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Long-Term Use of LVADs Induces Heart Muscle Regeneration

Researchers at UT Southwestern Medical Center have found that long-term use of a left ventricular assist device (LVAD) by patients with heart failure may induce regeneration of heart muscle by preventing oxidative damage to a cell-regulator mechanism. Their study appears online in the *Journal of the American College of Cardiology* .

The study looked at pre- and post-LVAD samples of heart muscle in 10 patients with heart failure. Senior researcher Dr. Hesham Sadek, assistant professor of internal medicine at UT Southwestern, and colleagues examined the paired tissue samples for markers of DNA damage and cell proliferation.

LVADs are mechanical pumps that are sometimes implanted in patients who are awaiting heart transplants. LVADs substitute for the damaged heart by pumping blood throughout the body. Dr. Sadek et al. explained that, by assisting the damaged heart, LVADs would alleviate oxidative damage that occurs within the heart-muscle cells.

“We looked at markers of what is called the DNA damage response in cardiomyocytes (heart-muscle cells) of these patients,” Dr. Sadek said. “The response is composed of a cascade of proteins that is activated in response to DNA damage and in turn shuts off the ability of cardiomyocytes to divide. We found that patients who were on LVAD for more than six months had significantly decreased levels of DNA damage response.”

Dr. Sadek's team also examined the paired tissue samples for markers of cell division. They observed that patients who were on LVADs for six months or longer had a remarkable increase — nearly triple — in cardiomyocyte proliferation.

“This result shows that patients with mechanical assist devices have the ability to make their muscle cells divide,” Dr. Sadek pointed out. “And the obvious question now is, ‘Are these hearts regenerating? Could LVADs be used as a cure for heart failure?’”

Heart failure is a debilitating and deadly disease in which the heart, as a result of injury, cannot pump blood efficiently and hence cannot provide sufficient oxygen to organs throughout the body. About 6 million people in the United States are living with heart failure, according to the American Heart Association. The number is expected to soar within the next 20 years as the population ages and as heart-attack treatments improve and more people survive heart attacks.

“Putting in a mechanical pump rests the heart and apparently sends a signal to make new heart cells. This is the first time that this phenomenon has been shown to occur in human heart failure,” said Dr. Pradeep Mammen, associate professor of internal medicine at UT Southwestern and co-senior author of the study, which builds on earlier work with mice that demonstrated that newborn mammalian hearts are capable of a strong, regenerative response to injury by activating cell division.

The earlier studies further showed that the ability to respond to injury is lost due to changes in circulation that occur after birth, which lead to a more oxygenated environment in the heart, ultimately causing oxidative damage to the cellular machinery that controls heart-muscle regeneration.

Dr. Sadek's new research is “exciting,” according to Dr. Joseph Hill, Chief of Cardiology at UT Southwestern. "The findings raise the prospect of reawakening otherwise quiescent cardiac muscle cells, coaxing them into regenerating new and healthy cells. This has been an overarching objective of the field for many years. The next step will be to leverage these exciting results to rebuild the failing heart,” explained Dr. Hill, professor of internal medicine and molecular biology.

The study is supported by grants from the National Institutes of Health (NIH) and the Foundation for Heart Failure Research.

Dr. Sadek and Dr. Mammen are members of the newly established Hamon Center for Regenerative Science and Medicine, made possible by a $10 million endowment gift from the Hamon Charitable Foundation. The Center’s goal is to understand the basic mechanisms for tissue and organ formation, and then to use the knowledge to regenerate, repair, and replace tissues damaged by aging and injury.

Source: UT Southwestern Medical Center
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Published on : Sat, 24 Jan 2015