**Role of Echocardiography in Epidemiologic Studies and Clinical Trials: An Historical Perspective**

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Non-invasive transthoracic echocardiography (TTE) for assessment of subclinical and clinical heart disease – initially, left ventricular (LV) mass, geometry and function – dates from the 1980’s. In parallel, TTE successfully demonstrated in hypertensive patients reduced LV mass and improved outcomes with antihypertensive therapy. Transesophageal echocardiography (TEE) has been invaluable in intra-operative/interventional trials. Many important uses of TTE/TEE and contributions from our collaborations are summarized in Tables 1 and 2. Challenges have included poor echocardiography windows, sonographer and reader measurement variability, temporal drift, regression-to-the mean, etc. Promising newer study applications include global image telemetry, strain deformation imaging, hand-held and potentially wearable echocardiography devices.

Table 1 - Important uses of TTE and TEE in Epidemiologic Studies and Clinical Trials

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| 1. *Epidemiology*: Characterize cardiac structure and function; identify echo prognostic parameters (e.g., in Framingham, Cornell, Helinski and CHS) |
| 2. *Hypertension*: Measure LV mass, systolic and diastolic function and assess treatment effects |
| 3. *Valvular Disease*: Assess prevalence, risk factors for development; assess prosthetic valve hemodynamics (for FDA, etc.) |
| 4. *CHD/MI*: Assess disease impact on LV remodeling/function; assess drug, catheter-based and surgical interventions; stress echo for ischemic vulnerability, myocardial viability, etc. |
| 5.  *Heart Failure:* Assess LV systolic and diastolic function, LV remodeling, mitral regurgitation, and treatment effects – including reverse remodeling; assess candidates for CRT, other devices |
| 6. *Toxicity*: Assess effects of cancer, chemo/radiation therapy, diabetes, etc. |
| 7. *Other*: Diet drug valvulopathy, echo contrast agents, atrial fibrillation,TEE-guided cardioversion, interventional device (PFO and LAA closure, CRT, mitral clip, etc.) and surgical trials |

Abbreviations: CHD = coronary heart disease, CHS = Cardiovascular Health Study, CRT = cardiac re-synchronization therapy, echo = echocardiography, FDA = U.S. Food and Drug Administration, LAA = left atrial appendage, LV = left ventricular, MI = myocardial infarction, PFO = patent foramen ovale

Modified after Gottdiener,…Gardin, et al: *JASE* 17(10):1086, 2004.

Table 2 – Selected Cohort Studies involving our Collaboration

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| **Study** | **Population** | **Echocardiography findings** |
| CHS | Elderly US adults:  Bi-ethnic AA and C cohort | * Elucidated prevalence of HFpEF, HFrEF, CHD and AV disease * Predictive value of LV mass, geometry and systolic function for HF, stroke and overall CVD events |
| CARDIA | Young US adults:  Bi-ethnic AA and C cohort | * Elucidated prevalence of MVand AV disease, MVP and HCM. * Higher prevalence of LV mass in AA, associated with obesity and higher BP * Predictive value of LV systolic function for incident HF 10 years later |
| HF-ACTION | HFrEF patients  (LVEF < 35%) | * Association of LV diastolic dysfunction with exercise MVO2 |
| Echo NoRMAL | International cohort collaboration:  Adult populations | * Elucidated normal TTE values in Euro, SA, and EA populations * Demonstrated lower range of stroke volume(s) in SA |
| DIET DRUGS Phentermine/fenfluramine (phen/fen) and Dexfenfluramine | Multicenter phen/fen  and dexfenfluramine  cessation studies | * Prevalence of AR= 9 - 14% (mild = 8 - 12%) versus 4% in controls; regression or no change noted 1 year later |

Abbreviations: AA = African American, AR = aortic regurgitation, AV = aortic valve, BP = blood pressure, C = Caucasian, CARDIA = Coronary Artery Risk Development in Young Adults, CHD = coronary heart disease, CHS = Cardiovascular Health Study, CIMT = carotid intima-media thickness, EA = East Asian, Echo NoRMAL = Echocardiographic Normal Ranges Meta-analysis of the Left Heart, Euro = European, HF = heart failure, HF-ACTION = Heart Failure ACTION, HFpEF = heart failure with preserved ejection fraction, HFrEF = heart failure with reduced ejection fraction, SA = South Asian