

Is the SYNTAX Score a Predictor of Long-term Outcome after Coronary Artery Bypass Surgery?

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ABSTRACT

Background: The SYNTAX score was introduced to measure the complexity of coronary artery disease. Although a high SYNTAX score is indicative of a worse long-term outcome after percutaneous coronary intervention (PCI), it remains unclear whether it is also true for coronary artery bypass grafting (CABG).

Methods: We analyzed 200 consecutive CABG patients who underwent operations in 2002. Demographic and intraoperative data, perioperative outcomes, and 5-year outcomes were obtained. The SYNTAX score was calculated retrospectively by reviewing the original diagnostic angiograms. After excluding patients who had undergone CABG or PCI treatment within 6 months before surgery, we included 154 patients in the study. Patients were partitioned into tertiles according to the SYNTAX score (low, ≤ 18 ; intermediate, >18 - 26 ; high, >26). Cox regression analysis was used to identify baseline and procedural predictors for the combined end point of 5-year major adverse cardiac and cerebrovascular events (MACCE) and its components. Cumulative event rates were estimated by Kaplan-Meier methods.

Results: The mean ($\pm$ SD) age was 66.6 ± 8.5 years, the mean ejection fraction was $56.4\% \pm 13.6\%$, and the mean logistic EuroSCORE was $4.2\% \pm 4.7\%$. The SYNTAX score ranged between 2 and 52. The overall survival rate was 94.8% at 1 year and 84.1% at 5 years. The rate of freedom from MACCE was 92.9% and 78.0% at 1 and 5 years, respectively. Only a higher EuroSCORE, a New York Heart Association class of III to IV, and smoking could be identified with Cox regression as risk factors for MACCE during follow-up. The overall survival and MACCE rates of the 3 SYNTAX score subgroups were not significantly different.

Conclusions: Complex coronary pathology as measured by the SYNTAX score did not affect the long-term outcome after CABG in this study.

INTRODUCTION

By reducing the incidence of restenosis (a major disadvantage of bare-metal stent technology) and by treating patients who have drug-eluting stents (DES) with modern antiplatelet agents, the use of percutaneous coronary intervention (PCI) with DES has been thought to challenge coronary artery bypass grafting (CABG) for the treatment of patients with multivessel disease and left main stenosis. Consequently, the practice of “off-label” PCI outside the current guideline indications has increased in recent years and is thought to account for 30% to 60% of a routine interventional cardiology practice [Kappetein 2006; Brodie 2008; Ko 2009]. Comparisons of PCI with CABG for multivessel disease in various randomized and registry studies have nevertheless revealed strong evidence that CABG remains superior to PCI, even when DES are used [Briguori 2007; Javaid 2007; Brener 2008; Hannan 2008]. Although the identification of distinctive predictors of adverse early or long-term outcomes in PCI with DES is still under discussion, there is wide consensus that the complexity of coronary artery disease (CAD), although difficult to measure, strongly correlates with the advent of major adverse cardiac and cerebrovascular events (MACCE) after PCI.

The SYNTAX score was recently developed as a comprehensive angiographic scoring tool to quantify the complexity of CAD and to assist in patient selection and risk stratification [Valgimigli 2007]. Although the experience with this score has been limited to date, it is a promising classification system for the detailed description of the anatomical severity of CAD. It was recently demonstrated that PCI patients presenting with SYNTAX scores >26 had a significantly higher postprocedural MACCE rate and that the SYNTAX score independently predicted outcome [Valgimigli 2007]. These findings were recently confirmed with the randomized population of the SYNTAX study [Serruys 2009]; however, the early and late prognostic impacts of the SYNTAX score for CABG patients are still unknown. The aim of the present study was therefore to evaluate whether a complex pathology of the coronary arterial tree expressed by the SYNTAX score was a risk factor for an adverse long-term outcome after coronary artery surgery, as has already been shown for PCI patients at 1 year after the procedure [Valgimigli 2007].

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METHODS AND PATIENTS

We retrospectively analyzed 200 consecutive patients who had been referred for coronary surgery in 2002 and for whom the original coronary angiograms were available. The study protocol was approved by the local institutional review board. After exclusion of patients with previous cardiac surgery, an emergency indication, stent implantation within 6 months before surgery, incomplete files, or impossibility of gaining follow-up, we were able to include 154 patients in the study.

Data for demographic, intraoperative, perioperative parameters had been prospectively recorded in the hospital database. Additionally, the SYNTAX score was retrospectively calculated from the preoperative angiograms by a team of 3 experienced cardiac surgeons. These surgeons were not the same surgeons who performed the operations in 2002. The SYNTAX score is a comprehensive anatomical assessment derived from various preexisting classifications. In brief, each lesion producing $\geq 50\%$ luminal obstruction in vessels ≥ 1.5 mm in diameter is defined according to the modified American Heart Association coronary tree segment classification and is separately scored with respect to bifurcational, trifurcational, or aortic ostial localization; chronic occlusion; vessel tortuosity; lesion length; calcification; and thrombus formation. Finally, the score of each lesion is added to obtain the patient's total SYNTAX score. Thus, higher SYNTAX scores are indicative of complex coronary artery disease.

A yearly patient follow-up to at least 5 years was obtained by written or telephone contact and was focused on major cardiac events and recurrent angina. MACCE included death from all

causes, myocardial infarction, repeat revascularization, and cerebral stroke. The 5-year follow-up rate was 100%.

Continuous variables were estimated as the mean $\pm$ SD, and the data were evaluated by 1-way analysis of variance. Discrete variables were reported as counts and/or percentages, and differences were assessed by means of the chi-square test or the Fisher exact test, as indicated.

In a first step, we performed univariate and multivariate Cox regression analysis that included as potentially influencing factors the EuroSCORE, the SYNTAX score, arterial hypertension, smoking status, New York Heart Association functional class, Canadian Cardiovascular Society class, diabetes mellitus, and previous stent implantation.

In a second step, we divided the patients into 3 SYNTAX score groups (≤ 18 , >18 -26, and >26). These divisions were based on the distribution in our study population and on a recently published PCI series by Valgimigli and colleagues [2007], but they varied from those of the data analysis used in the SYNTAX study [Seruys 2009]. Cumulative event rates (overall survival, occurrence of MACCE, and angina) were estimated by the Kaplan-Meier method and compared by means of log-rank tests. Data were analyzed with SPSS software (version 13.0; SPSS, Chicago, IL, USA) and Microsoft Excel software (Redmond, WA, USA).

RESULTS

Demographic and perioperative data for all of the patients and the different SYNTAX score subgroups are summarized in Tables 1 and 2. The groups showed no significant differences for any of the criteria.

Table 1. Baseline Clinical Characteristics Stratified to SYNTAX Score*

Variable	SYNTAX Score				P
	All (n = 154)	≤ 18 (n = 58)	>18 -26 (n = 46)	>26 (n = 50)	
Age, y	66.7 $\pm$ 8.5	67.0 $\pm$ 8.9	67.5 $\pm$ 6.7	65.5 $\pm$ 9.4	.50
Male sex, %	75.3	69.0	76.1	82.0	.29
Body mass index, kg/m ²	28.3 $\pm$ 4.1	28.2 $\pm$ 3.7	28.3 $\pm$ 4.3	28.5 $\pm$ 4.4	.93
Arterial hypertension, %	95.5	87.9	95.7	96.0	.18
Hyperlipidemia, %	81.2	75.9	82.6	86.0	.54
Renal insufficiency, %	1.3	1.7	0.0	2.0	.49
Occlusive arterial disease, %	30.5	32.8	30.4	28.0	.86
Diabetes, %	44.8	43.1	45.7	46.0	.80
Current smoker, %	14.3	17.2	13.0	12.0	.52
Ex-smoker, %	39.0	27.6	45.7	46.0	.46
Prior myocardial infarction, %	45.5	37.9	56.5	44.0	.23
Ejection fraction $<30\%$, %	5.2	1.7	4.3	10.0	.15
Additive EuroSCORE	3.7 $\pm$ 2.5	3.6 $\pm$ 2.2	3.5 $\pm$ 2.0	4 $\pm$ 3.1	.56
Logistic EuroSCORE, %	4.2 $\pm$ 4.8	3.8 $\pm$ 4.5	4.7 $\pm$ 4.8	4.1 $\pm$ 5.1	.66
3-Vessel disease, %	66.9	60.3	58.7	82.0	.022
Left main disease, %	11.0	10.3	10.9	12.0	.96

*Data are presented as the mean $\pm$ SD where indicated.

Table 2. Operative Data Stratified to the SYNTAX Score*

Variable	SYNTAX Score				P
	All (n = 154)	≤18 (n = 58)	>18-26 (n = 46)	>26 (n = 50)	
Operation time, min	160 ± 46.2	160 ± 56.7	154 ± 43.6	164 ± 33.9	.56
OPCAB, %	37.0	41.4	45.7	24.0	.06
CPB time, min	76 ± 23.3	77 ± 27.6	70 ± 17.6	79 ± 21.8	.29
Cross-clamp time, min	45 ± 14.2	45 ± 16.1	42 ± 12.1	48 ± 13.9	.42
Distal anastomoses, n	2.6 ± 1.1	2.5 ± 1.2	2.5 ± 1.0	2.8 ± 0.9	.13
LIMA use, %	95.5	93.1	95.7	98.0	.17
BIMA use, %	11.7	12.1	4.3	18.0	.04*
Radial artery use, %	29.9	27.6	26.1	36.0	.37
Total arterial revascularization, %	36.4	46.6	30.4	30.0	.08
Perioperative IABP support, %	3.2	3.4	0.0	6.0	.03
Rethoracotomy for bleeding, %	1.3	0.0	0.0	4.0	.02
Ventilation time, h	12.5 ± 8.7	14.4 ± 11.0	11.8 ± 6.8	10.8 ± 7.0	.08
Blood transfusion, %	40.9	46.6	39.1	36.0	.44

*Data are presented as the mean ± SD where indicated. OPCAB indicates off-pump coronary artery bypass grafting; CPB, cardiopulmonary bypass; LIMA, left internal mammary artery; BIMA, both internal mammary arteries; IABP, intra-aortic balloon pump.

Table 3. Clinical End Points in Hospital, at 30 Days, at 1 Year, and at 5 Years*

Variable	SYNTAX Score				P
	All (n = 154)	≤18 (n = 58)	>18-26 (n = 46)	>26 (n = 50)	
30-Day MACCE, %	2.6	1.7	0.0	6.0	.16
1-Year MACCE, %	7.1	6.9	6.5	8.0	.96
5-Year MACCE, %	20.8	19.0	21.7	22.0	.91
Death, %	14.9	13.8	17.4	14.0	.85
Death or MI, %	16.2	13.8	19.6	16.0	.73
Death or repeat revascularization, %	18.8	19.0	19.6	18.0	.98
5-Year death or recurrent angina, %	26.6	29.3	30.4	20.0	.43

*MACCE indicates major adverse cardiac and cerebrovascular events; MI, myocardial infarction.

Thirty-Day Outcome

The overall 30-day mortality rate was 2.6% (3 patients). Causes of death were low cardiac output (2 patients) and respiratory failure (1 patient). Table 3 summarizes the major perioperative complications.

Long-term Outcome

The total follow-up time was 685 patient-years. The cumulative survival rate was 94.8% (95% confidence interval [CI], 91.3%-98.3%) at 1 year and 84.1% (95% CI, 78.0%-90.1%) at 5 years.

Independent predictors of death during follow-up were a high preoperative EuroSCORE (odds ratio [OR], 1.8/point; 95% CI, 1.4-2.3; $P = .0001$), current smoking (OR, 29.0; 95% CI, 4.6-182.4; $P = .0001$), and ex-smoker (OR, 10.2; 95% CI, 2.3-46.1; $P = .02$) (Figure 1).

Independent risk factors for MACCE during follow-up were a higher EuroSCORE (OR, 1.5/point; 95% CI, 1.2-1.9; $P = .0001$), current smoking (OR, 21.9; 95% CI, 4.7-101.3; $P = .0001$), ex-smoker (OR, 8.9; 95% CI, 2.5-30.9; $P = .001$), and New York Heart Association class III or IV at the time of operation (OR, 6.7; 95% CI, 1.6-29.1; $P = .0001$).

The SYNTAX score subgroups demonstrated no significant differences with respect to survival, freedom from MACCE, or freedom from MACCE and angina recurrence (Figure 2).

DISCUSSION

Data from randomized controlled trials comparing DES to bare-metal stents have shown significant reductions in repeat intervention with the use of DES and with comparable

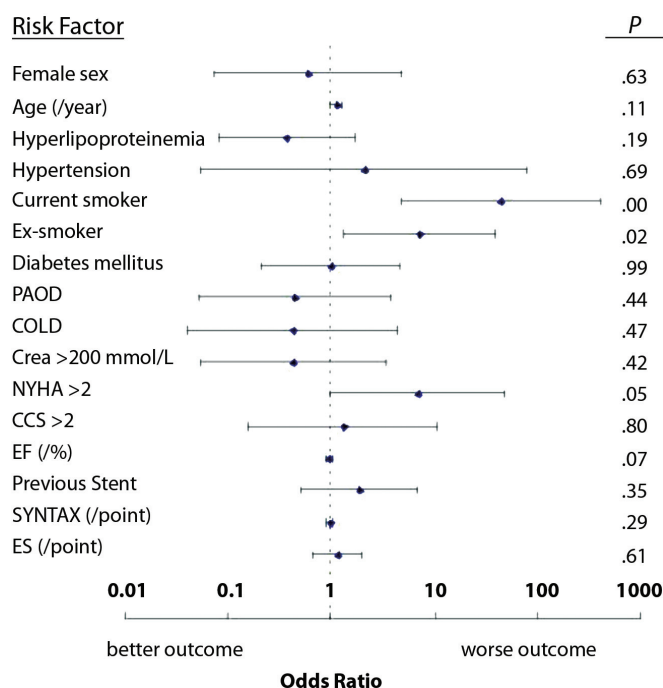


Figure 1. Results of univariate linear regression analysis for major adverse cardiac and cerebrovascular events after 5 years. PAOD indicates peripheral artery occlusive disease; COLD, chronic obstructive lung disease; Crea, creatinine; NYHA, New York Heart Association; CCS, Canadian Cardiovascular Society; EF, ejection fraction; ES, EuroSCORE.

death and myocardial infarction rates [Stettler 2007]. These improvements have led to expanding the use of PCI in patients with complex coronary anatomy, even though most randomized trials exclude such patients. According to contemporary guidelines, the suitability for a particular revascularization approach is dependent on a number of factors. The interventional cardiologist is particularly interested in the coronary anatomy (eg, the presence of chronic total occlusions, bifurcation disease, tortuosity, and calcification), whereas the surgeon is more concerned with the presence of comorbidities (eg, chronic obstructive pulmonary disease, renal impairment, recent stroke) and the availability of suitable graft conduits, all of which may negatively affect surgical outcome.

The SYNTAX score was developed by a team of cardiologists and cardiac surgeons. It was designed to assess the anatomical complexity and, to a lesser extent, the functionality of the coronary artery bed. The intention was to make patients comparable with respect to their coronary pathology. Thus far, the role of the SYNTAX score for therapeutic decisions and/or patient guidance has not been clarified. It is particularly unclear whether the SYNTAX score can provide a means of prognostic significance for patients after CABG surgery and whether therapeutic strategies (eg, surveillance intervals) can be deduced from the score. The SYNTAX score has been shown to be an independent predictor of MACCE after PCI [Valgimigli 2007]. A higher SYNTAX score can also predict periprocedural myocardial injury after PCI [van Gaal 2008].

It remains unclear, however, what kind of coronary pathology is the key predictor of poor outcome in PCI patients. Additionally, the critical SYNTAX score limit for PCI treatment is unknown. Post hoc analyses of SYNTAX score subgroups may help define coronary characteristics that favor either CABG or PCI in patients with 3-vessel/left main disease.

No long-term results regarding the relation between SYNTAX score and postoperative outcome have yet been reported. Two recent studies provide insight into 1-year results after cardiac surgery with respect to the SYNTAX score. Lemesle and colleagues [2009] found no difference in MACCE rates after 1 year for different SYNTAX score groups in patients with 3-vessel disease and concluded that the SYNTAX score had no prognostic value after coronary surgery. On the other hand, Birim and colleagues [2009] identified the SYNTAX score as a good predictor for the occurrence of MACCE within 1 year after CABG surgery in patients with left main disease.

In a larger group of randomized patients—the surgical arm of the SYNTAX study—the 1-year MACCE rate was demonstrated not to be influenced by the SYNTAX score [Serruys 2009].

The intention of our study was to correlate the SYNTAX score with long-term results after cardiac surgery. A clear predictive value of the SYNTAX score (as has been shown for postprocedural outcome after PCI) also could not be found for patients after surgical revascularization in our study. Furthermore, patients with a higher SYNTAX score demonstrated no trend toward a higher risk for the occurrence of MACCE or angina recurrence during a 5-year postoperative period. On the other hand, the well-known risk factors for postsurgical outcome, mainly reflected by the EuroSCORE, had a strong prognostic significance.

In conclusion, our study found no relationship between a higher SYNTAX score and a worse postoperative long-term outcome. It provides more support for the assumption that surgical revascularization is an excellent therapeutic option, independent of the complexity of CAD. Of course, this conclusion needs to be confirmed with long-term results from larger trials, such as the SYNTAX trial.

LIMITATIONS

The study was retrospective in nature because the SYNTAX score was developed only recently, and the intention was to obtain a 5-year follow-up. The number of patients was relatively small. A larger trial might demonstrate additional significant differences. The patient population consisted only of patients who were referred for surgery and for whom PCI was not considered as an alternative option. The SYNTAX score was calculated by cardiac surgeons. Although they were independent from the surgeries, a possible bias cannot be completely excluded. Furthermore, the patient population included not only patients with de novo 3-vessel CAD, and therefore comparability to the population of the SYNTAX trial is limited.

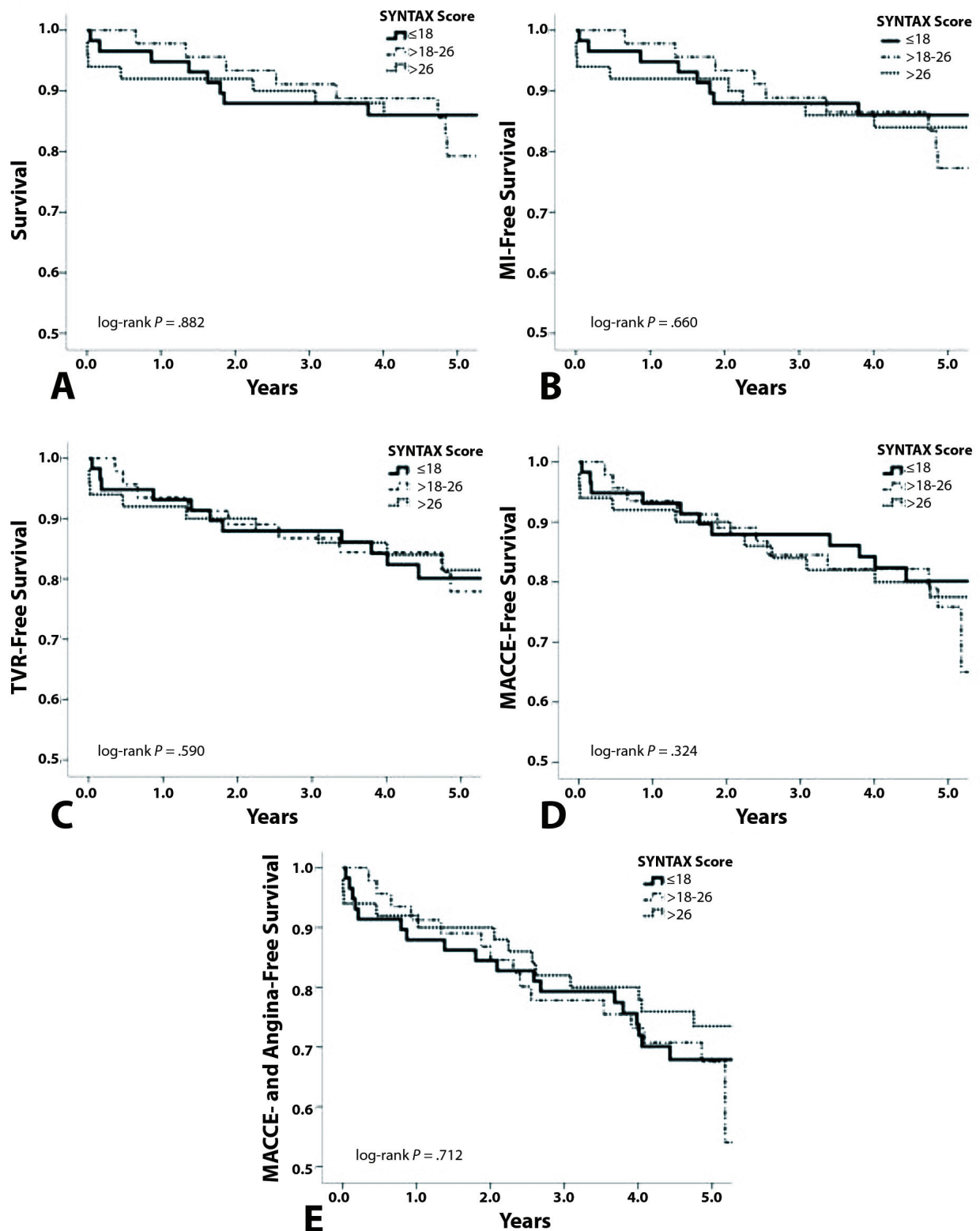


Figure 2. Adverse events over 5 years stratified to SYNTAX score subgroups and depicted as Kaplan-Meier plots of overall survival (A), myocardial infarction (MI)-free survival (B), target vessel revascularization (TVR)-free survival (C), major adverse cardiac and cerebrovascular event (MACCE)-free survival (D), and freedom from MACCE and angina (E).

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