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Prognostic Value of the SYNTAX Score in Patients With Acute Coronary Syndromes Undergoing Percutaneous Coronary Intervention

Analysis From the ACUITY (Acute Catheterization and Urgent Intervention Triage StrategY) Trial

Tullio Palmerini, MD,*† Philippe Genereux, MD,† Adriano Caixeta, MD,† Ecaterina Cristea, MD,† Alexandra Lansky, MD,‡ Roxana Mehran, MD,§ George Dangas, MD,§ Dana Lazar, MD,† Raquel Sanchez, MD,† Martin Fahy, MSc,† Ke Xu, PhD,† Gregg W. Stone, MD†

Bologna, Italy; New York, New York; and New Haven, Connecticut

Objectives We sought to investigate the predictive value of the SYNTAX (Synergy Between PCI With Taxus and Cardiac Surgery) score (SS) for risk assessment of 1-year clinical outcomes in patients with non–ST-segment elevation acute coronary syndromes undergoing percutaneous coronary intervention (PCI).

Background In the SYNTAX trial, the SS was effective in risk-stratifying patients with left main and triple-vessel coronary disease, the majority of whom had stable ischemic heart disease.

Methods The SS was determined in 2,627 patients with non–ST-segment elevation acute coronary syndromes undergoing PCI in the angiographic substudy of the ACUITY (Acute Catheterization and Urgent Intervention Triage StrategY) trial. Patients were stratified according to tertiles of the SS: <7 (n = 854), ≥7 and <13 (n = 825), and ≥13 (n = 948).

Results Among patients in the first, second, and third SS tertiles, the 1-year rates of mortality were 1.5%, 1.6%, and 4.0%, respectively ($p = 0.0005$); the cardiac mortality rates were 0.2%, 0.9%, and 2.7%, respectively ($p < 0.0001$); the myocardial infarction (MI) rates were 6.3%, 8.3%, and 12.9%, respectively ($p < 0.0001$); and the target vessel revascularization (TVR) rates were 7.4%, 7.0%, and 9.8%, respectively ($p = 0.02$). By multivariable analysis, the SS was an independent predictor of 1-year death (hazard ratio [HR]: 1.04, 95% confidence interval [CI]: 1.01 to 1.07; $p = 0.005$), cardiac death (HR: 1.06, 95% CI: 1.03 to 1.09; $p = 0.0002$), MI (HR: 1.03, 95% CI: 1.02 to 1.05; $p < 0.0001$), and TVR (HR: 1.03, 95% CI: 1.02 to 1.05; $p < 0.0001$). The SS affected death, cardiac death, and MI both within the first 30 days after PCI and between 30 days and 1 year, whereas it affected TVR primarily within the first 30 days. The predictive value of an increased SS was consistent among multiple pre-specified subgroups.

Conclusions In patients with non–ST-segment elevation acute coronary syndromes undergoing PCI, the SS is an independent predictor of the 1-year rates of death, cardiac death, MI, and TVR. (Comparison of Angiomax Versus Heparin in Acute Coronary Syndromes [ACS]; NCT00093158) (J Am Coll Cardiol 2011;57:2389–97) © 2011 by the American College of Cardiology Foundation

Prospectively developed for the SYNTAX (Synergy Between PCI With Taxus and Cardiac Surgery) trial, the SYNTAX score (SS) is an angiographic scoring system to rank the complexity of the coronary anatomy (1). The SS was not originally conceived as a method to predict outcomes related to anatomic characteristics (2), but rather to

From the *Istituto di Cardiologia, Policlinico S. Orsola, Bologna, Italy; †Columbia University Medical Center and the Cardiovascular Research Foundation, New York, New York; ‡Yale University School of Medicine, New Haven, Connecticut; and the §Mount Sinai Medical Center, New York, New York. The ACUITY trial was funded by The Medicines Company and Nycomed. Dr. Mehran is a consultant to Abbott Vascular, AstraZeneca, Cardiva, Cordis, Ortho-McNeil, The Medicines Company, and Regado Biosciences; and has received a research grant from Sanofi/Bristol-Myers Squibb. Dr. Dangas has received honoraria from The Medicines Company, Cordis, and Sanofi/Bristol-Myers Squibb; and is a consultant to AstraZeneca. Mr. Fahy, and Drs. Xu, Cristea, Lazar, and Sanchez are employed by the Cardiovascular Research Foundation. Dr. Stone serves on the scientific advisory boards for and has received honoraria from Abbott Vascular and Boston Scientific; and is a consultant to The Medicines Company. All other authors have reported that they have no relationships to disclose.

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Abbreviations and Acronyms

CABG = coronary artery bypass graft

CI = confidence interval

HR = hazard ratio

LVEF = left ventricular ejection fraction

MI = myocardial infarction

NSTEACS = non–ST-segment elevation acute coronary syndromes

PCI = percutaneous coronary intervention

ROC = receiver-operator characteristic

SS = Synergy Between PCI With Taxus and Cardiac Surgery score(s)

TIMI = Thrombolysis In Myocardial Infarction

TVR = target vessel revascularization

allow a detailed and objective assessment of the coronary vasculature (3). Subsequent reports have demonstrated that the SS may be an effective tool for predicting the risk of major ischemic events in patients undergoing percutaneous coronary intervention (PCI) with stable ischemic heart disease and multivessel or left main disease (3–10).

Patients with non–ST-segment elevation acute coronary syndromes (NSTEACS) may have significant morbidity and mortality, even with an early invasive management strategy. Prospective risk stratification is essential to estimate patient prognosis, to aid in clinical decision making, and to ensure quality control. Indeed, although clinical predictors of ischemic outcomes in patients with NSTEACS have been previously reported (11–15), the role of angiographic variables is less well defined. In this context, no previous study has assessed the prognostic utility of the SS in patients with NSTEACS undergoing PCI. We therefore sought to investigate the impact of the SS on ischemic outcomes in patients with NSTEACS undergoing PCI from the multicenter, prospective randomized ACUITY (Acute Catheterization and Urgent Intervention Triage StrategY) trial.

Methods

Study protocol. The ACUITY trial design was previously reported in detail (16). Briefly, the ACUITY trial was a multicenter, prospective, randomized trial of patients with moderate and high-risk NSTEACS who were managed with an early invasive strategy. Patients were randomly assigned before coronary angiography to heparin (unfractionated or low molecular weight) plus a glycoprotein IIb/IIIa inhibitor, bivalirudin plus a glycoprotein IIb/IIIa inhibitor, or bivalirudin monotherapy with provisional glycoprotein IIb/IIIa inhibitor use. Angiography was performed in all patients within 72 h of randomization. Depending on coronary anatomy, patients were then treated with PCI, coronary artery bypass graft (CABG) surgery, or medical therapy. In patients undergoing PCI, the choice of either bare metal or drug-eluting stents was per operator discretion. Dual antiplatelet therapy with aspirin and clopidogrel was strongly recommended for at least 1 year. All major adverse events were adjudicated by an independent clinical events committee blinded to treatment assignment.

Objectives, patients, and angiographic analysis. The primary objective of the present analysis was to evaluate the impact of the SS on the risk of individual ischemic outcomes, including 1-year all-cause death, cardiac death, myocardial infarction (MI), and target vessel revascularization (TVR). We included only the subgroup of PCI patients in whom quantitative coronary angiography (17) was performed in the formal angiographic substudy of the ACUITY trial by experienced core angiographic laboratory technicians (Cardiovascular Research Foundation, New York, New York) blinded to treatment assignment and clinical outcomes. Because the SS score has been validated only for patients with native coronary artery disease, patients with a history of CABG were excluded.

For the present study, the SS for each angiogram was assessed by 3 experienced interventional cardiologists blinded to treatment assignment and clinical outcomes. Each lesion with ≥50% diameter stenosis in vessels ≥1.5 mm in diameter was scored using the SS algorithm fully described elsewhere (1). The Fleiss kappa statistic (18) (tertile partitioning), determined for the 3 readers from 50 films read independently, was 0.57, signifying interobserver reproducibility comparable to that previously reported from the SYNTAX trial (19).

Statistical analysis. Continuous data are presented as mean ± SD and were compared using the Student *t* test or the Mann-Whitney rank-sum test, as appropriate. Categorical variables were compared by the chi-square or the Fisher exact test. Patients were grouped into tertiles of SS. One-year outcomes were determined using Kaplan-Meier methodology and compared using the log-rank test. Receiver-operator characteristic (ROC) curves were also constructed to assess the predictive accuracy of the SS for 1-year all-cause mortality, cardiac mortality, MI, and TVR. The minimized absolute value of (sensitivity-specificity) was chosen as the optimal ROC cutoff point. Stepwise Cox multivariable regression analyses were performed to assess the association between the SS and 1-year all-cause mortality, cardiac mortality, MI, and TVR. The following variables were included in the models: SS (as a continuous variable), age, male sex, white blood cell count, hemoglobin levels, current cigarette smoking, diabetes, renal dysfunction, left ventricular ejection fraction (LVEF), baseline troponin elevation, ST-segment deviation, previous MI, previous PCI, and type of stent (drug-eluting vs. bare-metal stent). Landmark analyses of all-cause death, cardiac death, MI, and TVR were performed using Kaplan-Meier methodology in 2 periods of interest: from PCI to 30 days and from 31 days to 1 year. Statistical analyses were performed using SAS version 9.1 (SAS Institute, Cary, North Carolina). A p value <0.05 was considered statistically significant.

Results

Quantitative coronary angiography was performed in 6,921 patients enrolled in the ACUITY trial angiographic substudy, including 3,826 patients who underwent PCI. After

excluding patients who had undergone previous CABG surgery (n = 862) and those for whom the SS could not be calculated due to technical reasons (n = 337), 2,627 patients remained for whom the SS was determined for the present analysis.

The SS ranged from 0 to 59, with a mean of 11.5 ± 8.4 and median of 9. Clinical and angiographic characteristics of patients stratified by SS tertiles are shown in Table 1. Compared with patients in the lower tertile, those in the upper tertile were older and more likely to have diabetes mellitus, renal dysfunction, baseline troponin elevation, ST-segment deviation, higher Thrombolysis In Myocardial Infarction (TIMI) risk score, and lower LVEF. Patients in the upper tertile were also more likely to have longer lesions, bifurcation lesions, thrombus-containing lesions, and heavily calcified lesions than those in the lower 2 tertiles. There were no significant differences in discharge medication use of aspirin, clopidogrel, and ticlopidine across SS tertile.

1-year clinical outcomes. At 1-year follow-up, the rates of all-cause death, cardiac death, MI, and TVR in the overall cohort were 2.4%, 1.3%, 9.3%, and 8.1%, respectively. Clinical outcomes stratified according to SS tertiles are shown in Table 2 and in Figures 1A to 1D. Event rates were significantly higher in the upper tertile than in the intermediate or lower tertiles, whereas no significant difference existed between the intermediate and lower tertiles. As shown in Table 3, after adjusting for possible confounders, the SS was an independent predictor of 1-year all-cause mortality (hazard ratio [HR]: 1.04, 95% confidence interval [CI]: 1.01 to 1.07; p = 0.005), cardiac mortality (HR: 1.06, 95% CI: 1.03 to 1.09; p = 0.0002), MI (HR: 1.03, 95% CI: 1.02 to 1.05; p < 0.0001), and TVR (HR: 1.03, 95% CI: 1.02 to 1.05; p < 0.0001).

ROC curves and landmark analyses. ROC curve analysis demonstrated a significant association between the SS and 1-year all-cause mortality, cardiac mortality, MI, and TVR. As shown in Table 4, the optimal SS cutoff value ranged from 10 to 13 depending on the outcome considered. The 1-year rates of all-cause death, cardiac death, MI, and TVR were 4.0%, 2.7%, 12.9%, and 9.8% in patients with an SS ≥13, respectively, and 1.5%, 0.5%, 7.3%, and 7.2% in those with an SS <13 (for death, p < 0.0001; for cardiac death, p < 0.0001; for MI, p < 0.0001; for TVR, p = 0.006).

Landmark analyses of clinical outcomes are shown in Figures 2A to 2D. The rates of death, cardiac death, and MI were increased in patients with a higher SS, both within the first 30 days after PCI and between 30 days and 1 year (Figs. 2A to 2C), whereas the rates of TVR were elevated in patients with a high SS principally within the first 30 days after PCI (Fig. 2D). As shown in Figure 3, the predictive value of an increased SS for cardiac death, MI, and TVR was consistent among multiple pre-specified subgroups, including the elderly and patients with a low LVEF, diabetes, renal dysfunction, and positive biomarkers. There was no significant interaction between the SS and each of these patient subgroups.

Discussion

The present study is the first to assess the SS for risk prediction of ischemic outcomes in patients with moderate- and high-risk NSTEACS undergoing PCI. The main findings of this study are the following. 1) The SS was strongly associated with adverse outcomes after PCI in NSTEACS; even after adjustment for clinical variables, the SS was an independent predictor of 1-year all-cause death, cardiac death, MI, and TVR. 2) Both the 30-day and 1-year rates of death, cardiac death, and MI were increased in patients with a high SS, whereas an increased SS was associated with an increased TVR, primarily within the first 30 days after PCI. 3) The predictive value of the SS was consistent across numerous subgroups of patients.

Several studies have identified clinical and laboratory variables that correlate with a poor prognosis in patients with NSTEACS. Advanced age (12), clinical presentation (15), previous aspirin use (11), electrocardiogram performed at hospital at admission (13), and biochemical evidence of myocyte necrosis (14) have been consistently reported to be predictors of reduced survival in this population. The prognostic role of anatomic and angiographic variables has been less extensively studied and is unsettled. Recently, Lansky et al. (20) reported that baseline angiographic characteristics provide substantial incremental predictive value for 1-year ischemic outcomes in patients with NSTEACS treated with PCI, CABG surgery, or medical therapy (20). In contrast, a recent study from the National Cardiovascular Data Registry reported that angiographic factors add little incremental predictive value for in-hospital mortality after PCI (21). The present large-scale study demonstrates that the SS is a powerful angiographic predictor in patients with NSTEACS undergoing PCI. The discrepant results between the National Cardiovascular Data Registry study and the present analysis may be explained by the fact that the National Cardiovascular Data Registry study appraised only individual angiographic variables, whereas the SS provides a broad integration of coronary lesion complexity and atherosclerotic burden. Angiographic factors may yield relatively little incremental prognostic value when considered individually, whereas they may provide major prognostic value when considered additively as an integrated score.

Before the present study, the SS had previously been associated with the occurrence of major ischemic events, mostly in stable patients with multivessel and left main coronary artery disease (3–7,9), but not specifically in patients with NSTEACS. Recently, the SS was found to

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Table 1 Clinical and Angiographic Characteristics of Patients According to SYNTAX Score Tertiles

	Tertile I, <7 (n = 854)	Tertile II, ≥7 and <13 (n = 825)	Tertile III, ≥13 (n = 948)	p Value
Age, yrs	59.3 ± 11.5 (854)	60.0 ± 11.7 (825)	62.6 ± 11.7 (948)	<0.0001
Male	63.9% (546/854)	68.0% (561/825)	70.4% (667/948)	0.01
Hypertension	64.5% (572/886)	66.2% (545/823)	66.0% (626/948)	0.72
Diabetes mellitus	25.4% (216/850)	29.6% (243/821)	30.3% (286/943)	0.04
Insulin-treated	7.5% (64/850)	7.8% (64/821)	8.2% (77/943)	0.88
Hypercholesterolemia	56.6% (476/841)	56.2% (458/815)	55.8% (520/932)	0.94
Current smoker	38.2% (325/851)	37.2% (306/823)	31.1% (294/944)	0.003
Previous myocardial infarction	28.3% (237/836)	26.9% (218/809)	31.6% (294/931)	0.09
Previous percutaneous coronary intervention	51.1% (437/853)	42.6% (351/823)	38.8% (367/947)	<0.0001
Renal dysfunction	12.4% (99/796)	15.0% (116/774)	18.7% (166/888)	0.002
Left ventricular ejection fraction	56.1 ± 9.8 (671)	54.3 ± 10.6 (645)	50.6 ± 12.7 (767)	<0.0001
Baseline troponin elevation	51.3% (368/717)	62.0% (440/710)	67.7% (571/843)	<0.0001
ST-segment deviation ≥1 mm	22.5% (192/854)	24.4% (201/825)	28.9% (263/932)	0.005
TIMI risk score				
Low (0–2)	18.0% (122/678)	15.6% (108/691)	15.1% (115/762)	0.29
Intermediate (3–4)	61.2% (415/678)	60.9% (421/691)	55.8% (425/762)	0.06
High (5–7)	20.8% (141/678)	23.4% (162/691)	29.1% (222/762)	0.0008
Antithrombotic medication				
Bivalirudin	65.9% (563/854)	66.1% (545/825)	65.1% (617/948)	0.89
Unfractionated heparin	20.8% (178/854)	19.0% (157/825)	19.2% (182/948)	0.58
Enoxaparin	12.8% (109/854)	13.2% (109/825)	13.8% (131/948)	0.80
GPI	65.7% (561/854)	68.8% (568/825)	68.1% (646/948)	0.34
No. of vessel disease	1.3 ± 0.5 (854)	1.5 ± 0.6 (825)	1.9 ± 0.8 (948)	<0.0001
Multivessel disease	22.4% (191/854)	40.6% (335/825)	66.9% (634/948)	<0.0001
LAD disease	34.4% (294/854)	61.9% (511/825)	75.5% (716/948)	<0.0001
Cx disease	38.5% (329/854)	39.2% (323/825)	55.3% (524/948)	<0.0001
RCA disease	51.6% (441/854)	46.4% (383/825)	59.4% (563/948)	<0.0001
Left main coronary artery disease	0.9% (8/854)	0.6% (5/825)	1.4% (13/948)	0.26
No. of lesions	2.8 ± 1.8 (853)	3.7 ± 2.0 (824)	4.6 ± 2.2 (946)	<0.0001
Extent of disease, mm	30.7 ± 20.6 (848)	39.8 ± 26.8 (804)	48.9 ± 28.8 (927)	<0.0001
No. of treated vessels	1.1 ± 0.3 (835)	1.2 ± 0.4 (796)	1.3 ± 0.5 (897)	<0.0001
Any drug-eluting stent	81.6% (697/854)	87.2% (719/825)	85.9% (814/948)	0.004
Total no. of drug-eluting stents	0.9 ± 0.6 (854)	1.1 ± 0.7 (825)	1.3 ± 0.8 (948)	<0.0001
Any bare-metal stent	12.3% (105/854)	13.1% (108/825)	16.5% (156/948)	0.03
Total no. of bare-metal stents	0.1 ± 0.4 (854)	0.1 ± 0.4 (825)	0.2 ± 0.5 (948)	0.006
Lesion length >20 mm	16.1% (159/987)	18.9% (198/1,049)	25.4% (332/1,307)	<0.0001
Severe tortuosity	0.4% (4/988)	0.4% (4/1,066)	0.2% (3/1,369)	0.68
Thrombus	10.9% (108/989)	15.4% (164/1,065)	19.0% (260/1,371)	<0.0001
Severe calcification	1.8% (17/967)	2.3% (24/1,036)	4.4% (60/1,352)	0.0003
Ulceration	4.1% (40/987)	4.5% (48/1,065)	4.8% (65/1,366)	0.72
Aneurysm	0.8% (8/989)	1.1% (12/1,065)	1.2% (16/1,366)	0.67
Bifurcation present	13.7% (135/988)	23.8% (260/1,094)	23.9% (327/1,367)	<0.0001
Baseline QCA				
Reference vessel diameter, mm	2.78 ± 0.57 (989)	2.75 ± 0.53 (1,072)	2.72 ± 0.54 (1,376)	0.03
Minimal lumen diameter, mm	0.80 ± 0.47 (989)	0.72 ± 0.46 (1,072)	0.64 ± 0.46 (1,376)	<0.0001
Diameter stenosis, %	71.2 ± 15.4 (989)	73.8 ± 15.8 (1,072)	76.0 ± 16.4 (1,376)	<0.0001
Final QCA				
Reference vessel diameter, mm	2.83 ± 0.56 (984)	2.79 ± 0.53 (1,072)	2.76 ± 0.54 (1,364)	0.01
Minimal lumen diameter, mm	2.40 ± 0.55 (983)	2.33 ± 0.53 (1,072)	2.25 ± 0.58 (1,364)	<0.0001
Diameter stenosis, %	15.3 ± 9.7 (983)	16.5 ± 10.6 (1,072)	18.4 ± 13.9 (1,364)	<0.0001

Data are mean ± SD (N) or % (n/N). Renal dysfunction is defined as a calculated creatinine clearance rate <60 ml/min determined by the Cockcroft-Gault equation.

Cx = circumflex artery; GPI = glycoprotein IIb/IIIa inhibitor; LAD = left anterior descending artery; QCA = quantitative coronary angiography; RCA = right coronary artery; TIMI = Thrombolysis In Myocardial Infarction.

Table 2 1-Year Clinical Outcomes According to SYNTAX Score Tertiles

	Tertile I, <7 (n = 854)	Tertile II, ≥7 and <13 (n = 825)	Tertile III, ≥13 (n = 948)	p Value for Trend	p Value for Tertile I vs. II	p Value for Tertile II vs. III	p Value for Tertile I vs. III
Major adverse cardiovascular events	15.9% (127)	16.6% (134)	22.9% (213)	<0.0001	0.41	0.0006	<0.0001
Death	1.5% (12)	1.6% (13)	4.0% (37)	0.0005	0.79	0.003	0.001
Cardiac death	0.2% (2)	0.9% (7)	2.7% (25)	<0.0001	0.09	0.005	<0.0001
Myocardial infarction	6.3% (52)	8.3% (67)	12.9% (120)	<0.0001	0.11	0.002	<0.0001
Q-wave	1.1% (9)	1.1% (9)	2.7% (25)	0.009	0.95	0.02	0.01
Non–Q-wave	5.2% (43)	7.2% (58)	10.3% (96)	0.0002	0.09	0.02	<0.0001
Death or myocardial infarction	7.3% (61)	9.5% (77)	15.0% (140)	<0.0001	0.11	0.0004	<0.0001
Target vessel revascularization	7.4% (56)	7.0% (55)	9.8% (89)	0.02	0.93	0.02	0.02

Values are % (n). Major adverse cardiovascular events denotes cardiac mortality, myocardial infarction, or target vessel revascularization.

independently predict major ischemic events and mortality in the all-comers population of the LEADERS (Limus Eluted from A Durable versus Erodable Stent Coating) trial (22). Distinctive aspects of our study compared with its predecessors are the higher number of patients enrolled, with the ACUITY angiographic substudy representing the largest quantitative coronary angiography study to date in any setting; exclusive evaluation of NSTEACS patients undergoing PCI; appraisal of the SS in the prognosis of individual ischemic outcomes (rather than just composite

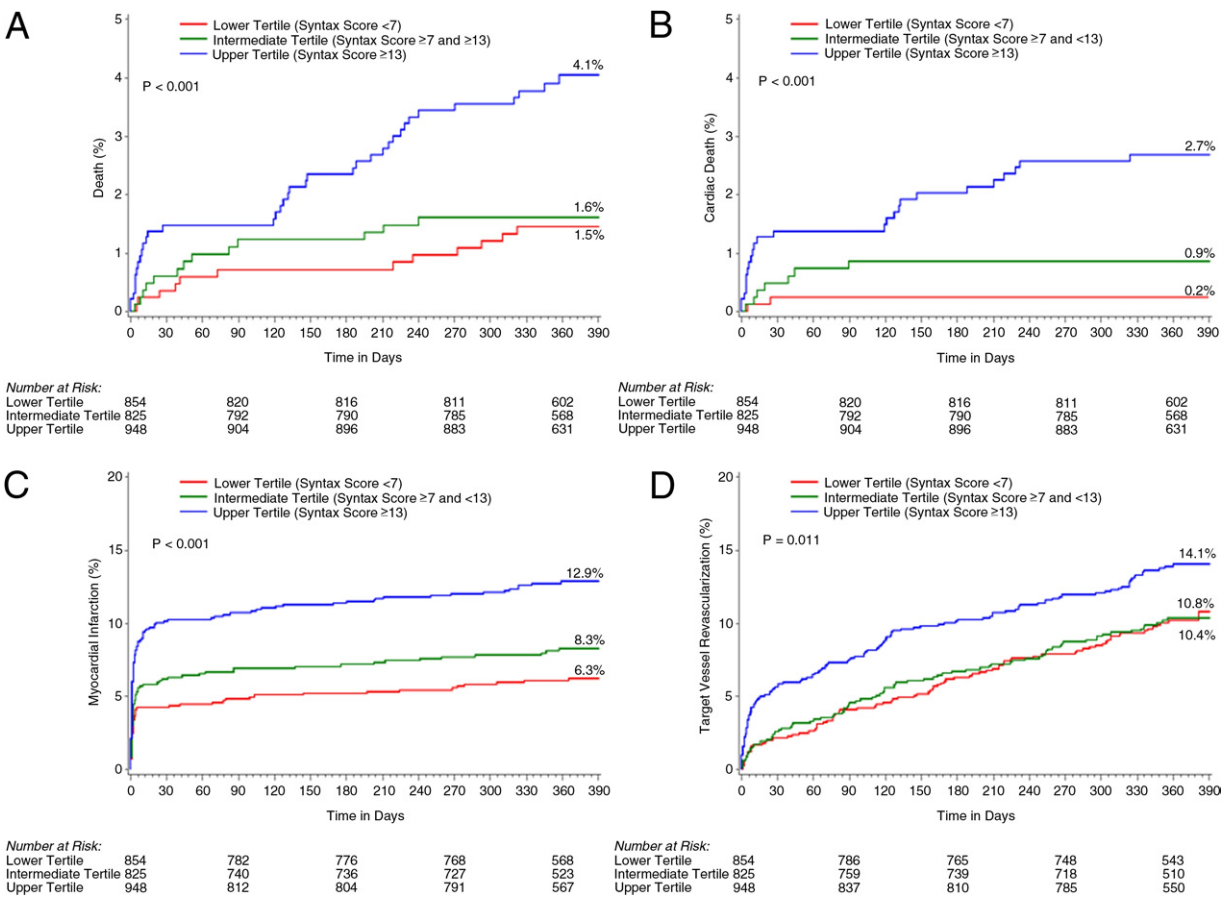

Figure 1 Kaplan-Meier Curves Showing Cumulative Event Rates Through 1 Year

All-cause mortality **(A)**, cardiac mortality **(B)**, myocardial infarction **(C)**, and target vessel revascularization **(D)** stratified by tertiles of SYNTAX score. Event rates were significantly higher in the upper tertile of SYNTAX score than in the intermediate or lower tertiles, whereas no significant difference existed between the intermediate and lower tertiles.

Table 3 Independent Predictors of 1-Year Clinical Outcomes

	Hazard Ratio (95% CI)	p Value
All-cause mortality		
SYNTAX score	1.04 (1.01–1.07)	0.005
Age (per 10-yr increments)	2.07 (1.55–2.78)	<0.0001
Diabetes	2.41 (1.34–4.31)	0.003
Left ventricular ejection fraction	0.97 (0.95–0.99)	0.02
Current cigarette smoking	2.15 (1.08–4.25)	0.03
Cardiac mortality		
SYNTAX score	1.06 (1.03–1.09)	0.0002
Age (per 10-yr increments)	1.76 (1.21–2.54)	0.003
Diabetes	2.47 (1.15–5.28)	0.02
Left ventricular ejection fraction	0.96 (0.94–0.99)	0.006
Current cigarette smoking	2.63 (1.12–6.19)	0.03
Myocardial infarction		
SYNTAX score	1.03 (1.02–1.05)	<0.0001
Age (per 10-yr increments)	0.85 (0.74–0.97)	0.02
Previous PCI	1.40 (1.04–1.89)	0.03
Renal insufficiency	2.65 (1.85–3.80)	<0.0001
Baseline biomarker elevation or ST-segment deviation	1.48 (1.04–2.09)	0.03
Target vessel revascularization		
SYNTAX score	1.03 (1.02–1.05)	<0.0001
Age (per 10-yr increments)	0.81 (0.72–0.92)	0.0007
Renal insufficiency	1.68 (1.18–2.40)	0.004
Previous PCI	1.90 (1.49–2.41)	<0.0001

CI = confidence interval; PCI = percutaneous coronary intervention.

ischemic events); and inclusion of patients with relatively lower SS values. Regarding the latter point, although in earlier studies, the mean SS ranged from 20 to 30 (3–7,9), in our study, the mean SS was 11. It is noteworthy that relatively low SS cutoff points in the present study (ranging from 10 to 13) possessed significant accuracy in predicting individual adverse ischemic outcomes. As a continuous variable, the SS was independently associated with 1-year all-cause death, cardiac death, MI, and TVR. Of note, only 60 patients (2.3%) undergoing PCI in the present study had an SS of ≥33, demonstrating the rarity of this practice outside of the SYNTAX trial.

The rates of all-cause mortality, cardiac mortality, and MI were increased in the higher SS cohort both within the first 30 days after PCI and between 30 days and 1 year. The increased 30-day rates of death and MI in patients with high SS may be explained by the higher procedural risk associated with complex lesions. A high SS is also a marker for diffuse atherosclerosis, which likely contributed to the worsened late prognosis. Because the SS includes anatomic variables strongly associated with restenosis (including the number of lesions, bifurcations, ostial disease, and so on), we were surprised that higher SS were not associated with increased rates of TVR after 30 days. This observation is consistent with some (22) but not all (9,23) previous studies and thus requires additional investigation. Because in the ACUITY trial all revascularizations categorized as TVR were by definition unplanned, staged procedures had no impact on the 30-day rate of TVR. All studies, however, have consistently shown an increased rate of TVR within 30 days after PCI in patients with a high SS.

Current risk scores for NSTEACS are based only on clinical, biochemical, and/or electrocardiographic variables (11,24). The SS, in contrast, is a pure angiographic measure of anatomic coronary complexity. These considerations notwithstanding, the present study demonstrates that the SS is a powerful independent predictor of adverse ischemic outcomes during 1-year follow-up in patients with NSTEACS undergoing PCI, even after adjustment for clinical variables. The present study thus demonstrates that in addition to clinical variables, angiographic factors also are important for risk-stratifying NSTEACS patients undergoing PCI.

Along with the SS, advanced age, diabetes, and reduced LVEF were independent predictors of all-cause and cardiac death, and renal insufficiency was an additive independent correlate of MI and TVR. Thus, risk scores incorporating both clinical and angiographic variables may be more accurate than those including either alone. In 2 previous studies in different patient cohorts, the prognostic utility of the SS was improved by integrating it with the Euroscore (25) or a modified ACEF (age, creatinine, and ejection fraction) score (23). Whether this holds true for patients with NSTEACS deserves further investigation. One advantage of the SS, however, is that it was created before the SYNTAX trial and then prospectively validated. The modified (post-hoc) clinical and angiographic risk scores require prospective validation and comparison with the SS before they are accepted into routine clinical practice.

Study limitations. As a retrospective analysis from a prospective, randomized trial, the results should be considered hypothesis generating. Although we corrected for measured

Table 4 Receiver-Operator Characteristic Curve Analysis Demonstrating the Association Between SYNTAX Score and Individual Adverse Ischemic Outcomes

	AUC	p Value	Optimal Cutoff Value	Sensitivity, %	Specificity, %
All-cause death	0.64	<0.0001	11	60	59
Cardiac death	0.72	<0.0001	13	68	63
Myocardial infarction	0.61	<0.0001	11	61	57
Target vessel revascularization	0.58	0.0001	10	56	54

AUC = area under the curve.

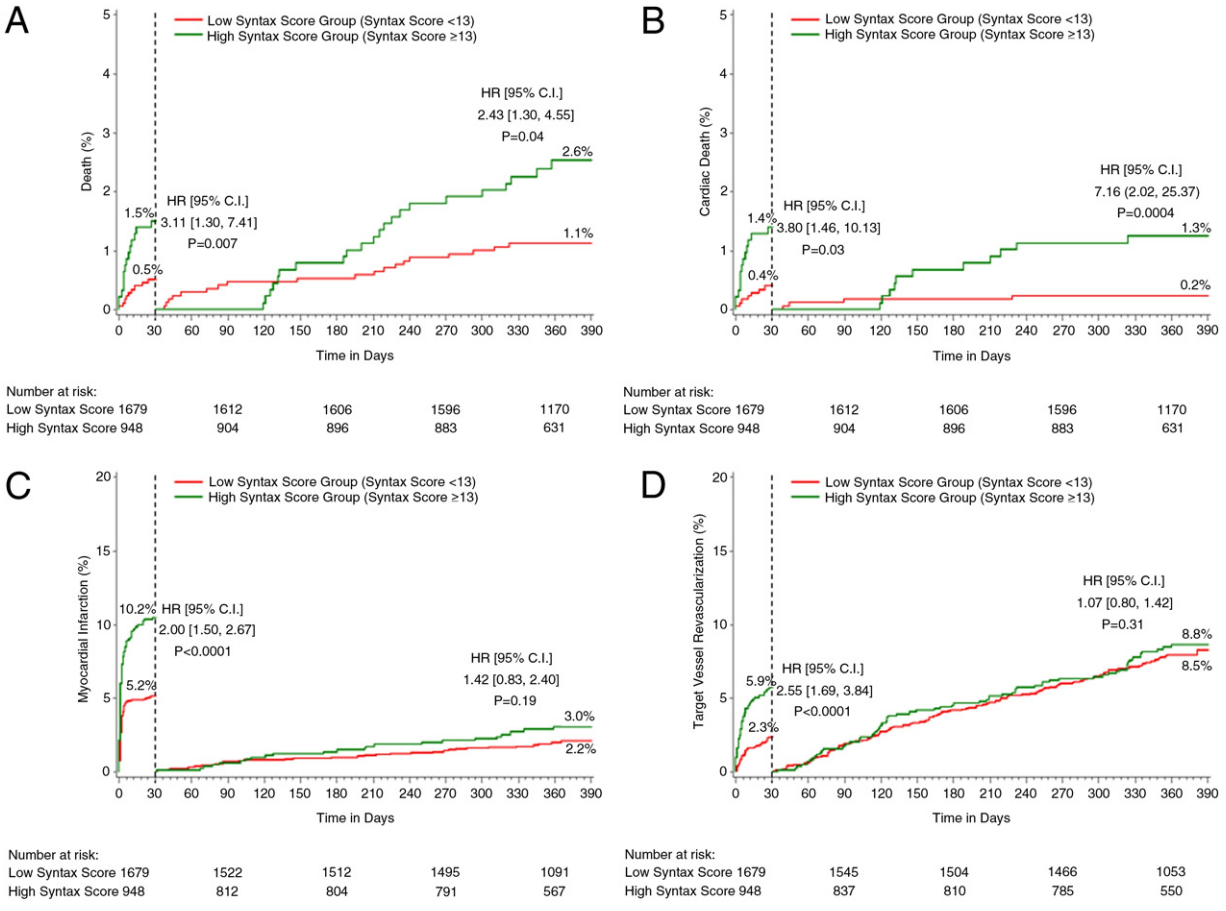

Figure 2 **Landmark Analyses**

All-cause mortality **(A)**, cardiac mortality **(B)**, myocardial infarction **(C)**, and target vessel revascularization **(D)** within 30 days from percutaneous coronary intervention and between 30 days and 1 year in patients with high versus low SYNTAX scores. The rates of death, cardiac death, and myocardial infarction were increased in patients with a higher SYNTAX score both within the first 30 days after the procedure and between 30 days and 1 year, whereas the rates of target vessel revascularizations were elevated in patients with a high SYNTAX score principally within the first 30 days after percutaneous coronary intervention.

covariates in the multivariable model, unmeasured confounders may still persist.

Choice of stent was not randomized in the ACUITY trial, and the patient cohort in the present analysis was drawn from the U.S.-based angiographic substudy in which a higher proportion of drug-eluting stents was used than in the entire ACUITY trial. However, multivariable adjustment for selection of drug-eluting stent versus bare metal stent use did not affect the results. A recent study suggested that incomplete revascularization may be associated with worse clinical outcomes in patients with multivessel disease and high SS undergoing PCI (26). Data on completeness of revascularization were not systematically collected in the ACUITY trial, and therefore we could not evaluate the impact of this variable on 1-year outcomes. Patients who had undergone previous CABG surgery were not included because the SS algorithm was developed only for patients with native coronary artery disease. All total occlusions were scored as having unknown duration; many of these occlusions in the ACUITY trial were likely of short duration, leading to overestimation of the SS. The SS is calculated by visual lesion assessment, and therefore interobserver variability may affect its reproducibility (19). Finally, whether these findings may be extended to NSTEACS patients treated conservatively or with CABG deserves further investigation.

Conclusions

In patients with moderate- and high-risk NSTEACS undergoing PCI after an early invasive management strategy, the SS is an independent predictor of 1-year mortality, cardiac mortality, MI, and TVR, even after correcting for clinical variables. As such, the SS may be a useful tool for risk stratification in this patient population.

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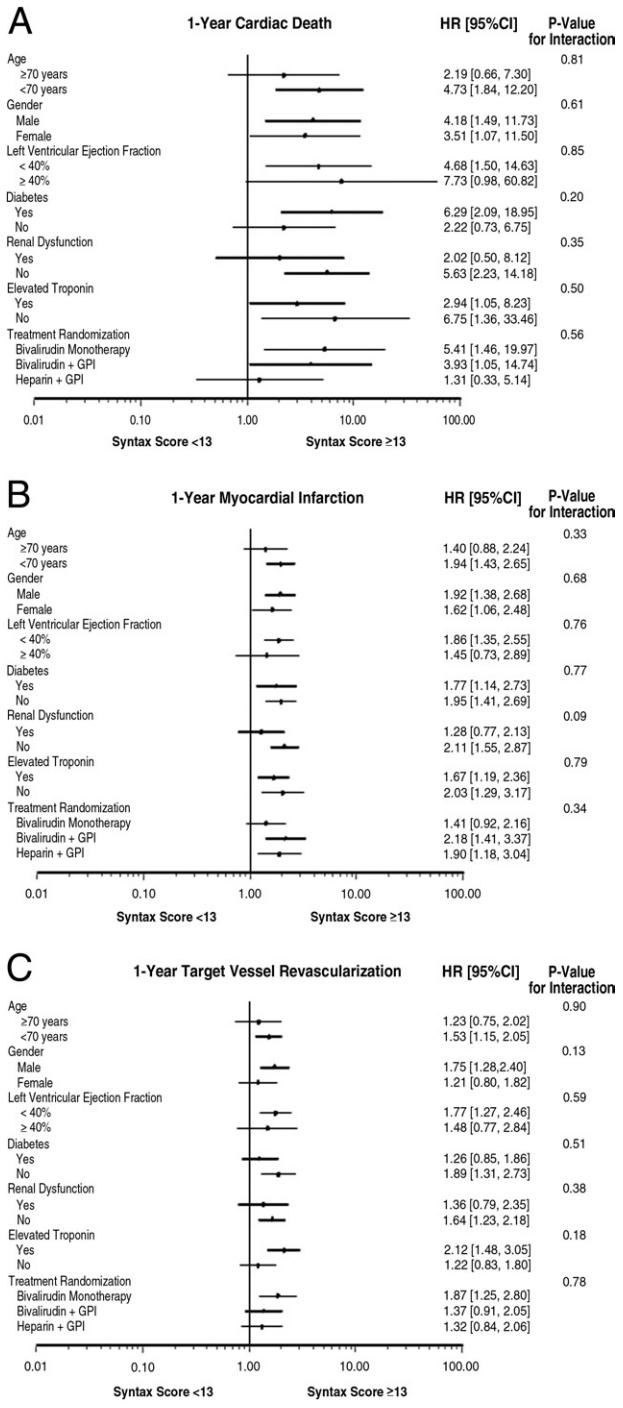

Figure 3 **Impact of SYNTAX Score in Pre-Specified Subgroups of Patients**

Adjusted 1-year cardiac mortality **(A)**, myocardial infarction **(B)**, and target vessel revascularization **(C)** according to high versus low SYNTAX scores. The predictive value of an increased SYNTAX score for cardiac death, myocardial infarction, and target vessel revascularization was consistent among multiple pre-specified subgroups. CI = confidence interval; GPI = glycoprotein inhibitor; HR = hazard ratio.

Reprint requests and correspondence: Dr. Gregg W. Stone, Columbia University Medical Center, New York-Presbyterian Hospital, The Cardiovascular Research Foundation, 111 East 59th Street, 11th Floor, New York, New York 10022. E-mail: gs2184@columbia.edu.

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Key Words: acute coronary syndromes ■ coronary angioplasty ■ SYNTAX score.