**ROLE OF AUTOPHAGY IN THE HUMAN HEART EXPOSED TO IATROGENIC ISCHEMIA/REPERFUSION INJURY**

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Although originally described as a survival mechanism, recent reports documented that autophagy may contribute to the pathogenesis of various heart conditions. To evaluate in the human heart exposed to warm blood cardioplegic arrest (WBCA) the occurrence of autophagy associated with on-pump cardiac surgery, twenty-four patients undergoing on-pump CABG surgery were classified into groups A and B, receiving 45-55 minutes and 90-105 minutes of WBCA, respectively. Two sequential biopsies were obtained from the right atrium: at the start of grafting (internal control) and 10 minutes after release of aortic cross-clamp. Autophagy was quantified by immunohistochemistry, as well as Western Blot (WB) analysis, using a monoclonal LC3 antibody. Myocyte autophagy, revealed by staining with a monoclonal LC3 antibody, was virtually absent in control specimens, but was detected in 4.7±1.6% and 9.1%±2.4% of the entire myocyte population from group A and B, respectively (p<0.01). LC3 positive vacuole formation was observed to start at one nuclear pole, before becoming bipolar and involving the cytosol (group A). Subsequently, the autophagic process extended also to the nuclei, which, in the final stages, underwent a progressive vacuolization and disintegration, assuming a peculiar “strawberry like aspect” (autophagic cell death; group B). In line with this finding, WB analysis documented that cleavage of endogenous LC3, which was minimal or absent in control samples, increased of 2.3 fold in group A and reached a zenith of 4.7 fold in group B (p<0.001).

In conclusion, WBCA caused myocyte autophagy, whose magnitude and severity are proportional to the length of cardioplegic arrest.