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Impact of surgical ventricular reconstruction on sphericity index in patients with ischaemic cardiomyopathy: follow-up from the STICH trial

Jin-Oh Choi[1,2], Richard C. Daly[3], Grace Lin[1], Brian D. Lahr[4], Heather J. Wiste[4], Thomas M. Beaver[5], Attilio Iacovoni[6], Marcin Malinowski[7], Ivar Friedrich[8], Jean L. Rouleau[9], Roberto R. Favaloro[10], George Sopko[11], Irene M. Lang[12], Harvey D. White[13], Carmelo A. Milano[14], Robert H. Jones[14], Kerry L. Lee[15], Eric J. Velazquez[16], and Jae K. Oh[1,2]*

[1]Echocardiography Core Laboratory, Division of Cardiovascular Disease, Mayo Clinic, Rochester, MN, USA ; [2]Division of Cardiology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea; [3]Division of Cardiovascular Surgery, Mayo Clinic, Rochester, MN, USA; [4]Division of Biomedical Statistics and Informatics, Mayo Clinic, Rochester, MN, USA; [5]Division of Thoracic and Cardiovascular Surgery, University of Florida, Gainesville, FL, USA; [6]CardioVascular Department, Ospedale Papa Giovanni XXIII, Bergamo, Italy; [7]Department of Cardiac Surgery, Medical University of Silesia, Katowice, Poland; [8]Krankenhaus der Barmherzigen Brüder, Nordallee, Trier, Germany; [9]Montréal Heart Institute, Université de Montréal, Montréal, Canada; [10]University Hospital Favaloro Foundation, Buenos Aires, Argentina; [11]National Institutes of Health/National Heart, Lung and Blood Institute, Bethesda, MD, USA; [12]Department of Internal Medicine, Medical University of Vienna, Vienna, Austria; [13]Green Lane Cardiovascular Service, Auckland City Hospital, Auckland, New Zealand; [14]Department of Surgery-Cardiothoracic, Duke Clinical Research Institute, Duke University Medical Center, Durham, NC, USA; [15]Department of Biostatistics and Bioinformatics, Duke Clinical Research Institute, Duke University Medical Center, Durham, NC, USA ; and [16]Department of Medicine-Cardiology, Duke Clinical Research Institute, Duke University Medical Center, Durham, NC, USA

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Aims We sought to evaluate associations between baseline sphericity index (SI) and clinical outcome, and changes in SI after coronary artery bypass graft (CABG) surgery with or without surgical ventricular reconstruction (SVR) in ischaemic cardiomyopathy patients enrolled in the SVR study (Hypothesis 2) of the Surgical Treatment for Ischemic Heart Failure (STICH) trial.

Methods and results Among 1000 patients in the STICH SVR study, we evaluated 546 patients (255 randomized to CABG alone and 291 to CABG + SVR) whose baseline SI values were available. SI was not significantly different between treatment groups at baseline. After 4 months, SI had increased in the CABG + SVR group, but was unchanged in the CABG alone group (0.69 ± 0.10 to 0.77 ± 0.12 vs. 0.67 ± 0.07 to 0.66 ± 0.09, respectively; $P < 0.001$). SI did not significantly change from 4 months to 2 years in either group. Although LV end-systolic volume and EF improved significantly more in the CABG + SVR group compared with CABG alone, the severity of mitral regurgitation significantly improved only in the CABG alone group, and the estimated LV filling pressure (E/A ratio) increased only in the CABG + SVR group. Higher baseline SI was associated with worse survival after surgery (hazard ratio 1.21, 95% confidence interval 1.02 – 1.43; $P = 0.026$). Survival was not significantly different by treatment strategy.

Conclusion Although SVR was designed to improve LV geometry, SI worsened after SVR despite improved LVEF and smaller LV volume. Survival was significantly better in patients with lower SI regardless of treatment strategy.

Keywords Sphericity index • Surgical ventricular reconstruction and STICH

*Corresponding author. Division of Cardiovascular Diseases, Mayo Clinic, 200 First St SW, Rochester, MN 55905, USA. Tel: +1 507 284 1226, Fax: +1 507 284 3968, Email: oh.jae@mayo.edu

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Introduction

In patients with ischaemic cardiomyopathy, left ventricular (LV) remodelling occurs preferentially along the short axis of the left ventricle and results in a dilated ventricle with a more spherical shape, which is associated with poor outcomes.[1,2] Surgical ventricular reconstruction (SVR) is a technique to attempt to reverse LV remodelling and to restore the more efficient geometry of the left ventricle in patients with previous large anterior myocardial infarction and apical akinesia or dyskinesia.[3] However, the data from the Surgical Treatment for Ischemic Heart Failure (STICH) trial did not demonstrate survival benefit from adding SVR to coronary artery bypass grafting (CABG) compared with CABG alone in that patient population, despite improved LVEF and smaller LV volumes with SVR.[4] Moreover, a subgroup analysis based on baseline echocardiography measurements suggests that SVR may improve clinical outcome in patients with an early stage of LV remodelling and LV end-systolic volume (LVESV) index of $\leq$60 mL/m^2, but not in patients with a larger left ventricle.[5,6]

The sphericity index (SI), which is a ratio of the LV short-axis to the long-axis dimension, has been used to evaluate the geometry of the left ventricle, and a higher SI value indicates a more globular shape of the left ventricle and poor prognosis.[2] Therefore, the purpose of this report is to determine how SVR affects the SI in patients with ischaemic cardiomyopathy enrolled in the SVR study (Hypothesis 2) of the STICH trial and what impact the baseline SI had on the clinical outcome of the patients after CABG with or without SVR.

Methods

Patient selection

Between September 2002 and January 2006, patients with an LVEF $\leq$35%, apical dyssynergy, and coronary artery disease amenable to CABG were enrolled in the SVR hypothesis of the STICH trial and randomized to CABG + SVR or CABG alone. Patients were recruited from 122 clinical sites in 26 countries. The qualifying LVEF for enrolment was determined by the clinical sites using any available imaging modalities within 3 months of enrolment. More detailed inclusion and exclusion criteria and randomization strata for the STICH trial have been published elsewhere.[4,7] The median duration of follow-up of the patients was 4 years. The primary endpoints in the current analysis were overall mortality and change of SI at 4-month follow-up. In this analysis, we excluded patients if their baseline SI was unavailable. To ensure that the subset of patients for the analysis of changes in SI and other echocardiographic variables was not compromised by early surgical death (early post-surgical death is more common in patients with higher risks such as larger LV size and higher SI at baseline), we defined a subgroup of patients who underwent surgery and remained alive to undergo follow-up imaging of the LV size and shape using paired evaluations of SI in patients with adequate quality of echocardiography allowing LV volume measurement.[6]

Echocardiography

Transthoracic echocardiography (TTE) was performed at baseline, 4 months (between 2 and 6 months), and 2 years (between 18 and 30 months) following surgery, and TTE images were submitted to the Echocardiography Core Laboratory for analysis. All TTE measurements were performed by the Echocardiography Core Laboratory according to standardized methods as recommended by the American Society of Echocardiography.[8,9] All measurements and analyses were performed without knowledge of treatment assignment, clinical, or other laboratory data. Echocardiographic measurements were acquired and averaged over three cardiac cycles if sinus rhythm was present, and 3–5 cardiac cycles for patients in AF.

Left ventricular dimensions and sphericity index

The LV SI, which was a pre-defined echocardiographic variable in the STICH trial, was calculated as the ratio of the LV short-axis dimension (numerator) and the long-axis dimension (denominator) measured at the end-diastolic period. Therefore, the more spherical the left ventricle becomes, the higher the SI. The LV minor short-axis dimension was measured from the two-dimensional parasternal long-axis view of the left ventricle near the junction of the head of the papillary muscle and chordae. The long-axis dimension of the left ventricle was measured from the apical four-chamber view from the mitral annulus to the apex (*Figure 1*). For follow-up SI after SVR, the long-axis dimension was measured from the mid-portion of the mitral annulus to the centre of the LV apex in the apical four-chamber view, which might be different from the longest dimension of the left ventricle.

Left ventricular volume and ejection fraction measurement

The LVEF was measured by the Simpson's biplane volumetric method whenever possible. Either a combination of apical four- and two-chamber views (preferentially) or a combination of apical four-chamber and long-axis views was used. If two apical views were not available, only one apical view was used for the Simpson's single plane method. The LV endocardial border was traced contiguously from one side of the mitral annulus to the other, excluding the papillary muscles and trabeculations. LVEF was determined from LV volumes accordingly, which were indexed by body surface area.

Statistical analyses

Descriptive statistics on baseline data were reported as mean ± standard deviation, median (interquartile ranges), or number (percentage), as appropriate. Two-group comparisons of baseline characteristics between the two types of surgeries were tested using the Student's *t*-test or Wilcoxon Rank Sum test for continuous data or a χ^2 test for categorical variables. All comparisons of treatment strategy were analysed based on the intent-to-treat approach. As the primary variable of interest, a measured value of SI at baseline was required for inclusion in these analyses. Since a possible selection bias could limit the generalizability of results from this subset, analyses comparing the characteristics of those with and without an SI value were performed (see Supplementary material online, *Table S1*). For all analyses, $P < 0.05$ was considered statistically significant.

For SI and other echo parameters, the change in value between baseline and 4-month follow-up was assessed on the subset in which both measures were available. Likewise, the change between 4-month and 2-year follow-up values was analysed, though fewer subjects with

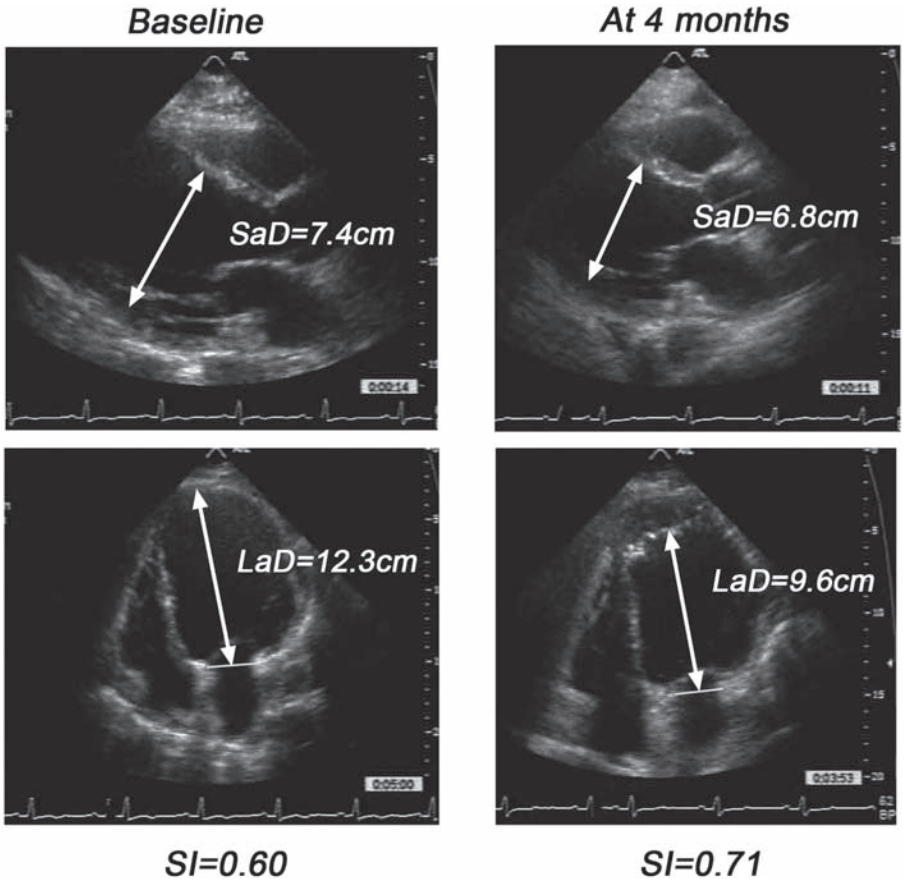

Figure 1 Measurement of the sphericity index (SI). The LV short-axis dimension (SaD) was measured near the junction between the papillary muscle head and the chordae in parasternal long-axis view, and the long-axis dimension (LaD) from the mitral annulus to the apex by drawing a line at the mid-portion of the annular plane to the centre of the LV apex in the apical four-chamber view. The SI was calculated at baseline (left panels) and 4 months after surgery (right panels) measuring the LV parasternal long-axis view (upper panels) and apical four-chamber view (lower panels) at end-diastole. Note that despite a slight decrease in SaD, a greater reduction in LaD results in an increase of SI at 4 months.

those paired measures were available. We tested for a significant change between paired measures using a paired *t*-test, and for a significant difference in the change between surgery groups using a two-sample *t*-test. Pearson correlation coefficients were used to assess whether baseline LVESV index was associated with baseline SI or with changes in SI from baseline to 4 months within surgery groups and whether changes in echocardiographic variables over time were linearly related to changes in SI. For these analyses, the grade of mitral regurgitation was quantified as a numerical variable as follows: 0 for none, 1 for mild, 2 for moderate, 3 for moderately severe, and 4 for severe mitral regurgitation. Likewise, the grade of diastolic dysfunction was coded as a numerical variable with a grade of 0–4. An indeterminate grade of diastolic function or mitral regurgitation was treated as missing data, thereby excluding those subjects from the corresponding analyses.

The influence of SI on overall survival was evaluated with Cox proportional hazards regression, both unadjusted and adjusted for conventional confounders including age, sex, and body mass index. To study whether the effect of SI on the endpoint was differential with respect to surgery type, we fit a model with an interaction term between SI and surgery type and tested its significance. A linear effect of SI was assumed in these regression models since a p-spline plot revealed no clear evidence of a non-linear relationship between the log of the mortality hazard function and numerical values of SI.[10] For descriptive purposes, survival was estimated by the Kaplan–Meier method for categories of SI, divided at the median, and plotted over time.

Results

Baseline echocardiographic data

A total of 1000 patients were enrolled in the SVR arm, and randomized to the CABG alone ($n = 499$) or CABG + SVR group ($n = 501$). Of these, 937 underwent baseline TTE, 724 at 4 months and 561 at 2 years following surgery (*Figure 2*). Baseline characteristics for the study population have been published previously.[4] After exclusion of 391 subjects whose image was poor for measurement of SI [unable to measure the LV long-axis ($n = 222$) or short-axis dimension ($n = 265$); 96 subjects were missing both], we included 546 study subjects whose baseline SI was available. Study subjects were

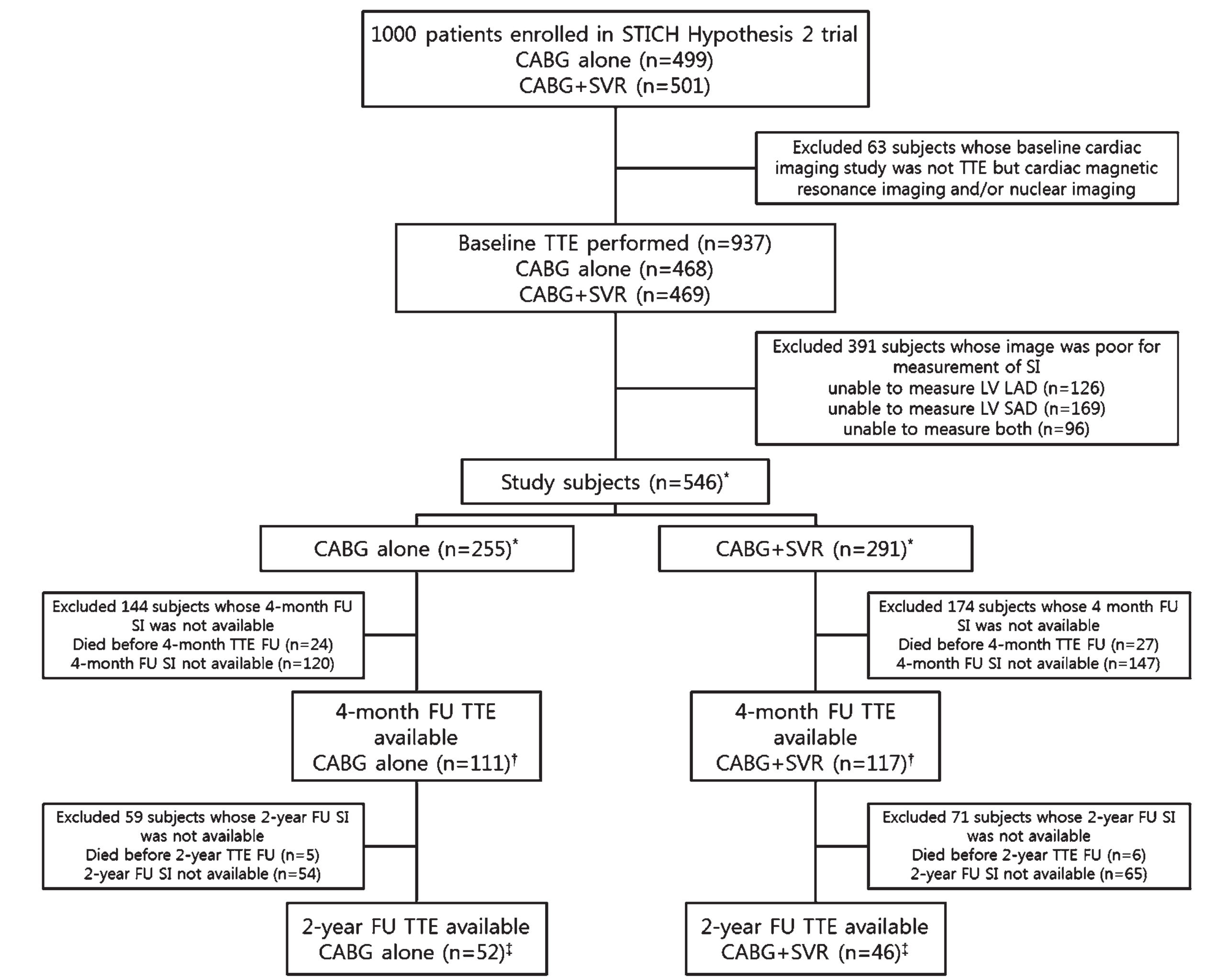

Figure 2 Flow diagram for analysis of the current study. *Study subjects included for outcome analysis for sphericity index. †Study subjects included for the changes in sphericity index from baseline to 4-month follow-up. ‡Study subjects included for the changes in sphericity index from 4-month to 2-year follow-up. CABG, coronary artery bypass graft surgery; FU, follow-up; LAD, long-axis dimension; SAD, short-axis dimension; SI, sphericity index; STICH, Surgical Treatment for Ischemic Heart Failure; SVR, surgical ventricular reconstruction; TTE, transthoracic echocardiography.

younger, less frequently male, had lower body mass index, and were more frequently randomized to the CABG + SVR group compared with those without a baseline SI measure (see Supplementary material online, *Table S1*). Also, despite no significant differences in baseline LVEF, those patients with baseline SI had a slightly larger LV volume, increased E/A ratio, shorter deceleration time, and more significant mitral regurgitation and diastolic dysfunction compared with patients in which baseline SI could not be measured.

For the 546 subjects included in the primary analyses ($n = 255$ with CABG alone, $n = 291$ with CABG + SVR), baseline echocardiographic data according to the treatment group are shown in *Table 1*. At baseline, there were no significant differences in LVEF, LV volumes, SI, or echocardiographic parameters for diastolic function between the CABG alone group and the CABG + SVR group.

Changes in left ventricular volume, ejection fraction, and sphericity index

Changes in echocardiographic variables from baseline to 4-month follow-up are presented according to the treatment group in *Table 2*, *Figure 3*, and Supplementary material online, *Table S2*. Baseline characteristics of the patients who were excluded from this analysis due to not having a 4-month follow-up SI measured are also shown in the Supplementary material online, *Table S3*. There were no significant differences in mean time from baseline to 4 months echocardiography (4.3 ± 0.5 months for CABG alone and 4.4 ± 0.6 months for CABG + SVR, $P = 0.06$), and from baseline to 2 years follow-up echocardiography (24.6 ± 1.2 months for CABG alone and 24.6 ± 1.1 months for CABG + SVR, $P = 0.87$) between groups. The LVESV index was significantly reduced at 4 months

Table 1 Baseline characteristics of study subjects in the STICH trial surgical ventricular reconstruction evaluation with available baseline sphericity index according to treatment strategy

Variable	Overall		CABG		CABG + SVR		*P*-value
	n	Mean ± SD or *n* (%)	*n*	Mean ± SD or *n* (%)	*n*	Mean ± SD or *n* (%)	
Age at randomization (years)	546	60.6 ± 9.6	255	60.4 ± 9.6	291	60.7 ± 9.6	0.78
Male gender	546	450 (82.4%)	255	204 (80.0%)	291	246 (84.5%)	0.16
Body mass index (kg/m^2)	546	26.9 ± 4.1	255	27.2 ± 3.9	291	26.7 ± 4.2	0.14
Body surface area (m^2)	546	1.92 ± 0.21	255	1.93 ± 0.20	291	1.92 ± 0.21	0.33
Creatinine (mg/dL), median (Q1, Q3)	545	1.06 (0.90, 1.26)	254	1.05 (0.90, 1.21)	291	1.06 (0.91, 1.28)	0.58
LVEF (%)	509	29.4 ± 8.3	238	29.3 ± 8.1	271	29.4 ± 8.5	0.83
LVEDV (mL)	509	228.0 ± 70.6	238	227.8 ± 67.1	271	228.2 ± 73.6	0.94
LVESV (mL)	509	163.5 ± 61.7	238	163.6 ± 59.9	271	163.5 ± 63.4	0.98
LVEDV index (mL/m^2)	509	119.3 ± 36.3	238	118.4 ± 33.8	271	120.1 ± 38.3	0.60
LVESV index (mL/m^2)	509	85.6 ± 32.1	238	85.0 ± 30.4	271	86.2 ± 33.5	0.69
LVEDD or short-axis dimension (cm)	546	6.37 ± 0.82	255	6.37 ± 0.79	291	6.36 ± 0.85	0.90
LVESD (cm)	515	5.35 ± 0.95	240	5.35 ± 0.93	275	5.35 ± 0.96	0.94
LV long-axis dimension (cm)	546	9.35 ± 0.97	255	9.38 ± 0.93	291	9.32 ± 1.00	0.45
Sphericity index	546	0.68 ± 0.09	255	0.68 ± 0.08	291	0.69 ± 0.10	0.42
RWT	527	0.30 ± 0.08	252	0.29 ± 0.08	275	0.30 ± 0.08	0.47
Left atrial volume (mL)	378	81.6 ± 29.0	175	81.6 ± 30.0	203	81.6 ± 28.2	0.99
E velocity (m/s)	479	0.76 ± 0.24	222	0.76 ± 0.25	257	0.75 ± 0.24	0.63
A velocity (m/s)	455	0.66 ± 0.25	212	0.66 ± 0.25	243	0.66 ± 0.26	0.89
E/A ratio, median (Q1, Q3)	454	1.13 (0.71, 1.80)	212	1.16 (0.72, 1.78)	242	1.03 (0.71, 1.83)	0.62
Deceleration time (ms)	445	177.5 ± 49.4	208	181.4 ± 51.0	237	174.2 ± 47.8	0.12
e′, septal (m/s)	294	0.05 ± 0.02	138	0.05 ± 0.02	156	0.05 ± 0.02	0.73
e′, lateral (m/s)	278	0.06 ± 0.03	133	0.06 ± 0.03	145	0.06 ± 0.03	0.12
E/e′ septal, median (Q1, Q3)	271	15.6 (11.4, 20.0)	128	15.9 (12.0, 21.8)	143	15.0 (10.0, 20.0)	0.40
E/e′ lateral, median (Q1, Q3)	263	12.5 (9.3, 16.7)	124	12.9 (10.0, 17.8)	139	12.0 (8.6, 16.7)	0.16
MR grade	539		252		287		0.12
None		114 (21.2%)		63 (25.0%)		51 (17.8%)	
Mild		261 (48.4%)		118 (46.8%)		143 (49.8%)	
Moderate		92 (17.1%)		42 (16.7%)		50 (17.4%)	
Moderate to severe		36 (6.7%)		17 (6.7%)		19 (6.6%)	
Severe		17 (3.2%)		8 (3.2%)		9 (3.1%)	
Indeterminate		19 (3.5%)		4 (1.6%)		15 (5.2%)	
Diastolic function grade	545		254		291		0.87
Normal		2 (0.4%)		1 (0.4%)		1 (0.3%)	
1		142 (26.1%)		67 (26.4%)		75 (25.8%)	
2		191 (35.0%)		91 (35.8%)		100 (34.4%)	
3		138 (25.3%)		60 (23.6%)		78 (26.8%)	
4		1 (0.2%)		1 (0.4%)		0 (0.0%)	
Indeterminate		71 (13.0%)		34 (13.4%)		37 (12.7%)	
PASP (mmHg)	151	42.8 ± 15.2	69	40.6 ± 14.3	82	44.7 ± 15.7	0.10
MV repair/replacement	546	104 (19.0%)	255	42 (16.5%)	291	62 (21.3%)	0.15

Mean ± standard deviation or count (percentage) are shown unless otherwise noted.
A, late mitral inflow velocity; CABG, coronary artery bypass graft surgery; E, early mitral inflow velocity; e′, early mitral annular velocity; LVEDD, left ventricular end-diastolic dimension; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic dimension; LVESV, left ventricular end-systolic volume; MR, mitral regurgitation; MV, mitral valve; PASP, pulmonary artery systolic pressure; RWT, relative wall thickness; SVR, surgical ventricular reconstruction.

after surgery in both the CABG + SVR (83.2 ± 33.5 mL/m^2 to 67.7 ± 27.8 mL/m^2, $P < 0.001$) and CABG alone (84.2 ± 28.0 mL/m^2 to 79.2 ± 32.2 mL/m^2, $P = 0.037$) groups, but the change was significantly greater in the CABG + SVR group ($P = 0.002$). LVEF increased significantly in the CABG + SVR group (29 ± 9% to 35 ± 11%, $P < 0.001$) but not in the CABG alone group (30 ± 8% to 32 ± 10%, $P = 0.11$). Likewise, the LV long-axis dimension was significantly decreased in the CABG + SVR group (9.3 ± 1.1 cm to 8.2 ± 1.0 cm, $P < 0.001$) but not in the CABG alone group (9.5 ± 0.9 cm to 9.4 ± 0.9 cm, $P = 0.10$). In contrast, the LV short-axis dimension (LV end-diastolic dimension) was significantly decreased in the CABG alone group (6.4 ± 0.7 cm to 6.2 ± 0.8 cm, $P = 0.007$) but not in the CABG + SVR group (6.3 ± 0.8 cm to 6.2 ± 0.8 cm, $P = 0.08$), although these changes was not

Table 2 Changes in echocardiographic variables from baseline to 4 months according to treatment strategy

Variable	CABG		CABG + SVR		*P*-value[a]
	n	Mean ± SD[b]	*n*	Mean ± SD[b]	
Sphericity index	111	−0.01 ± 0.08	117	0.08 ± 0.10†	<0.001
LV long-axis dimension (cm)	111	−0.12 ± 0.77	117	−1.1 ± 1.1†	<0.001
LVEDD or short-axis dimension (cm)	111	−0.17 ± 0.67†	117	−0.10 ± 0.61	0.37
LVESD (cm)	98	−0.17 ± 0.75*	108	−0.16 ± 0.80*	0.96
LVEF (%)	101	1.8 ± 11.2	94	5.6 ± 9.6†	0.012
LVEDV (mL)	101	−9.4 ± 45.3*	94	−26.2 ± 52.0†	0.017
LVESV (mL)	101	−9.1 ± 45.9*	94	−29.1 ± 44.0†	0.002
LVEDV index (mL/m^2)	101	−5.1 ± 24.3*	94	−14.0 ± 27.3†	0.017
LVESV index (mL/m^2)	101	−5.1 ± 24.1*	94	−15.5 ± 23.0†	0.002
RWT	107	0.03 ± 0.10†	110	0.01 ± 0.10	0.09
Left atrial volume (mL)	57	−1.5 ± 23.6	44	1.0 ± 30.6	0.63
E velocity (m/s)	88	0.10 ± 0.30†	96	0.17 ± 0.34†	0.16
A velocity (m/s)	80	0.11 ± 0.33†	88	−0.03 ± 0.26	0.001
E/A ratio	80	−0.09 ± 0.89	88	0.45 ± 1.2†	0.001
Deceleration time (ms)	80	16.2 ± 63.3*	83	−4.7 ± 74.0	0.06
MR grade	102	−0.34 ± 1.1†	106	−0.07 ± 1.00	0.06
Diastolic function grade	78	−0.01 ± 0.80	90	0.18 ± 0.92	0.16

A, late mitral inflow velocity; CABG, coronary artery bypass graft surgery; E, early mitral inflow velocity; LVEDD, left ventricular end-diastolic dimension; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic dimension; LVESV, left ventricular end-systolic volume; MR, mitral regurgitation; RWT, relative wall thickness; SVR, surgical ventricular reconstruction.
[a]*P*-value of comparison of changes of variables between treatment strategies from two-sample *t*-test.
[b]*P*-value of change within group is from a paired *t*-test: $^*P < 0.05$, $^\dagger P < 0.01$.

significantly different between groups ($P = 0.37$). Accordingly, SI worsened after 4 months in the CABG + SVR group (0.69 ± 0.10 to 0.77 ± 0.12, $P < 0.001$) but did not significantly change in the CABG alone group (0.67 ± 0.07 to 0.66 ± 0.09, $P = 0.24$). In general, among the subsets who additionally had 2-year data, echocardiographic measurements did not change significantly from 4 months to 2 years, with the exception of a slight increase in LV end-diastolic dimension in the CABG + SVR group (6.07 ± 0.70 cm to 6.22 ± 0.72 cm, $P = 0.011$; *Figure 3*).

In both treatment arms, baseline levels of SI and indexed LVESV were positively correlated (*Figure 4*). However, the change in SI was not significantly associated with baseline LVESV index.

Changes in mitral regurgitation and diastolic function

Mitral valve repair and/or replacement was performed during the surgery in 62 (21.3%) patients of the CABG + SVR group, which was not significantly different compared with the CABG alone group [42 (16.5%) patients, $P = 0.15$]. However, mitral regurgitation grade was significantly decreased in the CABG group (1.3 ± 1.1 to 0.9 ± 0.7, $P = 0.003$) but did not significantly change in the CABG + SVR group (1.2 ± 0.9 to 1.1 ± 1.0, $P = 0.50$). Despite the within-group change of mitral regurgitation grade, the difference in change in mitral regurgitation between treatment groups was only of marginal statistical difference ($P = 0.06$).

There were significant differences in changes in diastolic function parameters from baseline to 4 months according to the treatment strategy. In particular, the E/A ratio, which estimates LV filling pressure, increased significantly in the CABG + SVR group (1.3 ± 0.9 to 1.8 ± 1.1, $P < 0.001$), suggesting a higher diastolic filling pressure, but did not significantly change in the CABG alone group (1.4 ± 0.9 to 1.3 ± 0.8, $P = 0.35$). These trends did not change when we excluded the patients who underwent mitral valve repair and/or replacement from the paired comparisons. Interestingly, changes in the grade of mitral regurgitation and LV diastolic dysfunction had weak but statistically significant correlations with change in SI from baseline to 4 months ($r = 0.17$, $P = 0.025$ and $r = 0.16$, $P = 0.020$, respectively) among all subjects combined.

Sphericity index and outcome

Lower baseline SI was associated with better overall survival after surgery (hazard ratio 1.21, 95% confidence interval = 1.02–1.43, $P = 0.026$; *Figure 5*, *Table 3*). Survival was not affected by treatment strategy ($P = 0.94$) nor was the effect of SI on survival different by treatment group ($P = 0.27$). Neither SI at 4-month follow-up nor change in SI from baseline to 4 months had a significant association with overall survival after 4 months in landmark survival analyses.

Discussion

The major findings of the current data are that survival was worse in patients with increased ventricular sphericity regardless of treatment strategy, and that SI increased in the SVR patients

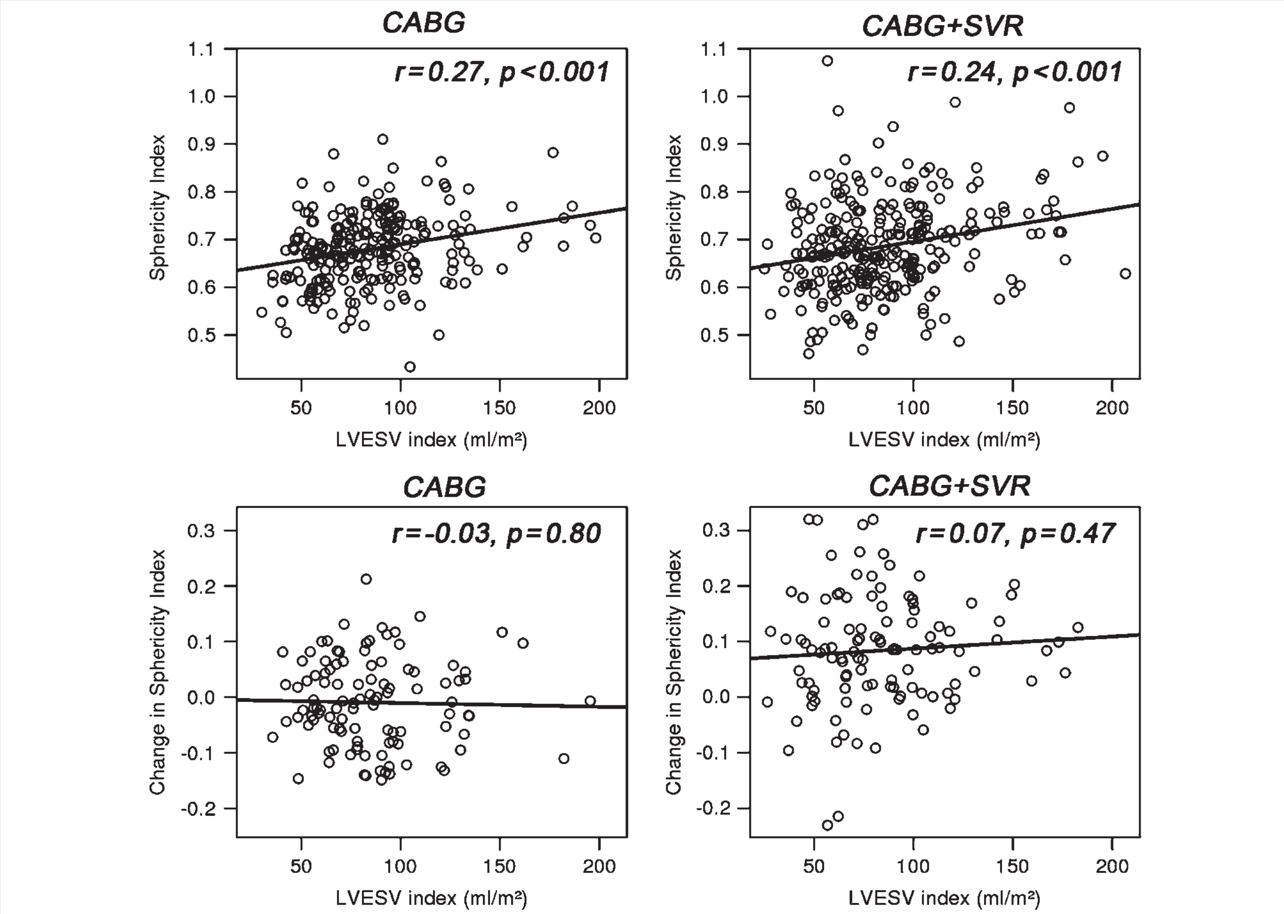

Figure 3 Changes in echocardiographic variables. Mean values along with 95% confidence intervals of echocardiographic variables at baseline and 4-month follow-up (left side in each graph) and at 4-month and 2-year follow-up (right side in each graph) are noted according to the treatment groups. Upper panels show the changes in sphericity index (SI) together with those of the LV short-axis and long-axis dimension, which are the numerator and denominator of SI, respectively. Lower panels show changes in LV end-systolic volume (LVESV index), LVEF, and deceleration time of early mitral inflow velocity. Note that even though a reduced LVESV index and improved LVEF were noted, SI became worse in the CABG + SVR group. Deceleration time was increased only in the CABG group. *indicates $P < 0.05$ from a paired *t*-test within treatment group. Blue lines indicate the CABG alone group and red lines the CABG + SVR group. CABG, coronary artery bypass graft surgery; SVR, surgical ventricular reconstruction.

most probably due to the significant shortening of the LV long-axis without shortening of the LV short-axis.

Previous studies have identified larger LV volumes, restrictive diastolic filling, advanced heart failure symptoms, and abnormal LV geometry as predictors of poor outcomes in patients undergoing SVR.[11–15] STICH is the largest surgical trial in patients with ischaemic cardiomyopathy directly comparing the impact of CABG alone vs. CABG + SVR. The results of STICH demonstrate that increased SI was associated with worse survival, independent of age, sex, and body mass index for the patients with ischaemic cardiomyopathy undergoing surgical revascularization. The results of STICH also suggest that the negative impact of abnormal LV geometry on mortality is independent of and not significantly different whether SVR is added to CABG or not.

Initially, SVR was believed to reverse LV remodelling by eliminating the akinetic or dyssynergic zone of the left ventricle and therefore reducing LV cavity size with a more efficient shape. However, there were controversies about the usefulness of this procedure, with the only previous study of a small number of patients showing that SI became worse after SVR.[14,16] In this analysis of STICH data, LV end-systolic and diastolic volumes were reduced and LVEF improved after CABG + SVR, as expected. The decrease of LV volume after SVR was probably due to reduction in the LV long-axis dimension as there was only an insignificant decrease in short-axis dimension. Although LV volume was reduced after SVR, its shape most probably became more globular and SI increased at follow-up. Considering that diastolic function is usually more related to the longitudinal motion of the left ventricle, findings that the reduction in LV long-axis dimension and increased SI were associated with worsening grades of diastolic dysfunction are noteworthy.[17] Indeed, as the left ventricle becomes more globular, LV wall tension generally increases and is

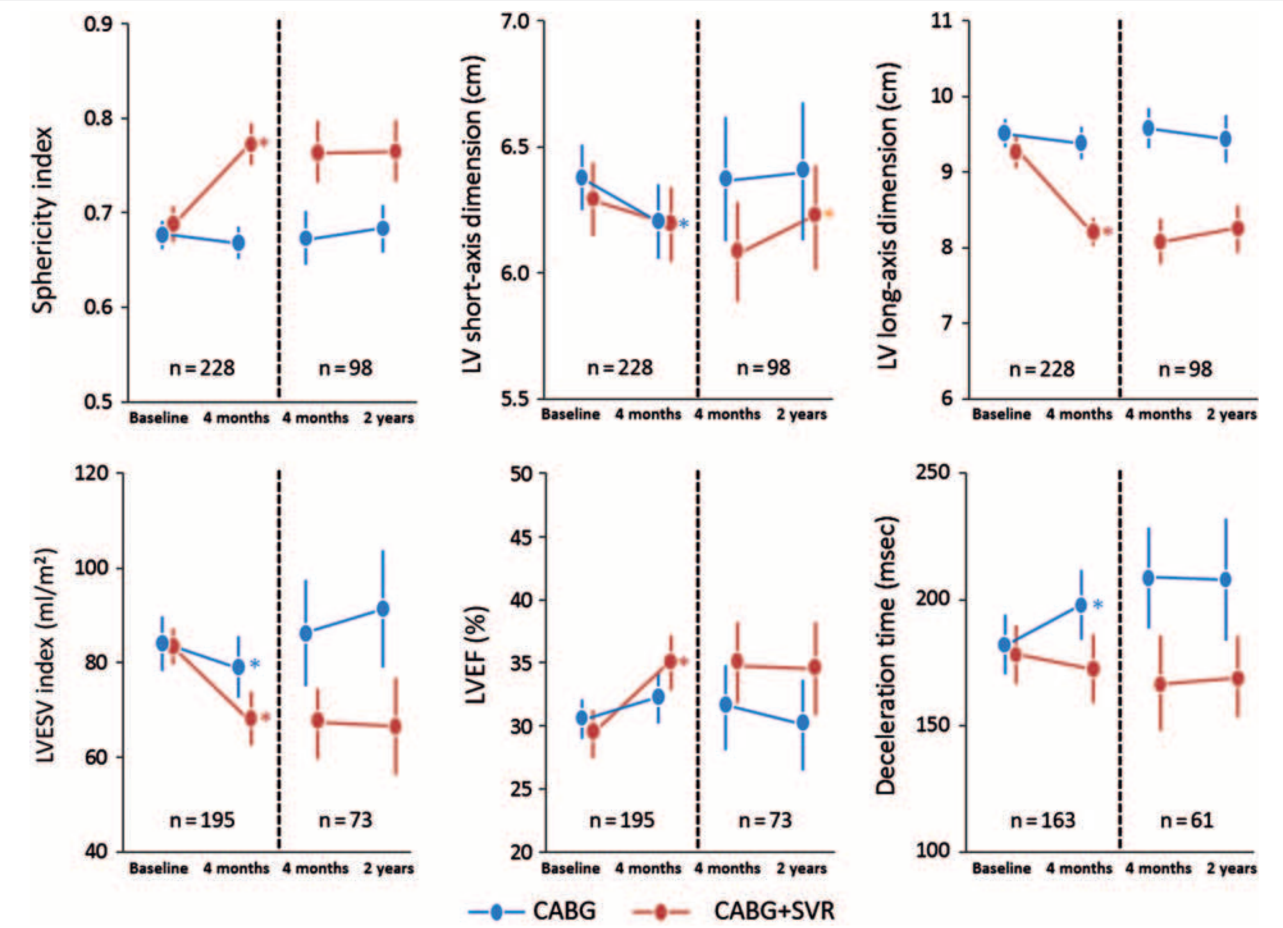

Figure 4 Associations of baseline LV end-systolic volume (LVESV) index with baseline sphericity index (SI) (upper panels) and change in SI from baseline to 4 months within treatment groups (lower panels). Pearson correlation coefficients along with *P*-values are shown at the top of each panel. Linear regression lines are also shown for each panel.

followed by more severe diastolic dysfunction and/or mitral regurgitation, which was consistent in the current data.[14,18,19] Increased LV wall tension could also have adverse effects on myocardial blood flow.[20] This counter-intuitive change in LV shape towards a less efficient globular shape after SVR was evident irrespective of the baseline LVESV index (*Figure 4*). In contrast, SI was not significantly changed in the CABG alone group, although there was a small but statistically significant reduction in LV short-axis dimension.

Although a smaller LV volume and better LVEF usually indicate better outcome, after SVR these changes were not translated into a survival benefit in STICH. This lack of benefit in survival with the addition of SVR may have been a result of the left ventricle becoming more spherical (with an increase in SI) and worsening of LV diastolic dysfunction or filling pressure (as assessed by the E/A ratio) in the CABG + SVR group and a significant improvement in the severity of mitral regurgitation being documented only in the CABG alone group. Indeed, worse diastolic dysfunction and significant mitral regurgitation are well-known clinical predictors of poor outcomes in patients with heart failure, such that the beneficial effects in terms of LV volume and LVEF in patients with CABG + SVR may have been offset by the worse effects on diastolic function and mitral regurgitation.

Previously our report from STICH trial showed that patients with a smaller left ventricle had a benefit from SVR in contrast to the previous expectation that SVR would be useful the patients with advanced LV remodelling.[6] This subgroup of patients with early stage of LV remodelling could partly explain why there were no significant differences in clinical outcome between CABG + SVR and CABG alone groups in spite of worse geometry, diastolic function, and mitral regurgitation. However, as there was no significant interaction effect between treatment strategies and baseline SI on overall survival, it is difficult to say whether the outcome of CABG + SVR was even worse in the patients with higher baseline levels of SI compared with those with lower values. These insignificant results might be from the small number of patients evaluated at 4-month echocardiography or relatively short follow-up periods. However, our data might support that artificial modification of LV geometry by SVR could not change the clinical outcome of the patients with ischaemic cardiomyopathy.

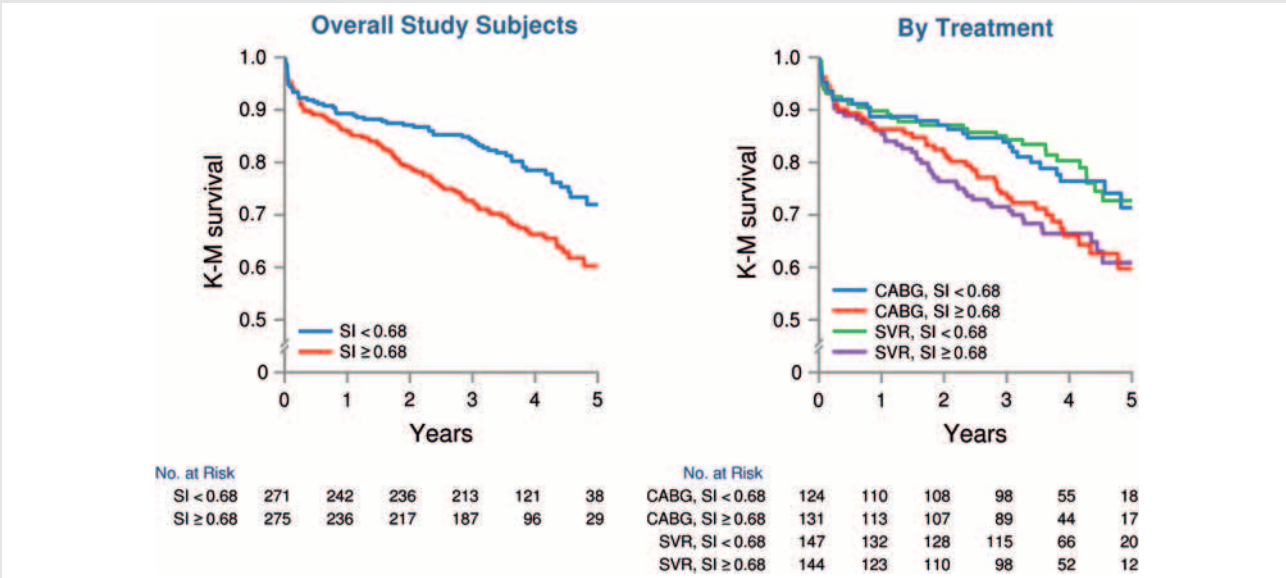

Figure 5 Kaplan–Meier curves for overall survival according to the median baseline sphericity index (SI) in overall study subjects (left panel) and within treatment strategy (right panel). The age-, sex-, and body mass index-adjusted hazard ratio from Cox regression analysis is 1.21 (95% confidence interval 1.02 – 1.43, $P = 0.026$) per 0.1 increase of SI. However, there was no significant interaction between treatment and SI in predicting overall survival ($P = 0.27$).

Table 3 Cox proportional hazard models for overall survival

Variable	No. of events	No. of patients	Unadjusted		Age, sex, and BMI adjusted	
			HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Sphericity index, per 0.1	546	156	1.20 (1.01 – 1.42)	0.041	1.21 (1.02 – 1.43)	0.026
Treatment CABG + SVR vs. CABG	546	156	0.98 (0.72 – 1.35)	0.92	0.99 (0.72 – 1.35)	0.94
Sphericity index at 4 months, per 0.1	228	39	1.13 (0.86 – 1.48)	0.39	1.18 (0.85 – 1.63)	0.33[a]
Change in sphericity index from baseline to 4-month echo, per 0.1	228	39	1.15 (0.85 – 1.57)	0.37	1.13 (0.83 – 1.55)	0.44

There was no significant interaction with treatment and sphericity index in predicting overall survival ($P = 0.27$).
BMI, body mass index; CABG, coronary artery bypass graft; CI, confidence interval; HR, hazard ratio.
[a]Adjustment was also made for baseline sphericity index.

Interestingly, only a few cases with higher baseline LVESV index (>90 mL/m^2) showed reduced SI at 4 months after surgery and those who experienced reduction of SI had a relatively small LVESV index at baseline (*Figure 4*). This finding might provide an insight into why the clinical course after SVR was better in the patients with a small LVESV index or less advanced LV remodelling in the previous reports.[6]

Study limitations

There were several limitations in the current analysis. First, baseline SI measurement was available in only 55% of the patients who were originally assigned to the SVR arm of the STICH trial. There was also considerable loss of patients for the follow-up measurements of the echocardiographic variables. One reason for this is that LV dimensions were measured in the Echocardiography Core Laboratory only when the echocardiography images taken for that measurement were completely satisfactory. As the study subjects in which baseline SI measurements were available had slight but statistically significantly different baseline characteristics from those not included (see Supplementary material online, *Table S1*), the study results may not be generalizable to the entire set of patients enrolled in the STICH trial. Nevertheless, since there were no noticeable group imbalances in baseline echocardiographic characteristics between treatment groups in patients for whom an SI was obtainable, this selection did not appear to bias the group comparability of our primary analyses. A number of additional cases were excluded from the paired comparison analyses of SI between baseline and 4 months and between 4 months and 2 years. This was mainly due to the frequency of very poor echocardiographic windows for good images after surgery and the fact that we could not evaluate the changes in those who died during the follow-up. This resulted in lack of sufficient statistical power to detect the significant associations between survival and SI at 4 months or change of SI from baseline to 4 months. Therefore, it is difficult to conclude whether this lack of significant association with survival was due to a small number of follow-up patients or no actual clinical impact of increased SI after SVR on overall survival in this study. Follow-up echocardiography was performed in relatively wide ranges of time periods; between 2 and 6 months for the 4-month follow-up and between 18 and 30 months for the 2-year follow-up. This wide range of time points might have resulted in deviation from actual values at 4 months and 2 years after surgery. However, as there were no significant differences in echocardiographic follow-up days between groups, this limitation might have little effect on the difference in changes of echocardiographic variables between groups. There were 12 (2.2%) patients who did not receive CABG and 26 (4.8%) patients who crossed over between CABG + SVR and CABG alone groups, but, when the analysis was repeated based on as-treated, the results did not change significantly from the current analysis in terms of changes of SI, grade of mitral regurgitation and diastolic dysfunction, and effect of SI on overall survival (data not shown). Follow-up measurement of SI especially after SVR could be very challenging since the original LV apex was cut off after SVR. Therefore, there were possibilities of the new LV apex being different from the original one, which might result in over- or underestimation of the LV long-axis dimension and SI. Finally, although every surgeon in the trial was trained in SVR according to the protocol to standardize the surgical technique, the actual operative technique might be different from centre to centre, which might have some differential effect on the change of LV geometry. Despite these limitations, our results provide an insight into geometric and haemodynamic alteration after CABG + SVR in terms of the impact of the baseline SI on clinical outcome and the impact of SVR compared with CABG alone on subsequent SI as well as other echocardiographic parameters.

Conclusions

This analysis of the STICH trial shows that higher baseline SI was associated with worse survival in patients with ischaemic cardiomyopathy and anterior wall akinesia/dyskinesia, undergoing surgical revascularization, whether or not SVR was performed. Although SVR was designed to improve LV geometry, SI worsened after SVR despite improved LVEF and a smaller LV volume. The worsening of SI with SVR was accompanied by worsening of diastolic function and less improvement in mitral regurgitation.

Supplementary Information

Additional Supporting Information may be found in the online version of this article:

Table S1 Demographic and baseline echocardiographic characteristics in study subjects with baseline echocardiographic data by availability of sphericity index

Table S2 Comparison between echocardiographic variables measured at baseline and 4 months according to treatment group

Table S3 Demographic and baseline echocardiographic characteristics in study subjects with baseline sphericity index (SI) by availability of 4-month SI and survival status at 4 months among those without 4-month SI

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