Abstract: 5S

Respiratory Modulated Pacing Improves Outcomes In Sheep With Reduced Ejection Fraction Heart Failure

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Heart failure is a leading cause of mortality and morbidity globally. Heart rate is dynamic, with greater heart rate variability (HRV) being a positive prognostic indicator of cardio-vascular health. HRV changes rhythmically with breathing, termed respiratory sinus arrythmia (RSA). This is an evolutionary conserved phenomenon prominent in children and healthy adults but absent in many cardiovascular diseases, including heart failure. We hypothesised that pacing the heart with novel respiratory modulated pacing would improve outcomes in heart failure with reduced ejection fraction compared to conventional monotonic pacing.

Heart failure was induced in adult Romney sheep by a microembolisation technique. Eight to ten weeks post embolization sheep were implanted (under anaesthesia 2.5-3% isoflurane) with an arterial pressure probe, diaphragmatic electrodes, aortic flow probe, coronary artery flow probe, a pacing lead on the left atria, and split into three groups. RSA paced (n = 5), monotonically paced (n = 5), and time control (n = 5). One week baseline recording was followed by four weeks of pacing, and one week off-pace, before terminal experiments and tissue collection. All recordings were in conscious animals. Respiratory modulated pacing was generated by a proprietary device (Ceryx medical) which receives input from the diaphragmatic electrodes to pace the heart with real time respiratory modulation.

RSA pacing resulted in a significant increase in cardiac output (4 weeks of pacing: Δ RSA: 1.4 ± 0.5, Δ Mono: -1.2 ± 1.0, Δ TC: -0.2 ± 1.2 L/min), and ejection fraction (4 weeks of pacing: ΔRSA: 10.6 ± 9.2, Δ Mono: -4.8 ± 4.5, ΔTC: -3.0 ± 3.4 %) compared to monotonic pacing, with no difference in heart rate between groups. The increase in cardiac output was not associated with a change in MAP, indicating total peripheral resistance was reduced. RSA also caused a significant reduction in apnea incidence, suggesting improvement in respiratory instabilities.

Reinstalling RSA may be a novel therapeutic target for improving outcomes in heart failure and opens the possibility of new device-based therapies in other diseases of cardiac inefficiency. We propose that the next generation of pacemakers should incorporate respiratory modulation.