrees of TR are usually due structural deficiency and damage to the valvular apparatus such as Ebstein anomaly, tricuspid valve endocarditis and torn leaflets from repeated right heart biopsies.

Management of TR depends on the cause of TR. For less than moderate degrees of TR medical treatment should be optimized. For severe TR, surgical treatment includes annuloplasty, valve repair and replacement.
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TAVI--WAVE OF THE FUTURE OR TIME FOR A DEEP BREATH?
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TAVI has emerged as an alternative to surgical aortic valve replacement (AVR) for high risk patients with aortic stenosis. This presentation will review the efficacy of TAVI in relation to surgical AVR in regards to prosthetic durability, strokes, vascular complications, cost, perivalvular leaks, and conduction abnormalities.
TRANSESOPHAGEAL ECHOCARDIOGRAPHY FOR TRANSCATHETER AORTIC VALVE REPLACEMENT

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TEE is critical for the success of TAVR.
TEE is critical for aortic annulus sizing, guiding the delivery, coaxiality, position and deployment of the transcatheter heat valve and evaluation of complications post TAVR
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ASYMPTOMATIC SEVERE AORTIC STENOSIS: OPERATE OR WAIT?
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Calcific aortic stenosis is now the main cause of aortic stenosis in the majority of patients, due to declining incidence of rheumatic fever. Risk factors such as hyperlipidemia play an important role in the progression of aortic stenosis. According to the most recent American College of Cardiology/American Heart Association guidelines, peak velocity greater than 4 m/sec, a mean gradient of more than 40 mmHg and a valve area of less than 1.0 cm is considered hemodynamically severe aortic stenosis. Aortic valve surgery promptly should be done in symptomatic patients due to dismal prognosis without operation. Features such as high aortic valve calcium and positive exercise test identify asymptomatic patients who would benefit from early aortic valve surgery. Due to improvement in surgical techniques and better prosthesis, aortic valve surgery can now be offered at low risk to a selected group of asymptomatic patients with severe aortic stenosis. Currently percutaneous aortic valves are used in very high-risk patients with severe symptomatic aortic stenosis. Their role may expand in the future, depending on the improvements in design and operator experience. Whether advances in molecular cardiology lead to novel therapies in preventing calcific aortic stenosis in the future remains to be seen.
Mitral regurgitation (MR) is a common degenerative valve disease and increasing as aging population grows. Because surgery is the only curative modality, determining optimal time for surgery is critical for these patients. Current guidelines recommend surgery according to symptomatic status, left ventricular (LV) ejection fraction and size; surgery is recommended if patient has severe MR and is symptomatic or shows LV ejection fraction < 60% or LV end-systolic dimension > 45mm. Thanks to recent advances in surgical technique and perioperative management, surgical indication is getting wider especially in experienced centers. There have been several reports indicating that early surgery seems to be beneficial regardless of symptomatic status and LV function if the valve is repairable and surgical risk is low. However, the strategy of early surgery has several problems. First, although surgical mortality is markedly decreased, its morbidity is not negligible and thus the quality of life should be deteriorated in some of the patients. For example, chronic pain or depression is not uncommon after cardiac surgery. Second, the evidence for benefit of early surgery is not concrete. All the reports were based on retrospective analysis and had many potential biases. Third, the diagnosis of severe MR is not without errors in clinical practice. Doppler echocardiography has several important limitations in the diagnosis of MR. Therefore, if surgery is performed solely based on the result of Doppler echocardiography, unnecessary surgery is inevitable. In conclusion, although early surgery is an attractive strategy, it should be applied in selected patients.
MAJOR NON-CARDIAC SURGERY IN PATIENTS WITH AORTIC STENOSIS - SAME AS 20 YEARS AGO?

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Severe aortic stenosis has been long recognized as a risk factor for perioperative mortality and morbidity. Current ACC/AHA Guidelines recommend that elective noncardiac surgery be postponed for AS patients until after aortic valve surgery, due to an estimated mortality risk of noncardiac surgery at approximately 10%. However, these recommendations are based on studies that are now couple decades old, echocardiographic criteria for defining severe aortic stenosis have since changed, and improvements in surgical and anesthesia techniques have led to a decrease in overall surgical mortality and morbidity. Recent data suggest the perioperative risk associated with severe aortic stenosis in the contemporary era is significantly lower than originally described.
SURGICAL TIMING FOR INFECTIVE ENDOCARDITIS

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Despite advances in medical and surgical treatment, infective endocarditis (IE) remains a serious disease that carries considerable mortality and morbidity. The role of surgery has been expanding in IE and early surgery is strongly indicated for IE patients with congestive heart failure or uncontrolled infection, but no randomized trial has been conducted to clarify the indications and optimal timing of surgery because of ethical, logistical and financial constraints.

The Early Surgery versus Conventional Treatment in Infective Endocarditis (EASE) trial was designed to compare clinical outcomes of early surgery and conventional treatment strategy for IE patients with a high risk of embolism. Patients with left-sided IE, severe valve disease and large vegetation were randomly assigned on a 1:1 basis to early surgery (37 patients) or to conventional treatment (39 patients). The primary end point was a composite of in-hospital death and embolic events that occurred within 6 weeks from randomization. The primary end point occurred in 1 (2.7%) patient of the early surgery group and in 9 (23.1%) of the conventional treatment group (hazard ratio [HR], 0.248; 95% confidence interval [CI], 0.069-0.883; P=0.031).

The EASE trial demonstrated that early surgery performed within 48 hours after diagnosis reduced the primary end point of death and embolic events by effectively decreasing systemic embolisms in patients with IE. Moreover, these improvements in clinical outcomes could be achieved without increase in operative mortality or recurrence of IE. Additional larger randomized trials are needed to evaluate the effectiveness of early surgery in complicated IE.
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THE WORK UP OF ASYMPTOMATIC WOLFF-PARKINSON-WHITE SYNDROME
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Background: Asymptomatic ventricular pre-excitation (aVPE) is a conduction abnormality that results in sudden death due to rapid conduction down the accessory pathway during atrial fibrillation (AFib). The purpose of this study was to identify a cost effective approach to risk assessing aVPE patients.

Methods: A cost effectiveness analysis performed using a decision tree model comparing aVPE patients undergoing a transvenous electrophysiology study (TVEPS) vs. step wise risk assessment (exercise stress test(EST), transesophageal electrophysiology study (TEEPS) and TVEPS if risk could not be determined). TEEPS followed EST when VPE did not disappear and TVEPS followed TEEPS when Afib not induced or risky. Efficacy of EST was 15%, ability of TEEPS at inducing Afib was 88%; with 78% having no risk. Costs were 2009 Medicare reimbursement rates with cost of EST $ 277, TEEPS $990, and TVEPS $4035.

Results: The step wise approach involving EST, TEEPS and TVEPS when necessary is the most cost-effective method of identifying aVPE patients at risk with an expected cost of $2,174 compared to $4,035 for those initially undergoing TVEPS. Combining efficacy and cost data on these patients, this approach (EST- TEEPS - TVEPS) results in an average savings of $1,861 per patient. This step wise approach remained cost effective as long as TEEPS efficacy rate is > 31% on patients not screened out at EST.

Conclusions: This step wise approach (EST-TEEPS-TVEPS) is the most cost effective way to risk assessment of aVPE patient. This approach yields an average savings of $1,861 per patient.
ATRIAL FIBRILLATION AS A GENETIC DISEASE

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In decades past, recognition that AFIB may be a primary genetic disease in otherwise healthy individuals was not recognized. Data from the Framingham Heart Study first demonstrated the genetic contribution to the arrhythmia, reporting that a parental history of AFIB is associated with a 1.85-fold increased risk of developing the arrhythmia in offspring. The risk of developing the arrhythmia in the presence of a sibling with lone AFIB is increased 70-fold in males and 34-fold in females. The contribution of genetics to the development of AFIB in the absence of traditional risk factors such as hypertension and valvular heart disease, so called *lone* or *healthy heart* AFIB, appears to be much greater. Following the recognition of a genetic contribution to the development of AFIB, the last 8 years has led to a surge in the identification of genetic culprits responsible for both familial and sporadic, *healthy heart* AFIB. This presentation will review the novel mechanisms of atrial fibrillation as discovered through genetics research.
IS THERE A PERFECT APPROACH FOR ABLATION PERSISTENT ATRIAL FIBRILLATION?
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Ablation of paroxysmal atrial fibrillation that remains symptomatic despite tolerated antiarrhythmic medication is widely utilized with reasonable success. However, ablative approach in persistent atrial fibrillation remains unclear. Pulmonary vein isolation remains the cornerstone but what additional procedures need to be done to enhance the poor success rate remains inconclusive. Fractionated atrial electrogram, linear lines and more recently rotor modulation have all been proposed by several groups. This review will focus on the strengths and weakness of these approaches.
THORACOSCOPIC BIATRIAL MAZE PROCEDURE – A NOVEL MINIMAL-INVASIVE REMEDY WITH PROMISING MIDTERM RESULTS
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Minimal Access atrial fibrillation has undergone significant progression in last few years. The lesion set has progressed from simple pulmonary vein (PV) isolation to a more comprehensive lesion set, which can be placed epicardially, and more closely replicates the left atrial lesions of the Cox maze III. Less-invasive access has progressed from bilateral mini thoracotomies initially described by Wolf and coworkers, to a totally thorascopic approach initially described by Puskas and coworkers. Besides antral lesions, complete box lesion is produced connecting all pulmonary veins. Furthermore, left atrial isthmus lesion set is created by connecting the both superior pulmonary veins to the non/left coronary commissure of the aortic valve. This triangle is on the dome of the left atrium and connected to the fibrous skeleton of the heart. Next the pericardial ganglionic plexi are tested and ablated, and entrance and exit block is confirmed using intraoperative electrophysiological interrogation. Lastly, the left atrial appendage is excluded under Transesophageal echocardiogram using a dedicated left atrial. In 2012, fourteen patients with previous unsuccessful electrophysiological ablation for persistent or longstanding persistent atrial fibrillation underwent thoracoscopic Maze using aforementioned protocol. The average hospital stay was three days, and there was no stroke, myocardial infarction or mortality. 14-day-holter monitors were collected at 3, 6 and 12 month, confirming all patients being in normal sinus rhythm. One patient required electrophysiological ablation of persistent atrial flutter, with subsequent cure of the atrial flutter. No patient has had recurrence of atrial fibrillation in the follow-up.
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LEFT ATRIAL APPENDAGE CLOSURE
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Atrial fibrillation is a frequent cause of stroke. The mechanism in non-valvular atrial fibrillation is thrombus formation in the left atrium. Ninety percent of left atrial thrombi occur in the left atrial appendage. Anticoagulation with vitamin K antagonists has been demonstrated to substantially reduce the stroke risk in patients with atrial fibrillation (up to 60%). However, it is accompanied by significant logistical challenges related to required frequent laboratory monitoring, drug-drug and diet-drug interactions. More importantly, it is associated with a bleeding risk including intracranial hemorrhage. Therefore, it is not surprising that a large number of patients at risk for stroke are not treated with anticoagulation. Though new anticoagulants, particularly direct thrombin antagonists and Factor Xa inhibitors have a wider therapeutic range and do not require routine monitoring, they are also associated with significant bleeding risk. Moreover, those patients who have the highest stroke risk are also at greatest risk for bleeding. Hence, alternative methods to reduce the stroke risk in patients with atrial fibrillation are needed. Most recently, percutaneous left atrial appendage occlusion either via endocardial or combined endo- and epicardial approach has explored with one randomized trial demonstrating non-inferiority to anticoagulation with warfarin. The aim of this presentation is to review the role of percutaneous left atrial appendage closure for the prevention of strokes in the setting of atrial fibrillation.
ANTICOAGULATION IN PATIENTS WITH LEFT VENTRICULAR SYSTOLIC DYSFUNCTION AND SINUS RHYTHM: WHEN?

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Left ventricular systolic dysfunction and chronic systolic heart failure predispose to intraventricular thrombus formation and embolization resulting in stroke. Current guideline recommends the use of oral anticoagulants in patients with atrial fibrillation and history of previous thromboembolism. However, anticoagulant treatment in patients with left ventricular systolic dysfunction with sinus rhythm and without history of previous thromboembolism is still on debate. Review of epidemiologic data, which shows increased risk of embolic events shortly after diagnosis of heart failure and case reports support the hypothesis that initiation of systolic left ventricular dysfunction may lead to transient increase of thromboembolic events. Possible mechanisms cover the decrease of left ventricular filling pressure and positive inotropic effects of afterload reducing drugs and positive inotropic drugs. This treatment might facilitate detaching of fresh thrombi from the left ventricular cavity. Accordingly, patients with newly diagnosed left ventricular systolic dysfunction in sinus rhythm and without previous thromboembolic events should be closely followed up for several months, and temporary anticoagulant treatment should be considered to prevent thromboembolic events.
CRYPTOGENIC STROKE--COULD LONG TERM MONITORING UNCOVER THE CAUSE
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"Cryptogenic Stroke" is defined as an ischemic stroke that is not attributable to a cardioembolic source or large or small vessel disease whose cause remains undetermined after an extensive cardiovascular and hematologic search for the cause. Approximately, 20-25% of ischemic strokes are "cryptogenic" with some due to unrecognized or undetected atrial fibrillation. The amount of atrial fibrillatory burden is often small and difficult to identify owing to its often asymptomatic, sporadic, and unpredictable occurrence. The most frequent monitoring techniques used to detect atrial fibrillation may not be adequate to determine if unrecognized atrial fibrillation is the underlying cause of a stroke. Prolonged invasive monitoring may provide better detection. Previous and on-going studies supporting the role of prolonged monitoring will be discussed.
Orthostatic hypotension (OH) can be a vexing problem for both patients and their cardiovascular providers. As it often presents with syncope or presyncope, these patients are often referred to cardiologists to help with the regulation of their blood pressures. Neurogenic OH (excluding PH due to neurally mediated episodes) is primarily a problem of the elderly. Given the aging of the population in the Western world, neurogenic OH is already starting to become more prevalent both in clinics and in terms of hospital admissions.

In this session, a clinical approach to orthostatic hypotension will be offered. Different clinical presentations will be reviewed, as well as when one should be concerned about autonomic failure. Data will be offered on some treatment options. Associated and confounding problems, including supine hypotension will also be discussed in the context of optimal management of the patient.
ASSOCIATION OF CORRECTED QT INTERVAL WITH LONG-TERM MORTALITY IN PATIENTS WITH SYNCOPE

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Introduction: The electrocardiographic parameters QRS duration, QRS-T angle and QTc can predict mortality in patients with cardiovascular disease. The prognostic value of these parameters in hospitalized patients with syncope needs investigation.

Methods: We retrospectively studied 590 consecutive patients hospitalized with syncope. After excluding patients with baseline abnormal rhythm, QT-prolonging medications, and missing data, 459 patients were analyzed. Baseline demographic characteristics, co-morbidities, medication use, San Francisco Syncope Rule (SFSR) and Osservatorio Epidemiologico sulla Sincope nel Lazio (OESIL) score and data on mortality were collected. The categorical and continuous variables of the 2 groups of patients with prolonged QTc and normal QTc interval were analyzed by Fischer’s exact test and Mann-Whitney Test. A stepwise Cox regression model was used for time to death analysis.

Results: Of 459 patients, prolonged QTc interval was observed in 122 (27%). Mean follow-up was 41 months. Patients with prolonged QTc interval had higher prevalence of cardiovascular disease, OESIL score, high risk SFSR, hypertension, dyslipidemia, coronary artery disease, congestive heart failure, and increased mortality. Stepwise Cox regression analysis showed that significant independent prognostic factors for time to death were prolonged QTc interval (P=0.005), age (P=0.001), diabetes mellitus (p=0.001) and history of malignancy (p=0.006). QRS duration and QRS-T angle were not independent predictors of mortality.

Conclusion: A prolonged QTc interval is an independent predictor of long-term mortality in hospitalized patients with syncope.
LONG TERM EFFICACY OF ATRIAL BASED PACING AND BETA BLOCKER THERAPY TO PREVENT SUDDEN CARDIAC DEATH IN CONGENITAL LONG QT SYNDROME

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Introduction: Limited data exist for congenital long QT syndrome (LQTS) treated with combination of beta blockade and continuous pacing. We examine the outcome of a cohort of patients at our institution treated with the combination of a beta blocker and atrial based pacing at a high rate.

Methods: Long term clinical course of patients with LQTS treated with beta blockers and atrial pacing was examined to identify recurrent syncope, cardiac arrest, sudden cardiac death or the need to upgrade to a defibrillator.

Results: A total of 30 patients with LQTS (age 26.8 ± 21.3 years; 21 females) were identified with varying presentations - syncope (n=16); torsade de pointes (n=7); cardiac arrest (n=6); family history (n=1). All patients had a pacemaker implanted. Lower rate was set to a mean of 89 ± 9 bpm [≥ 90 (n=20); ≥80 (n=9); 70 (n=1)]. 21 patients were programmed in the AAI mode, with the rest in the DDD (n=6) or DDI (n=3) modes. Over a mean follow up of 9.7 ± 6.6 years, no patient had recurrent syncope, cardiac arrest or sudden cardiac death. None of the patients required upgrade to an ICD. 4 patients died during follow up from known unrelated causes.

Conclusion: A combination of beta blocker therapy and atrial based pacing at a high rate is highly effective in preventing sudden death in patients with congenital LQTS. This approach may be particularly beneficial in the young population, in whom, implantation of a pacemaker rather than an ICD may enhance device longevity and avoid inappropriate ICD therapies.
Objectives: To test whether reducing oxidative stress attenuates diabetic cardiomyopathy.

Background: Cardiac oxidative stress is an early event associated with diabetic cardiomyopathy. Sulforaphane (SFN) and MG132 have gained attention by their anti-oxidative effects via activation of Nrf2 pathway.

Methods and results: FVB mice were intraperitoneally injected with multiple low doses of streptozotocin to induce Type 1 diabetes or directly given subcutaneous injection of Angiotensin II (Ang II) for 2 months. Hyperglycemic or Ang II-treated mice and age-matched control mice were treated with or without SFN for 3 months and then kept for additional 3 months without SFN (i.e.: 6 months of diabetes). SFN significantly prevented diabetes- or Ang II-induced high blood pressure, cardiac dysfunction and remodeling at both 3 and 6 months. SFN up-regulated Nrf2 expression and transcription activity and also almost completely prevented diabetes- or Ang II-induced cardiac oxidative damage. OVE26 transgenic Type 1 diabetic mice at 3 months old were given with and without low-dose MG132 for 3 months. Diabetic mice showed significant cardiac dysfunction and remodeling along with systemic and cardiac oxidative damage and inflammation. All of these pathogenic changes were reversed by MG132 treatment that significantly increased cardiac Nrf2 expression and activation and decreased the expression of Iκ-B and the nuclear accumulation and DNA binding activity of NF-κB in the heart.

Conclusion: These results suggest that SFN and MG132 have preventive and therapeutic effect on diabetic cardiomyopathy in diabetic mouse models, probably through the up-regulation of Nrf2-dependent anti-oxidative function and the down-regulation of NF-κB-mediated inflammation.
DOES THE ETIOLOGY OF RECIPIENT CARDIOMYOPATHY OR LEFT VENTRICULAR HYPERTROPHY POST TRANSPLANT PREDICT THE LONG TERM INCIDENCE OF CORONARY ALLOGRAFT VASCULOPATHY?

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Cardiac allograft vasculopathy (CAV) continues to be a major problem post transplant, limiting long term survival. In our study, we aimed to investigate the possible correlation between CAV and etiology of recipient cardiomyopathy (CMP) and if left ventricular hypertrophy (LVH) in the transplanted heart is a predictor of CAV. Retrospectively, we reviewed the transplant database of a tertiary care academic center from 2003 to 2011. Primary outcome was CAV, defined as ≥ 60% stenosis in ≥ 1 major coronary vessel or >30% in more than 1 vessel. The following variables were analyzed for their association with the outcome: donor and recipient age, gender, body mass index, smoking, diabetes, hypertension, dyslipidemia, chronic kidney disease, cytomegalovirus/Epstein Barr virus serology and frequency of acute cellular rejection episodes within 12 months from transplantation. LVH is defined as interventricular septal and posterior wall thickness >1.2 cm on echocardiogram obtained 12 months from the date of transplant. Logistic regression analysis was utilized to examine the association between LVH and CAV and also with the etiology of recipient CMP. We included 85 patients (mean age 46 (±12), male= 64, female=21). 61(71%) patients had HTN, 56 patients had dyslipidemia, 51 (60%) had LVH. The rate of CAV was 27% with a mean follow up of 4.3 (±2.9) years. The percentage of ischemic etiology of recipient was 47%, nonischemic was 53%. The results of the study indicated that the incidence of CAV does not correlate with etiology of recipient cardiomyopathy and progression of LVH in the first year of transplant.
TAKOTSUBO CARDIOMYOPATHY: ANALYSIS FROM THE NATIONAL INPATIENT SAMPLE 2009-2010

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Objective: Aim of our study was to determine the prevalence, in-hospital mortality and predictors of mortality for patients with Takotsubo cardiomyopathy (TC) in the United States.

Background: TC is characterized by left ventricle apical ballooning with elevated cardiac biomarkers and electrocardiographic changes suggestive of an acute coronary syndrome. There is paucity of data on the prevalence and predictors of mortality in TC.

Methods: All patients diagnosed with TC in the Nationwide Inpatient Sample (NIS) 2009 – 2010 database using International Classification of Diseases (ICD) 429.83 were included in the study. Acute critical illnesses included were sepsis, acute cerebrovascular disease, acute respiratory insufficiency and acute renal failure. Chronic conditions were diabetes, hypertension, dyslipidemia, tobacco, alcohol use, anxiety and hyperthyroidism. Multivariate logistic regression analysis was done to analyze predictors of mortality.

Results: The prevalence of TC was 0.03% (n=13804) of all hospital admissions. The mean age was 66.6 years with women (67.1) older than men (62.5) (p<0.001). Mean length of stay was 6.28 days, with men staying longer than women (8.2 versus 6.03 days; p= 0.0024). In-hospital mortality rate was 4.5%, with men having higher mortality than women (10.5% versus 3.7%; p=0.0002). Interestingly, dyslipidemia (OR 0.450, p=0.006) along with acute cerebrovascular disease (OR 6.95, p=0.000), acute renal failure (OR 4.12, p=0.000) and acute respiratory insufficiency (OR 10.41, p=0.000) predicted mortality after adjusting for demographics, acute critical and chronic illnesses.

Conclusion: TC was present in 0.03% of all hospital admissions in the United States. Independent predictors of in-hospital mortality were dyslipidemia and acute critical illnesses.
PROGNOSTIC VALUE OF FRAGMENTED QRS COMPLEX ON ECG OF HYPERTROPHIC CARDIOMYOPATHY PATIENTS WITH ICD

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Background: Fragmented QRS (fQRS) on an electrocardiogram (ECG) is associated with worse outcomes in ischemic and non-ischemic cardiomyopathy. Our hypothesis is fQRS is associated with more frequent arrhythmic events among hypertrophic cardiomyopathy (HCM) patients with an implantable cardioverter-defibrillator (ICD).

Methods: Patients at Indiana University with HCM who received an ICD between January 1, 2000 and December 15, 2011 were studied retrospectively with chart reviews of medical history, ECG data, echocardiography data, and ICD records. fQRS was defined as notched R or S waves or RSR` pattern in at least 2 contiguous ECG leads. Appropriate device therapy or death marked a cardiac event. Chi-square and student's t-test were used in analysis.

Results: Thirty four HCM patients with an ICD were studied, 15 of whom were male (44%). Mean age at implant of ICD was 45±16.5 years, 28 patients (82%) received an ICD for primary prevention, and 6 patients received an ICD for secondary prevention. fQRS was present in 15 patients (44 %). Compared to the non-fQRS group, the fQRS group had lower ejection fraction (57% vs 64%; P value: 0.20), thicker septum (2.2 cm vs 1.9 cm, P value: 0.18), and larger left atrial diameter (4.7 cm vs. 4 cm; P value: 0.1). In the fQRS group, 6 patients had a cardiac event (40%) including one death, compared to 3 patients in the non-fQRS group (16%); (P value: 0.14).

Conclusion: Among HCM patients with an ICD, those with fQRS have worse echocardiographic parameters and more arrhythmic events than those without fQRS.
LIRAGLUTIDE POSTCONDITIONING IS MORE EFFECTIVE THAN EXENDIN-4 IN LIMITING REPERFUSION INJURY IN BOTH WKY AND SHR-SP RATS WITH LEFT VENTRICULAR HYPERTROPHY

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Introduction: Exendin-4 (exe4) postconditioning has been shown to limit reperfusion injury (RI) in experimental and clinical settings. Left ventricle hypertrophy (LVH) may be associated with increased RI. Our objective was to study exe4 and liraglutide postconditioning (PostC) in hearts with LVH, isolated from hypertensive SHR-SP (hypertensive LVH) rats.

Methods: Hearts isolated from WKY and SHR-SP rats were subjected to LAD occlusion-2 hrs reperfusion, with exe4 0.3 nM or liraglutide 0.3 nM present during the first 15 min in treated hearts.

Results: BP and heart/body weight ratio were increased in SHR-SP compared to WKY rats (p<0.0001 for both parameters). Infarcts were larger in SHR-SP than in WKY (65.7 +/-3.2, N=7 vs 37.1 +/-3.4, N=12 respectively; P<0.05). Exe-4 and liraglutide PostC decreased infarct size (IS) after 35 min ischemia in WKY (p<0.05). Liraglutide and preconditioning, but not Exe-4, decreased IS after 35 min in SHR-SP (p<0.05). Exe4 PostC decreased IS after 15 min ischemia in SHR-SP (p<0.05). In WKY hearts, exe4 treatment significantly decreased diastolic contracture and increased left ventricle developed pressure. Liraglutide, but not exe4, decreased diastolic pressure in SHR hearts. Degree of Akt phosphorylation was smaller in LVH hearts compared to normal hearts.

This data suggests that liraglutide was more effective than exe4 in limiting reperfusion injury in both WKY and SHR-SP. In both WKY and SHR-SP hearts there was a loss of response to PostC by exe4 with increasing ischemia time and infarct size. This loss of response to PostC occurs earlier in hypertrophy hearts.
SENSITIVITY AND SPECIFICITY OF COMMONLY USED EKG CRITERION TO ASSESS LEFT VENTRICULAR HYPERTROPHY IN CENTENARIANS

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Background: The centenarian population is increasing, and patients ≥100 years old are encountered more frequently in clinical practice. Cardiovascular disease is the most common cause of death in this subset of patients. We previously reported the echocardiographic characteristics of centenarians and found a high prevalence of hypertrophied left ventricles (LVH) in the elderly. We decided to assess the best EKG criteria to detect LVH in centenarians.

Methods: We retrieved the admission EKGs and echocardiograms of all centenarians between 1998 to 2009 from our database (of 30,798 records), and detected 72 centenarians. We identified the echocardiograms showing LVH and then compared 3 common criteria (Romhilt-Estes, Sokolow-Lyon, Cornell) to assess left ventricular hypertrophy from the EKGs by comparing the proportions of correctly identified LVH by using Z-statistics.

Results: We found a very high prevalence of left ventricular hypertrophy (87.5%) in centenarians. We determined that the Sokolow-Lyon criteria were the most sensitive and specific to identify left ventricular hypertrophy in centenarians (Sensitivity 84%, Specificity 89%, Positive predictive value 98%; p<0.05 for all comparisons).

Conclusion: Our data suggests that there is a very high prevalence of LVH in centenarians (even in those without clinical hypertension) and the Sokolow-Lyon criteria were the most effective in correctly identifying LVH in centenarians.
A CASE OF FATAL FULMINANT MYOCARDITIS PRESENTING AS AN ACUTE ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION AND PERSISTENT VENTRICULAR TACHYARRHYTHMIA ASSOCIATED WITH INFLUENZA A (H1N1) VIRUS IN A PREVIOUSLY HEALTHY PREGNANT WOMAN

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Several studies have reported influenza A (H1N1) virus as a cause of fulminant myocarditis. We report the first fatal case of fulminant myocarditis presenting as an acute ST-segment elevation myocardial infarction and ventricular tachyarrhythmia associated with influenza A (H1N1) in a previously healthy pregnant woman. A 38-year-old Asian woman, gravida 3, para 1-0-1-1, presented with flu-like symptoms. Initially, she developed wide-complex tachycardia requiring several defibrillations and was later intubated. Electrocardiogram showed ST-segment elevation. Coronary angiogram was negative and a pulmonary angiogram ruled out pulmonary embolism. Fetal compromise was noted on the monitor, and the patient underwent an emergent cesarean section. She subsequently expired. Autopsy confirmed severe myocarditis. Further testing confirmed influenza A (H1N1) virus. This case of a rare, yet lethal, complication of H1N1 infection underscores the importance of increased awareness among health care professionals to provide pregnant women with vaccination and prompt treatment.
A 45-year-old female presented with sudden onset of severe chest discomfort and associated diaphoresis, headache and sinus congestion. The patient received sublingual nitroglycerin with subsequent relief of the pain. Initial EKG showed normal sinus rhythm with 1 mm ST-elevations in lead II and lead aVF and 1 mm ST-depression in lead V1 with associated T-wave inversion. Initial Troponin I and CK-MB were elevated at 7.82 and 55.2 respectively and, 6 hours later, Troponin I increased to 13.44 and CK-MB to 75.7. Cardiac catheterization revealed normal coronary arteries and a normal ejection fraction. During hospitalization, she developed right-sided facial palsy. Her Lyme titers were positive. After treatment with ceftriaxone, her symptoms resolved.

Discussion: This is an unusual case of Lyme myocarditis associated with markedly elevated Troponin I and normal left ventricle function without conduction abnormalities. Higher level of Troponin I related to Lyme myocarditis just has been previously reported once in the literature. At the best of our knowledge no cases of myocarditis mimicking acute coronary syndrome with high levels of Troponin I and neurologic compromise has been described. In retrospect, the prodromal symptoms and more than one system involved were the clue to the diagnosis which was confirmed by serology. The prognosis seems to be favorable with adequate therapy. However, Lyme myocarditis may be a challenging diagnosis in endemic areas in patients with risk factors presenting with chest pain, EKG changes and positive cardiac markers. Lyme carditis should be considered in the differential diagnosis of patients presenting with clinical symptoms suggestive of acute coronary syndromes.
IS TAKOTSUBO CARDIOMYOPATHY A POTENTIAL SIDE EFFECT OF ANTIDEPRESSANT?

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Objectives: Our aim was to identify cases of Takotsubo Cardiomyopathy secondary to antidepressant use through literature review and analysis.

Background: Many cardiovascular toxicities of antidepressants have been identified, but their relationship with Takotsubo Cardiomyopathy and heart failure still remains unclear. Methods: We have reviewed literature published on PubMed between January 1980 and November 2012 using the following keywords: antidepressant, serotonin reuptake inhibitor, tricyclic antidepressant, Takotsubo Cardiomyopathy. Ten case reports were identified. Each case report was reviewed and variables for analysis were collected. Results: 70% (7) of the cases were related to SNRI use and 20% (2) were related to Tricyclic antidepressant (TCA) use. 40% of the cases were associated with antidepressant overdose and 50% were related to regular dose. Among the 5 cases that were not related to medication overdose, the medication was started recently in 3 out of 5 cases (60%) or the dose was increased within a month in 1 out of 5 cases (20%). The mean interval of either starting or increasing the dose of medication was 10 days prior to admission (4 patients). On imaging studies, 80% (8 out of 10) of patients had typical Takotsubo Cardiomyopathy and 20% (2 out of 10) had reverse Takotsubo Cardiomyopathy. Conclusion: We found that not only were overdose and serotonin syndrome the likely causes, even the therapeutic dose of antidepressant could be a cause of Takotsubo Cardiomyopathy. Physicians should consider Takotsubo Cardiomyopathy as a potential side effect when prescribing antidepressants.
TELMISARTAN DELAYED INACTIVATION OF CARDIAC NAV1.5 RESULTING CARDIAC DYSFUNCTION

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Telmisartan is an angiotensin II receptor blocker and partial peroxisome proliferator-activated receptor gamma agonist that modulates the renin-angiotensin-aldosterone system. It is used primarily to manage hypertension, diabetic nephropathy, and congestive heart failure. Recent studies have reported that myocardial infarction (MI) has occurred in telmisartan-treated patients. The purpose of the study was to investigate the specific conditions and underlying mechanisms that may result in telmisartan-induced MI. We evaluated the effect of telmisartan on whole hearts, cardiomyocytes, and cardiac sarcolemmal ion channels. Hearts of 8-week-old male Sprague–Dawley rats were perfused with 3, 10, 30, or 100 μM telmisartan or losartan, or normal Tyrode’s solution (control) for 3 hours. We found that telmisartan induced myocardial infarction, with an infarct size of 21% of the total at 30 μM (P<0.0001) and 63% of the total area at 100 μM (P<0.001). Telmisartan also induced cardiac dysfunction (e.g., decreased heart rate, diminished coronary flow, hypercontracture, and arrhythmia). Confocal microscopy demonstrated that 30 μM telmisartan significantly elevated intracellular Ca²⁺ level leading to hypercontracture and cell death. Patch clamp analysis of isolated cardiomyocytes revealed that telmisartan induced Na⁺ overload by slowing the inactivation of voltage-gated Na⁺ current (Iₚₜ), activating the reverse-mode of Na⁺-Ca²⁺ exchanger activity, and causing Ca²⁺ overload. Telmisartan significantly delayed inactivation of the voltage-gated Na⁺ channel causing cytosolic Na⁺ overload, prolonged action potential duration, and subsequent Ca²⁺ overload. Above 30 μM, telmisartan may potentially cause cardiac cell death and MI.
CAVEOLIN-1/ABC-A1 COMPLEX-MEDIATED CHOLESTEROL EFFLUX OF LIPID-LADEN CELLS AND DRUG DEVELOPMENT FROM CHINESE HERBAL MEDICINE

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It is well known that the balance between cholesterol efflux and uptake determines the progression of atherogenesis. Therefore, the cholesterol efflux remains a major target for atherosclerotic treatment, which results in regression of atherosclerotic plaques and reduces acute cardiovascular events. Considering multiple factors involved in cholesterol efflux, we have proposed a new model called "one center and four systems" integrating transportation and networking regulation in VSMCs and macrophages. This model helps us understand the dynamic process of atherogenesis and facilitates drug development. Thus, we synthesized a lipid-modulating compound CurNic through attaching the nicotinic acid groups to curcumin. Our molecular simulation study has revealed that CurNic had high dock efficiency with cholesterol transport-related proteins, such as Caveolin-1, Annexin-II, HDL-3 and MMP-9 with the LibDock/PoseDock values of 134/89, 104/69 and 116/88, respectively. In apoE-/- mice, we found that treatment with CurNic significantly increased the levels of HDL and HDL-C for up to 36%, which effects were more significant than that by niacin alone. Most importantly, CurNic treatment inhibited plaque formation in apoE-/- mice. Like lovastatin, CurNic treatment also decreased serum levels of LDL-C, TC, TG, CRP, IL-6 and IL-10. In cultured SMCs, CurNic was found to inhibit cell proliferation and arrest cells in the G0/G1 phase. Our further results showed that its cell cycle inhibition likely resulted from inhibition of the activities of MAPK and Cyclin D1 expression and stimulation of Caveolin-1 expression. Taken together, our results suggest that CurNic has anti-atherosclerotic effects through a potential mechanism involving lipid-lowering and anti-inflammatory actions.
CDK5-MEDIATED HYPERPHOSPHORYLATION CONTRIBUTES TO THE LOSS-OF-SIRT1 FUNCTION DURING THE DEVELOPMENT OF ENDOTHELIAL SENESCENCE

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Background: During vascular aging, endothelial cells lying on the inner surface of the blood vessels present a senescent phenotype, triggering and accelerating atherosclerosis development. The anti-aging activity of SIRT1, a NAD-dependent deacetylase, is lost during the occurrence of endothelial senescence (Circ Res 2010;106:1384-93). The present study aims to investigate the molecular mechanisms underlying the loss-of-SIRT1 function in senescent endothelial cells.

Methods and Results: In senescent primary porcine aortic endothelial cells (PAECs), the phosphorylation of SIRT1 at serine 47 (S47) was significantly enhanced. Phosphorylation at S47 was stimulated by agents promoting senescence, attenuated by drugs with anti-senescence properties, and critically involved in regulating the intracellular localization of SIRT1. Cyclin-dependent kinase 5 (CDK5) was responsible for modulating the phosphorylation of SIRT1 at S47. Knocking down or inhibition of CDK5 alleviated endothelial senescence and attenuated the expression of inflammatory genes in PAECs. Chronic treatment with roscovitine (a CDK5 inhibitor) blocked the development of cellular senescence and atherosclerosis in aortae of hypercholesterolemic apolipoprotein E deficient mice.

Conclusion: CDK5-mediated hyperphosphorylation of SIRT1 facilitates the development of endothelial senescence and atherosclerosis.

MOLECULAR MECHANISMS UNDERLYING THE PRO-ATHEROGENIC ACTIONS OF INTERFERON-GAMMA

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Objectives: To investigate the molecular mechanisms underlying the pro-atherogenic actions of interferon-gamma (IFN-gamma) on human macrophages.

Background: IFN-gamma is a key pro-atherogenic cytokine as revealed by numerous in vitro and in vivo studies. The cytokine affects all stages of the disease, including foam cell formation and regulation of plaque stability. In addition, the anti-atherogenic effects of lipid lowering drugs are in part due to inhibition of IFN-gamma actions. It is therefore essential that the mechanisms underlying the pro-atherogenic effects of this cytokine are fully understood.

Methods: The studies used the human THP-1 cell line and primary cultures of human monocyte-derived macrophages. Molecular mechanisms were delineated using a combination of RT-qPCR, western blot analysis, biochemical assays, promoter analysis, use of pharmacological inhibitors and RNA interference assays.

Results: IFN-gamma promoted macrophage foam cell formation by stimulating the uptake of modified lipoproteins and inhibiting the efflux of cholesterol from foam cells. Inhibition or knockdown of extracellular signal-regulated kinase (ERK) attenuated several IFN-gamma-induced events: phosphorylation of signal transducer and activator of transcription-1 (STAT1) on serine 727; the expression of key genes implicated in atherosclerosis; and the uptake of modified lipoproteins. In addition, transfection of DNA constructs specifying for dominant negative forms of several components of the ERK pathway attenuated IFN-gamma-induced activation of STAT1 responsive promoters.

Conclusions: These studies provide novel insights into the mechanisms underlying IFN-gamma actions on macrophages in atherosclerosis.

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Objectives: Omega-3 fatty acid products containing eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) have been shown to reduce the risk of cardiovascular disease, in part, by stimulating the endothelial formation of nitric oxide (NO), a potent vasoprotective factor. This study determined the mechanism leading to endothelial NO synthase (eNOS) activation in response to the highly active EPA:DHA 6:1 product. Methods: Vascular reactivity was assessed in organ chambers, vascular oxidative stress using the redox-sensitive probe, dihydroethidine, and the phosphorylation level of target proteins by Western blot.

Results: EPA:DHA 6:1 caused pronounced endothelium-dependent relaxations in porcine coronary artery rings. Relaxations to EPA:DHA 6:1 were slightly but significantly reduced by an eNOS inhibitor, not affected by inhibition of endothelium-dependent hyperpolarization and abolished by both treatments. Relaxations to EPA:DHA 6:1 were reduced by inhibitors of oxidative stress (MnTMPyP, PEG-catalase), an inhibitor of either Src kinase (PP2) or PI3-kinase (wortmannin), and intracellular copper chelating agents (neocuproine, tetrathiomolybdate), and were insensitive to cyclooxygenase inhibition (indomethacin), an iron chelating agent (desferroxamine), and a zinc chelating agent (histidine). EPA:DHA 6:1 induced phosphorylation of Src, Akt and eNOS at Ser 1177 in cultured coronary artery endothelial cells; these effects were inhibited by MnTMPyP and PEG-catalase. EPA:DHA 6:1 induced the endothelial formation of ROS in coronary artery sections, this effect was inhibited by MnTMPyP, PEG-catalase, and intracellular copper chelating agents.

Conclusion: EPA:DHA 6:1 causes endothelium-dependent NO-mediated relaxations in coronary artery rings, and this effect involves an intracellular copper-dependent event triggering the redox-sensitive PI3-kinase/Akt pathway to activate eNOS.
It is known that CaCC regulates agonist-stimulated contraction and myogenic tone in vascular smooth muscle cells. The physiological functions of CaCC in blood vessels are not fully revealed due to the lack of specific channel blockers and the uncertainty of its molecular identity. In this study, we investigated the effects of TMEM16A on cerebrovascular remodeling in rat basilar smooth muscle cells BASMCs isolated from 2-kidney, 2-clip renohypertensive rats, by using Whole-cell patch-clamp, and TMEM16A cDNA and small interference RNA (siRNA) transfection strategy. Our results demonstrated that knockdown of TMEM16A but not bestrophin-3 attenuated CaCC currents. The activity of CaCC in BASMCs was decreased and the CaCC activity negatively correlated with the blood pressure and the medial cross sectional area in basilar artery during hypertension. Both upregulation of CaMK II activity and downregulation of TMEM16A expression contributed to the reduction of CaCC in hypertensive basilar artery. Western blot results revealed that angiotensin II repressed TMEM16A expression in BASMCs. Knockdown of TMEM16A facilitated, whereas overexpression of TMEM16A inhibited, angiotensin II induced cell cycle transition and cell proliferation. TMEM16A affected cell cycle progression mainly through regulating the expression of cyclin D1 and cyclin E. The present data suggest that TMEM16A CaCC is a negative regulator of cell proliferation. Downregulation of CaCC may play an important role in hypertension-induced cerebrovascular remodeling, suggesting modification of the activity of CaCC may be a novel therapeutic strategy for hypertension-associated cardiovascular diseases, such as stroke.
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Arrestins play a central role in desensitization of G-protein-coupled receptors and form complexes with several signaling proteins such as Src, ERK1/2 and JNK3 MAP kinase signaling pathway. Previously, we reported that visual arrestin was co-purified with selected glycolytic enzymes and also the presence of arrestin like proteins (ALP) in cardiac tissues. Here, the soluble extract of bovine’s myocardial tissues analyzed by ACA-34 gel filtration, immuno-affinity column, Hydroxylapatite (HA)-Ultrogel chromatography, SDS-PAGE, ELISA, western blot and a sandwich immune assay for quantification of ALP in different regions such as left and right atriums and ventricles of the bovine heart (n= 3), we showed that; 1) Cardiac muscle contained a 50 kDa ALP at a concentration of 751 pg/mg of soluble extract protein, 2) ALP purified by immunoaffinity contained alpha-enolase (48kDa); 3) This observation confirmed using HA-chromatography in that arrestin-enolase complex eluted whit 100mM of phosphate buffer. 4) Anti arrestin and anti enolase antibodies decreased the cardiomyocyte proliferation in vitro, phenomenon amplified when cells are treated by Okadoic acid, an inhibitor of phosphatase. 5) Visual arrestin and enolase being autoantigens in retina and neuronal tissues respectively, we detected high level of autoantibodies (4.7% for arrestin and 6.9% for alpha-enolase) in serum of patients with heart disease (n=157). In conclusion, the data suggest that arrestin like proteins can interact with alpha-enolase, interaction which can influence the signal transduction and glycolytic pathway in cardiac muscles. This complex also can be a candidate for induction of cardiac autoimmune diseases.
Heart failure has developed into a global disease that requires a global response. A better understanding of the molecular mechanisms underlying heart failure could lead to new therapeutic options for this dreadful disease. The Grb2-associated binder 1 (Gab1), a scaffolding adaptor protein, plays an important role in cytokine and growth factor receptors-mediated signal transduction in cardiac cells. To examine the physiological and pathological role of cardiac Gab1 in adult animals, we generated cardiac-specific Gab1 knockout (Gab1-cKO) mice. Cardiac Gab1 deficiency in mice causes age-dependent progressive dilated cardiomyopathy and heart failure at ages 3-6 months. Moreover, under mechanical stress with transverse aortic constriction (TAC) at a young age before the onset of heart failure, Gab1-cKO mice suffer severe dilated cardiomyopathy. Mechanistically, there were loss of mitochondrial membrane potential and an increase of cardiomyocyte apoptosis in the Gab1-cKO heart. Transmission electron microscopy studies of the heart tissue from Gab1-cKO mice showed damaged mitochondria with cristae lysis and apparent abnormal internal membrane whorls. Signaling studies revealed that proapoptotic genes including p38MAPK and caspase 3 were activated in the Gab1-cKO heart. Quantitative PCR analysis demonstrated that anti-apoptotic genes such as Bcl2 were down-regulated, whereas pro-apoptotic genes such as Bax were up-regulated in Gab1-cKO heart. Collectively, our finding suggests that Gab1 is a crucial regulator of cardiac function through maintaining mitochondrial integrity and cell survival to prevent heart failure.
THE MOLECULAR MECHANISM OF THE ANTI-OXIDATIVE EFFECTS OF CATECHIN ON PALMITIC ACID-INDUCED CYTOTOXICITY IN ASTROCYTES

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Aims: Metabolic syndrome (MS) encompasses a group of problems which will put a person at a high risk of developing cardiovascular diseases, including heart attack and stroke. Effective prevention or treatment of MS significantly reduces the risk for developing serious complications. Palmitic acid (PA) is a saturated fatty acid, when being excessive, is a significant risk factor for development of MS or stroke. However, damage by MS to astrocytes is relatively unexplored. Catechin is an effective antioxidant which would be beneficial to neurons subjected to reactive oxygen species (ROS) damage as well as on cardiovascular diseases. This study was to identify the mechanism(s) of PA-induced cytotoxicity in rat astrocytes and also to assess the protective effects of catechin.

Methods: Cell apoptosis assessed by TUNEL assay. Cytosolic Ca2+ in astrocytes was measured with Fura-2 method. Intracellular ROS was detected by fluorescence spectrophotometry. Mitochondria membrane potential (MMP) measured by MMP Assay Kit. The p < 0.05 were considered significant (ANOVA).

Results: Exposure of astrocytes to PA (100 µM) for 24 h resulted in approximately 50 % cell death. Cell death was apoptotic (TUNEL) and unrelated to endoplasmic reticulum (ER) stress and cytosolic Ca2+ elevation. Exposure of astrocytes to PA for 30 min to 5 h was associated with significant mitochondria membrane potential (MMP) collapse and ROS production. Co-treatment of astrocytes with catechin (300 µM) significantly prevented PA-induced MMP collapse, ROS production and cell death.

Conclusions: Our results suggest that PA-induced cytotoxicity in astrocytes may involve MMP collapse and ROS production, which can be prevented by catechin.
REMOTE CARDIAC INJURY MEDIATED BY NEUROGENIC PATHWAY: A CARDIAC DELETERIOUS EFFECT AND PREVENTS STRATEGY

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Objects. This study sought to determine the molecular and neuronal basis, which brain ischemia induced remote cardiac injury via carotid artery vascular surgery.

Background. To date there are no basic science studies addressing the deleterious effect of remote vascular surgical procedure upon myocardial ischemia/reperfusion (I/R) injury, though clinical observations support that such effects exist. We previously described carotid artery vascular surgery upon infarct size after I/R called remote cardiac injury (RCI). In the present study, we elucidate mechanisms underlying this phenomenon.

Methods and Results. A minimally traumatic mouse model of myocardial I/R injury was used to ascertain the effect of remote surgical procedures, carotid artery vascular surgery upon I/R injury. Cytokines knockout mice were employed to determine the effect of TNF-α, IL-1, IL-6, BK1R and β-adrenergic signaling. Sympathetic ganglion blocker (Hex) is used to address this possibility of a ganglion transmission in RCI. We show that the myocardium deleterious effect is initiated by the unilateral carotid artery vascular surgery, and requires neurogenic pathway while rule out an essential diffusible humoral factor as the cause of cardiac deterioration after I/R. Our results demonstrate RCI is independent of TNF-α, IL-1, IL-6, β-adrenergic, or BK1R signaling. Finally, our data support our development of an inductive approach to steer the discovery of novel signaling components in this study.

Conclusion. Certain surgical vascular surgery (i.e. carotid artery vascular ligation) induced at a remote site contributes to MI that may reflex a novel therapeutic strategy to prevent myocardium deleterious.
TISSUE PERFUSION IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION: THE ROLE OF FIBRINOGEN LEVEL IN CORONARY ARTERY REVASULARIZATION AFTER THROMBOLYTIC THERAPY AND RESCUE PERCUTANEOUS CORONARY INTERVENTION

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Background: Tissue reperfusion following thrombolytic therapy (TT) or percutaneous coronary intervention (PCI) can be affected by thrombus burden and impaired microcirculatory reperfusion. The Fibrinogen plays a major role in this process and we investigated its association after TT and rescue PCI.

Methods: A 276 patients diagnosed with acute-STEMI underwent TT and subsequently rescue PCI. The baseline fibrinogen concentration was obtained and the patients were classified to no-reperfusion group [by ECG criteria, measured as the degree of ST segment normalization, defined as =<50% ST-segment resolution as an evidence of failed TT]; and reperfusion group [which is defined as >50% ST-segment resolution as successful TT].

Results: Baseline fibrinogen concentration was significantly higher in the no-reperfusion group than in the reperfusion group by ECG criteria (367 ±190.07 mg/dl vs 248.8 ±104.9 mg/dl, p=0.001). The subsequent rescue PCI in the no-reperfusion group; showed an angiographic evidence of 31.2% total occlusion with clot burden in the infarct-related artery with a higher fibrinogen level (392.2 ±39.2 mg/dl vs 308.5 ±136.7 mg/dl; p=0.012). The no-reperfusion group had also a significant previous use of statin therapy (21.4% vs 8.5%, p=0.005) and B-blocker usage (20.3 vs 9.5%; p=0.019). No other angiographic parameters were showing any significant relation with the no-reperfusion group. After logistic regression analysis, only the fibrinogen level (univariate p= <0.001, multivariate p=< 0.001) retained statistical significance as an independent predictor of no-reperfusion.

Conclusion: Elevated baseline fibrinogen concentration is an independent risk factor of myocardial no-reperfusion or failed TT in STEMI patients initially treated with thrombolytic therapy.
PATHOLOGICAL EFFECT OF ENDOTHELIAL-TO-MESENCHYMAL TRANSITION ON THE CYSTIC KIDNEY

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Objectives: We research on pathological effects of endothelial to mesenchymal transition (EndMT) on cystic kidney. Furthermore, we try to find novel genes inducing endMT on it.

Background: EndMT is a phenomenon that an endothelial cell loses its characteristic and acquires mesenchymal cell specific feature. It is known to be crucial for heart development. However, as it was found that endMT was involved in the cardiac fibrosis in 2007, pathological effect of endMT has been unveiled in other organs. Kidney is the organ composing urinary system. A functional and structural unit of the kidney is called nephron, which consists of epithelial tubules and blood vessels. Majority of kidney diseases entail renal fibrosis which impairs renal function. In 2008, it was reported that renal fibrosis considerably results from endMT.

Methods: We got mRNA and protein from mouse cystic kidney tissues. Expression level of mesenchymal markers was checked by real time RT PCR and western blot. Extent of endMT was observed by immunostaining with antibodies for mesenchymal markers (FSP1, Vim, etc.) and endothelial cell marker (CD31).

Results: Expression level of mesenchymal markers in mouse cystic kidney was higher than that in mouse normal kidney. Furthermore, endMT occurred much more in the cystic kidney tissue.

Conclusions: Like other chronic kidney disease, cystic kidney entails renal fibrosis. EndMT considerably contributes to renal fibrosis in the cystic kidney. To find out the novel inducer gene for endMT can help understanding its pathological effect on the cystic kidney.
Complement-C1q TNF-related protein (CTRP) is expressed at high levels in obese adipose tissues, and its expression is induced by proinflammatory cytokines including TNF and IL-1. In the previous study we investigated stimulation of aldosterone production by CTRP, since it was observed that CTRP was specifically expressed in the zona glomerulosa of the adrenal cortex, where aldosterone is produced. CTRP increased aldosterone production through induction of CYP11B2 which is a late-limiting enzyme for aldosterone production. Now we investigate whether CTRP expression affects cardiac muscle generation. First of all, we generated CTRP heterozygote mice to know CTRP-regulated genes and gene signature. CTRP upregulates Chad, Cyp2A4, NR4A1, and SCGB3A1 were upregulated and SLC5A, KAP, ALDOB were downregulated. To know gene signature of up- and down-regulated genes list of genes were analyzed using DAVID. Now we are focusing on muscle generation-related genes.
INTERFERENCE OF DOXORUBICIN WITH CARDIAC AMPK SIGNALING – A CULPRIT FOR DOXORUBICIN CARDIOTOXICITY?

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Anthracyclines, in particular doxorubicin, are the most effective anticancer drugs. However, a serious side effect of this therapy is severe cardiotoxicity. Despite almost 50 years of research, elucidation of cardiotoxicity associated with anthracyclines remains a challenge in terms of involved mechanisms and prevention. Our studies in isolated perfused rat heart, and heart from doxorubicin-treated rats provide evidence that persistent alterations in protein kinase cell signaling may be a key element in development of cardiotoxicity. Although doxorubicin induces energetic, oxidative and genotoxic stress in the heart, activity of the energy stress sensor AMP-activated protein kinase (AMPK) is paradoxically down-regulated. AMPK inhibition is, at least partially, due to the regulatory cross-talk with Akt and MAPK pathways, which are activated by doxorubicin largely by DNA damage signaling via DNA-PK. Combined inhibition of AMPK and activation of Akt and MAPKs leads to activation of growth-stimulating mTOR signaling. Such a signaling pattern increases cellular energy deficits and, via active mTOR signaling, generates pro-hypertrophic signals, both potentially contributing to the cardiotoxic phenotype.
Background: Cilostazol, a phosphodiesterase III inhibitor, have been used for adjunctive dual anti-platelet therapy (DAT) after percutaneous coronary intervention (PCI). The elevation of cAMP by cilostazol might lead to tachyarrhythmia. However, its clinical implications have never been investigated.

Methods: The pilot study included 174 patients undergoing elective PCI in a prospective and randomized design. Patients were allocated in a 1:1 ratio to the triple anti-platelet therapy (TAT, cilostazol and DAT) or the DAT. At baseline and at 6-month, 24-h holter was measured. Primary end-points were heart rate (HR) and number of ventricular premature capture (VPC) and secondary end-points were numbers of non-sustained ventricular tachycardia (NS-VT), atrial premature capture (APC), and supraventricular tachycardia (SVT).

Results: 84 were allocated to the DAT group and the remaining 92 were allocated to the TAT group after elective PCI. Clinical and 24-h holter baseline was similar between the 2 groups. However, after follow-up of 6-month, HR and number of VPC in the TAT group higher than those of DAT group (HR, 68.9 ± 9.3 bpm vs. 74.1 ± 11.7 bpm, p = 0.005 and VPC, 79.7 ± 201.0 vs. 510.8 ± 1618.8, p < 0.001). There were no significant differences in the numbers of NS-VT, APC, and SVT between the 2 groups.

Discussion: TAT after PCI increased HR and number of VPC, compared with DAT. In patients with tachycardia and frequent VPC, the use of cilostazol, as an add-on to the DAT, should be more cautious.
MAJOR BLEEDING IN ACUTE CORONARY SYNDROMES: INCIDENCE, PREDICTORS AND PROGNOSTIC VALUE
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Background: Hemorrhagic complications have been strongly linked with subsequent morbidity and mortality in patients with acute coronary syndromes (ACS). Objectives: To determine the incidence and predictors of major bleeding and its impact on outcomes, including mortality, in patients with ACSs.

Methods: Patients (n = 200) with ACS, clinical data, management strategies, complications and outcome were reported in case report form. Factors associated with major bleeding were identified using logistic regression analysis and impact of major bleeding on outcomes, including mortality was reported.

Results: Bleeding occurred in 41 pts (20.5%), and was classified as nuisance (15 pts, 7.5%), minor (21pts, 10.5%) and major bleeding (5pts, 2.5%). Advanced age (p=0.02), interventional coronary procedures (p= 0.001), low BMI (p= 0.047), Clopidogrel loading > 300mg (p= 0.006) and renal insufficiency (p= 0.04) were independently associated with a higher risk of major bleeding. Bleeding was independently associated with an increased risk of hospital and 30 day incidence of death, MI and stroke (p= 0.03). Patients with major bleeding showed higher frequency of blood transfusion (p= 0.0001), discontinuation of antithrombotics (p = 0.0001), mortality (p= 0.0001), and MI (p = 0.02). Haemoglobin decrease at cut off point of 3.4 gm predicted major complications with sensitivity 91% and specificity 88% with AUC of 0.9 and (p= 0.0001).

Conclusions: Major bleeding is a powerful independent predictor of in-hospital and 30 day mortality in patients with ACS. Advanced age, renal insufficiency, high clopidogrel loading and invasive coronary procedures are independent risk factors for major bleeding in ACS patients.
CLOPIDOGREL: A CAUSE OF RECURRENT RHEUMATISM
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Background: Clopidogrel (CPD) and aspirin are the mainstay of dual agent anti-platelet therapy in current cardiology practice. CPD most commonly causes increased bleeding, gastritis and rash. We report a unique case of CPD related recurrent arthritis.

Methods: Case report and literature search

Case: A 64-year-old man reported fever, right shoulder pain and neck stiffness for one day. He underwent percutaneous transluminal angioplasty and insertion of drug eluting stents 2 weeks prior, at which time CPD was added to his therapy. History revealed an episode of similar illness after a loading dose of CPD was given to him a year before. Fever and a markedly limited range of motion at the shoulder joint was demonstrated. The next day he developed arthritis in bilateral wrist joints. Radiographs of the joints showed only degenerative changes. Sterile synovial fluid with few white cells was aspirated from the shoulder joint. Blood counts, electrolytes and tests of kidney and liver functions were within normal limits. ESR (89mm) and CRP (15mg/dl) were elevated. Uric acid concentration (4.4 mg/dl) was normal. Alternate diagnoses were ruled out with appropriate testing. CPD was discontinued in favor of Prasugrel with good symptomatic relief. There was no recurrence of symptoms in the 2 weeks of follow up.

Conclusion: Literature search resulted in 10 reported cases of arthritis caused by clopidogrel but only one of them report a recurrence. Our case describes a unique incidence of recurrent arthritis caused by clopidogrel.
ULTIMATE SIMPLE STRATEGY FOR BIFURCATION LESION
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Background: Coronary bifurcation lesions have a higher risk of procedural complications with a greater restenosis rate. Most bifurcation lesions are currently treated via a simple approach. However, if treated with one stent, side branch ostium stenosis is often a major problem. The benefit of side branch intervention remains uncertain. We investigated our simple one-stent strategy which, if at a minimum achieves Thrombolysis In Myocardial Infarction 3 (TIMI3) flow in all branches, can be performed in the presence of side branch ostium stenosis.

Methods: From January 2004 to October 2011, we treated 226 true bifurcation lesions with drug-eluting stents (n=161) or bare metal stents (n=65). Our strategy was very simple: if we achieved TIMI3 flow in the side branch, ostium stenosis was allowed. Clinical and angiographic follow-up were completed at 6 months. Major adverse cardiac events and quantitative coronary angiographic data were compared.

Results: Baseline clinical and angiographic characteristics were similar. MACE did not differ (p=0.54), while the 6-month total restenosis rate was significantly higher in the BMS group (27.7% vs 13.0%, p<0.01). Moreover, late lumen loss of the side branch ostium was significantly less frequent in the DES group (-0.10±0.46mm vs 0.17±0.51mm, p<0.05). Improved side branch ostium lumen diameter was recognizable at 6 months post-procedure in 65.8% of the DES but only 35.4% of the BMS group (p<0.01).

Conclusion: For treating bifurcation lesions, our simple strategy with DES significantly improves and maintains side branch ostium lumen diameter for at least 6 months post-procedure as compared with BMS.
THE ROLE OF PATIENT CHARACTERISTICS IN SELECTIVE DIAGNOSTIC CORONARY ANGIOGRAPHY BY FEMORAL VERSUS RADIAL ACCESS

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Objectives: To evaluate the comparability of radial access (RA) versus femoral access (FA) in performing selective coronary angiography (SCA) based on patient characteristics.

Background: RA for diagnostic SCA might be, sometimes, technically challenging resulting in higher level of radiation and contrast used when compared to FA. The role of patient characteristics (such as age, sex, weight, height and body mass index (BMI)) in choosing between the 2 approaches is not well known.

Methods: We performed a descriptive review of 361 randomly selected patients, who underwent SCA between 2010 and 2012. We compared both groups by logistic regression analysis of contrast dose, radiation dose, and radiation based on patient age, sex, weight, height and BMI.

Results: Patient characteristics are charted in the Table. When RA and FA was compared, patient characteristics such as age, sex, weight, height and BMI had no role in fluoroscopy time, radiation dose, or in contrast dose. Same results were reproduced when patients were divided into four quartiles within their age, height, and BMI groups.

| Total (n=361) Femoral (n=185) Radial (n=176) P value |
| Age 58.43 (12.29) 59.10 (12.09) 57.72 (12.51) 0.443 |
| Sex (n=361) 0.441 |
| Male 251 132 (52.59) 119 (47.41) |
| Female 110 53 (48.18) 57 (51.82) |
| Wt 91.48 (24.39) 90.15 (25.05) 92.03 (24.17) 0.572 |
| Ht 2.22 (9.91) 2.72 (13.84) 1.70 (0.11) 0.962 |
| BMI 30.75 (7.42) 30.00 (7.05) 31.53 (7.73) 0.107 |

Conclusions: RA approach is as good as FA in performing SCA in terms of contrast and radiation dose used, regardless of the patient characteristics. RA approach can be offered to all patients.
STUDY THE UPPER EXTREMITIES VARIATION AND ITS ROLE IN TRANSRADIAL ANGIOGRAPHY PROCEDURE

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Introduction: transradial coronary angiography has several benefits such as reduction in access site complications especially in fully anticoagulated patients. The presence of arterial anomalies in upper limb arteries has important role in procedural success. Methods: retrograde trans-arterial sheath injection was done in patients with transradial coronary angiography. Arterial anomalies in the upper limb evaluated in frequency and their effect on cannulation time, the time of catheter passage to ascending aorta, Angiography time, fluoroscopy time, and contrast material volume used.

Results: 165 consecutive patients were studied, 116(70.3%) male and aged 56.7±11.1 years. With 96.6% success rate in procedure. Totally 59 anomalies were observed in 44 patients (26.7%). Radial artery by itself had 25 anomalies (15.1%). The most frequent anomaly was abnormal origin of radial artery in 14 patients (8.5%) followed by tortuosities in 10 ulnar (6%), 9 brachial (5.4%), 7 radial (4/2%), 5 subclavian (3%) and 3 brachiocephalic arteries (1.8%). There also were 4 loops in ulnar artery (2.4%) and one in radial and brachial arteries (each 0.6%). Other anomalies include 4 patients (2.4%). Except cannulation time (p=0.97) there were associations between anomalies and each of other times (p=0.001) and contrast volume (p=0.009). Anomalies didn’t have any effect on procedural Success rate and just in one patient with sulclavian loop procedure changed to femoral approach (p=0.19).
AGE-RELATED DEVIATION IN ACTUAL INGUINAL LIGAMENT COURSE (ARC)

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The inguinal ligament (IL) is traditionally depicted by a straight line extending from the anterior superior iliac spine (ASIS) to pubic tubercle (PT). Its demarcation is important during arterial access to minimize the risks of retro-peritoneal hemorrhage. We hypothesize the IL does not travel a straight course but is bowed downward secondary to gravity and abdominal wall laxity. 20 CT scans of the abdomen and pelvis were reviewed. Images were reconstructed to determine the actual course of the IL utilizing Terracon software. The IL was identified and maximal intensity projection reconstructions were used to establish the transition from the external iliac artery to the common femoral artery in multiple views. The lowest point of the inferior epigastric artery loop was defined as the actual IL. The expected IL was marked by a straight line from the ASIS to PT. The vertical distance from actual IL to the expected IL was measured and correlated. Average patient age was 50.4 years. Increasing age demonstrated increased downward bowing of the actual IL from the expected IL course (r=-0.618, p < 0.01, df=18). There is a weak correlation with weight that did not reach statistical significance (r=-0.26, p=0.3, df=15). A linear regression equation to predict deviation by age has been developed (-0.165 * age + 4.276) The actual IL does not follow a straight course from ASIS to PT but is bowed downward. This difference is most closely related to age. Operators must be mindful of this downward bowing during vascular access.
UNUSUAL TREATMENT OF POSTOPERATIVE BLEEDING AFTER CARDIAC SURGERY: RIGHT CORONARY ARTERY STENTING WITH COVERED STENTS

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A 50-year-old man visited the emergency service because of palpitations and left chest pain. A transthoracic echocardiogram was performed and detected a right atrial (RA) mass that infiltrated the RA free wall and that protruded into the RA. For further evaluation of this mass, magnetic resonance imaging and computed tomography were performed. These explorations showed a large excentric tumor in the RA free wall, protruding into the RA. The tumor extended into the right atrioventricular groove. Coronary angiography showed a right coronary artery with collateral circulation to a big mass. The surgery was performed under standard extracorporeal circulation. The RA was excised and the tumour could only be partially resected because it extended right ventricle free wall and tricuspid valve annulus. The RA was reconstructed using bovine pericardium and after declamp a persistent bleeding was observed. Because the bleeding control was no possible, we decided to close the chest and to perform a right coronary angiography which had revealed an important free extravasation of contrast into the pericardium through the collateral circulation. These branches were tackled successfully by covered stents and post-covered stent angiogram showed complete cessation of contrast extravasation. The postoperative course was uneventful and after asymptom-free survival of eleven months the patient presented with bone metastases.
ARTERIAL WALL THICKENING DURING MENOPAUSE TRANSITION REFLECTS IRON ACCRUAL AND ATHEROSCLEROSIS RISK

Objective: To study the role of iron in atherosclerosis using MRI in perimenopausal women.

Background: Women are typically 5-10 years older than men at age of first atherosclerotic event. One factor contributing to this sex difference may be monthly loss of iron, a key mediator of LDL oxidation, in premenopausal women. The non-contrast MRI biomarker T2* shortens with increased tissue iron. We measured carotid artery T2* in a cohort of perimenopausal women to determine if shortened T2* predicts arterial wall disease.

Methods: Prospectively-enrolled women with atherosclerosis risk factors and 1-6 menstrual cycles in the past year underwent longitudinal assessment including MRI for carotid artery wall T2* and wall volume, a measure of arterial disease.

Results: 87 women, aged 49.8±3.8 years, completed all baseline and 12-month follow-up studies. Median number of menstrual cycles in the prior 12 months decreased from 4 to 1 (p<0.001) and total iron binding capacity decreased (414±63 to 403±59ug/dL, p=0.02). Carotid artery T2* shortened (22.7±3.2 to 21.1±2.5ms, (p<0.001), and arterial wall volume increased (670±130 to 690±114mL, p=0.04). Dietary iron intake averaged 12.1±5.3mg/d and did not significantly influence outcome measures. While bioavailable estradiol decreased (0.66[0.33-2.43] to 0.52[0.32-0.92]pg/mL, p<0.01), this hormonal change did not predict arterial wall volume increase (r=0.13, p=0.27). Shortened T2* predicted wall volume increase (r=0.34, p<0.01) even after adjusting for baseline Framingham-derived risk score (r=0.32, p<0.01).

Conclusions: Over 12 months of perimenopause, a non-invasive biomarker of arterial wall iron has predictive value for arterial wall disease beyond risk factors and hormonal changes. Further studies of iron’s mechanistic role in atherosclerosis leveraging T2*-MRI can support novel preventive strategies addressing iron homeostasis.
CARDIOVASCULAR DISEASE AND SPINAL CORD INJURY: RESULTS FROM A NATIONAL POPULATION HEALTH SURVEY

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Objectives: While several studies have shown a higher prevalence of risk factors for cardiovascular disease (CVD) in individuals with spinal cord injury (SCI), little is known about the prevalence of CVD itself and corresponding risk estimates in those with SCI. The objective of this study was therefore to evaluate the association between CVDs (heart disease and stroke) and SCI in a large representative sample.

Methods: Data was compiled from over 60,000 individuals from the 2010 Cycle of the cross-sectional Canadian Community Health Survey (CCHS). Multivariable logistic regression analysis was conducted to examine this relationship, adjusting for confounders, and using probability weighting to account for the CCHS sampling method. Results: After adjusting for age and sex, SCI was associated with a significant increased odds of heart disease (Adjusted odds ratio [OR]=2.72, 95% Confidence Interval (CI) [1.94, 3.82]) and stroke (Adjusted OR=3.72, 95% CI [2.22, 6.23]).

Conclusions: These remarkably heightened odds highlight the exigent need for targeted interventions and prevention strategies addressing modifiable risk factors for CVD in individuals with SCI.
Background: There is not enough data on the relation between waist circumference (WC) and the risk and severity of coronary artery disease (CAD) among the Egyptian population.

Aim of the work: To Study the relation between waist circumference, risk and severity of coronary artery disease as assessed by coronary angiography in an Egyptian cohort.

Patient and Methods: The study included 500 consecutive Egyptian patients with suspected or known CAD who underwent diagnostic coronary angiography. Severity of coronary artery disease was assessed by Gensini score (GS). All patient were subjected to: Clinical examination, measurement of body weight, height, body mass index (BMI), (WC) and serum lipid profile.

Results: Within the examined 500 patients, 368 (73.6%) were male (mean age: 55.08 SD9.89 years) and 132 (26.4%) were female (mean age: 55.26 SD8.88 years). Mean (WC) in females was (102.93SD8.88 cm), while in males it was (99.38SD9.88cm). One hundred patients (20%) had normal coronary angiogram (GS=0), 190 (38%) had mild disease (Gs<32), 108 (21.9%) had moderate disease (GS =32-58), and 102 (20.4%) had severe disease (GS >58). There was a significant positive correlation between GS and increased WC, metabolic syndrome, male sex, increasing age, DM and dyslipidemia but not with BMI, family history of CAD or hypertension. Multivariate analysis revealed that male sex, dyslipidemia, diabetes mellitus, (WC) and increasing age were independent predictors of the angiographic severity of CAD.

Conclusion: There was a significant positive correlation between increased waist circumference, presence and severity of coronary artery disease among adult Egyptian patients independent of body mass index.
Objectives: The objective of this study was to find any relationship between higher BMI and waist to hip ratio (WHR) with the occurrence and severity of coronary artery disease (CAD).

Background: For decades it has been assumed that high body mass index (BMI) is a risk factor for CAD, but findings of some recent studies were paradoxical.

Methods: This study was a cross-sectional prospective study that included 414 patients with suspected coronary artery disease in whom coronary angiography was performed in our hospital. The mean ± SD of their ages were 61.2 ± 27.4 years (range 25-84 years) and 250 (60.4%) of them were male. Regarding cardiovascular risk factors 113 (27.3%) had a history of diabetes mellitus (DM), 162 (39.1%) had hypercholesterolemia, 238 (57.4%) had hypertension, 109 (26.3%) were current smoker and 24 (5.8%) had a family history of CAD. The mean ± SD of patients BMI was 26.04 ± 4.08 (range 16-39) and mean ± SD of patients’ WHR ranged from 0.951 ± 0.07 to 0.987 ± 0.05. Severity of CAD according to SYNTAX and Duke score were 17.7 ± 9.6 (range 0-64) and 3.2 ± 1.7 (range 0-12) respectively.

Results: Our findings in this study were in favor of negative correlation between severity of CAD and BMI according to both SYNTAX and Duke score (p<0.001 and p=0.001 respectively). However there was a positive correlation between WHR and severity of CAD according to Duke score (p=0.03).

Conclusions: BMI does not have positive correlation with the severity of CAD, but WHR has.
MATRIX METALLOPROTEINASE 9 (MMP9), TISSUE INHIBITOR OF MMP (TIMP1) IN SERUM AT PATIENTS WITH SUBCLINICAL ATHEROSCLEROSIS

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Objective. Assessment of matrix metalloproteinase 9 (MMP-9), tissue inhibitor of MMP (TIMP1) in serum at patients with subclinical atherosclerosis. 45 participants were examined. Intima-media thickness of the common carotid artery (IMT CCA) is measured at duplex scanning (HD3, Phillips). Each patient was assigned to one of two groups on basis of IMT CCA. Group I consisted of men without atherosclerosis (mean IMT <1 mm) (n = 16 males, mean age 61, 2 ± 6, 7 years), and group II consisted of patients with subclinical atherosclerosis (mean IMT >1 mm) (n = 29 males, mean age 64, 4 ± 9, 6 years). Concentration MMP-9, TIMP-1 in serum was determined on standard methods with standard test-systems ELISA for immunosorbent assay (BCMDiagnostics, Bender-MedsystemsGmbH, Austria). Measurement conducted on spectrophotometer (Hospitex, Italy). All venous blood samples drawn after a 12-hour overnight fast was immediately refrigerated.

Results. MMP-9 protein expression levels were significantly higher in the group II when compared with group I (398, 78 + 61, 13 ng/ml and 130, 55 + 43, 83 ng /ml, respectively, p < 0,001). TIMP-1 expression levels were significantly higher in the group II when compared to group I (187, 76+87, 56 ng/ml and 144, 39+98, 65 ng/ml, p <0, 05). IMT CCA positively correlated with MMP-9 and TIMP-1 expression (p = 0,023 and p = 0,032 respectively).

Conclusion. MMP-9, TIMP-1 can be used as noninvasive markers for detection of subclinical atherosclerosis. The identified relationships suggest the possibility of determining these parameters as additional diagnostic criteria for complex examination.
Depression and Risk of Cardiovascular Diseases Among Men Aged 25-64 Years: WHO Program MONICA – Psychosocial

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Objectives. We sought to examine the relationship between depression symptoms and the risk development of arterial hypertension (AH), myocardial infarction (MI) and stroke among men ages 25 to 64 years.

Methods: Within the framework of program WHO MONICA-MOPSY was examined representative sample of men 25-64 years old (1994 year). Total sample was 657 persons. Depression symptoms were measured with the use of the MONICA-psychosocial Interview Depression scale. The incidence of new cases of AH, MI and stroke was revealed at 14-year follow-up. Cox-proportional regression model was used for an estimation of hazard ratio (HR).

Results: Prevalence of depression in cohort of men with AH was - 28.9%, with MI - 65.8% and with stroke – 70.6%. The risk of AH within 5 years in group of men with high level of depressive symptoms, in compared with those with low depressive symptoms was 6.7 times higher, 10 years HR=4.2, 14 years HR=2.1. The risk of MI within 5 years HR=2.26, 10 years HR=2.4, 14 years HR=2.6. The risk of stroke within 5 years was 6.4, 10 years HR=5.2, 14 years HR=1.4 (p<0.05).

Most frequently of cardiovascular diseases occurred in men with higher negative psychosocial factors, i.e. widowers, divorced, those with primary and not-completed secondary school education and those engaged in hard and moderate manual labor as well as pensioners.

Conclusion: Depression is a predictor of cardiovascular diseases in middle-age men. The risk of development of cardiovascular diseases in group of men with depression was 2.5-6 times higher than without it.
THE RELATIONSHIP BETWEEN CAROTID INTIMA-MEDIA THICKNESS AND CARDIAC SYNDROME X

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Background: Cardiac Syndrome X (CSX) describes patients presenting with typical exertional chest pain, a positive stress test, and angiographically normal or non-obstructed epicardial coronary arteries in the absence of coronary spasm. Aetiology of CSX is still a matter of controversy and its relation to early atherosclerosis has not been fully investigated.

Aim: This study was performed to characterize the relation of carotid intima media thickness in patients with cardiac syndrome X compared to cardia wise asymptomatic controls.

Methods and results: We studied 25 consecutive CSX patients (mean age 52±5 years, 13 women) and 25 healthy controls (mean age 51±6 years, 10 women). The two groups were comparable for baseline clinical variable and coronary artery disease risk factors except for an increased incidence of hypertension (68% vs. 16%, P < 0.01), and diabetes mellitus (52% vs. 8%, P < 0.01) in patients with CSX compared to control group respectively. Common carotid IMT values were significantly higher in patients with CSX compared to controls (0.9 [0.55–1.78] mm vs. 0.61[0.46–1.16] mm, P<0.001). This difference remained significant even after exclusion of patients with hypertension and diabetes mellitus. Three patients in CSX group had carotid atherosclerotic plaques with none in the control group.

Conclusions: This study showed that compared to control subjects, patients with CSX have increased mean common carotid artery IMT. It demonstrated the usefulness of CIMT in predicting CSX patients. It raises the possibility that the pathogenesis of CSX may be an early form of atherosclerosis involving the coronary microvasculature.
RELATIONSHIP BETWEEN BONE MINERAL DENSITY AND RISK FACTORS OF Atherosclerosis AND CARDIOVASCULAR DISEASE IN KOREAN POSTMENOPAUSAL WOMEN

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We investigated the associations between bone mineral density and the risk factors for cardiovascular disease in Korean postmenopausal women who were enrolled in a health promotion center of a university hospital from January, 2012 to December, 2012. The risk factors of atherosclerosis and cardiovascular disease were a current smoker, no regular exercise, obesity, abdominal obesity, hypercholesterolemia, low levels of high density lipoprotein cholesterol, high levels of low density lipoprotein cholesterol, hypertriglyceridemia, hypertension, and diabetes mellitus. Metabolic syndrome was used as an endpoint of the risk factors for cardiovascular disease. The bone mineral density measures of the subjects were assessed using dual-energy X-ray absorptiometry. Data on their lifestyle, their current medical diseases and their medications was collected during a personal interview with using a questionnaire at the initial examination. Height, body weight, waist circumference, blood pressure, fasting blood glucose and the serum lipid profiles were measured. In the adjusted analysis with including age and the body mass index, blood pressure and the triglyceride level had a close correlation with bone mineral density. After adjustment for age, waist circumference, systolic- and diastolic blood pressure, bone mineral density revealed significant correlation with the presence of metabolic syndrome. Bone mineral density measures in Korean postmenopausal women with no prior history of cardiovascular disease were inversely related to metabolic syndrome, independent of age, waist circumference, systolic- and diastolic blood pressure, total cholesterol and triglyceride as risk factors for cardiovascular disease.
PRESENCE OF ANOMALOUS CORONARIES DO NOT INCREASE THE RISK FOR ATHEROSCLEROSIS

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2. CareMore Arizona

Background: It is unclear if anomalous coronary arteries are at higher risk in developing atherosclerosis. The aim of this study is to determine whether the coronary artery anomaly predisposes to development of atherosclerosis.

Methods: Using retrospective chart review, all patients with anomalous coronary arteries recognized during coronary angiography between years 2000 to 2007 were analyzed. Prevalence of significant atherosclerotic coronary artery disease (defined as more than 50% luminal narrowing) was compared between normal and anomalous coronaries. Results: A total of 147 patients with anomalous coronary arteries were found. Right coronary artery (RCA) was the most common anomalous artery 128 of 148 (86.5%) in our dataset. There was no difference in the occurrence of atherosclerosis between anomalous or non-anomalous coronaries. Significant atherosclerosis was present in 59 of the 148 anomalous coronary arteries (37.8%), and 112 of the 293 non-anomalous coronary arteries (38.2%, p=0.9).

Conclusion: Based on our study, there is no evidence that anomalous coronary arteries are more likely to have significant atherosclerosis in comparison to normal coronary arteries.
DOES BASELINE PR INTERVAL IMPACT OUTCOMES AFTER CARDIAC RESYNCHRONIZATION THERAPY?

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Introduction: Not all heart failure patients improve after cardiac resynchronization therapy (CRT). Patients with short baseline (pre-CRT) PR intervals may require shorter programmed AV delays to preempt native dyssynchronous conduction, causing truncated transmitral flow due to early left ventricular (LV) contraction. However, patients with prolonged baseline PR intervals have more advanced conduction disease and may improve less after CRT.

Methods: Clinical, ECG and Echocardiographic (Echo) variables were retrospectively analyzed in 103 patients pre- and post-CRT. Patients were sorted into groups: pre-CRT PR < 200 ms (n=66) and pre-CRT PR ≥ 200 ms (n=37).

Results: Groups matched at baseline except for slower heart rate (HR), shorter QRS duration, larger left atrial (LA) size, and worse mitral regurgitation (MR) in PR ≥ 200 group. Overall, LV ejection fraction (LVEF) improved with CRT (Pre-CRT=23.7%, Post-CRT=32.2%, P<0.001). However, patients with pre-CRT PR < 200 ms had greater improvements in LVEF, LVESD, and MR grade.

Conclusions: Baseline PR interval may have important effects on CRT response. Patients with PR intervals < 200 ms had better outcomes in LV function. More preexisting conduction disease may be a more powerful marker of poor outcomes compared to the effects of short AV delay and truncated transmitral flow.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre-CRT PR &lt; 200 (n=66)</th>
<th>Pre-CRT PR ≥200 (n=37)</th>
<th>P value</th>
<th>Post-CRT PR &lt; 200</th>
<th>Post-CRT PR ≥200</th>
<th>P value</th>
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<tr>
<td>Age</td>
<td>68.1</td>
<td>68.1</td>
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<tr>
<td>Gender (M, F)</td>
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<td>27, 10</td>
<td>0.51</td>
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<td>19.18</td>
<td>0.22</td>
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<td>Mean F/U (days)</td>
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<td>281.7</td>
<td>285.6</td>
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<tr>
<td>HR</td>
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<td>68.7</td>
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<td>ΔLVEF</td>
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<tr>
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<td></td>
<td></td>
<td>-0.16</td>
<td>-0.03</td>
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</table>

*P=0.02 †P=NS
THE FATE OF INNOCENT BYSTANDER LEADS AFTER LASER LEAD EXTRACTION
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Objective/Background: The effect of laser lead extraction on the long term survival of adjacent, non-extracted (“innocent bystander”) leads has not been previously reported. Inadvertent trauma to the innocent bystander leads at the time of laser lead extraction may lead to a decrease in their long term survival.

Methods: Patients with implantable cardioverter-defibrillators (ICDs) who had undergone revision or upgrade between January 2008 and December 2010 by a single operator (JS) at our institution were identified. A group of patients with an innocent bystander lead(s) was compared in a case controlled format with a similar group of patients who had existing leads that we reused at the time of device revision or upgrade, without the use of the laser.

Results: In the reviewed period, 16 laser lead patients with a total of 24 innocent bystander leads were identified. Four out of these 16 patients were found to have an innocent bystander lead that failed (mean follow-up of 24 months). In the control group, 40 patients underwent implantation of a new lead without laser lead extraction; here, 60 reused leads were identified. None of the reused leads failed (mean follow-up of 25 months). (P value = 0.0099)

Conclusion: This finding implies that laser lead extraction can negatively impact the lifespan of the innocent bystander leads. If confirmed in a larger trial, this finding could occasionally impact the decision to extract a given lead.
Objective: To compare the efficacy of two pacing protocols, MVP versus DDDR with long AV delay in patients with sinus node dysfunction.

Background: Dual chamber pacing in sinus node dysfunction could result in ventricular pacing. Managed ventricular pacing (MVP) is a pacing protocol designed to reduce ventricular pacing which might be harmful.

Method: Patients with sinus node dysfunction who had pacemaker implantation at Siriraj Hospital, Thailand, were randomized to have their pacemaker programmed to either MVP (MVP on) or DDDR with long AV delay (MVP off) mode. In the latter group, the AV delay was increased to ensure that there was no ventricular pacing or to a maximum of 300 milliseconds. After 3 months the patients were switched to another mode for the same duration. The primary outcome was ventricular pacing percentage (%VP) comparing between MVP mode and DDDR with long AV delay.

Results: Fifty patients were enrolled to the study. Twenty-seven (54%) were female. There was no difference in %VP between the two pacing mode (6.51% for MVP on versus 5.48% for MVP off, p=0.264). However, the patients in the MVP off group had higher six minutes' walk distance (272.81+81.33 versus 251.36+79.62, p=0.008). Other parameters included left atrial diameter, left ventricular systolic function, and brain natriuretic peptide level were also similar between the two groups.

Conclusion: There was no difference in %VP between MVP and DDDR with long AV delay pacing mode. However, the patients in the latter group had higher six minutes walk distance.
Background: This audit was carried out at a district general hospital. In the absence of an acute cardiology service the aim was to elucidate whether cardiology patients attending the emergency department (ED) were appropriately managed. The audit focused on rhythm disturbances commonly seen on ECG.

Objectives: The main outcomes were to determine ED staff knowledge of indications for permanent pacemaker (PPM) insertion, and to compare this knowledge across all grades. Methods: Using the European Society of Cardiology Guidelines on Cardiac Pacing and Cardiac Resynchronisation Therapy as a gold standard, a 15 question survey was created. Each question was a clinical scenario with answer options of A= no action required, B= non urgent referral, and C= urgent referral to cardiologist.

Results: Twenty one members of ED staff completed the survey scoring an average of 62.7%. Marks ranged from 8.5 (consultants) to 10.3 (senior house officers). Of the total 315 responses, 65% of incorrect answers included unnecessary or inappropriately urgent referrals. However, 21% of referrals were delayed or simply not made. Following a teaching session, subsets of original participants were re-tested on incorrectly answered questions. The average mark pre teaching session of 41.2% improved significantly to 80%.

Conclusions: These findings highlight that further education is required across all grades. A teaching session improved knowledge. Extrapolating these findings, it is hoped that an electronic teaching session will help to reduce unnecessary referrals, and ensure appropriate and timely cardiological referrals.
UNWINDING LIFE IN THE HEART; A CASE OF INTERNAL CARDIOVERTER-DEFIBRILLATOR LEAD MALFUNCTION
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Background: Internal cardioverter-defibrillator (ICD) lead malfunctions such as disintegration and externalization of the coils are rare but serious complications noted with Riata ICD leads, and are of growing concern.

Case Report: A 63-year-old, pacemaker dependent woman presented with complaint of hearing “beeping sounds” from her ICD. Interrogation of her defibrillator revealed a gradual increase in the lead impedance of over 2000 ohms, from the past five months prior to this presentation. The ICD lead fluoroscopy showed externalization of the ICD lead components between proximal and distal coils, a rare finding that has been recently reported in the literature with St. Jude Medical Riata ICD leads. She subsequently underwent a successful ICD lead replacement.

Discussion: Although extremely uncommon, few pacemaker and ICD lead manufacturers had malfunctioning leads resulting in a series of advisories and recalls. There is a rare possible risk for serious injuries and death resulting from inappropriate sensing, failure to capture or to deliver shock, and perforation of the heart. As a result, the medical community has faced with serious medical, psychological and financial burden. Most recent examples for such serious problems are Telectronics Accufix pacing leads, Medtronic’s Sprint Fidelis lead, and St. Jude Medical Riata ICD lead malfunctions. Conclusion: Externalization of the ICD lead is rare, but is a potentially serious complication of the newer ICD systems. There is no consensus if patients who already have these leads implanted, should have them replaced. Due to significant medico-legal risks involved, a clear communication between patients and their physicians is essential.
EPICARDIAL RHYTHM DEVICES (ERD), AN ALTERNATIVE FOR HEMODIALYSIS PATIENTS

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Objectives: Sudden cardiac death in the dialysis population comprises 25\% of all-cause of mortality. The epicardial approach for cardiac rhythm device leads may be preferred over transvenous leads.

Background: The transvenous route has been the most frequently used method for insertion of Cardiac Rhythm Device (CRD) leads. However, this route can cause major problems including central venous stenosis and cardiac device infection during episodes of dialysis access-related bacteremia.

Methods: This is a case report where a 56 year-old man on chronic hemodialysis presented with episodes of cardiac arrest due to ventricular fibrillation. He had had an amputation due to osteomyelitis and an arteriovenous-graft (AVG) infection of the right upper extremity in the past. At present evaluation he had a left upper extremity AVG. Results: Vascular evaluation revealed right subclavian vein and superior vena cava stenoses. Along with the presence of a left upper extremity AVG, this posed a dilemma regarding safety and usefulness of a transvenous rhythm device. An ERD-AICD was placed and one year later there were no cardiac or infectious events reported. Conclusions: Epicardial leads should be considered in hemodialysis patients who require a new CRD or replacement of existing transvenous CRD leads. Transvenous CRD leads can cause central venous stenosis and are vulnerable to contamination during AVG or tunneled hemodialysis catheter-related bacteremia. Because these complications are not infrequent in hemodialysis patients an alternative pathway is warranted. Epicardial leads do not traverse through the central veins and are not directly exposed to blood flow and do not cause central venous stenosis.
THE EFFECT OF AEROBIC TRAINING ON ENDOTHELIUM-DEPENDENT VASODILATATION IN CORONARY ARTERY DISEASE PATIENTS AFTER REVASCULARIZATION

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2. Angiography ward, Naft Hospital, Ahvaz, Iran

Background: because endothelium dependent vasodilation in coronary artery disease (CAD) patients after revascularization has not been studied enough, the aim of this study was to evaluate it.

Methods. This experimental study was conducted on patients with CAD (3 month after CABG and PCI) and students of medical school in 2011. The subjects were three groups. 20 patients were randomized into underwent training and control groups also 10 healthy young adults men underwent training compared to patients groups. Endothelium dependent dilation of the brachial artery was determined by using high-resolution vascular ultra-sonography through flow-mediated vasodilatation (FMD) after induction of ischemia, and the data were analyzed using SPSS, dependent t-test and ANCOVA.

Results: The findings showed that at baseline, FMD was reduced in revascularized patients, when compared with healthy young men, after 8 weeks, and exercise training significantly improved FMD in patients underwent training group [from 4.31±1.45 (SD)% to 6.15±0.773 (SD)%, p<0.05] and substantially increased the same in healthy young men [from 9.18±1.45% to 11.72±1.72%, p<0.05]. However, in the control group, the FMD remained unchanged, and even after aerobic training, it did not significantly modify the brachial artery diameter in these group.

Conclusion. Our study demonstrates that endothelial dysfunction persists in CAD patients after revascularization and aerobic training can improve endothelial function in different vascular beds in CAD patients and healthy young men. This may contribute to the benefit of regular exercise in preventing and restricting cardiovascular disease.
ANALYSIS OF THE RELATION BETWEEN VO₂MAX. AND LACTATE AFTER PHYSICAL EFFORT TEST IN ELDERLY
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2. University of Sao Paulo, Sao Paulo, SP, Brazil

Objectives: To analyze the relation of maximal oxygen uptake (VO₂max.) and lactate after maximum physical effort test in a group of elderly.

Background: With aging, physical abilities decrease, reducing the VO₂max. and the lactate.

Methods: Healthy elderly were submitted to a test of maximum physical effort in an electric treadmill. The lactate and VO₂max. were measured immediately after the exertion, analyzed in chemical analyzers. For statistical analysis of the correlation of the variables VO₂max. and lactate, it was used the “Pearson Correlation” and “Student t test” to detect any difference, with a significance level of 5%.

Results and Conclusions: We analyzed a sample of 17 elderly, with average age of 69.6 years (± 5.2), 64.7% female and 35.3% male. The VO₂max. average was 20.8 (± 3.9) ml.Kg.min⁻¹, being 20.2 (± 3.3) ml.Kg.min⁻¹ for women and 21.9 (± 5.0) ml.Kg.min⁻¹ for men, not showing significant differences between genders (p = 0.46). The average lactate was 4.7 (± 1.8) mg/dL, being, 4.6 (± 2.1) mg/dL for seniors (female) and 4.8 (± 1.3) mg/dL for seniors (male), with no significance (p= 0.77). There was a low correlation between VO₂max. and lactate (r = 0.25) when these variables were associated, with no gender distinction. However, when the sample was stratified, the associations show differentiated correlations for men (r = 0.68) and women (r = 0.07). The male cases showed a good correlation, indicating better association of these physical exhaustion indicators for patients (male) over 60 years old.
Background: The Finnegan score (FS) was proposed to assess neonatal abstinence syndrome (NAS) and is independent of the heart rate variability (HRV). We evaluated whether HRV is decreased in cases undergoing withdrawal compared to the controls and whether HRV changes are able to detect opiate withdrawal earlier than FS.

Methods: This is an observational study comparing HRV and FS. Twenty four controls and 25 cases were enrolled based on enrollment criteria. FS, and a rhythm strip were obtained at four hour intervals. N-N intervals were tabulated and time-domain analysis was performed.

Results: There were no differences in demographics between the groups. There is a higher average heart rate (AHR), decreased average N-N intervals, lower square root of the mean squared differences (RMSSD), and decreased standard deviation of N-N intervals (SDNN) among the cases compared to controls (p< 0.05). FS was positively correlated with higher AHR and decreased SDNN (p<0.05). In addition, higher average N-N intervals, higher SDNN, and higher RMSSD were noted among the controls (p<0.05) compared to cases within the first 24 hours, before reaching FS threshold for medical therapy.

Conclusion: HRV is decreased in NAS patients with opiate withdrawal compared to controls. FS was positively correlated with decreased HRV parameters. In addition, decreased HRV is present within the first 24 hours and presents earlier than a threshold FS in those requiring treatment. Therefore, incorporation of HRV parameters into the NAS score may allow for earlier detection and treatment of NAS patients.
PRENATAL DIAGNOSIS AND OUTCOMES OF FETUSES WITH TRICUSPID ATRESIA SINGLE CENTRE EXPERIENCE

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2. Main Center of Family Medicine, Prishtina, Kosovo

Introduction: Tricuspid atresia (TrA) is a congenital heart disease where there is no direct communication between the right atrium and right ventricle. Aim of this presentation was retrospective analysis of diagnosis, features and outcomes of fetuses with TrA diagnosed in our clinic.

Method and materials: Between January 2001 and December 2012 in our Clinic were studied around 326 fetal cases with congenital heart disease (CHD), and in 23(7.0%) were found to have TrA. Age of gestation at time of diagnosis was 16-38 weeks gestation. Retrospectively were analyzed characteristics and outcomes of 18 cases with known follow-up.

Results Characteristics: Three fetuses were twins, 2 fetuses were triple. Five fetuses(21.7%) had restrictive interatrial communication and balloon atrioseptostomy immediately were performed. Twelve of them had heart failure already at presentation, due to restrictive communication. All fetuses had nonrestrictive VSD, 5 of them had additional muscular restrictive VSD. Five fetuses (17.4%) had transposition of great arteries with nonrestrictive VSD, 8 fetuses (34.8%) had pulmonary stenosis, 2 (8.7%) had pulmonary atresia, 9 were (39.1%) with patent ductus, one with aortic coarctation, 6 had associated extracardiac anomalies.

Outcomes: Seven pregnancies (30.4%) were terminated, 6 with extracardiac anomalies. Out of 16 fetuses that continued pregnancies, 3 died in utero, 3 died shortly after birth and 3 died in second month of life waiting for surgery. The remaining 10 cases were operated with palliative procedures (shunt or pulmonary band). All they underwent surgery (Glenn operation or Fontan procedure). Total intrauterine and postnatal mortality, with terminated pregnancies was 16/23(69.6%).
UNDER ESTIMATION OF ATRIAL SEPTAL DEFECT CLOSURE DEVICE SIZE IN LARGE ATRIAL SEPTAL DEFECTS REQUIRING DEVICES ≥ 27 MM

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Cairo University, Cairo, Egypt

Objective: To report on difficulties of closure device size selection in patients with larger defects sizes ≥ 27 mm.

Background: Large ASDs in adults represent a small minority in most reports. Supporting rims of larger ASDs appear less capable of supporting bigger closure devices.

Methods: 62 consecutive patients were referred for ASD closure using Occlutech device. Patients were divided into two groups based on ASD size by TEE. Group A (43 patients) with devices < 27 mm and group B (19 patients) with devices ≥ 27 mm.

Results: Patients in group A were 8.3+1.8 years and 17.5 + 3.5 kg. Mean ASD diameter was 16 +2 mm. Median device size was 16 mm (range 6-24 mm). Device was successfully placed in all 43 patients using standard device size selection criteria. During mean follow-up of 12+3 months, no major complication were observed. Patients in group B were all > 18 years. ASD was successfully closed in 18 patients after 21 percutaneous attempts. In one patient, defect was surgically closed after percutaneous attempt was aborted. Another 2 patients needed two attempts to successfully close defect with device size 40 mm. In the remaining 16 patients 7 patients needed one step-up of estimated device size by TEE due to failure of measured rim to support the bigger device. During a mean follow-up of 5+1 months, no major complication were observed.

Conclusions: Transcatheter closure of larger ASDs is technically more challenging and frequently needs one step-up in device size selection to maintain device stability.
CHARACTERIZATION AND EVALUATION OF DUCTUS ARTERIOSUS STENTING IN NEONATES AND INFANTS WITH DUCT-DEPENDENT CYANOTIC CONGENITAL HEART DISEASE

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¹ Universidad Libre Seccional Cali, Colombia
² Imbanaco Medical Center, Columbia

Introduction and Objectives: Patients with duct-dependent cyanotic congenital heart disease need persistence in its permeability to ensure the flow either pulmonar or systemic system. Prostaglandin E1 infusion is generally effective for this use however is time. If achieved patency of the ductus arteriosus, with Ductal stenting can be performed palliation with minimal complications compared to surgery modified Blalock-Taussig. Objective: Characterization and Evaluation of ductus arteriosus stenting in neonates and infants with duct-dependent cyanotic congenital heart disease

Methods and Materials: 37 newborn patients with duct-dependent cyanotic congenital heart disease handled between 1 January, 2008 – 31 December, 2012 (5 years), in Imbanaco Medical Center in the city of Cali, Colombia.

Results: Ductal stenting was successful in 26 patients. Mean age was 28 ± 21.1 days and the average weight was 3.4 ± 1.9 kilograms. With this procedure, only one patient died immediately after the procedure. No major complications during stenting procedure, but were 9 hospital deaths, these occurred 2 to 14 days after stent implantation and were due to other conditions unrelated to the procedure. 10 patients underwent surgery modified Blalock-Taussig shunt after implantation of ductal stent failed. The average length of the stent was 17 ± 5.2mm (8 to 30mm) and diameter of 5 ± 1.3mm (3.5 to 10mm). The average procedure time was 60 minutes (range 30-130 minutes) and average fluoroscopy time was 20 minutes (range 8-40 minutes).

Conclusions: Ductal stenting becomes a useful and important tool to use in the patient with duct-dependent cyanotic congenital heart disease as an alternative to traditional surgical management, with lower rates of complications and mortality.
P308 REMOTE MONITORING IN CARDIOLOGY

291 USING THE IPHONE AS A HEART RHYTHM MONITOR. CAN I SEE P WAVES IN MY PHONE?
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Penn State Hershey Heart & Vascular Institute, Hershey, PA, USA

Objectives: describe our experience identifying P waves in electrocardiographic (ECG) recordings using the Alive ECG rhythm monitor (AliveCor).
Background: Alive ECG is an FDA approved ambulatory cardiac rhythm monitor that records a single channel (lead I) ECG rhythm strip using an iPhone.
Methods and results: Forty three recordings (10-30 secs) corresponding to 10 healthy volunteers and 10 volunteer cardiology patients were reviewed to identify the quality of the recording and registration of P or flutter waves. Heart rate corresponded 100% with palpation in volunteers and surface ECG in patients. P waves were identified in 38 (88.4%) recordings, all in sinus rhythm. No P wave was detected in 5 (11.6%) recordings, one sinus rhythm with low voltage P waves in the surface ECG, two with excessive baseline noise and two in atrial flutter. Overall recording quality was classified as good in 60.5 %, regular 34.8% and poor 9.3%. Quality was compromised by baseline noise and oscillation. Older individuals recorded more noisy signals. Poor contact, hand and arm tension holding the electrodes and tremors compromised the quality of the recording. One recording was performed using ECG patch electrodes attached to the volunteer and the device itself, connected with electrical wires and alligators. The recording obtained had no noise and was comparable with standard hospital monitors.
Conclusions: smartphone based wireless ECG rhythm monitoring holds promise. Individual coaching may be required to optimize the quality of the recording. Validity for detecting atrial arrhythmias and low voltage P waves should be further investigated.
Recognition that cardiovascular disease is the leading cause of mortality in women has stimulated major interest and improvement in the detection, prevention, and treatment of CVD in women. Certain aspects of this subject require further clarification and will be considered in this presentation: 1) CVD is the chief cause of death in women after the age of 75 yr, and prior to this age it is preceded in this statistic by cancer. 2) Because the toll of CVD is so high after 75 y.o., averaged over the lifetime, CVD is the leading cause of mortality in women. 3) MI, and especially fatal MI, is rare in premenopausal, nondiabetic, nonsmoking women. 4) CVD frequency rises sharply ~10 yr post-menopause but always lags behind that of men. 5) Primary prevention of CVD in women, as in men, is based on the traditional risk factors and despite its limitations, the Framingham risk score is a useful initial approach to risk estimation and can be refined by addition of family history and metabolic syndrome. 6) Women (and the elderly) have an increased frequency of atypical symptoms of ACS but the majority of this population presents with typical symptoms. 7) The first diagnostic method for CAD in women who can exercise and have a normal baseline ECG should be the exercise treadmill test, as recommended by ACC/AHA guidelines. 8) Current guidelines recommend similar treatment of women and men for most aspects of ACS and favor initial conservative therapy for women with a low risk presentation. 9) Recent data demonstrate an identical frequency of coronary microvascular dysfunction in the two sexes with chest pain and nonobstructive CAD. 10) The markedly increased frequency of Takatsubo cardiomyopathy in postmenopausal women than other segments of the population has not yet been clarified.
Stable ischemic heart disease (SIHD) is a new term in vogue; and one must address not only the impact of treatment on symptoms and quality of life but also on mortality and other serious adverse cardiovascular outcomes (SACO) such as myocardial infarction (MI) and stroke. Lifestyle alterations (abstinence of smoking, regular exercise and lipid modifying treatment with statins, reduce the incidence of SACO. But modifying abnormal lipids with niacin, or fibrates or raising HDL cholesterol with CTEP blockers, do not decrease SACO. Daily aspirin use in patients with SIHD and adequate control of blood pressure also reduce SACO. Antianginal agents reduce angina frequency and increase exercise tolerance but have little impact on mortality with only few exceptions, such as the use of beta blockers and ACE inhibitors after an acute MI and in patients with reduced left ventricular systolic function. Compared to optimal medical treatment, coronary revascularization, even in patients with diabetes and SIHD, does not reduce mortality or rates of MI but does relieve patient symptoms more effectively at least for the short term. Older medications such as allopurinol and colchicine have shown benefit in recent trials, but large outcome trials are needed before recommending their routine use. Individualization of treatment which takes into consideration patients’ lifestyle and presence of comorbidities which impact outcomes, and influence selection of treatment strategy, is critical in providing the best available treatment to patients with SIHD.
While physicians generally treat cardiovascular disease and risk factors with conventional medications such as statins and beta blockers, patients often use complementary or integrative therapy such as fish oil, vitamins, enzymes, and chelation therapy. This $45 billion industry is based on the belief that non-allopathic therapies can lower cardiovascular risk in addition to, or in lieu of, conventional therapy. The NIH Center for Complementary and Alternative Medicine supports therapy "for which there is some high-quality scientific evidence of safety and effectiveness"; however, most integrative therapies do not meet this test. Prospective studies support a minor role for omega3 fatty acids, a Mediterranean diet, and possibly vitamin C supplementation to reduce cardiovascular risk in selected individuals. No evidence to data supports the routine use of multi-vitamins, coenzyme Q, vitamin D or chelation therapy. The critical role of addressing conventional risk factors should not be abridged by unproven integrative therapies.
MEDICAL RISK FACTOR CONTROL IN LARGE TRIALS OF DIABETIC PATIENTS UNDERGOING CORONARY REvascularization

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Over the past 2 decades, significant progress has been made in the medical management for patients with coronary artery disease (CAD). Despite guidelines that recommend specific targets for control of risk factors, specifically blood pressure targets in hypertensive patients, low-density lipoprotein (LDL) for those with hyperlipidemia, and glycemic control (HbA1C) in diabetic patients, current large cohort studies demonstrate that a significant proportion of patients do not achieve target risk factor control. In this report, we further evaluate the data from three federally funded trials that focus on optimal medical therapy in patients with coronary artery disease and discuss potential barriers to achieving these targets. In this analysis, data from COURAGE, BARI-2D, and FREEDOM trials, specifically evaluating the proportion of patients that fail to achieve guideline-based targets for blood pressure, LDL, and HbA1C, were obtained from the respective principal investigators. Baseline and 1-year data from 2287 patients enrolled in COURAGE, 2368 patients in BARI-2D, and 1901 patients in FREEDOM trials, will be compared. Data from the 3 trials demonstrate that a significant number of patients fail to achieve targets for important cardiovascular risk factors as recommended by national guidelines even when optimal medical therapy is offered in the setting of large-scale clinical trials.

Future initiatives to improve control of risk factors are necessary and should be a key objective of future clinical trials in patients with CAD who are eligible for coronary revascularization.
PTEN AND STATINS INDUCED NEW ONSET DIABETES
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Background: High-dose statin therapy increases the incidence of new-onset diabetes. Studies in animal models have suggested that prolonged statin therapy upregulates Phosphatase and Tensin Homologue on Chromosome 10 (PTEN) expression. PTEN levels are also elevated in the heart, aorta and skeletal muscles of animals with diabetes, as well as the myocardium of diabetic patients. Increasing intracellular cAMP levels with subsequent activation of protein kinase A (PKA) decreases PTEN expression. We assessed whether prolonged treatment with high-dose statins induces diabetes and upregulates PTEN in the skeletal muscle of rats receiving Western Diet and whether concomitant treatment with cilostazol (CIL, a phosphodiesterase-3 inhibitor that increases cAMP levels) will attenuate these effects.

Methods: Rats received normal diet or Western diet without (control) or with rosuvastatin (ROS, 10 mg/kg/d), CIL (10 mg/kg/d), or ROS+CIL for 30 days.

Results: Western diet alone caused significant increase in glucose, GHbA1c and insulin. These levels were significantly higher in the ROS group. Western diet alone increased PTEN expression and decreased P-Akt levels. Levels of PTEN were significantly higher and P-Akt lower in the ROS than the control group. CIL normalized fasting glucose, GHbA1c and insulin levels and attenuated the changes in PTEN and P-Akt concentrations in the ROS+CIL group.

Conclusions: Long-term high dose statins can induce diabetes by upregulating PTEN that attenuates Akt activation. CIL attenuates these changes. Further studies are needed to assess the effects of increasing cAMP levels by GLP-1 activation or CIL to prevent induction of diabetes by statins.
Coronary artery disease prevention and treatment has received extensive study over the past few decades. However, many of the landmark studies have excluded geriatric patients by design. This has left a huge gap in data as to how to manage these patients. With the aging of the population, evidence-based practice is difficult to define in these patients. Recently, some studies have targeted older patients to define optimal medical as well as interventional/revascularization treatment. In addition, we have a better understanding of the potential risk of bleeding in the older patient. This will translate into better management of these patients with better assessment of the risk to benefit ratio.
Non-contrast-enhanced CT for coronary artery calcification (CAC) as a marker of coronary atherosclerosis has been studied extensively in the primary prevention setting. With rapidly evolving multidetector CT technology, contrast-enhanced coronary CT angiography (CCTA) has emerged as the non-invasive method of choice for detailed imaging of the coronary tree. In this review, we systematically evaluate the role of CAC testing in the age of CCTA in both asymptomatic and symptomatic patients, across varying levels of risk. Although the role of CAC testing is well established in asymptomatic subjects, its use in evaluating those with stable symptoms that represent possible obstructive coronary artery disease is controversial. Nevertheless, available data suggest that in low-to-intermediate risk symptomatic patients, CAC scanning may serve as an appropriate gatekeeper to further testing with either CCTA (if no or only mild CAC present) versus functional imaging or invasive coronary angiography (when moderate or severe CAC present). In a similar fashion, low risk patients and those with atypical chest pain presenting to the ED setting can be safely discharged in the setting of CAC=0. However, the true value of CAC=0 in ruling out disease in stable and acute settings need to be assessed in randomized clinical trial setting.
CENTRALIZED, STEPPED, PATIENT PREFERENCE–BASED TREATMENT FOR PATIENTS WITH POST–ACUTE CORONARY SYNDROME DEPRESSION: CODIACS VANGUARD RANDOMIZED CONTROLLED TRIAL

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Background: Controversy remains about whether depression can be successfully managed after acute coronary syndrome (ACS) and the costs and benefits of doing so. We determined the effects of providing post-ACS depression care on depressive symptoms and health care costs.

Methods: We performed a multicenter randomized controlled trial with 150 patients with elevated depressive symptoms (Beck Depression Inventory [BDI] score >10) 2 to 6 months after an ACS. Patients were recruited from 7 centers across the United States between March 2010, and January 2012. Patients were randomized to 6 months of centralized depression care (patient preference for problem-solving treatment given via telephone or the Internet, pharmacotherapy), stepped every 6 to 8 weeks, (active treatment group; n=73) or to locally determined depression care after physician notification about the patient’s depressive symptoms (usual care group; n=77).

Results: Depressive symptoms decreased significantly more in the active treatment group than in the usual care group (differential change between groups, -3.5 BDI points; 95% CI, -6.1 to -0.7; P = .01). Mental health care estimated costs were higher for active treatment, but overall health care estimated costs were not significantly different (difference adjusting for confounding, -$325; 95% CI, -$2639 to $1989; P=.78).

Conclusions: This kind of depression care is feasible, effective, and may be cost-neutral within 6 months; therefore, it should be tested in a large phase 3 pragmatic trial.

Trial Registration: clinicaltrials.gov Identifier: NCT01032018
Microencapsulation of stem cells offers a means to protect stem cells from early destruction by inflammatory products after acute ischemic events and also enables immunoprotection of stem cells without the need for immunosuppression. However, alginate microencapsulated stem cells typically contain 30-100 stem or progenitor cells and are too large, i.e., 300-500 micron diameter, for intracoronary or intramyocardial delivery. Our laboratory has recently developed a novel microfluidic device that enables “on-chip” alginate microencapsulation of individual microencapsulated stem cells on the order of 40-50 microns. Unlike previous microfluidic devices, stem cell encapsulation is rapid and using a pressure controlled valve prevents nozzle clogging to enable high throughput encapsulation. Viability testing of microencapsulated mesenchymal stem cells was >90% at 3 days post-encapsulation. By impregnating the microcapsule with clinical approved contrast agents such as perfluorocarbons, barium sulfate, or iron, the capsules can be visualized during injection with ultrasound, X-ray, or MRI on clinical imaging systems. A prototype single cell encapsulation using superparamagnetic iron oxides (SPIOs) were injected transendocardially using MRI-guidance on a clinical 3T scanner (Trio, Siemens, Germany) in a normal pig. The prototype therapeutic could be visualized during direct injection by MRI. However, at one week post-injection the capsules were no longer visible, most likely due to the low iron content hindering sufficient MRI sensitivity. The new proposed single stem cell microencapsulation shows promise for the administration of allogeneic or xenogenic stem or progenitor cells to the myocardium for cardiac regenerative therapy.
The present study tested the hypothesis that induction of autophagy in the heart prior to an ischemic insult by producing therapeutic amount of ER stress would ameliorate/reduce subsequent lethal myocardial ischemic reperfusion injury [similar to ischemic preconditioning]. Initially, we performed a dose-response study with both tunicamycin and thapsiagargin to determine the optimal dose for inducing autophagy for cardioprotection, which was 0.3 mg/kg). The Sprague Dawley rats were divided into six groups: Group I & II: control for tunicamycin and thapsiagargin [injected with saline], Group III & IV: [tunicamycin – that produces ER stress by increasing glycosylation: 0.3 mg/kg cardioprotective, 3 mg/kg detrimental], and Group V and VI [thapsiagargin-that produces ER stress by altering Ca\(^2+\) homeostasis: 0.3 mg/kg cardioprotective, 3 mg/kg detrimental]. After 48 h, the rats were subjected to M-mode echocardiography followed by isolated working heart preparation. The isolated hearts were subjected to 30 min ischemia followed by 2 h of reperfusion while left ventricular function was continuously monitored. At the end, the hearts were either subjected to measurement of infarct size or cardiomyocyte apoptosis. A part of the hearts [from different set of experiments] was used for transmission electron microscopy, confocal microscopy or Western blot analysis. The results of the present study indicate that tunicamycin and thapsiagargin irrespective of the doses, induced sufficient ER stress as evidenced by the activation of eIF2a and PERK as noted by their increased phosphorylation. Such ER stress potentiated autophagy in the heart as evidenced by the increased LC3II, beclin 1 and Atg6. This was also supported by the transmission electron microscopy, which clearly showed production of autophagosomes. These results were echoed by the confocal microscopy that showed upregulation of eIF2a and beclin-1. The autophagy produced with lower doses of tunicamycin and thapsiagargin in the face of myocardial ischemia/reperfusion resulted in the reduction of ischemic reperfusion injury as evidenced by improved left ventricular function and reduced myocardial infarct size and cardiomyocyte apoptosis. In concert there was an induction of GRP78 and activation of Bcl-2 and Akt. The higher doses, on the other hand were detrimental for the heart and were associated with the induction of the expression of CHOP and led to a down-regulation of Akt and Bcl-2. The results thus displayed the proof of concept that induction of autophagy by ER stress [therapeutic amount] prior to ischemia [similar to ischemic preconditioning] would reduce subsequent lethal ischemic reperfusion injury.
CARDIAC TISSUE HYPOTHYROIDISM- A MAJOR PLAYER IN DIABETIC CARDIOMYOPATHY
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Objectives and Background: Thyroid dysfunction is common in individuals with diabetes mellitus (DM) and may contribute to the associated cardiac dysfunction. However, little is known about the extent and pathophysiological consequences of low thyroid conditions on the heart in DM.

Methods and Results: DM was induced in adult rats by streptozotocin (STZ) following nicotinamide (N) pre-treatment. One month after STZ/N, rats were randomized to the following groups: STZ/N or STZ/N + 3 µg/kg/day T3 orally; age-matched vehicle treated rats served as non-diabetic controls (C). After 2 months T3 treatment (3 months post DM induction), LV function was assessed by echocardiography and LV pressure transducer. Despite normal serum thyroid hormone (TH) levels, STZ/N led to reductions in myocardial tissue content of THs (T3 & T4: 39% & 17% reduction vs. C, respectively). Tissue hypothyroidism in the DM hearts correlated with increased D3 deiodinase (which converts THs to inactive metabolites) and TH transporter expression, re-expression of the fetal gene phenotype, reduced arteriolar resistance vessel density, and diminished cardiac function. Physiologic T3 replacement largely restored cardiac tissue TH levels (T3 & T4: 43% & 10% increase vs. STZ/N, respectively), improved cardiac function, reversed fetal gene expression, and preserved the arteriolar resistance vessel network without causing overt symptoms of hyperthyroidism.

Conclusion: Cardiac dysfunction in chronic DM may be associated with tissue hypothyroidism despite normal serum TH levels. Physiologic TH replacement appears to be a safe and effective adjunct therapy to prevent cardiac remodeling and dysfunction induced by experimental DM.
Diabetes mellitus (DM) is a major public health problem. Diabetes impairs angiogenesis in response to myocardial infarction (MI). The formation of functional vessels by growth factors induced angiogenesis is still a challenging topic. Studies have shown decrease in the capillary density in human infarcted diabetic hearts as compared to the non-diabetic with a similar history of cardiac events and resultant death. Emerging evidence from our laboratory supports the anti-oxidative, anti-apoptotic, growth regulatory and VEGF triggering potential of thioredoxin-1 (Trx1) in the diabetic myocardium. It has been reported that the modulation of Trx-1 activity by its inhibitory, interacting partner TXNIP contributes to the hyperglycemia mediated oxidative stress. However, the role of Trx-1 and TXNIP in hyperglycemia mediated oxidative stress in the diabetic myocardium is unclear. In the present study we used pro-angiogenic gene therapy approach to reverse diabetes-mediated impairment of angiogenesis in the infarcted diabetic rat myocardium.

We used mono-gene therapy, Thioredoxin-1 (Trx1), in streptozotocin-induced diabetic rat after inducing MI. Myocardial function was measured by echocardiography 30 days after the intervention. The Ad-Trx1 administered group exhibited reduced fibrosis, oxidative stress, and apoptosis compared to the non-treatment group. The extent of angiogenesis was increased compared to wild type. Echocardiographic analysis 4 weeks after myocardial infarction revealed improvement in functional parameters such as ejection fraction, fractional shortening, and E/A ratio in the gene-therapy group compared with the non-treatment group. Our preclinical data demonstrates the efficacy of Trx1 gene therapy in increasing angiogenesis and reducing ventricular remodeling in the infarcted diabetic myocardium.
DNA TOPOISOMERASE II INHIBITORS INDUCE MACROPHAGE ABCA1 EXPRESSION AND CHOLESTEROL EFFLUX---AN LXR-DEPENDENT MECHANISM
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ATP-binding cassette transporter A1 (ABCA1) facilitates cholesterol efflux and thereby inhibits lipid-laden macrophage/foam cell formation and atherosclerosis. ABCA1 expression is transcriptionally regulated by activation of liver X receptor (LXR). Both etoposide and teniposide are DNA topoisomerase II (Topo II) inhibitors and are chemotherapeutic medications used in the treatment of various cancers. Interestingly, etoposide inhibits atherosclerosis in rabbits by unclear mechanisms. Herein, we report the effects of etoposide and teniposide on macrophage ABCA1 expression and cholesterol efflux. Both etoposide and teniposide increased macrophage free cholesterol efflux. This increase was associated with increased ABCA1 mRNA and protein expression. Etoposide and teniposide also increased ABCA1 promoter activity in an LXR-dependent manner and formation of the LXRE-LXR/RXR complex indicating that transcriptional induction had occurred. Expression of ABCG1 and fatty acid synthase (FAS), another two LXR-targeted genes, was also induced by etoposide and teniposide. In vivo, administration of mice with either etoposide or teniposide induced macrophage ABCA1 expression and enhanced reverse cholesterol transport from macrophages to feces. Taken together, our study indicates that etoposide and teniposide increase macrophage ABCA1 expression and cholesterol efflux that may be attributed to the anti-atherogenic properties of etoposide. Our study also describes a new function for Topo II inhibitors in addition to their role in anti-tumorigenesis.
FAILURE TO OVEREXPRESS UROCORTIN FOLLOWING CARDIOPLEGIC ARREST MAKES THE HEART OF DIABETIC PATIENTS UNDERGOING ON-PUMP CORONARY ARTERY BYPASS GRAFTING MORE SUSCEPTIBLE TO APOPTOSIS AND CARDIAC DYSFUNCTION

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Background. Molecular mechanisms responsible for the reported worse outcome of diabetic patients (DMP) after on-pump cardiac surgery (OPCS) remain unknown. Opposite effects have been reported for Urocortin (Ucn)/PKCε and PKCδ, the former being cardio-protective and the latter pro-apoptotic.

Aim. We investigated the role of PKCε and PKCδ in Ucn-induced cardio-protection in DMP and non-diabetic patients (NDMP) after OPCS.

Methods and Results. Two sequential biopsies were obtained from the right atrium of 27 DMP and 22 NDMP before Cardio-Pulmonary bypass (CPB) and 10 minutes after declamping. In post-cardioplegic NDMP, Ucn was induced at both mRNA and protein levels (p<0.01); conversely, post-cardioplegic induction was not observed in DMP (p=NS) and pre-cardioplegic levels of Ucn were 50% lower than NDMP (p<0.05). In NDMP, cardioplegic arrest increased PKC-ε mRNA and protein (p<0.05), while overexpression of PKC-δ was not seen. In contrast, DMP showed increased expression of PKCδ (p<0.01) with no change in PKCε. Phosphorylation and mitochondrial relocation of PKCε were only detected in post-cardioplegic samples from NDMP, while nuclear and mitochondrial translocation of activated PKCδ was mainly evident in post-cardioplegic samples from DMP. Apoptosis was over 2-fold higher in post-cardioplegic samples from DMP than NDMP. Apoptotic myocytes were Ucn-negative and exhibited nuclear and mitochondrial relocation of PKCδ, while enhanced PKCε/mitochondrial colocalization was observed in viable, Ucn-positive, myocytes. The leakage of troponin I documented in DMP was higher than in NDMP, although not statistically significant. Furthermore, despite a similar incidence of perioperative AMI, DMP did not show postoperative improvement of either systolic or diastolic function, which instead was seen in NDMP.

Conclusion. We report that in DMP, cardioplegic arrest failed to induce myocyte over-expression of Ucn and PKCε, but was associated with induction and mitochondrial relocation of PKCδ, resulting in apoptosis. Failure to over-express Ucn makes the DMP more susceptible to apoptosis and cardiac dysfunction, thus contributing to the reported worse postsurgical outcomes.
PI3K INHIBITORS AS NOVEL CANCER THERAPIES: IMPLICATIONS FOR CARDIOVASCULAR MEDICINE
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Background: The PI3K signaling cascade has fundamental roles in cell growth, survival and motility and increased PI3K activity is an important and common contributor to tumorigenesis and cancer progression. This pathway also has a significant role in physiological hypertrophy, myocardial contractility and metabolism in the heart and is a central determinant of pathological remodeling in the cardiovascular system.

Methods and Results: PI3K inhibitors are a promising class of anti-cancer drugs, although systemic inhibition of the PI3K pathway demands careful attention to possible adverse side effects of inhibiting these ubiquitously expressed proteins. Here we review the growing body of basic research on the role of PI3K signaling in the heart and give an overview of the different therapeutic strategies being developed for cancer using PI3K inhibitors, including pan and isoform selective inhibitors, combination PI3K/mTOR inhibitors and the use of PI3K inhibitors in combination therapies with other anti-cancer therapies. We focus on the clinical implications for treating patients with pre-existing cardiac risk factors or co morbidities with PI3K inhibitors.

Conclusions: PI3K inhibitors are novel cancer drugs which are likely to lead considerable toxicity to the cardiovascular system especially in elderly patients and those with preexisting cardiovascular disease.
PROTEIN TRANSDUCTION DOMAINS; TARGETED VS. NON-TARGETED TISSUE DELIVERY

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The ability of certain proteins to cross cell membrane barriers was a chance finding reported over 20 years ago. This ability, also termed protein transduction, is localized to 6-30, basic, cationic peptide motifs, known as protein transduction domains (PTDs). In general, PTDs can be classified into 3 types: cationic peptides of 6-12 amino acids in length comprised predominantly of arginine, ornithine and/or lysine residues; hydrophobic peptides such as leader sequences of secreted growth factors and cytokines; and cell-type specific peptides, identified by screening of peptide phage display libraries, also known as phage display or biopanning. These three types of transduction peptides have many different applications including delivery of therapeutic proteins and drugs, delivery of fluorescent or radioactive compounds for imaging, and improving uptake of DNA, RNA and even viral particles. In general the cationic peptides appear to be more efficient but have the drawback of being non-specific. Peptides felt to be tissue specific and identified through screening of large phage libraries appear to be relatively more tissue-specific though at the expense of efficiency. In this review an introduction to PTD technology with focus on phage display as a powerful tool to target tissue, without the need for characterizing the target molecule or receptor apriori, will be presented. In addition the potential for PTDs to serve as diagnostic and therapeutic agents will be high-lighted.
MIR-24 UP-REGULATION UNDERLIES EXCITATION-CONTRACTION UNCOUPLING IN HEART FAILURE
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Chronic heart failure is a complex clinical syndrome with impaired myocardial contractility. Failing cardiomyocytes exhibit decreased efficiency of Excitation-contraction (E-C) coupling. The down-regulation of junctophilin-2 (JP2), a structural protein anchoring the sarcoplasmic reticulum (SR) to T-tubules (TTs), has been identified as a major mechanism underlying the defective E-C coupling. We found that miR-24, a microRNA up-regulated in heart failure, is an immediate upstream suppressor of JP2. Bioinformatic analysis predicted two potential binding sites of miR-24 in the 3'-untranslated regions of JP2 mRNA. Luciferase assays confirmed that miR-24 suppressed JP2 expression by binding to either of these sites. In the aortic stenosis model, miR-24 was up-regulated in failing cardiomyocytes. Adenovirus-directed over-expression of miR-24 in cardiomyocytes decreased JP2 expression and reduced Ca2+ transient amplitude and E-C coupling gain. Stereological analysis of transmission electron microscopic images showed that the volume density and the surface area of junctional SR were decreased in miR-24 over-expressed heart cells. Moreover, the spatial span of TT-SR junctions was markedly reduced. In vivo silencing of miR-24 by a specific antagonir in an aorta-constricted mouse model effectively protected cardiomyocytes from structural and functional E-C uncoupling, and prevented the mouse from developing heart failure. As miR-24 is a member of the miR-23a~27a~24-2 cluster regulated by calcineurin-NFATc3 signaling, this finding mechanistically links upstream heart failure signaling to the ultimate defect in cardiomyocyte contractility, and suggests novel therapeutic strategies against heart failure.
EFFECTS OF RESUSCITATION TIME ON OUTCOMES IN CARDIAC ARREST PATIENTS UNDERGOING THERAPEUTIC HYPOTHERMIA

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Background: Therapeutic hypothermia (TH) improves neurological outcomes and has become standard of care in treatment of patients with cardiac arrest. Neurological recovery after cardiac arrest in patients undergoing TH is difficult to predict within the first 72 hours. We studied the effects of resuscitation time on neurological outcomes and mortality in this population.

Methods: Data were prospectively collected on consecutive cardiac arrest patients undergoing TH between June 2009 and July 2012. Resuscitation time was defined as time from when the patient was found until return of spontaneous circulation. Glasgow Pittsburgh Cerebral Performance Score (CPC) of 1-2 defines mild or no neurological injury, while CPC of 3-5 defines moderate to severe neurological injury or death. Univariate and multivariate logistic regression was used to calculate crude and adjusted (for age, gender, diabetes, coronary artery disease, stroke, arrest location, presence of shockable rhythm) odds ratios for CPC 3-5 and 30-day mortality.

Results: Resuscitation time longer than 20 minutes was significantly associated with moderate to severe neurological injury or death on univariate (OR 3.69; CI: 1.40-9.71; p=0.008) and multivariate analysis (OR 5.85, CI: 1.64-20.86; p=0.006), and with increased 30-day mortality rate on univariate (OR 5.52; CI: 1.94-15.72; p=0.001) and multivariate analysis (OR 10.49; CI: 2.41-45.62; p=0.002).

Conclusion: Identifying factors which predict outcomes in cardiac arrest patients treated with TH could aid in early prognostication and decision making. Our study suggests that prolonged resuscitation time in this population may help to predict unfavorable outcomes, such as worse neurological injury and early death.
HIGHLY LETHAL NKX2.5 MUTATION
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Introduction: To date, several disease-related mutations in NKX2.5, a cardiac-specific homeobox gene, have been documented in patients with a variety of congenital heart disease (CHD). The most commonly reported phenotypes are secundum atrial septal defect (ASD) and atrioventricular conduction disease (AVCD). Reports of sudden cardiac death (SCD) have been attributed to progressive conduction disease preventable with pacemaker therapy.

Methods: We report a family with a novel NKX2.5 mutation causing CHD, ventricular arrhythmias, and SCD despite pacemaker therapy.

Results: We have documented NKX2.5 Gln181His missense mutation in nine phenotypically affected members of a single family with a strong family history of SCD, CHD, and AVCD. Prior to genotyping, four family members died suddenly, two despite pacemaker therapy. SCD occurred at ages 23, 29, 44, and 45 years. Observed phenotypic characteristics of genotype-positive patients included: ASD, ventricular septal defect, aortic coarctation, tricuspid atresia (with heart failure requiring cardiac transplantation), supraventricular tachycardia, progressive AVCD, and ventricular tachycardia documented on ICD recording. Age at presentation ranged between 5 months and 44 years. AVCD was seen as early as infancy. Thus far, two phenotypically unaffected family members have tested negative for the mutation.

Conclusions: Our findings strongly suggest a new association of this NKX2.5 mutation with SCD from ventricular arrhythmia. This observation has significant implications for choice of therapy for affected individuals, specifically use of implantable cardiac defibrillators, and broadens the observed phenotypic spectrum of NKX2.5 mutations.
Background: Recent studies have linked Azithromycin to an increased risk of cardiovascular death in patients with high baseline cardiovascular risk factors. Given the high frequency of use of azithromycin in medical practices, a closer look at this association is imperative. The aim of this study is to summarize available evidence on the association between azithromycin and risk of death.

Method: Two authors independently conducted a comprehensive search of the Cochrane Library PUBMED, MEDLINE, and published proceedings from major cardiology meetings from January 1980 to September 2012. The Begg’s and Egger’s tests with visual inspection of the funnel plot were used to assess for publication bias. All analyses were performed using REVMAN 5.1. Results: Six studies involving 14,799 patients were included in the analysis. Five studies reported all-cause mortality and three studies reported cardiovascular death in their subset analysis. Azithromycin therapy duration ranged from 3 days to 12 months. Follow-up duration was 6 to 46.8 months. There were 354 deaths in azithromycin group compared to 402 in placebo group, (RR 0.88, 95% CI 0.77-1.01). There were 5,431 patients combined in the studies that reported cardiovascular death, 48 deaths in azithromycin group, compared to 50 in placebo group (RR 0.96, 95% CI 0.65-1.42). There was no evidence of publication bias in all the analyses. Results: This study shows that there is insufficient evidence in support of an association between Azithromycin use and increased risk of cardiovascular death. Future large studies with appropriate comparison groups and adequate follow-up are needed.
EFFECTS OF MILD THERAPEUTIC HYPOTHERMIA ON ELECTROCARDIOGRAPHIC PARAMETERS AMONG POST-CARDIAC ARREST PATIENTS SECONDARY TO ACUTE MYOCARDIAL INFARCTION

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The Mild Therapeutic Hypothermia (TH) in patients after cardiac arrest due to Acute Myocardial Infarction (THAMI) study assessed the safety and efficacy of TH in improving over-all hospital survival among post-cardiac arrest patients due to myocardial infarction (MI). This study evaluated the electrocardiographic and arrhythmogenic potential of TH among post-cardiac arrest patients due to acute MI using electrocardiographic parameters. This is a prospective cohort subanalysis of THAMI study involving post cardiac arrest MI patients from March to December 2012. A total of 22 patients (68% male, mean age 64.34±13), 12 underwent TH and 10 maintained on normothermia, were included. Measures of arrhythmogenic potential of TH was determined using electrocardiographic parameters such as heart rate, PR interval, QRS complex, QT interval, corrected QT (QTc), RR interval, P/QRS ratio, Osborn wave, and presence of arrhythmia. Baseline clinical characteristics were similar in both groups. QTc prolongation in the hypothermia group showed significant trend during TH compared to normothermia group (TH 528±12.2 vs No TH 468±2, p= 0.03). With regards to development of arrhythmias (atrioventricular block, right bundle branch block, premature atrial conduction, junctional rhythm, ventricular fibrillation, atrial fibrillation, ventricular tachycardia) no significant difference was noted between the two groups (p= 0.09). Likewise, there were no statistically significant differences in the PR interval, QRS complex, RR interval and P/QRS ratio between the two groups. This study showed that post-arrest MI patients treated with therapeutic hypothermia had significant QTc prolongation during TH but did not show any noteworthy tendency to develop hemodynamically significant arrhythmias.
Objectives: The aim of this study was to compare the clinical characteristics, treatment and outcomes of patients with Out of Hospital Cardiac Arrest (OHCA) admitted to a single center in the Middle East over a 20-year period.

Methods: This was a retrospective analysis of the 20-year registry data (Jan 1991 to Dec 2010) of consecutive OHCA patients hospitalized at Hamad General Hospital and Qatar Heart Hospital.

Results: 987 patients were admitted with OHCA, representing 2.4% of the ACS admissions. The mean age was 57 years with 27% females, 56% Middle Eastern Arabs and 31% South Asians. Compared with the non-cardiac arrest admissions, OHCA patients were likely to have diabetes mellitus (42.8% vs. 39.1%; P = 0.02), prior myocardial infarction (21.8% vs. 19.2%; P = 0.04) and chronic kidney disease [CKD] (7.4% vs. 3.9%; P = 0.001), but were less likely to have dyslipidemia (16.9% vs. 25.4%; P = 0.001). The most common preceding symptoms were chest pain (27%) and dyspnea (25%). 47% of the patients had no preceding symptoms. Shockable rhythm was present in 25% and STEMI in 30%. 38% of the STEMI was treated with thrombolysis and 11% underwent PTCA. 53% had severe left ventricle impairment (EF < 35%) with 43% presented with cardiogenic shock. In-hospital mortality was 60%.

Conclusions: Out-of-hospital cardiac arrest was associated with higher incidence of diabetes, prior MI and CKD; and very high in-patient mortality. It affected younger age group with half of the patients had no preceding symptoms.
META-ANALYSIS TO DETERMINE CRITICAL TASER BARB DISTANCE FOR MYOCARDIAL CAPTURE

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Introduction: TASERs are widely used by law enforcement to incapacitate combative individuals. Because they deliver high frequency current, they have the potential to precipitate sudden death through the induction of ventricular arrhythmias. Reports in the literature have reached disparate conclusions regarding the safety of TASERs, and the relationship between location of energy delivery and myocardial capture remains incompletely described.

Methods: To determine the association between myocardium-to-barb distance (MBD) and cardiac capture, we searched Medline for peer-reviewed studies reporting the cardiac effects of TASERs published before 6/1/2011. Final analysis was limited to studies that described the anatomic location of the barbs and performed ECG monitoring during shock delivery. Two independent reviewers determined the MBD, estimating the distance between the interventricular septum and closest electrode.

Results: We identified 2,832 shocks among 37 studies (25 human, 12 pig model). Of 558 shocks under cardiac monitoring and with barb location, 118 shocks resulted in cardiac capture. All episodes of capture resulted from barb positioning over the anterior chest or upper abdomen. Shocks resulting in capture were closer to the myocardium than shocks not associated with capture (median (IQR), 2.0 (1.5 – 4.0) cm versus 2.7 (2.0 – 3.0) cm, \( p = 0.004 \)). No shock with MBD > 5 cm resulted in capture.

Conclusions: Cardiac capture in TASER use depends on the distance between the heart and barb electrode and does not occur when the electrode is greater than 5 cm from the myocardium. These results have important implications for TASER training and utilization policies.
LEFT VENTRICULAR PACING SHOULD BE AN OPTION IN PATIENTS UNDERGOING CARDIAC RESYNCHRONIZATION THERAPY

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Introduction: A substantial number of patients who undergo cardiac resynchronization therapy (CRT) fail to demonstrate any benefit. We speculated that this in large part may be related to the adverse effects of incorporating right ventricular pacing as part of the algorithm.

Method: We compared the effects of right ventricular pacing (RV), simultaneous pacing of the right and left ventricle (V-V 0), left ventricular pacing 60 msec ahead of RV pacing V-V 60) and left ventricular pacing only (LV). Effects of these pacing modalities on global left ventricular function (EF) and regional wall motion contraction using longitudinal strain (speckle tracking) and 3D echocardiograms.

Results: 372 patients were studied. Mean age 69 years, 71% males and 65% with ischemic heart disease. There was a progressive improvement in left ventricular EF (RV 22%, V-V 0 32%, V-V 60 38% and LV only 40%). Regional segmental contraction improved only modestly with V-V 0, whereas a dramatic improvement was noted with LV only pacing. V-V 60 was better than V-V 0 but not as good as LV only. The greatest improvement was seen in septal contraction with both LV only and V-V 60. The changes noted were independent of baseline ECG morphology, QRS duration and etiology of LV dysfunction.

Conclusion: This study demonstrates that incorporating RV pacing in patients undergoing CRT is detrimental. Minimizing or removing the influence of RV pacing and utilizing LV pacing alone provides the greatest benefit and may be a consideration particularly in patients failing to respond to CRT therapy.
TOPICAL ANTIBIOTIC AND SKIN ANTISEPTIC PROPHYLAXIS AFTER PLACEMENT OF CARDIAC ELECTRONIC IMPLANTABLE DEVICE (CEID): A PROSPECTIVE RANDOMIZED TRIAL
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Objective: To evaluate the efficacy of topical antibiotic prophylaxis in the prevention of surgical site infection after CEID implantation procedures.

Background: Combined systemic and topical antibiotic prophylaxis is routinely used in cardiac electronic implantable device (CEID) procedure, but very few studies have assessed prophylactic use of topical antibiotics after CEID implantation.

Methods: This was a prospective randomized, placebo-controlled, single center, single operator study. All patients (n=1008) received standard systemic antibiotic prophylaxis. After the procedure, patients were randomized into four groups and received various topical prophylaxes. All patients were followed for at least 12 months. Surgical site inflammation and infection were graded based on degree of inflammation, discharge, wound cultures, and blood cultures.

Results: 58 patients developed surgical site inflammation and infection. Thirteen have superficial wound culture positive infections with staphylococcus species. Only one had pocket infection with Pseudomonas bacteremia. The surgical site infection rates were higher in those with procedure time over 110 minutes, associated with 2.3 times more likelihood of infection (p = 0.01). Patients with an associated malignancy are associated with 3.6 times more likelihood of infection (p = <0.01).

Conclusions: Routine topical antibiotic prophylaxis shows no significant benefit during CEID implantations. Patients with malignancy and longer procedural times are more likely to developed infection. There is a trend for less CEID infection with the cephalic approach. Systemic antibiotics with staphylococcal coverage are needed for prophylaxis as most of the wound culture positive infections are caused by staphylococcus species.
Background: Imaging pts with pacemaker or AICD's is mostly taboo in MRI environment. However, current PM lead and generator improvements along with knowledgeable personnel in PM safety suggests MRI procedures can be performed successfully. However, safe performance, notwithstanding risks, leads one to question if results from MRI provide additional clinical information to warrant risk. Hypothesis Imaging patients with a PM/AICD via MRI is safe and crucial to establish clinical diagnosis.

Methods: Of 29 pts imaged (GE, Milwaukee,WI): 3 (dependant PM), 3 (AICD), 4 (AICD/PM), 2 (single lead) and 17 (dual-chamber PM). Three pts underwent MRI twice. Each pt was performed in dedicated CV-MR Suite under strict Cardiology supervision. EP reconfigured PM/AICD to appropriate asynchronous mode/therapies under Cardiology guidance. MRI sequence: SAR <2.0W/kg.

Results: All pts completed MRI without AE/SAE's. PM/AID's were interrogated demonstrating impedance, thresholds, amplitudes and shock impedances were unchanged pre to post scanning. Average MRI:20±55min. Regarding case population, 20(69%) were neurology while 9(31%) were cardiac. After review from the 20 neurology cases comparing to prior CT, angio and/or myelogram, 15(75%) pts benefited: 12(60%) MRI's altered clinical diagnosis resulting in improved outcomes. The remaining 5(25%) MRI's provide no additional information. Comparing cardiac cases to prior cath, TEE, TTE and stress, all 9(100%) pts’ diagnoses were enhanced via CV-MR: 5(56%), CMR dramatically improved pt care. Thus, there was an 83% benefit ratio via MRI.

Conclusions: We propose not only are PM/AICDs no longer taboo in MRI environments but in proper settings, they are markedly effective with life-altering and life-saving consequences.
Objective: To evaluate the performance of DF4 lead system (DF4LS)

Background: The DF4LS allows a single connection between the implantable cardioverter defibrillator (ICD) lead and the pulse generator. We compared the performance and safety parameters of DF4LS with conventional three core (DF1) leads.

Methods: ICD database at our center was analyzed and patients receiving ICDs with the DF4LS (St Jude Medical 7120Q, 7121Q) were included. Controls were drawn from ICDs implanted in the same time period with DF1 leads. R-wave sensing, pacing thresholds, lead and coil impedances, and defibrillation threshold (DFT) at implant were recorded. Patients were followed at 2 weeks and 3 months post implantation and every 6 months thereafter. Any peri-procedural and long-term adverse event was recorded.

Results: 99 patients with DF4 and 54 with DF1 ICD lead systems were followed up for a mean duration of 4.6 months. Subjects (84.3% male) had a mean age of 64.3 ± 11.3 years. The DF4LS had lower implant as well as mean thresholds (0.66±0.28 vs. 0.77±0.36 V, p<0.05; 0.69±0.23 vs. 0.80±0.45 V, p<0.05). Mean DFT was lower in the DF4 group (14.6±1.6 vs. 16.4±4.3; p=0.001). The sensing threshold and pacing impedances were not significantly different in the two groups. No patient in the DF4 group required a lead/device revision while 2 patients did in the DF1 group.

Conclusion: DF4LS were found to perform well with a better adverse effect profile. The findings of lower pacing and defibrillation threshold may be beneficial in terms of device longevity, but need to be proven in prospective trials.
ROLE OF IMPLANTABLE LOOP RECORDER IN THE MANAGEMENT OF ATRIAL FIBRILLATION
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Introduction: Despite advances in atrial fibrillation therapeutics, hemorrhagic events are devastating in elderly, high-risk patients. No current guidelines exist on discontinuing anticoagulation, and this retrospective study explores the use of implantable loop recorder (ILR) in that population.

Method: Fifty-six consecutive patients who had prior complications of, or refusal of long-term anticoagulation and ILR placement were reviewed. Inclusion criteria were duration of follow-up at least 6 months. Two groups were then formed; patients off-anticoagulation (Group 1) and on-anticoagulation (Group 2). ILR data was analyzed for atrial fibrillation burden (Low burden – Less than 10 minutes per month), risk factors and incidence of stroke/transient ischemic attack (TIA).

Results: Among 28 patients included in final analysis, 53.6% of patients were off anticoagulation (Group 1) and in sinus rhythm at ILR placement. The mean age was 76.8 years and mean CHA2DS2-VASc score was 3.5 (Group 1, 3.2 vs. Group 2, 3.9). Average duration of follow-up was 14 months (Range 6 - 33 months). Seventy-one percent of total patients (Group-1, 80% vs. Group-2, 61.5%) had low burden atrial fibrillation for at least 6 months. There were no significant differences in risk factors, but atrial fibrillation burden was lower in Group-1. No stroke or TIA was reported.

Conclusion: In carefully selected patients at high risk of hemorrhagic events or who refuse anticoagulation, ILR may play a role to monitor atrial fibrillation burden, and thus discontinue anticoagulation without a significant increase in the risk of stroke/ TIA.
STRATEGY OF CARDIOVERSION AND ANTI-ARRHYTHMIC DRUG THERAPY FOR ATRIAL FLUTTER/FIBRILLATION INDUCED TACHYCARDIA MEDIATED CARDIOMYOPATHY – A SINGLE CENTER EXPERIENCE

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Introduction: Tachycardia mediated cardiomyopathy is a known complication of atrial flutter/fibrillation. There is very little data to guide therapy of this condition. We evaluated the safety and efficacy of a strategy of external cardioversion followed by anti-arrhythmic drug therapy in patients with tachycardia mediated cardiomyopathy.

Methods: After IRB approval, patients who underwent external cardioversion for atrial flutter/fibrillation between 2009-2012 were reviewed. Tachycardia mediated cardiomyopathy was defined as the presence of left ventricular ejection fraction less than 0.40 in the absence of other causes of cardiomyopathy. Demographic variables, type and duration of atrial fibrillation, type of anti-arrhythmic drugs used and success of rhythm control strategy were assessed. Data was analyzed using descriptive statistics.

Results: A total of 37 patients (30 male, 7 female) were identified. Mean age was 57.7 ± 11.8 years. Atrial flutter/fibrillation was persistent in 81% (n=30) with a median duration of 13.5 months. Mean ejection fraction at baseline was 0.32±0.07. Restoration of sinus rhythm occurred after the first shock in 97.3% (36/37) patients. Sinus rhythm was maintained in 82.3% at 1 month and in 76.1% at 6 months. Improvement in LV ejection fraction (>0.40) occurred in 76.1% (16/21) patients. No anti-arrhythmic drug side effects, ischemic strokes or deaths occurred during follow-up.

Conclusion: A strategy of cardioversion followed by anti-arrhythmic drug therapy and anticoagulation appears to be safe and effective in this cohort of patients with tachycardia mediated cardiomyopathy. Future studies should evaluate the efficacy of rate versus rhythm control in this condition.
MICROBIOLOGICAL DIFFERENCES OF POCKET VS. NON-POCKET CARDIOVASCULAR IMPLANTABLE ELECTRONIC DEVICE INFECTIONS

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Objective: To evaluate the unique microbiological features of pocket vs. non-pocket cardiovascular implantable electronic devices (CIEDs) related infections in order to elucidate the differences.

Background: A steady expansion in the use of CIEDs, particularly in the elderly, has led to an increased number of device-related infections. While such complications are routinely reported as a single entity, they actually comprise a rather heterogeneous group. We postulated that certain microbiological characteristics are associated with distinct CIED-related infection subgroups.

Methods and Results: We reviewed record of 434 patients undergoing device extraction for CIED-associated infection at a tertiary referral center between 1991–2008; 296 individuals (68%) had infection involving the pocket site (pocket infection group). Blood, wound, and tissue cultures, collectively and individually, were used to identify the pathogens in 384 (88%) out of 434 patients. Culture negative infections (16.2% vs. 1.4%, P < 0.001) and polymicrobial infections (15.9% vs. 5.8%, P =0.003) were more commonly observed in pocket infection group. Non-pocket infection group usually isolated a single pathogen compared to pocket infection group (92.8% vs. 67.9%, P < 0.001). As expected, non-pocket infection group also demonstrated more significant clinical symptoms and signs of systemic infection compared to pocket infection group.

Conclusions: In our patient population of CIED-related infections requiring extraction, a significant difference in the microbiology depending on the involvement of the pocket site was noted. These findings may suggest a different pathogenesis of pocket vs. non-pocket CIED-related infections and may define them as clinically different disease states.
CVD RISK PREDICTION

CORONARY ARTERY CALCIUM DENSITY AND CARDIOVASCULAR DISEASE EVENTS

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Background: Coronary artery calcium (CAC) measured by computed tomography (CT) has strong predictive value for incident cardiovascular disease (CVD) events. The standard CAC score is the Agatston, which is weighted upward for greater calcium density. However, some data suggest increased plaque calcium density may be protective for CVD.

Methods - We analyzed the independent associations of CAC volume and CAC density with incident hard coronary heart disease (CHD) and all hard CVD events in a multiethnic population of 3398 men and women who had at least some CAC on their baseline CT scan.

Results - During a median of 7.6 years of follow-up, there were 175 CHD events and an additional 90 other CVD events. With both CAC volume and density scores in the same multivariable model, the CAC volume score showed a strong independent association with incident CHD and all CVD, with hazard ratios of 1.77 (p<.0001) and 1.62 (p<.0001) respectively per standard deviation increase. Conversely, the density score showed a strong and independent inverse association, with hazard ratios of 0.73 for CHD (p=.006) and 0.72 for CVD (p=.0003) per standard deviation increase. Receiver Operating Characteristic curve analyses showed significantly improved risk prediction after addition of the density score to the multivariable model.

Conclusions - Increased density of CAC was associated with lower risk of incident CHD and CVD at any given volume of CAC. CAC scoring systems should be modified to include density as a protective factor, which will improve CVD risk prediction.
Carotid artery ultrasound intima-medial thickness (IMT) measurements are reported to add predictive value to traditional risk factors for predicting myocardial infarction and stroke. Recently, we reported that the Lifetime Risk algorithm was superior to both 10-year and 30-year Framingham Risk Score (FRS) algorithms in assigning subjects with carotid or femoral plaques to the high-risk FRS category for women aged 20-to-60 years and for men aged ≤50 years (Postley, … Gardin. J Am Coll Cardiol 2012;59:A420). Furthermore, in the elderly Cardiovascular Health Study cohort, addition of carotid IMT measurements modestly improved 10-year risk prediction for stroke and cardiovascular disease (CVD) beyond a basic FRS model—mainly by down-classifying risk in those not experiencing stroke or CVD. However, addition of information regarding presence or absence of plaque added no incremental benefit to carotid IMT measurements in this cohort (Gardin, et al. Circulation 2012;126:A16019). In our experience, addition of femoral artery to carotid artery ultrasound increased detection of plaques by 31% in men and 56% of women aged 50-64 years (Postley, Gardin, et al. J Am Soc Echocardiogr 2009;22:1145-51).

The progression rate of carotid IMT is associated with relative risk for CVD clinical outcomes. In addition, reduction in carotid IMT progression in lipid-lowering trials has been associated with a reduction in CVD events. However, a meta-analysis (Constanzo, et al. J Am Coll Cardiol 2010;56:2006-20) has questioned the reported association of regression or slowed progression of carotid IMT with reduction in CVD events.

Remaining challenges include the need: (1) to further define the independent predictive value of carotid measurements over clinical (e.g., Framingham) risk assessments and newer serologic markers; (2) to determine comparative performance of carotid ultrasound versus other imaging modalities (e.g., magnetic resonance imaging); (3) to further develop imaging measures of plaque bioactivity; and (4) to establish that use of these imaging techniques favorably impacts on CVD outcomes in a cost-effective manner.
Type 2 diabetes (T2DM) is associated with substantial increases in morbidity and mortality from coronary heart disease (CHD) and has been considered a CHD risk equivalent by the US National Cholesterol Education Program. The East-West Study originally showed persons with diabetes but no prior myocardial infarction had a similar risk of future CHD events as those with a prior myocardial infarction and no diabetes. However, recently meta-analyses note those with T2DM are at only about half the risk for CHD events as those with a known myocardial infarction. Moreover, global risk assessment shows one-half of females and one-third of males with T2DM to be a low to intermediate risk. In fact, there is a ten-fold variation in risk (0.4% to 4% annually) of CHD events according to the extent of subclinical atherosclerosis as evidenced by coronary artery calcium; the one-third of those with diabetes who do not have coronary calcium have CHD risks as low as many without diabetes or metabolic syndrome; conversely, those with coronary calcium scores of 400 or greater are at 10-fold greater risk for CHD events. These data support the role of global risk assessment and screening for subclinical atherosclerosis (eg, using coronary calcium screening) in those with T2DM.
RISK FACTORS FOR CARDIOVASCULAR DISEASE IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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Heart disease is the most common cause of death in patients with chronic kidney disease (CKD), particularly in those receiving dialysis. Atherosclerotic cardiovascular (CV) disease (CVD) accounts for a large number of these deaths. Atherosclerosis is accelerated in patients with CKD due predominantly to the high prevalence of traditional CVD risk factors in the CKD population. CKD aggravates pre-existent traditional risk factors such as hypertension and dyslipidemia due to secondary renal parenchymal hypertension and secondary dyslipidemia. In addition, a variety of non-traditional risk factors that occur commonly in CKD patients contribute to CV risk. These include hyperhomocysteinemia, increased oxidative stress, endothelial cell dysfunction, inflammation, activation of the renin-angiotensin-aldosterone and sympathetic nervous systems and vascular calcification. Recent studies suggest that CKD itself may be an independent risk factor for CVD, particularly coronary heart disease. Many therapies aimed at CV risk factor modification that have been successful in reducing CV risk in the general population are less effective or ineffective in favorably modifying CV risk in CKD.
THE HIGH CORONARY DISEASE RISK OF SOUTH ASIAN AMERICANS
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Objective and Background: Prevalence data and case-control studies suggest high coronary artery disease (CAD) risk in South Asians (SA) but prospective studies remain sparse. We performed a comprehensive prospective analysis in a large population.

Methods: We studied incident CAD hospitalizations in a multi-ethnic California cohort of 126,088 persons that supplied baseline data in 1978-85. Cox proportional hazards models adjusted for 11 covariates (age, sex, smoking, alcohol, BMI, education, marital status, blood pressure, blood cholesterol, blood glucose, and leukocyte count) were used to study 7,658 persons hospitalized for CAD through 2008. The models yielded hazard ratios (HR) and 95% confidence intervals (CI).

Results: For CAD the adjusted HR (CI) for SAs versus white persons was 2.32 (1.76-1.84, p<0.001). For other Asian American ethnic groups the HRs were: Chinese = 0.74 (p<0.001), Japanese = 0.84 (p=0.1) Filipino = 1.14 (p=0.048), and Other Asian = 0.76 (p=0.2). The SA risk of CAD was substantially higher in separate models versus blacks, Hispanics, and each other Asian group, ranging from a HR of 2.3 vs Filipinos to 3.3 vs Chinese and with p<0.001 vs each. There was also consistency in models stratified by sex, baseline age, smoking, presence of baseline CAD history/symptoms, or acute myocardial infarction/other CAD.

Conclusions: South Asian Americans are at substantially higher risk than any other ethnic group. While unexplained, the findings warrant vigorous public health action.
MENTAL STRESS INDUCED MYOCARDIAL ISCHEMIA AND ITS TREATMENT
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This presentation will discuss the most recent findings of mental stress induced myocardial ischemia (MSIMI) and its response to antidepressant. MSIMI is prevalent and a risk factor for poor prognosis in patients with clinically stable coronary heart disease (CHD). With the NHLBI funded REMIT (Responses of Myocardial Ischemia to Escitalopram Treatment) study that has been recently completed, we learned that MSIMI occurred in 43.45%, whereas exercise-induced ischemia occurred in 33.79% (p=0.002) of the study population (N=310). Women (odds ratio [OR]: 1.88), patients who were not married (OR: 1.99), and patients who lived alone (OR: 2.24) were more likely to have MSIMI (all p<0.05). One hundred twenty seven patients with MSIMI were randomized to take escitalopram or placebo (1:1) of 6 weeks. At the end of 6-week, a larger percentage of patients taking escitalopram (29.7%) did not show MSIMI, compared to 14.3% in patients taking placebo (OR: 2.53, 95% confidence interval: 1.04-6.15). Number needed to treat is 6. Escitalopram in addition resulted in significant alteration of platelet serotonin receptor transporter function, reduction in mental stress induced heart rate, rate-pressure product, and increase of positive emotions (ps<0.05). REMIT study demonstrated that MSIMI is more common than exercise-induced ischemia in patients with clinically stable CHD. Women, unmarried men, and individuals living alone are at higher risk for MSIMI. Further, 6-week escitalopram treatment reduces occurrence of MSIMI in CHD patients.
Objective: To discuss the bidirectional risks involving cardiac and cognitive diseases. Cognitive dysfunction has been shown with coronary artery disease, heart failure and atrial fibrillation. Studies have shown subclinical cardiovascular disease with a lower cardiac index but within the normal range, and left ventricular dysfunction in the absence of overt heart failure have been associated with cognitive dysfunction. An independent association was shown between natriuretic peptide levels and cognitive decline in the absence of previous stroke or coronary artery disease. Procedures like valve surgeries and coronary artery bypass grafting has been associated with post-surgical cognitive impairment. Cardiac transplantation and ventricular resynchronization therapy have been shown in some small studies to improve cognitive function. Inhibition of the central renin angiotensin system aldosterone system seems to limit cognitive decline. Neural networks play a role in the regulation of cardiovascular function. Neurotransmitters play a role in the regulation of cardiovascular system both in health and disease. Autonomic dysfunction can occur in all dementias and with sustained orthostatic hypotension can play a role in cardiovascular diseases. Orthostatic hypotension has been associated with coronary artery disease, myocardial infarction and heart failure. Autonomic dysfunction involving the interaction between sympathetic and parasympathetic system, may be playing a role in the evolution and outcome of many cardiovascular diseases. Conclusion: Evidence is evolving that the pathological risks that affect heart brain connection may be bidirectional.
Cardiovascular disease remains the leading killer of both men and women in the United States. However, compared to men, women have higher rates of morbidity and mortality with cardiovascular disease. Whether these differences are due to sex/gender differences whether they are due to differences in comorbidity can be debated. Studies such as the WISE study have shed light on important gender differences in the etiology of heart disease in women compared to men, including a higher prevalence of microvascular disease than previously thought. Specialized diagnostic testing might be needed to evaluate ischemia in women. Recent trial evidence also suggests that strategies for primary prevention in women might be different than in men. Future clinical trials need to address both the similarities and differences in prevalence, etiology, and treatment of heart disease in men and women.
BODY MASS INDEX AS PREDICTOR OF TOTAL AND CARDIAC MORTALITY IN PATIENTS WITH CARDIOVASCULAR DISEASE: A META ANALYSIS OF 49 STUDIES

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Background/Objective: Clinical studies have reported conflicting results between association between obesity as measured by body mass index (BMI), and total mortality and cardiovascular mortality in patients with cardiovascular disease (CAD and CHF). We investigated the extent and nature of this association through a systematic review of published literature.

Methods: We searched the Pub Med, CENTRAL and EMBASE databases for studies from 1966 to September 2012 that reported rate of total mortality or cardiac mortality, among various categories of BMI (low, normal weight (reference), overweight, obese, and severely obese) in patients with cardiovascular diseases (CAD and CHF).

Results: Forty nine cohort studies (N=284,831) were included for analysis. Patients with a low body mass index (BMI) (i.e., <20) had an increased relative risk (RR) for total mortality (RR =2.3614 [95%CI 1.958-2.848]), cardiovascular mortality (RR=1.9129 [95%CI 1.3584-2.6935]); while severely obese patients (BMI≥;35) had highest risk for cardiovascular mortality (3.1859 [1.7019-5.9639]) and cardiovascular mortality (0.7345 [0.5951-0.9065]) compared with those for people with a normal BMI. Overweight patients (BMI 25–29.9) had no increased risk for total mortality (0.7154 [0.6686-0.7654]) or cardiovascular mortality (0.8505 [0.7606-0.9511]).

Conclusion: Clinical outcomes were better among overweight and mildly obese cardiac patients. This could be due failure of BMI to adequately assess the degree of adiposity.
DIFFERENCES IN PLATELET microRNA PROFILES AFTER ASPIRIN USE ARE ASSOCIATED WITH DIFFERENCES IN WHOLE BLOOD AGGREGATION AND MIGHT IDENTIFY ASPIRIN RESISTANCE  
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Background: Re-instant stenosis is known to be a major problem. It is thought to be related to aspirin. It is known, that there are individual differences in the response of platelets to aspirin. Whether the response of platelets to aspirin translates to differences in miRNA expression is not known yet. We therefore, studied the influence of aspirin on microRNA expression levels and platelet function, in isolated platelets of healthy volunteers.  

Methods: We measured relative expression levels of platelet microRNAs using microarrays before and after two weeks of aspirin use (100 mg, once daily) in 15 healthy individuals (age 45-65 years). Additionally, we performed in vitro whole blood aggregation studies to determine whether the observed difference in microRNA profile before and after aspirin use, could be linked to platelet function. Whole blood from the same individuals, in the absence of aspirin, was tested using Multiplate® aggregometry and was incubated with indometacine to mimic aspirin use.  

Results: Based on aspirin-induced changes in microRNA profile, two subgroups could be distinguished: a group of individuals (n=9) with similar (SIM) and a group with different (DISSIM) (n=6) miRNA profiles before and after aspirin use. The SIM group had significantly reduced ADP-mediated aggregation as compared to the DISSIM group, after indometacine administration.  

Conclusion: Differences in platelet microRNA profiles after aspirin use are related to differences in ADP-mediated indometacine-treated whole blood aggregation. This could imply that differences in miRNA profiles might identify individuals with aspirin resistance.
ASSOCIATION STUDY OF 10 SELECTED GENE VARIANTS WITH ANGIOGRAPHIC SEVERITY OF CORONARY ARTERY DISEASE

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Objectives and background: More than 40 gene variants were associated with the coronary artery disease (CAD) in genome-wide association studies (GWAS). We aimed to examine in the Central European population possible associations of 10 selected single nucleotide polymorphisms (SNPs) previously identified by GWAS with the angiographic severity of CAD.

Methods: We included 173 consecutive patients (61% men, mean age 64±17 years) who underwent selective coronary angiography. To express the angiographic CAD severity Gensini score (GS) was calculated. The following SNPs were determined by high-resolution melting method: ANRIL (rs4977574), SORT1 (rs599839), LDLR (rs1122608), ABO (rs579459), ADAMTS7 (rs4380028), LPA (rs10455872), LIPA (rs1412444), MRPS6 (rs9982601), MIA3 (rs17465637), and PHACTR1 (rs12526453). Results: 58% of 173 subjects had at least one significant (>50%) coronary artery stenosis (angioCAD+). ANRIL rs4977574 was associated with a 9 points higher GS per risk G-allele (95% CI: 2.1-15.7, p=0.011) and PHACTR1 rs12526453 with an 8 points higher GS per risk C-allele (95% CI: 0.1-16.1, p=0.048) in age-, sex- and risk factor-adjusted additive genetic model. Odds ratio for presence of angio CAD+ was 2.13 (95% CI: 1.28-3.57, p=0.003) per G-allele of ANRIL rs4977574 A/G. ABO rs579459 was borderline associated with an increased prevalence of myocardial infarction per C-allele (OR 1.76, 95% CI: 1.04-3.00, p=0.034) in age- and sex-adjusted model.

Conclusions: In our pilot study in the Slovakian population, the ANRIL (9p21) and PHACTR1 variants were associated with the angiographic severity of coronary artery disease independently of the traditional risk factors.

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GENETIC VARIANTS IN FBN-1 AND RISK FOR THORACIC AORTIC DISSECTION AND NON-DISSECTING ANEURYSM: THE YALE STUDY

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Background: A recent genome wide association study (GWAS) found that single nucleotide polymorphisms (SNPs) in the FBN-1 gene, encoding Fibrillin-1, were associated with thoracic aortic dissection (TAD), thoracic aortic non-dissection aneurysm (TAA), and thoracic aortic aneurysm or dissection (TAAD); the largest effect was for association with TAD. We investigated whether two independent tagging SNPs (rs2118181 and rs10519177) in FBN-1 are associated with TAD, TAA, and TAAD in the Yale study.

Methods: We genotyped 636 TAAD cases (496 TAA and 140 TAD) and 275 disease-free controls collected in United States, Hungary, and Greece and analyzed the association of the FBN-1 SNPs with TAD, TAA, and TAAD using logistic regression models that adjusted for sex and study center.

Results: Odds ratios (95% CI) for carriers of the risk variant of the rs2118181 SNP, compared with noncarriers, were 1.76 (1.09-2.85), 1.21 (0.82-1.79), and 1.32 (0.91-1.93) for TAD, TAA, and TAAD, respectively. The second SNP, rs10519177, was not associated with any endpoint. In a combined analysis of the Yale study and published GWAS results, the odds ratios for TAAD were 1.75 (1.53-2.01) and 1.41 (1.18-1.67) for rs2118181 and rs10519177, respectively.

Conclusions: In the Yale study, rs2118181 in FBN-1 was strongly associated with TAD but not with TAA or TAAD; rs10519177 was not associated with any endpoint. Further investigation of these genetic variants is warranted.
MACROPHAGES TRANSMIT POTENT PROANGIOGENIC EFFECTS OF oxLDL IN VITRO AND IN VIVO INVOLVING HIF-1α ACTIVATION: A NOVEL ASPECT OF ANGIOGENESIS IN ATHEROSCLEROSIS

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Background: Neovascularization has been linked to the progression and vulnerability of atherosclerotic lesions. Angiogenesis is increased in lipid-rich plaque. Hypoxia-inducible factor alpha (HIF-1α) is a key transcriptional regulator responding to hypoxia and activating genes, which promote angiogenesis, among them vascular endothelial growth factor (VEGF). Oxidized low-density lipoprotein (oxLDL) is generated in lipid-rich plaque by oxidative stress. It triggers an inflammatory response and was traditionally thought to inhibit endothelial cells. New data, however, suggest that oxLDL can activate HIF-1α in monocytes in a hypoxia-independent fashion. We hypothesized that HIF-1α activation in monocyte–macrophages could transmit proangiogenic effects of oxLDL linking hyperlipidemia, inflammation, and angiogenesis in atherosclerosis.

Methods and Results: First, we examined the effect of oxLDL on HIF-1α and VEGF expression in monocyte–macrophages and on their proangiogenic effect on endothelial cells in vitro in a monocyte–macrophage/endothelial co-culture model. OxLDL strongly induced HIF-1α and VEGF in monocyte–macrophages (23±5 vs. 0.0±0 %; P<0.05) and VEGF (37±6 vs. 4±2 %; P<0.05) compared to untreated controls under normoxic conditions and significantly increased tube formation in co-cultured endothelial cells. HIF-1α inhibition with chetomin reversed this effect. Second, we demonstrated a direct proangiogenic effect of oxLDL in the in vivo matrigel plug angiogenesis assay (29±4 mm of blood vessels per high power field compared to 1±0.5 mm in growth factor-depleted matrigel alone, p<0.05). Again, HIF-1α inhibition with chetomin abrogated the proangiogenic effect of oxLDL (6±1mm vs. 29±4mm; p<0.05). Third, in a rabbit atherosclerosis model, we studied the effect of dietary lipid lowering on arterial HIF-1α and VEGF expression. The administration of low-lipid diet significantly reduced the expression of both HIF-1α and VEGF, resulting in decreased plaque neovascularization.

Conclusions: Our data point to oxLDL as a proangiogenic agent linking hyperlipidemia, inflammation, and angiogenesis in atherosclerosis. This effect is dependent on macrophages and, at least in part, on the induction of the HIF-1α pathway.
A GENETIC RISK SCORE FOR ATRIAL FIBRILLATION IS ASSOCIATED WITH CARDIOEMBOLIC STROKE

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Objectives: To determine whether a genetic risk score (GRS) for atrial fibrillation (AF) is associated with the risk of cardioembolic stroke (CES) in the Vienna Stroke Registry (VSR) cohort.

Background: Four single nucleotide polymorphisms (SNPs), rs2200733, rs10033464, rs2106261, and rs13376333, are associated with AF with genome-wide significance. Of these, rs2200733 and rs10033464 were also associated with CES in independent studies. Since AF is a risk factor for CES, we evaluated a GRS that combined the genetic risk for AF of four SNPs for an association with CES.

Methods: The genotypes of the four SNPs were determined for 202 CES cases and 815 controls in the VSR. A weighted AF GRS was calculated by summing the natural log of the risk estimate for each risk allele present in an individual. The association between the GRS (in tertiles) and CES was assessed by logistic regression.

Results: The risk alleles of rs2200733, rs10033464, rs2106261, and rs13376333 contribute 0.54, 0.33, 0.22, and 0.12, respectively, to the AF GRS which ranged from 0 to 1.65 among the VSR individuals. The GRS tertiles were 0 to 0.12 (bottom), >0.12 to 0.54 (middle), and >0.54 (top), respectively. Individuals in the top and the middle GRS tertiles had an increased risk for CES with odds ratios of 1.72 (95% CI 1.18-2.51) and 1.36 (95% CI 0.91-2.03), respectively, compared with individuals in the bottom tertile. The trend test p value was 0.005.

Conclusion: A genetic risk score of AF was associated with cardioembolic stroke in the Vienna Stroke Registry.
THE ASSOCIATION OF A GENETIC RISK SCORE WITH ATRIAL FIBRILLATION IN TWO HYPOTHETICAL POPULATIONS

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Objective: To evaluate two hypothetical study populations, one general (30,000 subjects, 6.6% incidence rate) and one high-risk (400 subjects, 20% incidence rate), for investigating the association between a genetic risk score (GRS) and atrial fibrillation (AF).

Background: Four single nucleotide polymorphisms (SNPs), rs2200733, rs10033464, rs2106261, and rs13376333, are associated with AF with genome-wide significance. A GRS that combines the risk ratios, versus separate risk ratios for these SNPs, could better characterize the genetic risk of an individual.

Methods: Genotypes and AF status for each individual in the hypothetical populations were generated assuming allele frequencies from the HapMap project, risk ratios of the risk alleles from the literature, and assumed incidence rates. A weighted AF GRS was calculated for each individual by summing the natural log of the risk ratio for risk alleles carried. Using 500 and 10,000 simulations for the general and the high-risk populations respectively, the power to detect an association between the GRS and AF, and the expected risk ratios associated with the top and middle tertiles, compared with the bottom tertile of the GRS, were estimated.

Results: The odds ratios for AF for individuals in the top and middle tertiles, compared with the bottom tertile of the AF GRS were estimated to be 2.06 (95% CI 1.82-2.30) and 1.30 (95%CI 1.15-1.46), respectively. There were 100% and 77% power to detect the association in the general and the high-risk populations respectively.

Conclusion: Two hypothetical populations appeared suitable for investigating the association between an AF GRS and AF risk.
A NOVEL LAMIN A/C MUTATION IN A DUTCH FAMILY WITH PREMATURE Atherosclerosis

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Background: Premature atherosclerosis sometimes runs an autosomal dominate course within families. Despite that, no major genetic defect has been identified yet. It has been suggested that many different genes might be related to premature atherosclerosis and therefore, no major gene effect can be anticipated. We report a novel lamin A/C (LMNA) mutation, c.667G>A, in a family with extensive premature atherosclerosis, diabetes mellitus and steatosis hepatis.

Methods: In silico analysis (using Alamut version 2.2), co-segregation analysis, electron microscopy, extensive phenotypic evaluation and literature comparison were used to determine the significance of this mutation.

Results: The father of three siblings died at the age of 45 years. The three siblings and the brother and sister of the father were referred to the cardiovascular genetics department, because of the premature atherosclerosis and dysmorphic characteristics observed in the father at autopsy. Clinical evaluation revealed a LMNA mutation in the father and the two sons and showed atherosclerosis, insulin resistance and hypertension in the father and dyslipidemia and hepatic steatosis in all individuals with the mutation. Furthermore, skin biopsies of both sons showed nuclear blebbing.

Conclusion: Based on the facts that in silico analysis predicts a possibly pathogenic mutation, the mutation co-segregates with the specific disease characteristics, fibroblasts of mutation carriers showed nuclear blebbing and a similar phenotype was reported to be due to certain missense mutations in LMNA, we conclude that the novel mutation we found is a pathogenic mutation, resembling Dunnigan-type familial partial lipodystrophy.
Objective: To elucidate the potential of small non-coding RNAs, known as microRNA (miRNA), as a regulator of bone-marrow derived mesenchymal stem cell (MSC) phenotype.

Background: MSCs have been implicated in a variety of cardiovascular diseases, from cardiac fibrosis to in-stent restenosis and transplant vasculopathy, predominantly through the acquisition of a myofibroblast phenotype. We have previously shown that MSCs display a myofibroblast phenotype in vitro in addition to increased miRNA-301a expression. In this context, the mechanism of MSC-myofibroblast differentiation is unclear; however, miRNA expression has been shown to influence differentiation of other cell types. We therefore hypothesize that miRNA expression changes coincide with and influence the MSC to myofibroblast transformation.

Methods: MSCs were isolated from the sternum of patients undergoing open heart surgery and were cultured in standard DMEM/F12 with 20% FBS. Cells were transfected using 50nM concentrations of control and pre-miR-301a. MSC structure and function was assessed with collagen gel contraction and MTT assays, immunofluorescent staining, qRT-PCR and western blotting.

Results: mir-301a expression was decreased in MSCs possessing myofibrblast characteristics, compared to less differentiated cells. Compared to scramble controls, overexpression of miR-301a resulted in reduced collagen gel contraction and increased proliferation. Mir-301a overexpression also decreased non-muscle myosin IIa, smooth muscle myosin and the myofibroblast marker ED-A fibronectin.

Conclusions: Our results suggest a mechanistic role for miR-301a in regulating the proliferative versus differentiated phenotype of bone marrow derived mesenchymal stem cells. Further experiments are required to determine a potential therapeutic role for miR-301a.
THE EFFECTS OF GENDER, CALCIUM CHANNEL BLOCKERS AND DIGOXIN ON DOFETILIDE THERAPEUTIC EFFICACY AND OUTCOMES: AN ACAP-TIKOSYN REGISTRY ANALYSIS

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Introduction: Dofetilide, a potent class III anti-arrhythmic drug has been available for atrial fibrillation management for over a decade; however it is not widely used since studies regarding factors affecting its efficacy and safety are scarce.

Methods: We prospectively followed 130 patients who were admitted to our institution for dofetilide loading according to the FDA approved protocol. The drug was administered every 12 hours with electrocardiograms 2 and 6 hours after each dose. Initial dosage was dependent on initial QTc, 500 mcg if QTc <450ms and 250 mcg if QTc >450ms, and the dose was subsequently adjusted per protocol. Logistic regression, ANOVA and KM curves were used.

Results: The cohort had 105 (81%) males; mean age was 63 ± 12 years, 53% had hypertension, 42% had Dyslipidemia, 16% were diabetics, and 15% had coronary artery disease. Interestingly, the conversion rate of dofetilide to sinus was 87.5%, which increased to 95% in patients concomitantly receiving calcium channel blockers [CCB], (OR = 15.3; p=0.01); however rate significantly dropped to 83% when patients received digoxin in addition to dofetilide, (OR = 0.23; p=0.04). Females had significantly higher incidence of Torsades de pointes (TdP) events compared to males, KM curve (Hazard Ratio = 16.1; 95%CI = 1.7 - 14.5, p=0.007). The mean Follow Up was 1040 days.

Conclusions: Common rate control drugs significantly affect the efficacy of dofetilide; CCB improves and digoxin decreases its conversion rates. Females on dofetilide have increased risk for Tdp when compared to men; mechanisms are to be investigated.
INTEGRATED CHRONIC CARE MANAGEMENT IN PATIENTS WITH ATRIAL FIBRILLATION: AN EFFECTIVE TREATMENT STRATEGY


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Background: Integrated chronic care management is a necessary, systemic approach to face future capacity problems and high healthcare costs in patients with chronic disease, like atrial fibrillation (AF). Such approach in AF is not available yet. Therefore a nurse-led, guideline-based, software supported AF outpatient service was developed.

Methods: A randomised controlled trial, following PROBE design, was conducted. In total, 712 patients were randomly assigned to the AF Clinic or the usual care group. In the AF Clinic patients underwent protocolized clinical testing, were seen by a nurse specialist, supervised by a cardiologist. In the usual care patients were treated by a cardiologist in the regular outpatient setting. The primary endpoint was a composite of cardiovascular death and hospitalization.

Results: At baseline, mean age was 67±13, and 418 pts (59%) were male. Underlying diseases: hypertension 380 pts (53%), heart failure 50 pts (7%), CAD 71 pts (10%), stroke 89 pts (13%). At follow-up, 51 pts (14.3%) had reached their primary endpoint in the AF-Clinic group versus 74 pts (20.8%) in the usual care group; (HR 0.65, 95% confidence interval (CI) 0.45-0.93). Cardiovascular hospitalization occurred in 48 (13.5%) versus 68 pts (19.1%) (HR 0.66, CI 0.46-0.96) and death in 4 (1.1%) versus 14 pts (3.9 %), respectively (HR 0.28, CI 0.09–0.85).

Conclusion: The AF-Clinic improves clinical outcome and survival, and prevents hospitalization in patients with AF compared to usual care. Key to the success is the comprehensive intervention focusing on patient education, guideline adherence and teamwork between nurse specialist, cardiologist and patient.

(Clinicaltrials.gov: NCT00753259).
Pulmonary vein isolation (PVI) is an effective treatment for atrial fibrillation (AF), however, there is no consensus on the definition of success or follow-up strategies. Existing data are limited to intermittent Holter or trans-telephonic monitoring with reliance of patients symptoms.

Objectives: We sought to determine the outcomes of AF ablation and post-ablation AF surveillance with a leadless implantable cardiac monitor (ICM).

Methods: Sixty-five patients with drug refractory AF underwent pulmonary vein isolation. An ICM was implanted subcutaneously post-ablation to assess AF recurrence. AF recurrence was defined as > 1 AF episode with a duration of > 30 S. The device-stored data was downloaded weekly over the internet and will transmitted events were reviewed.

Results: A total of 2105 AF automatic and patient activated AF episodes were analysed over a follow-up of 18 +/- 4 months. Of these episodes, 63% were asymptomatic. Furthermore, only 49% of the patient-activated episodes were AF. AF recurrence was highest in the first 4 weeks and substantially decreased 6 months post-ablation. The overall freedom from AF recurrence at the end of follow-up was 54%. When 48 h Holter recordings were compared with the device stored episodes, the sensitivity of the device to detect AF was 95% and the specificity was 62%.

Conclusion: The ICM provides an objective measure of AF ablation success and provides excellent sensitivity in AF detection. A significant percentage of AF episodes post-ablation are asymptomatic.
FREQUENCY OF ATRI-VENTRICULAR BLOCK COMPlicating ST ELEVATION MYOCARDIAL INFARCTION

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ST segment elevation myocardial infarction (STEMI) can be associated with conduction disturbances including atrioventricular block (AVB). AVB can occur as frequently as in 14% of patients with inferior wall STEMI and is usually associated with increased mortality but these data antedate modern area of catheter-based reperfusion therapy. The aim of this study was to ascertain the frequency of AV conduction disease complicating STEMI in the area of rapid reperfusion with primary percutaneous intervention. We have analyzed retrospectively 223 consecutive patients presenting with STEMI to our institution. 72 (41%) patients had an anterior STEMI, 98 (56%) patients had an inferior STEMI and 9 (5%) had a lateral STEMI. Most of the patients (87%) were African-American. Mean door-to-balloon time was 77±38 minutes. Only 10 patients (4.4%) required temporary pacing at presentation. Out of the 10 patients, 8 presented with complete AVB. Nearly all of them (7) had an inferior STEMI, and one had a lateral STEMI. No patients with an anterior STEMI had an AVB. Only one patient required permanent pacing. Logistic regression analysis identified female gender and posterior extension of the infarct as predictors for the need of temporary pacing. AV nodal conduction abnormalities were infrequently seen in our STEMI population undergoing reperfusion with PCI. Overwhelming majority of conduction abnormalities resolved without sequelae. Furthermore, the presence of AVB did not seem to be associated, as previously thought, with increased in-hospital mortality. This may be due to faster recovery of flow in the infarct related artery that is achieved with catheter based reperfusion.
ENHANCED ABLATION IN PULMONARY VEIN ANTRUM GUIDED BY MAGNETIC NAVIGATION IMPROVES LONG-TERM OUTCOME OF PAROXYSMAL ATRIAL FIBRILLATION

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Objective: Electrical reconnection between pulmonary vein and left atrium is one of the main causes of the recurrence of paroxysmal atrial fibrillation (PAF) after radiofrequency catheter ablation. The aim of the study is to evaluate the effect of enhanced ablation in pulmonary vein antrum (PVA) guided by magnetic navigation on the long-term outcome. Methods: Forty patients with refractory non-valvular PAF was randomized into regular ablation group (RAG, male 15, 67.3±9.6 yrs) and enhanced ablation group (EAG, male 14, 68.1±7.9 yrs). PVA isolation was achieved by creating single PVA ablation circle in RAG and closed double PVA ablation circles in EAG. Left and right sided pulmonary veins were isolated as one unit respectively. Cool saline irrigated magnetic ablation catheter, CARTO 3 mapping system and Niobe II magnetic navigation were used in both groups. Lasso mapping catheter was used to confirm PVA isolation. Amiodarone was canceled in three months after procedure. Symptom-driven electrocardiography and regular Holter monitoring were used to follow up all patients.

Results: Forty patients got 100% PVA isolation without complications by single procedure. Ablation energy delivery time were longer in RAG than in EAG (568.3±110.6 vs 725.2±161.7 seconds, P<0.05). During the follow-up of 17.3±3.6 months, symptom-driven electrocardiography was more frequent in RAG than in EAG (11 vs 5, P<0.05). PAF recurrence rate confirmed by regular Holter monitoring was higher in RAG than in EAG 20.0% vs 0.0%, P<0.01).

Conclusions: Enhanced ablation in PVA by magnetic navigation could improve long-term outcome of PAF.
Objectives: To compare radiofrequency catheter ablation (RFCA) to cryocatheter ablation (CCA) therapy for treatment of cavotricuspid isthmus-dependent type 1 Atrial Flutter (AFL). The use of CCA therapy in this setting has been increasing.

Methods: Studies evaluating RFCA and CCA for treatment of type 1 AFL were identified and collected by searching MEDLINE, EMBASE and the Cochrane Library. A mean difference and 95% confidence interval was calculated for continuous variables while a common odds ratio and 95% confidence interval was calculated for odds ratio variables.

Results: 7 studies were included from final analysis. Procedural time was significantly less in RFCA group compared to CCA group (134.4 min vs 166.7 min, std mean diff -0.69, p = 0.01). Acute success rate was significantly higher in RFCA group compared to CCA group (92.7% vs 85.5%, OR 2.06, p = 0.01). Significantly higher long term success rate was also noted in RFCA group compared to CCA group (85.4% vs 75.1%, OR 2.15, p = 0.002). Pain perception using Pain-VAS score was significantly higher in RFCA group compared to CCA group (15.4 vs 0.4, std mean diff 2.22, p <0.00001). Conclusion: RFCA therapy required shorter procedural time and was associated with higher acute and long term follow up success rates when compared to CCA therapy for treatment of type 1 AFL. CCA therapy was less painful than RFCA therapy.
SAFETY AND FEASIBILITY OF ADENOSINE ADMINISTRATION DURING HYBRID ATRIAL FIBRILLATION ABLATION TO TEST DORMANT PULMONARY VEIN CONDUCTION

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Objectives: To test the safety and feasibility of adenosine administration during a combined simultaneous thoracoscopic surgical and transvenous catheter atrial fibrillation (AF) ablation.

Background: Adenosine administration after pulmonary vein isolation (PVI) with unipolar radiofrequency energy (RF), reveals acute recovery of conduction to the pulmonary veins (PV) in up to 25% and predicts AF recurrence. This testing may increase long term success rate of ablation procedures. To date, no study has evaluated adenosine administration in a hybrid AF ablation setting using a bipolar RF device to isolate the PVs.

Methods and results: 10 patients (mean age 56 years, 9 men) with AF (60% paroxysmal AF) underwent a hybrid ablation. At least 30 minutes after bilateral PVI using a bipolar RF clamp (Atricure, West Chester, OH) and once sinus rhythm was restored with additional linear lesions if necessary, acute PV reconduction was assessed using adenosine and a circular mapping catheter (Lasso, Biosense Webster, Diamond Bar) placed endocardially at the ostium of the PV. A total of 40 PVs were checked with 15 to 21mg of adenosine administrated per PV. None of the 40 PVs tested showed any dormant PV potential after adenosine administration. No complications occurred.

Conclusions: The use of adenosine in a hybrid AF ablation setting, is feasible and safe. In this small series of patients, the use of a bipolar RF clamp results in no acute PV reconduction after adenosine administration.
If a left atrial appendage (LAA) thrombus is identified prior to cardioversion (CV) or ablation despite anticoagulation, standard practice is for more aggressive anticoagulation followed by transesophageal echocardiography (TEE) to ensure thrombus dissolution. This usually requires 3-4 weeks. A 46 year old man with dilated cardiomyopathy, left ventricular ejection fraction of 11%, and recurrent persistent atrial fibrillation (AF) despite amiodarone was re-admitted with decompensated heart failure secondary to AF, only 2 weeks post CV. The plan was to repeat CV, followed by left atrial circumferential ablation (LACA) after a few days for hemodynamic stabilization. However, TEE identified LAA thrombus (Figure A). Low molecular weight heparin was added to warfarin for 2 weeks but the thrombus persisted (Figure B). As his heart failure worsened despite rate-control, it was felt that CV or ablation could not be delayed further for thrombus dissolution. Due to the high risk of embolic complication, a decision was made to attempt systemic thrombolysis. IV alteplase was administered with no immediate complications. Two days later the thrombus had dispersed (Figure C). CV resulted in short-term hemodynamic and clinical improvement, enabling successful LACA to be undertaken. This case illustrates the efficacy of systemic thrombolysis for resistant LAA thrombus in a highly symptomatic AF patient. Thrombolysis may be considered where delay for anticoagulation prior to CV or ablation may be detrimental, but the risk of intervention in the presence of thrombus is deemed too high. Each case must be judged on its own merits in terms of risk and benefit.
Objective: Determine the complication risks of transseptal puncture (TSP) using single plane fluoroscopy during electrophysiology studies in pediatrics and congenital heart disease (CHD).

Background: TSP is commonly used to access the left heart for catheter ablation procedures. The specific complication risks of this procedure have not been determined.

Methods: This was a retrospective cohort study of patients undergoing TSP during electrophysiology study (EPS) at the University of Michigan congenital heart center between 1999 and 2011. Both fluoroscopic and non-fluoroscopic systems were used.

Results: There were 385 left heart ablation procedures. The total cohort was divided into a pediatric subgroup (less than 18yrs old with normal cardiac anatomy) and a subgroup of patients with CHD. Exclusions included 13 adults without CHD, 6 procedures using an alternative imaging modality and 5 procedures using retroaortic access. There were 321 pediatric TSP procedures (median age 13 yr, range 1 mo to 17 yr) and 40 TSP procedures in the CHD group (median age 28 yr, range 3-73). There was 1 complication directly attributable to TSP: needle perforation of the left atrium without development of effusion in a normal heart. Post-procedure echocardiograms were performed routinely in 358 (99%) of cases showing only trivial effusions in 7 (1.8%).

Conclusions: Over 12 years of TSP in pediatric and congenital heart disease patients using single plane fluoroscopy shows the risk to be low with a 0.3% (95% CI 0, 0.9%) risk for all direct complications.
Introduction: RP interval during narrow complex tachycardia, measured by surface EKG is often used to differentiate between the two types of AV node dependant tachycardia (AVNRT and AVRT). An RP interval < 80 ms commonly suggests presence of a typical AVNRT. We hypothesized that the above criteria may not apply to elderly patients. Methods: EKGs from thirty consecutive patients referred to EP laboratory were reviewed and analyzed. Baseline EKG intervals while in sinus rhythm (SR) and RP interval during confirmed typical AVNRT were measured in leads II and V1.

Results: The mean age of patients was 59 ± 15 years. 9 out of 30 patients (30%) were ≥ 70 years old. PR interval during SR did not differ between patients < 70 and ≥ 70 years: 148 ± 22 ms vs 150 ± 26 ms (p=NS). QRS duration was longer in patients ≥ 70 vs < 70 years: 105 ± 10ms vs 94 ± 11ms (p=0.0012). RP interval was significantly longer in patients ≥ 70 vs < 70 years old: 83 ± 16 ms vs 58 ± 10ms (p=0.0014). 6 out of 9 patients ≥ 70 years, had an RP interval ≥ 80 ms while no one in the group of < 70 years old: 66% vs 0% (p<0.001).

Conclusions: RP interval < 80 ms measured on surface EKG during narrow complex tachycardia is a useful criteria for identifying typical AVNRT in patients < 70 years old, but may not be applicable in elderly individuals. Further studies may be required to explain this finding.
Objective: This study aims to evaluate strut coverage according to the use of different statins and low density lipoprotein cholesterol (LDL-C) level following drug-eluting stent (DES) implantation.

Backgrounds: No randomized data exists regarding strut coverage after DES implantation according to specific statin use or LDL-C levels.

Methods and Results: A total of 60 patients were randomly allocated into Sirolimus eluting stents (SES) and Biolimus eluting stents (BES) and then each stent group was randomly assigned with Pitavastatin (2mg/day) or Pravastatin (20mg/day) group. Follow-up OCT was performed to assess stent strut coverage 6 months after DES implantation [pitavastatin (n=25) vs. pravastatin (n=27)]. There were no significant differences in the percentage of uncovered struts between pitavastatin (19.4 ± 14.7%) and pravastatin (19.0 ± 15.2%, p=NS) group. However, Pearson correlation analysis revealed that lower achieved LDL-C level (r=0.558, p=0.009) and higher LDL-C reduction (r=0.464, p=0.045) were significantly correlated with a lower percentage of uncovered struts in SES, but not in BES. Furthermore, multiple linear regression revealed that attainment of LDL-C level <70mg/dL was significantly correlated with a lower percentage of uncovered struts after adjusting follow-up duration, types and size of DES, inflammation marker, presence of diabetes, and initial diagnosis (p=0.042).

Conclusions: Irrespective of types of used statin, a lower LDL-C, especially < 70mg/dL, might have a protective effect against delayed stent coverage after SES implantation but not BES.
THE ANATOMICAL SIGNIFICANCE OF EARLY NORMALIZATION OF THE ST DEPRESSION IN THE RECOVERY PERIOD

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Objective: We sought to examine the angiographic correlation of the early recovery phenomenon in exercise treadmill tests (ETT).

Background: We showed early ST segment normalization during recovery had similar summed stress scores to those with normal ETT. This implied that early normalization of the ST segment signifies an unrecognized false positive based on functional data. Methods: Those who had angiography 6 months prior and up to 1 year after exercise MPI were included. Normal was defined as a negative ETT. Positive ETT were stratified on the degree of ST depression at 1 min in recovery (Persistence: >1mm; Early normalization <1mm). Angiographic data included number of stenotic vessels and high-risk findings (left main and 3VD). Clinical characteristics were compared using ANOVA for continuous and Chi-Square test for categorical variables. Number of diseased vessels was compared with Fisher’s exact test.

Results: Normal group had greater proportion of normal coronaries while Early Normalization had more single VD. High-risk anatomy occurred in 5.9% of Normal, 7.4% of Early Normalization which was significantly different from Persistence group at 39.3%. The difference between the Normal and Early Normalization was not statistically significant (p=0.969).

Conclusion: Although ST segment depression of >1mm at peak exercise indicates a positive ETT, the degree of ST segment depression at 1 minute into recovery appears to be a better indicator of high-risk angiographic findings. Early normalization of ST depression in recovery was not significantly different from normal ETT with respect to the presence of 3VD or left main CAD.
EXAMINATION OF CAVI MEASUREMENT IN PATIENTS UNDERGOING INITIAL CORONARY ANGIOGRAPHY

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Objective: The cardio-ankle vascular index (CAVI) was developed as a new, blood-pressure-independent index of arterial stiffness and is used for the quantitative evaluation of blood vessel elasticity and arterial stiffness. In this study, we examined the relationship between CAVI and the severity of coronary artery disease (CAD) in patients undergoing initial coronary angiography (CAG).

Subjects and Methods: The subjects were 231 consecutive patients who underwent initial CAG for the purpose of diagnosing CAD. CAVI was measured in the catheterization laboratory prior to CAG. Significant stenosis was defined by greater than or equal to 75% organic stenosis on the coronary angiogram, and severity was classified as 0-, 1-, 2- and 3-vessel disease based on the number of affected coronary branches.

Results: Subjects with multi-vessel disease had significantly lower HDL-C levels and significantly higher CAVI values than those with 0-vessel disease. In addition, simple correlation analysis revealed correlations between CAVI and age, systolic blood pressure, eGFR, difference in systolic blood pressure between the left and right upper arms, and the number of affected coronary branches. Furthermore, multivariate analysis revealed that CAVI was significantly associated with age and the number of affected coronary branches.

Conclusions: CAVI well reflects the severity of CAD. Furthermore, blood pressure data obtained by CAVI measurement may indicate the worsening of peripheral arterial disease associated with the severity of CAD.
IS D DIMER TEST RELIABLE FOR DIAGNOSIS OF DEEP VENOUS THROMBOSIS?

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The patients hospitalized at Intensive Care Unit (ICU) for treatment of severe diseases are considered to have high risk for deep venous thromboembosis (DVT). For diagnosis of DVT, Duplex ultrasonography (DUS) or D dimer test is very useful. However, the patients at ICU have high coagulability by original severe diseases, and show high D dimer concentration. Then, we evaluated usefulness of D dimer test and DUS for diagnosis of DVT at ICU.

Methods: The 31 patients who are treated at ICU for severe disease were studied. DUS and D dimer test were done before administration of heparin or warfarin. All patients had severe diseases including sepsis, severe inflammatory disease, cerebral vascular diseases etc.

Results: By DUS, DVT was detected in 20 patients (DVT group). D dimer concentration was 20.54±7.6 µg/ml (mean±SD) in DVT and 17.34±9.0 µg/ml in non DVT group (NDVT)(NS). The number of patients with D dimer concentration of more than 10 µg/ml was 14(70%) in DVT and 6(55%) in NDVT. That of patients with D dimer concentration of more than 20 µg/ml was 9(45%) in DVT and 4(36%) in NDVT. Out of 11 patients with D dimer concentration of less than 10 µg/ml, 5 patients (45%) developed DVT. Conclusions: In the patients with severe diseases, D dimer test is not reliable for diagnosis of DVT at ICU. DUS is necessary to detect thrombus in deep leg veins.
GLOBAL LONGITUDINAL STRAIN SPECKLE TRACKING IN CONSIDERING ADVERSE CARDIOVASCULAR EVENTS DURING FOLLOW SHORT TERM IN PATIENTS WITH ACUTE CORONARY SYNDROME

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Method: A prospective, longitudinal, observational assessment of ACS patients over 18 years admitted to the Hospital "Dr. Domingo Luciani" evaluated by two-dimensional echocardiography in the first 48 hours and 3 months from February to July 2012.

Results: 61 patients with ACS were assessed baseline echocardiographic measurements were made with traditional parameters and SLG. We followed 47 patients and found a significant improvement SLG in those with NSTEMI vs STEMI (-18.26% vs -14.37. P <0.02) and patients with STEMI who received fibrinolysis vs those not receiving (-15.72 vs. -13.02% . p <0.01). In revascularized patients ejection fraction (EF) on average at 3 months was higher (56% vs. 42%. P <0.002) as well as the SLG (-18.15% vs -14.27%. P <0.01). The sensitivity (27%) and specificity (95%) of the SLG significantly predicted death better than EF and WMSI (p <0.04). Patients with SLG > -12.5% are 4.5 times more likely to die from cardiovascular causes than those with value < -12.5% (p <0.03).

Conclusions: The SLG has high specificity in predicting cardiovascular death before 3 months follow-up in patients with acute coronary syndrome.
USEFULNESS AND LIMITATION OF ANKLE-BRACHIAL INDEX FOR DIAGNOSIS OF PERIPHERAL ARTERY DISEASE
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The usefulness of ABI (ankle-brachial index) test for diagnosis of peripheral artery disease (PAD) has not been established in the patients with tibioperoneal obstructive disease. Then we evaluated usefulness of ABI test in the patients with PAD.

Methods: We evaluated 18 PAD patients with obstruction of anterior tibial artery (ATA) and/or posterior tibial artery (PTA) (27 obstructed lesions)(group A). On the other hand, 14 PAD patients with femoral or iliac obstructive disease igroup B, 18 lesions. PAD was diagnosed by duplex ultrasonography (DUS) and computerized tomography angiography (CTA).

Results: ABI was 0.95±0.03(mean±SE) in group A and was 0.71±0.05 in group B (P<0.0001). ABI was 1.06±0.02 in the patients with only obstruction of ATA (AA group) (n=12), 0.94±0.03 in the patients with only obstruction of PTA (AB group) (n=7),and 0.79±0.02 in those with obstruction of both ATA and PTA (AD group) (n=8). ABI of AD group was lower than that of AP or AA (P=0.0005 or 0.0001 respectively) and ABI of AP was lower than AA (P=0.05).

Conclusions: Usefulness of ABI is limited for diagnosis of PAD in the patients with tibial obstructive disease. PAD may exist in the patients with ABI of more than 0.9. ABI of the double tibial obstructive disease was lower than that of ATA or PTA obstructive disease alone, and similar to that of iliofemoral obstructive disease. DUS is mandatory for diagnosis of PAD.
Effects of Radial Artery Anatomical Variations on Transradial Cardiac Catheterization

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Background: Trans-radial cardiac catheterization (TRCC) approach has been used more frequently. This approach has unique technical challenges especially for new users. Most of the technical difficulties are related to radial anatomical variations causing spasm, difficulty engaging and procedure achievement.

Methods and Results: We did evaluate the incidence of anatomical variations of the right artery (RA) and its effects on the TRCC. A total of 300 consecutive patients who underwent TRCC in our academic institution were analyzed by radial angiogram after access and after the antispasmic medications. Overall, anatomical variations were seen in 29 patients (9.6%); 24 cases of high origin of the RA from the axillary artery (8%) that did not cause any technical difficulties compared to normal bifurcation, and 5 cases of radioulnar loop (1.6%) requiring access change in 4 of the cases. 64 pts (21%) had tortuous innominate artery which resulted in more contrast use and more fluoroscopy time compared to non-tortuous artery. Radial spasm was present in 55 cases (18%) requiring more vasodilators use and access switch in only 4 cases. It was difficult to engage one of the coronaries in 63 cases requiring more contrast use, more fluoroscopy time and multiple catheter use. Engagement difficulty was mainly due to RA spasm and tortuous innominate artery. TRCC failed in 10 patients (3%). The average radial artery size was 2.9 mm, the average ulnar artery size was 2.7 mm.

Conclusion: In TRCC, Radioulnar loop, radial spasm and tortuous right innominate artery were associated with technical difficulties and challenge.
RECANALIZATION OF CHRONIC TOTAL OCCLUSIONS BY A SYSTEM OF HIGH-FREQUENCY VIBRATION

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Background: Failure of CTO recanalization still occurs in approximately 25–50% of coronary CTO cases. The CROSSER System consists of a reusable Generator which converts AC line power into high-frequency vibration. The coronary CROSSER Catheter is 1 mm in diameter, 6 Fr guide catheter compatible, and has a blunt stainless steel tip.

Methods: We present the first 4 consecutive lesions in three patients in our center with CTO treated by CROSSER catheter as an alternative to other system of recanalization.

Results: Four lesions were treated in three patients. Two men and one woman. The mean age was 66 ± 13 years. The diagnosis on admission was stable angina in all cases and the treated arteries were the left anterior descending artery in two cases and the right coronary artery in the other one. The average time of use of the device was 2.33 ± 1.5 minutes: two minutes in the first patient, five minutes in the second one and three minutes in the last one. The therapy following CROSSER was the stenting in all cases with TIMI 3 flow in arteries treated. There were not periprocedural complications (periprocedural MI, clinical perforation, cardiac tamponade or death). Length of stay post procedure was 1.33 ±0.58 and 30 days MACE was 0%.

Conclusion: We conclude that high-frequency vibration using the CROSSER catheter is a safe and effective alternative therapy for patients with CTO with decreased procedure time, minor use of contrast and shorter fluoroscopy time compared with conventional devices.
Objectives: To present a novel, alternative endovascular treatment strategy for atherosclerotic carotid artery aneurysmal disease.

Background: Carotid artery stenting has become a safe and effective alternative for the treatment of carotid artery disease. The management of aneurysmal or ulcerated defects, when associated with atherosclerotic lesion, however, remains unclear.

Methods: A 64-year-old male with a history of prior ischemic stroke, for which he underwent right carotid endarterectomy with patch angioplasty 3 years earlier, presented with symptomatic high-grade stenosis of the right internal carotid artery (ICA). A pre-procedural CTA confirmed a >80% stenotic lesion with an associated sacular defect suggestive of an ulcerated lesion vs pseudoaneurysm. Selective carotid angiography with adjunctive IVUS examination confirmed a >80% eccentric stenosis with a sacular defect at the superior margin of the prior endarterectomy patch. Under combined distal and proximal embolic protection with flow reversal, the lesion was successfully crossed and stented with an 8x30mm Abbott Xact self-expanding nitinol stent. Repeat angiography showed excellent results in regard to stenosis reduction to <10% residual. There was, however, a persistent filling of the sacular defect behind the stent struts that was postulated could serve as a nidus for clot formation. A 7x25mm Gore Viabahn PTFE self-expanding covered stent was then deployed within and overlapping preceding nitinol stent and post-dilated at moderate atmospheres. Angiography demonstrated good apposition and complete obliteration of the sacular formation.

Results and Conclusions: This case illustrates a novel endovascular treatment option for carotid lesions associated with pseudoaneurysm or ulcerative features. There is paucity of data to guide management in similar circumstances and the optimal strategy is unknown.
Disruption of atherosclerotic plaques could play an important role in the pathogenesis of dissection and Pseudoaneurysms occurring after coronary stenting. Currently, there are no established guidelines regarding the management of Ascending aortic pseudo aneurysm, but most authors recommend surgical treatment even in asymptomatic patients.

We report the case of a 46-year-old man with risk factors for coronary artery disease of ex-smoking, obesity, hyperlipidemia and peripheral arterial disease. His past medical history was remarkable for a non-ST elevation myocardial infarction, treated four months previously with percutaneous coronary intervention and four sirolimus-eluting stent implanted to treat stenosis of the right coronary artery. Two months later he was referred to our hospital because of persistent fever. Computed tomography angiography was performed and revealed the presence of a pseudoaneurysm of the ascending aorta involving the right coronary sinus of Valsalva. The patient underwent surgical intervention under extracorporeal circulation. At surgery the aorta was not dilated and in the aortic wall Atherosclerotic fragments were predominantly seen. The entry of the Pseudoaneurysm was closed with bovine pericardial patch. Surgical intervention was successful and he was discharged home without significant issues. At the two-month follow-up visit the patient was asymptomatic. A follow-up visit and a computed tomography has been recommended at 6 months. The forceful manipulation of the guide catheter seemed to be the Pathophysiologic mechanism of the Pseudoaneurysm involving the right coronary sinus of Valsalva.
THE POSITIVE INFLUENCE OF EARLY TRAINING IN THE COMFORT LEVEL OF DOING DIAGNOSTIC ANGIOGRAPHY BY RADIAL ACCESS IN COMPARISON TO FEMORAL ACCESS

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Objectives: To evaluate the hypothesis that with early training fellows develop equitable competency in radial access versus femoral access in doing diagnostic angiography.

Background: Radial access in doing diagnostic coronary angiography has shown to be technically challenging and this has been shown to result in higher level of radiation exposure and contrast dose.

Methods: We did a retrospective, descriptive review of transfemoal versus transradial approach in doing diagnostic coronary angiography between July 2012 to December 2012 among fellows of various levels of training.

Results: Among the randomly selected 227 patients who underwent selective coronary angiography 104 had transradial approach and 123 had transfemoral approach. There was no statistically significant difference in fluro dose, floro time among these two groups, but the contrast dose was significantly higher in transradial approach coronary angiogram. The flurodose, fluro time, and contrast dose was non significantly higher in the radial group among the first year fellows but they were equal in second and third year fellows.

Conclusions: With early initiation training fellows have increasing and comparable proficiency in transradial approach against transfemoral approach in doing selective coronary angiography.
EFFECT OF THERAPEUTIC LIFESTYLE CHANGE ON HIGH DENSITY LIPOPROTEIN CHOLESTEROL IN PATIENTS WITH METABOLIC SYNDROME

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Introduction: Therapeutic lifestyle change (TLC), especially diet control has been primarily focused on lowering LDL cholesterol levels, and the effect on patients with metabolic syndrome is not well established.

Objective: This study was to elucidate the effect of 4 week TLC diet on metabolic syndrome.

Method: This study was single arm trial including subjects with metabolic syndrome taking 4 week TLC diet. Metabolic syndrome was defined as the presence of at least 3 out of 5 risk factors according to the NCEP-ATP III guidelines. One session of individualized education was presented by skilled nurse with brochure that described detailed information about TLC diet.

Result: 67 subjects with metabolic syndrome were enrolled. Changes in body weight were not significant. Fasting blood glucose levels were not altered. TLC did not resulted in significant changes in total cholesterol and triglyceride. But, TLC led to significant reduction in LDL cholesterol levels (from 161.1±21.2 to 147.6±25.1mg/dL, P<0.001, -6.6%), and significant elevation in HDL cholesterol levels (from 37.7±6.8 to 41.8±8.4mg/dL, P=0.001, +12.1%).

Conclusion: Four weeks' TLC intervention, which was provided with one session of education by skilled nurse, improved lipid profile (especially HDL cholesterol) in metabolic syndrome. Our findings indicate that the importance of less intensive, inexpensive and easily accomplishable education method should not be underestimated from the early stage of intervention.
THE EVALUATION OF THE USE OF A LIPID TRACKING MATRIX TO IMPROVE PROVIDER ADHERENCE TO LIPID GUIDELINES
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Background: Heart disease is the leading cause of death in men and women in the United States. Significant research into the risk factors for cardiovascular disease has been conducted, and the effect of hyperlipidemia on cardiovascular risk has been well documented. Recent research has shown that there is a lack of adherence to lipid guidelines by primary care providers. Failure to follow clinical guidelines for lipid disorders leads to increased cardiovascular morbidity and mortality.

Objective: The objective of the project was to evaluate whether a simple, paper-based, lipid-tracking matrix could improve provider adherence to current lipid guidelines.

Methods: This descriptive study used a pre/post-test design. Baseline adherence to lipid guidelines was determined by chart review of a random sample of practice patients. The lipid-tracking matrix was placed on the charts of all patients seen for routine office visits during a 4-week period. After the lipid-tracking matrix collection period was completed, a random sample of those patients was reviewed to reassess provider adherence to lipid guidelines. The post-implementation data was compared to the baseline data.

Results: The use of the lipid-tracking matrix did demonstrate an improvement in provider adherence to lipid guidelines as demonstrated by an increase in the number of patients who had a documented LDL goal (p<0.0001).

Conclusion: In practices without electronic medical records (EMR), this simple, inexpensive, paper-based matrix can be used to improve provider adherence to lipid guidelines. In addition, this matrix can be used to inform future EMR interfaces.
LIPOPROTEIN FRACTIONS AND SUBFRACTIONS AND HEART PROTEASES IN ACUTE LIPEMIA AND MURINE MODEL OF ATHEROSCLEROSIS

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Objectives: serum of 85 CBA mice with acute lipemia and early atherosclerosis induced by poloxamer 407 (P-407) administrations in CBA mice.

Background: According to Otvos et al. (2002), lipoprotein (LP) fractions were divided on the following four main classes: high density LP (HDL), low-density LP (LDL), very-low-density LP (VLDL) and chylomicrons or seven subfractions: HDL$_3$, HDL$_2$, LDL, Intermediate-Density LP (IDL), VLDL$_{3-5}$, VLDL$_{1-2}$, and chylomicrons. According to Otvos (2002) LP fractions and subfractions are useful in diagnosis of early atherosclerosis onset.

The aim: to evaluate effect of acute, subacute and chronic mode of poloxamer 407 (P-407) treatments on lipoprotein fractions and subfractions in murine models of lipemia or/and onset of atherosclerosis.

Methods and Results. A novel small-angle X-ray scattering method (Siemens, Germany) for the determination of the fractional and subfractional composition of lipoprotein-cholesterol (LP-C) and lipoprotein-triglyceride (LP-TG) fractions and subfractions was used (Tuzikov et al., 2002). Compared to acute lipemia induced by P-407 atherosclerosis development was characterized by steady increase in atherogenic subfractions typical for atherosclerosis in humans according to Otvos (2010). The difference between human and experimental data was in HDL subfractions, elevated in experimental atherosclerosis as result of inhibition of lipoprotein lipase (Johnston, 2010). Significant increase in heart cathepsins B and D was shown in experimental atherosclerosis. Conclusion: Small-angle X-ray scattering approach (SAXS) was useful in revealing early changes in LP-C and LP-TG subfractions in atherosclerosis in experimental murine models.
BLOOD PRESSURE (BP) RESPONSE TO EXERCISE IN PATIENTS WITH END STAGE RENAL FAILURE: IMPACT OF AUTONOMIC NEURAL CONTROL MECHANISMS

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Purpose: We aimed to investigate the BP response to exercise and its relation with the balance of sympathetic and parasympathetic activities which contributes to the exercise intolerance in end stage renal disease (ESRD) patients.

Method: 43 ESRD patients in chronic haemodialysis program without diabetes or CAD and 35 healthy control patients included in the study. In all subjects, heart rate(HR) response to valsalva maneuver, HR variation with deep inspirium were evaluated and symptom limited exercise test were performed. Exercise induced vasopressor reaction, exercise capacity, chronotropic index and HR recovery were assessed.

Results: Resting systolic BP(SBP), and diastolic BP(DBP), SBP and DBP in peak exercise were 132±20 vs 120±9 mmHg (p=0.001), 83±12 vs 74±8 mmHg(p=0.001), 158±23 vs 91±12 mmHg(p<0.05), 168±17 vs 100±12 mmHg(p=0.009) in ESRD patients and control group, respectively. Maximum increase in SBP and DBP in peak exercise, HR response to valsalva maneuver and deep inspirium are found to be decreased in ESRD group, compared to the control group. ( 36±2 vs. 48±12 mmHg, 7±12 vs 25±10 mmHg, 1.0±0.7 vs 1.1±0.7; 10.3±3.5 vs. 14±3.5, p<0.05 in patients with ESRD and control group, respectively). HR response to deep inspirium was found to be related to SBP and DBP in peak exercise (p=0.0001). Significant relationship was detected between exercise capacity with resting DBP and with HR response to maneuvers in ESRD patients(p<0.001).

Conclusion: Exercise capacity, HR index and BP increase during exercise were lower in ESRD patients. In ESRD, blunting of blood pressure response to exercise was related to changes in autonomic neural control.
UNVEILING THE MYTH OF THE J-SHAPED RELATIONSHIP BETWEEN BLOOD PRESSURE AND CARDIOVASCULAR RISK

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Objectives: Several studies found that too great a reduction of clinic blood pressure (BP) by treatment increased cardiovascular (CVD) risk, concluding a J-shaped relationship between treatment-induced BP reduction and CVD outcomes. We investigated the relationship between achieved BP and CVD risk in normotensive subjects and hypertensive patients treated at different times of the day.

Methods: A total of 3344 subjects (1718 men/1626 women), 52.6+/−14.5 years of age were prospectively studied throughout a 5.6-year median follow-up. Hypertensive participants were randomized to ingest all hypertension medications upon awakening or at least one at bedtime. BP was measured for 48h at baseline, and again annually or more frequently (quarterly) after adjustments in treatment.

Results: A J-shaped relationship was detected between total CVD events and achieved clinic and awake BP mean only for patients ingesting all medications upon awakening. In normotensive subjects and patients of the bedtime-treatment regimen group the risk of CVD events progressively diminished with decrease in clinic and awake BP mean. The adjusted hazard ratio of CVD events was significantly lower with the progressive reduction in the asleep BP mean in all three groups.

Conclusions: Clinic and ambulatory BP values of normotensive individuals and those achieved in hypertensives undergoing a bedtime hypertension treatment-regimen are not associated with a J-shaped relationship with CVD risk. The proposed J-curve seems to be a manifestation of overtreatment in the morning of elevated BP to achieve the misleading therapeutic goal of progressive reduction in clinic BP level and disregard entirely of asleep BP control.
PARTICIPATION OF SENSORY NERVES IN DIFFERENT MODELS OF FRUCTOSE-INDUCED AND NO-DEFICIENT HYPERTENSION

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Objectives. The aim: to evaluate the role of sensory nerve in the development of hypertension following fructose-induced metabolic syndrome and NO-deficient rats. 54 Wister male rats were used; groups: 1. control (intact rats); 2. NO-deficient rats (L-NAME drinking rats); 3. The desensitization + L-NAME; 4. L-NAME + stimulation; 5. Fructose-fed rats (FFR); 6. The desensitization + FFR; 7. FFR + the stimulation.

Methods and Results: NO-deficient rats: L-NAME (N\textsubscript{\textsubscript{u}}-Nitro-L-arginine methyl ester hydrochloride (0.02% solution to drink, 6 weeks). FFR - fructose (12.5% solution, to drink, 10 weeks). Glucose tolerance was assayed by glucose (intraperitoneal) tolerance test (GTT). Systolic blood pressure (BP) was measured by a tail-cuff apparatus (Coda, Kent Scientific, USA). The desensitization and the stimulation of sensory nerves were induced with capsaicin, desensitization - 150 mg/kg, the stimulation - 1 mg/kg/day, for 3 days. FFR showed glucose intolerance. The desensitization and the stimulation of sensory nerves improved glucose intolerance. Systolic BP (mmHg) increased in FFR and NO-deficient rats as compared to control rats: 142.8 ± 5.1 (FFR), 140.3 ± 1.9 (L-NAME), vs control 123.6 ± 2.9 mm. The desensitization decreased BP in FFR (116.7 ± 3.9) and increased in NO-deficient rats (164.7 ± 3). The stimulation reduced BP in the both models of hypertension.

Conclusion: The results showed participation of capsaicin-sensitive nerves and their different role in fructose-induced hypertension and NO-deficient hypertension.
SOME ISSUES ON ARTERIAL HYPERTENSION HEALTH CARE SERVICE IN MONGOLIA

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Background: Since arterial hypertension has high prevalence in country, we need to emphasize the some issues of health care service of the arterial hypertension.

Purpose: The survey is aimed to investigate and clarify causes of uncontrolled hypertension

Materials and methods: Our survey was cross sectional survey and multiple staged sampling was conducted. The study frame was over 18 years old population of 4 regions of Mongolia. In order to investigating the uncontrolled hypertension prevalence and its impact factors, we have chosen over 18 years old adults as following international standard by standard questionnaire. The questionnaire has 45 questions dividing into 6 parts.

Results: We have investigated 1635 people. There has 643 males and 992 females. The arterial hypertension prevalence were higher in the Khangai region 36.5% than eastern region 28% and dominantly in women 59.6%.

Out of total subjects, 6.2% were newly diagnosed with hypertension and were unaware of their condition. Out of total subjects, 27.1% had hypertension but they did not follow their physicians instructions. Regional differences were statistically significant (P=0.03): Of the survey respondents, 8.2% of population had uncontrolled high blood pressure but were taking medications. In this case there were no significant differences between the regions. Out of the 1103 patients with the arterial hypertension, 48.3% respondents are taking their medication daily. In our survey 58.8% of respondents admitted that at times they would forget to obtain their medication, 63.9% of respondents admitted to not taking medications because they were unable to obtain the medication as physician recommended. Finally 73.2% respondents admitted to stopping medications when they felt well or their symptoms disappeared. Of the patients who getting medication, 74.4% are using the antihypertensive drugs but 25.6% are using the non antihypertensive medication.

Conclusion: The prevalence of treated uncontrolled hypertensive patients were 8.2%, out of them 58.8% forget to get the medication, this result shows that there has higher personal impact for hypertension control.
SYNERGIC EFFECTS OF LEVAMLODIPINE AND BISOPROLOL ON BLOOD PRESSURE REDUCTION, ORGAN PROTECTION AND STROKE PROTECTION IN RATS

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Background: The objective of this work was to study the synergic effects of levamlodipine and bisoprolol on blood pressure reduction, organ protection in spontaneously hypertensive rats (SHR) and test the effects of combination with levamlodipine and bisoprolol on stroke in rats.

Methods: Blood pressure was continuously monitored in conscious SHR. Systolic blood pressure (SBP) and heart period (HP) were monitored in conscious rats before and after drug administration. To observe the protection of drugs against ischemic cerebral injury, rats were subjected to middle cerebral arterial occlusion half an hour after drug administration; 24h later, the infarct size were measured. For long-term treatment study, drugs were delivered via rat chow in stroke prone-spontaneously hypertensive rats (SHR-SP). The survival time of each rat was recorded.

Results: A single dose of levamlodipine (from 1 mg/kg), bisoprolol (from 0.125 mg/kg), and their combinations significantly decreased blood pressure. The levamlodipine-induced tachycardia and the bisoprolol-induced bradycardia were temporized by the combination of these two drugs. Upon chronic treatment, this combination also decreased blood pressure variability and reduced organ damage. SBP was significantly reduced by combination therapy with levamlodipine and bisoprolol both in SHR-SP and SAD rats. Neutralization on heart rate was observed in combination. In SHR-SP, BRS was enhanced in levamlodipine alone and combination. In long term treatment study, the lifespan of SHR-SP in combination was notably longer than that in other groups. Conclusion: Levamlodipine and bisoprolol produce synergic effects on blood pressure reduction and organ protection in SHR, combination of levamlodipine and bisoprolol has a better protection on stroke.
Hypertension is common but, with early detection and treatment, it is rare to see malignant hypertension. A 40 year old female presented with shortness of breath for one day. His past medical history was unremarkable. On presentation, this patient’s blood pressure was 280/180 mmHg, with a mean of 213 mmHg. Physical examination was bilateral crackles of the lung with pitting pedal oedema. Blood tests showed: Haemoglobin 10.3 g/dl, White cell count 10.08 g/dl, Platelets 71000, Creatinine 512 and LDH 1161. The patient’s initial treatment consists of glyceryltrinitrate and intravenous frusemide. His mean arterial pressure decreased to approximately 170 mmHg during the first hour, shortness of breath improved with the control of elevated mean arterial pressure. The patient was started on intravenous labetalol, over the next 24, the patient’s blood pressure was brought down to 140/90 mmHg and his shortness of breath improved significantly. Blood peripheral smear was significant for ongoing haemolysis. Renal biopsy was malignant hypertensive nephropathy with thrombotic microangiopathy. 2D echocardiography showed left ventricular hypertrophy. On follow up the platelet count was normal.

This case report highlights that malignant hypertension is a medical emergency which can present with features resembling a wide variety of diseases, including thrombotic thrombocytopenic purpura and hemolytic uremic syndrome. Using appropriate management to control the elevation in blood pressure can help reveal the underlying diagnosis.
IMPACT OF HYPERTENSION ON CARDIAC FUNCTION AND EXERCISE CAPACITY IN WOMEN

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Background: The purpose of this study is to evaluate the relationship between cardiac structure and function and exercise capacity in women with hypertension and normal women.

Methods: One hundred and twenty four women were divided to 2 groups - 61 normal control women with body mass index (BMI) < 25 Kg/m² (group A), 63 women with hypertension and BMI< 25 Kg/m² (group B). All study subjects were taken echocardiography and treadmill exercise test. Peak velocity of early (E) and late (A) mitral inflow and early (Ea) and late (Aa) diastolic tissue velocity of mitral annulus and left ventricular ejection fraction (LVEF) were measured. Exercise duration and METs were analyzed to evaluate exercise capacity.

Results: LVEF was not significantly different between two groups. Group B showed significantly higher A velocity (0.71±0.19 vs. 0.65±0.17 m/sec, p=0.04) and significantly lower Ea velocity (0.068±0.019 vs. 0.078±0.023 m/sec, p=0.013) compared with group A. METs and exercise duration were not significantly different between two groups. METs showed positive correlation with Ea velocity in group A and B. BMI showed negative correlation with Ea and Aa velocity in group B. However, BMI showed positive correlation with Aa velocity in group A.

Conclusions: Hypertension influence diastolic function but did not influence exercise capacity in women. Augmented atrial function according to weight increase may be attenuated by hypertension in women.
Introduction: We present a patient with a pattern of admissions for recurrent hypertensive crises during the winters for the last 4 years.

Case Presentation: In November, a 39Y/O obese male with past medical history significant for hypertension diagnosed 4 years ago, diabetes and plaque psoriasis presented to the emergency room with blood pressure elevated to 209/130. Physical examination revealed extensive plaque psoriasis. Rest of the examination was unremarkable. Laboratory data revealed elevated troponins. EKG showed no acute ST-T wave changes. Workup for known causes of hypertension was negative and it was basically concluded that his psoriasis which gets worse in winters was contributing to his hypertensive crisis.

Discussion: Psoriasis patients with hypertension have been shown to be 5 times more likely to be on monotherapy antihypertensive regimen, 9.5 times more likely to be on dual, 16.5 times more likely to be on triple and 19.9 times more likely to be on quadruple therapy. This association may be attributed to Angiotensin II that regulates vascular tone and stimulates the release of inflammatory cytokines including Endothelin-1 which has been correlated with psoriasis activity and oxidative stress resulting in destruction of endothelium dependent vasodilatation. Psoriasis has been known to get more severe in winters and our case highlights this resulting in hypertensive crisis emphasizing the need for better hypertension control in winters. Hypertensive patients with psoriasis should be encouraged to keep a log of their blood pressures so that antihypertensive regimen can be tailored accordingly. Further studies are necessary to define the nature of the relationship between psoriasis and hypertension.
Purpose: Recent studies have shown that lower body mass index (BMI) is associated with higher mortality rate in ICU patients, and patients admitted for pneumonia. However, whether BMI has an impact on mortality in patient with pulmonary embolism (PE) is unknown. We aimed to examine the association between BMI and mortality in patients diagnosed with PE.

Methods: 156 patients diagnosed with PE from 2010 to 2012 were included in this retrospective study. The demographic data, clinical manifestation, laboratory findings, and all-cause mortality at 3 months were collected. Appropriate descriptive statistics and statistical tests were performed.

Results: From 156 patients (42.9% male, mean age 59.6±19 years old, mean BMI = 31.5±8.9 kg/m²), 22 patients (14.1%) died within 3 months after being diagnosed with PE. Mean BMI in patients who died was lower compared to patients who survived (25.8 vs 32.5 kg/m², p = 0.002). There was no difference between age, gender, and ethnicity in these 2 groups. In binary logistic regression analysis, being overweight or obese (BMI > 25 kg/m²) was an independent variable associated with surviving at 3 months (OR = 3.65; 95%CI: 1.1-11.7, P = 0.029).

Conclusions: Multiple studies have revealed the association between BMI and outcome in patients in many populations. In our study, we found that being overweight or obese is associated with surviving at 3 months. The exact mechanism is unknown but many hypotheses have been proposed. This study suggests that BMI can be used as prognostic indicator for patients with PE.
Background: Obstructive sleep apnea (OSA) is a well established risk of cardiovascular morbidity and mortality. The effect of OSA on EKG has not been well studied. The aim of our study is to investigate the impact of continuous positive airway pressure (CPAP) on EKG in patients with significant OSA.

Methodology: We conducted a retrospective study using the sleep lab database in our academic center. 700 patients with OSA were randomly selected, of which 243 patients had moderate or severe OSA and prescribed CPAP, 337 patients had mild OSA, and 120 had normal study. Using T test we compared different EKG parameters in patients with moderate or severe OSA before and 6 to 12 months after the initiation of the CPAP treatment. From the 243 patients, 148 have documentation of CPAP compliance. The rest of the patients with no or questionable compliance were excluded.

Results: Mean PR interval has dropped significantly in the study group from $(123.34\pm24.95)$ before CPAP treatment to $(85.46\pm40.99)$ after being complaint with the CPAP treatment for 6 to 12 months $(p=0.01)$. Similar trend was noticed in the QRS and QTc durations, but without being statistically significant. When comparing other EKG parameters, there was no statistically significant difference.

Conclusion: CPAP treatment was associated with significant reduction is the PR interval duration in patients with moderate to severe OSA compliant with the treatment. The rest of the parameters were not statistically significant. A larger sample size is needed to confirm other relations observed in the study population.
QRS COMPLEX MORPHOLOGY IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Background and Objectives: An increased rate of ventricular arrhythmias and conduction disturbances is documented in patients with obstructive sleep apnea (OSA), being related to altered electrical properties of myocardium and altered sequence of depolarization creating a substrate for triggering arrhythmias. We aimed to evaluate the QRS complex morphology in patients with OSA.

Methods: The study population consisted of 199 consecutive patients examined in the sleep laboratory, divided into quartiles according to the apnea/hypopnea index (AHI): Group Q1: AHI 0.7-1.9 #/h; Group Q2: AHI 11.0-32.3 #/h; Group Q3: AHI 32.3-63.0 #/h; Group Q4: AHI 65.1-157.8 #/h. Resting 12-lead ECG was recorded, the QRS parameters analyzed included amplitude, QRS spatial vector magnitude (QRSmax), electrical axis (EA), and three ECG criteria for left ventricular hypertrophy (ECG-LVH) based on amplitude criteria: Sokolow-Lyon index, Cornell voltage and Gubner criterion.

Results: The QRS values were very low with respect to normal values, and there were no significant differences between the groups. The prevalence of a positive diagnosis by accepted ECG-LVH criteria was extremely low. The values of EA were significantly shifted gradually to the left (Q1: 40.1±19.8; Q2: 34.5±18.0; Q3: 27.6±15.3; Q4: 31.6±16.2). QRS morphology showed a variety of intraventricular conduction defects, including QRS notching, non-specific conduction defects and patterns of left/ or right bundle branch blocks.

Conclusions: The OSA patients displayed significant changes in QRS complex morphology characteristic for depolarization sequence deterioration indicative of considerable electrical remodeling that could be identified before the arrhythmia occurs. Support: Slovak Ministry of Education VEGA 1/0111/12, APVV 0134-11
USE OF A RESPIRATORY VOLUME MONITOR TO ASSESS RESPIRATORY COMPETENCE IN CARDIAC SURGERY PATIENTS AFTER EXTUBATION

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Background: Patients who have cardiac surgery are mechanically ventilated postoperatively. Early postoperative extubation is currently recommended in anesthesia guidelines. No current technology can accurately, non-invasively, measure respiratory competence after extubation. Pulse oximetry has been helpful, but this is a late indicator of respiratory compromise. A novel, non-invasive, Respiratory Volume Monitor (RVM) has been shown to deliver accurate continuous, real-time minute ventilation (MV), tidal volume (TV) and respiratory rate (RR) measurements and provide an objective measure of respiratory competence.

Objective: The RVM will accurately reflect MV, TV and RR in cardiac surgery patients before and after extubation.

Methods: RVM traces were recorded from patients before and after cardiac surgery. Continuous monitoring began on admission to the unit and was ended at 24 hours after extubation. RVM based MV, TV & RR were calculated from 30-second segments. MV, TV & RR were also continuously recorded from the ventilator prior to extubation. The RVM was calibrated to each patient using the readings from the ventilator.

Results: During mechanical ventilation, the RVM measured TVs strongly correlated with the ventilator TVs (r=0.97). Following extubation the patient’s breathing became more erratic and TVs and MVs decreased. Within one hour all patients studied showed a marked recovery of MV and TV.

Conclusions: RVM based MV, TV and RR correlated well with similar data collected from ventilators. After extubation, RVM shows promise as a means to monitor respiratory competence of intubated and non-intubated patients, and has implications for improving patient safety.
STATINS THERAPY AND THE SEVERITY OF PULMONARY EMBOLISM

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Purpose: The preventive effect of statins on pulmonary embolism is controversial. Recent studies revealed statins decreases incidence of pulmonary embolism (PE) but no one has reported the effect of statins on the severity of PE. The aim of this study is to determine the association between statins and the severity of PE.

Methods: Retrospective medical records review of 156 patients diagnosed with PE determined the severity by simplified pulmonary embolism severity index (SPESI). The length of hospital stay and all-cause mortality were also compared between statins and non-statins use. The demographics, clinical manifestation, laboratory findings, and treatment were also collected.

Results: From 156 patients (mean 59.6±19 years old, 42.9% male), 35 patients were on statins therapy (statins group). There is no statistical significant in high SPESI risk between statins and non-statins users (65.7% vs 53.8%, p = 0.21). The average length of hospital stay are 7.9 days and 7.2 days (p = 0.69) in statins and non-statins groups respectively. All-cause mortality rate is also comparable among 2 groups (14.3% vs 13.4%, p = 0.9). No difference between age, gender and ethnicity in statins compared to non-statins group.

Conclusions: Even though there is supportive evidence of statins in the prevention of PE by the proposed mechanism of reduction of inflammatory and platelet aggregation. No association of statins and the severity of PE, the length of hospital stay and all-cause mortality was shown in this analysis.
Impact of Obstructive Sleep Apnea on the Heart Structure by Echocardiography Findings

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Background: Obstructive sleep apnea is a well-established risk factor for cardiovascular morbidity and mortality. The aim of our study is to investigate the impact of obstructive sleep apnea (OSA) on different echocardiography parameters.

Methodology: In this study, we performed a retrospective analysis of 700 patients with OSA randomly selected from our sleep lab database in our tertiary academic center. 243 patients had moderate or severe OSA for which a continuous positive airway pressure machine (CPAP) was prescribed and used. The rest of the patients had mild OSA (n= 337) for which CPAP was not needed and 120 had normal sleep study. Using T-test we compared different echo parameters between the patients with moderate or severe OSA (Group 1) and patients with mild or no OSA (Group 2).

Results: When comparing echo parameters between the 2 groups, the right ventricular systolic pressure (RVSP) and the right atrial size tend to be higher in Group 1 but the difference was not statistically significant. There was no statistically significant difference in regards to RV function and size, diastolic and systolic function. Mean Aortic root diameter was significantly higher in Group 1 (3.383±0.05) compared to Group 2 (3.1±0.07) (p = 0.0022).

Conclusion: In our study, among all the echo parameters, the only significant finding was a larger aortic root diameter in patients with moderate and severe OSA vs mild or no OSA regardless of CPAP treatment. A larger sample size is needed to confirm other relations observed in the study population.
SILDENAFIL DECREASES PULMONARY HYPERTENSION AFTER ACUTE PULMONARY EMBOLISM IN CHRONIC HYPOXIA

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Background During chronic hypoxia smooth muscle cells in the pulmonary vessels proliferate and the compliance of pulmonary vessels is decreased. We hypothesize that decrease of pulmonary vessel compliance results into increased pulmonary perfusion pressure response to acute PE. Our aim was to determine the influence of cGMP-specific phosphodiesterase type 5 inhibitor Sildenafil on pulmonary hypertension after acute PE in rat lungs exposed to 5day hypoxia.

Methods Using the model of in vivo PE we measured perfusion pressure changes and the level of pulmonary vasoconstriction on isolated perfused rat lungs in 5 groups: NN-control group (n=6), H-5day hypoxia (n=6), E-PE (n=6), HE-PE after 5day hypoxia (n=6), HES-PE after 5day hypoxia, administration of Sildenafil (n=6). Sildenafil was applied by gastric gavage during 5 day hypoxia. The level of pulmonary vasoconstriction was measured after administration of sodium nitropruside into perfusion solution of isolated rat lungs.

Results Animals exposed to chronic hypoxia (group HE) had significantly higher basal perfusion pressure after PE than the embolised animals without chronic hypoxia exposition (group E). However, perfusion pressure in group HES (sildenafil administration) was significantly lower than in group HE. There was no significant difference in vasoconstriction value among all groups after PE.

Conclusion The increase of pulmonary perfusion pressure after PE was higher in rats, which were exposed to chronic hypoxia. Administration of Sildenafil during chronic hypoxia decreased pulmonary hypertension after PE. This effect is probably caused by decreased compliance rather than by the change in vasoconstriction of pulmonary vessels.
Background: Takotsubo Syndrome (TS) most commonly affects women and is characterized by left ventricular (LV) dysfunction in a clinical setting suggesting an acute coronary syndrome. Sporadic cases of pharmacologically induced TS (PITS) have been reported but full characterization of PITS has not occurred. Such investigation may provide insight into mechanisms and treatment of TS.

Purpose: Characterize PITS with respect to presentation, outcome, and instigating agents.

Methods: Local cases were combined with literature review of PITS cases. For each case sex, age, presentation, presumed causal agent, electrocardiography, ejection fraction (EF), LV contraction abnormalities, and outcome were compiled.

Results: Seventy six patients (88% female) were identified. Agents causing PITS were epinephrine alone (37%) or in combination with other catecholamines (5%), dobutamine (21%), or other catecholamine enhancing agents (33%). Administration errors caused 33% of PITS. All dobutamine induced PITS occurred during stress echocardiography. ST segment elevation (46%) was common. Apical ballooning occurred in 59%. The mean EF was 33+/−11%. 48% developed congestive heart failure (CHF) and 35% required hemodynamic support. Mortality was infrequent (1.3%). All survivors normalized their EF.

Conclusions: Most PITS occurs with correct dosing rather than administration error. Epinephrine is the most frequent causal agent. LV dysfunction with CHF requiring hemodynamic support is common. The strong female preponderance mirrors spontaneous TS and suggests an increased female susceptibility at the myocardial level. Thus measures to limit excessive beta adrenergic simulation from any cause should be made in patients with a spontaneous or iatrogenic TS history.
IGNORE A TICK BITE AT YOUR HEART’S PERIL

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Background: Lyme disease is the most commonly reported vector-borne disease in the United States. Ten percent of patients with untreated Lyme disease (LD) develop cardiac sequelae that can be prevented by early diagnosis and appropriate treatment. We present a clinical vignette demonstrating the serious cardiac complications of inadequate treatment and favorable outcome with guideline based management. 28- year-old woman presented to her physician with fever and rash over chest for two days. She recalled tick bites over the past 6 weeks. She was treated with cephalexin for cellulitis. Two weeks later she presented to our emergency department (ED) with dizziness. Physical examination showed a heart rate of 40 beats/minute and a blood pressure of 92/58 mm Hg. 12-lead electrocardiogram (ECG) showed sinus rhythm with complete heart block. Transcutaneous pacing was started followed by transvenous pacemaker. A clinical diagnosis of lyme carditis was made and patient received empiric therapy with 7 days of intravenous ceftriaxone. Lyme titres were strongly positive and western blot results confirmed LD. Serial ECGs subsequently showed improvement in the severity of heart block with first degree AV block on day 4. Transvenous pacing was discontinued. The patient was discharged on oral doxycycline for 3 weeks with resolution of AV block upon follow-up.

Conclusion: 85% of cases with carditis demonstrate early cutaneous manifestations of LD. Adhering to the Infectious Disease Society of America guidelines regarding management of LD will potentially minimize the serious cardiac complications. There is increased need for awareness about these guidelines.
DIFFERENTIATING ISCHAEMIC FROM IDIOPATHIC DILATED CARDIOMYOPATHY USING DIFFERENT ULTRASONIC MODALITIES

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Objective: This study was performed to define the value of various cardiovascular ultrasonic modalities including transthoracic and transoesophageal echocardiography (TEE) and duplex scanning in differentiating idiopathic from ischaemic cardiomyopathy (ICM).

Background: Patients with left ventricular systolic dysfunction due to coronary artery disease, and those with idiopathic dilated cardiomyopathy (DCM) may present with identical manifestations. Their differentiation is by no means an academic exercise, and has important therapeutic and prognostic implications.

Methods and Results: The study included 48 patients with a mean age of 52.1±11.2 years, with males representing 79%. On the basis of coronary angiography, 31 patients had ICM and 17 DCM. Segmental wall motion abnormalities (SWMA) were more prevalent in the ICM group (p=0.002). Using TEE, 11 coronary plaques were detected in the ICM group with none seen in the DCM group (p<0.05), while 15 aortic plaques were seen in the ICM group with one in the DCM group (p=0.009). The mean right and left common carotid artery intima media thickness was significantly greater in the ICM group (p=0.027, and p=0.008 respectively). Seventy four percent of the ICM group and 18% of the DCM group had carotid plaques (CP) (p=0.001). Femoral plaques (FP) were more frequent in the ischaemic (65%), than the DCM group (6%) (P=0.002). Multivariate regression analysis revealed that predictors of ICM were SWMA (r=0.57, p=0.002, B=0.44), CP (r=0.74, p=0.001, B=0.20), FP (r=0.78, p=0.002, B=0.27), and coronary plaques (r=0.81, p<0.05, B=0.17).

Conclusions: Differentiation of ischaemic cardiomyopathy from idiopathic dilated cardiomyopathy is possible using non-invasive cardiovascular ultrasonic modalities.
AN ASSOCIATION OF TAKOTSUBO CARDIOMYOPATHY AND USE OF ANTIDEPRESSANTS

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Objectives: The aim of this study was to identify the association of Takotsubo Cardiomyopathy and antidepressants use.

Background: The association between Takotsubo Cardiomyopathy and antidepressants still remains unclear despite its theoretical causality.

Methods: We retrospectively reviewed the medical records of Takotsubo Cardiomyopathy patients from January 2010 to December 2012. All data and variables concerning clinical presentation were collected and descriptively analyzed.

Results: A total of 49 Takotsubo Cardiomyopathy patients were retrospectively identified through chart review. Among these patients, 13 patients (26.5%) were on antidepressants upon admission. 11 patients (22.4%) were on SSRI/SNRIs and 2 patients (4%) were on bupropion. 1 case was related to antidepressant overdose and the others (24.4%) were related to the therapeutic use of antidepressants. Peak troponin level was 3.89 ± 3.6 ng/mL and peak CK-MB was 9.25 ± 7.4 ng/mL. On imaging studies, 100% had typical apical hypokinesis, and the mean ejection fraction was 37.9 ± 11.9%. Only 1 patient had severe cardiogenic shock requiring intra-aortic balloon pump; other patients were discharged after recovery. Antipsychotics were continued after discharge in 5 patients and discontinued in the other patients.

Conclusion: We found that antidepressant use, especially SSRI/SNRI use, may possibly be related to Takotsubo Cardiomyopathy. Physicians should consider Takotsubo Cardiomyopathy as a possible side effect when prescribing antidepressants. A prospective cohort study or randomized control trial is warranted to confirm this finding.
A 29 year African-American male presented with a three-month history of palpitations, weight loss, fatigue, dyspnea and night sweats. His physical exam revealed left conjunctiva congestion and bilateral crackles in his lungs. EKG showed non-sustained ventricular tachycardia and CT chest revealed severe bilateral fibrosis of lung parenchyma. Transbronchial biopsy revealed non-caseating granulomas, confirming the diagnosis of sarcoidosis. Several episodes of non-sustained VT were documented. Cardiac MRI showed delayed gadolinium enhancement in the myocardium, highly suggestive of cardiac sarcoidosis. The patient was started on systemic steroids and methotrexate. An ICD was placed due to inducible sustained polymorphic ventricular tachycardia on cardiac electrophysiology.

Discussion: Cardiac sarcoidosis is present in only 5% of cases of clinical sarcoidosis. However, autopsy reports indicate subclinical cardiac involvement in up to 20–30% and in populations like Japanese up to 60%. Conduction abnormalities and ventricular arrhythmias are the most common causes of sudden death in these patients. There are no established criteria for specific diagnosis of cardiac sarcoidosis. The Japanese Ministry of Health proposed guidelines for diagnosis based either in histological confirmation by endomyocardial biopsy which has a low sensitivity due to the patchy involvement; or histological confirmation of extra-cardiac sarcoidosis plus presence of conduction abnormalities or ventricular arrhythmias. Our patient met the diagnostic criteria for the latter.

Conclusion: Early recognition of cardiac sarcoidosis is challenging but vital because of high risk and lack of predictability for sudden cardiac death. Any patient with sarcoidosis should be evaluated for presence of conduction abnormalities and other arrhythmias.
DILATED CARDIOMYOPATHY IN BECKER MUSCULAR DYSTROPHY (CASE REPORT)
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Background: Becker Muscular Dystrophy (BMD) was first described in 1955 by a German Neurologist and Geneticist, Peter Emil Becker (1908-2000). The incidence of this rare x-linked muscular dystrophy is 3 in 100,000 live male births. The most common cardiac presentation is cardiomyopathy (occur in 50% of cases) and conduction disorders. In the archives of the Philippine Heart Center, the most common etiology of dilated cardiomyopathy was found to be ischemic (59% of cases). In the same study, non-ischemic cause of dilated cardiomyopathy was found in 41% of cases with following etiologies: idiopathic (77%), alcoholic (13%), myocarditis (2%) and peripartum (4%). Cardiomyopathy from Becker Muscular Dystrophy is rarely encountered.

Case: This is a case of a 27 year-old male who was diagnosed with Becker Muscular Dystrophy during his childhood. He developed gradual progressive muscle weakness with decrease in basal functional capacity. Diagnosis of dilated cardiomyopathy was based on the clinical and echocardiographic findings. He was later admitted due to ventricular tachycardia.

Diagnostics: The chest x-ray showed cardiomegaly with an increased cardiothoracic ratio. Laboratory examination showed markedly elevated creatine kinase isoenzymes: CK-MM = 4319 IU/L, CPK=4399 IU/L, CPK-MB=80 IU/L. The ECG showed sinus rhythm with frequent polymorphic ventricular ectopic beats, first degree AV block and an incomplete right bundle branch block. Two dimensional echocardiography showed generalized hypokinesia with severely depressed systolic function (EF=25% by Simpson’s, 22% by Teicholz formula). There was dilated left ventricular cavity (LVMi of 132 grams/m², LVEDD=6.9cm) and left atrium (LAVI=29ml/m²). The sphericity index was 1.23.

Conclusion: Becker Muscular Dystrophy is rare, however the knowledge of the disease progression including the development of cardiomyopathy and conduction disorders (atrial and ventricular arrhythmia) will aid the clinician in the management and enable to anticipate probable sequelae.
CLINICAL PROFILE, MANAGEMENT, AND OUTCOMES OF PATIENTS WITH CHRONIC HEART FAILURE REFERRED TO A TERTIARY CARE HEART FAILURE CLINIC IN SAUDI ARABIA: SUBSTUDY OF THE HEARTS REGISTRY

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This is a sub-study of a prospective registry, heart function assessment registry trial in Saudi Arabia (HEARTS) and included all consecutive patients followed in the HFC between September 2009 and December 2011. Only patients with HF who were at high risk for re-admission were enrolled in the clinic. We evaluated clinical outcomes including death and re-admission rates in a subset of HF patients followed in the HFC at 1 year.

Results: 436 patients were enrolled with mean age 56.14±15.4 years, 71.79% were men and 96.57% were Saudis. The main etiologies of HF were ischemic heart disease (37.9%), non-ischemic dilated cardiomyopathy (42.7%), and hypertension (8.0%). The overall 1 year mortality rate in a subset of patients (347 patients) was 9% and the 1 year re-admission rate 37% in the same subset. The prescription rate of evidence based therapies before admission to HFC, at discharge from 1st visit and at 1 year follow up was 90%, 91% and 94% for beta-blockers, 79%, 80% and 86% for ACEi/ARBs and 44%, 45% and 42% for spironolactone respectively.

Conclusions: Our high-risk chronic heart failure patients were younger, have high rate of DM, and predominantly have LV systolic dysfunction compared with developed countries. The rate of evidence-based therapies use was reasonable, but the ICD/CRT implantation rate was low. Further improvements in management and potentially clinical outcomes, are yet to be shown with long-term follow-up at the HFC.
TAKOTSUBO SYNDROME (OR APICAL BALLOONING SYNDROME) SECONDARY TO ZOLMITRIPTAN

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Takotsubo syndrome (TS) also known as broken heart syndrome is characterized by left ventricle apical ballooning with elevated cardiac biomarkers and electrocardiographic changes suggestive of an acute coronary syndrome (i.e. ST-segment elevation, T waves inversions and pathologic Q waves). We report a case of 54-year-old woman with past medical history of mitral valve prolapse and migraines who was admitted to the hospital for substernal chest pain and electrocardiogram demonstrated < 1mm ST segment elevation in leads II, III, aVF, V5, and V6 and positive troponin I. Emergent coronary angiogram revealed normal coronary arteries with moderately reduced left ventricular ejection fraction with wall motion abnormalities consistent with TS. Detailed history obtained retrospectively revealed that usually the patient took zolmitriptan sparingly only when she had migraines. Patient otherwise reported that she is quite active, rides horses and does show jumping without any limitations in her physical activity. There was no evidence of any recent emotional or physical stress or status migrainosus.

Readers may argue that migraine headaches could be the etiologic agent since they maybe a risk factor for TS as described in few case reports. However in this patient similar previous migraine headaches have not been associated with TS. We propose that the high dose of zolmitriptan and the migraine headaches may have a synergistic effect accentuating coronary vasospasm and in turn cause TS.
EFFECTS OF IF CURRENT BLOCKER IVABRADINE IN HIGH AND INTERMEDIATE RISK PATIENTS UNDERGOING VASCULAR SURGERY

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Background: Patients undergoing vascular surgery constitute a particular challenge. Several trials showed a significant beneficial effect of beta-blockers in these patients. Perioperative use of ivabradine may be associated with several advantages.

Objective: to evaluate the efficacy of ivabradine in high and intermediate risk cardiac patients undergoing vascular surgery in comparison to standard care beta blocker therapy.

Methods: Seventy one patients underwent vascular surgery were prospectively studied and received beta blockade alone, beta blockade plus ivabradine or ivabradine alone before and 30 days after vascular surgery.

Results: Preoperative heart rate was significantly lower in beta blockade plus ivabradine and ivabradine groups compared to beta blockade group (63.5±3.8 and 64.4±4.65 versus 70.9±9.1 beat/min, p=002), and we found that the most important predictor of postoperative events was patients that not achieving the target heart rate (P= 0.02, Odds ratio= 6.75, 95% CI: 1.4-34). The target heart rate (<65 bpm) was achieved in (70%) of patients received beta blockade plus ivabradine and (64%) of patients with ivabradine alone (p= 0.01), while only 31% with beta Blocker strategy alone. In the present study, the patient with beta blockade strategy had 62.5% of cardiac complications.

Conclusions: Ivabradine may improve the postoperative outcome; these benefit independent of beta blocker dose and it offer the patient with better heart rate without hemodynamic deterioration. The patients that were not achieving preoperative target heart rate are the best to predict the postoperative complications.
CLINICAL OUTCOMES AND IMPACT ON LEFT VENTRICULAR FUNCTION, IN PATIENTS WITH MULTI-VESSEL DISEASE AND SEVERE LV DYSFUNCTION; A COMPARATIVE STUDY OF PERCUTANEOUS CORONARY INTERVENTION VERSUS CORONARY-ARTERY BYPASS GRAFTING: A SINGLE CENTER EXPERIENCE FROM SAUDI ARABIA

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Purpose: Left ventricular dysfunction (LVD) a predictor of adverse outcome in patients (pts) with multi-vessel disease (MVD). Coronary artery bypass grafting (CABG) first line strategy in pts with LVD and MVD. Percutaneous coronary intervention (PCI) is acceptable alternative. We compared outcomes and LV function in pts undergoing PCI, CABG or Optimal Medical Therapy (OMT) at tertiary care centre.

Methods: Retrospective analysis of pts n=68 with MVD and LVD Ejection Fraction (EF) ≤35% since 2006. The primary end-point was composite of major adverse cardiac, cerebrovascular events, death, MI, stroke and repeat revascularization (MACCE) in PCI n=26, CABG n=26 and OMT n=16. P <0.05 significant.

Results: Mean follow up 24 months. Males 85%, Diabetics 78%, hypertensive 75% and advanced Heart Failure 16%. Mean syntaxscore 26, 37 and 31, Euroscore 7, 12 and 11 in PCI, CABG and OMT respectively. Most pts in OMT and PCI were declined CABG, by surgeons 61%, 27% or by pts 3%. MACCE: PCI: 19 %, CABG: 27% and OMT: 11%, PCI vs CABG P=0.2. PCI pts demonstrated pre EF: 26±7.7 post:32.3 ± 9.6, CABG: pre 29.4 ± 4.7 post 32.2 ± 9.9 and OMT pre 25.3±8.2 post 25 ± 9.6 (P=0.113, P=0.108). Mean EF improvement of 6.3% vs 2.8% and larger EF>10% improvement in PCI than CABG 31% vs. 12% P= 0.06.

Conclusion: Our pts with MVD and severe LVD undergoing PCI, CABG or OMT revealed similar clinical outcomes; however, EF improved more in PCI group compared with CABG. Further studies are needed to validate these results.
PERICARDIAL SYNOVIAL SARCOMA: CHALLENGES IN DIAGNOSIS AND MANAGEMENT
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Pericardial synovial sarcoma is a rare tumor with very poor prognosis. Recent evidence suggests that timely diagnosis and aggressive multimodal management may substantially improve patient outcome. We present our institutional experience of management of only the second reported case with a favorable outcome amongst the fifteen reported so far. 27-year-old male presented with dyspnea and cough of 3 weeks. Exam revealed tachycardia, distant heart sounds and elevated jugular venous pressure. Chest X-ray showed widened mediastinum. Transthoracic echocardiogram (TTE) noted large pericardial effusion with tamponade physiology. Therapeutic pericardiocentesis yielded hemorrhagic fluid. Computed Tomography (CT) of chest showed persistent pericardial effusion and a left anterior mediastinal mass. Left anterior thoracotomy, pericardial window and left anterior mediastinotomy were done, revealing a well-encapsulated gelatinous tumor originating from the pericardium. Morphological and immuno-histochemical profile showed the tumor to be a monophasic synovial sarcoma. Fluorescent In-Situ Hybridization (FISH) was positive for SS18 (SYT) gene rearrangement on chromosome 18q11, substantiating the diagnosis. Workup for metastases was negative. Patient was treated with neo-adjuvant chemotherapy and radiation with substantial reduction in the size of tumor. Patient underwent curative surgical resection and is doing well. In patients with pericardial effusions of unknown etiology multiple modalities of cardiac imaging must be employed if there is suspicion for a pericardial mass. CT and Magnetic Resonance Imaging (MRI) are useful to evaluate for pericardial thickening or masses in addition to TTE. Treatment of synovial sarcoma is not well established. Aggressive neo-adjuvant chemotherapy with Ifosfamide, radiation and surgical resection show best outcome.
SUCCESSFUL ASPIRATION AND RHEOYTIC THROMBECTOMY OF RENAL ARTERY INFARCTS

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Objectives. In renal thromboembolism; the classic treatment is anticoagulation with possible thrombolysis and surgical thrombectomy. The role of endovascular therapy remains controversial. There are only few anecdotal reports about the use of aspiration and rheolytic thrombectomy in the renal arteries. We herein would like to highlight and discuss the role of the latter.

Background. In renal thromboembolism and in situ thrombosis, the classic treatment has been anticoagulation with or without thrombolysis and surgical embolectomy. The use of antiplatelets and anticoagulants as the sole therapy has often not been sufficient to alleviate symptoms and renal dysfunction resulting from renal infarcts, and its effectiveness in thrombolysis is formally questionable. Open surgical revascularization has limited and specific indications in the current era due to significant morbidity and mortality.

Methods and results. We present a case of acute renal infarction resulting from systemic embolism secondary to atrial fibrillation. This was treated with percutaneous revascularization, including aspiration and rheolytic thrombectomy followed by stent placement, with excellent results.

Conclusion. We believe that with the successful results described in the few anecdotal reports about the use of aspiration and rheolytic thrombectomy in the renal arteries, those can be additional tools of great use in renal artery infarcts, even if considered off label, so far.
The beneficial effects of ACE inhibitors (ACEi) and AT1 receptor blockers (ARBs) are due to blockade of tissue Ang II. Such blockade is often incomplete, due to activation of feedback mechanisms within the RAS (‘Ang II escape’). Tissue angiotensin generation depends on the uptake of circulating renin, and renin inhibitors (RI) may already bind to renin before it reaches tissue sites, thereby effectively inducing RAS blockade. Indeed, the rise in renin (indicating the degree of RAS blockade) has been suggested to be larger during RI than during other RAS blockers, and tissue Ang II remained better suppressed. Yet, recently the ALTITUDE study was halted because the addition of a RI to an ACEi/ARB in diabetic patients with nephropathy did not yield additional benefit, and resulted in increased side effects, including hypotension and end-stage renal disease. These findings mimic earlier studies in high-risk patients with established cardiovascular disease or diabetes treated with an ACEi+ARB (ONTARGET trial) and in rodents treated with an ACEi+ARB on top of a low-salt diet. The latter study revealed that dual RAS blockade induced hypotension and renal failure, accompanied by massive rises in renin, depleting angiotensinogen. These deleterious effects were prevented by a high-salt diet. Clearly, we now need a full understanding of why dual blockade might be harmful and whether this applies to some or all patients. Second, we need to establish whether the three types of RAS blockers, when given separately, are identical. This talk will summarize the current status with regard to these topics.
OPTIMAL BLOOD PRESSURE GOALS IN PATIENTS AT HIGH RISK FOR CARDIOVASCULAR EVENTS

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The American College of Cardiology Foundation/American Heart Association 2011 expert consensus document on hypertension in the elderly recommended the blood pressure (BP) be less than 140/90 mm Hg in adults with hypertension younger than 80 years and the systolic BP reduced to 140-145 mm Hg if tolerated in persons with hypertension aged 80 years and older. At 24-month follow-up of 4,162 patients with acute coronary syndrome in PROVE IT-TIMI-22, the lowest cardiovascular events rates occurred with a BP between 130-140/80-90 mm Hg with a nadir of 136/85 mm Hg. With extended follow-up to 5 years of 6,400 diabetics with coronary artery disease in INVEST, mortality was 22.8% if the systolic BP was less than 130 mm Hg versus 21.8% if the systolic BP was between 130-139 mm Hg (p =0.04). At 4.6-year follow-up of 9,603 diabetics and 15,981 diabetics in ONTARGET, the lowest incidence of cardiovascular death occurred with a systolic BP of 135.6 mm Hg in diabetics and 133.1 mm Hg in nondiabetics. A meta-analysis of 2,272 patients with hypertensive chronic kidney disease showed that a BP less than 125/75 -130/80 mm Hg did not improve clinical outcomes more than a BP less than 140/90 mm Hg. At 2.5-year follow-up of 20,330 patients with recent non-cardioembolic ischemic stroke in PROFESS, compared with a systolic BP of 130-139 mm Hg, vascular death, myocardial infarction, or stroke was increased 16% (95% CI, 1.03-1.31) in patients with a systolic BP between 120-129 mm Hg.
NOVEL TECHNOLOGIES TO MANAGE BLOOD PRESSURE IN PATIENTS WITH AUTONOMIC DYSFUNCTION

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Autonomic dysfunction contributes to abnormalities in blood pressure and heart rate control in young and elderly populations and causes significant disability. Supine hypertension and orthostatic hypotension is a common picture in patients with autonomic failure and are difficult to manage. Volatile blood pressure in patients with afferent baroreflex failure is a challenge to control. Resistant hypertension can be difficult to treat pharmacologically. Postural tachycardia syndrome is a heterogeneous entity difficult to diagnose and manage. Novel signal and hardware technologies can improve management of autonomic baroreflex dysfunction and reduce health care costs. Spectral analysis of hemodynamic parameters is a powerful tool if used appropriately. Electrical nerve stimulation or smart infusions of vasoactive drugs are possible ways to prevent orthostatic hypotension. Electric field stimulation of carotid baroreceptors elicits a depressor response through sympathetic inhibition and can be applied to reduce hypertension. Endovascular renal nerve ablation has been developed to treat resistant hypertension. Studies are under way to prove the efficacy and safety of these interventions in different patients populations.

Wireless smart ambulatory autonomic health monitor systems utilizing accelerometer, impedance techniques, and blood pressure can help in the diagnosis and prevention of falls or syncope. These miniature wireless smart devices can potentially interface with therapeutic devices for blood pressure control. Bionic baroreflex systems, originally proposed decades ago, will be possible soon in human subjects. The integration of these techniques into a smart health care informatics system will complement and improve the management of the cardiovascular abnormalities associated with autonomic dysfunction in the clinic and at home.
ROLE OF INGESTION-TIME OF RENIN-ANGIOTENSIN BLOCKADE FOR REDUCING BLOOD PRESSURE AND CARDIOVASCULAR RISK

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Objectives: Significant treatment-time differences in the beneficial and/or adverse effects of at least six different classes of hypertension medications, and their combinations, are now known. In particular, bedtime ingestion of ACE inhibitors and angiotensin-receptor blockers (ARB) exerts greater therapeutic effect on asleep BP, a significant prognostic marker of cardiovascular (CVD) events. We evaluated the potential ingestion-time-dependent effects on CVD risk of the various classes of hypertension medications.

Methods: We prospectively studied 3344 subjects (1718 men/1626 women), 52.6+/−14.5 years of age, during a median follow-up of 5.6 years. Hypertensive participants were randomized to ingest all hypertension medications upon awakening or at least one at bedtime. BP was measured for 48h at baseline, and again annually or more frequently (quarterly) after adjustments in treatment.

Results: CVD risk was markedly lower in patients ingesting medications at bedtime. Greater benefits were observed for bedtime compared to awakening treatment with angiotensin-receptor blockers (ARB) (hazard ratio (HR): 0.29 [95% CI 0.17-0.51]; P<0.001). CVD risk was similar for all six classes of tested hypertension medications in patients randomized to ingest all of them upon awakening. Among patients randomized to ingest medications at bedtime, however, ARBs were associated with significantly lower HR of CVD events than ingestion of any other class of medication also at bedtime (P<0.017).

Conclusions: The chronotherapy of conventional hypertension medications constitutes a new and cost-effective strategy for enhancing the control of daytime and nighttime BP levels, normalizing the dipping status of their 24h patterning, and potentially reducing the risk of CVD events.
Hypertension is a major global public health concern and widespread disease number one. Especially, in the industrialized countries its prevalence will increase in the years ahead. Some 30-40% of the world’s adult population suffer from hypertension, and, of these, 10-15% suffer truly resistant hypertension. Several hypertensive patients are faced with lifelong intake of medicines for reducing their chances of suffering from heart attacks, renal insufficiency or stroke. Despite the daily pill intake of many antihypertensive drugs, nearly half of these patients continue to have inadequately controlled blood pressure. Hyperactivity of the sympathetic nervous system activates norepinephrine release from the kidneys and seems to be an important contributor for maintaining hypertension and its progression.

Catheter-based renal denervation is a new and very promising therapy option for patients with resistant hypertension. During the minimally invasive procedure, the tip of the catheter is directed into the distal renal artery and two minutes of RF energy is applied. The tip is withdrawn, circumferentially rotated within the artery, and a further two minutes of energy is applied, and so on all the way back through the renal artery. Usually four to six applications of the RF energy are applied per artery. The straightforward (procedure time approximately 45 minutes) procedure reduces blood pressure by up to 30 mmHg, which sustained over 36 months and increased the blood pressure control rate, without long-term adverse events. Interestingly, beside a dramatic blood pressure reduction, renal denervation also influences glucose metabolism. Recently, it has been shown that interventional renal denervation improves insulin sensitivity and glucose metabolism in patients with resistant hypertension. If further clinical trials and registries confirm these initial findings, catheter-based renal sympathetic denervation might be helpful in the management of hypertension and could be important in reducing the high cardiovascular morbidity and mortality in patients with resistant hypertension.
USE OF AMBULATORY BLOOD PRESSURE MONITOR (ABPM) FOR GUIDING CARDIAC PATIENT MANAGEMENT

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24-hours ambulatory blood pressure monitoring has been for years a useful tool to assess variability in blood pressure beyond office checks or self-measurement. We decided to investigate the impact of ABPMs on patient management. The common indication for applying the test was uncertainty of BP fluctuations over a course of 24 hours. Our retrospective study included 250 studies on 164 patients over the span of over 15 years. The study population was 60% male and 40% female and ranged from 18 to 89 years of age. In patients who had more than one test, the shortest span was 7 months. Tests were classified as normal (exhibiting satisfactory distribution of BP with minimal deviation), as abnormal high (over 50% of readings over 140), as abnormal low (with any readings below 80), or partially abnormal (mixed with under 50% of abnormal readings either high or low). The results showed that 49% of tests were satisfactory, 30% were abnormally high, 3% were abnormally low, and 18% were partially abnormal. The clinical assessment depended upon test results. In 50% of the tests, the patient was reassured and advised to continue current treatment; in 13%, a change in medication timing was advised; in 9%, an increase in medication dosage was indicated; in 3%, a decrease in medication was recommended; in 21%, a new medication was added, and in 4%, a behavioral change was advised. In conclusion, 24-hours ABPM is a valuable tool in assessing uncertainties of BP control based on office measurements.
Objectives: The potential beneficial effects of low-dose aspirin (ASA) in the prevention of preeclampsia have not been fully corroborated by trials usually carried out in low-risk women, testing 60 mg/day ASA presumably ingested in the morning, and including women randomized as late as at 26-32 weeks of gestation.

Methods: We conducted a double-blind, placebo-controlled, chronotherapy trial on 350 high-risk pregnant women, 13.5+/-1.4 weeks of gestation at recruitment, randomly assigned to one of six groups, defined according to treatment (placebo or ASA, 100 mg/day) and time of treatment: upon awakening, 8h after awakening, or at bedtime. Intervention started at 12-16 weeks of gestation and continued until delivery.

Results: Women ingesting ASA, compared to placebo, evidenced a significantly lower hazard ratio (HR) of serious adverse outcomes, a composite of preeclampsia, preterm delivery, intrauterine growth retardation (IUGR), and stillbirth (0.35, 95%CI [0.22-0.56]; P<0.001). There were non-significant differences in outcomes between placebo at any time and ASA upon awakening. These four groups combined showed highly significant greater event-rate of adverse outcomes than women ingesting ASA in the evening or at bedtime (HR: 0.19 [0.10-0.39]; P<0.001). There was no increased risk of hemorrhage with ASA relative to placebo (0.57 [0.25-1.33]; P=0.194).

Conclusions: Results indicate: (i) 100 mg/day ASA should be the recommended minimum dose for prevention of complications in pregnancy; (ii) ingestion of low-dose ASA should start at <16 weeks of gestation; and (iii) low-dose ASA ingested at bedtime, but not upon awakening, significantly reduces the incidence of preeclampsia, gestational hypertension, preterm delivery, and IUGR.
ANGIOGENIC FACTORS AND THE RISK OF ADVERSE OUTCOMES IN WOMEN WITH SUSPECTED PREECLAMPSIA

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Background—An imbalance in circulating angiogenic factors plays a central role in the pathogenesis of preeclampsia.

Methods and Results—We prospectively studied 616 women who were evaluated for suspected preeclampsia. We measured plasma levels of antiangiogenic soluble fms-like tyrosine kinase 1 (sFlt1) and proangiogenic placental growth factor (PlGF) at presentation and examined for an association between the sFlt1/PlGF ratio and subsequent adverse maternal and perinatal outcomes within 2 weeks. The median sFlt1/PlGF ratio at presentation was elevated in participants who experienced any adverse outcome compared with those who did not (47.0 [25th–75th percentile, 15.5–112.2] versus 10.8 [25th–75th percentile, 4.1–28.6]; P=0.0001). Among those presenting at less than 34 weeks (n=167), the results were more striking (226.6 [25th–75th percentile, 50.4 – 547.3] versus 4.5 [25th–75th percentile, 2.0-13.5]; P=0.0001). Among these participants the addition of sFlt1/PlGF ratio to hypertension and proteinuria significantly improved the prediction for subsequent adverse outcomes (area under the curve, 0.93 for hypertension, proteinuria, and sFlt1/PlGF versus 0.84 for hypertension and proteinuria alone; P=0.001). Delivery occurred within 2 weeks of presentation in 86.0% of women with an sFlt1/PlGF ratio greater than or equal to 85 compared with 15.8% of women with an sFlt1/PlGF ratio less than 85 (hazard ratio, 15.2; 95% confidence interval, 8.0 –28.7).

Conclusions—In women with suspected preeclampsia presenting at less than 34 weeks, circulating sFlt1/PlGF ratio predicts adverse outcomes occurring within 2 weeks and may be useful in risk stratification and management. Additional studies are warranted to validate these findings.
HYPONATREMIA IN PATIENTS WITH ACUTE DECOMPENSATED HEART FAILURE TREATED WITH ULTRAFILTRATION

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Background: Hyponatremia is common in heart failure and worsening during acute decompensated heart failure (ADHF) indicates poor prognosis. We assessed the effect of ultrafiltration (UF) on serum sodium in diuretic-resistant ADHF.

Methods: 100 patients on ultrafiltration divided into 2 groups: decrease in serum sodium, DSS (n=77) and not decrease in sodium, control (n=23). Patients started low sodium diet and 2L fluid restriction during UF treatment.

Results: 32 patients had hyponatremia (Na<135 mEq/L) prior to UF treatment. Overall sodium decreased by 3.13±5.23 mEq/L and 62 patients developed hyponatremia (Na<135 mEq/L) after UF. Baseline sodium (137.2 ± 3.8 vs. 133±4.4 mEq/L, p=0.04) and incidence of diabetes was higher in DSS group (68 vs. 45, p=0.04) and smaller number of DSS patients used nitrates during hospital stay (46 vs. 68, p=0.05). No difference in other baseline demographic, laboratory and echocardiographic characteristics between DSS and control groups. Rate and duration of UF and number liters removed did not differ, however, the DSS patients lost less weight (-6.7 ± 6.6kg vs. -9.4 ± 4.2 kg, p=0.03). No difference in LOS or survival between the groups during 12 months follow up (p=0.74)

Conclusion: Significant hyponatremia occurred frequently during UF and was associated with higher incidence of diabetes and lack of treatment with nitrates during hospitalization. DSS during UF may indicate poor adherence to sodium/fluid limitation in the study group.
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PROCEDURAL PARAMETERS DURING RENAL DENERVATION AND CHANGE OF BLOOD PRESSURE IN PATIENTS WITH RESISTANT HYPERTENSION

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Background: Aim of the study was to investigate procedural parameters of renal denervation (RDN) which may indicate an effective ablation of sympathetic nerve fibers and thereby reduction of blood pressure.

Methods: In a total of 201 patients (age 64.2±9.6 years, 56% male, BP 174±22/ 92±16 mm Hg) with resistant hypertension RDN with the Symplicity catheter was performed. Follow-ups were conducted after 3 (n=178) and 6 (n=162) months.

Results: The mean procedure time was 63.2 ±1.5 min. During RDN a mean of 92.7 ±2.9 ml contrast medium and a radiation dose of 4978 ±247 cGy*cm² was needed. Bilateral RDN was performed with a total number of ablations of 9.9 ±0.2, while 5 ±0.1 ablations were made in the right and 4.9 ±0.2 ablations in the left renal artery. Three (3M) and 6 months (6M) after RDN systolic blood pressure (SBP) was reduced by 18 ±2 (p<0.0001) and 20 ±2 (p<0.0001). Neither total number of ablations (r=0.15; p=0.053) nor number of right-sided (r=0.128; p=0.098) or left-sided ablation (r=0.113; p=0.145) correlated with the change of SBP after 6 months. A total of 53 patients (26%) had a reduction of SBP <10 mm Hg (non-responders). Concerning procedural parameters non-responders significantly differed from responders in dose of radiation (4003 ± 354 vs. 5336 ± 290 cGy*cm²; p=0.011) and amount of contrast medium (81 ± 4 vs. 96.4 ± 3.4 ml; p=0.013). No correlation existed between change of SBP and impedance or temperature during ablation.

Conclusion: Procedural parameters of renal denervation, in particular number of ablations, were not associated with change of SBP during follow-up.
SIMULTANEOUS MEASUREMENT OF MULTIPLE CIRCULATING MICRONAS IMPROVES PROGNOSTICATION IN SUBJECTS WITH HEART FAILURE

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Certain circulating microRNAs have been proposed as novel biomarkers in heart failure (HF). However, this is based on small cohort studies. Studies in large numbers of patients that also compare multiple circulating microRNAs have not yet been reported. Accordingly, we directly compared different circulating microRNAs in a large cohort of patients with stable HF and long-term follow-up. The study included 834 patients: mean age, 68.1±12.7 years; main etiology of HF ischemic heart disease, 43.8%; NYHA II/III (68%/24%), and mean LVEF, 35.4±13.6%. We measured 14 microRNAs in plasma samples by standard Q-PCR. During a median follow-up of 2.79 years, 328 patients died. Circulating levels of miR 423-5p, miR-129-5p, miR 22_3p and miR 320 all differed highly significantly between HF decedents versus survivors (p<0.001 for each), while circulating levels of miR-133a and miR-378 differed with p-values <0.05. miR-208a, miR-622 and miR 1254 did not differ significantly. Next, we compared these circulating microRNAs in a multivariable analysis including established prognosticators of HF like age, hemoglobin, serum creatinin and NTproBNP. In this multivariable analysis, combination of different microRNAs provided independent significant prognostication, with miR 22_3p and miR423-5p adding significant independent prognostic information (P<0.05). This first large study directly comparing multiple circulating microRNAs to NTproBNP shows that selected microRNAs provide additional prognostic information in a multivariable model. Recently, new platforms have emerged to clinically measure multiple circulating microRNAs in an affordable, quick and reliable manner. This opens the exciting possibility to measure a ‘mini-microRNA profile’ in daily clinical care as a novel way to prognosticate HF.
A NEW THERAPY FOR DIASTOLIC HEART FAILURE

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Despite the increasing prevalence of heart failure with preserved left ventricular function, there are no specific treatments, partially because the mechanism of impaired relaxation is incompletely understood. Evidence indicates that cardiac relaxation becomes altered in diastolic dysfunction as a result of changes in myofilament calcium handling in response to oxidative stress. During oxidative stress, nitric oxide synthase (NOS) becomes uncoupled secondary to tetrahydrobiopterin (BH4) oxidation, reducing cardiac nitric oxide (NO). Recently, we reported that hypertension-induced diastolic dysfunction was accompanied by cardiac BH4 depletion, NOS uncoupling, a depression in myofilament cross-bridge kinetics, and S-glutathionylation of myosin binding protein C (MyBP-C). BH4 ameliorated or prevented the diastolic dysfunction, and we hypothesized that the mechanism by preventing glutathionylation of MyBP-C. We used the deoxycorticosterone acetate (DOCA)-salt mouse model, which demonstrates mild hypertension, myocardial oxidative stress, and diastolic dysfunction. DOCA-salt mice exhibited diastolic dysfunction that was reversed after seven days of BH4 treatment. pCa50 for tension increased in DOCA-salt compared to sham but reverted to sham levels after BH4 treatment. Maximum ATPase rate and tension cost decreased in DOCA-salt compared to sham, but increased after BH4 treatment. Cardiac MyBP-C glutathionylation increased in DOCA-salt compared to sham, but decreased with BH4 treatment. MyBP-C glutathionylation correlated with the presence of diastolic dysfunction. In conclusion, our results suggest that alterations in myofilaments underlie diastolic dysfunction and that BH4 may be helpful in the treatment of heart failure with preserved left ventricular function.
PARTIAL ADENOSINE A1-RECEPTOR AGONISTS FOR THE TREATMENT OF HEART FAILURE
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Background: Adenosine (AD) elicits cardioprotection through A1-receptor (A1R) activation. Therapy with AD A1R agonists, however, is limited by undesirable actions of full agonism such as bradycardia. To overcome these side effects, efforts were focused on developing “partial” adenosine A1R agonists that elicit therapeutic benefits without side effects. We recently conducted pre-clinical studies to examine the effects of a partial AD A1R agonist, Capadenoson (CAP), on left ventricular (LV) function and remodeling in dogs with heart failure (HF).

Methods: Studies were performed in dogs with microembolization-induced HF randomized to 12 weeks oral therapy with CAP or to no therapy (Control). LV end-diastolic (EDV) and end-systolic (ESV) volumes, ejection fraction (EF), plasma norepinephrine (NE) and n-terminal pro-brain natriuretic peptide (nt-pro BNP) were measured before (PRE) and 12 weeks after initiating therapy (POST). LV tissue at POST was used to assess SERCA-2a activity, expression of mitochondria uncoupling proteins (UCP) and glucose transporters (GLUT-1 and GLUT-4).

Results: In controls, EDV and ESV increased and EF decreased significantly from PRE to POST. In CAP-treated dogs, EDV was unchanged; ESV decreased and EF increased significantly. CAP significantly increased SERCA-2a activity and expression of UCP-2 and -3, and GLUT-1 and -4 and decreased NE and nt-pro BNP.

Conclusions: Our studies showed that CAP improves LV function and prevents progressive remodeling without eliciting side effects. Improvement of LV function is mediated, in part, by improved myocardial energetics. The results support continued development of partial AD A1R agonists for the treatment of chronic HF.
Alterations in cardiac energy metabolism contribute to the impaired heart function observed in heart failure patients. The failing heart is both energy compromised, as well as inefficient at producing energy. Defects in the rates of O2 consumption and mitochondrial electron transport activity occur in advanced stages of heart failure, which decrease ATP generation. This results in an increase in glycolysis as a source of ATP production. Unfortunately, while glycolysis increases, the second part of the glucose metabolic pathway, glucose oxidation, decreases because it is a mitochondrial dependent process. As a result, an increased uncoupling of glycolysis from glucose oxidation enhances H+ and lactate production. This can decrease cardiac efficiency, as ATP produced by the heart is directed away from use by the contractile proteins towards use in clearance of the H+’s. One promising strategy to increase cardiac efficiency in the failing heart is to directly stimulate glucose oxidation, thereby improving the coupling of glycolysis to glucose oxidation. This can be achieved with agents like dichloroacetate, which stimulate pyruvate dehydrogenase, the rate-limiting enzyme involved in glucose oxidation, and improves cardiac efficiency and function in the failing heart. Alternatively, glucose oxidation can be stimulated indirectly by inhibiting fatty acid oxidation. Fatty acid oxidation inhibitors such as trimetazidine and perhexiline increase glucose oxidation in the heart, and have been shown to be beneficial in treating heart failure. As a result, enhancing glucose oxidation is a potential novel therapeutic approach to treating heart failure.
Advanced heart failure (AHF) is growing in magnitude and represents a major public health problem. AHF patients are heterogeneous with varying clinical presentations. Left ventricular assist device (LVAD) support is an accepted treatment of patients with AHF. Success with LVADs as bridge-to-transplant therapy has led to their successful use as an alternate to a transplant (ie, as destination therapy [DT]). The REMATCH trial showed a 48% reduction in all-cause mortality in patients receiving LVAD therapy versus OMM (P = 0.001). One-year survival was 52% in the LVAD group and 25% in the OMM group, whereas 2-year survival was 23% and 8%, respectively. However, the number of AHF that qualify for these advanced treatments is relatively small. Despite evidence based medical and pharmacologic advances the management of AHF remains challenging, especially in the ambulatory setting. There is an urgent need to develop strategies to reduce hospitalizations and re-admission rates for heart failure in general. AHF carries a high burden of symptoms, suffering, and death. Palliative care can complement traditional care to improve symptom amelioration, patient-caregiver communication, emotional support, and medical decision making. Palliative therapies is still underused in AHF treatment. Planning for adverse events and the end of life, can be integrated into HF care early in illness. Discussions that acknowledge the uncertainty of HF course and length of life and incorporate patient and family goals and values facilitates this planning. Clear processes for weighing potential benefits and burdens of interventions and therapies should accompany decision-making.
Volume overload leading to both hemodynamic and symptomatic congestion is the cause for hospitalizations in the majority of cases with heart failure (HF). Ultrafiltration (UF) has been traditionally used for removal of volume in patients with diuretics resistance and those who need removal of a large volume. Early European studies showed a rapid and controlled removal of fluid with UF with less neurohormonal activation compared to diuretics, restoration of diuretic responsiveness and improvement in exercise capacity. Two small studies in the US later demonstrated that early application of UF for patients with CHF was possible, well tolerated and resulted in a significant weight loss and shortening length of stay. These studies were followed by two larger studies, the first was the UNLOAD study which randomized 200 patients with hospitalized for HF to UF or diuretics. The study showed that effective removal of fluid with UF resulted in improved long term outcome with reduction of rehospitalizations and emergency room visits in 90 days. More recently the CARRESS study confirmed the ability for effective removal of fluid in patients with HF. Although UF was associated with an increase of serum creatinine this was not associated with an impact on outcome. This finding has confirmed results of a number of recent reports indicating that increased serum creatinine during successful management of volume overload and congestion is not associated with worsening of renal function and do not have an unfavorable effect on either short or long term outcome.
While peritoneal dialysis is an established therapy for management of patients with end stage renal disease, it has also been proposed as a means of fluid and sodium extraction in patients with heart failure and volume overload. A number of studies have used this therapeutic modality in various settings and have generally reported positive results. In this talk, there will be a brief review of the pathophysiologic mechanisms related to the use of peritoneal dialysis with regard to its ability for fluid management through removal of water and sodium. Different regimens, techniques, and options (e.g. choice of solution) will be mentioned in this part of the talk. Then, major European and North American studies on the role of peritoneal dialysis in management of patients with both end stage renal disease and heart failure are presented and their results will be discussed, followed by an analytical summary of these studies at the end of this part. Afterwards, the results of the most recent studies on the role of peritoneal dialysis in management of patients with heart failure, but without end stage renal disease, will be presented. Finally, there will be recommendations for future studies and the major unanswered questions that need to be addressed by these trials.
Caregivers, scientists and policy makers are committed to providing more patient-specific care. The Centre of Excellence for the Prevention of Organ Failure (PROOF Centre) was established to implement biomarker solutions that define risk, predict disease occurrence, diagnose, prognose, or refine our understanding of responses to therapies and other care interventions along the life cycle of heart, lung and kidney failure. The Centre’s experience and directions with regards to biomarker identification and clinical evaluation as “fit for purpose” has been based on work related to immune rejection of transplanted hearts and kidneys, and more recently arising from questions related to “acute COPD attacks” and various forms of heart failure. This presentation will highlight lessons learned from the PROOF Centre journey in applying its development process to bring new biomarker-based tools to the clinic:

- Seamless science, building on clinically-driven needs, well-phenotyped clinical cohorts, establishment of quality-assured, state-of-the-art platforms for biological interrogation, and rigorous data mining
- Translation of technology platforms that can be cost-effective and workable in real-world clinical laboratory settings
- Shared commitment of a diversity of clinicians, life and computational scientists, policy makers, health economists, technologists, and patients.
- Pursuing health system implementation by evaluating biosignatures for intellectual property value, interfacing with regulatory agencies, and entraining experts in health system implementation processes for new diagnostic tests
- Pushing to better understand the biology of injury and repair of hearts, lungs and kidneys, and enabling pharma in drug discovery
BENEFIT OF HEART RATE REDUCTION IN ISCHEMIC HEART DISEASE AND HEART FAILURE
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Elevated resting heart rate is an established marker of risk of morbidity and mortality in patients with ischemic heart disease (IHD) and/or heart failure (HF). In IHD lower heart rates are associated with a better survival and higher heart rates increase the likelihood of episodes of myocardial ischemia during daily life and the effectiveness of anti-ischemic treatments is related to the degree of heart rate reduction. For similar degree of heart rate reduction, ivabradine is more effective than beta-blockers in improving myocardial ischemia. Recent studies have shown that in patients with HF the risk of cardiovascular death or hospital admission for worsening HF increase by 16% for every 5 bpm increase. Studies in patients with HF included in beta-blockers trials have shown that prognosis is independently related to the degree of heart rate reduction. Recent studies have shown that heart rate reduction with ivabradine improves mortality and morbidity in HF and that ivabradine alone or in combination with carvedilol is more effective than carvedilol in improving exercise tolerance and functional class in these patients. In conclusion, heart rate is an important target in patients with IHD and in those with HF. The therapeutic effect of beta-blockers in these patients is related to the degree of heart rate reduction. Ivabradine is more effective than beta-blockers in improving myocardial ischemia for similar degrees of heart rate reduction and improves mortality and morbidity in patients with HF. In these patients ivabradine is more effective than beta-blockers in improving clinical status and functional capacity.
PREDOMINANT DIFFERENTIAL CAUSE OF DYSPNEA IN ATRIAL FIBRILLATION AND COINCIDENT COPD. INFLAMMATION, LATENT ISCHEMIA AND MYOCARDIAL DYSFUNCTION, THROMBOGENESIS, APOPTOSIS AND CARDIOVASCULAR REMODELING OR RESPIRATORY IMPAIRMENT?

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Objectives and Background: Cardiopulmonary dyspnea represents a vital diagnostic dilemma. This study aims to evaluate NT-ProBNP and other Biomarker serum levels, correlated not only with each other but also with cardiac, pulmonary function indices and blood gasses.

Methods: 33 patients, 20 males and 13 females, mean age 73 yrs, underwent 1) Serum evaluation of NT-ProBNP, Homocysteine (Hcy), Troponin-I (Tr-I), Metalloproteinase-9 (MMP-9), Erythropoietin (EPO), C-Reactive Protein (CRP), Tumor Necrosis Factor-a (TNF-a), Interleukin-6 (IL-6) and D-dimers 2) Echocardiography and 3) Pulmonary Function Tests and Blood Gasses.

Results: The results showed 1. Abnormal serum mean values of NT-ProBNP= 5.647 pg/ml, Hcy= 18,2 μmol/L, Tr-I = 1,1 ng/ml, MMP-9 = 910 ng/ml, EPO = 30mU/ml, CRP = 5 mg/dl, TNF-a = 44 pg/ml and D-dimers = 1,3 ng/ml 2. Echo LAD = 4,9 cm, RVSP = 46 mm Hg, and normal EF and LVID 3. Restrictive or Congestive changes of respiratory function 4) decreased PO2 and increased alveolo-arterial oxygen difference [P(A-a)O2]= 38 mm Hg 5. Significant correlation of a) NT-ProBNP with Hcy (r = 0,630) b) LAD with RVSP (r = 410), LVID (r= 0,410 ), MMP-9 (r= - 0,570 ) c) RVSP with MMP-9 (r= -0,660 ) and finally d) Tr-I with EF (r = -0,430 ) 6. No correlations were found with Respiratory Function Tests and Blood Gasses.

Conclusions: Increased serum values of NT-ProBNP and significant correlation with resulted abnormal Biomarker levels, also correlated with each other, conclude that the predominant type of existing dyspnea could be consequent to inflammatory, latent ischemic dysfunction, thrombogenesis, cellular damage guided apoptosis and cardiovascular remodeling. The reported dyspnea of cardiac origin is leading and/or further strengthening preexisted thrombogenetic dyspnea and chronic pulmonary hypertention, having been due to COPD. Both, further worsen cardiovascular remodeling, presented as cardiac dysfunction or dyspnea and heart failure mainly with preserved systolic function. However, abnormal respiratory function indices and blood gases distinguish themselves as independent factors of pulmonary dyspnea.

Clinical implications; Further studies should be carried out to classify reported values, distinguishing cardiac from pulmonary dyspnea in COPD and coincident AF.

COI: None
EFFICACY AND SAFETY OF IVABRADIN IN PATIENTS WITH IDIOPATHIC DILATED CARDIOMYOPATHY

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The aim of the study was to assess efficacy and safety of ivabradin treatment in patients with idiopathic dilated cardiomyopathy complicated with congestive heart failure. Methods: We studied 30 patients (mean age 54 ± 3 years) with idiopathic dilated cardiomyopathy with a LV ejection fraction ≤35 %, sinus rhythm, and heart rate ≥70 beats/min despite optimal medical therapy for heart failure. Patients assigned to treatment with ivabradin (Coraxan, "Servier", France) (n=15) till a target dose of 15 mg/day or resting heart rate of 60 beats/min or placebo (n=15) in a double-blind randomized fashioned. Duration of the study was 6 months.

Results: At the end of the study there was significant and sustained reduction of heart rate at rest (From 89±13 beats/min to 75±11) without a significant change of blood pressure level. Ivabradin therapy resulted in a significant improvement in LV ejection fraction compared with the placebo group. Exercise capacity measured by treadmill time and by distance walked in 6 minutes improved with ivabradin treatment and this was reflected in daily life as lower Living with Heart Failure Questionnaire scores with treatment. No cardiovascular side effects were observed in any patients while taking ivabradine.

Conclusion: These data, taken collectively, indicate that ivabradin represents a new therapeutic approach for patients with dilated cardiomyopathy and chronic heart failure.
Background: The potential benefits and risks of at least 1-year dual antiplatelet therapy (DAPT) duration after drug-eluting stent (DES) implantation remain uncertain.

Methods and Results: Pubmed, the Cochrane Central Register of Controlled Trials, ClinicalTrials.gov databases were searched from database inception to December 2011 for randomized controlled trials that compared longer DAPT versus shorter DAPT duration after DES. Unpublished data were obtained from investigators. Trial-specific odds ratios (ORs) with 95% confidence interval (CI) were calculated and pooled using fixed-effects or random-effects model as appropriate. Data were independently extracted by 2 reviewers. Three randomized controlled trials comprising 5622 participants were included. Compared with patients receiving short-term therapy, participants receiving longer DAPT duration had a pooled OR of 1.26 (95% CI, 0.88 to 1.80; P=0.21, random-effects) for the primary outcome of cardiac death, myocardial infarction or stroke, OR of 1.29 (95% CI, 0.85 to 1.93; fixed-effects) for all-cause death, 1.23 (95% CI, 0.78 to 1.93; fixed-effects) for cardiac death, 0.91 (95% CI, 0.58 to 1.42; random-effects) for myocardial infarction, 1.93 (95% CI, 1.01 to 3.69; fixed-effects) for stroke and 2.51 (95% CI, 1.10 to 5.71, fixed-effects) for TIMI major bleeding. The number needed to treat for an additional harmful outcome was 217.6 for stroke and 243 for TIMI major bleeding.

Conclusions: This meta-analysis provides no evidence of benefits with longer DAPT duration as compared with a shorter course of therapy. It also reports significant harms with respect to major bleeding and stroke associated with prolonged DAPT use.
CHARACTERISTICS OF PATIENTS WITH POST PCI HYPER-RESPONSIVENESS TO CLOPIDOGREL

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Objectives: To characterize predictors of clopidogrel hyper-responsiveness using Accumetrix VerifyNow P2Y12 testing after percutaneous coronary intervention (PCI) in a real world setting.

Background: Hyper-responsiveness to clopidogrel [Platelet Reactivity Units (PRU) ≤ 30] has not been studied carefully. There is still debate whether hyper-responsiveness increases the incidence of bleeding. Characteristics of patients with hyper-responsiveness to clopidogrel post PCI is lacking.

Methods: 657 consecutive patients had PCI and platelet function testing after initial background aspirin and ≥ 600 mg of clopidogrel. A daily maintenance dose of 75 mg clopidogrel was administrated. Patients’ characteristics and presentation [Acute coronary syndromes (ACS) vs. non ACS] were compared between hyper-responders and non-hyper-responders.

Results: Of the 657 patients [411 (63%) ACS vs. 246 (37%) non-ACS] 46 (7%) were hyper-responders to clopidogrel. Comparison between the two groups is presented in table 1.

Figure 1: Comparison of patients characteristics between both groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hyper-responders N=46 (7%)</th>
<th>Non Hyper-responders N=611 (93%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62.9±11.3</td>
<td>66±12.4</td>
<td>0.04</td>
</tr>
<tr>
<td>Gender (Men)</td>
<td>23 (50%)</td>
<td>369 (60%)</td>
<td>0.2</td>
</tr>
<tr>
<td>Smokers</td>
<td>15 (33%)</td>
<td>154 (25%)</td>
<td>0.29</td>
</tr>
<tr>
<td>HTN</td>
<td>37 (80%)</td>
<td>495 (81%)</td>
<td>0.85</td>
</tr>
<tr>
<td>DM</td>
<td>16 (35%)</td>
<td>220 (36%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>35 (76%)</td>
<td>445 (73%)</td>
<td>0.73</td>
</tr>
<tr>
<td>Prior MI</td>
<td>17 (37%)</td>
<td>249 (41%)</td>
<td>0.64</td>
</tr>
<tr>
<td>Prior PCI</td>
<td>24 (52%)</td>
<td>241 (40%)</td>
<td>0.12</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>5 (11%)</td>
<td>93 (15%)</td>
<td>0.52</td>
</tr>
<tr>
<td>CK (U/L)</td>
<td>417.4±559</td>
<td>623.6±1030</td>
<td>0.18</td>
</tr>
<tr>
<td>Troponin I (ng/ml)</td>
<td>17±30</td>
<td>25.2±58.2</td>
<td>0.23</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>102.2±35.9</td>
<td>93.6±43.8</td>
<td>0.32</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>46.1±15.1</td>
<td>40.7±14.7</td>
<td>0.01</td>
</tr>
<tr>
<td>Hg (g/dl)</td>
<td>13.12±2.09</td>
<td>12.8±2.18</td>
<td>0.17</td>
</tr>
<tr>
<td>PLT (K/ul)</td>
<td>255.6±69.9</td>
<td>225.5±71.6</td>
<td>0.004</td>
</tr>
<tr>
<td>BUN (mg/dl)</td>
<td>16.7±11.7</td>
<td>20±12.3</td>
<td>0.04</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>0.9±0.38</td>
<td>1.23±1.31</td>
<td>0.05</td>
</tr>
</tbody>
</table>

HTN- Hypertension; DM- Diabetes Mellitus; MI- Myocardial infarction; PCI- Percutaneous coronary intervention; CABG- Coronary artery bypass graft; CK- Creatine kinase; LDL- Low-density lipoprotein; HDL- High-density lipoprotein; Hg- hemoglobin; PLT- platelets; BUN- blood urea nitrogen.

Conclusions: Clopidogrel hyper-responsiveness post PCI is observed in less than 10% of patients. Those patients are younger with higher HDL and lower creatinine and BUN. Further studies are needed to evaluate the bleeding risk of those patients who are more responsive to clopidogrel on one hand but are younger and have less renal insufficiency on the other hand.
CO-EXISTENCE OF HYPO-RESPONSIVENESS TO ASPIRIN AND CLOPIDOGREL IN EMERGENCY ROOM IN PATIENTS WITH CORONARY ARTERY STENTING

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Objective: This study was conducted to evaluate the co-existence of hypo-responsiveness to aspirin and clopidogrel in patients on dual anti-platelet regimen for coronary artery stenting, and to examine other potential factors associated with this relationship.

Background: Dual anti-platelet regimen has been shown to reduce the major adverse cardiovascular events (MACE) after percutaneous coronary interventions (PCI), which is believed to be due to the efficacy of anti-platelet drugs. However, the variability of efficacy of anti-platelet drugs can lead to pharmacodynamic failure, which may translate into clinical failure.

Methods: Hypo-responsiveness to clopidogrel and aspirin were evaluated in a cohort of 533 consecutive patients with history of percutaneous intervention (PCI). P2Y12 reaction units (PRU) were measured to evaluate inhibition of platelet aggregation with clopidogrel, and aspirin reaction units (ARU) were measured to evaluate the inhibition of platelet aggregation by aspirin. ARU were available for 349 patients.

Results: Among 349 patients prescribed both aspirin and clopidogrel, 59 (16.9%) were hypo-responsive to aspirin (ARU equal or more than 550) and 135 (38.7%) were hypo-responsive to clopidogrel (PRU equal or more than 230) by platelet function assay. Clopidogrel hypo-responsiveness was a significant predictor of aspirin hypo-responsiveness; unadjusted (OR=2.15, p=0.008) or adjusted (OR=2.30, p=0.007) for gender, age, race, type I diabetes, type II diabetes, hypertension, smoking, CRF, and obesity. No variable besides clopidogrel hypo-responsiveness was significantly associated (p<0.05) with aspirin hypo-responsiveness.

Conclusions: There is a high prevalence of the co-existence of aspirin and clopidogrel hypo-responsiveness in patients presenting with chest pain. This relationship persists whether or not controlling for other potential risk factors of aspirin hypo-responsiveness.
ANTIPLATELET DRUG RESISTANCE IN ASIAN POPULATION
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Clopidogrel is the commonly used P2 Y12 receptor antagonist used in the treatment of ischemic heart disease and stroke. Poor metabolizers treated with clopidogrel exhibit higher cardiovascular event rates. Asian population has been found to show higher resistance to clopidrogrel. Present study was undertaken to find the prevalence of clopidogrel resistance in patients undergoing coronary angioplasty. 100 consecutive patients who underwent coronary angioplasty for acute coronary syndrome were selected for the study. All patients had 300 mg Aspirin and 600 mg for clopidogrel as loading dose. 150 mg aspirin and 75 mg twice daily of clopidogrel were given as the maintenance dose. Verify Now point of care platelet function study were done 5 days after starting of clopidogrel. Aspirin resistance was defined as more 550 aspirin resistance units and Clopidogrel resistance is defined more than 213 platelets resistance units. 79 % were male subjects 21% were women. 43 % were diabetics. 25% patients were aspirin resistant and 36% were resistant to clopidogrel. 7% showed dual antiplatelet resistance. Clopidogrel resistance was more common in female (P value <0.023). Clopidogrel resistance was significantly more common than aspirin resistance in diabetic subjects. Conclusion: Aspirin and clopidogrel resistance are common in Asian population. This should be taken into account in selecting antiplatelet drugs in patients following acute myocardial infarction irrespective of the management strategy. It is surprising that correlation between aspirin / clopidogrel resistance, genetic polymorphism, and clinical data do not correlate to explain the long term benefits of drug therapy.
Objectives: The aim of this study was to compare the bleeding risk associated with the use of bivalirudin and eptifibatide during percutaneous coronary intervention (PCI).

Background: Cardiovascular mortality has improved with the use of novel anticoagulant and anti-platelet medications in patients undergoing PCI but the risk of bleeding remains high.

Methods and Results: This was a retrospective case cohort study conducted at a community hospital. 1027 patients were identified who underwent PCI between January 2008 to December 2010. The primary outcome was procedural and non-procedural site bleeding. Global Utilization of Streptokinase and t-PA for Occluded coronary arteries (GUSTO) bleeding criteria was used to categorize the bleeding complications into mild, moderate and severe. Out of a total of 1027 cases of PCI, bivalirudin was used in 660 cases and eptifibatide was used in 345 cases. 31 cases of bleeding complications (incidence of 3%) were identified, 1 patient was excluded for receiving both bivalirudin and eptifibatide, and therefore, 30 cases were used for analysis. Of these, 10 were in association with the use of bivalirudin and 20 were in association with eptifibatide (odds ratio of 0.25; 95% confidence interval of 0.11-0.54; p=0.0001). 70% of bleeding cases in the bivalirudin group were severe (GUSTO criteria) as compared to only 35% cases in the eptifibatide group. There was no mortality associated with bleeding complications in either group.

Conclusion: Bivalirudin is associated with significantly less bleeding complications with PCI as compared to eptifibatide. However, the bleeding complications associated with bivalirudin tended to be more severe.
OBJECTIVES: In this study we sought to compare the clinical outcomes of anticoagulant use in patients undergoing transradial percutaneous coronary interventions (PCI). Background: Previous data does not support “stacking” of anticoagulants with femoral cardiac catheterizations, but there is a paucity of data with respect to the use of multiple anticoagulants when using a radial arterial approach. Bleeding complications and transfusions are causes of worse outcomes in patients undergoing PCI.

Methods: 225 patients at a high volume university medical center undergoing radial artery PCI were retrospectively divided into three different groups based on anticoagulant use - unfractionated heparin, low molecular weight heparin (LMWH), and both. Cardiology fellows obtained access in greater than 90% of all patients.

Results: All-cause mortality, vascular complications, bleeding events within 72 hours, and transfusion rates (GUSTO moderate bleeding) were not significantly elevated in any of the three groups.

Conclusions: In this single center study, the concurrent use of multiple anticoagulants does not result in increased adverse outcomes in transradial PCI.
Objective: To evaluate the pathological and electrophysiological abnormalities caused by different ischemic insults.

Background: Myocardial infarct was classified based on pathological, clinical and prognostic differences. Coronary microembolization has been associated with valvular endocarditis, cardiomyopathy, mural thrombus, arrhythmias, hypertension, diabetes, systemic lupus erythematosus and sickle cell diseases.

Methods and Results: In swine (n=32), the tip of the catheter was placed in the LAD. The animals were subjected to different ischemic insults, namely 90min LAD occlusion/reperfusion, delivery of 80µm microemboli, the combination of the 2 insults and controls. Acute and evolving changes in electrophysiological were monitored using Holter monitor. Contrast enhanced MR imaging followed by histopathology was performed to define viable myocardium 3 days later and images were analyzed using semi-automatic threshold method. MR images showed different patterns of enhancements; namely hyperenhancement in large infarct, hypoenhancement in microvascular obstruction zone at the infarct core, moderately enhancement in patchy infarct at the infarct border, depending on the pathologies (Fig. 1). It provided the following estimations of the extent of myocardial damage in LAD occlusion/reperfusion group (12.4±0.8% LV mass), microembolized LAD (8.8±0.5%) and in the combined intervention (15.7±1.1%). These findings support the recently published MR data in 144 patients with a prior MI. The electrophysiological abnormalities (ventricular and supraventricular ectopic activities) were not specific to the enhancement pattern or infarct size.


Fig. 1. MRI (top) show enhanced myocardial damage (white arrows) and patterns in large infarct (left), patchy microinfarct (center) and the combination with hypoenhanced microvascular obstruction zone (black (right). ECG abnormalities caused by microemboli (bottom). Grey arrowheads=single and black= couplet. Black lines =bigeminy and grey lines=LV run.
IMPACT OF RENAL INSUFFICIENCY ON 30-DAY OUTCOMES IN PATIENTS WITH ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION TREATED WITH PRIMARY PERCUTANEOUS CORONARY INTERVENTION

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Background: The benefits of primary percutaneous coronary intervention (PCI) in patients with ST-segment elevation myocardial infarction (STEMI) and renal insufficiency (RI) remain uncertain.

Methods: We reviewed 809 consecutive STEMI patients treated with primary PCI with (221) and without RI (588). RI was defined as an estimated glomerular filtration rate <60 ml/min/1.73m2.

Results: The RI group had a higher percentage of prior myocardial infarction (18.6% vs. 10.0%, P=0.0010), prior stroke (7.7% vs. 4.3%, P=0.049), multivessel coronary disease (41.6% vs. 31.8%, P=0.0088), all-cause (4.5% vs. 1.4%, P=0.0065) and cardiac 30-day mortality rates (4.1% vs. 1.2%, P=0.0087). Successful reperfusion rates were similarly high in both groups (91.9% and 93.5%, P=0.40), despite the significantly higher proportion of patients with door-to-balloon times >90 min (18.1% vs. 6.3%, P<0.0001) in patients with RI. Successful compared to unsuccessful PCI decreased the all-cause 30-day mortality rates in both patients with (3.0% vs. 22.2%, P<0.0001) and without RI (0.9% vs. 7.9%, P=0.0003). When reperfusion was successful, the cardiac 30-day mortality rate was not significantly greater in patients with RI than in those without (2.5% vs. 0.7%, P=0.051). By multivariate analysis, unsuccessful reperfusion (odds ratio, 8.08; 95% confidence interval 2.69-24.3; P=0.0002) independently predicted all-cause 30-day mortality, whereas RI (odds ratio, 2.43; 95% confidence interval 0.85-6.97; P=0.098) and door-to-balloon time >90 min (odds ratio, 2.50; 95% confidence interval 0.77-8.19; P=0.13) did not.

Conclusions: Extensive pre-existing atherosclerosis characterizes patients with RI developing STEMI. Aggressive PCI improves prognosis in patients with RI, and short door-to-balloon time is an important parameter conditioning the prognosis.
INDICATIONS AND SURVIVAL OF 90 YEAR OLDS UNDERGOING CORONARY ANGIOGRAPHY

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2. Albany Medical College, Albany, NY, USA

Background: The Elderly are the fastest growing segment of western population. 1 in 5 US Citizen will be elderly by the year 2030. Nonagenarians (>90 year old) are projected to grow to 18 million by the year 2050. Cardiovascular disease (CVD) is the leading cause of morbidity, mortality and reduced quality of life in this group. Despite higher incidence of CVD, scientific evidence is not as good regarding interventional treatment of the nonagenarians.

Methods: Medical history and clinical presentation were prospectively collected on 147 consecutive patients ≥90 years old at our institution; a tertiary care referral center, between 1995 and 2011. End point was time to death after coronary angiography. Kaplan-Meier survival statistics were conducted. Survival was obtained by linkage to the Social Security Death Administration Death Master File.

Results: Mean age was 92 (90-97) years. 61% were female. 15% had EF < 30%, 36% procedures were performed emergently, 47% were urgent and 17% were elective, 8% had a previous CVA. ST elevation MI (STEMI) was the most common indication for coronary angiography followed by Non-STEMI. Figure 1. Median survival after coronary angiography was 2.8 (0.7-5.1) years. There were 28.2 deaths per 100 person years of follow-up. Figure 2.

Conclusions: In this study majority of nonagenarians undergoing coronary angiography were for emergent or urgent indications. When performed in carefully selected patients coronary angiography may help reduce morbidity and mortality. Further study is needed in this rapidly growing segment of the population to evaluate the utilization and impact of interventional treatments.
EARLY STRINGENT GLYCEMIC CONTROL IMPROVES REPERFUSION IN PATIENTS WITH ACUTE ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION

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Background: Hyperglycemia in patients with ST-segment elevation myocardial infarction (STEMI) has been associated with no reflow.

Purpose: We tried to assess whether early stringent in hospital control of hyperglycemia would improve reperfusion after thrombolysis.

Methods: We enrolled 54 consecutive patients with acute STEMI who had admission blood glucose more than or equal 200 mg/dL. Streptokinase was given within 6 hours from the onset of chest pain. Patients were randomized either to early intravenous insulin infusion (initiated before thrombolysis) and continued for 24 hours with a target blood glucose 140-180 mg/dL then conventional control till hospital discharge or conventional glycemic control from the start. The single worst lead electrocardiogram before and 90 minutes after thrombolysis was analyzed.

Results: There was no statistical difference between the 2 groups regarding age, gender, major risk factors, location of infarction, or onset of thrombolysis. Patients in the intervention arm had a lower mean blood glucose level in the first 90 minutes (151.00 ±21.52 mg/dL versus 252.66 ± 65.51 mg/dL, p=0.0001). We found that patients in the intervention arm had a higher percent ST-segment resolution (62.62 ± 24.72, versus 29.22 ± 29.20, p=0.0001).

Conclusion: Early control of hyperglycemia improves reperfusion after thrombolysis in patients with STEMI.
COMPARING OUTCOMES IN MYOCARDIAL INFARCTION (NSTEMI) EARLY VERSUS DELAYED LEFT HEART CATHETERIZATION (COMED TRIAL)

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Background: In patients with NSTEMI, the importance of early versus delayed coronary angiography remains uncertain. Prior research has shown that cardiac biomarkers peak level is a simple and effective way of indirectly measuring clinical outcomes and is correlated with extent of infarct size and degree of ventricular dysfunction. We assessed the hypothesis that there is no significant difference between early versus delayed invasive intervention in patients presenting with NSTEMI in terms of peak cardio-marker levels and length of hospitalization.

Methods: A retrospective case analysis of patients presenting with NSTEMI at a University hospital were divided into five groups based on the time period between admission to cath lab. The primary variables analyzed were infarct size as measured by peak biomarker level along with ventricular dysfunction and mortality. Secondary variables analyzed were length of hospital stay. Statistical analysis was done using Pearson Correlation Coefficient (PCC) between these variables.

Results: A total of 1590 patients were analyzed. We observed that coronary angiography was performed in 91% of patients (n=1444). Pearson Correlation Coefficient (PCC) was noted to be mildly negative in terms of correlation with biomarker elevation and timing of coronary angiogram (-0.083 with Trop I and -0.127 with CK-MB). PCC was mildly positive in terms of length of hospitalization (0.11).

Conclusion: We conclude that early intervention and delayed intervention did not differ greatly in terms of peak biomarker elevation and length of hospitalization. Also there was no significant difference in all-cause mortality and systolic dysfunction.
Primary PCI is the treatment of choice for the majority of patients presenting with myocardial infarction. In many instances, the choice of revascularization strategy is complicated by the presence of multivessel disease, especially in the presence of additional comorbidities, chronic total occlusions and, infrequently, hemodynamic or electrical instability. Although currently discouraged by guideline statements and expert consensus, a strategy of immediate full revascularization is sometimes considered as a means of improving prognosis in patients with multiple potential infarct arteries and an inconclusive ECG or shock, or even as a means of enhancing the patient’s experience or in an effort at cost containment. Alternatively, a strategy of culprit-only PCI may be favored in an effort to reduce potential harm, reduce contrast and radiation exposure or even to provide the opportunity to further gauge patient baseline and socioeconomic characteristics to better tailor additional therapies. This discussion will focus on available data to support an initial strategy of culprit-only intervention, followed by individualization of revascularization and medical therapy over the ensuing weeks.
Fractional flow reserve (FFR) has become an extremely valuable tool for assessing the hemodynamic significance of intermediate native coronary lesions in patients with stable coronary syndromes. The correlation between FFR and symptom severity and future major cardiovascular events (MACE) are examined in view of the FAME-2 study results. The scientific gaps, potential pitfalls and misconceptions related to emerging FFR indications (left main disease, bifurcation stenting, acute coronary syndromes, multi-vessel disease, peripheral and renal artery disease) are delineated. Described are the most important developments related to FFR in 2012: instantaneous wave free ratio and non-invasive CT angiography based FFR. Future research to support current and emerging invasive and non-invasive FFR use is suggested.
HIGH SENSITIVITY TROPONINS: A STEP FORWARD OR A UNREQUESTED COMPLICATION?

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Progressive improvement in the analytical sensitivity of troponin (cTn) assays has led to a more rapid diagnosis of AMI and improved risk stratification in patients with NSTE-ACS, several authors have found that hs-troponin allow a faster and more accurate diagnosis of myocardial infarction (AMI), allowing detection of almost all MI in the first 3 to 6 hours. However, at the same time, hs-troponin has introduced the problem of a lower diagnostic specificity. It is of remarkable importance to consider that cTn is not a specific marker of AMI, caused by myocardial ischemia, but is a specificity as marker of myocardial damage, that could be due to other mechanisms. Therefore, hs-Tn assays are able to detect very small increases in the biomarker concentration and may result “positive” in a wide range of non-ischemic clinical conditions, acute and chronic, cardiac and extra-cardiac, such as pericarditis, myocarditis, tachyarrhythmias, heart failure, pulmonary embolism, stroke and sepsis thus current guidelines recommend that for a diagnosis of AMI, it is necessary to observe a rise and fall of hs-Tn. Persistent, but without a rise and fall pattern, elevation of hs-Tn can be found in patients with stable coronary artery disease (chronic renal failure, chronic heart failure and severe left ventricular hypertrophy. Therefore, hsTn significantly increase the detection of AMI but require a careful evaluation of possible false positive cases.
Plaque disruption including plaque rupture and erosion is known as a major mechanism of ACS onset. The plaque prone to disrupt is called vulnerable plaque and is detected as yellow plaque by angioscopy. Yellow plaques have thin fibrous cap. Yellow plaques may include both plaques prone to rupture and those prone to erode. The number of yellow plaques in the coronary artery is associated with future risk of ACS event. CKD patients are known to have more yellow plaques than non-CKD patients. On the other hand, statin can reduce the yellow color of those plaques and stabilize them. Although ACS is known to occur by the thrombosis at the disrupted plaque, there are so many silent plaque disruptions detected in the coronary arteries. Therefore, plaque disruption does not always cause ACS and some missing factors may be necessary for the onset of ACS. High blood thrombogenicity and vasospasm are supposed one of those factors. Indeed, ACS patients have very high blood thrombogenicity. We think stenosis presented by plaque burden and luminal area may also be an important factor, which is supported by some recent reports. Then, the reduction of stenosis by stenting may reduce the risk of future ACS event even if the stenosis is not severe enough to cause myocardial ischemia. I will discuss on these mechanisms of ACS onset mainly from the viewpoint of angioscopy.
Background: The management of acute coronary syndromes (ACS) patients has undergone major changes during the last decade. These changes reflect the results of numerous controlled clinical trials that established the basis for evidence-based guidelines.

Aims: To evaluate trends in the characteristics, management and outcome of patients with ACS hospitalized in all 26 Intensive Cardiac Care Units (ICCU) / Cardiology departments operating in public hospitals in Israel, during the last decade.

Methods: Data were derived from 6 biennial nationwide prospective community-based two-month ACS Israeli Surveys (ACSIS) performed between 2000 and 2010.

Results: During this period, there was a 23% decline in the number of patients admitted with ACS that was more pronounced for STE (-38%) than for NSTE patients (-14%). The mean age of the patients (64 years) has not changed. The prevalence of risk factors and CV comorbidity increased. There has been an increasing use of evidence-based medications during hospital stay and at discharge, and the use of PCI with stent implantation.

Primary reperfusion rate increased (from 56% in 2000 to 72% in 2010), and the mode of reperfusion significantly changed in favor of primary PCI (from 18% in 2000 to 97% in 2010). D2B time declined from 75 min to 68 min, while pre-hospital delay has not changed.

A significant reduction in short- and long-term mortality was observed; with a reduction in 30-day mortality (from 8.5 to 4.1%, OR_{adj} = 0.44 (0.32-0.61), and in 1-year mortality (from 13.5% to 7.8%, OR_{adj} = 0.52 (0.42-0.65). In-hospital complications declined except major bleeding that increased. Length of hospital stay declined.

Conclusion: ACSIS demonstrates that high degree of implementation and adherence to recommended guidelines is associated with a continuous improvement in short- and long-term outcome of ACS patients in Israel. Nonetheless, more efforts are needed to further improve the outcome of ACS patients.
Despite standard-of-the-art reperfusion therapy, most patients with ST elevation myocardial infarction (STEMI) present significant myocardial necrosis, and many of them experience adverse left ventricular remodeling and adverse outcomes. Coadjuvant therapies able to limit necrosis in these patients by reducing reperfusion injury are thus of great potential clinical interest. Preclinical studies have produced a wealth of information demonstrating that the cyclic GMP (cGMP) - PKG signal pathway is depressed at the time of reperfusion, and that its pharmacological stimulation limits reperfusion injury and infarct size. Clinical studies have shown that this pharmacological approach is capable to limit infarct size in patients with STEMI undergoing reperfusion therapy. Moreover, recent data indicate that cGMP signaling may have an important role in the cardioprotection afforded by other therapeutic strategies that have been found also able to limit infarct size in these patients, including ischemic postconditioning and remote ischemic conditioning. This presentation analyzes recent advances in the understanding of the mechanisms of cGMP-mediated protection against reperfusion injury and new ways to exploit them to limit infarct size and improve the prognosis of patients with STEMI.
Several studies have shown significant reduction in bleeding and vascular complications with transradial percutaneous coronary intervention (PCI) compared to a transfemoral approach. More recently, data from RIVAL and RIFLE-STEACS studies have suggested a mortality benefit in favor of transradial approach for patients undergoing PCI for ST elevation myocardial infarction (STEMI). However, the transradial studies demonstrating these benefits were performed at high volume radial centres with expert transradial operators in a select group of patients. The translation of these benefits to a wider patient population undergoing primary PCI by low to intermediate volume operators remains unclear. Available evidence shows that the transradial PCI is associated with greater technical challenges compared to a transfemoral approach resulting in a higher procedural failure rate. In addition, the amount of contrast media and radiation exposure is higher for transradial PCI. In an era, where door to balloon times are publically reported and used as quality indicators for STEMI care, the appropriate choice for vascular access in primary PCI carries utmost importance. In this presentation, the challenges and difficulties encountered during primary PCI by transradial approach will be presented. In addition, strategies to overcome complications associated with transradial PCI with a focus on appropriate patient selection and advanced technical skills will be discussed. The presentation would share data that would help the interventional cardiologist to deliver the benefits of transradial primary PCI observed in large studies without added procedural complexity or adverse clinical events.
PROTECTIVE EFFECT OF TELMISARTAN AGAINST ENDOTHELIAL DYSFUNCTION AFTER CORONARY DRUG-ELUTING STENT IMPLANTATION IN HYPERTENSIVE PATIENTS

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Objectives: The aim of this prospective, randomized study was to evaluate the effects of telmisartan on endothelial function after coronary drug-eluting stent (DES) implantation in hypertensive patients, compared to a calcium channel blocker, amlodipine. Background: DES implantation impairs local endothelial function, which may be associated with future cardiovascular events. Telmisartan, which has unique proliferator-activated receptor-gamma mediated effects in addition to its renin-angiotensin system inhibition effects, has favorable effects on endothelial function.

Methods: Fifty-one hypertensive patients with coronary artery stenosis but without coronary artery spasm, treated with a sirolimus-eluting stent, were randomly assigned to either the telmisartan (25 cases) or amlodipine (26 cases) treatment group. At baseline and at 3 months after DES implantation, endothelium-dependent and –independent vasomotion were evaluated by quantitative coronary angiography under the condition of medication withdrawal. The mean luminal diameter of a 20-mm coronary segment, beginning 5 mm distal to the stent, was measured before and after infusion of intracoronary acetylcholine (ACh: 10⁻⁷ mol/L, 10⁻⁶ mol/L) and then again after infusion of nitroglycerin.

Results: Blood pressure was comparable between groups at baseline and after 3 months. Vasoconstriction after ACh infusion at 3 months (impaired endothelial function) was less pronounced in the telmisartan-group than in the amlodipine-group (p<0.0001), although there was no significant difference between the two groups before DES implantation. The response to nitroglycerin did not differ between groups before or at 3 months after DES implantation.

Conclusions: Telmisartan significantly ameliorated endothelial dysfunction after DES implantation in terms of vasoconstriction induced by ACh compared to amlodipine.
INCIDENT HEART FAILURE MORTALITY ACCORDING TO RACE AND SEX AMONG OLDER ADULTS FROM THE CARDIOVASCULAR HEALTH STUDY

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Background: Among patients with heart failure (HF), mortality is lower in women vs. men. However, it is unknown whether the survival advantage in women compared with men is present in both whites as well as African-Americans with HF.

Methods: We examined adults older than 65 years with incident HF after enrollment in the Cardiovascular Health Study (CHS), a prospective, population-based study of cardiovascular disease. Of the 5,888 CHS participants, 1264 developed new HF and were followed for 3 years. We categorized participants into four race-sex groups and used multivariate analysis to examine whether 3-year total and cardiovascular mortality differed in the four groups after adjusting for sociodemographic factors, comorbidities and treatment. We also tested for sex-race interaction for each outcome.

Results: Among participants with incident HF, the mortality rates after HF were lower in women compared with men (for white women, African-American women, African-American men and white men: total mortality 35.5, 33.6, 44.4, and 40.5 per 100 person years respectively and cardiovascular mortality 18.4, 19.5, 20.2, and 22.7 per 100 person years respectively). After adjusting for covariates, women had a 15-20 percent lower risk of total and cardiovascular mortality compared with men but there was no significant difference in outcome by race. The sex-race interaction for either outcome was not significant.

Conclusions: Among older adults with HF, women have significantly better survival than men irrespective of their race suggesting that sex-based survival differences may be more important than race-based differences.
FACTORS AFFECTING MINNESOTA LIVING WITH HEART FAILURE SCORE
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Background: Heart failure is one of the major medical problems in US. Minnesota Living with Heart Failure (MLHF) score is a very useful tool to assess prognosis in these patients. However, very little data is available about various comorbidities which can affect MLHF score.

Patients and methods: We evaluated 458 patients enrolled in HF clinic between 2007 to 2012 with a retrospective chart review. There were 267 male patients and 160 female patients with average age being 63.2 years. We studied the effect of various comorbidities on 6MWT. Data was analyzed by using SAS software.

Results: Depression adversely affected MLHF at 6 and 12 months. Advancing age also affected MLHF at 12 months. Patients’ creatinine, diabetes and albumin levels did not have a significant clinical effect on MLHF. We also studied correlation between MLHF, NYHA class and ejection fraction (EF) amongst various subgroups. MLHF and NYHA correlated very well. MLHF and EF correlated negatively at 12 months. These two factors correlated at 6 months as well for diabetic and depressed patients. Baseline lower 6 minute walk test (6MWT) predicted higher MLHF score at 6 and 12 months. This negative correlation reached statistical significance in all subsets of patients with diabetes, chronic kidney disease, depressed and diastolic dysfunction. BNP had negative correlation with MLHF but did not reach any statistical significance.

Conclusion: Before administering MLHF questionnaire, pre-existing conditions like depression, functional status, 6MWT and EF should be kept in mind as they may affect the score adversely.
MARKED ELEVATION OF B-TYPE NATRIURETIC PEPTIDE IN PATIENTS WITH HEART FAILURE AND PRESERVED EJECTION FRACTION
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Introduction: Patients presenting with heart failure and preserved ejection fraction (HFpEF) often have moderate elevations in B-type natriuretic peptide (BNP). Elevations of BNP greater than 1000 pg/ml are seen infrequently, but are associated with worse outcomes and may reflect a greater burden of cardiac or renal disease. The aim of this study was to examine the clinical and laboratory characteristics of a cohort of patients with HFpEF and markedly elevated BNP.

Methods: A retrospective examination of 421 inpatients at a university hospital admitted with a diagnosis of HFpEF was performed. Clinical and echocardiographic data in patients with levels of BNP below and above 1000 pg/ml were compared.

Results: Patients with HFpEF and BNP above 1000 pg/ml comprised 28% of the population. These patients were characterized by impaired renal function (CKD IV or V in 43% of patients) and greater use of anti-hypertensive medications. However, 31% of patients with BNP above 1000 pg/ml had normal renal function; these patients were significantly older, more frequently female, had lower use of anti-hypertensive medications, and tended to have lower ejection fractions. Conversely, patients with HFpEF and BNP less than 100 pg/ml were younger and had preserved renal function. No echocardiographic indices differentiated any BNP groups.

Conclusions: BNP greater than 1000 pg/ml is seen in almost 1/3 of patients hospitalized with HFpEF. This elevation of BNP often reflects impaired renal function, but can also be seen in older patients with preserved renal function but relatively impaired systolic function.
Background: Epicardial adipose tissue (EAT) has been found to be associated with cardiac diseases including coronary artery disease & atrial fibrillation. The relationship of EAT with diastolic function has not been studied well.

Methods: We evaluated 500 consecutive echocardiograms to calculate maximum EAT thickness (EATmax) in parasternal long axis on 2D echocardiography over the right ventricle to quantify EAT. Diastolic function was estimated using transmitral flow & mitral annular tissue doppler in patients with preserved left ventricular function.

Results: EATmax & diastolic function was available in 307 patients with preserved LV systolic function (EF>45%). Diastolic function was normal in 67 patients (group 0). 184 patients had grade I diastolic dysfunction (group 1), 47 patients had grade II diastolic dysfunction (group 2) & 9 patients had grade III/IV diastolic dysfunction (included in group 2). ANOVA demonstrated significant between the group differences in EATmax. Post hoc test using Bonferroni correction showed significant differences in EATmax between group 0(0.57+0.26 cm) & group 1(0.76+0.26 cm) p <0.001 & between group 0 & group 2(0.76+0.24 cm) p value<0.001. There was a significant difference in EATmax between group with normal diastolic function & abnormal diastolic function (p value<0.001). Multivariate logistic regression was performed to assess predictors of abnormal diastolic function using variables of age, gender, EATmax & EF. Only age & EATmax were found to be significant predictors (p value 0.000 & 0.036 respectively; R2= 0.708).

Conclusion: In patients with preserved systolic function, increased quantity of EAT as assessed by echocardiography predicts abnormal left ventricular diastolic function.
Background: With the push toward bundled-service payments and pay -for- performance by Medicare, there is an even higher need to identify patients with acute decompensated heart failure (ADHF) at high risk for 30-day readmission. The aim of this study was to identify independent predictors of 30-day readmission for patients admitted with ADHF.

Method: We performed a retrospective analysis of patients (age equal to or greater than 18), admitted with a diagnosis of ADHF from April, 2011 to April, 2012. Univariate and multivariate logistic regression models were used to determine independent risk factors of 30-day readmission. Covariates with a P<0.05 on univariate analysis were entered in to multivariate analysis. Data analysis was performed with SPSS 16.0.

Results: The study included 310 patients; 149 men and 161 women. The mean age was 81±12.8, length of stay 5±4.4 days, and ejection fraction 50±18.9%. Overall 30-day readmission rate for ADHF in the study population was 9.4%. From a multivariate logistic regression model (age, gender, ethnicity, ejection fraction, atrial fibrillation, diabetes, hypertension, coronary artery disease, creatinine, Brain natriuretic peptide, AICD, hyperlipidemia), only diabetes (adjusted OR 2.65, 95% CI (1.16-6.05)) and ejection fraction (adjusted OR 0.98 95% CI (0.96-0.99)) remained independently associated with 30-day readmission.

Conclusion: This hospital-based study shows that diabetes and low ejection fraction are independent predictors of 30-day readmission. Patients with diabetes and low ejection fraction may require closer follow-up to limit ADHF related readmission.
A META-ANALYSIS ON THE EFFECTS OF TOLVAPTAN IN PATIENTS WITH CHRONIC HEART FAILURE

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Background: Vasopressin levels are often elevated in heart failure patients and left ventricular dysfunction and this may contribute to the increase in systemic vascular resistance via stimulation of the V1a receptor. Among the recent novel therapies for heart failure are the vasopressin receptor antagonists. Tolvaptan is an oral, non-peptide, selective vasopressin V2-receptor antagonist that causes aquarexis by acting on the distal nephron to increase secretion of electrolyte-free water. This meta-analysis will test the hypothesis that Tolvaptan is beneficial and result in clinical improvement in the treatment of heart failure.

Methodology: Included in this study are randomized controlled trials (RCTs) which compared the efficacy of Tolvaptan (30mg daily) with a placebo. We obtained relevant publications from PubMed, Cochrane and Australasian Medical Index. Abstracted data were assessed from the five (5) included studies using the JADAD Quality Scale. Outcome measured is (1) change in body weight and (2) change in serum sodium from baseline within 24 hours of initiating treatment and at the end of follow-up. Treatment of data was done using the Review Manager 5 software version 5.1.7. Analysis of the mean difference was used as effect measure.

Results: In this meta-analysis, the total pooled patient population was 4,899 patients, the largest proportion of which was from the EVEREST study. There were 2,281 patients assigned to the tolvaptan group and 2,279 patients assigned to the placebo group. The outcome of the mean difference in body weight after 24 hours and at end of follow-up was -0.93 (95% CI: -1.12 to -0.74) and -1.34 (95% CI: -1.66 to -1.02) respectively. The outcome of the mean difference in serum sodium after 24 hours of treatment and at end of follow-up was 3.05 (95% CI: 1.85 to 4.25) and 2.25 (95% CI: 0.83 to 3.66) respectively.

Conclusion: This meta-analysis had demonstrated significant weight reduction and increase in serum sodium in patients with heart failure treated with tolvaptan during the first day and up to the end of follow-up treatment. These are important properties that are useful to the armamentarium for the treatment of heart failure. This may be translated to favorable clinical implications in medical practice.
FACTORS PREDICTING 6 MINUTE WALK TEST IN PATIENTS WITH STABLE HEART FAILURE

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Background: Nearly 5 million Americans are living with heart failure. 6 minute walk test (6MWT) is a very useful and validated tool to assess prognosis in heart failure patients. However, very little data is available about various comorbidities which can affect 6MWT in these patients.

Patients and methods: We evaluated 458 patients enrolled in our HF clinic from 2007 to 2012 with a retrospective chart review. There were 267 male patients and 160 female patients with average age being 63.2 years. We studied the effect of various comorbidities on 6MWT. Data was analyzed by a professional statistician using SAS.

Results: During 1 year follow up, higher BNP levels predicted lower 6MWT at all 3 points of time. However, the correlation was significant only at baseline. For male patients, this was significant at 0 and 6 months. Mean score of 6MWT was higher among patients with albumin less than 3 g/dL at baseline; however it was reversed at 6 month and 1 year compared to patients with albumin more than 3. 6MWT was significantly lower in patients with diabetes at baseline. At 6 months, using linear regression test, 6MWT was lower amongst patients with depression and diastolic dysfunction. At 1 year, using linear regression analysis, 6MWT was significantly lower only in depressed patients.

Conclusion: 6MWT is a useful tool in HF assessment. However, various factors can affect it including diabetes, depression, BNP levels and diastolic dysfunction at different points in time which should be adjusted accordingly.
PROTEINURIA AND RENAL DYSFUNCTION AS PREDICTORS OF DIASTOLIC DYSFUNCTION

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Background: Proteinuria as well as renal insufficiency are well-established risk factors for cardiovascular morbidity & mortality. Their role in diastolic dysfunction (DD) isn’t well defined.

Aim: To investigate the association of proteinuria & Renal dysfunction with DD independently of diabetes mellitus (DM) & hypertension (HTN) as comorbidities.

Methods: We retrospectively reviewed 2,224 medical records of patients receiving Echocardiograms at a University hospital between 2008 and 2012. We excluded patients with a diagnosis of both DM and HTN. The patients were divided into two groups according to presence or absence of DD. Patients were classified into normal (n=713, 32.06%) & those with DD (n=1,511, 67.94%), including Impaired Relaxation (IR, n=1,243, 55.89%), Pseudonormal (PN, n=208, 9.34%), and Restrictive pattern (Res, n=60, 2.70%).

Results: We found proteinuria is more frequent in patients with DD patients (18.8%) vs. those without DD (12.6%, p=0.0020). The presence of GFR at 3 cutoff points (60ml/min, 30ml/min, and 15ml/min) was associated with DD & was statistically significant (31.45% vs 14.95%, p<.0001, 10.17% vs 5.79, p=0.0014, and 5.81% vs 2.89%, p=0.0052, respectively). The multivariable analysis showed proteinuria & age were associated with presence of DD, controlling for sex, obesity & GFR <60 (OR: 1.833, 95%CI 1.19-2.83, p=0.0060 & OR: 1.061, 95%CI 1.05-1.07, p<.0001, respectively).

Conclusions: Proteinuria & decreased GFR are associated with presence of DD when HTN & DM were excluded.
Background: The heart is an endocrine organ and secretes natriuretic peptide in response to wall stress of the atrium and ventricle. B-type natriuretic peptide (BNP) or N-terminal proBNP (NT-proBNP) is used as a diagnostic test for congestive heart failure (CHF). In our hospital, BNP has been replaced with NT-proBNP due to its stability in circulating blood and hence may be a better marker.

Methods: NT-proBNP was performed in 200 patients presenting to the hospital with chest pain or shortness of breath (SOB). Of these, 141 patients had SOB as the presenting symptom. Diagnosis of CHF was objectively confirmed by chest x-ray. 36 patients were excluded due to renal insufficiency. NT-proBNP was considered abnormal if greater than 450 in patients younger than 50 or more than 900 in patients 50 and older.

Results: Among 105 patients presenting with SOB excluding renal insufficiency, 36 out of 83 patients (43.4%) with abnormal NT-proBNP were confirmed to have CHF while only 1 out of 22 (4.5%) with normal NT-proBNP had CHF (odds ratio 16.1, p=0.008). A multivariable logistic regression model was fitted which included age, gender, and overweight status (BMI more than 25) as covariates. Neither age nor gender were statistically significant predictors of CHF, while overweight status had an adjusted odds ratio (AOR) of 2.4 (p=0.051). The AOR for abnormal NT-proBNP was 11.9 (p=0.020).

Conclusion: NT-proBNP is a highly informative biomarker for diagnosis of CHF in patients presenting with SOB.
HYPERKALEMIA AMONG HOSPITALIZED PATIENTS WITH ACE INHIBITORS AND ANGIOTENSIN - II RECEPTOR BLOCKER THERAPY
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Background: Angiotensin-converting enzyme inhibitors (ACEi) and angiotensin receptor blockers (ARB) are used widely for management of hypertension, heart failure and coronary artery disease (CAD). However, their use is associated with significant hyperkalemia.

Objective: To determine risk factors associated with hyperkalemia amongst all hospitalized patients on ACEi or ARB therapy.

Methods: All patients older than 18 years on ACEi or ARB therapy presenting with hyperkalemia either at admission or during hospitalization were included in the study. Patients with end stage renal disease on dialysis were excluded.

Results: Of 409 patients with hyperkalemia, 131 (32%) were noted to be on ACEi or ARB. 73.2% patients had hyperkalemia at admission and 26.8 % developed hyperkalemia during hospitalization. Mean serum potassium was 5.8 +/- 0.62 mg/dl. Major co-morbidities associated with hyperkalemia were hypertension (76.3%), chronic kidney disease (CKD)(55.7 %), diabetes mellitus (DM) (45.8%), (CAD) (39.6%), and atrial fibrillation (23.6%). 56.4% patients had acute renal failure and 42.7 % had metabolic acidosis. Patients were on following drugs associated with hyperkalemia: beta-blockers (68.7%), aldactone (16.7 %), potassium supplements (13.7%), digoxin (10.6%), heparin (10%), non-steroidal anti-inflammatory drugs (NSAIDS) (6%), azole antifungals (4.5%) and trimethoprim (3.8%). Mean duration prior to resolution of hyperkalemia was 10.8 hours. Seven patients required hemodialysis and 10 patients died during hospitalization.

Conclusion: ACEi and ARB therapy poses significant challenge as the indications for their use (CAD, CKD, DM) also increase the risk of hyperkalemia. Close monitoring for hyperkalemia is prudent to prevent life-threatening hyperkalemia in hospitalized patients when above listed drugs are concomitantly used.
The A2b adenosine receptor (A2bAR) is expressed in various cell types and is an established regulator of inflammation. Macrophages are central to the development of high fat diet-induced tissue insulin insensitivity and glucose intolerance. However, much is still to be explored as to which genes grant macrophages this property. We found that A2bAR knockout (KO mice fed a high fat Western diet (HFD) develop hallmarks of insulin resistance in liver, fat and muscle, as well as impaired glucose clearance, compared to control mice under the same diet. The mechanisms involved include macrophage A2bAR-induced changes in inflammation, and in the levels of sterol response element binding protein-1 and insulin receptor-2, with consequent effects on lipid synthesis and insulin signaling. Generation and analysis if a transgenic mouse model expressing the A2bAR gene in macrophages on an otherwise A2bAR null background showed that macrophage A2bARs are critical for improving high fat diet-induced changes in lipid homeostasis and insulin signaling. Importantly, activation of the A2bAR in vivo with a specific agonist improves glucose homeostasis in control wild type mice fed with HFD, suggesting a therapeutic application.
SILENCING CLC-3 PREVENTS APOPTOSIS INDUCED BY PALMITATE IN PREADIPOCYTES THROUGH THE ER STRESS PATHWAY, A POTENTIAL LINK BETWEEN OBESITY AND INSULIN RESISTANCE

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Objective: ClC-3 chloride channel, plays an important role in the regulation of cell volume, proliferation and apoptosis. Preadipocytes of type 2 diabetes show a tendency to enhanced apoptosis. We hypothesized that there is a relation between ClC-3 and insulin resistance, and one underlying mechanism may be associated with the modulation of free fatty acid-induced preadipocyte apoptosis by ClC-3.

Methods: Type 2 diabetes mellitus (T2DM) models in ClC-3 KO mice and rats were induced by fed with high-sucrose-high-fat diet combined with a low dose of streptozocin. The cellular apoptosis was detected by Annexin V-PI staining.

Results: Compared with the wild-type T2DM models, ClC-3 knockout T2DM mice displayed an improvement in insulin resistance, as evidenced by significant decrease in homeostatic model assessment of insulin resistance (HOMA-IR). In T2DM rat models, we further found that ClC-3 protein in adipose tissue is increased, and was positively correlated to HOMA-IR, but was not the case in liver and skeletal muscle. We further found palmitate-induced preadipocyte apoptosis was parallel to a significant increase in the endogenous expression of ClC-3 protein. Transfection with ClC-3 siRNA decreased and overexpression of ClC-3 facilitated apoptosis, caspase-3 activation, and increased ratio of Bcl-2/Bax in palmitate-treated preadipocytes. ClC-3 affected apoptosis mainly through regulating ER stress signaling proteins, Grp78, CHOP, phosphorylation of PERK and eIF2 [alpha].

Conclusion: These data suggested that chloride channel ClC-3 can modulate palmitate-induced apoptosis in preadipocytes via the ER stress pathway. Silencing of ClC-3 may play an important role in adipose-related insulin resistance.
GLUCOSE-INSULIN-POTASSIUM IMPROVES CARDIAC PERFORMANCE VIA INHIBITING HEXOSAMINE BIOSYNTHESIS IN PATIENTS UNDERGOING CARDIOPULMONARY BYPASS

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Background: Cardiopulmonary bypass (CPB) may cause profound hyperglycemia, which are associated with increased flux through the hexosamine biosynthesis pathway and elevated O-linked attachment of N-acetyl-glucosamine (O-GlcNAc) levels. Although the beneficial effects of glucose-insulin-potassium (GIK) in CPB have been described, the underlying mechanisms remain still unknown. This study was designed to explore whether GIK infusion improve cardiac performance via inhibiting HBP in patients undergoing CPB.

Methods and Results: 616 patients undergoing mitral valve replacement were randomly divided into GIK group (n=293) and control group (n=323). The trial was double-blind and conducted at a single center. GIK was administered starting after induction of anesthesia and finishing 24 hours following release of the aortic cross clamp. There was no significant difference in cardiac index between GIK and control group at 1 h and 6 h after CPB, whereas GIK treatment significantly enhanced cardiac index at 12 h and 24 h after CPB (2.63 vs. 2.32, 2.71 vs. 2.53, L/m², both P<0.05). Compared with control group, the incidence of abnormal cardiac enzyme rise in patients such as creatine kinase (12% vs. 30% in control group, P<0.01) and lactate dehydrogenase (22% vs. 34% in control group, P<0.01) was significantly reduced in GIK group. Moreover, GIK increased myocardial Akt phosphorylation and decreased the expression of glutamine fructose-6-phosphate amidotransferase (hexosamine pathway rate-limiting enzyme) and O-Linked Glycosylation of selected protein bands.

Conclusions: Perioperative treatment with GIK significantly improved cardiac performance which was associated with decreased flux through the hexosamine biosynthetic pathway and decreased O-Linked glycosylation of protein.
DOES DIABETES CAUSE ATRIAL FIBRILLATION?

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Background: Few studies have established association between DM and Atrial Fibrillation. The purpose of our study was to identify risk factors including DM control that could independently be associated with development of AF.

Methods: For our retrospective case-control study, data on 6602 pts with DM, including demographics, glycated hemoglobin levels (HbA1c) was recorded. Cases of DM with new onset AF (Group A; n=150) were compared with controls (Group B; n=1038). Mean HbA1c levels and cholesterol levels were calculated and statistical significance was established using ANOVA.

Results: 1276 out of 6602 (19.3%) pts had treated DM but no other co-existing risk factors for AF. 238/1276 (18.6%) were diagnosed with AF, from which 88 (36.9%) had pre-existing AF. 150/238 (63.1%) cases (Group A) with DM, had been newly diagnosed with AF. Out of 150 cases (Group A), 110 were African-Americans (73.3%), 26 (17.3%) were Hispanics. Mean HbA1c level in Group A (cases) was 8.234% (SD 2.288, 95% CI 8.108–8.464). Mean HbA1c level in Group B (controls) was 7.586% (SD of 2.918, 7.164-7.904). Difference between the two means was 0.648 (p value = 0.0025).

Conclusion: Poorer control of diabetes was found in pts with new onset AF when compared to controls. The development of AF is likely to be multifactorial and while the exact mechanism remains elusive, there is emerging evidence on the correlation between AF and DM. While larger studies are needed to evaluate the pathogenesis, our data clearly points towards a trend showing a causative effect.
EPICARDIAL ADIPOSE TISSUE: PREDICTOR OF METABOLIC SYNDROME IN THE ELDERLY

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Background/Objectives: Clinical studies have suggested an association between epicardial adipose tissue (EAT) and metabolic syndrome (MetS). However, most studies have focused on a younger population (median age <50 yrs). Therefore, we sought to examine the relationship between EAT thickness (EAT-th) and MetS in an elderly population (median age >70 yrs) using echocardiography.

Methods: We searched our database for the presence of EAT in consecutive patients referred for echo. We excluded patients with prior cardiac surgery or pericardial disease. EAT-th was determined in the parasternal long-axis view as previously described. MetS was defined by NCEP ATPIII guidelines.

Results: EAT-th was measured in 88 patients (30% male; 73±10 yrs; BMI 30.5±8 kg/m2). Mean EAT-th was higher in patients with MetS (9.4±3.7 vs 7.5±2.8 mm, p 0.008). In univariate analysis, EAT-th correlated with MetS (r 0.33, p 0.001), HTN (r 0.21, p 0.02), DM (r 0.33, p 0.001); in multivariate analysis, HTN (r2 0.22, p 0.02) and DM (r2 0.35, p 0.0001) correlated with EAT-th. The AUC for EAT-th as a predictor of MetS was 0.67 (std err 0.06; 95% CI 0.54-0.79; p 0.01); an EAT-th cutoff of 7.6 mm yielded a sensitivity of 71% and specificity of 56% for detecting MetS. Each increase in EAT-th by 10 mm increased the risk for MetS fivefold (p 0.01).

Conclusion: Our study confirms the correlation between EAT-th and MetS risk factors in an elderly population. If found, EAT could suggest an underlying metabolic disorder, which we believe should prompt further investigation with potential clinical impact.
SYNERGISTIC RELATIONSHIP WITH THE RISK OF CARDIOVASCULAR EVENTS BETWEEN DIABETES AND AMBULATORY BLOOD PRESSURE

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Objectives: Progressively elevated blood pressure (BP) and diabetes (DM) are two documented prognostic markers of increased cardiovascular (CVD) risk. However, the relationship between ambulatory BP (ABPM) and DM as potential synergistic factors for enhanced CVD risk has been scarcely investigated.

Methods: A total of 3344 subjects (1718 men/1626 women), 52.6+/-14.5 years of age, 607 with type 2 DM, were prospectively studied throughout a 5.6-year median follow-up. At baseline and annually thereafter, ambulatory BP was monitored for 48h. The Cox proportional-hazard analysis was used to estimate hazard ratios (HR) for CVD events associated with the awake and asleep systolic/diastolic (SBP/DBP) BP means for participants with and without DM.

Results: The analyses documented the: (i) expected increased adjusted HR of CVD events associated with progressively elevated awake and asleep SBP/DBP means; (ii) significantly greater slope of increasing risk with progressively elevated SBP/DBP in patients with than without DM; and (iii) progressively and significantly greater differences in the adjusted HR of total CVD events between patients with and without DM for awake SBP/DBP means >130/75 mmHg and asleep SBP/DBP means >110/65 mmHg. Furthermore, there was a significant interaction between DM and both the awake and asleep SBP/DBP means for patients above these threshold values (P<0.023).

Conclusions: This prospective study documents a synergic relationship with CVD risk between DM and increasing BP above the threshold BP values indicated above and, thus, provides evidence to utilize different ambulatory BP diagnostic thresholds for diagnosis of hypertension in patients with and without DM.
GLOBAL LONGITUDINAL STRAIN IS ALTERED IN DIABETES MELLITUS PATIENTS WITH NORMAL EJECTION FRACTION, STRATIFIED BY BMI: A SPECKLE TRACKING ECHOCARDIOGRAPHY STUDY

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Background: Obesity, creating a left ventricular volumetric overload, can be responsible of further damage on ventricular function in diabetic patients.

Objective: Aim of this study was to demonstrate the effect of BMI on left ventricular function in diabetic patients (DP).

Methods: Seventy asymptomatic DP (mean age: 61 +/- 8 yrs; 40% F; HB1Ac: 7.2 +/- 0.8; duration DM: 10 +/- 9 yrs) and 13 healthy controls (HC) (41% F; mean age: 58.5 +/- 10.0 yrs; BMI: 22 +/- 1) were evaluated. Patients were stratified according to BMI (A: BMI < 25; B: > 25 - < 30; C: > 30 Kg/m²). All patients performed conventional 2D echocardiography. Global longitudinal strain (GLS) was obtained by Speckle tracking imaging method.

Results: The EF was similar in the three groups, while it was significantly higher in A compared to control group (HC: 58 +/- 4 vs 63 +/- 8 yrs. p=0.03). LVMass indexed for height was significantly higher in C in comparison with HC (44 +/- 7 g/m2.7 vs. 37 +/- 4.5 g/m2.7; p<0.01). The stroke volume index was significantly lower in C vs A (C: 35 +/- 7ml/m2; A: 43.5 +/- 7ml/m2; p=0.01). GLS was significantly lower in diabetics but the significance was reached between group C and HC (HC: 21 +/- 1.01%; C: 18 +/- 2.1%; p<0.006).

Conclusions: In diabetic patients Obesity plays an additive role in affecting left ventricular function and remodeling. Conventional echocardiographic methods are not useful tools in identifying subtle LV dysfunction respective to GLS evaluation by Speckle Tracking echocardiography.
BARIATRIC SURGERY VERSUS NON-SURGICAL TREATMENT FOR OBESITY: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Introduction: The overall effects of bariatric surgery compared to non-surgical treatment for obesity are unclear. We aimed at quantifying the effects of bariatric surgery compared to non-surgical treatment for obesity.

Methods: We searched Medline, Embase, and the Cochrane Library from their inception to December 2012. Eligible studies were randomized controlled trials (more than 1 year follow-up) which included individuals with a BMI greater 30 kg/m², compared current bariatric surgery techniques to non-surgical treatment, and reported on body weight, cardiovascular risk factors, quality of life, or adverse events. Two investigators independently abstracted data and assessed risk of bias.

Results: The meta-analysis included 7 studies with 508 individuals (mean BMI: 34 to 48 kg/m²). Individuals allocated to bariatric surgery lost more body weight (mean difference [MD] -25 kg, 95% CI -31 to -20 kg) compared to non-surgical treatment, had a higher remission rate of type 2 diabetes (relative risk 11.9, 95% CI 2.1 to 66.7) and metabolic syndrome, greater improvements in quality of life and reductions in drug use. Triglycerides decreased more (MD -0.5, 95% CI -0.7 to -0.3 mmol/L) and HDL-cholesterol increased more (MD 0.16, 95% CI 0.1 to 0.2 mmol/L). Changes in blood pressure, total cholesterol or LDL were not different. Serious adverse events after bariatric surgery were relatively rare.

Conclusions: Bariatric surgery improves body weight, cardiovascular risk factors, and quality of life more efficiently than non-surgical treatment. Results are limited because only 7 RCTs could be included and apply only to younger individuals with a BMI greater 35 kg/m².
LEVELS OF OXIDATIVE STRESS AND ANTI-OXIDANT STATUS IN DIABETES MELLITUS PATIENTS

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Objective: To see the oxidative status of Diabetes Mellitus (DM) patients as persistent hyperglycemia is known to produce more free radicals and decrease the level of antioxidant enzymes which are associated with the development of various complications.

Methodology: Patients with duration of DM >1 year without any end organ failure were recruited. Along with detail clinical history and relevant systemic examination, specific additional investigations done were glycosylated hemoglobin (HbA1c), oxidative stress indicators like plasma malondialdehyde (MDA) & protein carbonyl (PC) content and protective antioxidant sulphydryl content (SH).

Results: Preliminary analysis was done in 90 DM patients (recruitment is still ongoing) with mean age of 55.2 ± 9.8 yrs and 3.2 yrs of DM duration. HTN was present in 60 patients (66.6%). Out of 31 (34.4%) SH measured pts, 27 (87.1%) pts had low SH (<509 µmol/L). SH level was low in DM pts (389.9±122.9 µmol/L) when compared to 25 controls (539±156 µmol/L) which was statistically significant (p <0.001). There was negative correlation to SH and HbA1c (r value -0.2). Out of 57 (63.3%) MDA measured pts, 14 (24.6%) pts had elevated MDA value (>4.5nanomole/ml). All 12 (13.3 %) PC measured pts had elevated values (Normal <1.0nmol/mg) with mean of 2.3±1.2. nmol/mg. PC levels were high when compared to controls which was statistically significant (p=0.01) but not MDA (p = 0.5).

Conclusion: Increased levels of PC and decreased levels of SH in DM may suggest increased levels of oxidative stress and decreased antioxidant capacity.
INDIVIDUALS WITH CORONARY ARTERY DISEASE AT A YOUNG AGE AND FEATURES OF THE METABOLIC SYNDROME HAVE AN INCREASED PROTHROMBOTIC POTENTIAL

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Background: The relation between coagulation and atherosclerosis has been extensively described. However, most literature on this issue shows conflicting results. It is known that obesity and hereby induced metabolic syndrome (MS), a risk factor for CAD, are related to a higher incidence of thrombo-embolic events. We hypothesized that individuals with premature CAD and features of MS have an increased prothrombotic potential.

Methods: We investigated 118 patients with premature CAD (before the age of 51 in men and 56 in women) and 50 healthy first-degree relatives and measured endogenous thrombin potential (ETP). Furthermore, we studied differences in ETP in these patients, with and without MS features, based on the NCEP guidelines. We adjusted our analysis for age, sex, smoking and oral contraceptives use.

Results: The adjusted general linear model (GLM) showed a positive association between the peak thrombin levels and the presence of premature CAD (B = 9.40; p<0.05). Furthermore, we were able to show, that CAD patients with MS features have increased ETP levels, both in comparison with healthy first degree relatives (B = 18.18; p<0.05) and with CAD patients without MS (B = 10.47; p<0.05). No difference could be observed between CAD patients without MS and healthy first-degree relatives.

Conclusion: This study shows that only individuals with premature CAD and MS features have an increased prothrombotic state.
PREVALENCE OF PERIPHERAL ARTERIAL DISEASE (PAD) BY MEANS OF ABI IN ASYMPTOMATIC TYPE II NORTH INDIAN DIABETICS AND ITS CORRELATION WITH CARDIOVASCULAR RISK MARKERS

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Aims: To evaluate the prevalence of PAD by means of ankle-brachial index (ABI) in T2DM patients.-stage I grade0 category0 (Fontaine’s stages & Rutherford categories classification of PAD) in North Indian population.

Methods: Between winter 2009 & summer 2012, 2778 asymptomatic (no complaints pertaining to PAD) Type II Diabetes patients were enrolled. Blood pressure, BMI, baPWV, HbA1c, Cholesterol, HDL, LDL & Triglycerides values were analysed. The ABI was measured with VP-2000/1000-Colin Corporation, hyayashi komaki, Japan. PAD was considered when ABI measured was <0.9 in either leg.

Results: We studied 2778 patients (1681 men and 1097 women; mean age 50.4±7.0 years; mean duration of diabetes 7.8±5.9 years). The prevalence of PAD was 14.2% with men having a slightly higher prevalence (14.9%), as compared to women (13.2%). ABI was found to be significantly correlated with age (r=0.15), duration of diabetes (r=0.09), PWV (r=0.13 for left and r=0.12 for right) and DBP (r=0.13). We did not find a significant correlation between measures of obesity (WHR) and PAD.

Conclusion: Using ABI, we found prevalence of PAD in 14.2% of type 2 diabetics which is comparable to western population. Risk factors significantly associated with PAD were - age, duration of diabetes, PWV and DBP. Considering ABI as a significant future CV risk marker, routine screening of diabetic population is advisable for future CV risk prevention.
CURCUMIN TRINICOTINATE REGULATE THE PROLIFERATION OF VSMCS VIA CAVEOLIN-1/ERK1/2 SIGNALING PATHWAY

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Objective: To detect the effects of curcumin trinicotinate (CurTn) on the VSMCs proliferation via Caveolin-1/ERK1/2 signaling pathway in vitro.

Background: The anomalous proliferation of VSMCs have been identified as a incentive that plays a predominant role in atherosclerosis formation. Thus, the discovery of a new and effective medicine that can suppress the proliferation of VSMCs is conducive to postpone the atherosclerosis.

Methods: CurTn, which purity is over 95%, synthesis by esterification of curcumin with niacin in our laboratory. VSMCs were cultured in DMEM medium with or without 10%NCS. SiRNA of caveolin-1 and PD98059 were adopt to inhibit the activation of caveolin-1 and ERK respectively. MTT assay was used to detect the viability of VSMCs. FCM was employed to observe the distribution of cell cycle. Western blotting was applied to analyze the expression of PCNA, Caveolin-1, ERK1/2 and CyclinD1.

Results: There were dose-dependent inhibitory effects on VSMC in five different concentrations of CurTn. This inhibitory effect reached plateau at 30μmol/L. CurTn increased the distribution proportion of cell cycle G0/G1 phase and decreased the percentage of cell cycle S phase. At the same time, CurTn elevated the expression of Caveolin-1 protein, and down regulated the expression of p-ERK1/2 and CyclinD1 protein, which is weakened by si-RNA of Caveolin-1 and inhibitor of ERK.

Conclusions: CurTn can inhibit the proliferation of VSMC through G1 phase cell cycle arrest. This effect may be result from the Caveolin-1/ERK1/2 signaling pathway. This work is supported by China National Natural Science Foundation (No. 30971170~No. 81173047,) and the construct program of the key discipline in hunan province.
ASSOCIATION BETWEEN CHRONIC PERIODONTITIS AND CORONARY ARTERY DISEASE

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Purpose: Cardiovascular and periodontal diseases are common inflammatory conditions in the general population. Inflammation plays a continuous role in the development, instability and rupture of atheromatous plaques, in atherosclerosis disease. Our aim is to evaluate the association between chronic periodontitis (CP) and coronary artery disease (CAD).

Methods: We carried a cross-sectional controlled study including 206 patients older than 18 years of age that had at least 6 natural teeth and had undergone coronary cineangiography. Patients were assigned to group I, II or III according to the presence of lesions in 1, 2 or 3 vessels. After that, a periodontist blinded to group assignments determined the presence of CP, which was defined according to the mean clinical attachment loss of teeth (CAL) and gingival inflammatory signs, as suggested by Armitage. They were classified as having gingivitis or initial, moderate or severe periodontitis. The Pearson chi-square, Student t, Mann-Whitney, and Fisher exact tests were used to analyze data statistically.

Results: Most patients were white (92%) men (60.2%), and their mean age was 60.3 years (64.6%). CAD was found in 126 (61.2%) of the sample (group I:17%; II:18.4%; III:42.1%), whereas CP was found in 99% of the patients (gingivitis:0.5%; initial CP:0.5%; moderate CP:24.3%; severe CP:73.8%). The sample was stratified according to mean Pobing Pocket Depth (2.61mm±0.72) and CAL (4.40mm±1.29) because of CP homogeneity. CAD and CP severity were statistically associated (p=0.0478). The association between CAD extension and CP severity was also significant (p=0.0296). Conclusions: CP is associated with CAD.
ATRIAL FIBRILLATION AND LA-SIZE ARE INDEPENDENTLY CORRELATED WITH THE AMOUNT OF PERICARDIAL ADIPOSE TISSUE

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Introduction: Pericardial adipose tissue (PAT) as visceral fat depot surrounding the heart serves as an endocrine active organ and is associated with inflammation. There is also growing evidence that atrial fibrillation (AF) is linked to inflammation, which can be a promoter of left atrial remodelling. The aim of this study was to evaluate a potential correlation of PAT to AF and left atrial remodelling represented by LA-size.

Methods: PAT was detected in 1095 patients (557 men, mean age 62.5±11.4) who underwent coronary artery calcium scanning for coronary risk stratification. LA-size was determined by two independent readers. Patients were subdivided in patients without AF and patients with paroxysmal and persistent AF.

Results: 289 patients showed AF. In a multivariate analysis PAT was a risk factor for AF (OR 1.53; 95% CI: 1.16 to 2.01, p = 0.003), independent from age, BMI, arterial hypertension. In patients with incremental AF burden (persistent AF) the odds ratio further increased, OR: 2.77; 95% CI: 1.83 to 4.26, p < 0.001. Multivariate analysis revealed also a significant association of LA-size with PAT (regression coefficient: 0.15 with 95% CI: 0.10 to 0.20, p < 0.001).

Conclusion: PAT is associated with AF, in particular persistent AF and LA-size. Our data suggest that PAT could be an independent risk factor for the development of AF and LA remodelling.
DOES THE EXTENT OF CALCIFIED PLAQUE AFFECT THE PERFORMANCE OF COMPUTED TOMOGRAPHIC CORONARY ANGIOGRAPHY?

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Objectives: Our study investigated the effect of calcified plaque on the diagnostic accuracy of 64 slice Coronary CT Angiography (CCTA).

Background: Diagnosis of coronary artery stenosis by CCTA in patients with extensive coronary artery calcium (CAC) has been challenging and only a few studies have specifically investigated this issue.

Methods: We included 427 patients who underwent both CCTA and invasive coronary angiography within 6 months for workup of anginal symptoms, at two Los Angeles medical centers from September 2006 to May 2010 or as part of the multicenter ACCURACY trial. The accuracy of 64 slice CCTA to detect coronary artery stenosis with invasive coronary angiography as the reference were calculated in different groups based on CAC.

Results: 97 patients had a CAC score of 0 (mean age 51.8), 97 had a CAC score of 1-100 (mean age 58), 98 had a CAC score of 101-400 (mean age 58) and 135 had a CAC score >400 (mean age 64). On a patient based model, the sensitivity and specificity in the four groups to detect 50% coronary artery stenosis were 100, 96.2, 91.1, 98.9 and 97.7, 87, 71.4, 58.7 % respectively.

Conclusion: The sensitivity of 64 slice CCTA remains preserved through all levels of CAC, however the specificity decreases with increased CAC due to blooming and beam hardening artifact. In patients with no calcification, CCTA rules out significant CAD with a NPV of 100%, largely obviating the need for any further testing.
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RISK STRATIFICATION WITH CALCIUM SCORING IN PATIENTS WITH SEVERE CHRONIC KIDNEY DISEASE

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Background: Coronary calcium is a well-established risk factor for future cardiovascular events. This study evaluates the predictive value of the calcium score (CS) in patients with severe chronic kidney disease (CKD).

Methods: 393 patients with severe CKD (eGFR <30ml/min/1.73m²; Group I) but without known cardiovascular disease (mean age: 63.0±18.9 years, 271 men) were examined. CS (Agatston method) was determined by 64-slice CT and compared to CS in a second group of 701 patients (mean age: 61.4±16.3 years, 453 men) without CKD (Group II). Major cardiovascular events (MACE: myocardial infarction and sudden cardiac death) in both groups were documented during follow-up of 6.2±1.3 years. The risk of MACE depending on CS was calculated.

Results: Mean CS in Group I was significantly higher compared to Group II (207±190 vs. 121±169, p=0.007). 71 (18.0%) patients in Group I had zero CS compared to 201 (28.7%) in Group II (p = 0.001). In Group I, 69 (17.6%) patients suffered from MACE, whereas in Group II 85 (12.1%) events occurred. Based on the CS in Group I odds ratio (OR) for MACE adjusted for conventional risk factors was 8.2 (95% CI: 7.1-13.7) for CS=400 and 15.5 (95% CI: 10.6-21.0) for CS=1000 without significant difference compared to OR in Group II: 8.6 (95% CI: 7.1-14.3) and 14.9 (95% CI: 9.7-19.1), respectively. No MACE was observed in patients with zero CS.

Conclusion: OR for MACE depending on CS was not different in patients with/without renal function impairment indicating that CS can be used for risk stratification independently.
Objective: To demonstrate the association between left ventricular (LV) thrombus and apical myocardial infarction using delayed enhancement MRI (DE-MRI).

Background: Patients with LV dysfunction bodes worsened prognosis from heart failure and sudden cardiac death. LV thrombus is further sequel that causes devastating conditions like systemic emboli. Cardiac magnetic resonance (CMR) has a promising role in clear delineation of thrombus and unique property in evaluation of infarct myocardium, a potential predictor of thrombus, especially apical infarction.

Methods: Patients with LV dysfunction, defined as LV ejection fraction (LVEF) <50%, referring for CMR were consecutively enrolled. The presence of LV thrombus was diagnosed by cine and DE-MRI techniques. Potential predictors including baseline characteristics, LV functional parameters, and infarct myocardium, were independently collected. The correlation between LV thrombus and these parameters was analyzed.

Results: A total of 500 patients (mean age 64.9±13.3 years, 68.4% male) were enrolled with mean LVEF 31.9±11.9%. LV thrombus was determined in 4.2%. There were significant positive association between LV thrombus and degree of dysfunctioning myocardial segments and extent of total myocardial scar and apical scar. Further, an inverse relationship with LVEF was significantly established. Using multiple logistic regression analysis, only apical scar remained an independent determinant (p<0.001).

Conclusions: This is the first to demonstrate apical myocardial scar as an independent predictor of LV thrombus in patients with cardiomyopathy. Cardiac MRI is a unique technique that has the highest accuracy in determination of apical scar. The presence of extensive apical myocardial scar warrants additional anticoagulant therapy warrants further investigation.
COMPARISON OF DIAGNOSTIC ACCURACY OF MULTISLICE CT ANGIOGRAPHY WITH CONVENTIONAL CORONARY ANGIOGRAPHY IN BYPASS GRAFT STENOSIS AFTER CORONARY ARTERY BYPASS GRAFT SURGERY

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Background: Conventional coronary angiography is the gold standard technique for evaluation of coronary artery anatomy. Multislice CT angiography is a new imaging technique for evaluating coronary arteries.

Objectives: Because the accuracy of CT angiography rather than conventional coronary angiography among bypass graft has not been studied enough we wanted to evaluate it.

Methods: This study was performed in Imam Khomeni Hospital of Ahvaz from 2007 to 2012. 143 arterial and venous grafts were assessed by CT angiography and conventional angiography from 53 patients with history of coronary artery bypass graft (CABG) surgery. All data were analyzed by SPSS version 17.

Results: Mean ages of men were 59.4±10 and women were 59.9±8 year. 34% was female and 66% was male. Sensitivity, specificity, positive and negative predictive value and diagnostic accuracy in CT angiography were 95%,100%,100%,86%,96% in proximal and 100%,100%,100%,100% in middle part and 71%, 96%,93%,83%,86% in distal part of arterial and vein graft bypasses.

Conclusion: Diagnostic accuracy of CT angiography in comparison with conventional coronary angiography may be good enough to be used in some selected cases with history of CABG. Although the best result was shown in the middle part of bypass grafts.
Objectives: To determine if single site maximum stenosis of coronary artery disease (CADmax) on coronary computed tomographic angiography (CTA) predicts coronary plaque burden measured by calcium score (CaS), CTA plaque burden score (PBS) or by counting the number of main coronary arteries with disease.

Background: The COURAGE trial showed coronary plaque burden and maximum coronary stenosis predicts adverse coronary events. CTA enables assessment of CAD stenosis and plaque burden but the relationship between these parameters has not been previously described.

Methods: We retrospectively reviewed the CTA of 147 subjects (mean age 58.2±10.6, 74% male) referred for screening. Prior analysis included CaS, PBS, and a count of the number of main coronary arteries (to a maximum of 4: left main, left anterior descending, right coronary artery, and circumflex artery) with any evidence of disease (0count) or greater than 50% stenosis (50count). PBS was obtained by summing CAD extent and severity from standard CTA segments. After review of all measurements for each patient, CADmax was categorized as 0%, 1-49%, 50-74% and 75-100% stenosis.

Results: CADmax was >0% in 79 (53%) patients. Multiple pair wise comparisons following analysis of variance comparison demonstrated an association between CADmax and CaS, PBS, 50count, and 0count. From regression, these relationships remained significant after adjustment for age and gender.

Conclusions: Single site maximum coronary stenosis on CTA predicts the total coronary burden independent of age and gender. This relationship held true regardless of the modality (CaS, PBS, 0count, 50count) used to assess coronary plaque burden.
THE INCREMENTAL PROGNOSTIC VALUE OF A NEGATIVE CARDIAC CT SCAN ON MAJOR ADVERSE CARDIAC OUTCOMES: A SAUDI EXPERIENCE

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Background: With the current advancements in the multiple imaging modalities, non-invasive cardiac testing has become the initial golden standard investigation for CAD assessment in the patients with low-to-intermediate risk category. To our knowledge there are no data available in the Kingdom of Saudi Arabia, especially in the Eastern Province, looking at the rates of major cardiac events following a negative scan. Methods: This was a retrospective observational registry performed in a single center in Saudi Arabia. The data was collected from the cardiac CT database identifying all the scans reported with non-obstructive CAD between January 2010 and December 2012. The patients’ charts were reviewed looking for any major cardiac events. Median follow up was 12.7 months.

Results: 143 patients identified with non-obstructive CAD in the pre-specified time frame. 62.9% were male. Mean age was 46.7±12 years. 23% were diabetic, 34.2% were hypertensive, 32.9% were dyslipidemic, 8.2% had a positive family history of IHD, 12.6% were smokers, and 4.9% had prior history of CAD. 1.4% of the total patient populations had prior CABG. 2.8% of the patients had prior PCI. There were 2 patients that were admitted for a diagnosis of ACS and went on to have further cardiac workup. One of those two patients underwent PCI. The other patient had non-obstructive CAD on angiography. These are consistent with a 0.7% risk of cardiac events following a negative scan.

Conclusion: The above findings demonstrate that the risk of major cardiac events after a negative cardiac CT scan is low and is in keeping with the international statistics available.
OPTIMIZATION OF LIVER IRON LOAD ASSESSMENT BY PIXEL-BASED T2* MRI IN THALASSEMIC PATIENTS

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Background: Iron over load is a major problem of treatment in patients with thalassemia. The accuracy of iron load estimation may suffer from the methodology of T2* measurement to investigate the precision of different approaches of T2* measurement in order to improve assessment of liver iron load.

Methods: 32 â– thalasemic patients (18 male) with the mean age of 20.0±6.5, were involved in this study. A multi-echo fast gradient echo technique on a 1.5T MRI system was used to measure liver iron over load. The T2* map of liver was reconstructed on a pixel-by-pixel basis. The T2* map and MRI image were utilized to determine accurate location of region of interest (ROI). The mean of T2* were computed from the ROIs. The reproducibility of calculated T2* values in two methods was obtained. Moreover, the mean of the pixel’s T2* was calculated in the entire liver parenchyma of one slice. The T2* value of entire slice was compared with the ROI approach.

Results: In the ROI based method, the CoV for the intra-observer reproducibility was 8.5% and for the inter-observer was 9.78%. In the pixel based method, the CoVs for intra-observer and inter-observer reproducibility were 2.79% and 3.91%. There was an acceptable correlation (r=0.96) between the T2* values calculated by the ROI and the entire slice.

Conclusions: The pixel-based approach is more precise to determine the appropriate placement of the ROI. The assessment of T2* in the entire slice reduces the user-based errors significantly.
IMPROVING THE COST EFFECTIVENESS OF CHEST PAIN CENTERS

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Background: Chest Pain Centers have the expressed goal of facilitating the rapid diagnosis and management of patients presenting with chest pain in a cost effective manner. We postulated that using nuclear stress tests to risk stratify all such patients was not cost effective.

Study population: Patients admitted to the Chest Pain Center for observation for evaluation of chest pain and who had subsequent myocardial perfusion imaging (MPI) within twenty-four hours at University of Pittsburgh Medical Center/St. Margaret were included in the study.

Methods: MPI in conjunction with stress testing was performed on a total of 301 patients admitted to observation status in the Chest Pain Center.

Results: 15 patients (5\%) were found to have an abnormal MPI. The very low rate of positive myocardial perfusion imaging (MPI) in patients admitted to the UPMC/St. Margaret Observation Unit in the Chest Pain Center is indicative of a very low risk population with a very low pre-test probability of coronary artery disease.

Conclusion: Recent recommendations of the American Heart Association and the American College of Cardiology have stressed the importance of applying appropriate use criteria (AUC) in the selection of patients for nuclear stress testing. Clearly utilizing the test for patients with a five percent rate of positivity is not cost efficient and indicates a failure to apply these criteria in the Chest Pain Center at our institution.
TO EVALUATE WHETHER A MILD, ISOLATED INFERIOR WALL DEFECT ON MYOCARDIAL PERFUSION IMAGING WITH OTHERWISE NORMAL CORONARIES ON A LEFT HEART CATHETERIZATION IS ASSOCIATED WITH A NON-DOMINANT RIGHT CORONARY ARTERY

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Objective: We hypothesize that a false positive mild inferior wall perfusion defect on a myocardial perfusion scan (MPS) may be associated with a non-dominant RCA (NDRCA).

Method: Our institute performs MPS using either treadmill exercise or regadenoson (Lexiscan). A 1-day rest/stress gated SPECT single isotope (99M Technetium Myoview) imaging protocol is utilized. We evaluated a total of 1271 MPS done between Feb 2012 and July 2012. Out of these, 187 had an abnormal MPS involving the inferior wall. From these 187, coronary angiography was performed on a total of 149 patients. 88 patients (47%) were found to have a mild, isolated inferior wall defect (either fixed or reversible). The other 61 patients were used as the control group.

Results: In the patients with a false positive mild inferior defect on MPS, a NDRCA was seen in 3 (3.4%) patients. None of the patients in the control group had a NDRCA with otherwise normal coronaries. The prevalence of a NDRCA with otherwise normal coronaries was more frequent in the study group, however this association was not significant (p=0.203).

Conclusion: Although we observed an increased prevalence of a NDRCA in patients with a false positive mild inferior wall perfusion defect on MPS, this association was not significant (p=0.203) when compared to the control group. Our study may have been underpowered and a larger prospective evaluation may be warranted to evaluate this interesting finding.
Primary prevention of coronary artery disease / risk factors for atherothrombotic disease

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SEDENTARISM AS A STRESS GENERATOR IN A YOUNG POPULATION OF CAMPINAS, SP -BRAZIL


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Objective: To evaluate the repercussion of sedentary habits in the lifestyle of children and adolescents, 7 to 18 years old, both sexes, from public schools of the city of Campinas, Brasil.

Methods: A cross-sectional epidemiological study with sampling from a school population pool was carried out. Eleven schools were randomly selected in central and peripheral city areas. The assessment protocol comprised a structured questionnaire, anthropometry, and a non fasting lipid profile. In 2010, 4699 students (47.14% of the male sex; mean age, 11.07±2.9 years) were evaluated.

Results: Reports showed that 67.25% of the children that practiced outside school physical activities did not present weight excess. Overweight (>+1SD ) and obesity (>+2SD ) prevalence rates were 15.7% and 16.0%, respectively. Sedentary habits (television, videogames and computers) corresponded to 3.29 hours daily. Low and moderate time for interaction with electronic devices (television, computers and video games) was up to 3.5 hours daily and moderate, intense and exaggerated was considered for more than 4 hours daily. Children that spent more time in front of screens also report having significant stress in the home environment (p<0.0001). A significant correlation between time spent in front of screens and stress in school was also true. (p<0.0001).

Conclusion: Physical activity is associated to a healthy life style in a young population, in opposition to sedentary habits generating stress and weight gain. Interventions are required to improve physical activities and reverse the unfavorable tendency of future cardiovascular risk and potential chronic degenerative pathologies in the adult population.
ANTIDEPRESSANT USE AND RISK OF CORONARY HEART DISEASE: A META-ANALYSIS

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Objectives: To perform a meta-analysis to determine whether antidepressants are associated with coronary heart disease risk among subjects without history of coronary heart disease.

Background: Antidepressants are among the most frequently prescribed drugs in the world, but their association with coronary heart disease has not been fully evaluated. Methods: A search of Medline, EMBASE, and the Cochrane Library between January 1, 1995 and January 1, 2013 was performed. Three authors reviewed independently and selected eligible observational studies, based on predetermined selection criteria. Relative risk (RR), and confidence intervals (CIs) were calculated using random-effects or fixed-effects models.

Results: 16 observational studies (6 case-control studies and 12 prospective cohort studies) published between 1995 and 2013 were included in the final analysis. There was no association between SSRI use and CHD risk overall (OR, 0.93; 95% CI, 0.65–1.33) or in subgroup meta-analysis of case-control studies (OR, 0.91; 95% CI, 0.60–1.37) and cohort studies (RR, 0.96; 95% CI, 0.59–1.55). In contrast, the use of TCA significantly increased CHD risk (OR, 1.51; 95% CI, 1.07–2.12). Subgroup meta-analysis by study design type revealed only case-control studies to demonstrate significantly increased CHD risk with TCA use (OR, 1.41; 95% CI, 1.37–1.45) based on the fixed-effects model. Conclusion: Meta-analysis of observational studies in a population with no history of coronary heart disease showed that TCA use was associated with an increased risk of coronary heart disease whereas SSRI use was not. Our finding should be confirmed in future randomized controlled trials.
Objectives: To explore the influence of depression (D) on relative risk of myocardial infarction (MI) and arterial hypertension (AH) in female population of 25-64 years in Russia.

Methods: Under the third screening of the WHO "MONICA-psychosocial" (MOPSY) program random representative sample of women aged 25-64 years (n=870) were surveyed in Novosibirsk. D was measured at the baseline examination by means of test “MOPSY”. From 1995 to 2010 women were followed for the incidence of AH and MI. Cox proportional regression model was used for assessment of relative risk (HR) of AH, MI.

Results: The prevalence of D in women aged 25-64 years was 55.2%. MI was developed in 2.2% of women, AH – in 33.4%. 16-years risk of MI development in women having D was 2.5-fold higher (HR=2.53; 95% CI:1.26-24.34; p<0.05) compared those without D. HR of AH in women with D over the first 5 and 10 years of study was 1.6-fold (95.0% CI: 0.86-2.98; p<0.05) and 1.74-fold higher (95.0% CI: 1.01-3.01; p<0.05) compared to those without D, respectively. The incidence rates of MI and AH were more likely in married women with D having incomplete higher/vocational education. Rates of AH was higher in “executive managers” (chi-square=4.38 df=1 p<0.05) and “easy manual laborers” with D (chi-square=4.61 df=1 p<0.05). Similar tendencies in occupational class were typical for MI.

Conclusions: The prevalence of D in women aged 25-64 years is more than 50%. Over 16 years of study women with D have significantly higher risk of MI and AH than without D.
SCREENING RATES OF HYPERLIPIDEMIA IN AT-RISK URBAN PEDIATRIC POPULATIONS

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Introduction: New lipid screening guidelines from the NHLBI suggesting universal screening between 9 and 11 years of age were endorsed by the American Academy of Pediatrics (AAP). Prior to these, the American Heart Association (AHA) and the AAP suggested obtaining a fasting lipid profile in children based on risk factors. We hypothesized that placing reminder cards on patient charts will increase compliance with the above guidelines.

Methods: We performed a retrospective chart review in the resident, attending, and adolescent patient clinics located in a high-risk urban hospital for three months to assess lipid screening rates. We then placed reminder cards on patient charts for the same clinics prospectively for three months to assess the screening rates. Demographics, risk factors, and screening information were collected and analyzed, with a p-value <0.05 being significant.

Results: Reminder cards improved screening rates and compliance with the AHA/AAP guidelines for hyperlipidemia in the resident clinic overall (X^2, p=0.016) and when comparing only patients who met criteria (X^2, p<0.005) but not in the adolescent or attending clinics. By logistic regression, older age and higher BMI were predictors (OR=1.2 and OR=12.7, respectively) of a lipid panel being obtained (p values < 0.01). There was no statistically significant increase in screening rates in the 9-11 year age group.

Conclusions: Reminder cards improved compliance with the AHA/AAP guidelines among resident physicians. Age and BMI influenced the physician’s decision to obtain a fasting lipid profile when criteria were met. Other methods must be explored to increase compliance with the guidelines.
Objectives: To evaluate the lipid profile in association with fish consumption in children from 7 to 18 years of age, of both sexes, in public schools of the metropolitan city of Campinas, Brasil.

Methods: A cross-sectional epidemiological study with sampling from a school population pool was carried out. Eleven schools were randomly selected in central and peripheral city areas. The assessment protocol comprised a structured questionnaire, anthropometry, and a non-fasting lipid profile. In 2010, 4699 students (47.14% of the male sex; mean age, 11.07±2.9 years) were evaluated.

Results: One fourth (25.89%) of the students reported meat ingestion once a week but 37.33% reported that fish was not even sporadically present in their diets. On the other hand, daily consumption of sweets and soft drinks was 26.62% and 26.77% respectively. Prevalence of overweight (>+1SD) and obesity (>+2SD) for the whole population was 15.7% and 16% respectively. A lipid profile was aleatorily performed in 2452 children. Medium values were: total cholesterol 130.5±33.2mg/dL, HDLc 42.86±14.48mg/dL, LDLc 80.12±30.29mg/dL, triglycerides 99.19±54.35mg/dL. While 3.61% of the children had total cholesterol above 200mg/dL and 6.26% LDLc above 130mg/dL, 47.31% presented with HDLc levels below 35mg/dL. On the other hand, the habit of eating fish correlated positively with higher HDLc levels: 42.6±14.5mg/dL and 47.1±15.5mg/dL for no consumption in opposition to daily consumption of fish (p=0.0233).

Conclusion: Parents should be warned of the repercussions of unhealthy diets in the lipid profile and change to more cardiovascular protective habits.
OUTCOMES OF CARDIAC REHABILITATION IN OBESE PATIENTS
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Introduction: Cardiac rehabilitation has been well proven to be beneficial in patients after major cardiac events or interventions. Obesity is a well-defined adverse risk factor for all the cardiovascular diseases.

Purpose: We want to analyze if obese patients had any difference in outcomes from cardiac rehabilitation.

Patients and methods: We collected data for patients enrolled in phase II cardiac rehabilitation program from 2010 to 2012. They were enrolled for 8 to 12 weeks. A total of 201 patients were enrolled but data was analyzed for 120 patients out of which 80 were males and 35 were females. Complete demographic data was not available for rest of the patients. 52 patients were obese and 33 were males amongst them.

Results: Out of all the obese patients, 24 patients had diabetes, 8 patients had CHF and 5 had depression. After cardiac rehabilitation, obese patients derived significant benefit in weight, waist circumference, diastolic bp, total cholesterol, exercise volume, LDL, triglycerides, glucose, METs and Beck’s depression score. Non-significant improvement was seen in systolic bp and HDL. These improvements were similar to non-obese individuals. On further analysis, BMI at the end of program was not associated with sex and comorbidities like diabetes, chronic kidney disease, CHF and depression. Obese patients lost more weight vs. non obese patients. They also had greater reduction in waist circumference vs. non obese patients.

Conclusion: Obese patients should be routinely referred to cardiac rehabilitation program. They derive comparable benefits as compared to non-obese patients.
COMPARISON OF VO2MAX., ENERGY BALANCE AND ANTHROPOMETRY IN PATIENTS OF A CHECK-UP PROGRAM

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Objectives: To compare the maximum oxygen uptake (VO2max.), BMI, body fat (BF), energy balance (EB) and waist circumference (WC) of patients of a program called fitness check-up.

Background: A “checkup” analyses risks of cardiovascular diseases. And a clear classification of physical fitness among sedentary and active people is important for physical exercise orientations.

Methods: The BF was measured by “dual energy X-ray absorption” (DEXA) and VO2max. by maximal cardiopulmonary exercise test. The energy balance was held by the difference between the relative energy expenditure and calorie uptake. The classification of the level of physical activity, active or sedentary, was done through a self-report and evaluated by an appraiser, with a reliable level of 95%.

Results and Conclusions: we analyzed 81 cases of male gender, with average age of 47 years old, 52% were sedentary. There was a better physical fitness in a group of active people (Mann-Whitney U=565.0; p=0.12). The sedentary differ from the active people also about the average of: BF (31.9% x 28.9%), WC (99.2cm x 93.9cm; p=0.031) and EB: (290.0 x -113.5cal; p=0.006). There was not a statistical difference about the age, waist-hip ratio and BMI. We conclude that for the studied cases, the physical fitness represented by VO2max. was better in cases physically active compared with sedentary patients, the same happened to anthropometric index and energy balance. The best correlation with sedentary and physical activity was effective with the classification of VO2max.
ABNORMAL INTRACELLULAR Ca2+ HOMEOSTASIS, CONDUCTION ABNORMALITIES AND ARRHYTHMIA IN RYR-P2328S ATRIA

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The present experiments explore for the mechanism of slowed conduction in murine RyR2S/S hearts modelling Catecholaminergic polymorphic ventricular tachycardia (CPVT). CPVT is a potentially lethal familial condition associated with mutations in the cardiac ryanodine receptor. It is accompanied by an increased incidence of atrial and ventricular arrhythmias. Recent reports in mice homozygous for the gain-of-function RyR2-P2328S mutation (RyR2S/S) demonstrated a similar arrhythmic tendency associated with increased diastolic cytosolic Ca2+ concentration [Ca2+]i and conduction slowing. The determinants of conduction velocity were investigated in RyR2S/S and compared to those in WT and slow-conducting Scn5a+/− hearts. Picosirius red staining demonstrated abnormal fibrosis in Scn5a+/− but not RyR2S/S or WT hearts. Immunoblot assays showed similar expression of Cx43 and Cx40 levels in the three genotypes. In contrast, Nav1.5 expression was reduced in both RyR2S/S and Scn5a+/− compared to WT atria. Intracellular microelectrode and loose-patch clamp recordings confirmed reduced fast Na+ channel function by showing reduced maximum rates of action potential depolarisation and reduced peak Na+ currents, respectively, in both RyR2S/S and Scn5a+/− atria compared to WT. Acute increases in [Ca2+]i produced by caffeine or cyclopiazonic acid treatment in the WT were also shown to reduce peak Na+ currents. The experiments presented here demonstrate chronic reductions in Nav1.5 expression and Na+ channel function in RyR2S/S atria. In addition, acute elevation of diastolic [Ca2+]i produced similar reductions in Na+ channel function. These findings suggest abnormal intracellular Ca2+ homeostasis produces slow-conducting arrhythmic substrates through both acute and chronic effects on Na+ channel function.
INCIDENCE OF ATRIAL TACHYARRHYTHMIAS IN PATIENTS WITH EARLY REPOLARIZATION SYNDROME AND BRUGADA SYNDROME: ANALYSIS OF PATIENTS WITH IMPLANTABLE CARDIOVERTER DEFFIBRILLATORS

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Background: Early repolarization syndrome (ERS) and Brugada syndrome (BrS) share many electrocardiographic and clinical characteristics. In a significant proportion of patients with BS, atrial tachyarrhythmias (ATAs) are documented, and often serve as important causes of inappropriate shock. The aim of this retrospective study was to evaluate the incidence of ATAs and ATA-induced inappropriate shocks (IS) ATAs in patients with ERS as compared with BrS.

Methods: We analyzed data from 47 patients with ERS or BrS and underwent implantable cardioverter defibrillator (ICD) implantation. The clinical data were analyzed for all events with ICD shocks.

Results: Seventeen patients with ERS (age 38.6 +/- 11.1, M=14) and 30 patients with BrS (43.6 +/- 11.3, M=29) were enrolled. Twelve patients experienced AF after defibrillation for ventricular arrhythmia (6 in ERS vs. 6 in BrS, P = NS). Three patients with BrS had paroxysmal AF. During mean follow-up of 5.3 +/- 4.5 years in the ERS and 4.4 +/- 4.0 years in the BrS, five patients received appropriate shock (3 in ERS vs. 2 in BrS, P = 0.25). There was no significant difference in the prevalence of ATAs between patients with ERS and BrS (9 in ERS vs. 12 in BrS, P = 0.54). Three of 17 (17.6%) ERS and 6 of 30 (20.0%) BrS patients received IS due to ATAs during this periods (P = 0.72). Conclusions: ATA occurred not infrequently in patients with ERS after ICD implantation. There were no significant differences in the occurrence of ATA and IS in patients with ERS as compared to those with BrS.
INCIDENCE, CLINICAL PRESENTATION AND OUTCOME IN TAIWANESE PATIENTS WITH LONG ASYSTOLE INDUCED BY HEAD-UP TILT TEST

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Background: Long systole during head-up tilt test is uncommon. When the duration is more than 5 seconds, it has been called "malignant". Although previous reports have demonstrated long asystole response is quite a benign course. Owing to most of these reports came from western countries, ethnic variation is possible. The clinical data about this subset of patients are reported herein.

Methods: head-up tilt test was employed for 604 patients with syncope of unknown origin. The protocol include 30 min passive tilt test and 30 min isoproterenol infusion which increased the heart rate up to 20% from baseline. The response patterns were analyzed and categorized. The prolonged asystole was searched. Follow up was made at the outpatient clinic or by phone call.

Results: Two hundred forty-two patients (40.1%) had positive response. 172 patients (71.1%) with mixed type, 60 patients (24.8%) with the vasodepressive type and only 10 patients (4.1%) with the cardioinhibitory type. Three patients (1.2%) had prolonged asystole. One young girl and two elderly males associated with atrial fibrillation. The young girl received midodrine treatment and stopped the medication 6 months later with only few recurrence of syncope. The two elderly received pacemaker implantation without syncope recurrence.

Conclusion: the incidence of long asystole during head-up tilt test in our patients was much lower than that of western countries. Head-up tilt test may be a helpful tool for evaluation of syncope in elderly patients with atrial fibrillation.
EFFECT OF DIFFERENT REGIMENS OF DIALYSATE POTASSIUM CONCENTRATION ON CARDIAC ARRHYTHMIA

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Background: Despite the substantial progress made in dialysis technology, cardiovascular diseases remain the single most common cause of death in chronic dialysis patients, the aim of this study was to evaluated the effects of two different regimens of dialysis potassium removal in patients with a tendency to develop arrhythmias during HD (haemodialysis).

Methods and Materials: There were 88 (36 men and 52 women) ESRD patients recruited for the study. They received regular hemodialysis three times per week at the hemodialysis units of a university medical center (Golestan hospital) during year 2011. We compared the arrhythmogenic effects of two dialysis techniques differing in dialysate potassium (K) content. We had two group: in group A, each patient underwent Acetate-Free filtration sessions with constant (3 mEq/l) K and group B had sessions with constant (2 mEq/l) K. Holter ECG recording and plasma electrolytes before and after HD measured.

Results: There was a significant reduction in SVC in the HD solution with constant (3 mEq/l) K as compared with constant (2 mEq/l) K.

Discussion: In conclusion, the use of a model of intra-HD potassium that is more close to potassium serum concentration of ESRD patients seems decreased the arrhythmogenic effect of HD in patients on regular HD treatment.
Background: Natriuretic peptide has been validated as a useful marker in the diagnosis of heart failure. Its role in guiding inpatient medical management is not well established.

Objective: Determine if natriuretic peptide-guided therapy is associated with improved outcomes for hospitalized heart failure patients.

Methods: Using a PubMed keyword search, prospective randomized clinical trials evaluating B-type natriuretic peptide (BNP) and amino-terminal pro-B-type natriuretic peptide (NT-proBNP) guided therapy were identified. Study endpoints include natriuretic peptide levels, all-cause mortality rates, and cardiovascular events (re-hospitalization and cardiovascular death).

Results: Initial search results were reduced from 1,282 to 11 studies. 11 trials (2,610 patients) comparing natriuretic peptide-guided therapy to standard therapy for heart failure patients were identified, with follow-up times ranging from 3 months to 3 years.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number of studies investigating outcome</th>
<th>Total # of patients in studies</th>
<th>Range of follow-up time (months)</th>
<th>Worsening of outcome (# Studies/Total)</th>
<th>No significant outcome difference (# Studies/Total)</th>
<th>Improvement of outcome (# Studies/Total)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natriuretic peptide levels</td>
<td>7</td>
<td>1266</td>
<td>3 – 24</td>
<td>0/7</td>
<td>5/7</td>
<td>2/7</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>10</td>
<td>2093</td>
<td>9 – 18</td>
<td>0/10</td>
<td>7/10</td>
<td>3/10</td>
</tr>
<tr>
<td>Cardiovascular events</td>
<td>8</td>
<td>2331</td>
<td>3 – 36</td>
<td>0/8</td>
<td>3/8</td>
<td>5/8</td>
</tr>
</tbody>
</table>

Conclusion: No adverse outcomes were noted in guided therapy compared to standard therapy. The majority of current studies do not show a difference between guided therapy and standard therapy in reducing measured natriuretic peptide levels and all-cause mortality rates. Natriuretic peptide-guided therapy does appear to be associated with reduced cardiovascular events compared to standard therapy in heart failure patients.
DIAGNOSTIC VALUES OF URINE AND PLASMA NT-proBNP IN HEART FAILURE PATIENTS
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Objectives: To evaluate diagnostic value of fresh urine levels of NT-proBNP for detecting heart failure.

Background: The plasma N-terminal probrain natriuretic peptide (NT-proBNP) level is a significant diagnostic and prognostic marker of heart failure (HF). However, there is still controversy on the urinary NT-proBNP as a simple test for diagnosis of HF.

Methods: We studied 97 patients with chronic heart failure (CHF) and 30 healthy control subjects. Urine and plasma levels of NT-proBNP were measured in all subjects.

Results: Only plasma but not urine NT-proBNP was significantly higher in CHF patients in comparison to controls (p<0.001). There was significant correlation between plasma NT-proBNP and fresh urine NT-proBNP (r=0.49, p<0.001). Due to receiver operating curve analysis, urine NT-proBNP could diagnose HF with area under curve (AUC) of 0.72±0.04 (p<0.001) with sensitivity, specificity, positive and negative predictive value (PPV and NPV) of 71.1%, 56.6%, 84.1 and 37.8 for a cut-off of 94.5 pg/mL. Plasma NT-proBNP had greater AUC (0.94±0.02, p<0.001) and better sensitivity, specificity, PPV and NPV (93.8%, 86.6%, 95.79 and 81.25 for cut-off of428 pg/mL).

Conclusion: This study confirms the correlation between urine and plasma NT-proBNP. Plasma NT-proBNP is still the best diagnostic marker with high sensitivity and specificity; however, urinary NT-proBNP could be used in the absence of plasma NT-proBNP for diagnosing HF.
ULTRAFILTRATION DOES NOT IMPROVE NEUROHORMONAL ACTIVATION IN ACUTE DECOMPENSATED HEART FAILURE

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Background: Blood urea nitrogen (BUN) has recently emerged as a marker of neurohormonal activation, which is considered the central pathophysiologic mechanism of acute decompensated heart failure (ADHF). Compared with conventional therapies, extracorporeal ultrafiltration represents a therapeutic strategy that is superior in symptomatic improvement of ADHF. However, there is no data on the impact of ultrafiltration on the underlying pathophysiologic mechanisms of ADHF and its potential effects on outcomes.

Methods: We searched articles cited in PubMed database from 1970 to 2012 using key words: “ultrafiltration” and “heart failure”. We then reviewed and compared the results of those studies which used the novel portable device approved by the Food and Drug Administration (FDA) exclusively for management of volume-overloaded patients with ADHF.

Results: A total of 60 relevant articles were identified on the use of ultrafiltration in the setting of ADHF. Nine studies using the FDA-approved ultrafiltration device were selected. BUN levels were not reported in 2 studies. Four studies reported no significant change in BUN, while 3 studies found an increase in BUN levels following ultrafiltration therapy. None of these studies directly evaluated the impact of ultrafiltration on neurohormonal status (e.g. serum arginine vasopressin levels) or long-term survival of patients with ADHF.

Conclusion: While the higher efficacy of ultrafiltration for improvement in symptoms has been demonstrated in patients with ADHF, currently available data does not support its beneficial impact on BUN. Further studies are needed to assess whether this observation translates into lack of improvement in long-term outcomes.
PREVALENCE AND HEMODYNAMIC SIGNIFICANCE OF MITRAL ANNULAR CALCIFICATION IN ELDERLY PATIENTS

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Background: Due to aging population with increasing co-morbidities, mitral annular calcification (MAC) is a frequent finding in echocardiography.

Objectives: Evaluate the relationship between severity of MAC and its hemodynamic significance in older patients with preserved ejection fraction.

Methods: We retrospectively reviewed medical records of patients who underwent echocardiographic study at Mayo Clinic from 2004-2011. 640 patients had mitral annular calcification after excluding patients with greater than moderate mitral regurgitation, more than mild aortic regurgitation, prosthetic valves, and sub-normal left ventricular ejection fraction (EF<50%).

Results: 117 (18%) patients had mild MAC, while 354 (55%) had moderate MAC while 169 (26%) patients had severe MAC. Age was not different between the groups (77±11 years; 76 ±10 years; 77 ±12 years=0.61). Mitral valve gradient was different between groups (3.1 mm Hg vs. 3.7 mm Hg vs. 5.2 mm Hg) (overall P < 0.0001)). Most patients (72%) had mild MS (MG < 5 mm Hg), some had moderate MS (26%) (MG 5-10 mm Hg) and very few (1%) had severe MS (MG>10 mm Hg). However, none of the patients in mild to moderate MAC group had severe mitral stenosis (MG > 10 mm Hg), while only 7 (4%) patients with severe MAC group had severe MS.

Conclusions: Although many older patients have MAC, only minority will develop severe mitral stenosis. Even in patients with severe mitral annular calcification, severe mitral stenosis is infrequent. Further studies are needed to examine the mechanism of mitral stenosis in patients with mitral annular calcification.
CLINICAL OUTCOMES OF MEDICALLY TREATED ACUTE AORTIC INTRAMURAL HEMATOMA


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4. Daegu Catholic Hospital, Daegu, Korea

Objective: The aim of this study was to evaluate the clinical outcomes of patients with acute aortic intramural hematoma (IMH) which were medically treated at the presentation.

Patients and Methods:
We analyzed 118 consecutive medically treated patients with acute IMH diagnosed by contrast enhanced computed tomography (CT) from four large centers in Daegu City. All of 74 type B and 44 of 46 type A IMH were intended to medical treatment at the presentation. Those patients were divided into two groups; type A (n=44, 37.3%) and type B (n=74, 62.7%). The change of aortic diameter and hematoma size, clinical outcomes were analyzed and compared between the groups.

Results: Baseline characteristics were not significantly different between two groups. During hospitalization, progression to aortic dissection (13.6% vs 2.7%, p = 0.051) and conversion to surgery (13.6% vs 1.4%, p=0.011) were higher in type A than type B. On CT findings, pericardial effusion (27%) and pleural effusion (25%) was higher in type B than type A. Short-term follow-up CT examination (mean 10 days) didn't show any differences in the rate of hematoma absorption and aggravation between the types. During the 2 year clinical follow up, morality rate was 13.2% in type A and 9.7% in type B (p=0.587).

Conclusion: Even in type A acute IMH, early medical treatment and surgical conversion only in a selected, complicated cases would be a favorable treatment option.
Objectives To examine the chronobiological rhythms of type A and B acute aortic dissection in a group of Iranian patients.

Background: Seasonal differences in the manifestations of some cardiovascular diseases, have been reported. However, there is still controversy on the type A and B acute aortic dissection.

Methods: Patients with acute aortic dissection between 2001 and 2011 were studied. The confirmation of the diagnosis of acute aortic dissection had been performed by computed tomography angiography, transesophageal echocardiography or aortography. Data were recorded and incidence of Stanford type A and B acute aortic dissection was compared between different seasons and months.

Results: Total number of patients with acute aortic dissection was 135 (94 Stanford type A and 41 Stanford type B). The mean age of the patients was 59.19±14.99 years. For Stanford type A aortic dissection a significant peak of 60 cases in cold months vs. 34 cases in warm months was found (P=0.007). However, there was no difference in the incidence of Stanford type B aortic dissection between the cold and warm months (P>0.05).

Conclusion: Stanford type A aortic dissection exhibits significant seasonal variations. This finding may have important implication for the prevention of acute aortic dissection by adapting treatment strategies to ensure maximal benefits during the vulnerable periods.
DEVICE COMPLICATION AMONG TRANSFEMORAL AND TRANSAPICAL ACCESS FOR TRANSCATHETER AORTIC VALVE REPLACEMENT: A META-ANALYSIS

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Intro Transcatheter aortic valve implantation (TAVI) has become an important alternative to traditional surgical aortic valve replacement, particularly in high risk patients. Currently, femoral access is the less invasive approach for the procedure, and transapical access is a feasible alternative option. Concerns regarding those access route include complications such as device embolization, coronary obstruction, "valve in valve", need for surgical intervention and procedural success. Large studies and databases comparing directly the 2 access are currently scarce. We aimed combine the available information in a meta-analysis.

Methods We searched PubMed, EMBASE, and Cochrane databases from 1966 through April 2013. The studied outcomes were device embolization, coronary obstruction, "valve in valve", need for surgical intervention and procedural success. We excluded studies that could have overlapped population from another one. We used Fixed or Random Effect analysis using the Cochrane Handbook of Systematic Reviews.

Results Out of 856 articles, seven studies presented the studied data and were included in the analysis. The pooled data provided a total of 9408 patients, 6770 underwent transfemoral approach and 2638 underwent transapical access. As demonstrated in Figure 1, device embolization, coronary obstruction, and need for surgical intervention did not differ between routes. There was a tendency of a second valve implantation on the transapical group (p:0.06). Although, procedural success also did not differ among the two groups.

Discussion Although transapical approach for TAVI is more invasive than percutaneous transfemoral access, there is no significant difference among them regarding complications and procedural success.
COMORBIDITIES AMONG TRANSFEMORAL AND TRANSAPICAL ACCESS FOR
TRANSCATHETER AORTIC VALVE REPLACEMENT: META-ANALYSIS
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Intro  Transcatheter aortic valve implantation (TAVI) has become an important alternative to
traditional surgical aortic valve replacement, particularly in high risk patients. It carries
complications, mainly related to the via of access for the valve deployment. Currently, femoral
access is the less invasive approach for the procedure, and transapical access is a feasible
alternative option. They carry different rates of comorbidities such as AMI, pacemaker
implatation, renal dialysis, and vascular complication. Therefore we aimed to compare the
literature information in a meta-analysis.

Methods  We searched PubMed, EMBASE, and Cochrane databases from 1966 through April
2013. The studied outcomes were AMI, pacemaker implatation, renal dialysis, vascular
complication. We excluded studies that could have overlapped population from another one. We
used Fixed or Random Effect analysis using the Cochrane Handbook of Systematic Reviews.

Results  Out of 856 articles, ten studies presented the studied data and were included in the
analysis. Pooled data provided a total of 9631 patients, 7075 underwent transfemoral approach and
2556 underwent transapical. As demonstrated in Figure 1, there was a 0.3 fold increase in odds for
renal dialysis on transpical group (p<0.01) and a tendency for increased odds for AMI as well
(p:0.06). There was a 3 increased fold on the transfemoral groups for vascular complication. There
was no difference among groups for pacemaker implantation.

Discussion  While transfemoral is a less invasive approach, it carries a higher risk for vascular
complication while transpical is more invasive and carries a higher risk for end organ damage.
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RHEUMATIC MITRAL STENOSIS IN A PATIENT WITH LEFT LUNG AGENESIS AND PERCUTANEOUS BALLOON MITRAL VALVOTOMY AS A CHOICE

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Background: Lung agenesis is a rare congenital malformation where single or both lungs are absent with no trace of bronchial or vascular supply. Rheumatic heart disease is sequelae of streptococcal infection and these combinations and the challenges posed by this duo and management aspects were never reported in any literature.

Clinical summary: A 36 year old male, chronic smoker comes to us with progressive dyspnoea of NYHA functional class ¾. On examination mid diastolic murmur noted at cardiac apex and absent breath sounds on left hemi thorax. ECG revealed isolated LAE and AF. chest x-ray & HRCT showed absent left lung and bronchus and left pulmonary artery. Echocardiogram & TEE showed thickened and calcified mitral valve with area of 0.9cm² peak and mean gradients were 18 and 12. No evidence of thrombus was noted. Wilkinson's valve score was 13. Spirometry showed FEV1 of <30 and FEV1/FVC <0.7. The unsuitable stenotic valve for percutaneous interventions, anaesthetic complications secondary to Agenitic lung, low FEV1 levels for posed complexity in selecting therapeutic strategy. As his symptoms progressed and bronchodilators & anti failure measures were failed patient was taken up for PTMC through trans septal approach with INOUE balloon as a last resort. The procedure was uneventful and post procedural valve area increased to 1.7cm² and mean gradient dropped to 5mmhg. Patient’s symptoms dramatically improved and asymptomatic for last 3 years.

Conclusion: This case study is reported for its rarity and role of percutaneous procedures in high Wilkinson’s score patients with other co-morbidities.
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NOREPINEPHRINE VS. DOPAMINE PRETREATMENT OF POTENTIAL HEART DONORS - IMPACT ON LONG-TERM OUTCOME

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Background: Optimized care for deceased heart-beating donors has the potential to improve outcome in organ transplantation.

Methods: To compare outcome of patients that received hearts from donors pre-treated with norepinephrine (Group I) to patients that received organs of donors pre-treated with dopamine (Group II), a matched-pair analysis with very strict matching criteria including all patients transplanted at our center between 8/1981-12/2010 was conducted. Donor characteristics were obtained from Eurotransplant donor information forms. For all matched pairs survival time, or time-to-event in case of death with additional documentation of its cause were recorded.

Results: 936 patients (759 male; 177 female; mean age: 47.5±15.4 years) were analyzed and 22 patient pairs (all male; mean age 55.4±7.5 years; range 23-67 years) could be matched. An overall of 11 deaths occurred (Group I: n=3; Group II: n=8) with no significant difference in Kaplan-Meier analysis as far as overall survival is concerned (p=0.1438). In a sub-group analysis of matched pairs where both siblings were able to complete a 5-years follow-up (n=19 pairs), Kaplan-Meier analysis revealed a significant superior long-term survival (>5 years) of patients that received hearts being pre-treated with norepinephrine (p=0.0369).

Conclusion: Neither dopamine nor norepinephrine pre-treatment of potential heart donors showed superior overall survival. In a sub-population of long-term survivors norepinephrine pre-treatment was associated with better survival in a rather small cohort of heart transplant recipients. Nonetheless our findings underscore the need of further prospective multicenter randomized trials to recommend a preferable adrenergic therapy.
PERIOPERATIVE INTRA-AORTIC BALLOON PUMP AND ASSOCIATION WITH IN-HOSPITAL 30-DAY MORTALITY AFTER CORONARY ARTERY BYPASS GRAFT SURGERY

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Background. Pre-operative intra-aortic balloon pump (IABP) support has been reported to improve survival in high risk patients undergoing coronary artery bypass graft surgery (CABG). However, the effect of perioperative IABP placement on hospital mortality and 30-day mortality remains unclear. Hence, we evaluated whether perioperative IABP use is associated with reduced in-hospital and 30-day mortality after CABG.

Methods. We reviewed data from our prospective cardiac surgery database of all patients (n=2793) undergoing CABG from January 2003 through December 2006.

Results. There were 313 patients who required IABP support either prior to [n=205], during [n=54], or after [n=41] CABG, with the timing of IABP implant unspecified for the remaining 13 patients. Ejection fraction was lower in the IABP group [49.5+/−14.1 vs 54.6+/−12.2 in non-IABP group, p<0.0001]. Euroscore was higher in the IABP group [8.4+/−3.7 vs 6.7+/−3.1 in non-IABP group, p<.0001], indicating a greater mortality risk. There was a significant association [by Chi-square analysis] between IABP use and in-hospital mortality [mortality 10.9% in IABP vs 0.77% in non-IABP group, p<0.0001]. However, there was no significant difference in 30-day mortality between the two groups [p = 0.68]. Likewise, although timing of IABP was significantly associated with in-hospital mortality [p<0.0001], there was no significant difference in 30-day mortality rates [p=0.49]. Intraoperative and postoperative IABP placements were independent predictors of in-hospital mortality.

Conclusions. Despite greater in-hospital mortality risk for the IABP group, there was no difference in 30-day mortality between the IABP and non-IABP groups, suggesting late survival benefit for the IABP group.
EXPLORATION OF THE HEART AREAS BY TC-99M MIBI SCINTIGRAPHY AFTER INTRACORONARY INFUSION OF AUTOLOGOUS CD133+ CELLS IN PATIENTS WITH MYOCARDIAL INFARCTION
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Autologous transplantation of bone marrow derived CD133+ was undertaken with the high degree of success for a cohort of patients with heart disease. CD133 mesenchymal cells were enriched using magnetic microbed anti-CD133 antibody from Bone marrow mononuclear cells (BMMNCs). Flow cytometry and immunocytochemistry analysis using specific antibodies revealed that these cells were essentially 89±4% CD133+ and 8±5% CD34+. CD133+/CD34+ BMMNCs secrete important bioactive proteins such as cardiotropin-1, angiogenic and neurogenic factors, morphogenetic proteins, pro-inflammatory and remodeling factors \textit{in vitro}. Single Intracoronary infusion of autologous CD133+/CD34+ BMMNCs are effective and reduce infarct size in patients as analyzed by Tc-99m MIBI myocardial scintigraphy. Majority of patients were treated via left coronary artery. 9 months after cell therapy, 5 out of 8 patients showed a net positive response to therapy in different regions of the heart. Uptake of Tc99 isotope and revitalization of the heart area in Inferoseptal region is more pronounced as compared to apex and anterosptal regions after intracoronary injection of the stem cells. The cell therapy approach proposed here is safe and should be practiced in conjunction with scintigraphy observation of areas of heart which respond optimally to the infusion of autologous CD133+/CD34+BMMNCs. (Funded by Tajikistan ministry of the health, Clinical trials, Gov. number, 01011&1058:D053).
Background. Risk stratification is an important aspect of management of syncope. Transthoracic echocardiography (TTE) has been used as part of several risk score systems. However, predictive value of routine TTE is not well studied.

Methods. We reviewed the outcome of 103 consecutive patients (age 71±17 years, 52% men) referred for TTE as part of inpatient diagnostic work up of syncope. Risk stratification was performed using San Francisco (SF), univariate and multivariate EGSYS (uEGSYS and mEGSYS) and OESIL scoring systems. Adverse outcomes (cardiovascular events or all-cause mortality) were evaluated at mean follow up duration of 28 months.

Results. Definitive or probable causes for syncope were found in 80 (77%) and only 1 was made on the basis of TTE results (severe aortic stenosis). Only 16 (15%) had an adverse event on follow up. No difference in rate of abnormal TTE was observed in those without (group I, n=87) or with (group 2, n=16) adverse events (87% vs 81%, p=NS). In 31 patients with prior TTE, no significant interval change was noted. Risk scores based on systems that incorporate TTE abnormalities into their calculation were not different between the 2 groups (uEGSYS 2.8±3.6 vs 4±3.4, p=0.23; mEGSYS 3.6±3 vs 4.6±2.4, p=0.14; OESIL 1.9±1.2 vs 2.3±0.9, p=0.19). However, SF scoring system that does not incorporate TTE results was significantly different between 2 groups (0.9±0.7 vs 1.4±0.7, p=0.02). Average cost of hospitalization for syncope was $7,664 ± 8,576 at a length of stay of 3±2.7 days.

Conclusion. Routine TTE has little impact on diagnosis, management, and risk stratification of suspected cardiac syncope.
THE UTILIZATION OF THE "ROSE RULE" IN IDENTIFYING HIGH RISK SYNCOPE PATIENTS
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Introduction: Current admissions practices for Syncope result in a marginal diagnostic benefit and consume health care resources. On average 30%-40% of these patients are admitted to the hospital, resulting in excess of 200,000 hospital admissions annually in the US. However to accomplish such a medical change in the care strategy, an essential step is to provide the E.D and urgent care physicians with well-considered “risk stratification” guidelines.

Methods: This study is a prospective multicenter study that was conducted between August 2010 and June 2011. A total of 113 patients were enrolled when they presented to Emergency departments in two medical centers. Patients were subsequently: admitted, referred for outpatient investigation or discharged according to current ED protocols. A post disposition follow up was implemented.

Results: A total of 113 syncope-patients were included in the study (51% females, 49% males), mean age was (69.5 years old). 50 patients (43%) were considered high risk by ROSE rule compared to 59 patients (51%) identified as high risk by San Francisco rule. The results showed a significant correlation between patients labeled as high risk via the Rose rule with regards to poor outcomes. However, this association was not paralleled when utilizing San Francisco rule (OR: 2.82; CI:1.29 to 6.18: P<0.01),(OR:1.24; CI:0.58 to 2.66: P<0.69) respectively.

Conclusions: The ROSE rule criteria adds only BNP assay to the standard evaluation of syncope in the Emergency Department. This study showed that measuring BNP in addition to standard investigations may assist in preventing unnecessary admissions.
VALUE OF POINT-OF-CARE ECHOCARDIOGRAPHY USING A POCKET-SIZED DEVICE IN A COMMUNITY CLINIC

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Background. Nearly 20% of the population of the United States is uninsured. Uninsured do not seek regular preventive care and management of their heart disease may be affected by delays in obtaining appropriate imaging studies. We aimed to determine whether point-of-care echocardiography using a pocket-sized device (V Scan, GE Healthcare) would facilitate early diagnosis and management of such patients.

Methods. 50 consecutive adults seen at a cardiology outpatient clinic (Age 56±15 years, 54% men, body mass index 30±6 kg/m2, 68% hypertensive, 68% hyperlipidemic, 40% diabetic, 48% active smoker) were included. Clinical, diagnostic and therapeutic decisions were formulated before and after echocardiography.

Results. Most patients were unemployed (54%) with 16% part-time employed, and 6% physically disabled. Optimal or diagnostic quality images were obtainable in 92%. Overall, in 76%, the information obtained by point-of-care echocardiography obviated the need for a formal study. In 14%, such information allowed therapeutic decision making at the same visit. Formal echocardiogram was ordered in 10 (20%) of whom 5 did not show up for study and in 5 it was done at a mean of 13 days.

Conclusion. High quality point-of-care echocardiography is feasible in cardiology clinic and it can lead to 1) substantial cost saving, 2) obtaining information that is complementary to detailed cardiovascular examination, and 3) reduction of turn-around time for therapeutic decisions that require echocardiographic assessment. This can potentially reduce the number of needed clinic visits and improve patient adherence to scheduled future follow up visits.
Purpose: An integrated literature review was conducted to identify the effect of yoga intervention on heart rate variability in adults.

Methods: Extensive computerized searches of diverse data bases (Ovid MEDLINE, PubMed, APA PsycNET, Alt Health Watch via EBSCOhost, CINAHL) were conducted including ancestry searches on previously reviewed articles and on all potential primary studies. The key terms used for the search were yoga and heart rate variability. These extensive computerized searches yielded 230 studies (Ovid MEDLINE-25, PubMed-31, APA PsycNET- 16, Alt Health Watch- 153, and CINAHL- 5). Out of the 230 studies, nineteen studies were included in the final analysis. Inclusion criteria: The inclusion criteria were: studies that included adults with age greater than 18 years, measured heart rate variability using any form of Yoga as an intervention, reported during the years 2000 through 2013, published in peer-reviewed scientific journals, and reported in English language.

Results: Heart rate variability indices showed significant shift in autonomic balance towards vagal dominance. Heart rate, systolic, diastolic and mean blood pressure decreased significantly. Yoga intervention reduced the indices of ventricular repolarization dispersion (QTd, JTd) in patients with arrhythmia. Significant reduction in stress, anger, depression, anxiety and neurotic symptoms were noted. Current research with yoga in cardiovascular diseases: In patients with paroxysmal atrial fibrillation, yoga improves symptoms, arrhythmia burden, heart rate, blood pressure, anxiety and depression scores, and several domains of quality-of-life (Lakkireddy et al., 2013). Future recommendations: More randomized control trials are needed to evaluate the impact of yoga on adults with cardiovascular diseases.
FEASIBILITY OF INTEGRATING CLINICAL RESEARCH INTO CLINICAL CARE IN THE HEART CENTRE AT ST PAUL’S HOSPITAL

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Background: The heart Centre (HC) at St Paul’s Hospital is a unique resource in the province, which provides complete care for British Columbians with all kinds of heart diseases. The purpose of this study was to design, develop, implement and evaluate a suitable and sustainable method to integrate patient and staff in the research process, and increase quality of cardiac care.

Methods: All patients in HC were asked for “Permission to be Contacted” for future research participation by a validated form. This study was carried out in three phases. During the first phase, a pilot study was conducted in Pacific Adult Congenital Heart (PACH) clinic to confirm feasibility. In the second phase, the study was carried out in Heart Failure (HF), PACH and Stress Laboratory clinics to develop a sustainable method of approaching patient and to create a suitable database. During third phase, established process was evaluated and implemented.

Results: Upon confirmation that the study is feasible, printable electronic consent forms with relevant traceable patient information and a secured and comprehensive electronic database were developed. The results showed that the consent rate was high in HFC (83%) compared to PACH (76%) and stress lab clinics (61%). The collected results of three clinics were evaluated and steps were taken for further improvement and consistency.

Conclusions: This study determined supports, barriers, challenges of integrating clinical research with clinical care and now potentially can form a model for other departments of the hospital in the future.
APPLICATION OF A SUSTAINABLE PATIENT AND STAFF ENGAGEMENT METHOD IN TRANSLATIONAL RESEARCH

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Background: Heart disease research exhibits an important role in improving patient care. Despite well recognized research benefits, less than 10 percent of patients in British Columbia are approached for consent to participate in health research. This study demonstrated that patient consent to participate in future research can be integrated into routine outpatient health clinic practice.

Methodology: This study was carried out in stress lab clinic at St Paul’s Hospital. First month of this 5 month project was conducted as a pilot study to determine it’s feasibility. During this study, no dedicated research personnel was assigned and work was completed by the existing staff. Over a 5 month duration, all patients that visited the clinic were asked for Permission To be Contacted (PTC) for future research participation. A simple one page PTC form was designed for ease of field data collection and to track patient’s response both in a hard-copy and digital format.

Results: Patient’s PTC rate increased from 51 to 63 percent and both patient’s decline to participate and incomplete form rates decreased 6 percent from beginning to the end of the study. The 100 percent staff’s involvement was a significantly factor in the achievement of improved study results.

Conclusion: Although PTC procedure was well supported by the staff and enabled completion of the study without hiring new dedicated research person, yet the overall objective of achieving greater than 80 percent patient’s research engagement could not be attained. A longer duration study is required for further improved research outcome.
Background: Patients with thrombotic events require anticoagulation, however, this decision is clinically complicated if there is a history of a recent bleed. Medical management of thromboembolic events with anticoagulation must be discussed in order to ensure the best outcome for the patient.

Case Report: We identified a 63 year old Caucasian female who had a history of a neglected, ulcerating breast cancer admitted for an uncontrolled left axillary bleed. During the hemorrhage, she became unresponsive and hemodynamically unstable. She then developed respiratory failure requiring intubation. During her hospital course, she developed atrial fibrillation and was started on amiodarone. She also had a previous deep vein thrombosis in the left subclavian vein which was found in October 2010. Radiation therapy for her advanced malignancy was started, at which time she became thrombocytopenic. A discussion regarding the initiation of anticoagulation ensued, and she was ultimately opted for treatment with enoxaparin.

Discussion: This case report is pertinent because the decision to anticoagulate can be complicated in situations like this. The guidelines for anticoagulation can be intricate with patients who have additional problems such as bleeds or dysrhythmias. Further investigations on general recommendations for anticoagulation in complicated cases, management of DVTs, and optimal options for anticoagulation will all be discussed in this case study. The goal is to provide a framework to help guide clinical decisions related to anticoagulation for patients to ensure the best outcome and care.
Background: Mitral valve repair has been associated with better preservation of left ventricular (LV) function for isolated mitral regurgitation (MR). The objective of this study was to evaluate an influence of preoperative LV function on mitral valve repair for isolated MR, especially change in grade of MR, postoperative LV dimension, ejection fraction (EF).

Methods: Forty-one patients undergoing mitral valve repair for isolated MR from January, 2004 through December, 2010 were divided into two groups. Patients with decreased preoperative LVEF (< 50%; group I, n=14, M: F=9:5, age 57±18) were compared with patients with normal preoperative LVEF (≥50%; group II, n=27, M: F=11:16, age 59±12). The etiology of regurgitation was degenerative (I/II: 10/22), rheumatic (1/2), endocarditis (0/3), ischemic (3/0). All patients underwent transthoracic echocardiography preoperatively; mean follow up was 32±30 months.

Results: There is one reoperation in both groups. Group I demonstrated significant decrease in MR grade (P<0.004), increase in LVEF (P<0.009), decrease in LV end diastolic dimension (LVEDD) (P<0.000) and decrease in LV end systolic dimension (LVESD) (P<0.001) postoperatively compared with preoperative condition. But, group I showed decrease in LVEF (P<0.028), increase in LVEDD (P<0.000), increase in LVESD (P<0.002) compared with group II postoperatively during follow up.

Conclusions: Mitral valve repair in patients with LV dysfunction and isolated MR are effective improvement of LV function, however there are not so much improve compared with the group of normal LV function. The LV function was restored to normal during follow up period even in patients with LV dysfunction.
Recently, we reported that embryonic and induced pluripotent stem (iPS) cells following transplantation into infarcted heart can inhibit apoptosis and differentiate into cardiac myocytes. iPS cells can have wide application in for the treatment options in regenerative medicine including doxorubicin induced cardiomyopathy. In the present study, we explored the use of iPS and ES cells cells or factors released from these cells have a potential for cardiac and neovascular cell type differentiation as well as to inhibit adverse cardiac remodeling. Our Doxorubicin induced cardiomyopathy in mice hearts shows a significant increase in cardiac adverse remodeling (apoptosis and fibrosis) and oxidative stress. These increased adverse effects on remodeled hearts were attenuated following cells or factors released from stem cells transplantation. Next, transplanted pluripotent stem cells demonstrated increase in cardiac myocyte differentiation and neovascularization originating from endogenous cardiac stem cells. Overall, our data provide strong evidences that transplanted iPS cells in the Doxorubicin induced cardiomyopathy provide beneficial effects via increasing cardiac regeneration as well as inhibiting adverse cardiac remodeling which results in improved heart function.
CYTOKINES AND THE ROLE OF IMMUNOMODULATION IN HEART FAILURE OF DIFFERENT ETIOLOGIES

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In the acute phase of myocardial infarction for a long time were described several patterns of activation of the immune response.

On the contrary less well known are the changes in both chronic ischemic patients presenting the aspect of the so called chronic ischemic cardiomyopathy as well as in the heart failure of any etiology.

Therefore it is interesting the exploration and understanding of the meaning of the factors that regulate immune response at long interval of time from acute phase.

Moreover the targets of pharmaceutical approach that modulate the immune response can have better probability to gain a more successful result, as the therapeutical approach has given no result until now as is the case of TNF alpha inhibitors.

For this reason we have decided to study a group of patients, 48 subjects (male to female ratio 5.25), ranging from 40 to 80 years, mean age 64, SD 9, with left ventricular dysfunction caused by different cardiac disorders; and a group of 28 healthy individuals as control group.

The levels of a number of biochemical markers were analysed and compared in the patient and control group (tumor necrosis factor alpha – TNF alpha, interferon gamma, IFN gamma, interleukin-6 IL-6, interleukin 10 IL 10).

The results have been the following: there were statistically significant difference in the levels of IFN gamma and IL-6 between the patients and healthy controls. Table 1. Graph 1-2.

Conclusions: The only difference between patients and healthy controls that has shown a parameter of higher level among control group was the IFN gamma level. IL-6 was higher as expected in patients, while no significant differences were observed for the levels of TNF alpha and IL 10.

Therefore one can speculate that the modulation of the interferon molecules family can have a favorable clinical effect in heart failure population.

Table 1: Mann Whitney test patients vs controls

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean (pg/ml)</th>
<th>Mean controls (pg/ml)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNF alpha</td>
<td>21.25</td>
<td>21.19</td>
<td>p=0.9 ns</td>
</tr>
<tr>
<td>IFN gamma</td>
<td>354.41</td>
<td>574.16</td>
<td>p= 0.0005</td>
</tr>
<tr>
<td>IL-6</td>
<td>3.65</td>
<td>1.49</td>
<td>p&lt; 0.0001</td>
</tr>
<tr>
<td>IL 10</td>
<td>17.57</td>
<td>17.28</td>
<td>p= 0.71 ns</td>
</tr>
</tbody>
</table>
GRAPH 1. Box and whisker plot IFN gamma patients (IFN-g) vs. controls (c IFN-g)

GRAPH 2. Box and whisker plot TNF alpha patients (TNF-a) vs. controls (c TNF-a)