Journal of Invasive Cardiology

Published on *Journal of Invasive Cardiology* (http://www.invasivecardiology.com)

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Created *12/01/2011 - 14:20*

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- Volume 23 - Issue 12 - December 2011 [2] [1]
- Posted on: 12/1/11
- 0 Comments
-

Section:
Original Contribution
Issue Number: Volume 23 - Issue 12 - December 2011 [3]
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Abstract: Background. The SYNTAX score (SXscore), an angiographic score reflecting coronary lesion complexity, predicts clinical outcomes in patients with left main or multivessel disease, and in patients with ST-segment elevation myocardial infarction undergoing primary PCI. The clinical SXscore (CSS) integrates the SXscore and clinical variables (age, ejection fraction, serum creatinine) into a single score. We analyzed these scores in elderly patients with acute coronary syndrome (ACS) undergoing primary PCI. The purpose of this analysis was not to decide which patients should undergo PCI, but to predict clinical outcomes in this population. **Methods.** The SXscore was determined in a consecutive series of 114 elderly patients (mean age, 79.6 ± 4.1 years) undergoing primary PCI for ACS. Outcomes were stratified according to SXscore tertiles: SX_{LOW} ≤15 (n = 39), 15< SX_{MID} <23 (n = 40), and SX_{HIGH} ≥23 (n = 35). The primary endpoint was all-cause mortality at 30 days. Secondary endpoints were nonfatal major adverse cardiac and cerebrovascular events (MACCE) at 30 days, and 1-year outcomes in patients discharged alive. **Results.** Mortality at 30 days was higher in the SX_{HIGH} group compared with the aggregate $SX_{LOW+MID}$ group (37.1% vs 5.1%; *P*<.0001), and in the CSSHIGH group compared with the aggregate

CSSLOW+MID group (25.5% vs 1.4%; *P*=.0001). MACCE rates at 30 days were similar among SXscore tertiles. The CSS predicted 1-year MACCE rates (12.1% for CSS_{HIGH} vs 3.1% for $CSS_{LOW+MID}$; *P*=.03). **Conclusions.** The SXscore predicts 30-day mortality in elderly patients with ACS undergoing primary PCI. In patients discharged alive, the CSS predicts risk of MACCE at 1 year.

J INVASIVE CARDIOL 2011;23(12):505-510

Key words: SYNTAX score, acute coronary syndrome, PCI, myocardial infarction

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Several validated patient-based scores have been proposed to predict risk in patients presenting with acute coronary syndrome (ACS) including ST-elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI).[1-5] Most of these scores rely predominantly or entirely on clinical variables such as Killip class, ST-segment changes, and serum creatinine levels, while not taking into account the characteristics of coronary lesions. Recently, the SYNTAX (Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery) score (SXscore) has been developed as a comprehensive angiographic scoring system for the prospective quantification of coronary lesions with respect to their number, location, and complexity.[6-8] The SXscore was initially tested in patients with multivessel disease or complex coronary lesions allocated to PCI or coronary artery bypass graft (CABG) surgery in the landmark SYNTAX trial.[6] Subsequently, this score was also validated for risk prediction in patients with multivessel disease,[9,10] left main disease,[11-18] and in an all-comers population undergoing PCI.[19] More recently, the SXscore was validated for risk stratification in patients with STEMI undergoing primary PCI.[20,21] In the latter setting, the SXscore was identified as an independent predictor of mortality, major adverse cardiac events, and stent thrombosis at 1-year follow-up. A further development was the integration of the SXscore and clinical variables into a single score, the clinical SXscore (CSS), which was calculated by multiplying the SXscore to a modified score including three independent factors (age, creatinine, and left ventricular ejection fraction; ACEF).[22] The ACEF score strongly predicted clinical outcomes in patients undergoing elective cardiac operations.[23] The CSS was shown to improve the ability of the SXscore to predict long-term outcomes in patients undergoing PCI.[22]

Previous studies using the SXscore and CSS have focused on long-term clinical outcomes after PCI. Here we assessed the ability of these scores to also predict short-term outcomes after this intervention. To address this question, we analyzed elderly patients with ACS undergoing primary PCI, who are notoriously at high risk of periprocedural complications.[24] In this cohort, we also analyzed clinical outcomes at 1-year follow-up in patients discharged alive from the hospital.

Methods

[4]**Study population.** All patients aged 75 or older (with the exception of a single 73-year-old patient) who were admitted at our institution with ACS and underwent primary PCI during 2007 and 2008 were included in the present analysis (n = 114; mean age, 79.6 ± 4.1 years). ACS and STEMI were defined according to the guidelines of the European Society of Cardiology.[25,26] Clinical characteristics at baseline are shown in Table 1. STEMI was diagnosed in 76.3% of all patients. The decision to perform PCI, to treat

additional coronary lesions beyond the infarct-related lesion, and to implant bare-metal or drug-eluting stents (DES) was at the discretion of the operator. There was no restriction on the number of implanted stents or on the total stent length. Patients who underwent previous PCI were included in this analysis. Exclusion criteria were previous CABG surgery or clinical indication for emergent CABG surgery.

Determination of SXscore and CSS. From the baseline angiogram, each coronary lesion causing ≥50% diameter stenosis in vessels ≥1.5 mm was scored separately and added together to yield the overall SXscore, which was calculated with the SXscore online calculator (http://www.syntaxscore.com [5]), described in detail elsewhere.[7,8] For each patient, all angiographic variables involved in the calculation of the SXscore were computed by two independent investigators who were blinded to all clinical data. Because patients with STEMI were excluded from the initial SXscore algorithm,[7] there currently is no extensively validated method of calculating the SXscore in this group of patients; however, we followed a method used for this purpose in two recent studies in STEMI patients.[20,21] If the infarct-related artery was occluded, it was scored as an occluded artery of <3-month duration. The CSS was calculated by multiplying the SXscore to a modified ACEF score (age/LVEF +1 if serum creatinine >2.0 mg/dL).

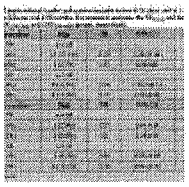
Study endpoints. The study's primary endpoint was mortality at 30-day follow-up. Secondary endpoints were mortality at 1-year follow-up in patients discharged alive from the hospital, and nonfatal major adverse cardiac and cerebrovascular events (MACCE), defined as a composite of target vessel revascularization, myocardial infarction, and stroke after the same follow-up periods.

Statistical methods. Data were described as mean and standard deviation (SD) if continuous and as counts and percentages if categorical. They were compared between SXscore groups by means of the test for trend. The predictive role of SXscore and CSS, categorized as lower/mid vs upper tertile, on 30-day mortality and rates of MACCE was assessed with the logistic model. The area under the ROC curve (AUC) was computed to measure model discrimination ability (the closer to 1, the better) and indirectly compare models. One-year survival and MACCE rate was described by means of the Kaplan Meier method and compared between groups with a Cox model. The Harrell's C statistic was computed to measure model discrimination ability (the closer to 1, the better) and indirectly compare models. For this analysis, patients discharged alive were included, with follow-up starting at discharge. Stata (*College Station*) was used for computation. A 2-sided $P<.05$ was considered statistically significant.

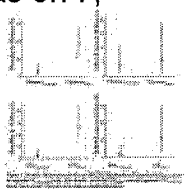
Results

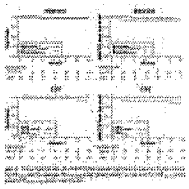
[6]**SXscore and CSS.** In a series of 114 consecutive elderly patients presenting with ACS and treated with primary PCI during 2007 and 2008, the SXscore ranged from 2.0 to 54.0. The SXscore tertiles were computed to SX_{LOW} <15 (n = 39), 15< SX_{MID} <23 (n = 40), and SX_{HIGH} >23 (n = 35). Cardiogenic shock and cardiac arrest were significantly more frequent in the SX_{HIGH} group compared with the SX_{MID} and SX_{LOW} groups (43.3% vs 10.0% vs 7.7% and 25.7% vs 7.5% vs 5.1%, respectively). Patients in the SX_{HIGH} tertile were less frequently on aspirin, clopidogrel, or statin therapy compared with lower tertiles. Other clinical characteristics did not significantly differ among SXscore tertiles. Angiographic data and PCI-related parameters are shown in Table 2. Three-vessel disease was significantly more prevalent in the SX_{HIGH} group compared with the SX_{MID} and the SX_{LOW} groups (42.9% vs 10.0% vs 7.7%, respectively). The CSS could be calculated in 104 patients, but not in 10 patients in whom LVEF was not measured.

This score ranged from 4.1 to 146.1. The CSS tertiles were defined as CSS_{LOW} <22.1 (n = 35), 22.1< CSS_{MID} <34.1 (n = 35), and CSS_{HIGH} >34.2 (n = 34).



[7]**Outcomes at 30-day follow-up.** Seventeen patients died within 30 days of the procedure (15 before and 2 after discharge from the hospital) and 5 patients had nonfatal MACCE during this period (2 of these died later). Mortality and rates of MACCE at 30-day follow-up are shown in Table 3 and Figure 1. They were significantly higher in the SX_{HIGH} group compared with the aggregate SX_{LOW} and SX_{MID} group. The AUC value was 0.77, indicating a good accuracy of the [8]method in this regard. The SXscore did not predict rates of MACCE at 30 days. Mortality rates at 30 days were significantly higher in the CSS_{HIGH} group compared with the aggregate CSS_{LOW} and CSS_{MID} group. The AUC value was 0.82, again indicating a good accuracy of the method for this endpoint. Similarly, rates of MACCE at 30 days were higher in the CSS_{HIGH} group compared with the aggregate CSS_{LOW} and CSS_{MID} group. The AUC value was 0.75.





[9]**Post-discharge outcomes.** Five patients, of those discharged alive, died within 1 year and 6 patients experienced nonfatal MACCE. The SXscore did not correlate with 1-year outcomes in these patients (Table 4 and Figure 2). However, the CSS predicted post-discharge rates of nonfatal MACCE (but not mortality) at 1 year.

Discussion

The present study shows that the SXscore is able to predict mortality at 30 days in elderly patients with ACS having primary PCI. These results are in general agreement with recent studies showing that the SXscore has risk predictive value both in patients undergoing elective PCI[6,9,10] and in those having primary PCI for ACS.[20,21] In addition, the SXscore has been associated with independent risk predictors, such as TIMI flow grade <3 and multivessel disease in patients having primary PCI.[27,28]

In the present study, patients in the high SXscore tertile had a higher prevalence of 3-vessel disease, cardiogenic shock, and cardiac arrest compared with those in the intermediate and low tertile. The well-established association between 3-vessel disease and cardiogenic shock[29] may explain, in part, the increase in the periprocedural risk in the high SXscore tertile. In addition, patients in the high SXscore tertile were less frequently on aspirin, clopidogrel, or statin treatment compared with other patients, which might have influenced early outcomes.

A combination with clinical variables (CSS) improved risk stratification using the SXscore at 30 days only marginally. This observation presumably reflects the predominant role of anatomic complexity of coronary lesions, relative to clinical risk factors, in determining periprocedural mortality. Conversely, the CSS, but not the SXscore, was moderately predictive of MACCE rates at 30 days, consistent with a significant impact of clinical risk factors on nonfatal events.

In 30-day survivors, the SXscore did not predict clinical outcomes at 1 year, consistent with a negligible role of the complexity of coronary lesions after discharge from the hospital. In these patients, however, CSS predicted nonfatal MACCE rates at 1 year, consistent with a persistent impact of clinical risk factors on nonfatal events beyond the periprocedural period.

Our findings add to recent data on the usefulness of the SXscore and CSS for risk stratification in patients with coronary artery disease. While originally developed to assess lesion complexity in patients having elective PCI, the SXscore was recently validated in patients with ACS including STEMI undergoing primary PCI.[20,21] The first dedicated analysis of the SXscore in patients with STEMI, published by Garg et al in 2011, showed that this score is a significant independent predictor of mortality, MACE, and any stent thrombosis out to 1-year follow-up.[20] Because primary PCI is the preferred treatment modality in this group of patients, the purpose of risk stratification using the SXscore in this setting is not to decide which patients should undergo PCI (the traditional use of this score), but rather to predict clinical outcomes in this population.[5]

Distinctive features of our analysis were the focus on elderly patients, who were not specifically studied in previous analyses, and early outcomes (30 days). With respect to the periprocedural risk, a recent study reported a correlation between the SXscore and periprocedural myocardial necrosis during PCI.[30] Our analysis of the survival data at 1 year, including both 30-day survivors and nonsurvivors, shows a predictive role of the SXscore at 1 year (not shown), in line with recent reports on patients with STEMI.[20,21]

In conclusion, the SXscore is able to predict early mortality in elderly patients with ACS undergoing primary PCI. This observation expands recent evidence of the usefulness of this angiographic score for periprocedural risk stratification to this specific group of patients.

Study limitations. We acknowledge the small size of our study cohort. Nonetheless, the number of patients was sufficient to reach statistically significant results and unambiguous conclusions, particularly with respect to 30-day mortality. However, post-discharge mortality was low in this series, hampering reliable statistical modelling.

Acknowledgments. Generous support by the Cecilia-Augusta Foundation, Lugano, Switzerland is gratefully acknowledged.

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Disclosure: The authors have completed and returned the ICMJE Form for Disclosure of Potential Conflicts of Interest. The authors report no conflicts of interest regarding the content herein.
Manuscript submitted July 19, 2011, provisional acceptance given August 15, 2011, final version accepted September 28, 2011.
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