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Therapy with bone marrow-derived stem cells does not improve short-term recovery after heart attack

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Administering to patients stem cells derived from their own bone marrow either three or seven days after a heart attack is safe but does not improve heart function six months later, according to a clinical trial supported by the National Institutes of Health.

The results of the trial, called Transplantation In Myocardial Infarction Evaluation (TIME), mirror a previous, related study, LateTIME, which found that such cells (called autologous stem cells) given two to three weeks after a heart attack did not improve heart function. Both TIME and LateTIME were conducted by the Cardiovascular Cell Therapy Research Network (CCTRN), sponsored by the NIH's National Heart, Lung, and Blood Institute.

The findings will be presented Tuesday, Nov. 6, at the American Heart Association (AHA) 2012 Scientific Sessions in Los Angeles and will appear concurrently in the Journal of the American Medical Association.

"This study was extremely valuable even though it did not provide a demonstrated health benefit after six months," said Sonia Skarlatos, Ph.D., deputy director of NHLBI's Division of Cardiovascular Sciences and member of the CCTRN. "Heart stem cell therapy research is still in its infancy, and results from early trials have varied greatly due to differences in the numbers of stem cells injected, the delivery methods used, and the compositions of the study populations. With TIME and

LateTIME, we have established both safety and baseline results in two large studies that followed the same procedures for growing and then administering stem cells. This standard will inform the next steps in research on the use of stem cells to repair damaged hearts."

"With this baseline now set, we can start to adjust some of the components of the protocol to grow and administer stem cell to find cases where the procedure may improve function," added fellow CCTRN member Jay Travese, M.D., of the Minneapolis Heart Institute, who will present the results at the meeting. "For example, this therapy may work better in different population groups, or we might need to use new cell types or new methods of delivery."

Skarlatos noted that another advantage of the TIME study is that CCTRN is storing samples of the stem cells taken from the participants. Investigators can examine the relationship between people who showed significant improvement during the study and the characteristics of their stem cells. Such a comparison may offer insights on the cell traits that are associated with clinical improvement.

Between July 2008 and February 2011, TIME researchers enrolled 120 volunteers (average age 57, 87.5 percent male) who suffered from moderate to severe impairment in their left ventricles – the part of the heart that pumps oxygen-rich blood to the body – and had undergone stenting procedures following heart attacks. Those selected for the trial were assigned randomly to one of four groups: day three after heart attack stem cell injection, day three after heart attack placebo injection, day seven after heart attack stem cell treatment, or day seven after heart attack placebo treatment. The researchers developed a method of processing and purifying the stem cells to ensure that participants in the stem cell groups received a uniform dose of 150 million cells about 8 hours after the cells were harvested from their bone marrow. This ensured that results would not be skewed by differences in the quantity

or quality of stem cells administered.

Researchers assessed heart improvement six months after stem cell therapy by measuring the percentage of blood that was pumped out of the left ventricle during each contraction (known as the left-ventricular ejection fraction, or LVEF). The study found no significant differences between the change in LVEF readings at the six-month follow-up in either the day three or the day seven stem cell groups compared with placebo groups or with each other. Every group showed about a three percent improvement in LVEF.

More information: Cardiovascular Cell Therapy Research Network: www.cctrn.org
The TIME study: clinicaltrials.gov/ct2/show/NCT00684021
The Late TIME study: clinicaltrials.gov/ct2/show/NCT00684060

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