

Special feature: Left Main Interventions

Prognostic performance of the Society of Thoracic Surgeons risk score in patients with left main coronary artery disease undergoing revascularisation: a post hoc analysis of the EXCEL trial



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KEYWORDS

- clinical trials
- death
- drug-eluting stent
- revascularisation
- risk stratification
- stroke

Abstract

Aims: Accurate risk prediction in patients undergoing revascularisation is essential. We aimed to assess the predictive performance of Society of Thoracic Surgeons (STS) risk models in patients with left main coronary artery disease (LMCAD) undergoing coronary artery bypass grafting (CABG) or percutaneous coronary intervention with everolimus-eluting stents (PCI-EES).

Methods and results: The predictive performance of STS risk models for perioperative mortality, stroke and renal failure was evaluated for their discriminative ability (C statistic) and calibration (Hosmer-Lemeshow goodness-of-fit-test; χ^2 and p-values) among patients with LMCAD undergoing PCI-EES (n=935) and CABG (n=923) from the randomised EXCEL trial. STS risk scores, in CABG patients, showed good discrimination for 30-day mortality and average discrimination for stroke (C statistic 0.730 and 0.629, respectively) with average calibration. For PCI, STS risk scores had no discrimination for mortality (C statistic 0.507), yet good discrimination (C statistic 0.751) and calibration for stroke. The predictive performance for renal failure was good for CABG (C statistic 0.82), yet poor for PCI (C statistic 0.59).

Conclusions: In selected patients with LMCAD from the EXCEL trial, STS risk models showed good predictive performance for CABG yet lacked predictive performance for PCI for perioperative mortality and renal failure. The STS stroke risk model was surprisingly more discriminating in PCI compared to CABG. Improved and procedure-specific risk prediction instruments are needed to accurately estimate adverse events after LMCAD revascularisation by CABG and PCI. ClinicalTrials.gov Identifier: NCT01205776

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Abbreviations

C statistic	concordance statistic
CABG	coronary artery bypass grafting
CAD	coronary artery disease
EACTS	European Association for Cardio-Thoracic Surgery
EES	everolimus-eluting stent
ESC	European Society of Cardiology
EXCEL	Evaluation of XIENCE versus Coronary Artery Bypass Grafting for Effectiveness of Left Main Revascularisation
LMCAD	left main coronary artery disease
O/E	observed/expected
OR	odds ratio
PCI	percutaneous coronary intervention
PROM	predicted risk of mortality
STEMI	ST-elevation myocardial infarction
STS	Society of Thoracic Surgeons
WHO	World Health Organization

Introduction

Accurate preoperative risk assessment is essential to decide between percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) surgery in patients with advanced coronary artery disease (CAD). This is particularly true now as PCI is increasingly accepted as a suitable alternative to CABG in selected patients with multivessel and left main coronary artery disease (LMCAD)¹⁻⁸. Moreover, it is unclear how risk score calculators perform in selected patients with isolated LMCAD undergoing revascularisation in the current era.

The randomised EXCEL (Evaluation of XIENCE versus Coronary Artery Bypass Grafting for Effectiveness of Left Main Revascularisation) trial showed that PCI with everolimus-eluting stents (EES) was non-inferior to CABG in patients with LMCAD and simple or moderate anatomic coronary complexity in terms of death, large myocardial infarction⁹, or stroke at an intermediate follow-up time of three years. Patients who underwent PCI had fewer major adverse events in the periprocedural period compared with those who underwent CABG, yet had a higher three-year rate of ischaemia-driven repeat revascularisation¹⁰. Patients at low risk of surgical complications may thus have a more favourable risk-benefit profile after CABG.

Multiple risk stratification tools have been developed to predict perioperative outcomes after CABG¹¹⁻¹⁴. These predictive models can guide cardiothoracic surgeons and cardiologists during Heart Team meetings to select the optimal treatment and predict their clinical outcomes, as recommended by the ESC/EACTS 2018 Guidelines on myocardial revascularisation^{6,15}.

It is unclear, however, whether the accuracy of isolated “CABG-only” STS risk models will remain as robust when applied in specific patient sub-cohorts (e.g., LMCAD EXCEL patients) treated with CABG or alternatively with PCI. We therefore sought to investigate the predictive performance of STS risk scores in patients who underwent CABG for LMCAD in the randomised

EXCEL trial. We also examined the utility of STS risk models in PCI-treated subjects to determine whether these models enable the identification of those patients best managed by one or the other revascularisation modality.

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Methods

STUDY DESIGN

The design and results of the EXCEL study have been reported previously^{10,16}. In brief, the EXCEL trial was a multicentre randomised trial that compared CABG to PCI with EES (XIENCE; Abbott Vascular, Santa Clara, CA, USA) in patients with LMCAD. The trial was approved by the local ethics committees of all participating sites and is registered at ClinicalTrials.gov (NCT01205776). The EXCEL trial randomised 1,905 patients with LMCAD and a low or intermediate SYNTAX score (≤ 32 , site-determined) to undergo CABG (n=957) or PCI with EES (n=948). Of the 957 patients randomised to CABG, 930 underwent revascularisation, with CABG being the primary procedure in 923 patients (as-treated). Of the 948 patients randomised to PCI, 942 underwent revascularisation and, of these, 935 patients underwent PCI as the primary procedure (as-treated). The current study included the as-treated randomised patients (CABG n=923 and PCI n=935) to assess whether 30-day clinical outcomes could be accurately predicted by the STS predicted risk of mortality (PROM), stroke, and renal failure risk models. STS risk scores were calculated by implementing the STS CABG risk models as per the specifications described by Shahian et al¹²; the accuracy of implementation was confirmed by robust cross-checking with the “online STS Adult Cardiac Surgery Risk Calculator” for “isolated coronary artery bypass”¹⁷. The definitions of death, stroke and renal failure used by the EXCEL trial are consistent with the definitions used by the STS adult cardiac surgery database.

STUDY ENDPOINTS

The primary endpoint was the predictive performance of the STS PROM and stroke risk scores in the as-treated LMCAD population that underwent CABG or PCI. The secondary endpoint was the predictive performance of the STS renal failure risk score in the CABG and PCI cohorts.

STATISTICAL ANALYSIS

Continuous variables were expressed as mean±standard deviation (SD), and discrete variables were expressed as percentage with frequency, unless otherwise stated. An unpaired t-test was used to compare mean outcomes, and the Wilcoxon two-sample test was used to compare median outcomes. Overall observed to expected (O/E) ratios were visualised by bar plots. The χ^2 test was used to calculate p-values and 95% confidence intervals (CI) on the difference in observed to expected proportions (O/E ratios) between treatment groups. An O/E ratio of >1 indicated underprediction of the clinical outcome by the STS risk score.

Each treatment group was split into quintiles based on the mean predicted STS risk scores, ranking subgroups from lowest predicted

risk scores to highest predicted risk scores. The PROM, stroke, and renal STS models were evaluated for their discriminating ability using the area under the receiver operating curve according to the “concordance” (C statistic) methodology. A C statistic outcome of 1.0 indicates perfect discriminative power, whereas 0.5 indicates no discriminative ability¹⁸. Risk model calibration competence was assessed using the Hosmer-Lemeshow goodness-of-fit test to examine the observed versus expected outcomes for all quintiles. Specifically for the Hosmer-Lemeshow goodness-of-fit test, a two-sided p-value of ≤ 0.05 indicates a statistically significant difference between observed and expected values; therefore, a p-value > 0.05 indicates better predictive performance. For all other statistical tests, a $p < 0.05$ was considered to be statistically significant. Statistical analyses were performed with SAS version 9.4 (SAS Institute, Cary, NC, USA).

Results

BASELINE AND PROCEDURAL CHARACTERISTICS

Baseline characteristics between the as-treated CABG and PCI groups were similar except for modest differences in New York Heart Association Class I, and distal left main stenosis anatomy (**Table 1**). Off-pump CABG was performed in 29.4% of the procedures; bilateral internal thoracic arteries were used in 22.4%. Mean post-procedural in-hospital stay was 8.3 ± 7.8 days for CABG and 2.2 ± 2.9 days for PCI ($p < 0.0001$) (**Supplementary Table 1**).

STS PROM RISK SCORES

The mean expected 30-day STS PROM scores were similar for patients who underwent CABG ($0.85\% \pm 0.76\%$) versus PCI ($0.90\% \pm 0.89\%$, $p = 0.21$). Observed 30-day mortality rates were also similar between CABG ($n = 10$, 1.1%) and PCI ($n = 9$; 1.0%) ($p = 0.83$). This resulted in comparable O/E ratios (1.27 vs 1.07, respectively, $p = 0.32$) (**Figure 1, Supplementary Table 1-Supplementary Table 3**). The STS PROM C statistic for CABG was 0.73 (**Figure 2A**) and 0.51 for PCI (**Figure 2B**). The Hosmer-Lemeshow goodness-of-fit test was 10.21 ($p = 0.25$) for CABG and 8.81 ($p = 0.36$) for PCI (**Figure 2C, Figure 2D**).

STS STROKE RISK SCORES

The mean expected 30-day STS stroke scores were $0.76\% \pm 0.54\%$ for CABG versus $0.77\% \pm 0.61\%$ for PCI patients ($p = 0.86$). Stroke occurred in 1.3% ($n = 12$) after CABG versus 0.6% ($n = 6$) after PCI ($p = 0.12$). Consequently, stroke O/E ratios were 1.70 for CABG and 0.83 for PCI ($p = 0.045$) (**Figure 1, Supplementary Table 2-Supplementary Table 4**). The C statistic for the STS stroke risk score was 0.63 for CABG compared with 0.75 for PCI (**Figure 3A, Figure 3B**). The Hosmer-Lemeshow goodness-of-fit test was 7.21 ($p = 0.51$) for CABG and 6.13 ($p = 0.63$) for PCI (**Figure 3C, Figure 3D**).

STS RENAL FAILURE RISK SCORES

No differences were found between the mean expected 30-day STS renal failure scores in the CABG cohort ($1.95\% \pm 2.13\%$) and

Table 1. Baseline clinical and angiographic characteristics.

Characteristics		CABG (n=923)	PCI (n=935)
Age, years		65.9±9.5	66.0±9.6
Female sex		22.1% (204/923)	23.9% (223/933)
Coronary artery disease risk factors	Hypertension	73.7% (680/923)	74.2% (694/933)
	Hyperlipidaemia	68.9% (635/921)	70.8% (661/934)
	Diabetes mellitus	27.7% (256/923)	30.2% (282/933)
	Medically treated	25.7% (237/923)	27.0% (252/933)
	Recent smoker	20.4% (187/915)	23.7% (220/930)
Preoperative risk factors	Family history of premature coronary artery disease	65.0% (506/779)	67.1% (521/777)
	Peripheral vascular disease	9.0% (83/919)	10.3% (96/932)
	Prior transient ischaemic attack or stroke	7.3% (67/923)	5.5% (51/934)
	Creatinine clearance (ml/min)	89.1±32.1 (908/923)	90.0±32.6 (922/935)
	Renal insufficiency ^c	15.1% (137/908)	17.4% (160/922)
	Dialysis	0.3% (3/923)	0.2% (2/933)
	Chronic obstructive pulmonary disease	8.4% (77/921)	6.9% (64/934)
	History of carotid artery disease	8.5% (78/919)	7.9% (74/931)
	History of anaemia ^a	8.8% (81/921)	10.6% (99/931)
	Body mass index, kg/m ²	28.5±5.0	28.8±4.9
Congestive heart failure	NYHA Class I ^b	0.7% (6/920)	1.7% (16/933)
	NYHA Class II	3.7% (34/920)	2.4% (22/933)
	NYHA Class III	1.7% (16/920)	2.8% (26/933)
	NYHA Class IV	0.2% (2/920)	0.1% (1/933)
Critical preoperative state ^d		2.0% (18/922)	1.1% (10/933)
Recent myocardial infarction ^e		14.8% (136/920)	15.0% (140/931)
STEMI		1.4% (14/917)	1.4% (13/928)
Non-STEMI		12.9% (118/917)	13.3% (123/928)
Coronary dominance, site assessed	Right	89.9% (816/908)	89.2% (814/913)
	Left	10.1% (92/908)	10.8% (99/913)
LM stenosis location, site assessed	Ostial	36.1% (333/923)	32.9% (308/933)
	Mid	18.6% (172/923)	20.3% (190/933)
	Distal ^f	51.9% (479/923)	59.1% (553/933)
	Bifurcation ^g	31.9% (294/923)	37.8% (353/933)
Left main diameter stenosis, site assessed	0 to <50%	0.4% (4/921)	0.3% (3/933)
	≥50 to <70%	16.8% (155/921)	16.7% (156/933)
	≥70%	82.7% (762/921)	83.0% (774/933)
SYNTAX score, site assessed		20.5±6.2	20.7±6.2
Low (≤22)		61.7% (569/922)	59.0% (551/934)
Intermediate (23-32)		38.3% (353/922)	41.0% (383/934)
High (≥33)		0% (0)	0% (0)
Left ventricular ejection fraction, site assessed		57.4±9.0	57.0±9.6

Values are % (n/N) or mean±standard deviation. ^aWorld Health Organization (WHO) criteria: haematocrit (Ht) at initial presentation: <13 g/dL (male) and <12 g/dL (female). ^bNYHA Class I: $p = 0.03$. ^cRenal insufficiency was defined as a creatinine clearance of <60 ml/min according to the Cockcroft-Gault equation. ^dCritical preoperative state: ventricular tachycardia, ventricular fibrillation, or aborted sudden death; preoperative cardiac massage; preoperative ventilation before anaesthetic room; preoperative inotropes or IABP; preoperative acute renal failure (anuria or oliguria <10 mL/h). ^eMyocardial infarction within seven days of randomisation. ^fLeft main stenosis lesion: distal ($p = 0.001$) and bifurcation ($p = 0.008$). All other p -values are non-significant. CABG: coronary artery bypass grafting; NYHA: New York Heart Association; PCI: percutaneous coronary intervention; STEMI: ST-elevation myocardial infarction

the PCI cohort (1.95%±2.35%, p=0.96). Observed renal failure rates, at 30 days, were 2.6% in patients who underwent CABG (n=24) and 0.6% in patients who underwent PCI (n=6) (p<0.001). Subsequently, renal O/E ratios were 1.34 for CABG and 0.33 for PCI (p=0.42) (Figure 1, Supplementary Table 3-Supplementary Table 5). The C statistic was 0.82 for CABG and 0.59 for PCI (Figure 4A, Figure 4B), and the Hosmer-Lemeshow goodness-of-fit test was 14.73 (p=0.065) for CABG (Figure 4C) and 11.98 (p=0.15) for PCI (Figure 4D).

Discussion

For patients with LMCAD undergoing revascularisation in the EXCEL trial, the perioperative STS PROM risk model for CABG patients showed good predictive performance based on the C statistic and was well calibrated according to the Hosmer-Lemeshow goodness-of-fit test, with modest underprediction of mortality among high-risk patients. Conversely, the STS PROM risk model was non-predictive after PCI with EES (C statistic 0.507; comparable to “flipping a coin”). In particular, perioperative mortality was overestimated by the STS PROM in the highest PCI

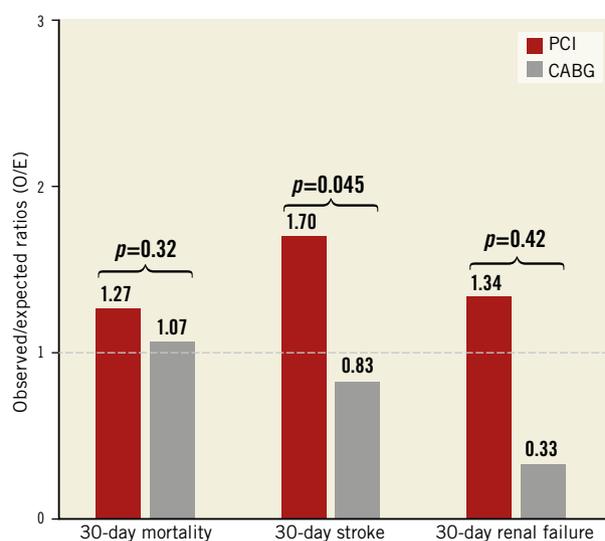


Figure 1. Observed to expected (O/E) ratios for 30-day all-cause mortality, 30-day stroke, and 30-day renal failure after coronary artery bypass grafting (CABG; n=923) and percutaneous coronary intervention (PCI; n=935).

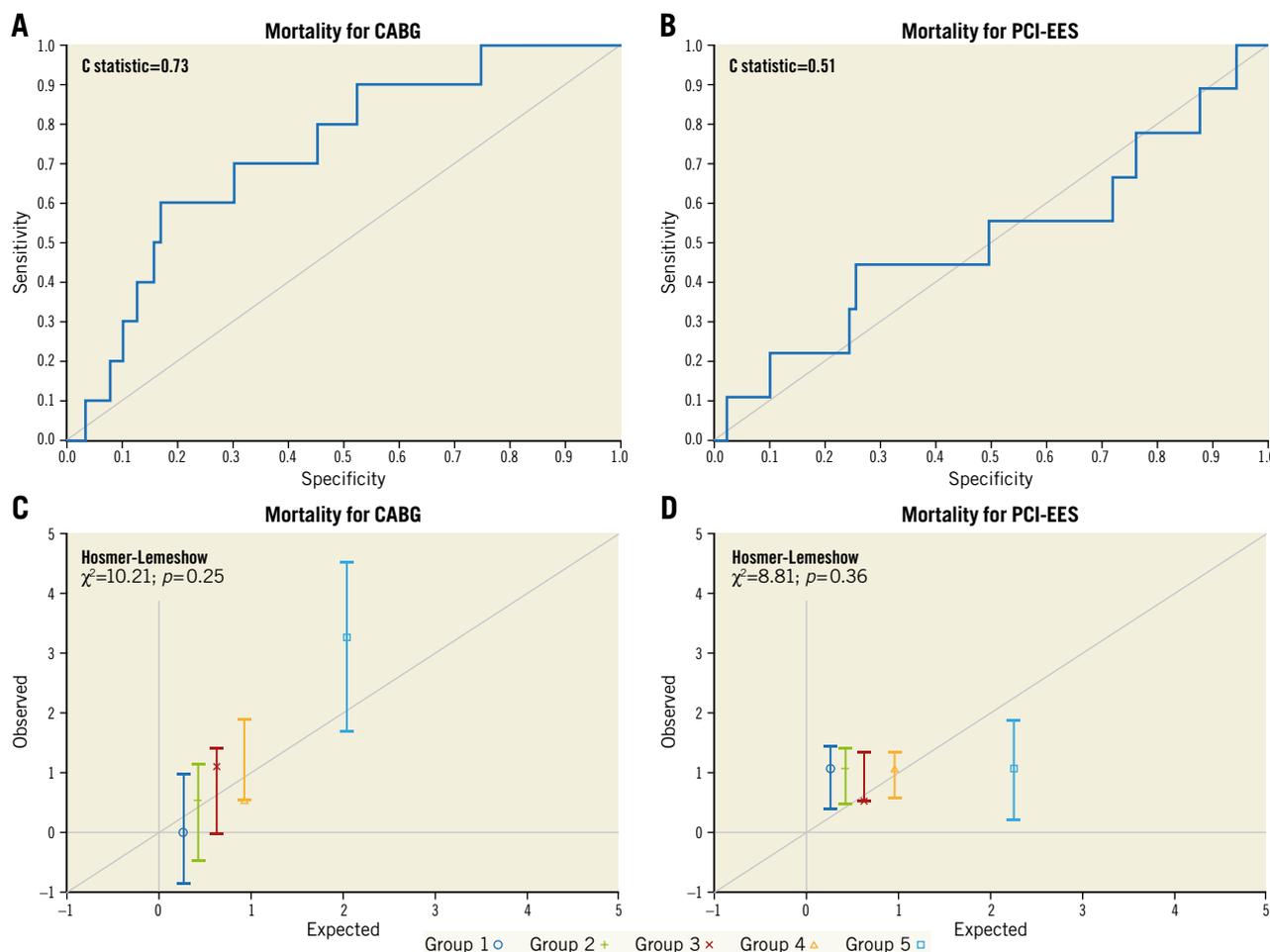


Figure 2. Representation of STS PROM score performance by C statistic (A & B) and Hosmer-Lemeshow goodness-of-fit tests (C & D) for coronary artery bypass grafting (CABG) and percutaneous coronary intervention with everolimus-eluting stents (PCI-EES). Panels C and D represent groups ordered by quintiles from the lowest predicted risk scores to the highest predicted risk scores.

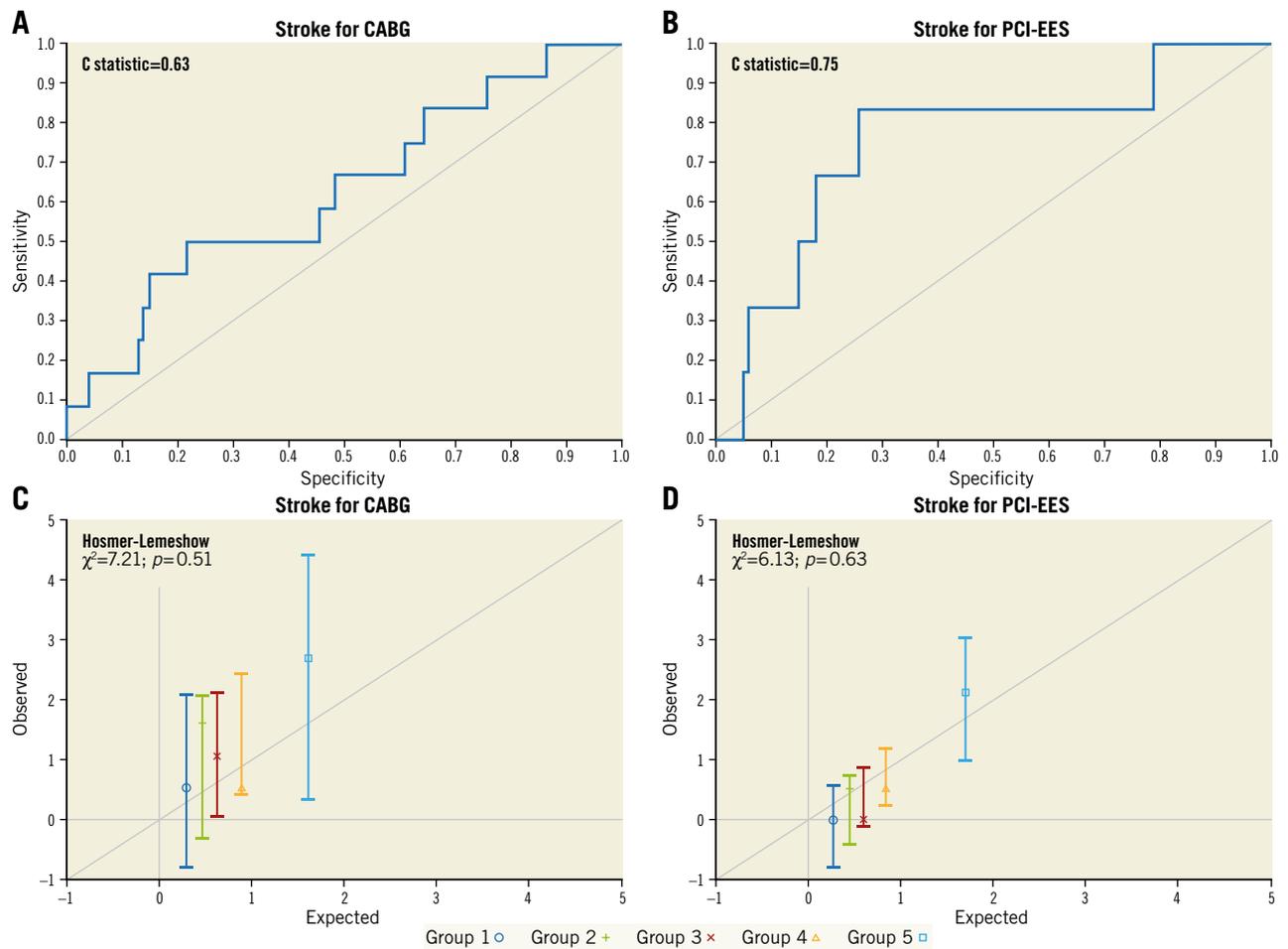


Figure 3. Representation of STS stroke risk score performance by C statistic (A & B) and Hosmer-Lemeshow goodness-of-fit tests (C & D) for coronary artery bypass grafting (CABG) and percutaneous coronary intervention with everolimus-eluting stents (PCI-EES). Panels C and D represent groups ordered by quintiles from the lowest predicted risk scores to the highest predicted risk scores.

risk quintile¹⁰; however, the number of very high risk patients was limited in EXCEL, potentially reducing the precision of the STS predictive ability in higher risk groups¹⁹. The predictive ability for stroke was reasonably good for both PCI and CABG. Finally, the predictive performance of STS renal failure risk scores was good in the CABG cohort, but poor in the PCI group. As the number of more complex patients with CAD who are discussed during Heart Team meetings increases, it is important to be able to predict the risk of adverse events after CABG or PCI accurately. Therefore, evaluating the predictive performance of the STS risk score calculator provides valuable insights into perioperative risk assessment in the contemporary revascularisation era.

The STS isolated CABG risk models were developed and validated for short-term outcomes (in-hospital or 30-day mortality and other major morbidity) based on a large, national-scale and all-inclusive isolated CABG surgery patient population derived from the STS adult cardiac surgery database over a period of time (one to three years)¹². It is therefore not surprising that STS risk models predicted outcomes less accurately in patients undergoing PCI with EES compared with those undergoing CABG. During structured Heart Team meetings, clinicians should combine the results

from the STS and other risk scores with clinical judgement and current guidelines to determine the optimal patient-tailored and evidence-based revascularisation decision^{6,15}. Besides, it is important to account for the expected increased short-term risk of surgical intervention versus potential differential long-term outcomes of available treatment options.

In the current study, stroke within 30 days occurred less often after PCI compared to CABG. This finding is in line with a prior large-scale meta-analysis reporting a significantly lower 30-day rate of stroke after PCI compared with CABG in LMCAD (odds ratio [OR] 0.36, 95% CI: 0.16-0.82, $p=0.007$)^{8,20}. Nonetheless, it was surprising that the STS risk model underestimated the risk of stroke at 30 days in patients who underwent CABG (O/E 1.70). The STS stroke risk model was developed and validated in an all-inclusive (LMCAD and non-LMCAD) patient population without including LMCAD as a predictor variable of perioperative stroke. Risk models developed in specific sub-cohorts (e.g., LMCAD only) can differ appreciably from models based on overall patient populations. In the EXCEL trial, the PCI cohort had a lower 30-day stroke rate ($n=6$, 0.6%) compared with CABG ($n=12$, 1.3%; OR 0.5, 95% CI: 0.19-1.33, $p=0.15$)⁹. The risk of

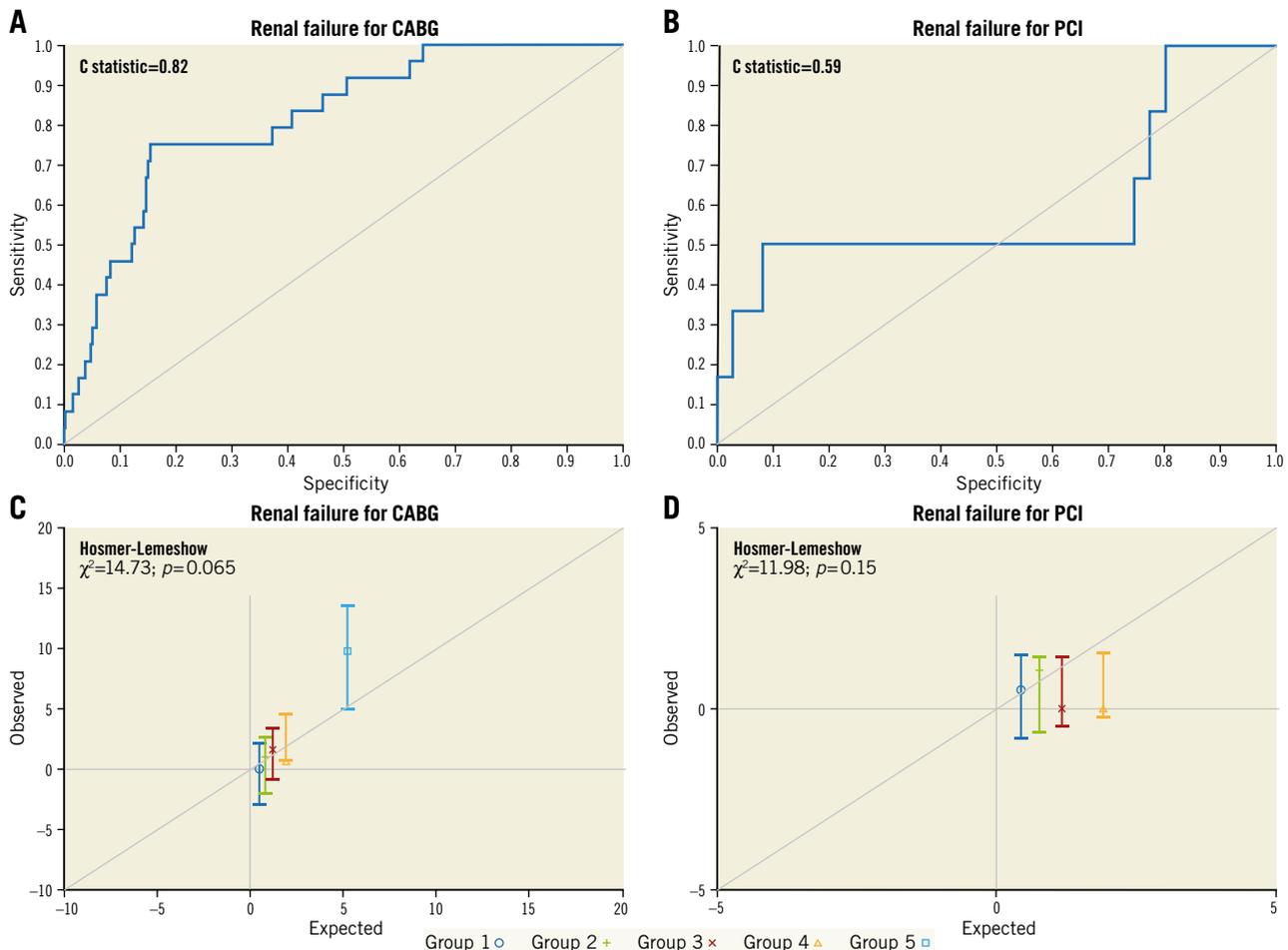


Figure 4. Representation of STS renal failure risk score performance by C statistic (A & B) and Hosmer-Lemeshow goodness-of-fit tests (C & D) for coronary artery bypass grafting (CABG) and percutaneous coronary intervention with everolimus-eluting stents (PCI-EES). Panels C and D represent groups ordered by quintiles from the lowest predicted risk scores to the highest predicted risk scores.

developing stroke is influenced by multiple underlying causes, in both CABG and PCI cohorts, such as (i) on-pump versus off-pump, (ii) usage of side-biting aorta clamp, (iii) single versus dual antiplatelet therapy, (iv) use of single versus bilateral internal thoracic arteries, (v) post-procedural atrial fibrillation, and (vi) femoral versus radial artery percutaneous access^{20,21}. STS risk models are solely based on demographic and preoperative CABG patient factors and comorbidity. Therefore, a different way of modelling is warranted to take into account all periprocedural factors influencing the risk of stroke.

Renal failure is a well-known and serious complication after cardiopulmonary bypass, and the excess use of contrast agents during PCI²² increases the risk of mortality and morbidity²³. A subgroup analysis of patients with versus without chronic kidney disease from the EXCEL trial showed that PCI compared with CABG was associated with lower rates of acute renal failure in patients with (2.3% vs 7.6%; OR 0.28, 95% CI: 0.09-0.87) versus without chronic kidney disease (0.3% vs 1.3%; OR 0.20, 95% CI: 0.04-0.90)²⁴. Nonetheless, no treatment interaction was identified (p for interaction=0.71). It is important to predict the risk of renal failure after revascularisation adequately in order to personalise treatment

strategies in individual patients. The predictive performance of the STS renal failure risk model was excellent in the CABG cohort; however, it performed poorly in the PCI cohort.

To date, no risk model has focused exclusively on predicting perioperative outcomes in patients with LMCAD. The CABG-specific STS risk model did not include LMCAD as a predictor of the risk for mortality, stroke, renal failure, and reoperation. Rather, it only included LMCAD-specific coefficients for “prolonged ventilation” and “any composite adverse outcome”¹². The SYNTAX score II did take LMCAD into account by grading the presence of a $\geq 50\%$ left main with the highest possible weighting factor, but this risk score was developed and validated for predicting long-term (four-year) mortality in patients with complex CAD¹⁴. To determine perioperative clinical outcomes for LMCAD patients more accurately, risk models specifically and separately created for the LMCAD-CABG and LMCAD-PCI patient populations will probably prove to be more discriminating.

Limitations

In the current study, the predicted STS risk scores were computed based on the 2008 STS risk models. The STS Adult Cardiac

Surgery Risk models were recently updated using a more recent patient population and considering a larger number of predictive variables²⁵. Since not all variables that were used in the updated STS models were collected in the EXCEL trial, it was not possible to evaluate the predictive performance of the 2018 STS CABG risk models in the EXCEL trial population. Furthermore, the EXCEL trial excluded patients with high site-determined SYNTAX scores; therefore, the results of this study cannot be generalised to such patients (SYNTAX score ≥ 33).

Conclusions

In selected patients with LMCAD from the EXCEL trial, STS risk models showed good predictive performance for CABG yet were non-predictive for PCI regarding perioperative mortality and renal failure. The STS stroke risk model was surprisingly more discriminating in PCI compared to CABG. Derivation and validation of treatment- and cohort-specific risk models are warranted for optimal prediction of perioperative clinical outcomes in patients with LMCAD requiring revascularisation, bearing in mind the between-treatment differences emerging beyond 30 days.

Impact on daily practice

In selected patients with LMCAD from the EXCEL trial, STS risk models showed good predictive performance for CABG yet lacked predictive ability for PCI regarding perioperative mortality and renal failure. The STS stroke risk model was surprisingly more discriminating in PCI compared to CABG. Derivation and validation of treatment- and cohort-specific risk models are warranted for optimal prediction of perioperative clinical outcomes of CABG and PCI in patients with LMCAD to guide clinical decision support better and to choose the best revascularisation treatment.

Guest Editor

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Conflict of interest statement

G.W. Stone has served as a consultant to Matrizyme, Miracor, Neovasc, V-wave, Shockwave, Valfix, TherOx, Reva, Vascular Dynamics, Robocath, HeartFlow, Gore, Ablative Solutions, Abiomed and Ancora; has received speaker honoraria from Amaranth and Terumo; holds equity/options in Ancora, Cagent, Qool Therapeutics,

Aria, Caliber, MedFocus family of funds, Biostar family of funds, Applied Therapeutics and SpectraWAVE; has served as a director for SpectraWAVE; and his employer, Columbia University, receives royalties for sale of the MitraClip from Abbott. P.W. Serruys reports receiving personal fees from Abbott, Biosensors, Medtronic, Micell Technologies, Qualimed, Sinomedical Technologies, St. Jude Medical, Stentys, Svelte, Philips/Volcano, Xeltis, and HeartFlow outside the submitted work. J. Sabik reports receiving personal fees from Medtronic, Edwards, and Sorin, and sits on the advisory board of Medtronic Cardiac Surgery. J. Puskas reports working as a consultant to Medtronic. A. Kappetein reports working as an employee of Medtronic, outside the submitted work. S. Head reports being an employee of Medtronic. The other authors have no conflicts of interest to declare. The Guest Editor is a consultant for Edwards Lifesciences.

References

- Hlatky MA, Boothroyd DB, Bravata DM, Boersma E, Booth J, Brooks MM, Carrie D, Clayton TC, Danchin N, Flather M, Hamm CW, Hueb WA, Kahler J, Kelsey SF, King SB, Kosinski AS, Lopes N, McDonald KM, Rodriguez A, Serruys P, Sigwart U, Stables RH, Owens DK, Pocock SJ. Coronary artery bypass surgery compared with percutaneous coronary interventions for multi-vessel disease: a collaborative analysis of individual patient data from ten randomised trials. *Lancet*. 2009;373:1190-7.
- Daemen J, Boersma E, Flather M, Booth J, Stables R, Rodriguez A, Rodriguez-Granillo G, Hueb WA, Lemos PA, Serruys PW. Long-term safety and efficacy of percutaneous coronary intervention with stenting and coronary artery bypass surgery for multivessel coronary artery disease: a meta-analysis with 5-year patient-level data from the ARTS, ERACI-II, MASS-II, and SoS trials. *Circulation*. 2008;118:1146-54.
- Capodanno D, Stone GW, Morice MC, Bass TA, Tamburino C. Percutaneous coronary intervention versus coronary artery bypass graft surgery in left main coronary artery disease: a meta-analysis of randomized clinical data. *J Am Coll Cardiol*. 2011;58:1426-32.
- Morice MC, Serruys PW, Kappetein AP, Feldman TE, Stahle E, Colombo A, Mack MJ, Holmes DR, Choi JW, Ruzyllo W, Religa G, Huang J, Roy K, Dawkins KD, Mohr F. Five-year outcomes in patients with left main disease treated with either percutaneous coronary intervention or coronary artery bypass grafting in the synergy between percutaneous coronary intervention with taxus and cardiac surgery trial. *Circulation*. 2014;129:2388-94.
- Cavalcante R, Sotomi Y, Lee CW, Ahn JM, Farooq V, Tateishi H, Tenekecioglu E, Zeng Y, Suwannasom P, Collet C, Albuquerque FN, Onuma Y, Park SJ, Serruys PW. Outcomes After Percutaneous Coronary Intervention or Bypass Surgery in Patients With Unprotected Left Main Disease. *J Am Coll Cardiol*. 2016;68:999-1009.
- Sousa-Uva M, Neumann FJ, Ahlsson A, Alfonso F, Banning AP, Benedetto U, Byrne RA, Collet JP, Falk V, Head SJ, Juni P, Kastrati A, Koller A, Kristensen SD, Niebauer J, Richter DJ, Seferović PM, Sibbing D, Stefanini GG, Windecker S, Yadav R, Zembala MO; ESC Scientific Document Group. 2018 ESC/EACTS Guidelines on myocardial revascularization. *Eur J Cardiothorac Surg*. 2019;55:4-90.
- Fihn SD, Blankenship JC, Alexander KP, Bittl JA, Byrne JG, Fletcher BJ, Fonarow GC, Lange RA, Levine GN, Maddox TM, Naidu SS, Ohman EM, Smith PK. 2014 ACC/AHA/AATS/PCNA/SCAI/STS focused update of the guideline for the diagnosis and management of patients with stable ischemic heart disease: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, and the American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *J Am Coll Cardiol*. 2014;64:1929-49.

8. Palmerini T, Serruys P, Kappetein AP, Genereux P, Riva DD, Reggiani LB, Christiansen EH, Holm NR, Thuesen L, Makikallio T, Morice MC, Ahn JM, Park SJ, Thiele H, Boudriot E, Sabatino M, Romanello M, Biondi-Zoccai G, Cavalcante R, Sabik JF, Stone GW. Clinical outcomes with percutaneous coronary revascularization vs coronary artery bypass grafting surgery in patients with unprotected left main coronary artery disease: A meta-analysis of 6 randomized trials and 4,686 patients. *Am Heart J*. 2017;190:54-63.
9. Moussa ID, Klein LW, Shah B, Mehran R, Mack MJ, Brilakis ES, Reilly JP, Zoghbi G, Holper E, Stone GW. Consideration of a new definition of clinically relevant myocardial infarction after coronary revascularization: an expert consensus document from the Society for Cardiovascular Angiography and Interventions (SCAI). *J Am Coll Cardiol*. 2013;62:1563-1570.
10. Stone GW, Sabik JF, Serruys PW, Simonton CA, Généreux P, Puskas J, Kandzari DE, Morice MC, Lembo N, Brown WM 3rd, Taggart DP, Banning A, Merkely B, Horkay F, Boonstra PW, van Boven AJ, Ungi I, Bogats G, Mansour S, Noiseux N, Sabaté M, Pomar J, Hickey M, Gershlick A, Buszman P, Bochenek A, Schampaert E, Pagé P, Dressler O, Kosmidou I, Mehran R, Pocock SJ, Kappetein AP; EXCEL Trial Investigators. Everolimus-Eluting Stents or Bypass Surgery for Left Main Coronary Artery Disease. *N Engl J Med*. 2016;375:2223-35.
11. Nashef SA, Roques F, Sharples LD, Nilsson J, Smith C, Goldstone AR, Lockowandt U. EuroSCORE II. *Eur J Cardiothorac Surg*. 2012;41:734-44.
12. Shahian DM, O'Brien SM, Filardo G, Ferraris VA, Haan CK, Rich JB, Normand SL, DeLong ER, Shewan CM, Dokholyan RS, Peterson ED, Edwards FH, Anderson RP; Society of Thoracic Surgeons Quality Measurement Task Force. The Society of Thoracic Surgeons 2008 cardiac surgery risk models: part 1--coronary artery bypass grafting surgery. *Ann Thorac Surg*. 2009;88:S2-22.
13. Ranucci M, Castelvécchio S, Menicanti L, Frigiola A, Pelissero G. Risk of assessing mortality risk in elective cardiac operations: age, creatinine, ejection fraction, and the law of parsimony. *Circulation*. 2009;119:3053-61.
14. Farooq V, van Klaveren D, Steyerberg EW, Meliga E, Vergouwe Y, Chieffo A, Kappetein AP, Colombo A, Holmes DR Jr, Mack M, Feldman T, Morice MC, Stahle E, Onuma Y, Morel MA, Garcia-Garcia HM, van Es GA, Dawkins KD, Mohr FW, Serruys PW. Anatomical and clinical characteristics to guide decision making between coronary artery bypass surgery and percutaneous coronary intervention for individual patients: development and validation of SYNTAX score II. *Lancet*. 2013;381:639-50.
15. Head SJ, Kaul S, Mack MJ, Serruys PW, Taggart DP, Holmes DR Jr, Leon MB, Marco J, Bogers AJ, Kappetein AP. The rationale for Heart Team decision-making for patients with stable, complex coronary artery disease. *Eur Heart J*. 2013;34:2510-8.
16. Kappetein AP, Serruys PW, Sabik JF, Leon MB, Taggart DP, Morice MC, Gersh BJ, Pocock SJ, Cohen DJ, Wallentin L, Ben-Yehuda O, van Es GA, Simonton CA, Stone GW. Design and rationale for a randomised comparison of everolimus-eluting stents and coronary artery bypass graft surgery in selected patients with left main coronary artery disease: the EXCEL trial. *EuroIntervention*. 2016;12:861-72.
17. Isolated CAB - STS Adult Cardiac Surgery Database. Available at: <http://riskcalc.sts.org/stswebriskcalc/calculate>. Last accessed October 2017.
18. Steyerberg EW, Vickers AJ, Cook NR, Gerds T, Gonen M, Obuchowski N, Pencina MJ, Kattan MW. Assessing the performance of prediction models: a framework for traditional and novel measures. *Epidemiology*. 2010;21:128-38.
19. Osnabrugge RL, Speir AM, Head SJ, Fonner CE, Fonner E, Kappetein AP, Rich JB. Performance of EuroSCORE II in a large US database: implications for transcatheter aortic valve implantation. *Eur J Cardiothorac Surg*. 2014;46:400-8.
20. Head SJ, Milojevic M, Daemen J, Ahn JM, Boersma E, Christiansen EH, Domanski MJ, Farkouh ME, Flather M, Fuster V, Hlatky MA, Holm NR, Hueb WA, Kamalesh M, Kim YH, Makikallio T, Mohr FW, Papageorgiou G, Park SJ, Rodriguez AE, Sabik JF 3rd, Stables RH, Stone GW, Serruys PW, Kappetein AP. Stroke rates following surgical versus percutaneous coronary revascularization. *J Am Coll Cardiol*. 2018;72:386-98.
21. Shoji S, Kohsaka S, Kumamaru H, Sawano M, Shiraishi Y, Ueda I, Noma S, Suzuki M, Numasawa Y, Hayashida K, Yuasa S, Miyata H, Fukuda K. Stroke After Percutaneous Coronary Intervention in the Era of Transradial Intervention. *Circ Cardiovasc Interv*. 2018;11:e006761.
22. Faggioni M, Mehran R. Preventing Contrast-induced Renal Failure: A Guide. *Interv Cardiol*. 2016;11:98-104.
23. Pickering JW, James MT, Palmer SC. Acute kidney injury and prognosis after cardiopulmonary bypass: a meta-analysis of cohort studies. *Am J Kidney Dis*. 2015;65:283-93.
24. Giustino G, Mehran R, Serruys PW, Sabik JF 3rd, Milojevic M, Simonton CA, Puskas JD, Kandzari DE, Morice MC, Taggart DP, Gershlick AH, Genereux P, Zhang Z, McAndrew T, Redfors B, Ragosta M 3rd, Kron IL, Dressler O, Leon MB, Pocock SJ, Ben-Yehuda O, Kappetein AP, Stone GW. Left Main Revascularization With PCI or CABG in Patients With Chronic Kidney Disease: EXCEL Trial. *J Am Coll Cardiol*. 2018;72:754-65.
25. Shahian DM, Jacobs JP, Badhwar V, Kurlansky PA, Furnary AP, Cleveland JC Jr, Lobdell KW, Vassileva C, Wyler von Ballmoos MC, Thourani VH, Rankin JS, Edgerton JR, D'Agostino RS, Desai ND, Feng L, He X, O'Brien SM. The Society of Thoracic Surgeons 2018 Adult Cardiac Surgery Risk Models: Part 1-Background, Design Considerations, and Model Development. *Ann Thorac Surg*. 2018;105:1411-8.

Supplementary data

Supplementary Table 1. Procedural characteristics.

Supplementary Table 2. STS expected risk scores for mortality, stroke and renal failure based on demographic and baseline characteristics.

Supplementary Table 3. STS mean predicted risk of mortality, observed mortality percentages, and the observed/expected mortality ratios for the as-treated CABG versus PCI patients.

Supplementary Table 4. STS mean predicted risk of stroke, observed stroke percentages, and the observed/expected stroke ratios for the as-treated CABG versus PCI patients.

Supplementary Table 5. STS mean predicted risk of renal failure, observed renal failure percentages, and the observed/expected renal failure ratios for the as-treated CABG versus PCI patients.

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Supplementary data

Supplementary Table 1. Procedural characteristics.

Characteristics	CABG (n=923)	PCI (n=935)	<i>p</i> -value
Time from randomisation to first procedure, days	6.7±14.3	3.3±5.3	<0.0001
Arterial access site ^a			
Femoral	—	72.9% (744/1,021)	—
Radial	—	26.9% (275/1,021)	—
Brachial	—	0.2% (2/1,021)	—
Number of vessels treated			
Left main	—	100.0%	—
Left anterior descending	98.8% (907/918)	28.3% (265/925)	<0.0001
Circumflex artery	88.2% (810/918)	16.6% (155/925)	<0.0001
Right coronary artery	37.8 (347/918)	26.7% (250/925)	<0.0001
Number of stents implanted per patient	—	2.4±1.5	—
Total stent length per patient (mm)	—	49.1±35.6	—
On-pump bypass duration (min)	83.5±45.0	—	—
Cross-clamp duration	54.9±27.3	—	—
Number of conduits used per patient			
Arterial conduits	1.4±0.6	—	—
Venous conduits	1.2±0.9	—	—
Off-pump CABG	29.4% (271/923)	—	—
Bilateral internal thoracic artery	23.5% (217/923)	—	—

Any radial artery used	6.0% (55/923)	—	—
Length of hospital stay (days)	8.3±7.8	2.2±2.9	<0.0001

Values are % (n/N) or mean±standard deviation.

^aAll procedures, including index and planned staged (1,021 procedures in 935 PCI patients with one or more procedures).

CABG: coronary artery bypass grafting; PCI: percutaneous coronary intervention

Supplementary Table 2. STS expected risk scores for mortality, stroke and renal failure based on demographic and baseline characteristics.

Variables	Entire population	<i>p</i> -value	Quintiles					<i>p</i> -value
			1	2	3	4	5	
Mortality								
CABG	0.85±0.76	0.21	0.26±0.04	0.42±0.05	0.62±0.07	0.93±0.12	2.03±0.95	<0.0001
PCI	0.90±0.89		0.27±0.05	0.41±0.05	0.62±0.08	0.95±0.14	2.25±1.17	<0.0001
Stroke								
CABG	0.76±0.54	0.86	0.27±0.07	0.45±0.05	0.62±0.05	0.88±0.10	1.60±0.60	<0.0001
PCI	0.77±0.61		0.26±0.07	0.44±0.04	0.60±0.05	0.83±0.09	1.71±0.74	<0.0001
Renal failure								
CABG	1.95±2.13	0.96	0.48±0.11	0.83±0.11	1.26±0.16	1.97±0.28	5.20±2.85	<0.0001
PCI	1.95±2.35		0.45±0.11	0.79±0.09	1.18±0.14	1.92±0.33	5.41±3.39	<0.0001

Values are mean±SD. For mortality and stroke primary endpoints, data were available for 923 CABG patients and 935 PCI patients. Scores represent predicted 30-day percentage rate unless otherwise noted.

CABG: coronary artery bypass grafting; PCI: percutaneous coronary intervention

Supplementary Table 3. STS mean predicted risk of mortality, observed mortality percentages, and the observed/expected mortality ratios for the as-treated CABG versus PCI patients.

	Coronary artery bypass grafting				Percutaneous coronary intervention			
	n	Expected	Observed	O/E	n	Expected	Observed	O/E
Entire population	923	0.85	1.07	1.27	935	0.90	0.96	1.07
Quintile 1	184	0.26	0	0	187	0.27	1.07	3.97
Quintile 2	185	0.42	0.54	1.28	187	0.41	1.07	2.60
Quintile 3	185	0.62	1.08	1.74	187	0.62	0.53	0.85
Quintile 4	185	0.93	0.54	0.58	187	0.95	1.07	1.12
Quintile 5	184	2.03	3.26	1.60	187	2.25	1.07	0.48

O/E: observed to expected ratio

Supplementary Table 4. STS mean predicted risk of stroke, observed stroke percentages, and the observed/expected stroke ratios for the as-treated CABG versus PCI patients

	Coronary artery bypass grafting				Percutaneous coronary intervention			
	n	Expected	Observed	O/E	n	Expected	Observed	O/E
Entire population	923	0.76	1.30	1.70	935	0.77	0.64	0.83
Quintile 1	184	0.27	0.54	1.99	187	0.26	0	0
Quintile 2	185	0.45	1.62	3.62	187	0.44	0.53	1.20
Quintile 3	185	0.62	1.08	1.75	187	0.60	0	0
Quintile 4	185	0.88	0.54	0.62	187	0.83	0.53	0.64
Quintile 5	184	1.60	2.72	1.70	187	1.71	2.14	1.25

O/E: observed to expected ratio

Supplementary Table 5. STS mean predicted risk of renal failure, observed renal failure percentages, and the observed/expected renal failure ratios for the as-treated CABG versus PCI patients.

	Coronary artery bypass grafting				Percutaneous coronary intervention			
	n	Expected	Observed	O/E	n	Expected	Observed	O/E
Entire population	923	1.95	2.60	1.34	935	1.95	0.64	0.33
Quintile 1	184	0.48	0	0	187	0.45	0.53	1.18
Quintile 2	185	0.83	1.08	1.30	187	0.79	1.07	1.35
Quintile 3	185	1.26	1.62	1.29	187	1.18	0	0
Quintile 4	185	1.97	0.54	0.27	187	1.92	0	0
Quintile 5	184	5.20	9.78	1.88	187	5.41	1.60	0.30

O/E: observed to expected ratio.