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Not too late to repair: Gene therapy improves advanced heart failure in animal model

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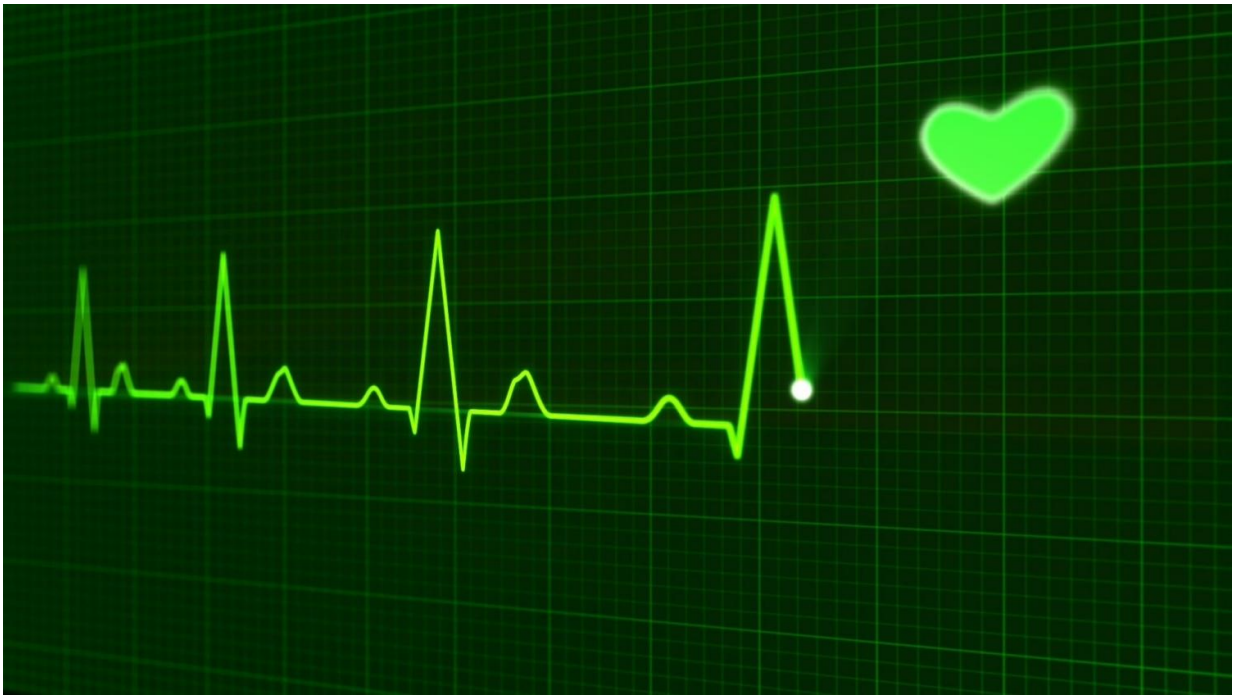

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Heart failure remains the leading cause of mortality in the U.S. During a heart attack blood stops flowing into the heart. Without oxygen, part of the heart muscle dies. The heart muscle does not regenerate; instead, it replaces dead tissue with a scar made of cells called fibroblasts that do not help the heart pump. If there is too much scarring, the heart progressively enlarges, or dilates, weakens and eventually stops working.

"The current thought is that advanced or chronic heart failure, a stage in which the cardiac muscle has become too weak, is a point of no return. The present understanding is that it is not possible to stimulate a heart in this condition to generate new heart cells to repair itself and that only palliative treatment is available to patients," said corresponding author Dr. Tamer M. A. Mohamed, associate professor of surgery and medicine and director of cardiac regeneration at Baylor College of Medicine.

"In this study published in the journal *Cardiovascular Research*, we show that advanced heart failure can be treated to improve cardiac function in an animal model."

In a previous study, Mohamed and his collaborators had successfully used gene therapy to improve acute cardiac dysfunction in animals. Their method effectively and specifically delivered genes that promote proliferation to heart cells, generating new heart muscle. This approach not only strengthened the heart improving its ability to keep the blood flowing, but also prevented typical subsequent congestion in the liver, kidneys and lungs in rats and pigs.

"In this study, we did something that had not been done before," Mohamed said. "We intervened with the same gene therapy but not during acute heart failure or early in the disease as in our previous experiments, but late in the disease during the chronic phase four weeks after cardiac injury had severely damaged the heart."

Four months after treating the animals, the researchers checked cardiac function and heart structure. "We were surprised to see evidence of significant heart cell proliferation, a marked reduction in scar size and a significant improvement in cardiac function," said first author Dr. Riham R E Abouleisa, assistant professor of surgery-cardiothoracic surgery at Baylor. "Although heart dilation and lung congestion associated with chronic heart failure were not improved, the treatment

partially improved liver and kidney functionality."

"The findings show for the first time that contrary to expectations, it is possible to induce heart cell proliferation during advanced states of heart failure and improve heart function, with some beneficial effects on the liver and kidneys' functions."

"Our work has important implications for the large group of patients with advanced heart failure for whom there are currently no treatments to improve their condition," Mohamed said. "This approach offers the possibility of developing future new therapies for this deadly disease."

More information: Riham R E Abouleisa et al, Gene therapy encoding cell cycle factors to treat chronic ischemic heart failure in rats, *Cardiovascular Research* (2024). DOI: 10.1093/cvr/cvae002

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