**THE INFLUENCE OF ACUTE MATRIX METALLOPROTEINASE ACTIVITY ON MYOCARDIAL DYSFUNCTION ASSOCIATED WITH URGENT CARDIAC SURGERY: CARDIOPROTECTIVE EFFECTS OF INHIBITION**

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Objective: Matrix metalloproteinase-2 (MMP2), a gelatinase involved in cell structure degradation, is emerging as an important player in acute ischaemia-reperfusion injury in the heart. We investigated whether MMP2 plays a role in cardiac dysfunction when previously infarcted hearts were subjected to additional elective global ischaemia. Methods: Left coronary artery occlusion was surgically induced in male Wistar rats. After 7 days, the hearts were removed and subjected to isolated Langendorff perfusion (20 mins), global ischaemia (30 mins) and reperfusion (60 mins) with or without &#963;-phenanthroline (an MMP inhibitor). Mechanical function (left ventricular developed pressure: LVDP) of the heart was monitored continuously by intraventricular balloon. MMP2 activity was measured (using zymography) in the initial 6 mls of coronary reperfusion effluent and in the heart tissue (using an MMP2 activity assay) at varying times of reperfusion.

Results: The final recovery (% pre-ischaemic LVDP) in infarcted hearts was significantly (p<0.05) lower (22±2%) than non-infarcted (39±2%) or sham (39±3%) hearts. MMP2 activity in infarcted hearts peaked at 5 mins of reperfusion (1.03ng/ml/gm of protein) and was significantly (p<0.05) higher than in normal (0.576ng/ml/gm) hearts. MMP2 release into the coronary effluent was also higher. Inhibition of MMP2 activity improved recovery of LVDP in infarcted hearts to 47±4% (p<0.05).

Conclusion: In infarcted hearts, additional elective global ischaemia, as occurs during cardiac surgery, reduced mechanical function with increased MMP2 activity. MMP2 inhibition ameliorated cardiac dysfunction, suggesting a role for MMP2. Clinically, inhibition of MMP2 activity may improve cardioprotection of patients undergoing cardiac surgery after an acute coronary event.