Study identifies new way to predict prognosis for heart failure patients

11 December 2013

Johns Hopkins researchers have identified a new way to predict which heart failure patients are likely to see their condition get worse and which ones have a better prognosis. Their study is one of the first to show that energy metabolism within the heart, measured using a noninvasive magnetic resonance imaging (MRI) test, is a significant predictor of clinical outcomes, independent of a patient's symptoms or the strength of the heart's ability to pump blood, known as the ejection fraction.

About half of the 5 million people suffering from heart failure in the United States have non-ischemic cardiomyopathy, which means that their heart failure is not due to blocked arteries.

"It is difficult to predict which people with non-ischemic heart failure will do poorly and be at a higher risk of death," says Robert Weiss, M.D., a cardiologist and professor of medicine at the Johns Hopkins University School of Medicine and senior author of the study. "Having a more precise way to determine a patient's risk would enable us to identify high-risk people earlier and tailor their treatments more specifically. And with a new target—impaired energy metabolism—we can also open the door to developing and testing new therapies for heart failure," he says.

In their study, described online on Dec. 11 in *Science Translational Medicine*, the researchers measured energy metabolism in the hearts of 58 patients using magnetic resonance spectroscopy. The patients were then followed for a median of 4.7 years to track heart failure hospitalization, heart transplantation, the placement of a ventricular assist device and/or death from all causes.

Specifically, the researchers examined how the energy that fuels heart muscle cells, known as adenosine triphosphate (ATP), reacted with the enzyme creatine kinase (CK). The role of CK is to maintain a constant energy supply in the beating heart. The researchers were able to measure the rate of ATP synthesis through the CK reaction within patients' heart cells noninvasively with magnetic resonance spectroscopy, a type of imaging that detects metabolism, or energy use, in organs and tissues without using contrast agents or ionizing radiation.

"We found that the rate of energy metabolism in heart muscle was significantly lower in those heart failure patients whose conditions got worse and needed hospitalization, implantation of a ventricular assist device or a heart transplant, or had died from their weakened heart," says co-lead author Paul Bottomley, Ph.D., professor and director of the Division of Magnetic Resonance Research at the Johns Hopkins University School of Medicine. "We believe that the rate of ATP delivery to the cells by CK can be used along with established methods to better predict heart failure events and improve the timing of intensive interventions for patients."

Established methods include the New York Heart Association (NYHA) Functional Classification system that places patients in one of four categories based on how much they are limited during physical activity, with symptoms that include shortness of breath and chest pain. The ejection fraction, which shows how well the heart can pump blood to the rest of the body, is also used as a prediction method. African-Americans are also in a higher risk category.

"The current methods used for prediction are not reflective of the underlying mechanism in the weak heart, and some of them are not very consistent in their predictive ability. That's why there's a need for new methods that could potentially be more specific," says co-lead author Gurusher Panjrath, M.D., who performed the work while at Johns Hopkins and is now an assistant professor of medicine and director of the Heart Failure and Mechanical Support Program at the George Washington School of Medicine & Health Sciences

in Washington, D.C.

The researchers say that even after correction for NYHA class, ejection fraction and race, reduced energy metabolism was a significant predictor of heart failure outcomes in their study.

"It makes sense that failing hearts with reduced energy supply are at increased risk of adverse outcomes, because the heart requires a lot of chemical energy to beat and function normally," says Weiss. "Now that our study has shown that energy metabolism in the human heart can be measured with an MRI scanner to predict heart failure outcomes, future studies are needed to determine the factors that impair energy metabolism in heart failure."

The researchers say this imaging method to measure energy metabolism could now be used in combination with other determinants of risk to provide a more complete picture of heart failure prognosis, helping doctors better plan the course of treatment for their patients.

According to the Centers for Disease Control, heart failure costs the nation an estimated $32 billion each year, including the cost of health care services, medications to treat heart failure and missed days of work. About half of the people who develop heart failure die within five years of diagnosis. The cause of non-ischemic heart failure, which is not due to blockages in coronary arteries and heart attack, is often unknown, but it can include high blood pressure, diabetes, infections and certain inherited conditions.

More information: "Metabolic Rates of ATP Transfer Through Creatine Kinase (CK Flux) Predict Clinical Heart Failure Events and Death," by P.A. Bottomley et al. *Science Translational Medicine*, 2013.

Provided by Johns Hopkins University School of Medicine