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Regional left ventricular function does not predict survival in ischaemic cardiomyopathy after cardiac surgery

David L. Prior¹, Susanna R. Stevens², Thomas A. Holly³, Michal Krejca⁴, Alexandros Paraforos⁵, Gerald M. Pohost⁶, Krysti Byrd², Tomasz Kukulski⁷, Robert H. Jones², Patrice Desvigne-Nickens⁸, Padmini Varadarajan⁹, Aman Amanullah¹⁰, Grace Lin¹¹, Hussein R. Al-Khalidi², Gabriel Aldea¹², Carlo Santambrogio¹³, Andrzej Bochenek⁴, and Daniel S. Berman¹⁴

¹Department of Medicine, St. Vincent's Hospital, University of Melbourne, Melbourne, Australia

²Duke Clinical Research Institute (SRS, RHJ, HRA) and Department of Surgery-Cardiothoracic (RHJ), Duke University School of Medicine, Durham, NC, USA ³Department of Medicine-Cardiology, Northwestern University Feinberg School of Medicine, Chicago, IL, USA ⁴1st Cardiac Surgery Department, Medical University of Silesia, Katowice, Poland ⁵Department of Surgery-Cardiac, University of Trier, Trier, Germany ⁶Department of Medicine-Cardiology, University of Southern California, Los Angeles, CA, USA ⁷Silesian Center for Heart Diseases, Silesian Medical University, Zabrze, Poland ⁸National Heart, Lung and Blood Institute, National Institutes of Health, Bethesda, MD, USA ⁹Department of Medicine-Cardiology, Loma Linda University Medical Center, Loma Linda, CA, USA ¹⁰Department of Medicine-Cardiology, Albert Einstein Medical Center, Philadelphia, PA, USA ¹¹Department of Medicine-Cardiology, Mayo Clinic, Rochester, MN, USA ¹²Department of Surgery-Cardiothoracic, University of Washington Medical Center, Seattle, WA, USA ¹³Department of Medicine-Cardiology, Policlinico San Donato, Milan, Italy ¹⁴Department of Medicine-Nuclear Cardiology, Cedars-Sinai Medical Center, Los Angeles, CA, USA

Abstract

Objectives—To define the prognostic contribution of global and regional left ventricular (LV) function measurements in patients with ischaemic cardiomyopathy randomised to coronary artery bypass graft surgery (CABG) with (N = 501) or without (N = 499) surgical ventricular reconstruction (SVR).

Methods—Novel multivariable methods to analyze global and regional LV systolic function were used to better formulate prediction models for long-term mortality following CABG with or without SVR in the entire cohort of 1000 randomised SVR hypothesis patients. Key clinical variables were included in the analysis. Regional function was classified according to the discreteness of anteroapical hypokinesia and akinesia into those most likely to benefit from SVR, those least likely and those felt to have intermediate likelihood of benefit from SVR.

Results—The most prognostic clinical variables identified in multivariable models include creatinine, LV end-systolic volume index (ESVI), age, and NYHA class. Addition of LV ejection

fraction, LV end-diastolic volume index and regional function assessment did not contribute additional power to the model. Subgroup analysis based on regional function did not identify a cohort in which SVR improved mortality.

Conclusions—ESVI is the single parameter of LV function most predictive of mortality in patients with LV systolic dysfunction following CABG with or without SVR in multivariable models that include all key clinical and LV systolic function parameters. Assessment of regional cardiac function does not enhance prediction of mortality nor identify a subgroup for which SVR improves mortality. These results do not support elective addition of LV reconstruction surgery in patients undergoing CABG.

Keywords

randomised clinical trial; coronary artery bypass grafting; ischaemic cardiomyopathy; surgical ventricular reconstruction; end-systolic volume index

Introduction

Surgical treatment is an important part of overall management of patients with left ventricular (LV) dysfunction due to coronary artery disease. Surgical treatment is most commonly coronary artery bypass graft (CABG) surgery, but in patients with anterior LV dysfunction, surgical ventricular reconstruction (SVR) may be added to CABG to reconstruct a more normal LV size and shape [1]. Observational evidence suggests that surgical reduction of LV size improves cardiac function, improves quality of life [2-4], and may decrease mortality. The randomised Surgical Treatment for Ischemic Heart Failure (STICH) trial, however, showed that routine addition of SVR to CABG in patients who have anterior regional dysfunction provided no additional benefit in survival or quality of life over CABG alone [2 3]. Possible reasons for these conflicting findings have been hotly debated and there remains great interest in determining whether a subset of patients who benefit from SVR can be found.

Indices of global systolic structure and function, such as LV end-systolic volume index and LVEF, are known to provide prognostic information in patients with heart failure due to ischaemic heart disease treated medically [4] or surgically [5]. Whether assessment of regional LV function adds prognostic value beyond that of global dysfunction in such patients is less clear. Some investigators have reported that assessment of regional LV function using a wall motion score index (WMSI) helps identify patients preoperatively who may benefit most from SVR [6]. This observation is confounded, however, by the fact that extensive segmental LV dysfunction and a high WMSI are commonly associated with large LV volumes and that WMSI provides an overall measure of LV function from the sum of its regional parts, but does not measure regional distribution of left ventricular dysfunction, which may be critical in deciding whether SVR is indicated.

Regional function is often difficult to quantitate accurately in all patients, especially if only one imaging modality is used. Wall motion in areas other than the anterior wall and apex also appear important, as the presence of posterior wall dysfunction may also compromise survival [7]. Whether mapping of function in anterior and apical ventricular segments which

are the target of the SVR can identify patients with greater likelihood of benefit from SVR is unknown. Apart from the STICH trial, no prospectively acquired database of baseline cardiac images has been available to identify patients who are proper candidates for SVR [8-10]. The 1000 patients in the STICH trial eligible for randomization to CABG with or without SVR, whose global and segmental LV function were well characterized by multiple imaging modalities, provide an ideal cohort in which to examine the prognostic utility of global and regional LV function when added to clinical variables predictive of patient survival. Moreover, this 1000-patient cohort, when compared to a 1036-patient cohort entered into the Society of Thoracic Surgeons' National Database during the enrollment interval of STICH, had similar baseline characteristics, thereby confirming the generalizability of the STICH SVR hypothesis conclusions [11].

This analysis of the SVR hypothesis 1000-patient cohort seeks to determine: 1) which measures of global LV systolic function best predict long-term survival after cardiac surgery; 2) whether characterization of segmental function adds independent prognostic information to that provided by prognostic clinical and global cardiac function variables; and 3) whether baseline parameters of segmental function identify a subgroup of STICH patients for whom the addition of SVR to CABG improves survival.

Methods

Patient Population

The STICH SVR hypothesis examined the effect of adding SVR to CABG in patients with ischemic heart disease suitable for CABG and an LVEF ≥ 0.35 with significant anteroapical akinesia or dyskinesia for whom adding SVR to CABG would be a reasonable, but not required operative treatment. All participants gave written informed consent, the study was approved by ethics committees responsible for the participating centers and this investigation conforms to the principles outlined in the Declaration of Helsinki. The main results have been published elsewhere [2] and reported that after a median follow-up of 3.6 years, death occurred in 141 (28%) of the 499 patients randomised to CABG and 138 (28%) of the 501 patients randomised to CABG with SVR (hazard ratio 1.00; CI, 0.79 to 1.26; $P = 0.98$). There were a total of 279 deaths observed in this cohort. Baseline clinical data used in multivariable modeling were complete for 98% of patients and baseline core lab LV ESVI data were complete for 87%. Imputations for missing data were performed so all study patients are represented in the final model (see Supplementary data Appendix 1).

Assessment of LV Function at Time of Randomisation

Baseline assessment of global and regional LV function was measured with echocardiogram (ECHO), gated myocardial perfusion single photon emission computed tomogram (SPECT), or cardiac magnetic resonance (CMR) by core laboratories blinded to treatment and outcome. All patients had a baseline LVEF from either a core lab image ($N=966$) or site-reported value on clinical case report forms ($N=34$). Reasons for incomplete baseline LV function data are depicted in figure 1. From 866 of the 1000 SVR hypothesis patients, one or more fair to excellent quality ECHO, SPECT, or CMR studies were received and processed by the core laboratories providing a baseline ESVI value. Clinical site-reported baseline

ESVI values were available on clinical case report forms for 58 additional patients so that values for baseline ESVI were available for 924 of the 1000 SVR hypothesis patients. ESVI was imputed for the remaining 76 patients using the following regression equation which was based on the observed relationship between LVEF and ESVI in the patients in whom ESVI was measured: $182.02 - (3.85 * \text{LVEF}) + (0.03 * \text{LVEF}^2) + (4.51 * \text{MR}) + (1.81 * \text{MI}) - (0.29 * \text{age})$ where MR (mitral regurgitation) and MI (previous myocardial infarction) take a value of 1 if present and 0 if absent (see Supplementary data Appendix 1). A scatterplot for the relationship between LVEF and ESVI is shown in Figure 2 where patients with measured ESVI are shown in black (N=924) and patients with imputed ESVI are shown in red (N=76).

Categorizing Regional Function by Suitability for SVR

For 812 of the 1000 patients who had fair or better core laboratory LV images collected at the segment level, regional LV function was assessed using a 1 (normal), 2 (hypokinesia), 3 (akinesia), 4 (dyskinesia) score that was mapped to a standardized 17-segment model [12]. Distribution and frequency of segmental akinesia and dyskinesia is shown in Figure 3. Regional function was classified by grouping patients into those who were most SVR-eligible (largest amount of discrete anteroapical akinesia or dyskinesia), those with least eligibility (smallest amount of discrete anteroapical akinesia or dyskinesia) and those with intermediate eligibility (fewer dysfunctional segments and less discrete transition from normal to dysfunctional segments). Amount of discrete anteroapical akinesia or dyskinesia was defined by summing the wall motion scores in segments 8, 13, 14, 15, 17.

To neutralize the confounding effect of large heart size with extensiveness of LV regional dysfunction, regional function was defined within deciles of increasing ESVI. Each decile was divided into thirds (groups of 33, 33, and 34 patients) as ordered from most to least dyskinesia in segments most likely to benefit from adding SVR to CABG (8, 13, 14, 15, 17). The 33, 33, and 34 patients from each of the 10 groupings by ESVI were combined into three cohorts numbering 330, 330, and 340 patients to reflect thirds of patients expected to be the **most**, **intermediate**, and **least** likely to receive benefit from adding SVR to CABG based on regional dysfunction criteria. Because, at a clinical level, patients without adequate regional wall motion assessment cannot be classified as suitable for SVR, they have been classified as **least** eligible. Thus the 340 patients in the group labeled as **least** eligible for SVR included the 188 patients without core laboratory assessment of regional function and 152 patients with the least discrete and smallest area of anteroapical regional dysfunction. With the exception of race, the baseline characteristics of patients with the least anteroapical dysfunction (least eligible) are similar to those with missing regional data (see Supplementary data Appendix 2). A sensitivity analysis was also performed excluding the patients without regional function data (see Supplementary data Appendix 3) and outcomes for those without regional data were also analysed separately.

Optimization of Baseline ESVI Prognostic Power Using Preliminary Multivariable Models

A preliminary model composed of baseline clinical characteristics and site reported LVEF was developed. Subsequently, site reported LVEF was substituted with various combinations of global and regional function measures to determine which functional measures maximized the contribution to prognosis of all 1000 patients in the context of clinical

variables. Since patients had LVEF and ESVI measures from more than one core lab, thirteen algorithms which gave priority to different imaging modalities and quality scores were substituted into the clinical model for all-cause death. Different combinations of LVEF, ESVI, EDVI, and SVR eligibility category based on regional function were also tested for their contribution to the model.

Results

Compliance with Randomised Treatment Assignment

Among the 499 patients randomised to CABG, 463 (92.8%) were compliant with the assigned treatment. Among the 501 patients assigned to CABG + SVR, 454 (90.6%) received their assigned operation (Table 1). A total of 979 patients received CABG with or without SVR. The reasons for non-compliance with treatment assignment are described in table 1.

Multivariable Model Results

Table 2 summarizes the results of multivariable modeling that began with identification of prognostic clinical variables, continued with introduction of multiple LV function variables, and concluded with maximization of the model prognostic strength by including the single algorithm of ESVI with the highest total model Chi square (if more than one ESVI value was available). The final model result showed that the addition of LVEF, EDVI, and regional function did not contribute prognostic information above that of baseline ESVI. Increasing blood creatinine over 1.0 mg/dL conveyed more prognostic information than ESVI. However, ESVI was more prognostic than age, heart failure class, presence of atrial flutter or fibrillation, diabetes, and six other clinical variables. The univariable relationship of all-cause death to baseline ESVI is depicted at 1, 3, and 5 years for the 979 patients who received surgery stratified by the operation received (Figure 4). Operative mortality was greatest among patients with the largest ESVI.

Comparison of Clinical Characteristics of 1000 Patients Grouped By SVR Eligibility

Baseline clinical and LV function characteristics of the three cohorts created to reflect the most, intermediate, and least SVR eligibility show no differences in baseline characteristics that would be likely to introduce bias toward a differential outcome from addition of SVR to CABG (Table 3). The strongest variables in the multivariable model were balanced among the three cohorts. EDVI and LVEF were similar among the three groupings, and thus the key difference between the groups was the distribution of regional function upon which the SVR eligibility categories was based. Correlations between baseline ESVI measured using the different imaging modalities have been published elsewhere [13].

Interaction of ESVI with Treatment Assignment

There was no significant interaction between baseline ESVI and surgery received ($p=0.88$). Figure 4 shows survival as a function of baseline ESVI at 1, 3, and 5 years of follow-up. All three paired curves share a similar shape with CABG + SVR having similar early survival in patients with the smallest baseline ESVI and CABG alone having visually greater early survival in patients with the largest ESVI.

Effect of Regional Function on Outcome

Regional cardiac function of patients grouped by the likelihood of benefit from SVR is shown in Figure 3. By definition, the most SVR-eligible 330-patient cohort had a high prevalence of akinesia or dyskinesia confined to the anteroapical segments. The 3 groups with a range of eligibility for SVR are well matched for ESVI and LVEF (Table 3). Despite confirmation that the data transform created at least 1 patient grouping with excellent SVR eligibility, no survival advantage for CABG + SVR occurred among even this most SVR-eligible cohort (Figure 5). Overall mortality was not different between the 3 SVR-eligibility groups, between the treatment received, nor their interaction ($p=0.45$); Mortality rates at 4 years were 27.4% in the most SVR eligible group, 28.9% in the intermediate group and 25.1% in the least-eligible group. Use of regional wall motion to rank patients by eligibility for SVR produced a cohort for which adding SVR to CABG would be expected to reduce mortality. However, in the most SVR-eligible cohort, the hazard ratio for CABG + SVR to CABG was 0.84 (0.55, 1.27). Similar results were seen in a sensitivity analysis that excluded the patients with missing regional function (see Supplementary data Appendix 3). Further, when outcomes were examined in the 188 pts excluded from the sensitivity analysis with missing regional data, 23/84 (27.4%) of those who received SVR died compared with 26/100 (26.0%) who received CABG alone ($p = 0.68$), a finding which was not different to those seen in the other groups. Four did not undergo operation.

Discussion

Although the prognostic importance of LV aneurysms was known during the 17th century, the impact of surgical intervention remains controversial in the 21st century [14] [15]. Once coronary revascularization became the primary objective of operations performed for CAD, LV aneurysms judged to pose a hemodynamic threat to patients undergoing CABG during the time of discontinuation of cardiopulmonary bypass were commonly treated with CABG and aneurysmectomy. Thus LV aneurysmectomy and subsequently its refinement, SVR, have been used for 50 years, but evidence for prognostic benefits of adding aneurysmectomy to CABG alone have been lacking outside non-randomised observational studies [16-18]. The SVR hypothesis of the STICH study showed that routine addition of SVR to CABG in those with suitable anatomy offered no survival advantage over CABG alone [2]. This analysis of the STICH SVR hypothesis sub-study fills in some of the gaps in knowledge in this area.

Using a novel analysis strategy which allows inclusion of mortality data from all randomised patients in the study, this analysis confirms that ESVI, a measure of global LV structure and function, is the most important cardiac determinant of subsequent survival following CABG with or without SVR, even when the prognostic model includes key clinical parameters known to influence outcome. This conclusion supports previous findings of the prognostic power of ESVI following acute myocardial infarction [4] and following CABG in ischaemic cardiomyopathy [19 20], and extends our understanding by considering ESVI in conjunction with important clinical variables. Novel findings include showing that assessment of regionality of LV dysfunction, grouped by involvement of the anteroapical myocardial segments targeted by the SVR procedure, offers no additional prognostic information over

ESVI for death in this patient group and that consideration of regionality does not identify a subgroup of the STICH cohort who may benefit from addition of SVR, both findings with practical implications for treatment of patients with ischemic cardiomyopathy.

Regional Function and Prognosis

The conclusion that regional function assessment does not add prognostic information to global function assessment differs from the conclusion from observational evidence of Klein et al. [6] who studied 101 patients undergoing SVR. They found that WMSI, but not ESVI or EDVI, predicted poor outcome, defined by death or poor functional capacity, at 1 year following SVR, a finding that they attributed to the ability of WMSI to measure regional variability of function and, in particular, function in areas remote to the anteroapical region. In contrast, we found that while ESVI, a global measure, was prognostically important in this type of cohort, assessment of regional function did not add to the prediction of death following surgery. Possible reasons for these differences include the fact that the study of Klein was significantly smaller than ours with lower statistical power and that WMSI, although often regarded as an index of regional function, in fact, provides a surrogate measure of global function which is simply derived as the sum of regional function in each of the wall segments. Unless a cluster of adjacent segments are identified with a high wall motion score, an elevated WMSI may simply reflect a dilated cardiomyopathy rather than a pattern of anteroapical regionality. For this reason, we grouped patients according to the regional distribution of dysfunction. When a combined endpoint of death or heart failure hospitalization was examined, this conclusion was not changed. Even the third of patients with a distribution of regional dysfunction that was characterized as “most SVR eligible” by experienced SVR surgeons did not identify a group that SVR improved survival. While the number of events were smaller and confidence intervals were broader within the eligibility subgroups based on regional wall motion, the lack of heterogeneity of treatment effect across the groups supports the validity of this conclusion. This STICH analysis is therefore the only study which has been able to examine the impact of regional function on outcomes in CABG with or without SVR in a randomised cohort as part of a multivariable model.

Inclusion of all Randomised Patients

This secondary observational analysis performed in this 1000-patient randomised cohort also addresses a major concern raised about the conclusions from the primary STICH-SVR outcome report [2]; that is, that sufficient detailed information was not provided to fully characterize global and regional baseline LV function in all 1000 patients, and patients who may have derived benefit from SVR were therefore not identified. In this study, we have used novel methodology to ensure that clinical and imaging data from all randomised subjects were optimally utilized to fully exploit the value of integrating parameters of LV global and regional structure and function with key clinical variables to predict death at five years following cardiac surgical revascularization with or without LV size reduction by SVR. The novel methodology used removes the confounding effects of the close relationship between global LV enlargement and LVEF when analyzing the impact of the extent and severity of regional dysfunction. It also allows outcome data for all 1000 SVR hypothesis patients to be included removing any bias which may be present due to exclusion of subjects in whom imaging findings are unavailable.

Because an ESVI value was not available on all patients, we used the calculated relationships with the measured value of LVEF to impute the most likely value of ESVI in a fraction of the patents and thereby account for all deaths among the complete 1000-patient cohort. Previous studies examining this question have excluded subjects for whom all the LV structure and function measures were not available [13]. Moreover, prior reports have not accounted for the strong relationship between the extent of regional wall motion abnormalities and systolic function [6]. We believe this analysis overcomes these weaknesses, confirms the importance of ESVI and confirms a neutral treatment effect of the addition of SVR to CABG.

Clinical Implications

Hernandez, et al. reported data from the Society of Thoracic Surgeons database of cardiac operations for 2,436 LV aneurysm repairs and identified 731 SVR operations that were performed outside the clinical trial setting during the 2002 to 2004 interval when the SVR hypothesis was actively enrolling patients [21]. They reported significant morbidity and mortality in relation to the use of the SVR operation in a real-world evaluation. The STICH trial results, including this analysis in which no subgroup who may benefit from SVR operation was found, suggest cardiac surgeons should carefully consider re-evaluation of indications for operations performed solely for the indication to decrease LV size. Myocardial revascularization alone appears to provide adequate benefit for most patients undergoing cardiac surgery for coronary artery disease.

Limitations

We have not included parameters of diastolic filling and right ventricular function in this report. Our use of the 17-segment description of regionality of LV dysfunction, which is a more granular description of regionality than the shape classifications of Di Donato, et al. [1], did not show prognostic significance. Moreover, exclusions to STICH trial enrollment of patients presenting in shock, patients with evolving myocardial infarction, and those with aortic valve disease limit extension of the conclusions to patients with these markers of higher operative risk. Our findings do not evaluate the value of adding SVR or LV aneurysmectomy to CABG in patients with a strong rationale for LV surgery, such as LV injury during median sternotomy, or unusual morbid conditions, such as intracavity thrombus or ventricular septal defects from an ischaemic etiology. There are also a number of patients with missing data requiring imputation (see Supplementary data Appendix 1) although sensitivity analysis suggests the overall conclusions are not altered by this. Finally, patient numbers and event rates are smaller as subgroup analysis is undertaken reducing the power to detect differences in treatment effect between groups.

Conclusions

Using a multivariable modeling approach incorporating imaging data from multiple modalities and allowing all 1000 STICH SVR hypothesis patients to be analyzed, we have shown that ESVI remains the best parameter of LV structure and function predicting outcome in patients undergoing CABG when considered in the context of other important clinical variables. Importantly, we have also shown that regional function assessment

incorporating the extent and the severity of anteroapical akinesia does not contribute significant prognostic information to that of ESVI alone and does not identify a group of patients for whom the elective addition of SVR improves mortality.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Abbreviations

CABG	coronary artery bypass grafting
CMR	cardiac magnetic resonance
ECHO	echocardiogram
EF	ejection fraction
LV	left ventricular

NYHA	New York Heart Association heart failure class
SPECT	gated single photon emission computed tomogram
STICH	Surgical Treatment for Ischemic Heart Failure trial
SVR	surgical ventricular reconstruction
WMSI	wall motion score index

Key Questions

What is already known about this subject?

Routine addition of surgical ventricular reconstruction (SVR) to coronary artery bypass grafting (CABG) does not reduce mortality in patients with ischaemic cardiomyopathy.

Whilst global measures of left ventricular (LV) structure and function such as end-systolic volume index (ESVI) predict survival in surgical and non-surgical patients with LV systolic dysfunction, it is unclear whether regionality of LV dysfunction provides additional prognostic information or identifies a patient sub-group who may benefit from SVR.

What does this study add?

We have shown that when added to important clinical parameters, ESVI is the strongest measure of global LV structure and function predicting mortality after CABG with or without SVR and the regional distribution of LV dysfunction does not add further prognostic information, nor identify a patient subgroup who may benefit from addition of SVR to CABG.

How might this impact on clinical practice?

Accurate quantification of ESVI provides important prognostic information about likely outcome of patients who undergo surgical treatment of ischaemic cardiomyopathy and should be routinely measured. There does not appear to be a role for routine addition of SVR in patients undergoing CABG and quantification of regionality does not help with this decision.

Baseline Core Laboratory Assessment of Left Ventricular Function in SVR Hypothesis Patients

N = 1000

Figure 1.

Availability of Baseline Cardiac Imaging Studies for Core Laboratory Assessment

Figure 2. Scatterplot of LVEF by ESVI values. Patients with a reported ESVI are plotted in blue and imputed ESVI values are plotted in orange.

Distribution of Regional LV Dysfunction in SVR Hypothesis Patients

Figure 3.

Regional LV Dysfunction Pattern in Three Patient Groups Based on SVR Eligibility – Segment 1 is the basal anterior segment. The distribution of dyskinesia as percentage of the 812 patients separated by SVR eligibility (top) and distribution of patients with akinesia with or without dyskinesia (bottom).

Figure 4. Relationship of ESVI to Survival by Operation Received at 1, 3, and 5 Years in 979 SVR Hypothesis Patients (21 patients received no operation) - Reference lines denote tertiles of ESVI.

Figure 5. Survival by Treatment Received in SVR Eligibility Groups Based on Regional Function (5A= most eligible, 5B= intermediate eligibility, 5C= least eligible) - Hazard ratios (95% CI) on each plot are for CABG+SVR versus CABG only. Treatment received-by-SVR eligibility group interaction p-value=0.45

Table 1
Hypothesis 2 Compliance with Treatment Assigned by Randomization in 1000 Patients

499 PatientsAssigned CABG			501 PatientsAssigned CABG + SVR	
Reason	Patients		Patients	Reason
Unknown	1	died before operation	5	3 definite cardiac cause
4 patients declined 3 patients worsened 1 provider decision	8	no operation at one year	7	5 patients declined 1 patient worsened 1 provider decision
9 provider decision	9	alternate operation chosen before operation	13	7 provider decision 3 patients declined 3 miscommunication
6 operative difficulties 12 operative findings	18	alternate operation chosen during operation	22	4 operative difficulties 18 operative findings
	36	did not receive assigned operation	47	
	463	assigned operation performed	454	
	92.8%	patients receiving assigned operation	90.6%	

917 (91.7%) of 1000 Hypothesis 2 patients received the assigned randomization treatment and 979 received surgery

Table 2
STICH Multivariable Model Predictive of All-cause Death in 1000 SVR Hypothesis Patients

Variable	HR	95% CI for HR	Chi- square	p
Creatinine, HR for 0.1 mg/dL increase between 1 and 1.6	1.16	1.10 - 1.22	27.8	<0.0001
ESVI, HR for 10 unit increase *	1.09	1.05 - 1.12	26.0	<0.0001
Age, HR for 10 year increase	1.42	1.24 - 1.63	25.1	<0.0001
Current NYHA heart failure class				
1	1.00	-		
2	1.19	0.70 - 2.03	28.1	<0.0001
3	1.67	0.99 - 2.82		
4	3.31	1.80 - 6.07		
Atrial flutter or fibrillation	1.86	1.38 - 2.51	16.3	<0.0001
Diabetes	1.50	1.17 - 1.92	10.0	0.0016
Haemoglobin, HR for 1 g/dL decrease below 14.3	1.15	1.05 - 1.26	9.8	0.0018
Mitral regurgitation				
None	1.00	-		
Mild/moderate	1.19	0.91 - 1.57	12.4	0.0020
Severe	2.55	1.51 - 4.29		
Myocardial infarction	1.62	1.10 - 2.38	6.0	0.0146
Hyperlipidaemia	0.74	0.57 - 0.95	5.4	0.0199
Stroke	1.64	1.06 - 2.53	5.0	0.0258
White (non-Hispanic)	1.60	1.05 - 2.45	4.7	0.0301
SVR eligibility category				
Least SVR eligible	1.00	-		
Intermediate eligibility	1.20	0.89 - 1.60	1.5	0.4767
Most SVR eligible	1.12	0.83 - 1.51		

* The ESVI comes from a selection algorithm giving preference to CMR as described by Oh [13], followed by echo, radionuclide, and site reported values to maximize the global chi-square of the multivariable model in the context of the other 11 variables significantly associated with mortality.

Table 3
Demographic, Clinical, and Cardiac Function Parameters in All 1000 Patients Grouped
by Regional Function*

Characteristic	SVR Hypothesis	Most SVR Eligible (N=330)	Intermediate SVR Eligibility (N=330)	Least SVR Eligible (N=340)
Age at randomization	62 (54 - 68)	62 (54 - 69)	60 (53 - 68)	62 (55 - 68)
Female	147 (14.7)	60 (18.2)	40 (12.1)	47 (13.8)
White (non-Hispanic)	876 (87.6)	294 (89.1)	291 (88.2)	291 (85.6)
Myocardial infarction	872 (87.2)	300 (90.9)	285 (86.4)	287 (84.4)
Diabetes	344 (34.4)	105 (31.8)	112 (33.9)	127 (37.4)
Hyperlipidemia	718 (72.0)	239 (72.4)	245 (74.5)	234 (69.2)
Hypertension	585 (58.5)	195 (59.1)	188 (57.0)	202 (59.4)
Stroke	56 (5.6)	26 (7.9)	17 (5.2)	13 (3.8)
Chronic renal insufficiency	85 (8.5)	27 (8.2)	31 (9.4)	27 (8.0)
Hemoglobin (g/dL)	13.7 (12.7 - 14.8)	13.7 (12.8 - 14.8)	13.8 (12.7 - 15.0)	13.7 (12.5 - 14.7)
Atrial flutter fibrillation	117 (11.7)	40 (12.1)	36 (10.9)	41 (12.1)
Mitral regurgitation				
None or trivial	364 (36.7)	128 (39.0)	107 (32.7)	129 (38.4)
Mild or moderate	591 (59.6)	189 (57.6)	207 (63.3)	195 (58.0)
Severe	36 (3.6)	11 (3.4)	13 (4.0)	12 (3.6)
Current NYHA heart failure class				
1	86 (8.6)	31 (9.4)	23 (7.0)	32 (9.4)
2	429 (42.9)	160 (48.5)	131 (39.7)	138 (40.6)
3	428 (42.8)	122 (37.0)	157 (47.6)	149 (43.8)
4	57 (5.7)	17 (5.2)	19 (5.8)	21 (6.2)
EDVI (algorithm 8)	109 (87 - 133)	110 (88 - 131)	110 (89 - 133)	106 (79 - 139)
ESVI (algorithm 8)				
Median (25 th , 75 th percentile)	78 (58 - 100)	78 (59 - 99)	78 (59 - 100)	78 (57 - 104)
Minimum, maximum	23, 281	25, 231	24, 268	23, 281
EF (algorithm 8)				
Median (25 th , 75 th percentile)	28 (23 - 34)	28 (23 - 33)	29 (22 - 35)	28 (23 - 33)
Minimum, maximum	4, 62	6, 62	4, 56	8, 61

* All p>0.05 (chi-square or Kruskal-Wallis tests) except myocardial infarction with p=0.036.