Usefulness of the SYNTAX Score for Predicting Clinical Outcome After Percutaneous Coronary Intervention of Unprotected Left Main Coronary Artery Disease

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Background—The SYNTAX score (SXscore) has been proposed recently as a valuable tool to characterize the coronary vasculature prospectively with respect to the number of lesions and their functional impact, location, and complexity. However, the prognostic value of SXscores in patients undergoing percutaneous coronary intervention of the left main artery has not been validated.

Methods and Results—We applied the SXscore in 255 consecutive patients who underwent percutaneous coronary intervention for left main disease and explored its performance with respect to their clinical outcome. Univariate and multivariate Cox proportional hazard regression analyses were performed to evaluate the relation between the SXscore and the incidence of cardiac mortality, the primary end point of the study, and major adverse cardiac events (MACE). At 1 year, the SXscore significantly predicted the risk of cardiac death (hazard ratio, 1.12/unit increase; 95% CI, 1.06 to 1.18; \( P < 0.001 \)) and MACE (hazard ratio, 1.59/unit increase; 95% CI, 1.02 to 2.48; \( P = 0.043 \)). After adjustment for potential confounders, a higher SXscore remained significantly associated with cardiac mortality (adjusted hazard ratio, 1.15; 95% CI, 1.05 to 1.26; \( P = 0.003 \)) and MACE (adjusted hazard ratio, 1.06; 95% CI, 1.02 to 1.10; \( P = 0.005 \)). C-indexes for SXscores in terms of cardiac death and MACE were 0.83 and 0.64, respectively. Using classification tree analysis, discrimination levels of 34 and 37 were identified as the optimal cutoff to distinguish between patients at low and high risk of cardiac death and MACE, respectively.

Conclusions—The SXscore is a useful tool to predict cardiac mortality and MACE in patients undergoing percutaneous revascularization of the left main coronary artery. (Circ Cardiovasc Intervent. 2009;2:302-308.)

Key Words: SYNTAX score | left main coronary artery | percutaneous coronary intervention

The SYNTAX score (SXscore) has been recently developed as a combination of several previously validated angiographic classifications aiming to grade the coronary anatomy with respect to the number of lesions and their functional impact, location, and complexity. Higher SXscores, indicative of a more complex condition, are likely to represent a bigger therapeutic challenge and to have a potentially worse prognosis in patients undergoing contemporary revascularization with percutaneous coronary intervention (PCI).

Clinical Perspective on p 308

The predictive value of the SXscore was recently validated on a series of patients undergoing PCI for 3-vessel coronary artery disease in the Arterial Revascularization Therapies Study Part II. However, a validation of this angiographic tool on a restricted series of patients with unprotected left main coronary artery disease undergoing PCI is lacking.

We sought to address this issue by applying the SXscore in patients who underwent percutaneous treatment for left main disease in our institution to examine its prognostic value in predicting in-hospital and long-term clinical outcomes. The performance of the SXscore was also explored in comparison with the modified lesion classification system of the American Heart Association/American College of Cardiology (AHA/ACC).

Methods

Patient Population

All consecutive patients undergoing PCI with either a sirolimus-eluting stent (Cypher, Cordis, a Johnson and Johnson Company, Miami Lakes, Fla) or a paclitaxel-eluting stent (Taxus, Boston Scientific, Natick, Mass) in left main coronary artery, from January 2003 to June 2008, at the Ferrarotto Hospital, Italy, were evaluated in this single-center study. The clinical outcome of a number of these patients was reported previously. The left main coronary artery was defined as unprotected if there were no patent coronary artery bypass grafts to the left anterior descending artery or left circumflex artery. A percutaneous approach rather than a surgical one was performed in the presence of suitable anatomy and lesion characteristics for stenting and one of the following conditions: (1) high surgical risk defined as a European system for cardiac operative risk evaluation...
>6 and/or previous bypass surgery with failure of conduits; or (2) patient refusal to undergo surgical revascularization. All patients were fully informed about the possible procedure-related risks and the alternative treatment options, and written informed consent was obtained from all patients.

Stent implantation was performed according to standard techniques, and the final interventional strategy was left entirely to the operator’s discretion. The use of intravascular ultrasound was used at the operator’s discretion. Lesions located at the ostium or shaft were treated with a single stent. Bifurcation lesions were treated by using one of the following strategies at the operator’s discretion: provisional T-stenting, T-stenting, V-stenting, or mini-crush stenting.5

Interventional strategy and administration of glycoprotein IIb/IIIa inhibitors were left to the discretion of the operators. Glycoproteins IIb/IIIa inhibitors were used in 36.7% of patients. An intravenous bolus of unfractionated heparin was administered at a dose of 70 units/kg immediately before PCI, and an additional bolus was given to achieve a target activated clotting time between 250 and 300 seconds. In case of abciximab administration, the loading dose of unfractionated heparin was 50 units/kg, and the target activated clotting time was 250 seconds. All patients were on aspirin (100 mg per day) that was continued indefinitely. A loading dose of 300 to 600 mg of clopidogrel was given the day before PCI in elective procedures or in the catheterization laboratory in emergent revascularizations and followed by 75 mg daily for 12 months. Alternatively, ticlopidine, at a dose of 250 mg twice daily, was given.

For 4 (1.5%) of 259 patients included in this registry, the diagnostic angiogram was not available or was of poor imaging quality. Thus, 255 patients were included in this analysis.

SXscore Calculation
The total SXscore was derived from the summation of the individual scorings for each separate lesion (defined as ≥50% stenosis in vessel ≥1.5 mm). Full details on SXscore calculation were reported elsewhere.4

All angiographic variables pertinent to SXscore calculation were computed by 2 of 3 experienced cardiologists who were blinded to procedural data and clinical outcome on angiograms obtained before the procedure. In case of disagreement, the opinion of the third observer was obtained, and the final decision was made by consensus.

Follow-Up, End Points, and Definitions
Information about in-hospital outcome was obtained from an electronic centralized clinical database. After discharge, all clinical follow-up data were collected prospectively by scheduled clinic evaluations or direct telephone interviews. Referring cardiologists, general practitioners, and patients were contacted whenever necessary for further information. All repeat coronary intervention and rehospitalization data were collected prospectively during follow-up and entered into the centralized computer system of our institution or by directly contacting the hospitals where the patients were admitted or referred. Clinical events were adjudicated by an independent clinical events committee.

The primary end point was the incidence of cardiac death considered as any death with a demonstrable cardiovascular cause or any death that was not clearly attributable to a noncardiovascular cause. We report the incidence of the primary end point both in-hospital and at follow-up.

The secondary end point was the incidence of major adverse cardiac events (MACE) defined as cardiac death, nonfatal myocardial infarction, or target lesion revascularization. Patients with >1 event were assigned the highest rank event. Periprocedural myocardial infarction was defined as a rise in troponin or creatine kinase-MB >3, the upper normal limit. Subsequent myocardial infarction was diagnosed in the presence of any elevation of troponin or creatine kinase-MB above the upper normal limit. Target lesion revascularization was defined as any repeat intervention (by coronary artery bypass graft or PCI) performed to treat a stenosis inside the implanted stent or within the 5-mm segments adjacent to the stent, including the ostium of the left anterior descending artery and/or left circumflex artery.

Statistical Analysis
Continuous variables are presented as mean±SDs or as median and interquartile range and were compared using Student’s unpaired t test or the Mann–Whitney rank sum test, as appropriate. The normality assumption for continuous variables was evaluated by the Kolmogorov-Smirnov test. Categorical variables are presented as counts and percentages and were compared with the χ² test when appropriate (expected frequency >5). Otherwise, Fisher’s exact test was used. Survival curves were generated by the Kaplan–Meier method, and the log-rank test was used to evaluate differences between groups. Patients lost to follow-up were considered at risk until the date of last contact, at which point they were censored.

To adjust for a range of potential confounders, multivariate analysis of independent predictors of cardiac death was performed with a Cox proportional hazard regression model. The assumption of the proportional hazard was verified by a visual examination of the log (minus log) curves, and the linearity assumption was assessed by plotting the Martingale residuals against continuous covariates. The variables considered as possible predictors included age, gender, smoking, diabetes, acute coronary syndrome, renal dysfunction, left ventricular ejection fraction, European system for cardiac operative risk evaluation, reference vessel diameter, lesion length, bifurcation lesion, emergent setting, complete revascularization as independent control variables, and the SXscore as the independent study variable of interest. The selection in the final model was based on a plausible association with the primary end point or a significant P value on univariate analysis. We report crude and adjusted hazard ratios (HRs) and corresponding 95% CIs.

The SXscore was studied with respect to a simple index of separation, defined as $P_{\text{worst}} - P_{\text{best}}$, assuming $P_{\text{worst}}$ as the predicted P of event for a patient in the group with the worst prognosis and $P_{\text{best}}$ as the predicted P of the same event for a patient in the group with the best prognosis.6

To assess the role of the SXscore in the context of the existing classifications, we compared its performance with that of the modified AHA/ACC lesions classification. For the purposes of this analysis, Type A stenoses were coded as 1 point, Type B1 stenoses as 2 points, Type B2 stenoses as 3 points, and Type C stenoses as 4 points, as described previously.2,7 Performance of the SXscore and the AHA/ACC score was analyzed in terms of discrimination and calibration. Model discrimination was measured by the c-statistic, and calibration was assessed by the Hosmer-Lemeshow goodness-of-fit test.

A classification tree procedure was used to identify the optimal predictive cutoff of the SXscore in terms of cardiac mortality and MACE. This method is an empirical, statistical technique based on recursive partitioning analysis.8 Because it does not require parametric assumptions, it can handle numeric data that are highly skewed or multimodal and categorical predictors with either an ordinal or nonordinal structure. In our context, it involved the segregation of different values of classification variables through a decision tree consisting of progressive binary splits. Every value of each predictor variable was considered as a potential split, and the optimal split was selected based on impurity criterion (the reduction in the residual sum of squares caused by a binary split of the data at that tree node).

For all analyses, a 2-sided P<0.05 was considered statistically significant. All data were processed using the statistical package for social sciences, version 15 (SPSS, Chicago, Ill).

Results
The overall SXscore in the studied population did not demonstrate a normal distribution (P<0.001) but a distinct right skewness (0.67±0.15), ranging from 8 to 57 with a median of 23 (interquartile range, 17 to 32) and a mean of 24.8±10.6 (95% CI, 23.5 to 26.1).

Baseline clinical and angiographic characteristics of the studied population stratified across SXscore tertiles (lowest tertile, ≤18; intermediate tertile, >18 to 27; and highest tertile, >27) are shown in Tables 1 and 2. Patients with high SXscores were older (P=0.004), were less likely to be smok-
Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>SXscore</th>
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<tbody>
<tr>
<td></td>
<td>Low (n=79)</td>
<td>Intermediate (n=91)</td>
<td>High (n=85)</td>
<td></td>
<td></td>
<td>P</td>
</tr>
<tr>
<td>Age, y</td>
<td>63±11</td>
<td>66±9</td>
<td>68±9</td>
<td>0.004</td>
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<tr>
<td>Male, n (%)</td>
<td>64(81)</td>
<td>67(74)</td>
<td>66(78)</td>
<td>0.516</td>
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<tr>
<td>Risk factors, n (%)</td>
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<td></td>
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<tr>
<td>Systemic hypertension</td>
<td>57(72)</td>
<td>58(64)</td>
<td>59(69)</td>
<td>0.481</td>
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</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>49(62)</td>
<td>58(64)</td>
<td>48(57)</td>
<td>0.592</td>
<td></td>
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</tr>
<tr>
<td>Present or previous smoking habitus</td>
<td>45(57)</td>
<td>40(44)</td>
<td>28(33)</td>
<td>0.008</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>21(27)</td>
<td>31(34)</td>
<td>32(38)</td>
<td>0.309</td>
<td></td>
<td></td>
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<tr>
<td>Creatinine&gt;2 mg %</td>
<td>8(10)</td>
<td>6(7)</td>
<td>7(8)</td>
<td>0.705</td>
<td></td>
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<tr>
<td>Medical history, n (%)</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Previous myocardial infarction</td>
<td>26(33)</td>
<td>36(40)</td>
<td>32(38)</td>
<td>0.658</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral artery disease</td>
<td>14(18)</td>
<td>16(18)</td>
<td>11(13)</td>
<td>0.628</td>
<td></td>
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<tr>
<td>Previous percutaneous coronary interventional</td>
<td>31(39)</td>
<td>29(32)</td>
<td>16(19)</td>
<td>0.015</td>
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<tr>
<td>Clinical presentation, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Silent ischemia</td>
<td>6(8)</td>
<td>10(12)</td>
<td>4(5)</td>
<td>0.300</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stable angina</td>
<td>42(53)</td>
<td>48(53)</td>
<td>59(69)</td>
<td>0.042</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unstable angina</td>
<td>24(30)</td>
<td>26(29)</td>
<td>14(17)</td>
<td>0.077</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>7(9)</td>
<td>7(8)</td>
<td>8(9)</td>
<td>0.917</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emergent PCI, n (%)</td>
<td>3(4)</td>
<td>4(4)</td>
<td>8(9)</td>
<td>0.235</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEF, n (%)</td>
<td>51±10</td>
<td>50±10</td>
<td>47±12</td>
<td>0.076</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EuroSCORE, %</td>
<td>4.3±2.6</td>
<td>4.7±2.8</td>
<td>5.7±3.1</td>
<td>0.005</td>
<td></td>
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</tr>
</tbody>
</table>

LVEF indicates left ventricular ejection fraction; EuroSCORE, European system for cardiac operative risk evaluation.

ers (P=0.008), had lower rates of previous PCI (P=0.015) and a higher European system for cardiac operative risk evaluation (P=0.005) when compared with those with lower SXscores. Not surprisingly, variables pertinent to complexity and extension of coronary artery disease were more pronounced in patients in the highest tertile.

In-Hospital Outcome

The rates of cardiac death during hospitalization were 0%, 1.1%, and 3.5% in patients with low, intermediate, and high SXscores, respectively. Also, the SXscore usefully stratified the rate of in-hospital MACE among tertiles (1.3%, 3.3%, and 4.7% in patients with low, intermediate, and high SXscores, respectively). One angiographically confirmed acute stent thrombosis was documented in the second SXscore tertile.

Long-Term Outcome

Twenty patients (7.8%) were lost to follow-up. The other patients were followed up for a mean duration of 18 months (ranging 3 to 57 months based on the date of enrollment). The cumulative incidences of cardiac mortality and MACE across the SXscore tertiles are shown in Figure 1. At 1 year, the rates of cardiac death were 2.5%, 1.1%, and 13.1% in patients with low, intermediate, and high SXscores, respectively (index of separation=0.106). In the same period, the incidence of MACE was 7.4% in the first tertile, 21.4% in the second tertile, and 20.4% in the third tertile (index of separation=0.130). Overall, by univariate Cox proportional hazard analysis, the SXscore significantly predicted the risk of cardiac death (HR, 1.12/unit increase; 95% CI, 1.06 to 1.18; P=0.001) and MACE (HR, 1.59/unit increase; 95% CI, 1.01 to 1.07; P=0.024) remained significantly different in relation to the SXscore.

Sensitivity Analysis

For analysis of sensitivity, 76 patients with a previous PCI were censored, and their long-term outcomes were reevaluated. The cumulative incidence of cardiac mortality (HR, 1.10/unit increase; 95% CI, 1.04 to 1.16; P=0.001) and MACE (HR, 1.04/unit increase; 95% CI, 1.01 to 1.07; P=0.024) remained significantly different in relation to the SXscore.
Multivariable Analysis

After adjustment for potential confounders, the SXscore remained significantly associated with cardiac mortality (adjusted HR, 1.15; 95% CI, 1.05 to 1.26; \( P = 0.003 \)) and MACE (adjusted HR, 1.06; 95% CI, 1.02 to 1.10; \( P = 0.005 \); Table 3). Although the SXscore was the only predictor of cardiac death at multivariable analysis, complete revascularization was found to be a predictor of a lower risk of MACE (adjusted HR, 0.34; 95% CI, 0.12 to 0.97; \( P = 0.044 \)).

AHA/ACC Score Versus SXscore

The overall AHA/ACC classification scheme ranged from 2 to 25, with a mean of 8.78 ± 4.51 points. A significant but not tight correlation was found with the SXscore (\( r = 0.67, P < 0.001 \); Figure 2).

Similar to the SXscore, the AHA/ACC score significantly predicted the rate of cardiac death (HR, 1.19/unit increase; 95% CI, 1.07 to 1.32; \( P = 0.001 \)) at 1 year. The rates of cardiac death were 3.3%, 1.3%, and 11.7% in patients with low, intermediate, and high AHA/ACC scores, respectively. In the same period, MACE (7.1% in the first tertile, 17.9% in the second tertile, and 25.3% in the third tertile, HR, 1.09/unit increase; 95% CI, 1.02 to 1.16; \( P = 0.016 \)) also varied significantly different according to the AHA/ACC score. After adjustment for potential confounders, AHA/ACC remained an independent predictor of cardiac death (adjusted HR, 1.19; 95% CI, 1.02 to 1.39; \( P = 0.032 \)) but failed to emerge as an independent predictor of MACE (adjusted HR, 1.07; 95% CI, 0.99 to 1.16; \( P = 0.084 \)).

Applied to our series, \( c \)-indexes for AHA/ACCs and SXscores in terms of cardiac death were 0.76 and 0.83, respectively, whereas the \( c \)-index in terms of MACE was 0.64 for both scores. Conversely, AHA/ACC scores showed a comparable calibration

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cardiac Death Hazard Ratio (95% CIs)</th>
<th>P</th>
<th>MACE Hazard Ratio (95% CIs)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>SYNTAX score</td>
<td>1.15 (1.05 to 1.26)</td>
<td>0.003</td>
<td>1.06 (1.02 to 1.10)</td>
<td>0.005</td>
</tr>
<tr>
<td>Age</td>
<td>0.96 (0.83 to 1.11)</td>
<td>0.55</td>
<td>0.96 (0.89 to 1.02)</td>
<td>0.20</td>
</tr>
<tr>
<td>Male gender</td>
<td>0.10 (0.01 to 1.22)</td>
<td>0.07</td>
<td>0.55 (0.19 to 1.56)</td>
<td>0.26</td>
</tr>
<tr>
<td>Smoke</td>
<td>2.40 (0.41 to 13.9)</td>
<td>0.33</td>
<td>1.25 (0.51 to 3.05)</td>
<td>0.63</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.72 (0.12 to 4.33)</td>
<td>0.72</td>
<td>0.75 (0.32 to 1.74)</td>
<td>0.50</td>
</tr>
<tr>
<td>Acute coronary syndrome</td>
<td>0.57 (0.05 to 6.56)</td>
<td>0.65</td>
<td>0.78 (0.29 to 2.13)</td>
<td>0.63</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>1.23 (0.89 to 1.41)</td>
<td>0.89</td>
<td>1.09 (0.84 to 1.38)</td>
<td>0.84</td>
</tr>
<tr>
<td>Left ventricular ejection</td>
<td>0.95 (0.87 to 1.03)</td>
<td>0.20</td>
<td>1.00 (0.97 to 1.05)</td>
<td>0.81</td>
</tr>
<tr>
<td>fraction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EuroSCORE</td>
<td>1.07 (0.62 to 1.84)</td>
<td>0.82</td>
<td>1.08 (0.81 to 1.43)</td>
<td>0.60</td>
</tr>
<tr>
<td>Reference vessel diameter</td>
<td>0.90 (0.08 to 3.95)</td>
<td>0.93</td>
<td>1.13 (0.40 to 3.17)</td>
<td>0.82</td>
</tr>
<tr>
<td>Lesion length</td>
<td>0.79 (0.63 to 1.29)</td>
<td>0.21</td>
<td>0.98 (0.91 to 1.07)</td>
<td>0.66</td>
</tr>
<tr>
<td>Bifurcation</td>
<td>1.25 (0.14 to 11.4)</td>
<td>0.85</td>
<td>1.25 (2.10 to 0.41)</td>
<td>0.41</td>
</tr>
<tr>
<td>Emergent setting</td>
<td>1.10 (0.89 to 3.34)</td>
<td>0.66</td>
<td>1.87 (0.22 to 6.81)</td>
<td>0.57</td>
</tr>
<tr>
<td>Complete revascularization</td>
<td>0.88 (0.60 to 1.52)</td>
<td>0.84</td>
<td>0.34 (0.12 to 0.97)</td>
<td>0.044</td>
</tr>
</tbody>
</table>
with respect to SXscores both in terms of cardiac mortality ($\chi^2$, 10.3; $P = 0.25$ versus $\chi^2$, 10.1; $P = 0.26$) and MACE ($\chi^2$, 10.9; $P = 0.21$ versus $\chi^2$, 10.5; $P = 0.23$).

**Classification Tree Analysis**

Of all tested univariate predictors of outcome, including AHA/ACC scores, SXscores emerged as the best single discriminator between patients with and those without clinical events. Using classification tree analysis, discrimination levels of 34 and 37 were identified as the optimal cutoff to distinguish between patients at low and high risk of cardiac death and MACE, respectively (Figure 3).

When stratified into the discrimination level suggested by classification and regression tree analysis, the HR for cardiac death was 15.84 (95% CI, 3.42 to 73.35; $P < 0.001$) in patients with high SXscores versus those with low SXscores. This finding was consistent across multiple prespecified subgroup (Figure 4) with the possible exception of patient with diabetes, distal disease, and complete revascularization.

**Discussion**

The idea of validating a prognostic model is generally taken to mean establishing that it works satisfactorily for
patients other than those from whose data the model was derived. However, the SXscore was created ad hoc to grade the complexity of coronary anatomy disease and actually tested only on a subgroup of the Arterial Revascularization Therapies Study Part II population, collecting patients with 3-vessel disease. Therefore, evidence of its generalizability and usefulness to assist in patient selection and risk stratification of patients with extensive coronary artery disease undergoing revascularization of the left main coronary artery is lacking.

The goal of this study was to investigate the validity of the SXscore for the prediction of in-hospital and clinical outcomes in the context of left main coronary artery disease using an external data set that could corroborate its relevance as a useful clinical risk tool. General reasons for wishing to make a prediction of the outcome of this subset of patients include (1) to inform treatment or other clinical decisions for individual patients; (2) to inform patients and their families; and (3) to create clinical risk groups for informing treatment or for stratifying patients by disease severity in clinical trials.

The most important findings of this report are the following. First, our results show that the SXscore predicted the rate of cardiac mortality, with patients in the highest tertile showing a significantly higher event rate both in-hospital and at long-term follow-up than do patients in the lowest tertile. This suggests that the SXscore may be a suitable tool to stratify early and late outcomes even in the context of left main coronary artery disease. These results were confirmed after adjustment for all potential confounders.

Second, the usefulness of the SXscore in predicting MACE when applied on left main patients is driven mainly by its ability to predict cardiac mortality across different strata rather than the power to anticipate the need for repeat revascularization. In fact, the SXscore did not significantly predict the 1-year rate of target lesion revascularization (5.0% in the first tertile, 19.6% in the second tertile, and 7.2% in the third tertile; HR, 1.00/unit increase; 95% CI, 0.96 to 1.05; \( P = 0.859 \)). Kaplan–Meier estimates showed that repeat revascularization in patients with intermediate SXscores mostly occurred from 6 to 8 months from the index procedure, suggesting that a routine angiographic follow-up may play a role in this subset, which conversely takes advantage of a lower competing risk of death as compared with the highest SXscore tertile.

A comparison of our results in terms of MACE with those of Arterial Revascularization Therapies Study Part II study would not be reliable because a different definition of the composite end point applied between the 2 studies. In fact, we chose to include target lesion revascularization rather than any revascularization in the definition of MACE, with the aim of ascertaining whether the propensity of developing left main restenosis might be expected on the basis of a higher complexity of coronary artery disease. By contrast, it is noteworthy that a characterization of the coronary vasculature with respect to the number of lesions and their functional impact and location seem to be more related to hard end points when left main patients are considered. This is consistent with the well known finding that the extent of coronary artery narrowing is a primary determinant of survival in patients with coronary artery disease.

A comparison of the index of separation in this study and in the Arterial Revascularization Therapies Study Part II accord-
ing to the outcomes stratified by SXscore tertiles shows that the 2 studies demonstrated slightly different findings when the SXscore was used to predict mortality (0.106 versus 0.010) and repeat revascularization (0.008 versus 0.092). These findings suggest that the SXscore may be more effective for predicting mortality in patients with unprotected left main coronary artery disease than in patients with 3-vessel disease. Conversely, the latter could take more advantage of the SXscore for predicting repeat revascularization.

When compared with the simpler AHA/ACC scoring system, the SXscore showed a similar performance, with the exception of a better ability to discriminate between patients at high risk of MACE and those at low risk. This finding was corroborated by the classification and regression tree analysis in which the SXscore emerged as the best single discriminator over all tested univariate predictors of outcome, including AHA/ACC score.

Some features of the SXscore warrant consideration when it is applied in clinical practice. First, in the SYNTAX algorithm there is no question for previous stenting. Therefore, it is not clear how to manage this very common situation when computing the SXscore. A sensitivity analysis conducted by censoring those patients who had previously undergone PCI showed that the usefulness of the SXscore in predicting clinical outcome in terms of MACE remained virtually unchanged. By contrast, the presence of a coronary bypass graft is a confusing factor when the SXscore is calculated. Because even this issue is not contemplated in the SYNTAX algorithm, we were urged to exclude from the analysis a discrete number of patients who are commonly seen in the real world. Therefore, standardization of the SXscore could benefit from the inclusion of a scoring for the presence of a previous coronary bypass.

Finally, the SXscore showed a better discriminatory capacity in low versus high tertiles than in intermediate versus lowest or highest tertiles. This is consistent with the findings of Valgimigli et al, who discussed this topic as the reflection of a power issue and suggests the need to dichotomize this variable to avoid overoptimism of the model and achieve the best distinction between patients with favorable and unfavorable outcomes. This concern is probably supported by the skewed distribution of SXscores as a continuous variable. Therefore, based on a classification and regression tree analysis, we propose a level of 34 as the best threshold to discriminate between patients at low and high risk of clinical events. In our series, patients with SXscore >34 faced a 16-fold increased risk of cardiac death than those with SXscore ≤34, with an appropriate stability across multiple subgroups.

Conclusions
This study demonstrated that the SXscore is a useful tool to predict cardiac mortality and MACE in patients undergoing percutaneous revascularization of the left main coronary artery.

Disclosures
There are no financial associations between the authors and any sponsor that might pose a conflict of interest in connection with the submitted article.

References

CLINICAL PERSPECTIVE
The SYNTAX score has been recently proposed as an aid in decision making for patients with complex coronary artery disease, such as 3-vessel or left main coronary artery disease. This study validates and supports the prognostic value of this angiographic tool in patient with left main coronary artery disease. We found that the SYNTAX score is able to stratify patients according to their 1-year risk of cardiac death or major adverse cardiac events after percutaneous coronary intervention, even after adjustment for potential confounders. On the basis of this analysis, we suggested a cutoff of 34 to identify patients who may potentially benefit from surgery because of their poor outcome estimated with percutaneous coronary intervention.
Usefulness of the SYNTAX Score for Predicting Clinical Outcome After Percutaneous Coronary Intervention of Unprotected Left Main Coronary Artery Disease

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