Vasoplegia induces high energy demand and depletes cardiac energetics: a new insight into physiological concepts of cardiac work and a model for acute heart failure?

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Topic(s):
Imaging

Background / Introduction
Hearts subjected to constant high workload will, over time, fail. We hypothesized vasoplegia would create a high cardiac energy demand and deplete cardiac energy reserves, a mechanism causing failure. With 31Phosphorus Magnetic Resonance Spectroscopy, we can measure energy: ATP usage (via creatine kinase flux) and reserves of phosphocreatine (PCr/ATP ratio).

Methods
Ten healthy volunteers were recruited: mean age 37, mean BMI 22.4, 5 male, 5 female. A nitrate vasodilator (Glyceryl trinitrate, GTN) was used to induce vasoplegia, with MRI and MRS measurements taken before and during.

Results
There was reduced preload (falls in end diastolic volume and right atrial area) and afterload (mean blood pressure fall 14mmHg, p <0.0001). Subjects mounted reflex tachycardia (mean heart rate rise 9bpm, p < 0.0001) and inotropy (mean baseline ejection fraction increase 5%, p = 0.0002) hence cardiac output and rate pressure product were maintained (baseline CO 6.24 ± 1.45 L/min vs GTN 6.49 ± 1.43 L/min, p = 0.37; baseline RPP = 6929 ± 976 mmHg.bpm vs GTN 7214 ± 1051 mmHg.bpm, p = 0.06).

There was a 58% increase in Creatine Kinase activity (kf) (baseline 0.158 s⁻¹ vs GTN 0.249 s⁻¹, p = 0.006) and CK flux (baseline 1.79 ± 0.78 umol/g/s vs GTN 2.59 ± 1.07 umol/g/s, p = 0.03), demonstrating increased ATP transfer. PCr/ATP fell (from 2.17 ± 0.2 to 1.99 ± 0.22, p = 0.027). Baseline PCr/ATP positively correlated with the change in stroke volume (R² = 0.66, p = 0.005) during administration of GTN. In addition, whilst at rest, CK kf correlated with rate pressure product (R² = 0.56, p = 0.03), there was no correlation seen during GTN.

Conclusions
We have shown vasoplegia increases energy demand upon the heart, despite unchanged cardiac output and rate pressure product. Further, we have shown a fall in Phosphocreatine/ATP ratio, suggesting this ATP transfer outstripped oxidative phosphorylation and the phosphocreatine pool was depleted in order to maintain ATP delivery. We speculate that progressive depletion of energetics in the context of high energy demand drives hearts under constant stress into failure.

In addition, we demonstrate that the magnitude of the resting phosphocreatine pool relates to ability to augment stroke volume during stress and suggest that this may be protective against a decline into failure. Further work is needed, but PCr/ATP may be an important biomarker for treatments that target myocardial energetics to protect against failure.
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