
Coronary microvascular function and myocardial metabolism in the pig model of pacing induced progressive LV dysfunction

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Dilated cardiomyopathy (DCM) is the third cause of chronic heart failure (HF) and is characterized by progressive ventricular dilation and functional impairment in the absence of coronary lesions and/or hypertension. Pacing-induced heart failure mimics many of the pathophysiological and molecular features of clinical non-ischemic dilated cardiomyopathy and is well-suited to perform combined in vivo and ex-vivo measurements and assays. The precise mechanisms responsible for the contractile dysfunction of idiopathic DCM are still not well defined. Research to date has mainly focused on 1) myocardial energy depletion and impaired energy substrate utilization; 2) myocardial ischemia. However, it is still debated whether these mechanisms are related to coronary microvascular dysfunction and/or mechanical dysynchrony. Increased glucose utilization and regional differences in contractile/perfusion function are well-known alterations of the failing heart and play an important pathophysiological role. We tested whether, similar to functional derangement, changes in glucose uptake develop following a regional pattern. Chronic HF was induced in 13 chronically instrumented minipigs by pacing the left ventricular (LV) free wall at 180 beats/min for 3 weeks. Regional changes in LV myocardial contractility, perfusion and stress were assessed by magnetic resonance imaging, whereas regional flow and glucose uptake were measured by positron emission tomography utilizing, respectively, the radiotracers [13N]ammonia and 18F-deoxyglucose. In heart failure, LV end-diastolic pressure was 20±4 mmHg, and ejection fraction was 35±4% (all P<0.05 vs. control). Sustained pacing-induced dysynchronous LV activation caused a more pronounced decrease in LV systolic thickening (7.45±3.42 vs. 30.62±8.73%, P<0.05) and circumferential shortening (-4.62 ± 1.0 % vs. -7.33 ± 1.2%, P<0.05) in the anterior/interior-lateral region (pacing site) compared with the inferoseptal region (opposite site). Conversely, flow was reduced significantly by ±32% compared with control and was lower in the opposite site region. Despite these nonhomogeneous alterations, regional endsystolic wall stress was uniformly increased by 60% in the failing LV. Similar to wall stress, glucose uptake markedly increased vs. control (0.24±0.004 vs. 0.07±0.01 μmol·min⁻¹·g⁻¹, P<0.05), with no significant regional differences. In conclusion, high-frequency pacing of the LV free wall causes a dyssynchronous pattern of contraction that leads to progressive cardiac failure with a marked mismatch between increased glucose uptake and regional contractile and flow dysfunction.

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Coronary microvascular function and myocardial metabolism in patients with dilated cardiomyopathy

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Dilated Cardiomyopathy (DCM) is a cardiac muscle disease characterized by reduced contractile function and dilation of the left or both ventricular chambers. Classical pathogenetic mechanisms of DCM, such as genetic etiology, viral etiology and autoimmunity, can be considered a leading cause of DCM only in the minority of patients. It has been recently hypothesized that coronary microvascular dysfunction, together with