Rebuilding blood vessels through gene therapy

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(Medical Xpress)—Diagnosed with severe coronary artery disease, a group of patients too ill for or not responding to other treatment options decided to take part in a clinical trial testing angiogenic gene therapy to help rebuild their damaged blood vessels. More than 10 years later, in a follow-up review of these patients, doctors at Baylor College of Medicine, Weill Cornell Medical College (where the clinical trial and review took place) and Stony Brook University Medical Center report the outcomes are promising and open the door for larger trials to begin.

The study, which appears online in the journal Human Gene Therapy, followed 31 Weill Cornell patients who were diagnosed with severe coronary artery disease and were given a direct injection into their heart muscle of gene therapy called adenovirus encoding angiogenic growth factor, or AdVEGF121. Study results show the five- and 10-year survival rate of those patients were just as good and, in some cases better, than what is seen in other groups with similar heart issues treated with traditional medical therapy.

"The results of this 10-year gene therapy study are important," said co-senior author Dr. Ronald G. Crystal, chairman and professor of Genetic Medicine at Weill Cornell Medical College. "After long-term follow-up, the patients who received angiogenic gene therapy appear to have improved outcomes. The study results give us greater insight into the safety and effectiveness of gene therapy to rebuild blood vessels in patients living with coronary artery disease."

"At the time when the trial began, there were no comparisons available to tell us what to expect, which is why we are so pleased with the results," said co-senior author Dr. Todd Rosengart, professor and chair of the Michael E. DeBakey Department of Surgery at Baylor College of Medicine, formerly of Stony Brook University Medical Center. "We only had an idea of what the outcome might be based on promising studies in the lab, so there was concern, but those who received this treatment really had no other treatment options."

The common treatment for severe coronary artery disease is coronary artery bypass surgery, which works by redirecting blood flow around the diseased or blocked area of the heart. However, for those involved in this trial, the blood vessels that normally would be used to redirect the flow of blood were not healthy enough to do so.

In the study, patients were divided into two groups. Group A received both conventional coronary artery bypass grafting and gene therapy, while group B received only gene therapy. There was no control group. The gene therapy helped rebuild weak and damaged blood vessels in these patients. Medical records, follow-up interviews and questionnaires were used to determine patient outcomes. For Group A, the survival rate was 40 percent and Group B was 31 percent at the 10-year follow-up mark. Of the 18 patients who died, causes of death ranged from cancer to cardiac related issues.

"While there were health issues that needed additional treatments, such as cardiac revascularization and implantable cardioverter-defibrillators among both groups, overall this group of individuals had an outcome greater than what we believe they would have if they had not received the gene therapy," Rosengart said.

"We found no evidence of safety issues that resulted from the gene therapy," Crystal said. "Given the concerns about gene therapies during

the time when this trial originated, this is one of the very few long-term gene therapy studies that is very encouraging from a patient safety basis."

According to researchers, the next step is further research to study larger groups of patients and to create a placebo control study to compare outcome results. Weill Cornell Medical College, Weill Cornell Medical College-Qatar and Baylor College of Medicine are collaborating on a new clinical trial currently in the planning stages.

Provided by Weill Cornell Medical College