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CLINICAL RESEARCH

A Patient-Level Pooled Analysis Assessing the Impact of the SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) Score on 1-Year Clinical Outcomes in 6,508 Patients Enrolled in Contemporary Coronary Stent Trials

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Objectives This study sought to assess the impact of the SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) score (SXscore) on clinical outcomes in patients undergoing percutaneous coronary intervention.

Background The SXscore has been demonstrated to have an ability to predict clinical outcomes in patients undergoing percutaneous revascularization. Current studies are limited by the relatively small number of patients in each SXscore group.

Methods Patient-level data from 7 contemporary coronary stent trials were pooled by an independent academic research organization (Cardialysis, Rotterdam, the Netherlands). Analysis was performed on a cohort of 6,508 patients treated with drug-eluting stents and who had calculated SXscores. Clinical outcomes in terms of death, myocardial infarction (MI), repeat revascularization, and major adverse cardiac events (MACE, a composite of death, MI, and repeat revascularization) were subsequently stratified according to SXscore quartiles: $SXscore_{Q1} \leq 8$ (n = 1,702); $8 < SXscore_{Q2} < 15$ (n = 1,528); $15 \leq SXscore_{Q3} < 23$ (n = 1,620); and $SXscore_{Q4} \geq 23$ (n = 1,658).

Results One-year outcomes were available in 6,496 patients (99.8%). At 1-year follow-up, all clinical outcomes including mortality, MI, repeat revascularization, MACE, and definite and any stent thrombosis were all significantly higher in patients in the highest SXscore quartile. Similar trends were observed in a subgroup of 2,093 patients (32.2%) who presented with an ST- or non–ST-segment elevation MI. The rate of MACE among patients with an SXscore >32 and ≤32 was 24.9% and 14.0%, respectively ($p < 0.001$). The SXscore was identified as an independent predictor of all clinical outcomes including mortality, MACE, and stent thrombosis ($p < 0.001$ for all).

Conclusions This study confirms the consistent ability of the SXscore to identify patients who are at highest risk of adverse events. (J Am Coll Cardiol Intv 2011;4:645–53) © 2011 by the American College of Cardiology Foundation

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The Synergy Between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) score (SXscore) is an angiographic scoring system that was developed to quantify the complexity of coronary artery disease (CAD) in patients undergoing coronary revascularization (1,2). The score was initially developed for use in the SYNTAX trial as a means of bringing together the cardiologist and cardiac surgeon to study, in great detail, the coronary angiogram of patients selected for enrollment (3). Subsequent analyses, however, have indicated that the SXscore can be used to assist in deciding the optimal revascularization strategy in patients with complex CAD (3,4), while also identifying those patients treated by percutaneous coronary intervention (PCI) who are at highest risk of adverse cardiac events (3–14). This ability to risk stratify patients has been evaluated in numerous studies, which include those with an all-comers design (8–10), and those more specifically enrolling patients with multivessel disease (5,6), complex CAD (triple-vessel and/or left main disease) (3,12–14), or those presenting with ST-segment elevation myocardial infarction (STEMI) (11). Importantly, the SXscore has consistently been identified as an independent predictor of major adverse cardiac events (MACE) and/or mortality at follow-up ranging between 1 and 5 years (5–13).

Abbreviations and Acronyms

CABG = coronary artery bypass graft

CAD = coronary artery disease

MACE = major adverse cardiac event(s)

MI = myocardial infarction

PCI = percutaneous coronary intervention

ST = stent thrombosis

STEMI = ST-segment elevation myocardial infarction

SXscore = Synergy Between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery score

TVR = target vessel revascularization

These assessments of the SXscore are limited however by the relatively small number of patients in each SXscore tertile, which have ranged from approximately 200 to 700 patients (5,8). In an effort to overcome these limitations, the present study pooled patient-level data from 7 contemporary coronary stent trials (3,15–20) where the SXscore was available, thereby enabling a more precise evaluation of the benefit of calculating the SXscore in patients treated by PCI.

Methods

Study design and patient population. We identified 7 contemporary coronary stent trials for which the SXscore was available (3,15–20): SIRTAX (Sirolimus-Eluting Stent Compared With Paclitaxel-Eluting Stent for Coronary Revascularization) trial, LEADERS (Limus Eluted From a Durable Versus Erodable Stent Coating) trial, RESOLUTE (Resolute All Comers) trial, ARTS II (Arterial Revascularization Therapies Study II), SYNTAX, STRATEGY (Single High-Dose Bolus Tirofiban and Sirolimus-Eluting Stent Versus Abciximab and Bare-Metal Stent in Myocardial Infarction) trial, and MULTISTRATEGY (Multicenter Evaluation of Single High-Dose Bolus Tirofiban Versus Abciximab With Sirolimus-Eluting Stent or Bare-Metal Stent in Acute Myocardial Infarction) study. Detailed individual study design and trial results are available elsewhere (3,15–20). In brief, all studies included patients with obstructive CAD that was amendable to coronary stent implantation, with drug-eluting stents used exclusively in all but 2 studies. Study inclusion criteria were deliberately heterogeneous ranging from an all-comers design (15–17), to studies only recruiting patients with complex CAD (3,18), or only those with STEMI (19,20). A summary of all studies, including pertinent inclusion and exclusion criteria, study stents, study procedures, and dual antiplatelet therapy regimes are shown in Online Table 1. All studies complied with the Declaration of Helsinki and were approved by the ethical review board in each institution. All patients provided written, informed consent for participation in the individual studies.

After identification of appropriate studies, the principal investigators of each study were subsequently contacted and individual patient data were requested on a broad range of core baseline clinical variables, procedural results, and clinical outcomes at 1-year follow-up. Clinical outcomes included data on death, myocardial infarction (MI), any repeat revascularization (either PCI or coronary artery bypass graft [CABG]), and stent thrombosis (ST). Death and MI were available from all studies, whereas any repeat revascularization was only available from 4 studies: ARTS II, SYNTAX, RESOLUTE, and LEADERS. Of the remaining 3 studies, 2—STRATEGY and MULTISTRATEGY—reported only clinically indicated target vessel revascularization (TVR) (19,20), whereas 1—SIRTAX—reported clinically and nonclinically driven target lesion revascularization and TVR (16). Data for ST was available from all studies. A summary of individual trial endpoints is shown in Online Table 2.

Patient-level-based data were subsequently transferred to an independent academic research organization (Cardialysis, Rotterdam, the Netherlands), where they were merged

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with a database containing the calculated SXscore and its components. Data from each trial were recoded by researchers (S.G., M.S., and T.d.V.), and finally, 2 researchers (S.G., P.W.S.) analyzed and interpreted the data.

SYNTAX score. The SXscore for each patient was calculated by scoring all coronary lesions with a diameter stenosis ≥50%, in vessels ≥1.5 mm, using the SXscore algorithm, which is described in full elsewhere (1,2) and is available on the SXscore Website (21). In the SYNTAX, LEADERS, and RESOLUTE studies, all angiographic variables required to calculate the SXscore were recorded prospectively by a team of 2 core laboratory analysts (Cardialysis) (3,15,17). In contrast, the SXscore in the SIRTAX, ARTS II, STRATEGY, and MULTISTRATEGY studies was calculated retrospectively by individual teams made up of 2 researchers (S.G., G.S., C.G., or M.V.) (16,18–20). Of note, at the time of the calculation, all investigators were blinded to clinical data, clinical presentation, and outcomes. In the event of disagreement, the opinion of a third analyst was sought, and the final decision was established by consensus. Core laboratory analysts and researchers have been shown on 2 occasions to have a similar degree of intraobserver variability (2,22).

The initial description of the SXscore calculation did not include patients presenting with STEMI or those with restenotic lesions. Patients with occluded infarct-related arteries were subsequently scored as occlusions of unknown duration in a similar manner as any chronically occluded artery. Similarly, patients with lesions due to restenosis or in-stent restenosis were scored in the same manner as if the lesion were a de novo lesion. Although this methodology was not described in the original description of the SXscore, it has previously been applied to other all-comers and STEMI populations (8–11).

Clinical endpoints and definitions. The primary endpoint of this pooled analysis was all-cause mortality at 1-year follow-up. The secondary endpoints included MACE, a composite of death, MI, and any repeat revascularization; a combined safety endpoint of death and MI; and the individual endpoints of MI, repeat revascularization (PCI or CABG), and stent thrombosis. In patients presenting with an MI, clinically indicated TVR is also reported.

Complete definitions are available in the individual study publications (3,15–20). Deaths from all causes are reported. As indicated in Online Table 3, there was a wide variation in the definition of MI between studies that reflects the heterogeneous study inclusion criteria, the variations in study design, and the different periods during which studies were performed. As all clinical events from each individual trial were adjudicated by independent clinical event committees, no attempt was made to readjudicate MI events in the different trials to compensate for the differences in individual definition of MI. Therefore, all MIs reported in the current study are as per individual protocol definitions. All repeat revascularization procedures were reported. The definitions of target lesion revascularization and TVR, and the criteria for a clinically driven revascularization used in the 5 studies reporting these outcomes (15–17,19,20) are provided in Online Table 2. All studies apart from the SYNTAX study reported ST defined according to the Academic Research Consortium definitions (23).

Statistical analysis. All patients with a calculated SXscore were included in the analysis. All variables were stratified according to SXscore quartiles. Discrete data were summarized as percent (frequencies), whereas continuous data were expressed as mean ± SD. Testing for (linear) trends was done by using generalized linear models with SYNTAX class as a covariable for continuous variables and the Cochran-Armitage test for trends in categorical data. The distribution of the SXscore was assessed for normality using the Kolmogorov-Smirnov test. Clinical outcomes are presented separately for all patients, those presenting with an MI (STEMI or non-STEMI), and those patients with an SXscore >32, which was the highest SXscore tertile in the SYNTAX study (3). Survival curves were constructed for time-to-event variables using Kaplan-Meier estimates and compared by the log-rank test. Patients lost to follow-up were considered at risk until the date of last contact, at which point they were censored. A Cox multivariate model

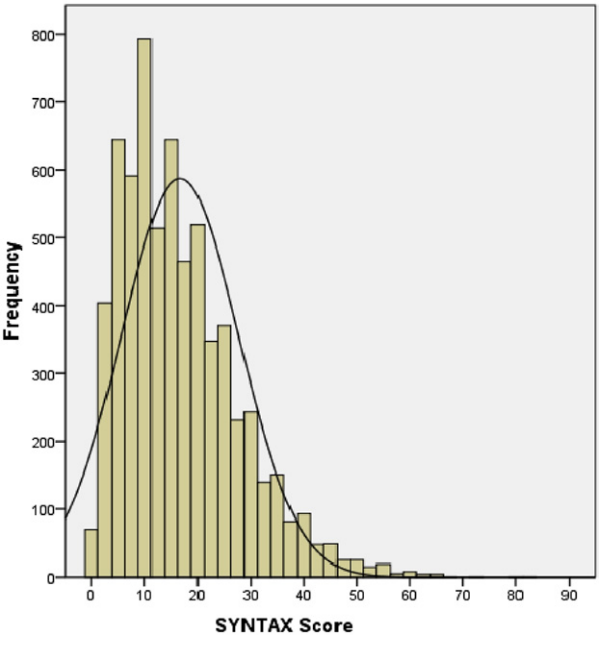

Figure 1. Distribution of the SYNTAX Scores Among the 6,508 Patients Enrolled in the Study

Histograms of the SYNTAX (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery) score with a superimposed normal curve. The score distribution is skewed to the right, and not normally distributed.

Table 1. Baseline Clinical Characteristics Stratified According to SYNTAX Score Quartile

Variable	SXscore ≤8 (n = 1,702)	8 < SXscore <15 (n = 1,528)	15 ≤ SXscore <23 (n = 1,620)	SXscore ≥23 (n = 1,658)	p Value
Baseline characteristics					
Male	73.7 (1,254)	74.3 (1,136)	76.1 (1,233)	77.0 (1,276)	0.01
Age, yrs	62.2 ± 10.7	62.8 ± 10.8	63.7 ± 10.7	66.5 ± 10.3	<0.001
Body mass index, kg/m^2	27.6 ± 4.3	27.9 ± 4.4	27.5 ± 4.3	27.7 ± 4.6	0.78
Risk factors					
Previous MI	28.9 (423/1,464)	29.3 (397/1,354)	30.4 (447/1,471)	33.3 (536/1,611)	0.007
Diabetes	18.7 (316/1,689)	20.4 (310/1,519)	24.5 (395/1,611)	29.2 (483/1,653)	<0.001
Hypertension	68.7 (1,159/1,686)	68.1 (1,032/1,516)	69.8 (1,120/1,605)	71.4 (1,177/1,648)	0.06
Hypercholesterolemia	65.4 (1,110/1,681)	63.1 (954/1,511)	65.8 (1,054/1,602)	68.1 (1,119/1,642)	0.04
Family history of ischemic heart disease	40.6 (396/976)	35.8 (312/871)	35.7 (353/988)	28.5 (338/1,188)	<0.001
Current smoker	36.0 (510/1,417)	33.6 (441/1,311)	32.3 (448/1,385)	22.9 (341/1,489)	<0.001
Peripheral vascular disease	5.9 (57/964)	7.2 (62/865)	7.0 (69/991)	9.1 (111/1,221)	0.007
Previous PCI	31.8 (468/1,470)	24.8 (339/1,369)	19.1 (285/1,492)	12.8 (208/1,623)	<0.001
Previous stroke	3.9 (34/879)	2.9 (24/830)	4.4 (43/974)	7.0 (87/1,240)	<0.001
Creatinine clearance, ml/1.73 m^2	95.0 ± 42.4	94.0 ± 35.1	89.7 ± 32.9	84.9 ± 31.7	<0.001
Creatinine >200 μmol/l	0.6 (8/1,392)	1.0 (14/1,367)	0.7 (11/1,487)	1.8 (28/1,576)	0.004
Ejection fraction	58.2 ± 11.0	56.2 ± 11.7	56.0 ± 12.6	55.5 ± 13.4	<0.001
SYNTAX score	5.0 ± 2.2	11.4 ± 1.7	18.3 ± 2.3	31.8 ± 8.3	<0.001
Indication for treatment					
Stable angina	38.5 (656)	36.5 (558)	35.6 (576)	42.1 (698)	0.07
Unstable angina	19.4 (330)	17.1 (262)	19.8 (321)	24.5 (406)	<0.001
ST-segment elevation MI	18.4 (314)	23.3 (356)	22.3 (362)	14.6 (242)	0.005
Non–ST-segment elevation MI	15.3 (261)	15.1 (231)	12.1 (196)	7.9 (131)	<0.001
Silent ischemia	9.9 (62/625)	9.7 (61/630)	9.8 (79/809)	8.6 (100/1,157)	0.37

Values are % (n), mean ± SD, or % (n/N).
MI = myocardial infarction; PCI = percutaneous coronary intervention; SXscore = SYNTAX score; SYNTAX = Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery.

was performed using the covariates sex, age greater than 65 years, diabetic status, urgency of procedure, SXscore, and use of a first-generation drug-eluting stent. A p value of <0.05 was considered significant, and all tests were 2-tailed. Data were analyzed with SAS (version 9.2, SAS Institute, Inc., Cary, North Carolina).

Results

The SXscore was available in 6,508 of 7,639 patients (85.2%) enrolled in the 7 individual studies. The main reasons for absent SXscores were missing baseline angiograms, the presence of prior surgical revascularization, or treatment with bare-metal stents. In total, the SXscore ranged from 0 to 83, with a mean ± SD of 16.7 ± 11.1 and a median of 15 (interquartile range: 8 to 23). The distribution of the SXscore is shown in Figure 1; the score was not normally distributed (Kolmogorov-Smirnov test $p < 0.05$). In this analysis, the 6,508 patients were divided according to their SXscore into quartiles defined as: $SXscore_{Q1}$ ≤8 (n = 1,702), 8 < $SXscore_{Q2}$ <15 (n = 1,528); 15 ≤ $SXscore_{Q3}$ <23 (n = 1,620); $SXscore_{Q4}$ ≥23 (n = 1,658).

Baseline angiographic and procedural characteristics. Baseline clinical, angiographic, and procedural characteristics of the study population, stratified according to SXscore quartiles, are shown in Tables 1 and 2. Table 2 demonstrates that indicators of lesion complexity, such as an ostial lesion, a total occlusion, and the presence of a bifurcation, were all significantly more common in the highest SXscore quartile, reflecting the higher calculated SXscore for these lesions.

Outcomes at 12 months. Clinical outcomes at 12 months, which were available in 6,496 patients (99.8%) and a subset of 2,093 patients (32.2%) presenting with an STEMI or a non-STEMI, are shown in Table 3, whereas cumulative survival curves for all patients and those presenting with an MI are shown in Figure 2 and Online Figure 1, respectively. Overall, the primary endpoint of death was significantly higher in the highest SXscore quartile (1.6% vs. 1.2% vs. 3.2% vs. 4.6%, $p < 0.001$). A similar trend was noted for all other clinical endpoints, including the safety composite of death/MI and overall MACE, a composite of death/MI and repeat revascularization. All clinical outcomes in patients presenting with an MI, apart from death and cardiac death, were also significantly worse in those patients in the highest SXscore quartile.

Table 2. Baseline Lesion and Procedural Characteristics Stratified According to SYNTAX Score Quartile

Variable	SXscore ≤8 (n = 1,702)	8 < SXscore <15 (n = 1,528)	15 ≤ SXscore <23 (n = 1,620)	SXscore ≥23 (n = 1,658)	p Value
Extent of disease					
Number of disease lesions	1.4 ± 0.7	2.3 ± 1.0	3.0 ± 1.2	4.1 ± 1.6	<0.001
1-vessel disease	69.6 (1185)	30.6 (467)	15.4 (250)	6.1 (101)	<0.001
2-vessel disease	25.7 (437)	49.6 (758)	42.4 (687)	24.9 (413)	0.11
3-vessel disease	2.7 (46)	17.2 (263)	40.4 (655)	66.7 (1,106)	<0.001
Lesion location					
Left main stem	0.4 (7)	3.8 (58)	6.2 (100)	21.1 (350)	<0.001
Right coronary artery	47.9 (816)	58.5 (894)	67.4 (1,092)	80.5 (1,335)	<0.001
Circumflex artery	33.9 (577)	49.3 (754)	63.4 (1,027)	81.7 (1,354)	<0.001
LAD artery	47.2 (803)	72.6 (1,110)	88.7 (1,437)	93.8 (1,555)	<0.001
Proximal LAD involvement	8.0 (136)	19.9 (304)	34.8 (563)	60.3 (1,000)	<0.001
All de novo lesions	92.7 (1,304/1,407)	93.9 (1,303/1,388)	95.3 (1,432/1,503)	96.5 (1,547/1,603)	<0.001
Lesion characteristics					
≥1 bifurcation lesion	18.9 (322)	48.7 (744)	60.9 (986)	71.6 (1,187)	<0.001
≥1 trifurcation lesion	0.5 (9)	2.0 (31)	3.2 (52)	8.0 (132)	<0.001
≥1 ostial lesion	1.8 (30)	3.9 (60)	4.2 (68)	8.1 (134)	<0.001
≥1 occlusion	7.9 (135)	21.1 (323)	33.1 (537)	42.9 (712)	<0.001
≥1 tortuous lesion	15.0 (256)	29.1 (444)	41.6 (674)	62.7 (1,039)	<0.001
≥1 lesion ≥20 mm	12.3 (209)	28.1 (430)	46.0 (745)	66.9 (1,109)	<0.001
≥1 calcified lesion	3.1 (52)	11.8 (180)	21.1 (342)	43.6 (723)	<0.001
≥1 lesion with thrombus	5.2 (88)	6.3 (97)	6.7 (108)	6.2 (103)	0.18
Procedural characteristics					
Number of stents implanted	1.7 ± 1.1	2.2 ± 1.5	2.9 ± 2.0	4.0 ± 2.3	<0.001
Total stent length, mm	24.6 ± 15.3	36.3 ± 24.0	51.7 ± 35.0	75.7 ± 46.3	<0.001
≥100 mm of stent implanted	0.4 (4/1,086)	2.1 (20/966)	9.7 (104/1,075)	24.9 (312/1,253)	<0.001
Post-procedural hospital stay, days	2.1 ± 2.8	2.5 ± 2.7	2.8 ± 3.3	3.8 ± 6.3	<0.001

Values are mean ± SD, % (n), or % (n/N).
LAD = left anterior descending artery; other abbreviations as in Table 1.

The rate of ST followed the same trend as other clinical outcomes, with the highest rate noted in SXscore$_{Q4}$. Of note, rates of ST were higher in all quartiles for patients presenting with an MI compared with the full patient cohort.

Clinical outcomes in patients with a SYNTAX score above and below 32. In the current analysis, 9.3% of patients had an SXscore >32. The clinical outcomes of patients with an SXscore above and below 32 are shown in Table 4, whereas cumulative survival curves are shown in Online Figure 2. All events were at least 1.5× more common in patients with an SXscore >32 ($p < 0.001$ for all), and overall approximately one-quarter of patients in this high-risk group experienced an event (death, MI, or repeat revascularization) within 12 months.

Multivariable analysis. The results of the Cox multivariable analysis are shown in Table 5. Following adjusting of the confounding factors: age >65 years, sex, urgency of procedure, diabetic status, and use of a first-generation drug-eluting stent, the SXscore remained an independent predictor of clinical outcomes such as mortality, MACE, and ST (any and definite).

Discussion

This study is the largest assessment of the SXscore in patients treated with PCI, and it confirms the ability of the SXscore to identify patients who are at highest risk of adverse events, irrespective of clinical presentation.

Several risk models have been developed for patients undergoing PCI; however, few, if any, have become embedded into regular clinical practice. Most of these risk models including the Mayo Clinic Risk Score, the EuroSCORE (European System for Cardiac Operative Risk Evaluation), and the National Cardiovascular Database Registry Cath-PCI risk score use a selection of clinical variables that have been identified as independent predictors of adverse outcome in those treated by PCI (24–30).

In contrast, the SXscore assesses the angiographic complexity of CAD and does not include any clinical variables in its calculation. The score was initially developed for the SYNTAX trial (3) to ensure the angiograms of patients selected for enrollment were appropriately scrutinized by members of the Heart Team, thereby ensuring patients

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Table 3. Clinical Outcomes at 1-Year Follow-Up Among All Patients and Those Presenting With an MI

Variable	SXscore ≤8 (n = 1,702)	8 < SXscore <15 (n = 1,526)	15 ≤ SXscore <23 (n = 1,617)	SXscore ≥23 (n = 1,651)	p Value
All patients					
Death	1.6 (28)	1.2 (19)	3.2 (52)	4.6 (76)	<0.001
Cardiac death*	0.8 (12/1,567)	0.8 (11/1,412)	2.3 (35/1,515)	3.6 (57/1,599)	<0.001
MI	2.9 (50)	3.2 (49)	3.8 (61)	6.1 (101)	<0.001
Any repeat revascularization†	7.7 (94/1,215)	8.7 (102/1,167)	11.4 (151/1,324)	15.4 (236/1,529)	<0.001
Death or MI	4.3 (73)	4.1 (62)	6.5 (105)	9.4 (156)	<0.001
Death/MI or repeat revascularization†	10.8 (131/1,215)	11.4 (133/1,167)	15.7 (209/1,324)	21.1 (323/1,529)	<0.001
ARC any stent thrombosis‡	1.3 (22/1,692)	1.9 (28/1,448)	3.1 (43/1,373)	4.9 (45/920)	<0.001
ARC definite stent thrombosis‡	0.6 (10/1,692)	1.2 (17/1,448)	1.5 (21/1,373)	2.9 (27/920)	<0.001
Patients presenting with MI§	n = 575	n = 587	n = 558	n = 373	
Death	2.4 (14)	1.7 (10)	5.6 (31)	4.3 (16)	0.006
Cardiac death*	0.9 (4/440)	1.1 (5/473)	3.9 (18/456)	2.8 (9/321)	0.005
MI	1.7 (10)	2.9 (17)	3.4 (19)	6.4 (24)	<0.001
Any repeat revascularization†	7.3 (21/287)	9.4 (33/351)	12.3 (43/349)	17.6 (50/284)	<0.001
Clinically indicated target vessel revascularization	2.8 (16)	4.4 (26)	6.5 (36)	9.7 (36)	<0.001
Death or MI	4.0 (23)	4.3 (25)	8.2 (46)	9.9 (37)	<0.001
Death/MI or repeat revascularization†	9.8 (28/287)	12.3 (43/351)	18.1 (63/349)	22.5 (64/284)	<0.001
ARC any stent thrombosis	1.4 (8)	2.2 (13)	5.0 (28)	5.9 (22)	<0.001
ARC definite stent thrombosis	0.7 (4)	1.4 (8)	2.7 (15)	4.3 (16)	<0.001

Values are % (n) or % (n/N). *Cardiac death not available in the STRATEGY and MULTISTRATEGY studies. †Any repeat revascularization was not available in the SIRTAX, STRATEGY, or MULTISTRATEGY studies. ‡Any stent thrombosis or definite stent thrombosis defined according to ARC was not available in the SYNTAX study. §Includes ST-segment elevation MI and non–ST-segment elevation MI. Patients with acute MI were excluded from the SYNTAX and ARTS II studies.

ARC = Academic Research Consortium; ARTS II = Arterial Revascularization Therapies Study II; MULTISTRATEGY = Multicenter Evaluation of Single High-Dose Bolus Tirofiban Versus Abciximab With Sirolimus-Eluting Stent or Bare-Metal Stent in Acute Myocardial Infarction; SIRTAX = Sirolimus-Eluting Stent Compared With Paclitaxel-Eluting Stent for Coronary Revascularization; STRATEGY = Single High-Dose Bolus Tirofiban and Sirolimus-Eluting Stent Versus Abciximab and Bare-Metal Stent in Myocardial Infarction; other abbreviations as in Table 1.

entered the appropriate arm of the trial. At the time of its development, it was hypothesized that the SXscore might help in identifying patients at highest risk of adverse events (1). Subsequent evaluations of the SXscore have confirmed this (3–14); however, studies have been hampered by relatively modest-sized patient cohorts, which for the purpose of analysis have been further subdivided into tertiles. Of note, the largest published assessment of the SXscore to date in patients treated with PCI, reported outcomes in 2,033 patients, with only 698 patients in the largest tertile (8). Importantly, the current pooled analysis has demonstrated findings consistent with previous evaluations of the SXscore, and to its strength, over 1,500 patients were present in each subgroup, alleviating some of the earlier concerns and ensuring robustness of the results. Furthermore, the identification of the SXscore as an independent predictor of clinical outcomes, including mortality MACE and ST, also provides further evidence to support the more routine use of the SXscore in the assessment of patients undergoing PCI.

This ability to identify patients at higher risk of adverse events has important clinical and research implications. From a clinical point of view, it enables physicians to more adequately inform or counsel their patients regarding the potential risk of adverse events and in the choice of revascularization procedure (CABG vs. PCI). Consequently, this should act as a trigger for more aggressive secondary preventive therapy, and lifestyle modification in those at highest risk, as well as close clinical monitoring of recurrent signs or symptoms of ischemia. Importantly, the present data also indicate that the SXscore is an independent predictor of ST, which speculatively might help identify those patients who would benefit most from assessment of platelet function together with more intensive, tailored and/or prolonged antiplatelet therapy. In clinical research, the ability to identify a population of patients with a particular anticipated event rate might help determine inclusion criteria for the design of more appropriately powered studies.

Previous studies that have assessed the SXscore and included a surgical treatment arm have concluded that SXscores >32/34 are the threshold above which patients fare better with CABG (3,4). In the present study, a one-tenth of the cohort had an SXscore over 32, and it is noteworthy that one-quarter of these patients experienced an event (death, MI, or repeat revascularization) within 12 months, confirming the poor outcomes associated with very high SXscores. In comparison, patients in the SYNTAX study with an SXscore >32, treated with CABG had a 1-year rate of major adverse cardiovascular and cerebrovas-

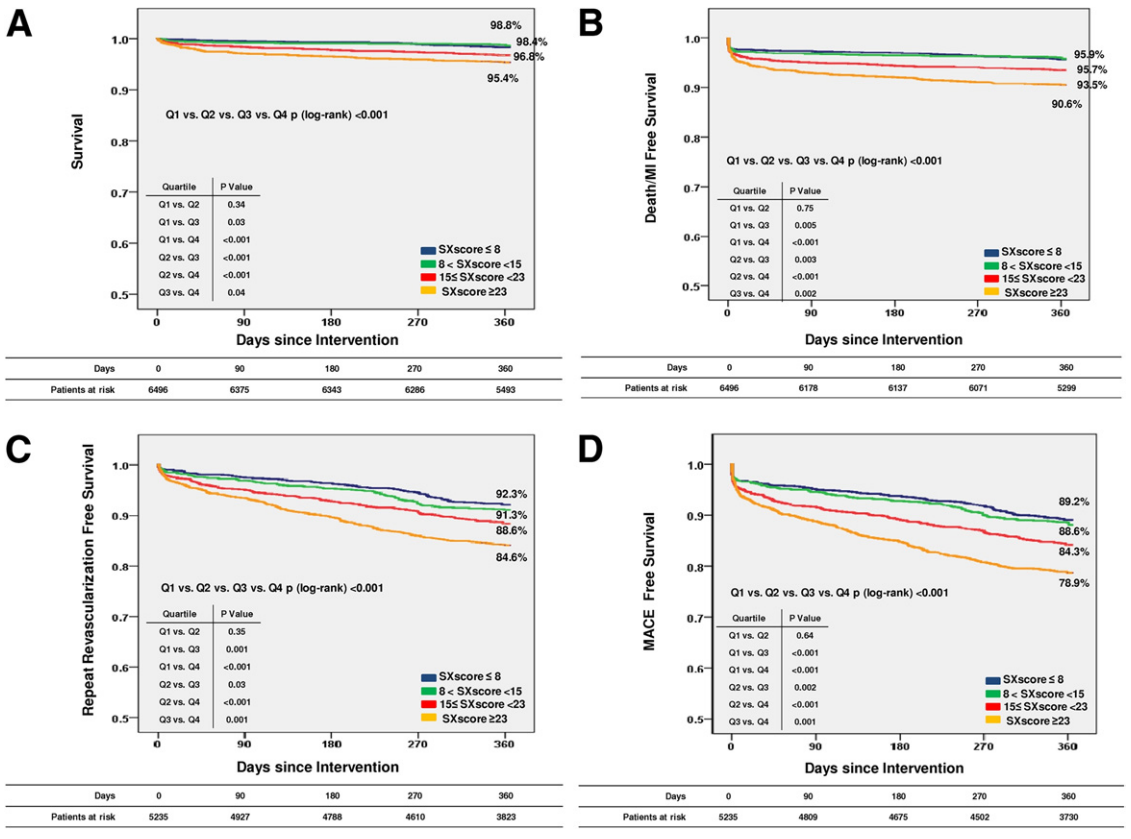

Figure 2. Kaplan-Meier Cumulative Curves

Kaplan-Meier cumulative curves for **(A)** death, **(B)** the composite of death and myocardial infarction, **(C)** repeat revascularization, and **(D)** major adverse cardiac events (MACE)—a composite of death, myocardial infarction, and repeat revascularization—at 1-year follow-up stratified according to SYNTAX score (SXscore) quartiles (Q). SYNTAX = Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery.

cular events of 10.7% (3). This disparity reiterates the importance of discussing the most appropriate method of revascularization, which in this complex subgroup of patients should ideally be CABG.

The absence of clinical variables has been raised as a limitation of assessing risk using just the SXscore. Consequently, several modifications to the SXscore have been proposed by combining it with risk models using patient variables such as the ACEF (Value of Age, Creatinine, and Ejection Fraction) score and EuroSCORE (31,32). Evaluations of these combined scores have shown promising early results; however, data are limited to initial evalua-

Table 4. Clinical Outcomes at 1-Year Follow-Up Among All Patients With SYNTAX Score Above and Below 32

Variable	SXscore ≤32 (n = 5,895)	SXscore >32 (n = 601)	RR (95% CI)	p Value
Death	2.3 (135)	6.7 (40)	2.58 (1.94–3.42)	<0.001
Cardiac death*	1.5 (85/5,508)	5.1 (30/585)	2.81 (2.05–3.86)	<0.001
MI	3.8 (222)	6.5 (39)	1.66 (1.23–2.24)	0.001
Any repeat revascularization†	10.3 (479/4,660)	18.1 (104/575)	1.76 (1.45–2.14)	<0.001
Death or MI	5.6 (330)	11.0 (66)	1.90 (1.50–2.40)	<0.001
Death/MI or repeat revascularization†	14.0 (652/4,660)	24.9 (143/575)	1.85 (1.55–2.20)	<0.001
ARC any stent thrombosis‡	2.3 (122/5,199)	6.8 (16/234)	2.82 (1.75–4.55)	<0.001
ARC definite stent thrombosis‡	1.3 (65/5,199)	4.3 (10/234)	3.19 (1.77–5.76)	<0.001

Values are % (n) or % (n/N). *Cardiac death not available in the STRATEGY and MULTISTRATEGY studies. †All repeat revascularization was not available in the SIRTAX, STRATEGY, or MULTISTRATEGY studies. ‡Any stent thrombosis or definite stent thrombosis defined according to ARC was not available in the SYNTAX study.

CI = confidence interval; RR= risk ratio; other abbreviations as in Tables 1 and 3.

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Table 5. Cox Multivariable Analysis

Clinical Outcome	Hazard Ratio for SYNTAX Score* (95% CI)	p Value
Death	1.40 (1.21–1.62)	<0.001
MI	1.33 (1.19–1.49)	<0.001
Any repeat revascularization	1.29 (1.19–1.39)	<0.001
Death or MI	1.33 (1.21–1.46)	<0.001
Death, MI, or repeat revascularization	1.30 (1.21–1.40)	<0.001
Definite stent thrombosis	1.64 (1.31–2.05)	<0.001
Any stent thrombosis	1.51 (1.28–1.78)	<0.001

*After adjustment of confounding factors: age >65 years, sex, urgency of procedure, diabetic status, and use of a first-generation drug-eluting stent.
Abbreviations as in Tables 1 and 4.

tions in small patient populations, and examination in large robust populations is currently lacking. An extension to this concept has recently been reported by Chen et al. (33) who included not only clinical and angiographic variables, but also procedural variables such as the stenting technique employed. Although these additional variables were shown to improve the accuracy of risk prediction, these operator-dependent variables cannot be reliably predicted before undertaking revascularization, and therefore, unacceptably, their inclusion moves the ability to accurately calculate risk to a time point after the procedure has been completed.

Study limitations. This study is limited by the absence of a CABG comparator arm, and by the limited duration of follow-up. Unfortunately, comparisons of the SXscore with clinical models such as the EuroSCORE and ACEF score, and combined scores such as the clinical SYNTAX score were hindered by the respective absence of recorded EuroSCOREs, and the large number of missing quantitative values for the left ventricular ejection fraction and/or creatinine clearance, both of which are needed to calculate the ACEF and clinical SYNTAX scores.

Conclusions

This study confirms the consistent ability of the SXscore to identify patients who are at highest risk of adverse events, irrespective of clinical presentation. These results provide important evidence to support the more routine use of the SXscore in any patient undergoing percutaneous coronary revascularization.

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Key Words: drug-eluting stent(s) ■ SYNTAX score.

APPENDIX

For supplementary information, tables, and figures, see the online version of this paper.