Circulation: Heart Failure

ORIGINAL ARTICLE

Society of Thoracic Surgeons Risk Score and EuroSCORE-2 Appropriately Assess 30-Day Postoperative Mortality in the STICH Trial and a Contemporary Cohort of Patients With Left Ventricular Dysfunction Undergoing Surgical Revascularization

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BACKGROUND: The STICH trial (Surgical Treatment for Ischemic Heart Failure) demonstrated a survival benefit of coronary artery bypass grafting in patients with ischemic cardiomyopathy and left ventricular dysfunction. The Society of Thoracic Surgeons (STS) risk score and the EuroSCORE-2 (ES2) are used for risk assessment in cardiac surgery, with little information available about their accuracy in patients with left ventricular dysfunction. We assessed the ability of the STS score and ES2 to evaluate 30-day postoperative mortality risk in STICH and a contemporary cohort (CC) of patients with a left ventricle ejection fraction ≤35% undergoing coronary artery bypass grafting outside of a trial setting.

METHODS AND RESULTS: The STS and ES2 scores were calculated for 814 STICH patients and 1246 consecutive patients in a CC. There were marked variations in 30-day postoperative mortality risk from 1 patient to another. The STS scores consistently calculated lower risk scores than ES2 (1.5 versus 2.9 for the CC and 0.9 versus 2.4 for the STICH cohort), and underestimated postoperative mortality risk. The STS and ES2 scores had moderately good C statistics: CC (0.727, 95% CI: 0.650–0.803 for STS, and 0.707, 95% CI: 0.620–0.795 for ES2); STICH (0.744, 95% CI: 0.677–0.812, for STS and 0.736, 95% CI: 0.665–0.808 for ES2). Despite the CC patients having higher STS and ES2 scores than STICH patients, mortality (3.5%) was lower than that of STICH (4.8%), suggesting a possible decrease in postoperative mortality over the past decade.

CONCLUSIONS: The 30-day postoperative mortality risk of coronary artery bypass grafting in patients with left ventricular dysfunction varies markedly. Both the STS and ES2 score are effective in evaluating risk, although the STS score tend to underestimate risk.

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Key Words: coronary artery bypass ■ coronary artery disease ■ heart failure ■ risk stratification

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WHAT IS NEW?

- In patients with severe left ventricular (LV) dysfunction (LV ejection fraction ≤35%) undergoing coronary artery bypass grafting (CABG), both the Society of Thoracic Surgeons (STS) score and EuroSCORE-2 are moderately effective in assessing individual 30-day postoperative mortality risk, but their predictive accuracy is somewhat less than that reported for the overall cardiac surgical population. Also, the STS score tends to underestimate risk.
- The lower 30-day postoperative mortality in a contemporary cohort of patients with an LV ejection fraction ≤35% undergoing CABG as compared with the STICH (Surgical Treatment for Ischemic Heart Failure) cohort (2002 to 2007), despite higher STS and EuroSCORE-2 scores, would suggest that 30-day postoperative mortality may be decreasing in such patients.

WHAT ARE THE CLINICAL IMPLICATIONS?

- Both scores can be used by surgical programs to benchmark their CABG 30-day postoperative mortality outcomes in this population, but because observed mortality most closely mimicked EuroSCORE-2 it may be superior to the STS score for benchmarking.
- The suggestion that 30-day postoperative mortality risk in such patients has decreased over the past decade should encourage a greater use of CABG in appropriate patients with severe LV dysfunction and coronary artery disease.

Thirty-day mortality for patients undergoing surgical myocardial revascularization is usually assessed with standard risk scores, such as the Society of Thoracic Surgeons (STS) score[1] or the EuroSCORE-2[2] and these have proven effective in assessing 30-day postoperative risk for a wide spectrum of patients undergoing cardiac surgery.[3–6] However, these scores included a relatively small number of patients with severely reduced left ventricular ejection fraction (LVEF) when being developed, and to our knowledge, no data have been published with regard to their relative efficacy in assessing 30-day postoperative risk in this population. Also, in evaluating the pre- and perioperative variables associated with 30-day postoperative mortality in STICH, many variables not included in either the EuroSCORE-2 or the STS score were strongly associated with outcomes raising the possibility that the influence of these variables could reduce the accuracy of the STS score and EuroSCORE-2 in these patients.[7] Finally, although the EuroSCORE-2 has excellent follow-up until hospital discharge, its follow-up 30-day postoperation is as low as 56.6%, such that deaths between hospital discharge and 30-day postoperation were not captured in all patients.[2] Analyses of the STS score would suggest that up to 10% of postoperative deaths occur from the time of hospital discharge to 30-day postoperation, a percentage that could be expected to be greater in high-risk patients.[8] Because of the growing number of patients undergoing CABG with coexisting severe LV dysfunction, and to more optimally individualize risk prediction, and thus improve assessment of the risk/benefit of CABG for such patients, evaluating the utility of 30-day postoperative mortality risk assessment with standard risk scores, specifically among patients with ischemic cardiomyopathy, is required.

Patients were enrolled in the STICH trial from 2002 to 2007. Their operative mortality was comparable to that reported at that time.[9–11] Since then, several reports suggest that mortality with CABG is decreasing despite increasing patient complexity[12,13] such that the 30-day postoperative mortality risk associated with CABG in patients with an LVEF ≤35% may be less than that reported in STICH. Accordingly, the performance of these risk scores in STICH trial patients should be accompanied by an evaluation in STICH-like patients treated outside of a trial in a more contemporary time period. The development of such a contemporary cohort (CC) would also permit the assessment of whether there is evidence of improvement in operative mortality since the STICH trial was performed in this high-risk population.

The objectives of this study were thus to assess and compare the ability of the STS score and EuroSCORE-2 to evaluate the risk of 30-day postoperative mortality in STICH patients and in a CC of patients with an LVEF ≤35% undergoing CABG outside of a trial setting.

METHODS

STICH CABG Cohort

The rationale and design of the STICH program of trials have been published previously.[14] STICH was a prospective, multicenter, randomized trial sponsored by the National Heart, Lung, and Blood Institute that recruited 2136 patients with coronary artery disease and a LVEF of ≤35% between 2002 and 2007 from 127 centers in 26 countries.[15] Two hypotheses were tested. Hypothesis 1 compared CABG plus optimal medical therapy versus optimal medical therapy alone in patients with an LVEF ≤35% that were amenable to CABG. It found CABG plus optimal medical therapy to reduce all-cause mortality compared with optimal medical therapy alone.[16,17] Hypothesis 2 compared CABG with and without surgical ventricular reconstruction in patients with an LVEF ≤35% and dominant akinesia or dyskinesia of the anterior wall requiring CABG. It found that surgical ventricular reconstruction did not improve outcomes in patients undergoing CABG.[18] The inclusion and exclusion criteria and the requirements for ensuring high-quality surgical revascularization have also been detailed previously.[14] Briefly, patients were required to have

coronary anatomy amenable to CABG and were excluded if they had left main coronary artery disease obstruction ≥50% or Canadian Cardiovascular Society angina class ≥3. Patients with cardiogenic shock or with a recent myocardial infarction (MI) thought to be an important cause of LV dysfunction were excluded from the trial.[14] The National Heart, Lung, and Blood Institute and the ethics committee at each recruiting institution approved the study protocol.

Of the 1534 patients in the STICH trial randomized to CABG with or without surgical ventricular reconstruction, 814 had CABG without concomitant procedures (surgical ventricular reconstruction or mitral valve procedure) or preoperative inotropes and constituted the STICH CABG cohort. Follow-up was performed at the time of hospital discharge or at 30 days after surgery if the patient remained hospitalized for ≥30 days, and at 4-month intervals for the first year of follow-up, and thereafter at 6-month intervals over the entire follow-up period.[14] There was 100% follow-up at 30-day postoperation.

Contemporary Cohort of Nontrial Patients With an LVEF ≤35% Having CABG

A CC was established for the specific purpose of the present analysis. A total of 1246 consecutive patients with a LVEF ≤35% who underwent CABG without concomitant procedures were recruited from 5 medical centers (the Montreal Heart Institute, Montreal, Canada, n=719 [2010 to 2017]; Jena Medical Centre, Jena, Germany, n=241 [2010 to 2017]; the Golden Jubilee National Hospital, Glasgow, United Kingdom, n=115 [2008 to 2017]; La Pitié-Salpêtrière Hospital, Paris, France, n=92 [2016 to 2017], and Georges Pompidou European Hospital, Paris, France, n=79 [2016 to 2017]). Patients with emergent or salvage procedures, critical/shock/resuscitation/inotrope dependent/acute MI were excluded from the analysis (n=2160; Figure 1). Of these, 3 of the participating centers (Montreal, Jena, and Glasgow) were initially involved in the STICH trial. Baseline clinical and biological characteristics were obtained from each site's computerized medical charts; values used being the closest to the date of surgery. Pre-, intra-, and postoperative management was based on an individual case-by-case analysis by each site's heart team. Follow-up was obtained either from individual follow-up or from an administrative database after appropriate institutional review board approval. Data were securely sent online as spreadsheets and centrally analyzed by the Duke Clinical Research Institute (Durham, NC). Follow-up was complete at 30 days in 1239 patients, the other 7 patients having been discharged stable to referring hospitals an average of 15 days (minimum 6 and maximum 28 days) postoperation, and were not considered for the present analysis. The ethics committee at each recruiting institution approved the study protocol.

Primary End Point

In the present study, the primary end point was 30-day postoperative mortality. Mortality was defined as any death within 30 days occurring after surgical procedure in any location: death from all-cause before discharge in the same hospital/facility, death after discharge to any other hospital/facility, or death after discharge at home.

Data Analysis

Patient characteristics were summarized by patient cohort (STICH and contemporary) and by quintile of risk predicted by the STS score and EuroSCORE-2. Unless otherwise noted, continuous variables were summarized as median (25th and 75th percentiles) and categorical variables were summarized as count (percentage). Differences in baseline characteristics across quintiles of risk are tested with χ^2 tests for categorical variables and Kruskal Wallis tests or ANOVA for continuous variables. Cohorts are compared with χ^2 tests for categorical variables and with Wilcoxon rank-sum or 2-sample *t* tests for continuous variables. Model discrimination was evaluated with the area under the receiver operating characteristic curve (C statistic) and its 95% CI from logistic regression.[19] Differences in predicted risk score between STS and EuroSCORE-2 for STICH and the contemporary cohorts were depicted in a mountain plot.[20] Mountain plot is simply an empirical distribution function curve folded at 50th percentile (ie, median).

STS and EuroSCORE-2 Scoring

The definitions used to calculate the STS score and EuroSCORE-2 are included in Table I in the Data Supplement. An imputed dataset was created using PROC multiple imputation in SAS v9.4 (SAS Institute, Inc, Cary, NC) with the method of fully conditional specification. Imputation performed separately for the STICH and contemporary cohorts using all available baseline and preoperative variables to inform the imputation. For STICH, patients in both hypotheses (H1 and H2) were included when imputing and in each cohort imputation was conducted before applying the exclusion criteria. In the CC, apart from pulmonary artery systolic pressure (PASP), there were few missing values for the calculation of both the STS and EuroSCORE-2, thus the scoring of the EuroSCORE-2 was repeated without the inclusion of PASP for a sensitivity analysis. In the CC, imputed values included PASP (N=302), New York Heart Association class (N=88), chronic lung disease severity (N=50), timing of past MI (N=29), preoperative intra-aortic balloon pump (N=54), type of atrial fibrillation (paroxysmal versus chronic, N=36), severity of mitral regurgitation (N=18), height and weight (N=7), peripheral vascular disease (N=3), cerebrovascular disease (N=2), diabetes mellitus (N=3), number of previous cardiac surgeries (N=1), and creatinine (N=1). Variables that needed to be imputed in STICH patients included mitral regurgitation severity (N=3), mobility (N=3), and acuteness of operation (N=1). Given the large percentage of missing PASP data in the STICH cohort, PASP was not imputed but assumed to be in the normal range when not available (N=660). Chronic lung disease was not documented in STICH and was assumed to be absent. Because of small percent of missing data, single random imputation rather than multiple imputation was conducted. Patient characteristics were manually entered into the online risk calculators for 15% of the CC to confirm that the scores matched those calculated programmatically.

To assess whether missing values would significantly lead to underestimation of 30-day postoperative risk, an exploratory analysis in which all missing values were awarded the most severe abnormality (worst case scenario) was performed. For example, all missing New York Heart Association values were

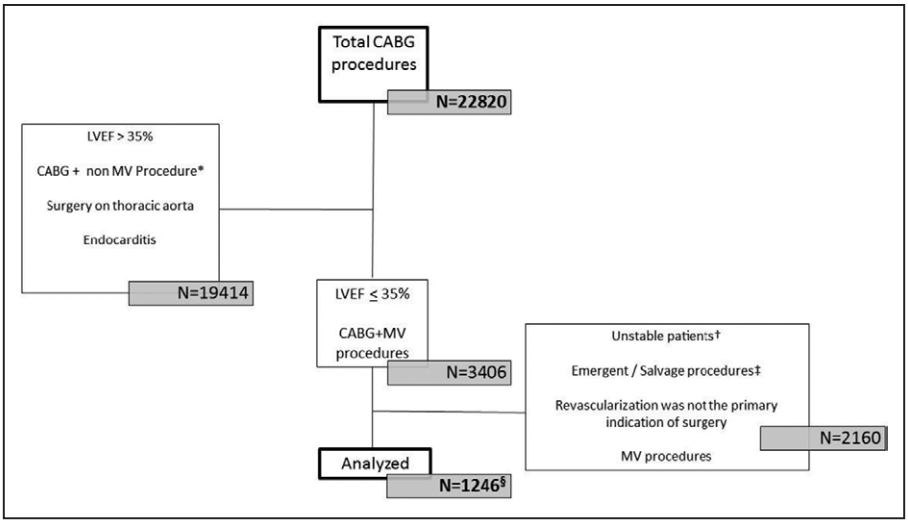

Figure 1. Inclusion process for patients in the contemporary cohort that had isolated coronary artery bypass grafting (CABG) for ischemic left ventricle (LV) dysfunction.

*Non-mitral valve (MV) procedure refers to any procedure combined with CABG other than repair/replacement of the mitral valve (surgical ventricular reconstruction [SVR], aortic valve/tricuspid valve repair or replacement, left atrial appendage closure, septal defect repair, tumor resection, and surgery on thoracic aorta). †Unstable refers to: any cardiopulmonary resuscitation or mechanical ventilation before the start of the procedure; preoperative shock, peripheral hypoperfusion or end-organ damage; critical preoperative state; surgery during the acute phase of myocardial infarction; any sustained ventricular arrhythmia or aborted sudden cardiac death. ‡Emergent refers to operation before the beginning of the next working day after decision to operate; salvage refers to patients requiring cardiopulmonary resuscitation before induction of anesthesia. §Seven patients were lost to follow-up within the first 30 d after surgery. LVEF indicates LV ejection fraction.

coded a class 4, all missing chronic obstructive pulmonary disease (COPD) values were awarded severe COPD, and so on.

Evaluating Predictive Value of STS Score and EuroSCORE-2

Logistic regression models were fit for mortality 30 days after CABG separately for the STICH and contemporary cohorts. The independent variable of interest was either STS score or EuroSCORE-2. Model calibration was assessed with Hosmer-Lemeshow goodness-of-fit tests (5 groups) and by plotting the predicted probability of 30-day death with the observed mortality rate in quintiles of predicted risk. The overall event rate is shown with a horizontal reference line.

Comparing Mortality Rates in Cohorts

To test whether the STICH and contemporary cohorts had different mortality rates after accounting for differences in risk score, a logistic model for 30-day mortality was built using cohort as an indicator variable and the (log-transformed) STS and EuroSCORE-2 scores as adjustment covariates. This model was used to estimate the odds ratio (95% CI) associated with being in the STICH cohort.

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

RESULTS

Baseline Characteristics and Outcomes

Baseline characteristics of both STICH (n=814) and contemporary (n=1246) cohorts are displayed in Table 1. Briefly, patients in the CC had slightly higher STS score (median 1.5 versus 0.9) and EuroSCORE-2 (median 2.9 versus 2.4) scores. They were older (67 versus 61 years), had more diabetes mellitus (45% versus 39%), hypertension (77% versus 59%), extracardiac arteriopathy (27% versus 20%), more extensive coronary artery disease, more unstable angina (8% versus 5%), had more intra-aortic balloon pump inserted preoperatively (13% versus 4%), and were more frequently considered urgent operations (27% versus 9%). Patients in the STICH cohort had a lower LVEF (28% versus 30%), more often a history of MI (80% versus 54%), more advanced New York Heart Association class, more severity of mitral regurgitation.

Mortality at 30 days in the STICH cohort was 4.8% (N=39) and in the CC was 3.5% (N=43), with no significant difference in mortality across centers (P=0.17). After adjusting for higher STS score and EuroSCORE-2 in the CC, there was a greater risk of 30-day postoperative death in STICH as compared with the CC (odds ratio: 2.21, 95% CI [1.35–3.61]; P=0.002).

EuroSCORE-2 and the STS Score in Patients With Ischemic HF

The distribution of predicted risk for the STICH cohort was largely below 2% for the STS score and below 4% for the EuroSCORE-2 (Figure 2). The distribution of patient risk for the CC was largely below 3% for the STS score, and below 5% for the EuroSCORE-2. The overall median value of the STS score for the 2 cohorts was significantly lower than the EuroSCORE-2 (1.23 versus 2.63, P<0.0001),

Table 1. Baseline Patient Characteristics and 30-Day Mortality by Cohort for Patients With Isolated CABG

	All Patients (N=2060)	STICH Cohort (N=814)	Contemporary Cohort (N=1246)	*P* Value
30-d postoperative mortality	82 (4.0%)	39 (4.8%)	43 (3.5%)	0.135
Age, y	65 (57, 72)	61 (54, 68)	67 (59, 73)	<0.001
Women	269 (13.1%)	105 (12.9%)	164 (13.2%)	0.863
Height, cm	170 (165, 176)	170 (165, 176)	170 (165, 176)	0.986
Weight, kg	80 (71, 91)	80 (70, 90)	81 (71, 92)	0.016
Body mass index,* kg/m^2	27.5 (24.6, 31.0)	27.2 (24.4, 30.4)	27.7 (24.7, 31.3)	0.005
Body surface area,* m^2	1.92 (1.79, 2.06)	1.92 (1.78, 2.05)	1.93 (1.80, 2.07)	0.067
Creatinine,* mg/dL	1.05 (0.90, 1.27)	1.10 (0.92, 1.27)	1.03 (0.87, 1.28)	0.017
Cockcroft-Gault creatinine clearance,* mL/min per 1.73m^2	77 (59, 100)	79 (61, 98)	76 (56, 101)	0.140
Ejection fraction, %	30 (25, 35)	28 (23, 35)	30 (25, 35)	0.001
Diabetes mellitus	879 (42.7%)	317 (38.9%)	562 (45.1%)	0.006
Non-insulin dependent	531 (25.8%)	194 (23.8%)	337 (27.0%)	0.103
Insulin dependent	348 (16.9%)	123 (15.1%)	225 (18.1%)	0.081
Hypertension	1443 (70.0%)	482 (59.2%)	961 (77.1%)	<0.001
Atrial fibrillation or flutter	231 (11.2%)	76 (9.3%)	155 (12.4%)	0.029
Myocardial infarction (MI)	1318 (64.0%)	650 (79.9%)	668 (53.6%)	<0.001
Extracardiac arteriopathy (PVD or stroke)	506 (24.6%)	166 (20.4%)	340 (27.3%)	<0.001
PVD	469 (22.8%)	130 (16.0%)	339 (27.2%)	<0.001
Cerebrovascular disease/stroke†	221 (10.7%)	58 (7.1%)	163 (13.1%)	<0.001
IABP	188 (9.1%)	29 (3.6%)	159 (12.8%)	<0.001
Number of diseased vessels (50%)				<0.001
0	3 (0.1%)	0	3 (0.2%)	
1	75 (3.6%)	56 (6.9%)	19 (1.5%)	
2	483 (23.4%)	228 (28.0%)	255 (20.5%)	
3	1499 (72.8%)	530 (65.1%)	969 (77.8%)	
Proximal LAD stenosis ≥75%	1383 (67.1%)	587 (72.1%)	796 (63.9%)	<0.001
Prior cardiac surgery	66 (3.2%)	27 (3.3%)	39 (3.1%)	0.814
Current NYHA class				<0.001
I	449 (21.8%)	85 (10.4%)	364 (29.2%)	
II	834 (40.5%)	401 (49.3%)	433 (34.8%)	
III	690 (33.5%)	297 (36.5%)	393 (31.5%)	
IV	87 (4.2%)	31 (3.8%)	56 (4.5%)	
Unstable angina	147 (7.1%)	42 (5.2%)	105 (8.4%)	0.005
Mitral regurgitation severity				<0.001
None or trace	1202 (58.3%)	328 (40.3%)	874 (70.1%)	
Mild (≤2+)	736 (35.7%)	420 (51.6%)	316 (25.4%)	
Moderate (3+)	114 (5.5%)	62 (7.6%)	52 (4.2%)	
Severe (4+)	8 (0.4%)	4 (0.5%)	4 (0.3%)	
Moderate or severe tricuspid regurgitation	43 (2.1%)	13 (1.6%)	30 (2.4%)	0.208
Pulmonary artery systolic pressure (PASP)‡	34 (30, 43)	37 (30, 46)	30 (30, 40)	<0.001
Any degree of aortic regurgitation	373 (18.1%)	113 (13.9%)	260 (20.9%)	<0.001
Poor mobility	198 (9.6%)	180 (22.1%)	18 (1.4%)	<0.001
Urgent operation	409 (19.9%)	70 (8.6%)	339 (27.2%)	<0.001
STS score	1.2 (0.7, 2.3)	0.9 (0.6, 1.6)	1.5 (0.8, 2.8)	<0.001
EuroSCORE-2	2.6 (1.7, 4.5)	2.4 (1.5, 3.8)	2.9 (1.8, 4.8)	<0.001

CABG indicates coronary artery bypass grafting; LAD, left anterior descending artery; NYHA, New York Heart Association; PVD, peripheral vascular disease; STICH, Surgical Treatment for Ischemic Heart Failure; and STS, Society of Thoracic Surgeons.

*In the contemporary cohort, height and weight are missing for 7 and creatinine is missing for 1.

†Stroke was only documented for patients in the STICH cohort.

‡PASP is missing for 302 patients in the contemporary and 660 patients in the STICH cohort.

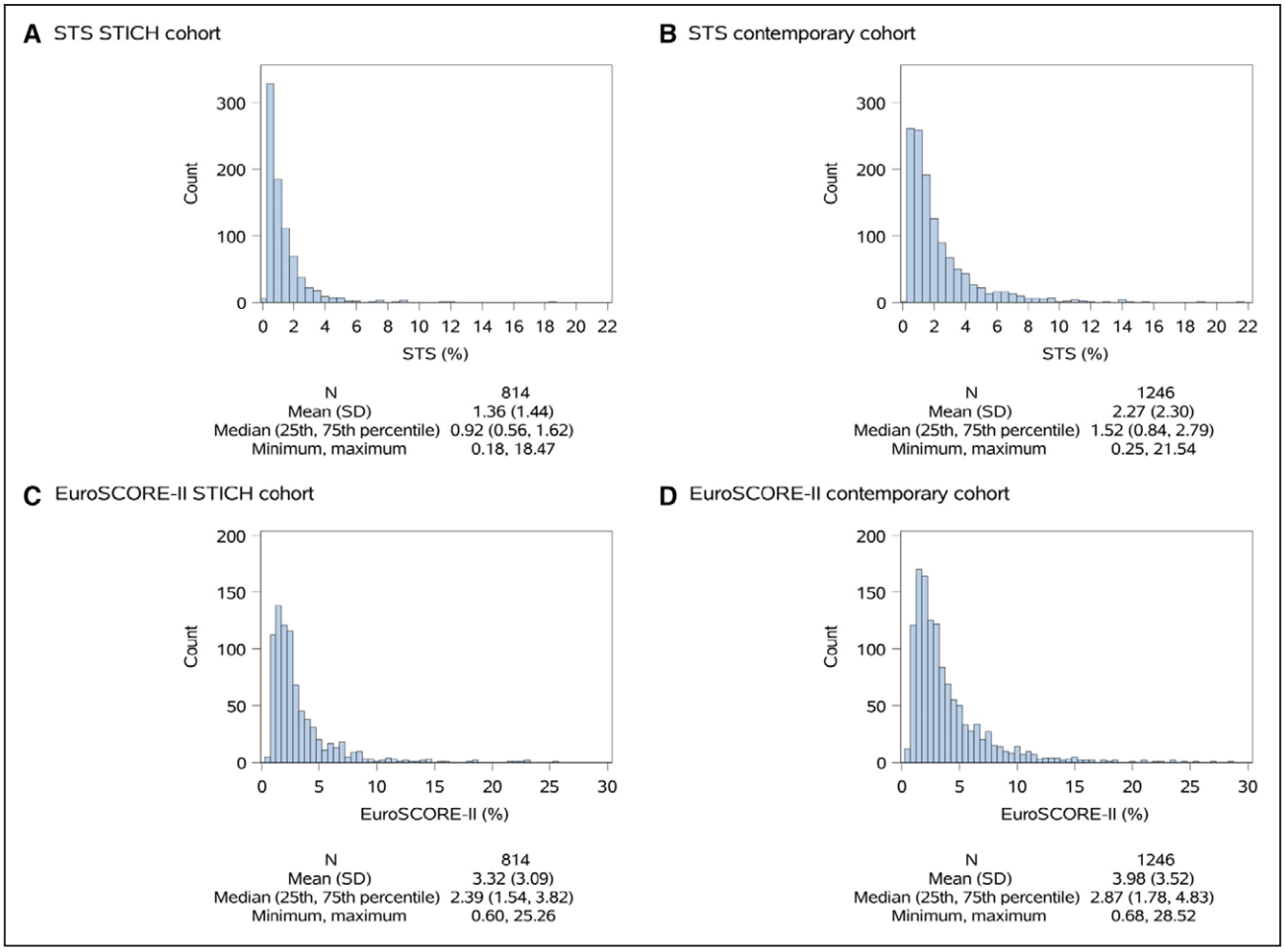

Figure 2. Distribution of scores across the STICH (Surgical Treatment for Ischemic Heart Failure; left) and the contemporary cohorts for patients with isolated coronary artery bypass grafting (CABG).
Distribution of Society of Thoracic Surgeons (STS) risk score and EuroSCORE-2 risk scores across the STICH (left, **A** and **C**) and the contemporary cohorts (right, **B** and **D**).

with the most striking difference being past the 50th percentile (Figure 3).

The C statistics for the STS score and the EuroSCORE-2 in predicting 30-day mortality in STICH patients and in the CC were similar (Table 2). In the STICH cohort, the STS C statistic was 0.744 (95% CI: 0.677–0.812), and the EuroSCORE-2 C statistic was 0.736 (95% CI: 0.665–0.808). In the CC, the STS C statistic of 0.727 (95% CI: 0.650–0.803) was similar to that of the EuroSCORE-2 C statistic of 0.707 (95% CI: 0.620–0.795). Including or excluding PASP in the EuroSCORE-2 did not alter the C statistic. Attributing worst case scenario values for missing variables did not significantly modify the C statistic of either the STS score or the EuroSCORE-2 in either cohort (STICH cohort: C statistic for the STS: 0.762 [0.694, 0.830], and for the EuroSCORE-2: 0.749 [0.675, 0.822]; and CC: C statistic for the STS: 0.733 [0.656, 0.810], and for the EuroSCORE-2: 0.706 [0.614, 0.797]).

The predicted versus observed mortality rate for both the STS score and EuroSCORE-2 appeared to be better for the CC than for the STICH cohort (Figure 4). In the STICH cohort, the predicted mortality with both the STS score and EuroSCORE-2 underestimated the observed mortality. In the CC, the mortality predicted by the EuroSCORE-2 showed a good fit to the observed mortality, whereas the mortality predicted by the STS score still underestimating observed mortality, but less than with the STICH cohort. Attributing worst case scenario for missing values did not completely correct the underestimation of actual 30-day postoperative risk with the STS score (Figure I in the Data Supplement). In both the primary and the sensitivity analyses, the underestimate of risk with the STS score in the STICH cohort is supported by significant *P* values from Hosmer-Lemeshow goodness-of-fit tests (*P*=0.021 and *P*=0.046, respectively).

Separating the CC patients by quintiles of risk according to the STS score (Table 3), or EuroSCORE-2 (Table 4), identified patients with greatly varying 30-day mortality risks, the lowest quintile of risk having a mortality of under 1%, and the highest quintile having mortality close to 8% or more.

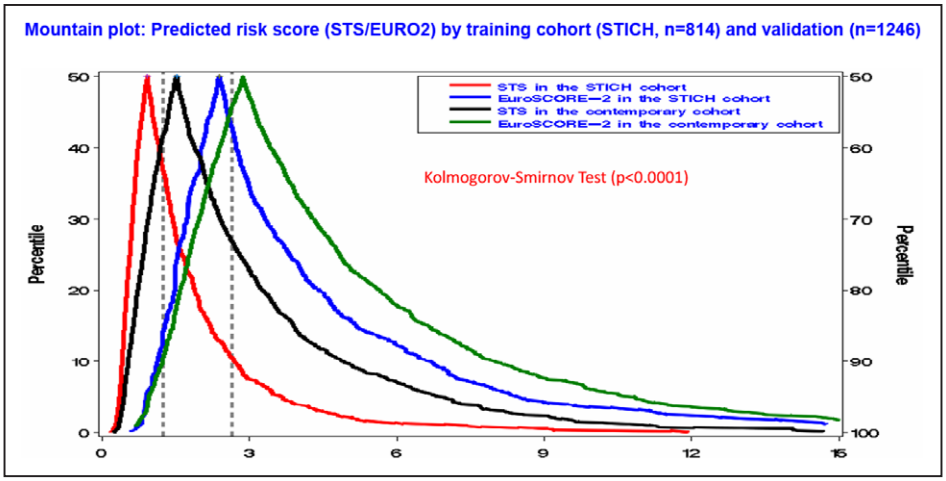

Figure 3. Cumulative distribution of the predicted risk of operative mortality assessed using the Society of Thoracic Surgeons (STS) risk score and the EuroSCORE-2 in both cohorts in patients with isolated coronary artery bypass grafting (CABG).
Red: the STS score in STICH (Surgical Treatment for Ischemic Heart Failure) patients, blue: the EuroSCORE-2 in STICH patients, black: the STS score in contemporary patients, and green: the EuroSCORE-2 in contemporary patients. Vertical dashed lines refer to median values for overall STS score (1.23) and EuroSCORE-2 (2.63).

DISCUSSION

This study demonstrates that the operative risk of 30-day postoperative mortality after CABG in patients with an LVEF ≤35% varies substantially from 1 patient to the next, being as low as 1% in nearly 20% of patients, but as high as 8% in close to 20% of patients. Both the STS score and EuroSCORE-2 are moderately effective in assessing this risk, but their performance is somewhat less predictive than that reported for the overall cardiac surgical population, with the STS more consistently underestimating the risk than the EuroSCORE-2. In the same patients, the EuroSCORE-2 consistently calculated significantly higher risk scores than the STS score, with its values more closely approximating the observed mortality. In a CC of patients with an LVEF ≤35% undergoing CABG, the predicted 30-day postoperative mortality (using either the STS score or the EuroSCORE-2) were higher than those of patients in the STICH trial, nevertheless, their observed mortality was less than that in STICH suggesting that operative mortality in such patients may have decreased since the STICH trial. Thus, assessing the risk of 30-day postoperative mortality after CABG with the use of the STS score or EuroSCORE-2 allows for more informed decisions, and should encourage more patients at lowest risk to proceed with CABG, and those at highest risk to consider alternate therapies. It should also facilitate benchmarking surgical outcomes in these patients and may also facilitate the choice of patients for the much-needed trial comparing CABG to percutaneous coronary intervention (PCI) in patients with severe LV dysfunction.

Table 2. The STS Score and the EuroSCORE-2 C-Index for Predicting 30-Day Mortality in STICH Patients and in the Contemporary Cohort

Score	C-Index (95% CI) for STICH Patients	C-Index (95% CI) for Contemporary Cohort
EuroSCORE-2 (without PASP)	0.734 (0.663, 0.805)	0.710 (0.626, 0.793)
STS Score	0.744 (0.677, 0.812)	0.727 (0.650, 0.803)
EuroSCORE-2	0.736 (0.665, 0.808)	0.707 (0.620, 0.795)

PASP indicates pulmonary artery systolic pressure; STICH, Surgical Treatment for Ischemic Heart Failure; and STS, Society of Thoracic Surgeons.

The Ability of the STS Score and EuroSCORE-2 to Identify Risk of CABG in Patients With an LVEF ≤35%

Risk assessment is mandatory for a tailored approach at the time of surgery in patients with coronary artery disease and low EF.[21] As such, risk stratification using specific tools has become the rule in cardiac surgery[22,23], the STS score and the EuroSCORE-2 being 2 common multivariable models used in this setting.[1,2] The STS model is a complex (>50 demographic and operative variables) and continuously updated model that allows for the prediction of postoperative mortality but also morbidity (such as the risk of renal failure or stroke). Although not updated on a regular basis, the EuroSCORE-2 is a more parsimonious model using only 18 variables, making it easier to calculate. Both the STS score and the EuroSCORE-2 have been widely validated in external populations,[3–6] generally yielding similar risk scores[24] and their relative calibration and discrimination performances recently proved to be similar on large samples of patients undergoing various cardiac procedures.[25] Moreover, they both seem to also predict long-term outcomes.[26–28]

In this study, both the STS Score and the EuroSCORE-2 performed moderately well in a population that has not previously been specifically addressed by either score, but with a C-index somewhat inferior to

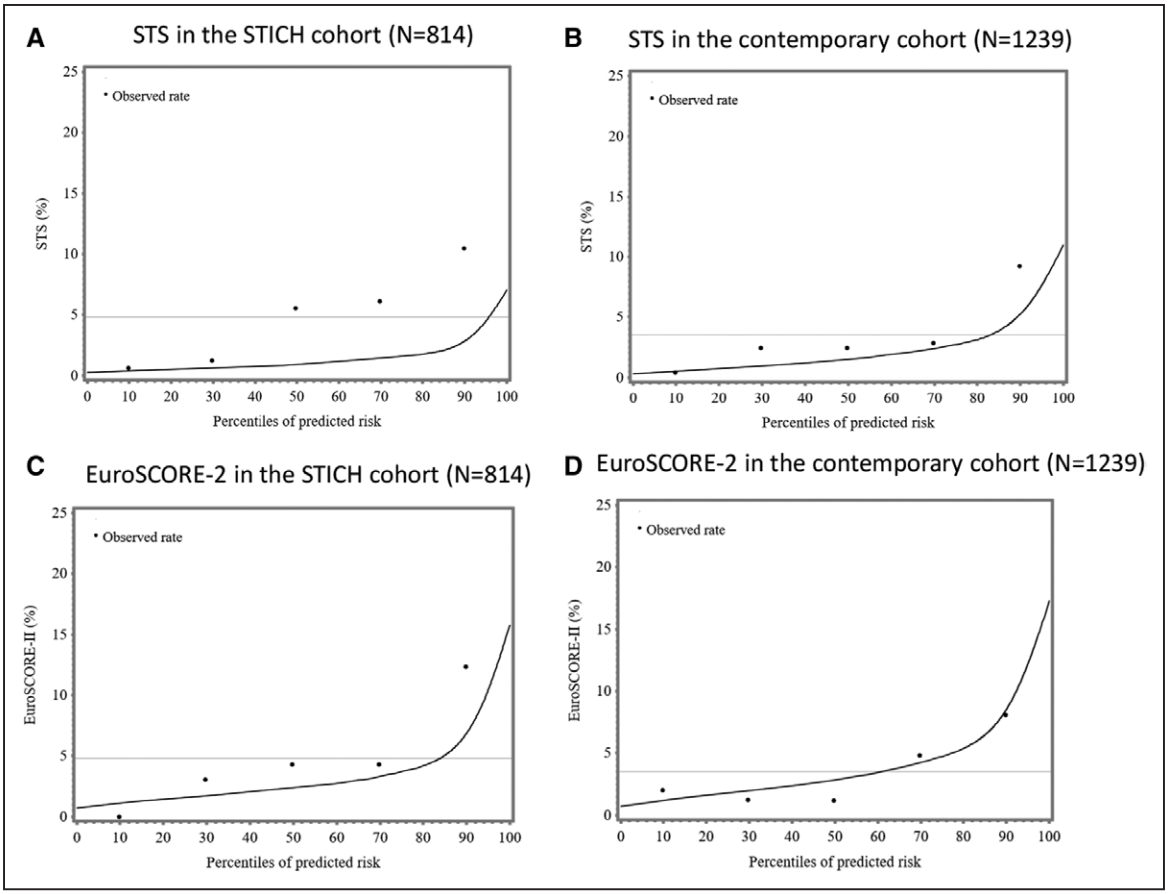

Figure 4. Comparison between actual and predicted 30-day postoperative mortality using the EuroSCORE-2 and the Society of Thoracic Surgeons (STS) risk score models in both cohorts (patients with isolated coronary artery bypass grafting [CABG]).
A and **C**, Actual vs predicted 30-day postoperative mortality in STICH (Surgical Treatment for Ischemic Heart Failure) patients (N=814). **B** and **D**, Actual vs predicted 30-day postoperative mortality in the contemporary cohort (N=1239, 7 patients were lost to follow-up).

that reported for overall cardiac surgical populations (where their C statistic is >0.80). The EuroSCORE-2 has previously been shown to be less accurate in terms of risk prediction[29] when applied to specific high-risk populations, and the results of the present analyses would suggest that in this population of patients with a low EF, this is also true for the STS score. Although methodological considerations may partly help explain less accuracy in high-risk patients,[30] one might hypothesize that these models were not built to accurately capture surgical risk of mortality in specific subgroups where certain risk factors carry an unusually large proportion of the risk.[29] Also, it may be that the exclusion of patients with variables of instability, such as those having emergent or salvage procedures, or with preoperative shock/resuscitation/inotrope dependence/acute MI may have had an impact.

The STS score appeared to more consistently underestimate risk as compared with the EuroSCORE-2, but both the STS score and EuroSCORE-2 significantly underestimated mortality in the STICH cohort, more than in the CC. This did not seem to be the result of the exclusion of important risk factors or imputation of missing values as an exploratory analysis where all missing values were attributed the worst possible score did not significantly modify the C statistic of either score in either cohort and did not fully correct the underestimation of mortality by the STS score. Although PASPs are known to be a risk factor for CABG, the inclusion or exclusion of it in the EuroSCORE-2 did not seem to modify the C statistic, perhaps because patients with high values were largely excluded from surgery and thus does not seem to explain the difference in scores.[31] These limitations notwithstanding, in the CC, the EuroSCORE-2 appeared to more accurately estimate risk, and may be better than the STS score for benchmarking 30-day postoperative mortality in these high-risk patients.

Variable and Changing Risk of CABG in Patients With an LVEF ≤35%

The overall 30-day postoperative mortality of STICH patients undergoing CABG (4.8%) was similar to or better than that reported by others in patients with HF and reduced LVEF.[9–11] Mortality in the CC for

Table 3. Baseline Characteristics and Outcomes of Patients According to Quintiles* of Risk for the STS Score

	Quintile 1 (N=412)	Quintile 2 (N=412)	Quintile 3 (N=412)	Quintile 4 (N=412)	Quintile 5 (N=412)	*P* Value
30-d postoperative mortality	2 (0.5%)	9 (2.2%)	17 (4.1%)	20 (4.9%)	34 (8.3%)	<0.001
Age, y	54 (49, 58)	60 (56, 64)	66 (60, 70)	70 (65, 74)	75 (70, 78)	<0.001
Women	16 (3.9%)	37 (9.0%)	41 (10.0%)	70 (17.0%)	105 (25.5%)	<0.001
Height, cm	173 (168, 177)	172 (167, 177)	171 (165, 176)	170 (164, 175)	167 (160, 173)	<0.001
Weight, kg	86 (78, 95)	83 (74, 95)	79 (70, 90)	78 (69, 88)	74 (65, 85)	<0.001
Body mass index, kg/m^2	29.0 (26.3, 31.8)	28.4 (25.4, 31.7)	26.8 (24.2, 30.6)	27.1 (24.3, 30.3)	26.4 (23.8, 29.8)	<0.001
Body surface area, m^2	2.00 (1.89, 2.11)	1.96 (1.85, 2.10)	1.92 (1.79, 2.05)	1.89 (1.76, 2.03)	1.83 (1.69, 1.97)	<0.001
Creatinine, mg/dL	0.95 (0.82, 1.08)	1.00 (0.88, 1.13)	1.04 (0.90, 1.23)	1.15 (0.95, 1.40)	1.30 (1.01, 1.58)	<0.001
Cockcroft-Gault creatinine clearance, mL/min per 1.73 m^2	108 (92, 126)	91 (75, 110)	76 (65, 92)	63 (53, 77)	50 (38, 63)	<0.001
Ejection fraction, %	30 (26, 35)	30 (24, 35)	29 (25, 35)	30 (25, 35)	30 (25, 33)	<0.001
Diabetes mellitus	134 (32.5%)	169 (41.0%)	178 (43.2%)	203 (49.3%)	195 (47.3%)	<0.001
Non-insulin dependent	106 (25.7%)	108 (26.2%)	107 (26.0%)	117 (28.4%)	93 (22.6%)	0.545
Insulin dependent	28 (6.8%)	61 (14.8%)	71 (17.2%)	86 (20.9%)	102 (24.8%)	<0.001
Hypertension	249 (60.4%)	278 (67.5%)	286 (69.4%)	304 (73.8%)	326 (79.1%)	<0.001
Atrial fibrillation or flutter	25 (6.1%)	30 (7.3%)	43 (10.4%)	55 (13.3%)	78 (18.9%)	<0.001
Myocardial infarction	274 (66.5%)	261 (63.3%)	257 (62.4%)	245 (59.5%)	281 (68.2%)	0.948
Extracardiac arteriopathy (PVD or stroke)	26 (6.3%)	53 (12.9%)	105 (25.5%)	132 (32.0%)	190 (46.1%)	<0.001
PVD	17 (4.1%)	46 (11.2%)	93 (22.6%)	126 (30.6%)	187 (45.4%)	<0.001
Cerebrovascular disease/stroke†	14 (3.4%)	23 (5.6%)	37 (9.0%)	46 (11.2%)	101 (24.5%)	<0.001
IABP	4 (1.0%)	30 (7.3%)	36 (8.7%)	46 (11.2%)	72 (17.5%)	<0.001
Number of diseased vessels (50%)						<0.001
0	0 (0.0%)	1 (0.2%)	1 (0.2%)	0 (0.0%)	1 (0.2%)	
1	35 (8.5%)	13 (3.2%)	9 (2.2%)	9 (2.2%)	9 (2.2%)	
2	133 (32.3%)	104 (25.2%)	102 (24.8%)	73 (17.7%)	71 (17.2%)	
3	244 (59.2%)	294 (71.4%)	300 (72.8%)	330 (80.1%)	331 (80.3%)	
Proximal LAD stenosis ≥75%	285 (69.2%)	275 (66.7%)	286 (69.4%)	264 (64.1%)	273 (66.3%)	0.246
Prior cardiac surgery	0 (0.0%)	1 (0.2%)	3 (0.7%)	14 (3.4%)	48 (11.7%)	<0.001
Current NYHA class						<0.001
I	124 (30.1%)	92 (22.3%)	96 (23.3%)	69 (16.7%)	68 (16.5%)	
II	181 (43.9%)	182 (44.2%)	172 (41.7%)	156 (37.9%)	143 (34.7%)	
III	103 (25.0%)	127 (30.8%)	128 (31.1%)	165 (40.0%)	167 (40.5%)	
IV	4 (1.0%)	11 (2.7%)	16 (3.9%)	22 (5.3%)	34 (8.3%)	
Unstable angina	12 (2.9%)	18 (4.4%)	39 (9.5%)	34 (8.3%)	44 (10.7%)	<0.001
Chronic pulmonary disease‡	8 (1.9%)	25 (6.1%)	37 (9.0%)	48 (11.7%)	99 (24.0%)	<0.001
Mitral regurgitation severity						0.086
None or trace	258 (62.6%)	225 (54.6%)	244 (59.2%)	237 (57.5%)	238 (57.8%)	
Mild (≤2+)	146 (35.4%)	171 (41.5%)	137 (33.3%)	143 (34.7%)	139 (33.7%)	
Moderate (3+)	7 (1.7%)	16 (3.9%)	27 (6.6%)	30 (7.3%)	34 (8.3%)	
Severe (4+)	1 (0.2%)	0	4 (1.0%)	2 (0.5%)	1 (0.2%)	
Moderate or severe tricuspid regurgitation	3 (0.7%)	6 (1.5%)	9 (2.2%)	11 (2.7%)	14 (3.4%)	0.003
PASP	32 (29, 41)	34 (30, 43)	33 (30, 43)	33 (30, 44)	35 (30, 45)	<0.001
Any degree of aortic regurgitation	54 (13.1%)	60 (14.6%)	73 (17.7%)	90 (21.8%)	96 (23.3%)	<0.001
Poor mobility	36 (8.7%)	33 (8.0%)	52 (12.6%)	33 (8.0%)	44 (10.7%)	0.398

(*Continued*)

Table 3. Continued

	Quintile 1 (N=412)	Quintile 2 (N=412)	Quintile 3 (N=412)	Quintile 4 (N=412)	Quintile 5 (N=412)	*P* Value
Urgent operation	26 (6.3%)	64 (15.5%)	80 (19.4%)	101 (24.5%)	138 (33.5%)	<0.001
STS score	0.5 (0.4, 0.5)	0.8 (0.7, 0.9)	1.2 (1.1, 1.4)	2.0 (1.7, 2.3)	4.0 (3.2, 6.0)	<0.001
EuroSCORE-2	1.3 (1.0, 1.7)	1.9 (1.5, 2.4)	2.7 (2.1, 3.4)	3.7 (2.7, 4.9)	6.8 (4.9, 9.9)	<0.001

IABP indicates intra-aortic balloon pump; LAD, left anterior descending artery; NYHA, New York Heart Association; PASP, pulmonary artery systolic pressure; PVD, peripheral vascular disease; STICH, Surgical Treatment for Ischemic Heart Failure; and STS, Society of Thoracic Surgeons.

*Quintiles are based on the scores in the combined dataset of contemporary and STICH cohorts. Quintile cut points are 0.609, 0.972, 1.55, and 2.685.

†Stroke was only documented for patients in the STICH cohort.

‡Chronic pulmonary disease was only documented for patients in the contemporary cohort.

patients undergoing CABG (3.5%) was lower than that of STICH patients despite having a higher STS score (1.5 versus 0.9) and EuroSCORE-2 (2.9 versus 2.4). After adjusting for the 30-day postoperative mortality risk scores, patients in the STICH cohort (surgeries in 2002 to 2007) had a significantly higher postoperative mortality (odds ratio: 2.21, 95% CI [1.35–3.61]; *P*=0.002) suggesting that for the same risk score, operative mortality has decreased since the STICH trial. This may also suggest that patients at higher risk are now sent for CABG as compared with 10 years earlier. Consistent with these findings is the reported decrease in mortality with CABG from 4.2% to 3.0% (29% reduction) in the STS database between the years 2002 to 2012,[13] and a consistent 3% mortality despite an increasing risk profile of patients undergoing CABG in Germany over a similar time period.[12] These differences are difficult to explain as in the field of cardiac surgery there have been no major anesthetic or technical advancements, and no major changes in cardioplegia types or delivery methods or other specific advancements that could explain the improvements in mortality. These changes may simply be the result of small improvements in patient selection, better timing and preparation of patients for surgery, greater use of arterial conduits, and better intraoperative and postoperative management.[13]

The probability that operative mortality has decreased in this high-risk population, and the ability to accurately assess the operative mortality risk of patients with an LVEF ≤35% has multiple significant implications for patients and the field. For patients at low risk it should encourage the use of CABG, and for higher risk patients, particularly those with significant angina, PCI or other options, rather than CABG, should seriously be considered despite registries suggesting that patients with a reduced LVEF that require revascularization generally fair better with CABG than with PCI.[32–36] A definitive recommendation should await a randomized comparative trial of CABG versus PCI in low-EF patients.[37] The apparent reduction in operative mortality in the CC, and the ability to assess individual patient risk with the STS score and EuroSCORE-2 should facilitate the much-needed trial of CABG versus PCI, which has also seen significant recent advances in this patient population.[38]

LIMITATIONS

Although this is the largest report of 30-day postoperative mortality risk assessment in patients with a reduced LVEF, the total number of events remains limited for both STICH and the contemporary cohorts. This notwithstanding, the similar C statistic for the STS score and EuroSCORE-2 in both cohorts suggests consistency across populations.

The STICH and contemporary cohorts excluded very unstable patients and patients undergoing a second procedure such that variables that assess acuity or a second procedure did not come into play and thus the present findings cannot be reliably applied to unstable patients or patients having a second procedure.

Finally, the information captured in the STICH trial did not include certain significant variables, such as the presence of paroxysmal atrial fibrillation (atrial fibrillation regardless of type was included), and the presence of COPD, so the true STS and EuroSCORE-2 scores may have been underestimated. This limitation notwithstanding, COPD and other potential variables not documented in STICH were considered in the CC (17.4% patients with COPD, N=217), and their inclusion had little impact on the predictive value of the different scores, perhaps because in such high-risk patients, those with significant COPD were excluded from CABG. Also, an exploratory analysis that attributed the worse score possible for missing values did not significantly modify the C statistics or fully correct for the underestimation of mortality risk with the STS score, supporting our conclusions.

CONCLUSIONS

The 30-day postoperative mortality risk of patients undergoing CABG with an LVEF ≤35% varies markedly from one patient to the next and is consistently calculated to be lower with the STS score than the EuroSCORE-2. Nevertheless, both the STS score and

Table 4. Baseline Characteristics and Outcomes of Patients According to Quintiles* of Risk for the EuroSCORE-2

	Quintile 1 (N=412)	Quintile 2 (N=412)	Quintile 3 (N=412)	Quintile 4 (N=412)	Quintile 5 (N=412)	*P* Value
30-d postoperative mortality	4 (1.0%)	10 (2.4%)	12 (2.9%)	18 (4.4%)	38 (9.2%)	<0.001
Age, y	58 (52, 63)	60 (54, 68)	65 (57, 70)	70 (62, 74)	72 (67, 77)	<0.001
Women	15 (3.6%)	31 (7.5%)	50 (12.1%)	70 (17.0%)	103 (25.0%)	<0.001
Height, cm	172 (167, 177)	172 (167, 177)	171 (165, 176)	170 (165, 176)	168 (162, 174)	<0.001
Weight, kg	86 (76, 95)	84 (73, 96)	80 (71, 92)	78 (69, 86)	75 (65, 85)	<0.001
Body mass index, kg/m^2	29.0 (25.9, 32.0)	28.4 (25.3, 31.9)	27.5 (24.6, 31.0)	26.8 (24.2, 29.8)	26.4 (23.8, 29.9)	<0.001
Body surface area, m^2	1.99 (1.87, 2.11)	1.97 (1.83, 2.10)	1.92 (1.79, 2.06)	1.89 (1.77, 2.00)	1.85 (1.71, 1.98)	<0.001
Creatinine, mg/dL	0.97 (0.83, 1.10)	0.98 (0.84, 1.14)	1.06 (0.90, 1.25)	1.10 (0.92, 1.34)	1.30 (1.02, 1.60)	<0.001
Cockcroft-Gault creatinine clearance, mL/min per 1.73 m^2	100 (88, 117)	92 (75, 111)	75 (61, 96)	67 (54, 81)	51 (39, 69)	<0.001
Ejection fraction, %	34 (30, 35)	30 (25, 35)	28 (25, 33)	29 (24, 33)	28 (22, 30)	<0.001
Diabetes mellitus	130 (31.6%)	166 (40.3%)	167 (40.5%)	193 (46.8%)	223 (54.1%)	<0.001
Non-insulin dependent	110 (26.7%)	109 (26.5%)	103 (25.0%)	117 (28.4%)	92 (22.3%)	0.319
Insulin dependent	20 (4.9%)	57 (13.8%)	64 (15.5%)	76 (18.4%)	131 (31.8%)	<0.001
Hypertension	256 (62.1%)	273 (66.3%)	286 (69.4%)	303 (73.5%)	325 (78.9%)	<0.001
Atrial fibrillation or flutter	37 (9.0%)	34 (8.3%)	38 (9.2%)	53 (12.9%)	69 (16.7%)	<0.001
Myocardial infarction	248 (60.2%)	265 (64.3%)	253 (61.4%)	268 (65.0%)	284 (68.9%)	0.015
Extracardiac arteriopathy (PVD or stroke)	6 (1.5%)	53 (12.9%)	85 (20.6%)	132 (32.0%)	230 (55.8%)	<0.001
PVD	6 (1.5%)	51 (12.4%)	78 (18.9%)	118 (28.6%)	216 (52.4%)	<0.001
Cerebrovascular disease/stroke†	1 (0.2%)	23 (5.6%)	33 (8.0%)	51 (12.4%)	113 (27.4%)	<0.001
IABP	16 (3.9%)	31 (7.5%)	33 (8.0%)	45 (10.9%)	63 (15.3%)	<0.001
Number of diseased vessels (50%)						<0.001
0	0 (0%)	1 (0.2%)	1 (0.2%)	0 (0.0%)	1 (0.2%)	
1	22 (5.3%)	13 (3.2%)	12 (2.9%)	13 (3.2%)	15 (3.6%)	
2	104 (25.2%)	126 (30.6%)	96 (23.3%)	77 (18.7%)	80 (19.4%)	
3	286 (69.4%)	272 (66.0%)	303 (73.5%)	322 (78.2%)	316 (76.7%)	
Proximal LAD stenosis ≥75%	274 (66.5%)	276 (67.0%)	284 (68.9%)	278 (67.5%)	271 (65.8%)	0.894
Prior cardiac surgery	0 (0%)	1 (0.2%)	3 (0.7%)	6 (1.5%)	56 (13.6%)	<0.001
Current NYHA class						<0.001
I	134 (32.5%)	111 (26.9%)	89 (21.6%)	64 (15.5%)	51 (12.4%)	
II	216 (52.4%)	183 (44.4%)	174 (42.2%)	149 (36.2%)	112 (27.2%)	
III	62 (15.0%)	113 (27.4%)	140 (34.0%)	174 (42.2%)	201 (48.8%)	
IV	0 (0%)	5 (1.2%)	9 (2.2%)	25 (6.1%)	48 (11.7%)	
Unstable angina	4 (1.0%)	25 (6.1%)	30 (7.3%)	38 (9.2%)	50 (12.1%)	<0.001
Chronic pulmonary disease‡	12 (2.9%)	26 (6.3%)	34 (8.3%)	72 (17.5%)	73 (17.7%)	<0.001
Mitral regurgitation severity						<0.001
None or trace	277 (67.2%)	253 (61.4%)	223 (54.1%)	227 (55.1%)	222 (53.9%)	
Mild (≤2+)	128 (31.1%)	141 (34.2%)	152 (36.9%)	153 (37.1%)	162 (39.3%)	
Moderate (3+)	7 (1.7%)	15 (3.6%)	34 (8.3%)	31 (7.5%)	27 (6.6%)	
Severe (4+)	0 (0%)	3 (0.7%)	3 (0.7%)	1 (0.2%)	1 (0.2%)	
Moderate or severe tricuspid regurgitation	2 (0.5%)	6 (1.5%)	8 (1.9%)	10 (2.4%)	17 (4.1%)	<0.001
PASP	30.0 (26.6, 37.0)	32.0 (29.0, 42.0)	35.0 (30.0, 44.5)	35.0 (30.0, 44.0)	36.2 (30.0, 48.0)	<0.001
Any degree of aortic regurgitation	43 (10.4%)	58 (14.1%)	82 (19.9%)	94 (22.8%)	96 (23.3%)	<0.001
Poor mobility	9 (2.2%)	34 (8.3%)	44 (10.7%)	47 (11.4%)	64 (15.5%)	<0.001
Urgent operation	23 (5.6%)	52 (12.6%)	72 (17.5%)	112 (27.2%)	150 (36.4%)	<0.001

(*Continued*)

Table 4. Continued

	Quintile 1 (N=412)	Quintile 2 (N=412)	Quintile 3 (N=412)	Quintile 4 (N=412)	Quintile 5 (N=412)	*P* Value
STS score	0.5 (0.4, 0.7)	0.8 (0.6, 1.2)	1.2 (0.9, 1.6)	1.9 (1.4, 2.6)	3.7 (2.6, 5.9)	<0.001
EuroSCORE-2	1.2 (0.9, 1.4)	1.8 (1.7, 2.0)	2.6 (2.4, 2.9)	3.9 (3.5, 4.5)	7.5 (6.2, 10.2)	<0.001

IABP indicates intra-aortic balloon pump; LAD, left anterior descending artery; NYHA, New York Heart Association; PASP, pulmonary artery systolic pressure; PVD, peripheral vascular disease; STICH, Surgical Treatment for Ischemic Heart Failure; and STS, Society of Thoracic Surgeons.

*Quintiles are based on the scores in the combined dataset of contemporary and STICH cohorts. Quintile cut points are 1.506, 2.2305, 3.11, and 5.066.

†Stroke was only documented for patients in the STICH cohort.

‡Chronic pulmonary disease was only documented for patients in the contemporary cohort.

EuroSCORE-2 are moderately effective in evaluating risk, although the STS tends to underestimate risk.

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