Research to assess safety and effectiveness of stem cells as potential treatment for heart failure

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Stem cells are being tested at the Medical University of South Carolina as a possible treatment for heart failure with a preserved ejection fraction, or HFpEF. The condition causes severe disability and kills half its victims within five years.

Research to test the safety and effectiveness of the treatment is being funded by the Department of Defense. HFpEF occurs earlier in veterans than civilians.

Cardiologist Michael Zile, M.D., who is directing the trial, said the funding underscores the growing importance of research involving this condition. HFpEF has been called an emerging epidemic. It shows up more often in women than men and appears to be more severe in African-Americans.

"To date, there are no management strategies that reduce morbidity and mortality or reduce disability in patients with HFpEF. These facts emphasize the presence of a large unmet need in our community. This is the challenge we're working to overcome by developing novel approaches to therapy," Zile said.

The MUSC team is working with investigators from the Cedars-Sinai Heart Institute and Capricor, the biotechnology company that makes the unique form of heart stem cells called cardiosphere derived cells, or CDCs.

The trial is called Regress-HFpEF, and enrollment is now underway at MUSC. Some people with HFpEF are so desperate for help that once word got out that this trial was about to begin, his team started getting calls from across the country.

"What's exciting is that we have an opportunity to change the function of the cells that actually make the patient ill," Zile said.

The $10 million Department of Defense grant is designed to come up with a better treatment for a really frustrating problem.

"I've had to look patients in the eye and say, 'You have a deadly disease that's going to kill you and limit your ability to live your life, and I have very little that will improve your symptoms and nothing that will keep you from being hospitalized or dying from this,'" Zile said.

"That represents, in my view, the most important unmet need in cardiology in 2016."

The trial will test a process developed by Eduardo Marban, M.D., of the Cedars Sinai Heart Institute. Cardiosphere-derived cells, or CDCs, which come from the muscle tissue of donor hearts, will be injected into the hearts of patients with HFpEF.

"The CDCs are delivery trucks," Zile said. And they're carrying what may be life saving packages.

In people with HFpEF, the heart muscle gets stiff and can't relax normally between contraction. That prevents the ventricles from filling with blood. It's also known as diastolic heart failure.

The culprit is malfunctioning heart cells. "They may be missing a protein peptide or making the wrong kind of protein or peptide," Zile said. "Or the controlling mechanisms, the RNA and DNA that control the production of these proteins and peptides, may be misaligned."

The CDCs will deliver good proteins, peptides, RNA and DNA. The hope is that they can reprogram cells in the patient's heart. "Instead of acting in a pathological way, they correct that," Zile said.

Heart failure affects about five million people in the U.S., according to the Heart Failure Society of America. While "failure" makes it sound like the heart has stopped working, it actually means that the heart is weakened and getting worse over time. About half of all heart failure patients have HFpEF.

Women are twice as likely as men to develop HFpEF, possibly because of a gender-specific way their bodies adapt to the high blood pressure that can come with aging. Veterans are more vulnerable, too, because they have a lot of

the conditions that result in HFpEF.

"They have a lot of hypertension, coronary disease, diabetes," Zile said. "Some of this comes from the fact that they're people who have served their country and suffered some disabling issue in many cases. And we know that veterans get heart failure preserved EF at a young age. In fact, they get it at least a decade earlier. The veterans get it at sixty and 50 instead of 70."

Zile hopes to enroll 40 people in the Regress HFpEF study, including veterans, MUSC Health patients and people from other institutions. "If people are at Roper or Trident or St. Francis or Summerville or anyplace else, and they have a patient who has heart failure preserved EF and they'd like us to provide some consultation and expertise, we're happy to do that," Zile said.

"We don't want to remove the patients from their physicians they're comfortable with. We just want to invite them to participate in this novel study."

Previous research by Zile and colleagues at Cedars-Sinai Heart Institute, published in the Journal of the American College of Cardiology Basic and Translational Science, found that the heart stem cell therapy worked in the lab, getting heart function back to normal. Now they want to find out if it works in patients.

The Regress HFpEF study is one of four projects underway at MUSC designed to improve treatment for people with HFpEF.

The others include:

-A study testing whether weight loss for patients with HFpEF reduces their symptoms

-The Paragon trial, which tests whether an investigational heart failure medicine made by Novartis can help people with HFpEF

-The Reduce LAP (left atrial pressure) trial, which evaluates whether a mechanical device can reduce left atrial pressure in patients with heart failure.

Data from the Regress HFpEf trial that Zile is directing will do more than test the effectiveness of heart stem cell infusions. It will also be sent to other laboratories where researchers will try to determine what specific changes are occurring that help the stem cell treatments work, find biomarkers to help predict which patients will do well with stem cell therapy, identify protein changes before and after the treatments and explore the role of calcium in HFpEF.

Zile said the overall goal is simple. "We want people to live longer and live better."

Source:
Medical University of South Carolina
