SVR Yields No Additional Benefit With Bypass

BY BRUCE JANCIN

ORLANDO — Coupling surgical ventricular reconstruction with coronary artery bypass grafting in patients with severe ischemic heart failure provided no survival or quality of life benefits over surgery alone in the largest randomized trial in cardiac surgery.

"These are definitive findings, and we have to conclude from them that there is no justification to offer [surgical ventricular reconstruction] to these patients, Dr. Robert H. Jones said in presenting the Surgical Treatment for Ischemic Heart Failure (STICH) trial results at the annual meeting of the American College of Cardiology.

STICH, funded by the National Heart, Lung, and Blood Institute, randomized 1,000 patients with left ventricular heart failure, an ejection fraction of 35% or less, and coronary artery disease suitable for coronary artery bypass grafting to CABG alone or CABG plus surgical ventricular reconstruction (SVR), an operation designed to reduce the size of the dilated ventricle and normalize the damaged heart's shape.

During the past decade, SVR has generated excitement among cardiac surgeons, based on the fact that beta-blockers, ACE inhibitors, and other highly effective medications for heart failure make the hypertrophic heart smaller and more normal-shaped. Surgeons reasoned that mechanically reshaping and downsizing the hypertrophic heart might similarly improve clinical outcomes.

"Now we know that it does not," said Dr. Jones, professor of surgery at Duke University, Durham, N.C. Dr. Jones was the principal investigator for the STICH trial (N. Engl. J. Med. 2009;360:1705-16).

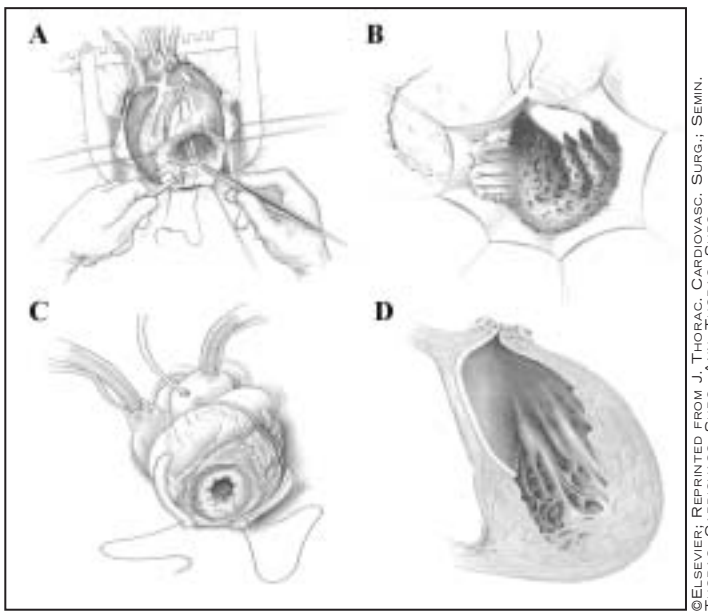
During a median follow-up of 48 months, the primary study end point of all-cause mortality or cardiac hospitalization occurred in 58% of the CABG-plus- SVR group and 59% of those who underwent CABG alone.

The STICH trial included an in-depth quality of life assessment led by Dr. Daniel Mark, director of outcomes research at the Duke Clinical Research Institute.

"We looked at a variety of different ways of assessing quality of life, including heart failure–specific quality of life, and found no evidence that the patients who received SVR on top of their bypass operation did any better or were in any way different in their long-term outcome out to 3 years compared to patients who got bypass surgery alone," he said.

Hospital costs averaged more than $14,500 higher in the SVR-plus-bypass group, mostly because they spent more time in intensive care, Dr. Mark added.

STICH is a milestone study not only because of its size and clarity, but also because it's the first major comparative effectiveness study examining two different cardiac surgical strategies, he said.



Surgical ventricular reconstruction methods shown here are Dor (A), Jatene (B), McCarthy (C), and Mickleborough (D).

" The tendency of cardiac surgery and, I think, other forms of surgery has been to evolve in an anecdotal fashion," Dr. Mark said.

Discussant Marvin A. Konstam said that the amount of reduction in end systolic volume achieved in the SVR recipients clearly indicates the STICH surgeons did an effective job of decreasing ventricular wall stress. It is noteworthy that this did not translate into improved outcomes, considering the abundant evidence that doing so pharmacologically does, he said.

This suggests that pharmacologic reduction of end systolic volume by reducing the amount of pathologic myocyte hypertrophy is a very good thing, but when a reduction in end systolic volume is achieved simply structurally it might not have the same benefit, said Dr. Konstam, chief of cardiology at Tufts Medical Center, Boston.

The STICH trial continues, with another 1,212 ischemic heart failure patients who have been randomized to intensive medical therapy alone or in conjunction with CABG. They will be followed for another 2 years. This study has potentially far-reaching impact for all of cardiovascular medicine, Dr. Jones stressed.

"If we find in another 2 years that intensive medical therapy has gotten so good that there's not much room for surgery to further improve outcomes, it's going to change a whole lot of cardiology," from noninvasive testing to how many cardiac caths get done, he said. ■

REVERSE Results Portend Expanded Indications for CRT

BY BRUCE JANCIN

ORLANDO — Cardiac resynchronization therapy improves key clinical outcomes in patients with mild heart failure, a randomized trial has shown.

In the European cohort of the Resynchronization Reverses Remodeling in Systolic Left Ventricular Dysfunction (REVERSE) trial, patients with cardiac synchronization therapy switched on had a 62% relative risk reduction in the combined end point of heart failure hospitalization or death compared with those assigned to CRT-off, at 24 months' follow-up, Dr. Cecilia Linde said at the annual meeting of the American College of Cardiology.

Patients with the CRT device turned on also had significantly improved left ventricular function, as reflected in their ejection fraction and end-diastolic and end-systolic volumes (see box). All these outcomes combined suggest that reverse ventricular remodeling had occurred, added Dr. Linde, professor of cardiology at Karolinska Hospital, Stockholm.

The European follow-up analysis, prespecified in the double-blind prospective REVERSE study, involved 262 patients who underwent implantation of a biventricular pacemaker and were then randomized 2:1 to have CRT switched on or off.

All subjects had New York Heart Association class II or previously symptomatic class I heart failure, a left ventricular ejection fraction of 40% or less, and a wide QRS interval of at least 120 ms. All were on optimal guideline-recommended medical therapy.

The goal of REVERSE was to learn whether heart failure patients who improved with medications to the point of being asymptomatic or mildly symptomatic could maintain that status with CRT. The answer, Dr. Linde said, is yes.

There was a 10% major complication rate related to the CRT devices in REVERSE. Lead dislocation, perforation of the coronary sinus, and other complications were concentrated in the left ventricular lead during the first year and the right lead in year 2.

The 12-month REVERSE results, presented last year, showed only a nonsignificant trend favoring better outcomes in the CRT-on group. Why the difference a year later?

"It takes time to have an effect in patients with asymptomatic or mildly symptomatic heart failure, so of course when you follow patients for 24 months you're going to find more than if you follow them for 12 months," she observed.

Today CRT is indicated for patients with class III or ambulatory class IV heart failure. Dr. Linde predicted that if the new REVERSE findings are confirmed in the Automatic Defibrillator Implantation With Cardiac Resynchronization Therapy (MADIT-CRT) trial and Rythmol SR Atrial Fibrillation Trial (RAFT), the indications for CRT will broaden to incorporate the large population of patients with class I and II heart failure along with a low ejection fraction and wide QRS interval.

Discussant Richard L. Page said he found it difficult to reconcile the enhanced LV function and improved clinical outcomes seen with CRT in REVERSE with the observed lack of functional and symptomatic improvement. The CRT on and off groups did not differ significantly at 24 months in the 6-minute walk test, Minnesota Living With Heart Failure Questionnaire, or NYHA class, noted Dr. Page, professor of medicine at the University of Washington, Seattle.

Dr. Jean-Claude Daubert of the REVERSE steering committee replied that since most patients were asymptomatic or mildly symptomatic at entry, there was little room for functional or symptomatic improvement.

"We suspect that to show functional benefit we'll need a much longer follow-up," said Dr. Daubert, professor of cardiology at Central University Hospital, Rennes, France.

REVERSE was sponsored by Medtronic. Dr. Linde and Dr. Daubert are consultants to, and are on the speakers bureaus for, Medtronic and St. Jude Medical. ■

Two-Year Outcomes in REVERSE Subanalysis

Outcome	CRT On	CRT Off
First heart failure hospitalization or death	12%	24%
Clinical worsening	19%	34%
LV ejection fraction (baseline 28%)	35%	30%
LV end-systolic volume (baseline 95 mL/m^2)	69.7	94.5
LV end-diastolic volume (baseline 131 mL/m^2)	103	132

Note: Based on a European cohort of 262 patients. All differences between groups are statistically significant.
Source: Dr. Linde