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ORIGINAL INVESTIGATIONS

Prognostic Value of *Site* SYNTAX Score and Rationale for Combining Anatomic and Clinical Factors in Decision Making

Insights From the SYNTAX Trial

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ABSTRACT

BACKGROUND The results of SYNTAX trial have been reported based on "corelab" calculated SS (cSS). It has been shown that reproducibility of SS is better among the core laboratory technicians than interventional cardiologists. Thus, the prognostic value and clinical implication of the "site" SYNTAX SS (sSS) remain unknown.

OBJECTIVES The study sought to evaluate the prognostic value and clinical implication of the sSS after percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) surgery in the randomized SYNTAX trial.

METHODS The sSS was calculated by the site investigators before randomization in the SYNTAX trial. New tertiles based on the sSS were defined with low (0 to 19), intermediate (20 to 27), and high (≥28) scores. The clinical endpoints were compared between PCI and CABG by Kaplan-Meier estimates, log-rank comparison, and Cox regression analyses using the new tertiles. The sSS-based SS II was calculated and its predictive performance was evaluated.

RESULTS The mean difference in cSS and sSS is 3.8 ± 11.2, with a mean absolute difference of 8.9 ± 7.8. In the overall cohort, using sSS there was a higher incidence of major adverse cardiac and cerebrovascular events (MACCE) at 5-year follow-up in the PCI group for low (31.9% vs. 24.5%; p = 0.054), intermediate (39.5% vs. 29.5%; p = 0.019), and high (43.0% vs. 31.4%; p = 0.003) tertiles, compared with the CABG group. Similarly, in the 3-vessel disease subgroup, 5-year MACCE rates were higher in PCI group in all tertiles. Conversely, in the left main subgroup, MACCE rates were similar for PCI and CABG groups in all tertiles. The sSS-based SS II (c-index: 0.736) had predictive performance similar to the cSS-based SS II (c-index: 0.744), with net reclassification index of -0.0062 (p = 0.79).

CONCLUSIONS Appropriate training and unbiased assessment are needed when using SS in clinical decision making. sSS and tertiles based on sSS showed poor discrimination among low, intermediate, and high-risk groups. However, combining clinical factors with sSS retained the predictive performance of SS II. (SYNTAX Study: TAXUS Drug-Eluting Stent Versus Coronary Artery Bypass Surgery for the Treatment of Narrowed Arteries; NCT00114972) (J Am Coll Cardiol 2014;64:423-32) © 2014 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

AUC = area under the receiver operating characteristic curves

CABG = coronary artery bypass grafting

CI = confidence interval

cSS = 'corelab' SYNTAX score

HR = hazard ratio

MI = myocardial infarction

MACCE = major adverse cardiac or cerebrovascular event(s)

NRI = net reclassification index

PCI = percutaneous coronary intervention

SS = SYNTAX score

sSS = 'site' SYNTAX score

SYNTAX = SYNergy Between PCI With TAXUS and Cardiac Surgery

ULMCA = unprotected left main coronary artery

3VD = 3-vessel disease

Interventional cardiologists and surgeons in the SYNTAX (SYNergy Between PCI With TAXUS and Cardiac Surgery) trial originally used the SYNTAX score (SS) to extract objective information from the coronary angiogram on the technical challenges posed by coronary anatomy to percutaneous coronary intervention (PCI) and to facilitate discussions made by the heart team (1). Subsequently, it became apparent that the SS had a prognostic value to predict short- and long-term outcomes (2–4). The European and American revascularization guidelines currently recommend the SS to guide the heart term in decision making (5–7). Moreover, high-risk SS category is a key inclusion/exclusion criterion, imposed by the U.S. Food and Drug Administration, in several ongoing randomized controlled trials, including EXCEL (Evaluation of Xience Prime or Xience V versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization), PARTNER-II (Placement of AoRtic TraNscathetER Valves), and SURTAVI (Surgical Replacement and Transcatheter Aortic Valve Implantation).

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Knowledge of variability in calculating SS is of paramount importance at a time of its widespread use as a clinical decision-making tool. Risk stratification of patients in the SYNTAX trial was based on "corelab" SS (cSS), which was calculated by the core laboratory technicians blinded to the treatment group. However, all sites participating in SYNTAX also had a "site" SS (sSS) calculated by the site investigators, who at that time had no knowledge of the prognostic significance of the SS. The discrepancy between cSS and sSS has been previously highlighted in the SYNTAX trial (8). Recently, Généreux et al. (9) have demonstrated that interventional cardiologists underestimate the number of lesions, bifurcation, and the presence of small-vessel disease, resulting in a lower SS than that reported by the core laboratory technicians. The significance and prognostic value of the sSS in the SYNTAX trial have not been evaluated.

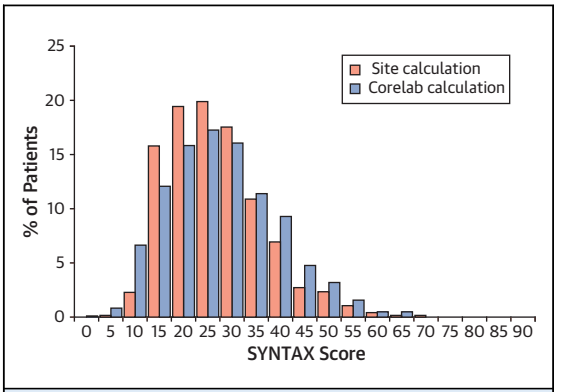

FIGURE 1 Distribution and Individual Difference of the cSS and the sSS

The mean SS was 28.7 ± 11.4 for the corelab and 24.9 ± 10.2 for the site. cSS = corelab SYNTAX score; SS = SYNTAX score; sSS = site SYNTAX score.

This study aimed to examine the difference between the cSS and sSS in the randomized SYNTAX trial and the prognostic performance of the sSS in assessing outcomes among patients undergoing PCI or coronary artery bypass grafting (CABG). We also investigated the predictive performance of the SYNTAX II score, a recently developed risk score that combines the anatomic SS with clinical variables to predict long-term outcome of PCI and CABG when calculated using either cSS or sSS.

METHODS

THE SYNTAX RANDOMIZED TRIAL. The SYNTAX trial (NCT00114972) was a prospective, multicenter, randomized trial to investigate subjects with unprotected left main coronary artery (ULMCA) disease (isolated or associated with 1-vessel, 2-vessel, or 3-vessel disease), or de novo 3-vessel disease (3VD) (10). Eligible patients were randomized on a 1:1 ratio to CABG (n = 897) or PCI with Taxus Express paclitaxel-eluting stent (Boston Scientific Corporation, Natick, Massachusetts; n = 903) and followed up for 5 years. The primary clinical endpoint of the SYNTAX trial was a composite

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