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Modified Spatial Organization of Cardiomyocyte in a Rat Model for Cardiorenal Syndrome

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Background:

Concomitant cardiac and renal dysfunction has been termed the cardiorenal syndrome (CRS), a major growing problem in chronic heart or renal failure (CHF/CRF) patients. CRF frequently leads to cardiac hypertrophy and diastolic dysfunction, yet insight into the pathogenesis of CRS remains limited. Under pathophysiological conditions, cardiac ultrastructural changes are markedly observed. Transmission Electron Microscopy (TEM) can be used to reveal intracellular changes of the contractile unit, the sarcomere, and of the spatial arrangement of organelles, e.g. mitochondria, and t-tubules. These changes may attribute to the contractile alterations that occur upon disease progression (e.g. damaged sarcomere structure may suggest reduction in contractile force).

Methods:

CRS Lewis rats underwent 5/6nephrectomy, 4 weeks prior to induction of left ventricular dysfunction (LVD) by LAD ligation, allowing CRF development prior to cardiac event. At time of necropsy, six weeks (short-term) or 8 months (long-term) post-MI, $1mm^2$of cardiac tissue obtained from the left septum of Sham, long/short-CRF, long/short-CRS and LVD rats were fixed for TEM processing according to standard protocol.

Results:

Control tissue showed regularly cross-striated myofibrils, condensed mitochondria, and numerous, well-organized t-tubules. Compared to Sham, LVD and short-CRS groups underwent massive internal reorganization: ruptured and damaged myofibrils, fused and clustered t-tubules, and swollen-damaged mitochondria. Further damage was observed in the long-CRF and long-CRS groups, presented by increased amount of swollen-damaged mitochondria and less organized myofibrils. Furthermore, long-CRF group exhibited spacious gap-junctions.

Conclusion:

Attenuated excitation-contraction coupling and its resultant decrease contraction force may be attributed to the disruption of t-tubules and sarcomere organization upon disease progression. Swollen mitochondria point-out to metabolic stress which may trigger apoptosis, intensify the loss of cardiac tissue. Spacious gap-junctionsmay implies to diminish electrical coupling between adjacent cardiomyocytes, which can lead to desynchronized contraction and arrhythmias.