The rationale and design of the Surgical Treatment for Ischemic Heart Failure (STICH) trial

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Received for publication March 28, 2007; accepted for publication May 11, 2007.

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J Thorac Cardiovasc Surg 2007;134:1540-7

0022-5223/$32.00

doi:10.1016/j.jtcvs.2007.05.069

Objectives: The rationale and design of the Surgical Treatment for Ischemic Heart Failure trial is described. Before the Surgical Treatment for Ischemic Heart Failure trial, less than 1000 patients with ischemic cardiomyopathy had been studied in randomized comparisons of medical therapy versus coronary artery bypass grafting. Trial data reflect how these therapies were delivered more than 20 years ago and do not indicate the relative benefits of medical therapy versus coronary artery bypass grafting in contemporary practice.

Methods: Randomization of consenting patients with heart failure, left ventricular ejection fraction of 0.35 or less, and coronary artery disease is based on whether patients are judged by attending physicians to be candidates only for coronary artery bypass grafting or can be treated with medical therapy without coronary artery bypass grafting. Patients eligible for surgical ventricular reconstruction because of significant anterior wall akinesis or dyskinesis but ineligible for medical therapy are randomly assigned to coronary artery bypass grafting with or without surgical ventricular reconstruction. Patients eligible for medical therapy are randomly assigned between medical therapy only and medical therapy with coronary artery bypass grafting. Patients eligible for all 3 are randomly assigned evenly to medical therapy only, medical therapy and coronary artery bypass grafting, or medical therapy and coronary artery bypass grafting and surgical ventricular reconstruction. Major substudies will examine quality of life, cost-effectiveness, changes in left ventricular volumes, effect of myocardial viability, selected biomarkers, and selected polymorphisms on treatment differences.

Results: Enrollment is now complete in both STICH hypotheses. Follow-up will continue until sufficient end points are available to address both hypotheses with at least 90% power. The primary outcome of hypothesis 2 is expected to be reported in 2009. The primary outcome of hypothesis 1 is expected to be reported in 2011.

Conclusions: The Surgical Treatment for Ischemic Heart Failure trial is a National Heart, Lung, and Blood Institute–funded multicenter international randomized trial addressing 2 specific primary hypotheses: (1) coronary artery bypass grafting with intensive medical therapy improves long-term survival compared with survival with medical therapy alone, and (2) in patients with anterior left ventricular dysfunction, surgical ventricular reconstruction to a more normal left ventricular size plus coronary artery bypass grafting improves survival free of subsequent hospitalization for cardiac cause when compared with that with coronary artery bypass grafting alone.

The revascularization of patients with coronary artery disease (CAD) with left ventricular (LV) systolic dysfunction (SD) and symptomatic heart failure (HF) has been the subject of much debate and surprisingly little research over the past 30 years.[1,2] Our current understanding of how best to treat these patients stems from

Abbreviations and Acronyms

CABG = coronary artery bypass grafting
CAD = coronary artery disease
CASS = Coronary Artery Surgery Study
EF = ejection fraction
H1 = hypothesis 1
H2 = hypothesis 2
HF = heart failure
LV = left ventricular
MED = medical therapy
NHLBI = National Heart, Lung, and Blood Institute
PCI = percutaneous coronary intervention
SD = systolic dysfunction
SVR = surgical ventricular reconstruction

subset analyses of the coronary artery bypass grafting (CABG)–medicine clinical trials performed in the 1970s and early 1980s and analyses of large registries of patients from the same era.[3-7] Although such analyses have generally demonstrated that patients with more advanced CAD and more severe LV dysfunction derive larger benefit from CABG relative to medical therapy (MED), in practice both cardiologists and surgeons have substantial uncertainty about whether these projected benefits are counterbalanced by the increased early risks of the surgical approach.

In 2002, the National Heart, Lung, and Blood Institute (NHLBI) funded the Surgical Treatment for Ischemic Heart Failure (STICH) trial to address 2 pressing clinical and policy questions regarding the management of patients with HF with surgically revascularizable CAD and decreased LV function: (1) Is contemporary CABG surgery superior to contemporary medical/secondary prevention therapy in prolonging survival in these patients? (2) Among patients with significant anterior wall dysfunction, does the addition of surgical ventricular reconstruction (SVR) to CABG improve hospitalization-free survival?

Materials and Methods

Study Design

In the absence of definitive data on the value of CABG in high-risk patients with LVSD, wide diversity exists among providers about how to select patients. Moreover, many patients who might be CABG candidates also have dominant anterior akinesia or dyskinesia that might be reasonable to reconstruct surgically at the time of CABG.[8] Therefore the STICH trial was designed to let physicians first determine whether potential STICH patients were amenable to CABG after their routine clinical assessment. A threshold LV ejection fraction (EF) of 0.35 or less was established, with no lower limit set to preclude study entry. Physicians are encouraged to use any cardiac testing necessary to decide whether an individual patient is a candidate for CABG, SVR, or both. This philosophy encourages the use of standard practice to identify patients for whom responsible physicians are at equipoise about MED, CABG, and CABG with SVR and ensures that the STICH cohort has characteristics that now pose the greatest uncertainty in clinical decision making for patients with ischemic cardiomyopathy. Moreover, all information now commonly used by clinicians in deciding on surgical treatment for a subset of patients with ischemic cardiomyopathy will be available so that the value added by each component to the decision-making process can be evaluated (Table 1).

Subjects meeting the broad inclusion criteria of CAD amenable to CABG with an LVEF of 0.35 or less, without a specific exclusion, are segregated into 3 strata (A, B, and C) depending on investigator-determined suitability for continued MED alone and eligibility for SVR (Figure 1). Eligibility for MED alone is defined by the investigator but generally excludes patients with an intraluminal left main coronary artery stenosis of 50% or greater or severe disabling angina (Canadian Cardiovascular Society Class ≥III) unresponsive to nonsurgical interventions. Eligibility for SVR is defined as dominant LV akinesia or dyskinesia amenable to SVR. Stratum A subjects are defined as suitable for MED with or without CABG, and consenting patients are randomly assigned in a 1:1 ratio between MED alone or with CABG. Stratum B subjects, defined as eligible for all 3 treatment options, are randomly assigned 1:1:1 to either MED alone, MED with CABG, or MED with CABG and SVR. Subjects eligible for CABG with and without SVR are randomly assigned 1:1 in stratum C to either CABG or CABG with SVR. After stratum eligibility is established and informed consent is obtained, treatment allocation is made to a specific therapy based on an undisclosed permuted block randomization scheme.

Study Population

The STICH trial is designed to enroll at least 2000 men and women aged 18 years and older who have CAD amenable to revascularization and LVSD defined by a clinically determined LVEF of 0.35 or less. STICH trial entry criteria are summarized in Table 2. Patients awaiting a planned percutaneous coronary intervention (PCI) to treat symptomatic CAD within the next 30 days are not eligible, although previous PCI is not an exclusion. Although planned operative treatment of the aortic valve excludes potential candidates, the decision to pursue operative management of any other valves, specifically the mitral valve, is left to the discretion of responsible physicians and surgeons.

Baseline and follow-up studies. After obtaining informed consent, baseline demographics, physical examination, laboratory data, and medical details, including procedural history and details, are collected, and all patients undergo any remaining requisite baseline studies (Table E1). Patients eligible for MED alone enrolled into strata A and B undergo baseline radionuclide perfusion and viability imaging and a modified Bruce protocol exercise stress test, if they are able to exercise. SVR-eligible patients enrolled into strata B and C preferably undergo baseline cardiovascular magnetic resonance or gated single photon emission computed tomographic perfusion imaging with follow-up at 4 and 24 months to assess postoperative size, shape, and function.

All STICH subjects will undergo echocardiography and blood sampling for neurohormonal, cytokine, and genetic analyses; a detailed quality-of-life assessment; and a 6-minute walk test, if appropriate, based on subject status. These baseline studies are