SYNTAX Score is associated with worse outcomes after off-pump coronary artery bypass grafting surgery for three-vessel or left main complex coronary disease

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Objective: The SYNergy between percutaneous intervention with TAXus drug eluting stents and cardiac surgery (SYNTAX) Score is a tool for risk stratification of patients according to the complexity of coronary lesions developed during the SYNTAX trial. We examined the influence of the SYNTAX Score on the incidence of major adverse cardiac and cerebrovascular events.

Methods: All patients with de novo left main or 3-vessel disease undergoing coronary artery bypass grafting from January 2005 to December 2008 at our institution (Hospital Clínico San Carlos, Madrid, Spain) were retrospectively assessed, and their SYNTAX Score was calculated. The influence of the SYNTAX Score on post-procedural and follow-up mortality and combined major adverse cardiac and cerebrovascular events (including death, myocardial infarction, cerebrovascular accident, and repeat revascularization) was identified by multivariate analysis. Balancing score analysis was performed to eliminate the effect of potential confounders.

Results: A total of 716 patients were enrolled. Mean SYNTAX Score was 34.5 (standard deviation, 6.7; range, 11.5–76). Three groups of patients were identified according to the score terciles: low (\leq 33), intermediate (33–37), and high (>37). These terciles scores differed greatly from those reported by the SYNTAX trial investigators. The multivariate analysis identified that the SYNTAX Score was associated with follow-up mortality (hazard ratio = 1.046, P = .015) and combined early and follow-up major adverse cardiac and cerebrovascular events (odds ratio = 1.079, P < .001; and hazard ratio = 1.034, P = .026, respectively). Balancing score-adjusted analyses demonstrated that the SYNTAX Score was independently associated with early and late major adverse cardiac and cerebrovascular events (odds ratio = 1.65, P < .001; and hazard ratio = 1.034, P = .027, respectively).

Conclusions: SYNTAX Score was remarkably high among patients undergoing surgical off-pump myocardial revascularization at our institution. In this subset of patients, a higher SYNTAX Score was associated with a higher incidence of in-hospital and follow-up major adverse cardiac and cerebrovascular events after coronary artery bypass grafting, but not with early or late mortality. (J Thorac Cardiovasc Surg 2011;142:e123-32)

Coronary artery bypass grafting (CABG) surgery is currently the treatment of choice for 3-vessel and left main coronary artery (LMCA) disease. However, recent developments in percutaneous coronary intervention (PCI) have made its endovascular treatment feasible. A CABG has also undergone advances, such as less invasive surgical access, use of arterial rather than venous grafts, and off-pump surgery. To reassess and compare the outcomes of both therapeutic options, the SYNergy between

and cardiac surgery (SYNTAX) trial was initiated in 2005. In this randomized multicenter trial, the outcomes of PCI using paclitaxel-eluting TAXUS stents and CABG for the treatment of 3-vessel and LMCA disease were compared. The SYNTAX Score is a comprehensive angiographic scoring system that assesses coronary lesion complexity within the context of this trial to select patients for one or the other option. In addition to showing acceptable reproducibility, the Syntax score has shown good predictive behavior. Thus, in a report of postprocedural and 1-year outcomes of surgical or PCI revascularization in the patients initially included in the SYNTAX trial stratified by SYNTAX Score, a lower major adverse cardiac and cerebrovascular events (MACCE)-free survival was recorded for the patients with the higher scores in the PCI group. 8 On the other hand, Mohr and colleagues 9 assessed the prognostic value of the SYNTAX Score in the SYNTAX trial CABG group and found no relationship between the

percutaneous intervention with TAXus drug eluting stents

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Abbreviations and Acronyms

AMI = acute myocardial infarction CABG = coronary artery bypass grafting

CI = confidence interval CK = creatine kinase

COPD = chronic obstructive pulmonary

disorder

CPB = cardiopulmonary bypass euroSCORE = European System for Cardiac

Operative Risk Evaluation

cerebrovascular events

HR = hazard ratio
IQR = interquartile range
LMCA = left main coronary artery
MACCE = major adverse cardiac and

OR = odds ratio

PCI = percutaneous coronary

intervention

SD = standard deviation

SYNTAX = SYNergy between percutaneous

intervention with TAXus drug eluting stents and cardiac surgery

score and 2-year follow-up survival. The predictive value of the score has been also studied in cohorts of patients different from those of the SYNTAX study undergoing PCI¹⁰⁻¹² and surgical revascularization for LMCA disease¹³ or 3-vessel disease.¹⁴ The present study was designed to assess the use of the SYNTAX Score to predict MACCE in the postprocedural course of patients undergoing CABG with de novo 3-vessel or LMCA disease.

MATERIALS AND METHODS Patients

All patients undergoing isolated CABG between January 2005 and December 2008 at the Hospital Clínico San Carlos (Madrid, Spain) were retrospectively assessed. Patients were enrolled if they had de novo 3-vessel, isolated LMCA, or LMCA disease with 1, 2, or 3 coronary vessels requiring surgical revascularization. Patients were excluded if they had undergone prior revascularization or single or 2-vessel disease. These criteria were similar to those of the original design of the SYNTAX trial.⁶ Before surgical intervention, written informed consent was obtained from all patients. The study protocol was approved by the institutional review board of our institution. Demographic, anthropometric, clinical, and surgical data were obtained from each patient. Postprocedural risk was estimated using the European System for Cardiac Operative Risk Evaluation (euro-SCORE).¹⁵ A list of all analyzed variables is provided in Table 1. The follow-up was completed between April 2009 and June 2009. For this purpose, patients were contacted by telephone calls or office visits during this period of time.

Coronary Artery Bypass Grafting Technique

Off-pump CABG surgery was always the first choice. Cardiopulmonary bypass (CPB) was conducted only in patients who showed hemodynamic

or electric instability that could not be corrected otherwise during surgery. Internal thoracic artery, saphenous vein, or radial artery grafts were harvested. Heparin was administered to achieve an activated clotting time of 300 to 350 seconds. First, the area of the anterior descending artery was revascularized. Next, distal anastomoses to the lateral, posterolateral, and diaphragmatic aspects were undertaken. Finally, proximal aspects were anastomosed to the ascending aorta with side clamping. Anastomoses were achieved by running suture, using a non-reabsorbable 7-0 monofilament (6-0 for sutures to the aorta). The heparin effect was reversed using protamine.

SYNTAX Score

By using the criteria of the SYNTAX trial, ⁷ we assessed all stenoses 50% or greater in any coronary vessel with a diameter of 1.5 mm or greater. For each patient, the score was retrospectively calculated by a single team comprising a heart surgeon and an interventional cardiologist (not blindly). The last coronary angiography before CABG procedure was used for score assessment. The SYNTAX Score was divided into 3 terciles according to its distribution in the population of patients included in the study.

Objective

The main aim of this study was to examine the effect of the SYNTAX Score on the outcomes of CABG for 3-vessel or left main disease. We recorded the incidence of the following major events during the postprocedural course (defined as the patient's hospital stay or the 30 days after surgery) and in the follow-up: (1) all cause death; (2) grouped MACCE, including (a) death; (b) acute myocardial infarction (AMI) (troponin I > 15 μ g/L in the first 12 hours, troponin I > 20 μ g/L in the first 24 hours or creatine kinase [CK]-MB 5 times greater than the upper limit of the normal range after CABG; CK to CK-MB value 5 times the upper limit of normal in the follow-up); ^{6,16} (c) permanent stroke (focal neurologic defect > 24 hours causing irreversible brain damage or permanent disability); ⁶ and (d) repeat revascularization (PCI or CABG). Only first event survival was assessed in the follow-up. Thus, repeated events were discarded.

Statistical Analysis

Continuous variables were compared with linear regression. Differences between qualitative variables were assessed using the chi-square test (linear trend if independent variable was ordinal) or Fisher's exact test (for expected frequencies < 5). Student t test, Mann–Whitney U test, or analysis of variance was used to compare quantitative (dependent) versus qualitative (independent) variables depending on normality and number of categories.

Potential confounding factors associated with the SYNTAX Score were identified using simple linear regression. Then, a balancing score 17 was developed using non-parsimonious multiple linear regression models that included those variables associated with the SYNTAX Score (P < .10) and first order interactions. The highest R^2 model was selected to develop the balancing score.

Risk factors for postprocedural events were identified by univariate and multivariate analyses. We performed a non-balanced binary logistic regression analysis including all variables found to be associated with postprocedural events in the univariate analysis (P < .20) and those associated with the SYNTAX Score (P < .05). The balancing score was included in the multivariate analysis to better discriminate potential confounders.

Event-free survival in the follow-up was assessed including both post-procedural and postdischarge events. Follow-up survival curves were produced according to the Kaplan–Meier method. Mantel–Haenszel log-rank tests were performed to analyze survival differences. Independent predictive factors for outcomes during the follow-up period were detected using a Cox proportional hazard model. Variables included in multivariate Cox model were those associated with the SYNTAX Score (P < .05) and those linked to the incidence of events in a univariate Cox model (P < .20). Again, to avoid further bias, the balancing score was included in the Cox analysis.

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