MR strategy gauges myocardial flux to show energy status of failing hearts

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CONTEXT: Adenosine triphosphate (ATP) is the basic energy currency of the heart. Creatine kinase (CK) reaction is a source of ATP, which is produced from phosphocreatine, a molecule that also serves as an intracellular chemical energy reservoir. Using MR spectroscopy, researchers at Johns Hopkins University have measured ATP synthesis through CK in normal, stressed, and failing hearts. The study, conducted by MRI research director Paul A. Bottomley, Ph.D., and cardiologists Dr. Robert G. Weiss and Dr. Gary Gerstenblith, found that ATP is significantly reduced in patients experiencing mild to moderate heart failure. The article was published in January in the Proceedings of the National Academy of Sciences.

RESULTS: Using a 1.5T scanner and a recently developed four-angle saturation transfer (FAST) method, phosphorus-31 MR spectroscopy was performed in 14 patients with no history of heart disease to measure cardiac CK flux over a physiologic range of stress. Six of the normal controls were administered intravenous dobutamine. Results showed that CK flux was faster among the normal patients than that estimated through oxidative phosphorylation. It did not increase when heart rate and blood pressure were doubled during dobutamine stress. However, ATP flux through CK was 50% lower among subjects with mild to moderate heart failure, leading Bottomley to conclude that failing hearts have an energy deficit. In some cases, the hearts had barely enough energy to function.

IMAGE: Cardiac MRI and P-31 spectra from FAST studies of a normal subject acquired at rest (A and B) and during dobutamine stress (C), and of a 37-year-old patient with class III heart failure at rest (D and E). Horizontal white lines in images denote the source of the spectra in the anterior myocardium. Arrows on the spectra identify the frequency of the saturating irradiation tuned to the g-ATP resonance (spectra at right) and, in a symmetric control location, relative to creatine phosphate or PCr (spectra on left). According to the spectra, the PCr signal with ATP saturation is directly proportional to the forward flux rate through the CK reaction. (Reprinted with permission of PNAS)

IMPLICATIONS: The study established that MR strategies can directly assess human myocardial CK energy flux, according to Bottomley. The deficit in ATP supplied by CK shows that failing hearts are "energy-starved," and therapies that reduce energy demand and/or increase energy transfer in failing hearts should be pursued.

"This is molecular imaging in its truest form," Bottomley said. "There are no contrast agents to deliver, no tags or cells that are stuck on things. This is the raw stuff."

Disclosures:

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