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Title: 0032 - RESEARCH

Demystifying The Conundrum of Reperfusion Injury

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Abstract: (Your abstract must use Normal style and must fit into the box. Do not enter author details)

Objective:

Myocardial ischemic reperfusion injury following coronary revascularization is a well-known phenomenon. It manifests as reperfusion induced ventricular arrhythmias, myocardial stunning, microvascular obstruction and lethal myocardial cell death. Lethal myocardial cell damage has been identified in STEMI patients where in therapeutic interventions applied solely at the onset of myocardial reperfusion reduces the infarct size by 40-50%. Reperfusion injury attenuates the full benefits of myocardial reperfusion during MI. However, very little is understood regarding the time course of reperfusion injury and the critical period during which interventions can mitigate myocardial damage. The objective of the study is to determine in vivo the time course of ischemic reperfusion injury.

Methods:

The time course of reperfusion injury was elucidated in a canine model. Real time visualization of injury was obtained using contrast cardiac MRI. The left anterior descending artery (LAD) was occluded using a 3.0mm PTCA balloon catheter (n = 12). Regional myocardial signal enhancement and function was recorded approximately every 10 min during 90 min of ischemia followed by 120 min of reperfusion, and again at 24 and 48 hours post reperfusion. A constant gadolinium infusion was administered during imaging. A catheter was inserted into the coronary sinus (CS) to measure creatine kinase (CK) leak across the coronary circulation (CS – LAD).

Results:

With occlusion of the LAD, the at-risk region became hypokinetic/akinetic. **Infarct Size:** Upon deflation of the balloon catheter (at the onset of reperfusion) the myocardium within the area 'at-risk' (of ischemia) began to swell into the lumen of the left ventricle, reaching a significance level within 20 minutes of reperfusion (P < 0.05; n=8). After 45 minutes of reperfusion, the infarct/LV% was 25.4 ± 8.0%. This was 76.2 ± 6.5% of the maximal change in infarct/LV% observed. The infarct/LV% continued to get larger reaching a maximum at 48 hours post reperfusion (32.7 ± 4.1%). **Cardiac Enzymes:** Within two minutes of reperfusion, the CK (CS – LAD levels) change measured 86.3 ± 71.3 IU as compared to (I90) immediately prior to deflation of the balloon 15.0 ± 7.2 IU. Peak CK leak (1346.3 ± 1050.0 IU; P < 0.05) occurred at 10 min of reperfusion. The CK change (CS-LAD CK levels) had the strongest correlation to infarct/LV % (Pearson's correlation r = 0.80) as compared to the CS (r = 0.66) and Art (r = 0.61). **Regional wall thickness:** Significant myocardial thickening, resulting from myocardial edema was achieved 15-120min post reperfusion. **Histopathology:** Ex vivo tissue analysis revealed evidence of necrotic cell death in the area at-risk are following reperfusion.

Conclusions:

This is the first study to demonstrate in real time the process of reperfusion injury. Based on imaging alone, the first 20-30min post revascularization appear to be when a large percentage of the reperfusion injury occurs. However in conjunction with cardiac enzymes, the first 10min following revascularization appears to be critical from lethal myocardial cell injury standpoint. This study provides conclusive real time in vivo critical period during which salvage interventions can be cardioprotective in terms of reducing infarct size post acute ischemia. We have also for the first time developed an in vivo canine model for ischemia reperfusion injury to further elucidate the process and develop cardioprotective interventions targeted towards mitigating reperfusion induced myocardial damage.