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Clinical Characteristics of Patients Undergoing Surgical Ventricular Reconstruction by Choice and by Randomization

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- Objectives** The aim of this study was to confirm the generalizability of the conclusions of the STICH (Surgical Treatment for Ischemic Heart Failure) trial.
- Background** Surgical ventricular reconstruction (SVR) added to coronary artery bypass grafting (CABG) did not decrease death or cardiac hospitalization in STICH patients randomized to CABG with (n = 501) or without (n = 499) SVR.
- Methods** Baseline clinical characteristics of 1,000 STICH SVR hypothesis patients and 1,036 STICH-eligible Society of Thoracic Surgeons (STS) National Cardiac Database patients undergoing CABG plus SVR were entered into a multivariate model equation to predict a mortality that placed these 2,036 patients in 1 of 32 risk at randomization (RAR) groups. The number of patients in each RAR group profiled the risk of STICH treatment arms and of STICH and STS STICH-eligible patients.
- Results** That 85% of the 1,000 STICH patients known to have no significant differences in baseline characteristics between the 2 treatment arms shared the same RAR group suggests that the RAR methodology has sufficient accuracy to compare RAR profiles of STICH and STS patients. RAR group was shared by 1,522 of 2,036 STICH and STS STICH-eligible patients (75%) who underwent CABG plus SVR. Differences in baseline characteristics responsible for more low-risk STICH patients and more high-risk STS patients were modest. Cox proportional hazard ratios of 1,000 STICH patients in 3 RAR groups suggested by STICH and STS RAR differences showed no differential treatment effect on survival across the low-, intermediate-, and high-risk groups.
- Conclusions** The STICH conclusion of no benefit from adding SVR to CABG applies to a broad spectrum of CABG-eligible patients with ischemic cardiomyopathy. (Comparison of Surgical and Medical Treatment for Congestive Heart Failure and Coronary Artery Disease; NCT00023595) (J Am Coll Cardiol 2010;56:499–507) © 2010 by the American College of Cardiology Foundation

Surgical ventricular reconstruction (SVR) is a technical refinement of left ventricular (LV) aneurysmectomy. The objective of SVR is to arrest or reverse progressive global cardiac dilation and heart failure by acutely reducing LV volume and wall stress and thereby minimize the deleterious effect of regional dysfunction on total cardiac performance. The National Institutes of Health–funded international

randomized STICH (Surgical Treatment for Ischemic Heart Failure) trial's SVR hypothesis objective was to

See page 508

evaluate whether adding SVR to coronary artery bypass grafting (CABG) benefited patients with dominant anterior

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**Abbreviations
and Acronyms**

CABG	= coronary artery bypass grafting
DDCD	= Duke Databank for Cardiovascular Diseases
LV	= left ventricular
LVEF	= left ventricular ejection fraction
RAR	= risk at randomization
STS	= Society of Thoracic Surgeons
SVR	= surgical ventricular reconstruction

dysfunction (1). The 1,000 participating patients were randomized to CABG alone (n = 499) or CABG plus SVR (n = 501) and followed for a median of 48 months for the primary outcome of death or cardiac hospitalization (2). Cardiac symptoms and exercise tolerance improved significantly from baseline to a similar degree in both groups after surgery. Although CABG plus SVR reduced mean LV end-systolic and end-diastolic volumes more than CABG alone, the primary outcome of death or cardiac hospitalization did not

differ between the 2 treatment groups (3). This result surprised many cardiovascular specialists, who raised questions regarding whether the results of the STICH trial should be generalized to the broad spectrum of patients with ischemic cardiomyopathy (4).

Patient eligibility for the STICH trial required coronary artery disease amenable to CABG and left ventricular ejection fraction (LVEF) ≤ 0.35 . SVR eligibility required dominant anterior akinesia or dyskinesia amenable to CABG. Patients considered to be SVR candidates who did not need CABG and patients judged as definitely needing CABG plus SVR were not eligible for STICH. SVR-eligible patients could have been randomized in STICH stratum C to CABG with or without SVR. All stratum C patients were analyzed only in the STICH SVR hypothesis cohort. Patients eligible for evidence-based medical therapy alone and for CABG with or without SVR were randomized among these 3 treatment options in stratum B. Stratum B patients had a 2 in 3 chance of randomization to the STICH SVR hypothesis. Stratum B patients randomized to evidence-based medical therapy alone were compared with CABG in the surgical revascularization hypothesis. Stratum B patients randomized to CABG provided primary outcome data for both hypotheses. Stratum B patients randomized to CABG plus SVR were only analyzed in the STICH SVR hypothesis.

Patients were judged “amenable to CABG” on the suitability of coronary stenoses for bypass and the benefit expected from surgical revascularization. Patients were judged “amenable to SVR” on the extent and severity of anterior regional dysfunction in the context of global dysfunction. Patients with anterior dysfunction as an equivalent component of global dysfunction were not SVR candidates. Wide variation was apparent in the decisions cardiovascular specialists made about which patients were amenable to undergo either or both procedures. However, coronary artery disease and LV functional assessments used to define eligibility for operations were always considered in the context of overall baseline clinical risk. The rationale for

specific randomization decisions at clinical sites cannot be known. However, the baseline characteristics of the patient population resulting from these 1,000 equipoise decisions about the value of adding SVR to CABG can be fully characterized. The purpose of this report is to profile the risk spectrum of the STICH SVR hypothesis randomized cohort to compare with that of the Society of Thoracic Surgeons (STS) STICH-eligible patients undergoing CABG plus SVR by clinical choice using data entered prospectively into the STS National Cardiac Database. Placing STICH randomized patients in the clinical context of patients treated by choice defines the degree to which the results of the STICH trial can be generalized to future decisions about adding SVR to CABG in patients with ischemic cardiomyopathy.

Methods

STICH patient enrollment and baseline clinical data acquisition. Between September 12, 2002, and January 24, 2006, 96 clinical sites randomized 1,000 patients to treatment with CABG alone (n = 499) or CABG plus SVR (n = 501) (2). Four countries (Poland, n = 288; the U.S., n = 200; Canada, n = 154; and Italy, n = 93) accounted for 735 of the 1,000 STICH SVR hypothesis patients (74%). STICH clinical sites used standardized definitions to enter structured responses describing baseline clinical characteristics of each randomized patient on pages 1, 2, and 4 of STICH case report forms (5). Deficiencies, out-of-range entries, or conflicting answers were queried and corrected. Sites received reimbursement only for query-clean case report forms. Site-monitoring visits used primary source documents to confirm the accuracy of data entered. Secondary SAS (SAS Institute Inc., Cary, North Carolina) data analysis files were formatted in tabular form.

Baseline clinical data were complete for 56 of 64 fields of demographic and clinical data. Four of the 8 variables with missing data were laboratory values for hemoglobin (n = 2), creatinine (n = 2), sodium (n = 4), and blood urea nitrogen (n = 228). Coronary angiographic assessment of the proximal left anterior descending coronary artery was unavailable in 1 patient. History of renal insufficiency (creatinine ≥ 1.5 mg/dl) was unavailable in 2 patients. History of hyperlipidemia was unavailable in 3 patients. The initial protocol required reporting of a site-determined end-systolic volume index. However, this assessment was not consistently present on cardiac catheterization reports. This requirement, which severely limited patient enrollment, was removed (1). Site end-systolic volume index data were reported for only 620 patients, but LVEFs were reported for all 1,000 patients. Percent akinesia or dyskinesia of the anterior wall was reported in 577 STICH SVR hypothesis patients. The STICH protocol version 2 permitted the enrollment of patients using a site-determined LVEF ≤ 0.35 from echocardiography, cardiac magnetic resonance, gated single-photon emission computed tomography, or

contrast ventriculography. Each site was required to submit an echocardiogram to the Echocardiography Core Laboratory. The submission of cardiac magnetic resonance and gated single-photon emission computed tomographic ventriculograms for core laboratory reading was strongly encouraged. The relationship of core laboratory cardiac imaging study results to the primary STICH SVR hypothesis outcome will be addressed in future reports. The LV functional and mitral regurgitation assessments described in this report were those available to clinicians at the sites to inform decisions about patient randomization. Only 693 patients performed 6-min walk tests at baseline, and symptoms during the tests were reported in 671 patients.

Identification of STS patients as STICH eligible. In 1989, the STS created a voluntary database to support the prospective entry of baseline clinical data on cardiac surgical patients using standardized definitions. In 2002, SVR operations were first entered separately from LV aneurysmectomy using the definition “procedure that restores the geometry of the heart after an anterior myocardial infarction.” The SVR also was described as “distinct from an anterior LV aneurysmectomy and from a Batista procedure that only produces LV volume reduction.”

To obtain STICH-eligible patients, the STS CABG database was searched for patients with LVEFs ≤ 0.35 who underwent CABG during the 1,231-day STICH SVR hypothesis patient enrollment interval and did not have the STICH exclusion criteria of: 1) need for aortic valve replacement; 2) recent myocardial infarction; 3) concomitant lung cancer resection; or 4) ongoing shock. STS patients with operations coded as LV aneurysmectomy were not included. STS patients with LVEFs < 0.10 also were excluded because of concern for spurious data. Of the 104,135 STS patients identified as STICH eligible, 103,043 (99%) underwent CABG without SVR. After the exclusion of 25 patients from the STS CABG plus SVR cohort who were also randomized into STICH and underwent CABG plus SVR, 1,036 STS STICH-eligible patients (1%) underwent CABG plus SVR by choice. Although STS STICH-eligible patients had baseline characteristics consistent with STICH eligibility, the clinical choice of a CABG operation provides no evidence that these patients met the STICH SVR hypothesis entry criterion of dominant anterior akinesia or dyskinesia amenable to SVR. All STICH SVR hypothesis patients could have been randomized to a CABG plus SVR option. Baseline clinical characteristics were tabulated to compare the STS patients by operation received by choice with those in the total 1,000-patient STICH SVR hypothesis population.

Risk at randomization (RAR) methodology. The RAR index was developed to place randomized STICH patients at their appropriate positions on the full spectrum of risk of all STICH patients (2). The application of STICH enrollment criteria to patients in the Duke Databank for Cardiovascular Diseases (DDCD) produced a STICH-eligible Duke patient population from which multivariate modeling

was developed to predict 5-year mortality, assuming absence of surgical treatment. Baseline values for all prognostically important variables of each STICH randomized patient were entered into the multivariate equation to predict their 5-year mortality at the time of randomization. Patients were placed in order of increasing predicted risk. An RAR index was created to separate 32 groups that equally shared one-thirty-second of total predicted deaths using the constraint that the entire predicted mortality of each patient was assigned to only 1 group. Individual values of baseline characteristics for each STS STICH-eligible CABG plus SVR patient were entered into the DDCD equation to obtain their predicted baseline mortality. This mortality was used to select the 32 STICH RAR groups with the high and low mortality window that encompassed the predicted mortality for each of 1,036 STS STICH-eligible patients who received CABG plus SVR by clinical choice. The 9 STS patients with lower predicted mortality than any STICH patient constituted RAR group 0, without STICH patient representation. No STS patient had a higher predicted mortality than STICH patients in RAR group 32. STICH and STS STICH-eligible CABG plus SVR patients in each RAR group were assumed to share a sufficiently similar probability of death to serve as interchangeable couriers of baseline risk for clinical decision making. Because STS STICH-eligible patients who received CABG by choice cannot be known to be SVR eligible, the risk profile methodology was applied only to STS patients undergoing CABG plus SVR by choice. Hereafter, this 1,036-patient cohort of STS STICH-eligible CABG plus SVR patients is called the STS CABG plus SVR patients.

The risk profile of 499 STICH SVR hypothesis patients assigned to CABG without SVR is compared with that of the 501 STICH SVR hypothesis patients assigned to CABG plus SVR to assess the variability of the RAR methodology in these patients known to have no differences at the $p < 0.05$ level between the 2 treatment arms for any individual baseline characteristic. The RAR profile of the 1,000-patient STICH SVR hypothesis cohort was compared with the risk profile of the 1,036 STS CABG plus SVR patients. Different representation of STICH and STS CABG plus SVR patients was apparent in RAR groups 0 to 9, 10 to 19, and 20 to 32. Baseline characteristics of STICH and STS CABG plus SVR patients in these 3 risk zones were tabulated separately to compare the magnitude of differences in clinical characteristics responsible for the observed mismatch between the risk spectrum of the STICH and STS CABG plus SVR cohorts. Finally, using the Cox regression model, hazard ratios with 95% confidence intervals were calculated for CABG plus SVR versus CABG alone for the 391 STICH patients in RAR groups 1 to 9, 323 STICH patients in RAR groups 10 to 19, and 286 patients in RAR groups 20 to 32 to statistically test whether there was a difference in the effect of CABG plus SVR compared with CABG depending on the baseline RAR.

Results

A histogram of 1,000 STICH SVR hypothesis patients sorted by RAR index of increasing risk is compared with the 32 RAR interval values of selected baseline characteristics in Figure 1. The 64 lowest-risk patients in RAR group 1 had a median age of 49 years, a median LVEF of 0.31, and a median Duke coronary disease index of 39 (1 \geq 75% stenosis with either proximal left anterior descending stenosis or 50% to 75% left main stenosis). No patient had renal insufficiency (creatinine \geq 1.5 mg/dl), 6 patients had mitral regurgitation, and only 6 patients had diabetes. The 13 highest-risk patients in the RAR group 32 had a median age of 73 years, a median LVEF of 0.20, and a median Duke coronary disease index of 91 (3 \geq 75% stenoses with either \geq 95% proximal left anterior descending stenosis or 50%–75% left main stenosis). All 13 RAR group 32 patients had renal insufficiency, 4 patients had moderate or severe mitral regurgitation, and 7 patients had diabetes. Moreover, severe heart failure and vascular disease were more prevalent in this highest risk RAR group. These different combinations of baseline cardiac and noncardiac variables explain the continuous spectrum of increasing risk for the decreasing numbers of patients assigned to each RAR interval.

The same RAR group was shared by 85% of the 499 CABG and 501 CABG plus SVR STICH patients (Fig. 2). The 15% of unmatched patients distributed throughout the full RAR spectrum reflects the magnitude of statistical variation among the 32 groupings of patients known to have no statistically significant difference of any single baseline characteristic (3).

The STICH randomized patients had clinical characteristics suggesting them to be lower-risk patients than either STS STICH-eligible population (Table 1). STICH patients were younger than the STS CABG cohort but similar in age to the STS CABG plus SVR cohort. LVEFs were 0.27 in STICH patients, 0.28 in the STS CABG cohort, and 0.24 in the STS CABG plus SVR cohort. The STICH trial enrolled fewer women and fewer patients with peripheral vascular disease, multivessel coronary artery disease, smoking histories, stroke histories, and prior CABG than either STS cohort. Moderate or severe mitral regurgitation was present in 18% of STICH patients, 16% of the STS CABG cohort, and 30% of the STS CABG plus SVR cohort.

The RAR profile of 1,000 STICH and 1,036 STS CABG plus SVR patients showed that 1,522 of the 2,036 STICH and STS STICH-eligible patients (75%) shared the same RAR group (Fig. 3). Because of 36 extra patients in the STS cohort, the 761 matching STICH SVR hypothesis patients represented 76% of their 1,000-patient cohort, but the 761 matching STS CABG plus SVR patients represented only 73% of the 1,036-ST patient cohort. The observation that only 10% more STS CABG plus SVR patients failed to match STICH SVR hypothesis patients than were observed to match between the 2 STICH SVR

hypothesis randomized cohorts suggests similarity of the STICH SVR hypothesis patients and the STICH randomized cohort. However, the mismatch identified more high-risk patients in the STS cohort and more low-risk patients in the STICH randomized patients.

Baseline clinical characteristics were compared for STICH SVR hypothesis patients and the STS CABG plus SVR patients in RAR groups 0 to 9, RAR groups 10 to 19, and RAR groups 20 to 32 (Table 2). The difference in patient baseline characteristics across the full risk spectrum of either the STICH or the STS patient cohort was substantially greater than the difference in baseline clinical characteristics between the STICH versus STS patient cohorts within any of the 3 RAR groups. For example, the difference in age between low- and high-risk groups was a mean of 13 years for STICH patients and a mean of 16 years for STS CABG plus SVR patients. However, mean age was only 3 years higher for STICH patients in RAR groups 0 to 9, 4 years higher for STICH patients in RAR groups 10 to 19, and the same for both cohorts in RAR groups 20 to 32. The incidence of 3+ or 4+ mitral regurgitation range for low- and high-risk groups was 6% to 36% for STICH patients and 8% to 45% for STS CABG plus SVR patients. These numeric changes are sufficient to explain greater numbers of high-risk STS CABG plus SVR patients but not sufficient to invalidate the application of STICH results to future patient management decisions.

For the STICH SVR hypothesis primary outcome, Cox model hazard ratios and 95% confidence intervals comparing STICH patients randomized to CABG plus SVR versus CABG alone in RAR groups 1 to 9 ($n = 391$), groups 10 to 19 ($n = 324$), and groups 20 to 32 ($n = 285$) demonstrated no interaction between treatment and level of baseline risk (Table 3). This evidence confirming the lack of a survival benefit from adding SVR to CABG over the broad spectrum of risk of the 1,000 SVR hypothesis patients confirms the previously reported STICH SVR hypothesis conclusions to be broadly generalizable to patients with ischemic cardiomyopathy over the full range of STICH SVR hypothesis baseline risk. This conclusion will remain important whether or not any core laboratory assessments of global and regional LV function analyzed in the context of all clinical baseline variables subsequently are shown to identify patients who receive benefit from adding SVR to CABG.

Discussion

Minimization of treatment bias is the major advantage of a randomized clinical trial over a well-conducted observational study. Drug safety and efficacy are tested incrementally to define the population for whom use or nonuse of the drug is safe and reasonable prior to conduct of large randomized trials. In contrast, randomized trials of the efficacy of operative procedures permit less standardization of the treatment before evaluation. Operations designed to

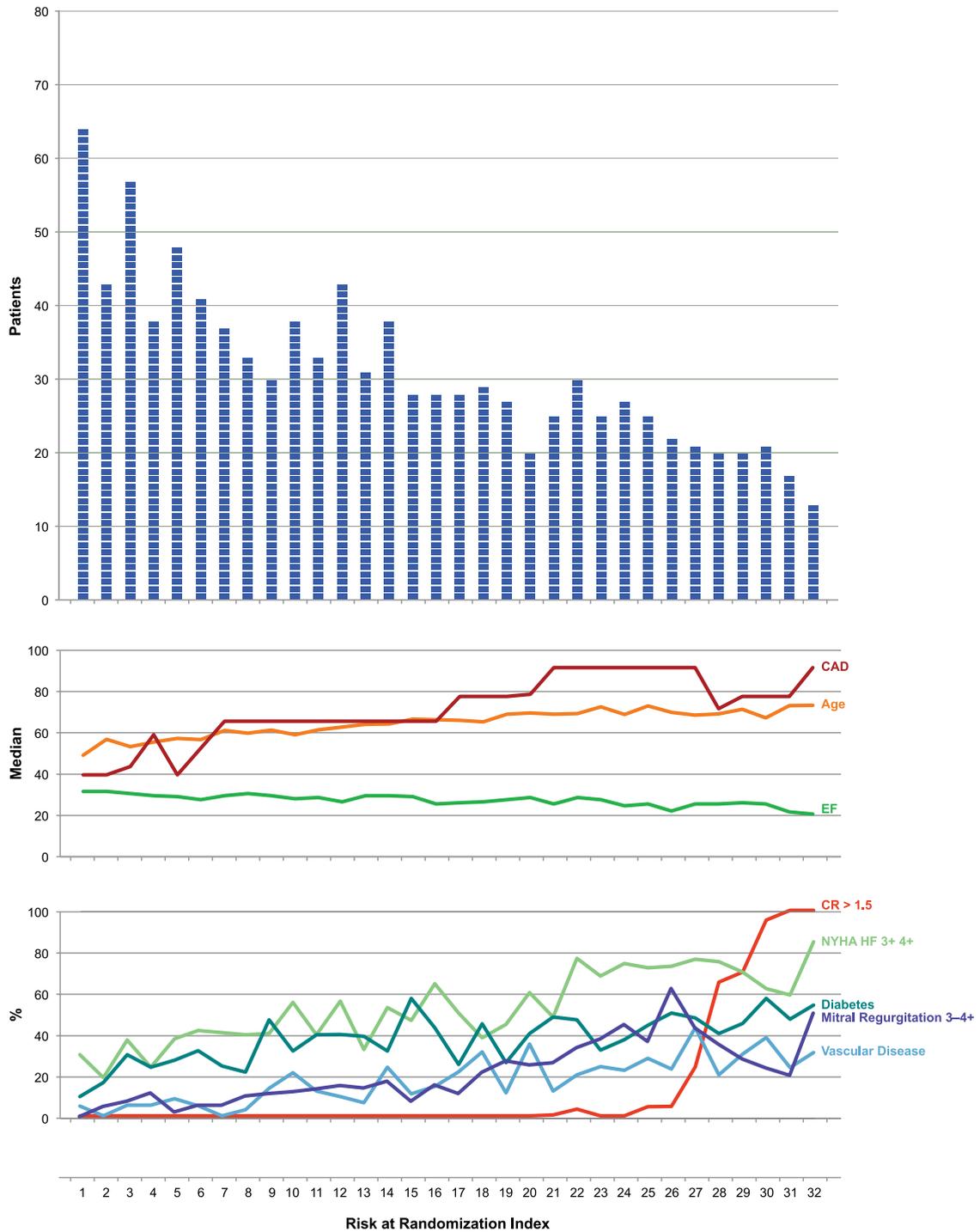


Figure 1 RAR Distribution of STICH SVR Hypothesis Patients Compared With Distribution of Values of Major Baseline Predictors of Risk for Each Interval

Histogram of individual STICH (Surgical Treatment for Ischemic Heart Failure) surgical ventricular reconstruction (SVR) hypothesis patients by risk at randomization (RAR) groups shows decreasing numbers of patients with increasing risk from RAR groups 1 to 32. The median age, ejection fraction (EF), and Duke coronary artery disease (CAD) index are depicted for each RAR group. The percentage of patients with baseline histories of specific cardiac and noncardiac disorders at baseline is depicted for each RAR group. CR = creatinine; HF = heart failure; NYHA = New York Heart Association.

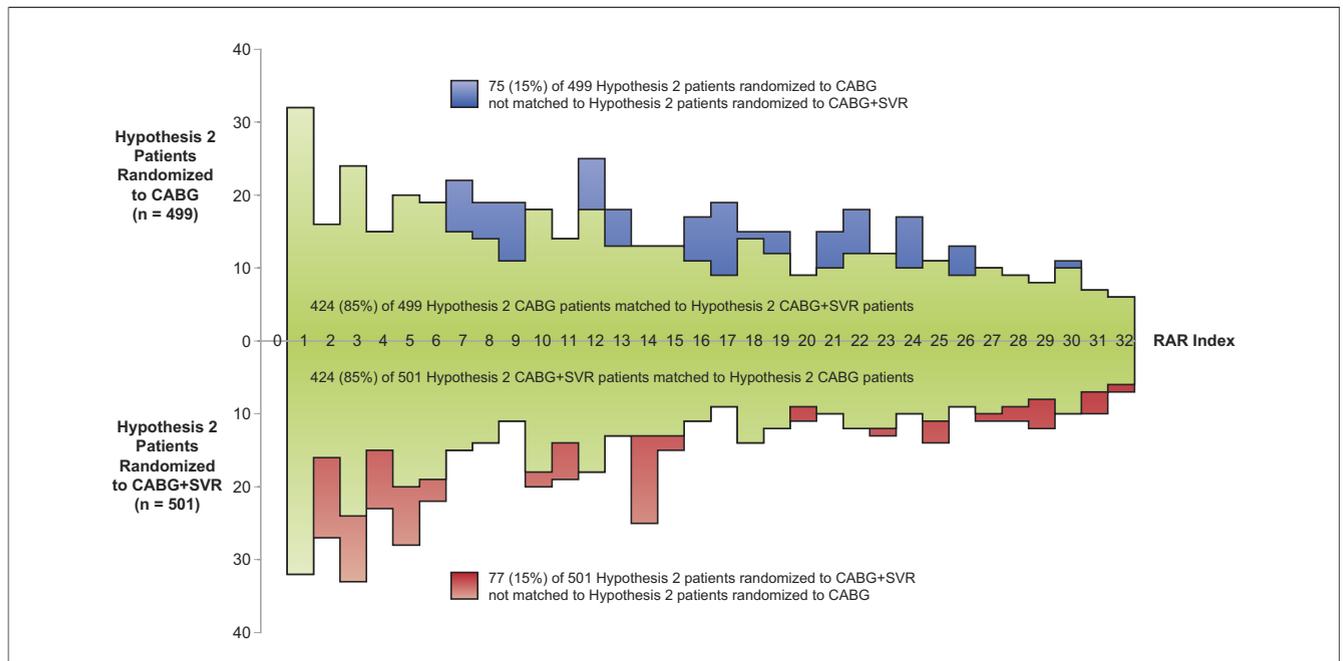


Figure 2 RAR Profile of STICH SVR Hypothesis Patients Compared by Randomized Treatment Assignment

Patients matched by randomized treatment assignment are plotted above in green (coronary artery bypass grafting [CABG]) and below (CABG + SVR) 0. Patients randomized to CABG not matched by CABG plus SVR patients are plotted above in blue. Patients randomized to CABG plus SVR not matched by patients randomized to CABG are plotted below in red. Abbreviations as in Figure 1.

favorably alter pathophysiologic processes must first be refined patient by patient so that the reason for performing an operation and its technical conduct evolve iteratively until it is considered to be indicated for selected patients as clinical practice. This evolutionary development of operative

procedures rarely proceeds to the point of clear consensus among surgeons that randomized evaluation of a surgical procedure is needed. Moreover, the perceived value of an operation may change over time. The earliest CABG operations were performed to relieve angina (6,7). Now CABG operations attempt to enhance coronary flow reserve and thereby decrease symptoms and increase patient survival. The earliest LV volume reduction operations were resections of large, thin-walled saccular aneurysms to reduce heart failure symptoms (8). As reperfusion therapy early in the course of acute myocardial infarction decreased the size and transmural extent of myocardial injury, operative techniques used for large saccular aneurysms have evolved to more effectively counter the deleterious geometric and wall stress effects of the scarred region on remote myocardium (9–12).

In 2001, the RESTORE group, composed of cardiologists and cardiac surgeons from 11 centers, reported on 439 patients undergoing SVR, with 89% also undergoing CABG (13). The operation was defined as one that “reduces ventricular size by excluding the non-contracting segment with an intraventricular patch.” Operative mortality was 6.6%. Only 27 patients were followed for 18 months, but the Kaplan-Meier estimate of survival was 89% for that interval. Freedom from rehospitalization for heart failure was 85% at 18 months. These investigators called for a randomized trial of SVR. Despite the absence of outcome data on a consecutive series of patients undergoing CABG

Table 1 Comparison of Baseline Characteristics of 1,000 STICH SVR Hypothesis Patients With STS STICH-Eligible Patients Treated by Choice With CABG or CABG Plus SVR

Variable	STS CABG (n = 102,964)	STICH SVR Hypothesis (n = 1,000)	STS CABG + SVR (n = 1,036)
Age (yrs)	65.7 ± 11.0*	61.6 ± 9.7	62.4 ± 10.8
LVEF	27.9 ± 6.5*	26.9 ± 5.9	23.6 ± 7.0*
Women	25%*	15%	21%*
Hypertension	77%*	59%	73%*
Peripheral vascular disease	21%*	15%	17%
Multivessel CAD ≥ 75%	97%*	80%	92%
Left main stenosis ≥ 0%	28%*	20%	15%†
Mitral regurgitation ≥ 3+	16%	18%	30%*
Diabetes	44%*	34%	42%*
Smokers	29%*	22%	28%*
Myocardial infarction history	70%*	87%	83%†
Stroke history	9%*	6%	9%†
Prior CABG	7%*	2%	10%*
Atrial fibrillation/flutter	11%	12%	9%†

Data are expressed as mean ± SD or %. *p < 0.001; †p < 0.05.

CABG = coronary artery bypass grafting; CAD = coronary artery disease; LVEF = left ventricular ejection fraction; STICH = Surgical Treatment for Ischemic Heart Failure; STS = Society of Thoracic Surgeons; SVR = surgical ventricular reconstruction.

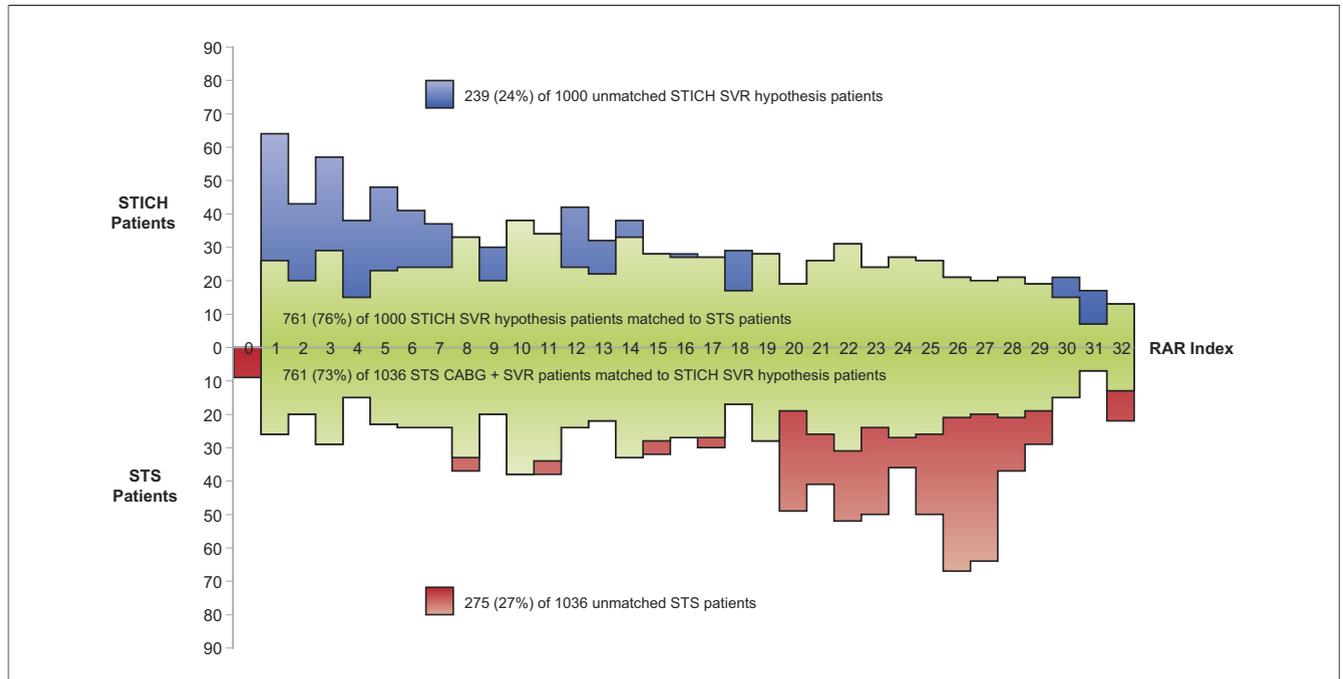


Figure 3 RAR Profile of 1,000 STICH SVR Hypothesis Patients Compared With 1,036 STS STICH-Eligible CABG Plus SVR Patients

The 761 STICH and 761 Society of Thoracic Surgeons (STS) CABG plus SVR patients who share the same RAR number are plotted from 0 (green). Excess STICH patients not matched by STS patients are plotted above in blue. Excess STS patients not matched by STICH SVR hypothesis patients are plotted below in red. Abbreviations as in Figures 1 and 2.

with and without SVR by choice, the editorialist agreed with the need for a randomized trial (14).

Hernandez et al. (15) reported the January 2002 to January 2004 STS database enrollment of patients with LV surgery using separate definitions for SVR and LV aneurysm repairs. LV aneurysm repairs were performed in 2,436 (77%) and SVR was performed in 731 (23%) of the 3,167 patients. The rate of reporting SVR grew from 15 patients/month in 2002 to 32 patients/month in 2004. Subsequent to this report, SVR use has stabilized and was 32 patients/month for patients enrolled in the STS database during 2008. During the 40.4-month STICH enrollment interval,

the U.S. investigators enrolled 5 patients/month, whereas all STS centers enrolled an average of 27 patients/month.

Demonstration that 75% of STICH and STS CABG plus SVR patients in this report had similar baseline risk suggests the STICH randomized cohort was representative of the overall group of patients considered to be candidates for CABG plus SVR during the time of STICH randomization. More unmatched STICH patients were present in the low-risk RAR groups, and more unmatched STS patients were present in the high-risk RAR groups. Hazard ratios that remain similar in patients grouped by low, intermediate, or high risk strongly indicate that no combi-

Table 2 Comparison of Baseline Clinical Characteristics in 3 Risk Groupings of STICH SVR Hypothesis Patients (n = 1,000) and STS CABG Plus SVR Patients (n = 1,036)

Baseline Clinical Characteristic	Lowest-Risk Patients (RAR Groups 0 to 9)		Mid-Risk Patients (RAR Groups 10 to 19)		Highest-Risk Patients (RAR Groups 20 to 32)	
	STICH Patients (n = 391)	STS Patients (n = 227)	STICH Patients (n = 324)	STS Patients (n = 289)	STICH Patients (n = 285)	STS Patients (n = 520)
Age (yrs)	55 ± 8	52 ± 8	64 ± 8	60 ± 9	68 ± 8	68 ± 9
LVEF	0.29 ± 0.05	0.26 ± 0.07	0.27 ± 0.06	0.25 ± 0.07	0.25 ± 0.06	0.22 ± 0.07
Women	52/391 (13%)	44/227 (19%)	56/323 (17%)	68/289 (24%)	39/286 (14%)	112/520 (22%)
Hypertension	211/391 (54%)	162/227 (71%)	197/323 (61%)	213/289 (74%)	177/286 (62%)	395/520 (76%)
Peripheral vascular disease	19/391 (5%)	11/227 (5%)	52/323 (16%)	32/289 (11%)	75/286 (26%)	133/520 (26%)
Multivessel CAD ≥50%	328/391 (84%)	193/227 (85%)	308/322 (96%)	271/289 (94%)	276/286 (97%)	513/520 (99%)
Left main CAD ≥50%	39/391 (10%)	21/227 (9%)	68/322 (21%)	52/289 (18%)	90/286 (32%)	88/520 (17%)
Mitral regurgitation ≥3+	21/362 (6%)	18/227 (8%)	46/301 (15%)	65/289 (22%)	96/266 (36%)	237/520 (46%)

Data are expressed as mean ± SD or as n (%).

RAR = risk at randomization; other abbreviations as in Table 1.

Table 3 STICH SVR Hypothesis Assessment of CABG Plus SVR Versus CABG in Subgroups Defined by RAR

RAR Subgroup	n	Hazard Ratio (95% CI)
1–9	391	0.92 (0.69–1.22)
10–19	324	1.13 (0.85–1.51)
20–32	285	0.99 (0.75–1.31)

p value for interaction = 0.60.
CI = confidence interval; other abbreviations as in Tables 1 and 2.

nation of baseline clinical variables with prognostic importance can reasonably be expected to help cardiac surgeons identify subgroups of patients who may benefit more from SVR added to CABG. However, the RAR index included the clinical site LVEF as the only LV functional parameter. Regardless of whether or not subsequent reports of ongoing work using core laboratory data from preoperative cardiac imaging studies identify an LV function marker of differential SVR treatment effect, the conclusion that no baseline clinical variable identifies any patient characteristic that marks differential outcome of CABG with or without SVR will not change. Similarity of baseline clinical characteristics of STICH and STS STICH-eligible patients confirms the generalizability of the STICH trial conclusions to patients with ischemic cardiomyopathy considered for CABG.

This report illustrates the enhanced value of the integration of information from both randomized trials and clinical registries. Clinical databases include cohorts of patients for whom entry into a randomized clinical trial would not be reasonable. Randomized trial results illustrate the influence of patient selection on variation in observed outcomes. For example, the operative mortality reported by Hernandez et al. (15) was 9.3%, compared with 5.2% in STICH (3). However, analysis of this STS patient cohort as STICH eligible would require elimination of data from emergency patients and patients operated on by cardiac surgeons with experience performing <5 SVR operations. Data reported by Hernandez et al. (15) suggest these STICH restrictions applied to STS patients would reduce the expected STS operative mortality to 7.2%. Moreover, the magnitude of lower baseline risk of STICH patients described in this report is adequate to explain the 2% lower operative mortality observed in the STICH randomized cohort compared with the STS CABG plus SVR cohort.

Study limitations. Definitions used to identify Duke patients as STICH eligible may have differed from those used to identify STS STICH-eligible patients. Moreover, a separate STS CABG plus SVR patient multivariate equation was not developed and calibrated, so that the equation developed on DDCD STICH-eligible patients may have had a consistent unrecognized bias when used to risk-profile STICH and STS CABG plus SVR patients. Separate matching of the Duke and STS patient selection definitions to STICH patient entry definitions did permit the use of a single multivariate equation to provide the predicted mortality that linked STICH and STS CABG plus SVR patients by their individual predicted mortality. This pre-

dicted mortality was used only to position each STICH SVR hypothesis and each STS CABG plus SVR patient into RAR groups defined by the same predicted risk ranges. That only 9 STS CABG plus SVR patients had lower predicted mortality and none had higher predicted mortality than any STICH randomized patient further suggests accuracy of risk profiling of these 2 patient populations.

Another limitation of the risk prediction used is that patients were matched using mortalities calculated for patients as if they would not have cardiac surgery, but all STICH SVR hypothesis and all STS patients were surgically treated. The purpose of this report was to link clinical decisions used to randomize STICH patients to the clinical care decisions clinicians will make for future patients. Therefore, predicted risk was based on clinical information available at a time when cardiac surgery was not yet certain to be the treatment chosen, reflecting the way STICH trial results should be used to make future decisions about the need for adding SVR to future patients who are similar to the STICH SVR hypothesis population.

Conclusions

STICH patients randomized to CABG with or without SVR have baseline clinical risk more similar to STS CABG plus SVR patients than STS CABG-only patients. The RAR profile shows a wide and similar range of risk for both STICH SVR patients and STS patients treated by choice with CABG plus SVR. Although 75% of these 2 patient cohorts shared the same RAR group, there were more low-risk STICH and more high-risk STS patients. Clinical characteristics responsible for these risk differences appear to be of minimal clinical significance. Regression analysis based on Cox proportional hazards ratios showed no significant interaction with respect to survival. Ongoing analysis will assess whether any aspect of global or regional cardiac function assessed by core laboratory evaluation of baseline cardiac images shows a different treatment effect of CABG with or without SVR with respect to the primary STICH SVR hypothesis outcome. The present study confirms the results of the STICH trial to be broadly generalizable to the ischemic cardiomyopathy population for whom CABG with SVR might be considered.

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Clinical Characteristics of Patients Undergoing Surgical Ventricular Reconstruction by Choice and by Randomization

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