Journal of the American College of Cardiology
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Published by Elsevier Inc.

Vol. 56, No. 4, 2010
ISSN 0735-1097/$36.00
doi:10.1016/j.jacc.2010.03.044

Value of the SYNTAX Score for Risk Assessment in the All-Comers Population of the Randomized Multicenter LEADERS (Limus Eluted from A Durable versus ERodable Stent coating) Trial

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Objectives We aimed to assess the predictive value of the SYNTAX score (SXscore) for major adverse cardiac events in the all-comers population of the LEADERS (Limus Eluted from A Durable versus ERodable Stent coating) trial.

Background The SXscore has been shown to be an effective predictor of clinical outcomes in patients with multivessel disease undergoing percutaneous coronary intervention.

Methods The SXscore was prospectively collected in 1,397 of the 1,707 patients enrolled in the LEADERS trial (patients after surgical revascularization were excluded). Post hoc analysis was performed by stratifying clinical outcomes at 1-year follow-up, according to 1 of 3 SXscore tertiles.

Results The 1,397 patients were divided into tertiles based on the SXscore in the following fashion: SXscore ≤8 (SXlow) (n = 464), SXscore >8 and ≤16 (SXmid) (n = 472), and SXscore >16 (SXhigh) (n = 461). At 1-year follow-up, there was a significantly lower number of patients with major cardiac event–free survival in the highest tertile of SXscore (SXlow = 92.2%, SXmid = 91.1%, and SXhigh = 84.6%; $p < 0.001$). Death occurred in 1.5% of SXlow patients, 2.1% of SXmid patients, and 5.6% of SXhigh patients (hazard ratio [HR]: 1.97, 95% confidence interval [CI]: 1.29 to 3.01; $p = 0.002$). The myocardial infarction rate tended to be higher in the SXhigh group. Target vessel revascularization was 11.3% in the SXhigh group compared with 6.3% and 7.8% in the SXlow and SXmid groups, respectively (HR: 1.38, 95% CI: 1.1 to 1.75; $p = 0.006$). Composite of cardiac death, myocardial infarction, and clinically indicated target vessel revascularization was 7.8%, 8.9%, and 15.4% in the SXlow, SXmid, and SXhigh groups, respectively (HR: 1.47, 95% CI: 1.19 to 1.81; $p < 0.001$).

Conclusions The SXscore, when applied to an all-comers patient population treated with drug-eluting stents, may allow prospective risk stratification of patients undergoing percutaneous coronary intervention. (LEADERS Trial Limus Eluted From A Durable Versus ERodable Stent Coating; NCT00389220). (J Am Coll Cardiol 2010;56:272–7)

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Manuscript received November 30, 2009; revised manuscript received March 22, 2010, accepted March 23, 2010.

The SYNTAX score (SXscore) is a comprehensive angiographic scoring system that is derived entirely from the coronary anatomy and lesion characteristics (1–3). It was initially designed to quantify lesion complexity; however, it is also able to predict major adverse cardiac events (MACE) after percutaneous revascularization in patients with multivessel coronary artery disease (4–6) and/or left main disease (7). More recent data indicate its ability to predict periprocedural myocardial infarction (MI) in patients undergoing elective percutaneous coronary intervention (8). In this substudy of the LEADERS (Limus Eluted from A Durable versus ERodable Stent coating) trial, in which the SXscore was collected prospectively in 1,397 all-comer patients, we assessed its prognostic value for MACE at 1-year follow-up.

Abbreviations and Acronyms

CI = confidence interval
HR = hazard ratio
MACE = major adverse cardiac event(s)
MI = myocardial infarction
SXhigh = SYNTAX score >16
SXlow = SYNTAX score ≤8
SXmid = SYNTAX score >8 and ≤16
SXscore = SYNTAX score
TVR = target vessel revascularization

Methods

Study population. LEADERS was a multicenter European noninferiority trial comparing the safety and efficacy of the BioMatrix Flex biolimus-eluting stent with a biodegradable polymer (Biosensors, Morges, Switzerland) with the Cypher Select sirolimus-eluting stent with a durable polymer (Cordis, Bridgewater, New Jersey) in 1,707 all-comer patients. Detailed study protocol can be found in the main report (9). The study complied with the Declaration of Helsinki and was approved by all institutional ethics committees. All patients provided written informed consent for participation in the trial.

SXscore and angiographic analysis. From the baseline diagnostic angiogram, each coronary lesion producing ≥50% diameter stenosis in vessels ≥1.5 mm was scored separately and added together to provide the overall SXscore, which was calculated prospectively using the SXscore algorithm (described in full elsewhere) (1–3). All angiographic variables pertinent to SXscore calculation were computed by blinded core laboratory analysts (Cardialysis B.V., Rotterdam, the Netherlands). The SXscore is not currently validated in patients with acute MI or previous percutaneous coronary intervention and coronary artery bypass graft. Core laboratory analysts were blinded to all clinical data, and therefore patients with occluded infarct–related arteries were scored as occlusions of unknown duration in a similar manner to any chronically occluded artery. Those patients with in-stent restenosis lesions were scored in the same manner as if the lesion was a de novo lesion.

Study end points. Definitions of all end points are provided elsewhere (9). The primary end point of this substudy was MACE, defined as the composite of cardiac death, MI, and clinically indicated target vessel revascularization (TVR) within 9 months. Secondary end points were any target lesion revascularization (both clinically and nonclinically indicated), any TVR, cardiac death, death from any cause, MI, stent thrombosis (defined according to the Academic Research Council [10]), device success, and lesion success.

The pre-specified principal outcome of the angiographic substudy was the in-stent percentage of diameter stenosis. Secondary angiographic outcomes were the in-segment percentage of diameter stenosis, minimal lumen diameter, late lumen loss, and binary restenosis.

Statistical analysis. A stratified post hoc analysis of clinical and angiographic outcomes was performed according to the tertiles of the SXscore (4,5). Dedicated software and visual coronary angiography served to determine the SXscore (1,2). All randomized patients without previous surgical revascularization (1,397 of 1,707) were included in the analysis. Angiographic outcomes were analyzed using SAS version 8 (SAS Institute, Cary, North Carolina) Proc Mixed for continuous and Proc Genmod for binominal outcomes, taking into account the within-patient correlation structure of these data. The Cox proportional hazards model was used to compare clinical outcomes among the groups. All analyses were performed using SAS version 8.02 by a dedicated statistician. All p values and confidence intervals (CIs) were 2-sided. Multivariate model included SXscore, diabetes, beta-blocker use, stent type, and the presence of acute coronary syndrome as covariates. Testing for (linear) trend was done by using generalized linear models with SYNTAX class as a covariable for continuous variables and the Cochran-Armitage test for trend in categorical data.

Results

SXscore and baseline characteristics. The SXscore was collected prospectively in 1,397 of the 1,707 patients (81.8%) enrolled in the LEADERS trial. The score ranged from 0 to 49, with a mean ± SD of 13.5 ± 8.7 and a median of 12 (interquartile range 7 to 19). In this post hoc analysis, the SXscore tertiles were defined as SXlow (SXscore ≤8) (n = 464), SXmid (SXscore >8 and ≤16) (n = 472), and SXhigh (SXscore >16) (n = 461). Baseline clinical and angiographic characteristics of the patients are listed in Tables 1 and 2.

1-year outcomes. The SXscore significantly predicted the rate of MACE at 360 days (Table 3, Figs. 1 to 4). There was a lower number of patients with MACE-free survival in the highest tertile of the SXscore (SXlow = 92.2%, SXmid = 91.1%, and SXhigh = 84.6%; $p < 0.001$). Death occurred in 1.5% of patients with SXlow, 2.1% of patients with SXmid, and 5.6% of patients with SXhigh (hazard ratio [HR]: 1.97, 95% CI: 1.29 to 3.01; p = 0.002). The rate of MI tended to be