Myocardial viability and impact of surgical ventricular reconstruction on outcomes of patients with severe left ventricular dysfunction undergoing coronary artery bypass surgery: Results of the Surgical Treatment for Ischemic Heart Failure trial

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Objectives: In the Surgical Treatment for Ischemic Heart Failure trial, surgical ventricular reconstruction plus coronary artery bypass surgery was not associated with a reduction in the rate of death or cardiac hospitalization compared with bypass alone. We hypothesized that the absence of viable myocardium identifies patients with coronary artery disease and left ventricular dysfunction who have a greater benefit with coronary artery bypass graft surgery and surgical ventricular reconstruction compared with bypass alone.

Methods: Myocardial viability was assessed by single photon computed tomography in 267 of the 1000 patients randomized to bypass or bypass plus surgical ventricular reconstruction in the Surgical Treatment for Ischemic Heart Failure. Myocardial viability was assessed on a per patient basis and regionally according to prespecified criteria.

Results: At 3 years, there was no difference in mortality or the combined outcome of death or cardiac hospitalization between those with and without viability, and there was no significant interaction between the type of surgery and the global viability status with respect to mortality or death plus cardiac hospitalization. Furthermore, there was no difference in mortality or death plus cardiac hospitalization between those with and without anterior wall or apical scar, and no significant interaction between the presence of scar in these regions and the type of surgery with respect to mortality.

Conclusions: In patients with coronary artery disease and severe regional left ventricular dysfunction, assessment of myocardial viability does not identify patients who will derive a mortality benefit from adding surgical ventricular reconstruction to coronary artery bypass graft surgery. (J Thorac Cardiovasc Surg 2014;148:2677-84)

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Supplemental material is available online.

The Surgical Treatment for Ischemic Heart Failure (STICH) trial demonstrated that in patients with ischemic cardiomyopathy and anterior wall akinesis undergoing coronary artery bypass grafting (CABG), the addition of surgical ventricular reconstruction (SVR) was not associated with a reduction in the rate of death or hospitalization for cardiac causes compared with results of CABG alone.[1] All patients in the SVR hypothesis of STICH were required to have global left ventricular (LV) dysfunction (ejection fraction $\leq$35%) and regional dysfunction with anterior

Abbreviations and Acronyms

CABG = coronary artery bypass grafting
CAD = coronary artery disease
LV = left ventricular
SPECT = single photon emission computed tomography
STICH = Surgical Treatment for Ischemic Heart Failure
SVR = surgical ventricular reconstruction

akinesia or dyskinesia, as determined by the recruiting investigators. However, whether these dysfunctional segments were composed of scarred or viable myocardium was not analyzed in the original report, because systematic application of a dedicated test for myocardial viability was not part of the original study design or a determinant of treatment assignment.

Although viable myocardium is expected to recover after revascularization, scarred tissue is not. Further, a large amount of scarred myocardium may contribute negatively to overall LV function by accelerating or worsening the process of remodeling and by reducing the mechanical contribution of normal or viable myocardium via tethering of adjacent segments. Therefore, excluding scarred anterior wall segments through SVR could result in hemodynamic and clinical improvement. Conversely, identification of myocardial viability in the same areas could lead to the retention of segments with the potential to recover after revascularization without SVR and contribute to improved LV mechanical function. Accordingly, distinguishing between viable versus scarred myocardium in the LV territory targeted for reconstruction may be critical for the success of the procedure and could identify a population who will preferentially benefit from SVR.

Single photon emission computed tomography (SPECT) is commonly performed in patients with LV dysfunction being considered for revascularization to identify areas of viable and scarred myocardium. Therefore, we tested in the STICH population the hypothesis that the presence of myocardial scar on SPECT identifies patients with coronary artery disease (CAD) and LV dysfunction who have the greatest benefit with CABG + SVR compared with CABG alone.

METHODS

Study Design

The rationale and design of the STICH trial have been described,[1-3] as have the methods of the viability substudy of the STICH revascularization hypothesis.[4] STICH was a multicenter, nonblinded, randomized trial sponsored by the National Heart, Lung, and Blood Institute. A total of 2136 patients were enrolled at 127 sites in 26 countries, all of whom were candidates for CABG. STICH involved 2 hypotheses regarding the role of surgery in patients with LV systolic dysfunction. All patients in STICH were eligible for CABG on the basis of clinical and coronary angiographic findings. The STICH revascularization hypothesis enrolled patients who were candidates for CABG or medical therapy, thus excluding patients with left main disease or unstable angina.[3] The STICH SVR hypothesis enrolled patients who were candidates for CABG who also had severe regional dysfunction of the LV anterior wall and were eligible for SVR.[1] In this arm of the trial, 1000 patients were enrolled, of whom 499 were assigned to CABG alone and 501 were assigned to CABG plus SVR. Myocardial viability testing was performed using SPECT in 267 of the 1000 patients, of whom 126 were assigned to CABG alone and 141 were assigned to CABG plus SVR. An independent core laboratory funded by the National Heart, Lung, and Blood Institute, in which investigators were unaware of study group assignments and the individual characteristics of patients, coordinated data collection and analysis for the SPECT studies.

Study Procedures

Four different clinically validated SPECT protocols for assessing myocardial viability were permitted at the enrolling sites. These included thallium imaging using a rest-redistribution or stress-rest-reinjection protocol,[5] a dual isotope protocol with rest-redistribution thallium imaging plus stress imaging with a technetium-99m perfusion tracer,[6] or imaging with a technetium-99m tracer at rest after the administration of nitroglycerin.[7] Images were stored digitally and sent to the STICH Radionuclide Core Laboratory at Northwestern University for analysis. Core laboratory measurement of regional tracer activity was performed on all SPECT studies using a 17-segment model of the left ventricle.[8] A myocardial segment was deemed viable if the tracer activity in that segment was 50% or greater of the activity in the segment with maximal activity. For thallium rest-redistribution imaging, a segment with activity less than 50% of the maximal myocardial activity on the redistribution images was also defined as viable if the improvement in activity from the rest to redistribution images was 12% or greater. Segments not meeting these criteria for viability were deemed to be scarred.

Myocardial viability on a per-patient basis was prospectively defined as the presence of 11 or more viable segments (≥65% of the entire left ventricle). When 7 or more segments were nonviable (≥41% of the left ventricle), the patient was considered to have insufficient mass of viable myocardium. This threshold was selected on the basis of previous retrospective data indicating that the likelihood for functional improvement after CABG is low when more than 40% of the LV myocardium is nonviable.[9]

Because the SVR procedure involves reconfiguring the anteroapical wall, we specifically explored the impact of anterior wall and apical scarring on the outcomes with CABG alone and CABG + SVR. For this analysis, viability was assessed using a 5-segment model in which the left ventricle was divided into septal, inferior, lateral, anterior, and apical segments (Figure E1).

Patient Follow-up and Outcomes

After enrollment, patients were followed every 4 months for the first year and every 6 months thereafter. The primary outcome was the composite of death from any cause or hospitalization for cardiovascular causes. The secondary end point was death from any cause. Definitions of the trial end points have been reported.[3] All end points were adjudicated by an independent clinical events committee. The comparisons of outcomes that were related to treatment were based on intention-to-treat analyses. Analyses that were based on actual treatment received were also performed to account for crossovers.

Statistical Analysis

Baseline patient characteristics are summarized as percentages for categoric variables and means and standard deviations for continuous variables. Comparisons of baseline data between (a) patients with and without a viability test, and (b) patients with and without myocardial viability, given that a test was obtained, were performed using the Pearson chi-square test for categoric variables and the Wilcoxon rank-sum test for continuous variables. Kaplan–Meier event curves for mortality and for death or cardiac