Usefulness of SYNTAX score II in complex percutaneous coronary interventions in the setting of acute coronary syndrome

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Background: **SYNTAX score II (SS II) integrates anatomical SS with clinical characteristics allowing an individualized prediction of long-term mortality.**

Aims: **We sought to assess to evaluate the usefulness of SS II in a real-world acute coronary syndromes (ACS) population with severe coronary artery disease (CAD) undergoing percutaneous coronary intervention (PCI).**

Methods: **From August 2011 to May 2013, out of 1591 consecutive patients admitted for ACS, 217 (13.6%) showed severe CAD (three-vessel disease and/or left main involvement). Among the latter, 100 patients underwent PCI and were enrolled into the study. SS II was calculated in all patients. One-year clinical follow-up was performed; major adverse cardiac and cerebrovascular events (MACCE) were defined as a composite of death, nonfatal myocardial infarction, stroke, or repeat revascularization.**

Results: **The median SS II was 29 (range, 14–59). Overall, MACCE occurred in 25% of patients (cardiac death 4%, myocardial infarction 4%, stroke 0%, and repeat revascularization 17%). The 1-year MACCE-free survival was significantly lower in patients with SS ($\geqslant$29), than in those with SS II (<29) (64.2% vs. 87.2%, respectively; $p = 0.007$). In multivariate Cox regression analysis, the presence of unprotected left main stenosis [hazard ratio 2.52, 95% confidence interval (CI): 1.02–5.85; $p = 0.031$] and SS II $\geqslant$29 (hazard ratio 2.74, 95% CI: 1.30–8.21; $p = 0.011$) were the only predictors of MACCE at 1-year clinical follow-up. The c-index of SS score II was 0.70 (95% CI: 0.58–0.81). For patients who experienced MACCE, the SS II reclassification improved by 36%, while in nonevent patients the reclassification improved by 22%. The net reclassification index was 0.24 ($p = 0.09$).**

Conclusion: **SS II might represent a useful tool to predict clinical events in not only ideal stable patients, but also an unrestricted, real world population of patients with ACS and severe CAD undergoing PCI.**

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Introduction

The anatomical synergy between percutaneous coronary intervention (PCI) with taxus and cardiac surgery (SYNTAX) score (SS) is advocated in both European and American revascularization guidelines [1,2] as an important tool that can help clinicians to establish the optimal revascularization approach in patients with complex coronary artery disease (CAD). The model has also been proposed as a predictor of clinical outcome following PCI [3]. However, it is well recognized that both anatomical and clinical variables are required to appropriately stratify the risk of patients undergoing PCI. Therefore, recent scores have been developed with the aim of integrating anatomical features with relevant clinical variables, to overcome the most obvious pitfalls of a system score only based on coronary angiograms [4,5]. Recently, seven clinical parameters [age, creatinine clearance, left ventricular ejection fraction (LVEF), presence of unprotected left main (ULM), peripheral vascular disease, female sex, and chronic obstructive pulmonary disease] have been added to SS to obtain SYNTAX score II (SS II) [4]. This new score is able to predict a statistically significant difference in long-term outcomes between patients undergoing coronary artery bypass graft (CABG) and those undergoing PCI [5,6].

However, SS II has been only validated in randomized trials, not in a real-world study; thus, excluding complex patients such as those with three-vessel disease and/or ULM involvement, particularly in the setting of acute coronary syndromes (ACS).

The aim of the current study was to evaluate the usefulness of SS II in a real-world population with severe CAD and ACS undergoing PCI.

Abbreviations

ACS	acute coronary syndrome
CABG	coronary artery bypass grafting
CAD	coronary artery disease
CI	confidence interval
LVEF	left ventricular ejection fraction
LAD	left anterior descending
MACCE	major adverse cardiac and cerebrovascular events
MI	myocardial infarction
NSTEMI	non ST-elevation myocardial infarction
PCI	percutaneous coronary intervention
rSS	residual Syntax score
SS	Syntax score
ST	stent thrombosis
STEMI	ST elevation myocardial infarction
TLR	target lesion revascularization
TVR	target vessel revascularization
ULM	unprotected left main

Methods

Study population

From August 2011 to May 2013, all patients admitted for ACS, at the Cardiology Department of Cannizzaro Hospital, Catania, were screened. Those with severe CAD, defined as showing three-vessel disease (stenosis $\geqslant$70%) and/or left main involvement (stenosis $\geqslant$50%) at coronary angiography, with an indication of PCI, were enrolled into the study. ACSs were defined according to the guidelines of the European Society of Cardiology [7,8]. Patients with cardiogenic shock (systolic blood pressure <90 mmHg and signs of tissue hypoperfusion) and previous CABG were excluded. All data were prospectively collected in a dedicated database.

The study was carried out according to the Helsinki declaration principles, and a written informed consent to coronary intervention and follow-up was obtained from all patients.

Determination of SS and SS II

From the baseline angiogram, each coronary lesion causing $\geqslant$50% diameter stenosis in a vessel with a caliber $\geqslant$1.5 mm, was scored to yield the overall SS, which was calculated with the SS online calculator [9]. For each patient, all angiographic variables involved in the calculation of SS were computed by two independent experienced interventional cardiologists blinded to clinical data.

The residual Syntax score (rSS) was calculated based on the remaining obstructive CAD after treatment with PCI; incomplete revascularization was defined as a rSS >0. The Δ Syntax score (ΔSS), representative of the burden of disease removed by PCI, was calculated by subtracting the rSS from the baseline SS.

All patients were assessed with echocardiogram (Philips IE33 Matrix, Philips Healthcare, Amsterdam, Netherlands), before discharge; and LVEF was evaluated using a modified Simpson method.

To calculate SS II, the anatomical SS was combined with the following variables: age, creatinine clearance, LVEF, presence of ULM disease, peripheral vascular disease, female sex, and chronic obstructive pulmonary disease; using the SS II nomogram, as previously described [4].

Procedure and medications

The decision to perform PCI or CABG was taken by the local heart team, consisting of two interventional cardiologists (not involved in the protocol), one cardiac surgeon, and one anaesthesiologist. In case of patient's refusal to undergo CABG, PCI was thus considered. According to our routine practice, staged revascularization was adopted in all cases: first, PCI of the culprit lesion was performed; then, delayed nonculprit-lesions angioplasty before patient discharge, often 3 days to 7 days later. In case of clinical and angiographic difficulties in distinguishing the culprit vessel, the different lesions judged to be critical were simultaneously treated.

During the study period, three types of drug eluting stents were used: everolimus-eluting stents (either Xience V, Abbott Vascular, Santa Clara, California, USA; or Promus, Boston Scientific, Boston, USA), zotarolimus-eluting stents (Resolute, Medtronic, Minneapolis, Minnesota, USA), and biodegradable polymer biolimus-eluting stents (either Nobori, Terumo, Tokyo, Japan; or BioMatrix Flex, Biosensors Inc., Newport Beach, California, USA).

PCI treatment was performed by two senior experienced interventionalists. The interventional strategy and the use of glycoprotein IIb/IIIa inhibitors or bivalirudin were entirely left to the operator's discretion. For patients who did not receive bivalirudin, an intravenous bolus of heparin was given to maintain an activated clotting time around 250–300 seconds. In addition to aspirin (300 mg), a loading dose of clopidogrel 600 mg, prasugrel 60 mg, or ticagrelor 180 mg was administered if the patient was not pretreated. Patients were thereafter maintained on clopidogrel 75 mg, prasugrel 10 mg, or ticagrelor 180 mg for 12 months, and aspirin 100 mg indefinitely. Statin therapy was prescribed in all cases.

Coronary angiograms

Visual coronary angiography analysis was performed by two operators not involved in the protocol. Angiographic success was defined as a residual stenosis <20% of the vessel diameter and thrombolysis in myocardial infarction flow Grade 3. Procedural success was defined as an angiographic success in the absence of death, myocardial infarction (MI), or target lesion revascularization (TLR) during in-hospital stay. Complete revascularization was defined as a restoration of thrombolysis in myocardial infarction Grade 3 flow with residual stenosis less <20% on visual assessment in the three coronary arteries and their major branches (branch diameter >2 mm), with rSS = 0.

Endpoints and definitions

A 1-year follow-up was performed: all patients were followed-up with telephone interviews; details about clinical outcomes were confirmed by reviewing hospital records or by the referring

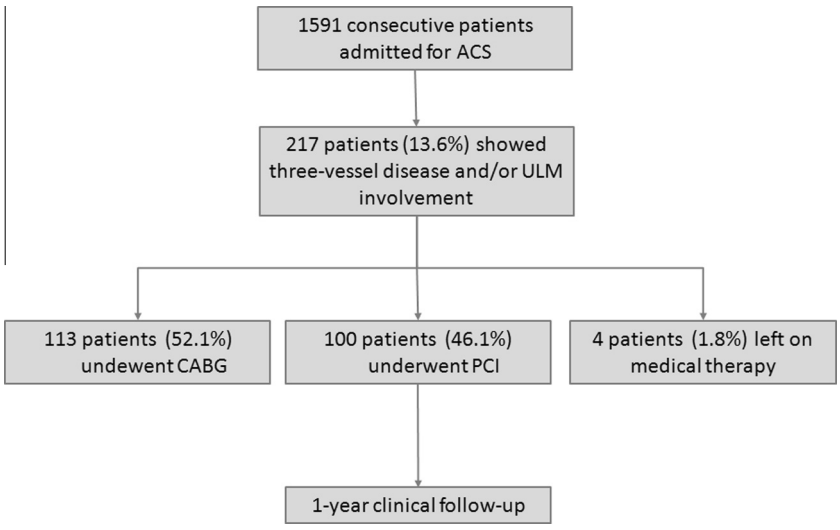

Figure 1. Chart of the study population. ACS = acute coronary syndrome; CABG = coronary artery bypass graft; PCI = percutaneous coronary intervention; ULM = unprotected left main.

physician; and data on all repeat interventions and hospitalizations were prospectively collected.

Major adverse cardiac and cerebrovascular events (MACCE) were defined as a composite of death, nonfatal MI, stroke, or repeat revascularization. Post-PCI MI and acute MI during follow-up were defined according to the consensus document on the third universal definition of MI [10]. Repeat revascularization included both TLR and target-vessel revascularization (TVR). TLR was defined as repeat PCI or CABG placement for restenosis at the treated lesions, or occurring within 5 mm of PCI sites. TVR was defined as a repeat intervention (percutaneous or surgical) to treat a luminal stenosis occurring in the coronary treated vessels beyond the target lesion limits. Definite/probable stent thrombosis (ST) (acute, subacute, and late) includes angiographic or postmortem evidence of ST according to the Academic Research Consortium recommendations [11].

Table 1. Baseline clinical characteristics of the study population.

	Total patients (n = 100)	SSII <29 (n = 47)	SS ⩾29 (n = 53)	p
Age (y) mean ± SD	66.3 ± 10.6	59.8 ± 9.1	72.0 ± 8.5	<0.001
Men, n (%)	81 (81)	40 (85.1)	41 (77.4)	0.233
Diabetes mellitus, n (%)	33 (33)	17 (36.2)	16 (30.2)	0.336
Hypertension, n (%)	59 (59)	21 (44.7)	38 (71.7)	0.005
Smoke, n (%)	39 (39)	24 (51.1)	15 (28.3)	0.017
Dyslipidemia, n (%)	77 (77)	35 (74.4)	42 (79.2)	0.371
Prior MI, n (%)	18 (18)	4 (8.5)	14 (26.4)	0.018
Prior PCI, n (%)	17 (17)	6 (12.7)	11 (20.7)	0.214
Chronic kidney disease, n (%)	11 (11)	0	15 (28.3)	<0.001
Peripheral vascular disease, n (%)	10 (10)	1 (2.1)	9 (17.0)	0.005
COPD, n (%)	9 (9)	4 (8.5)	5 (9.4)	0.577
LVEF, %, mean ± SD	50.7 ± 7.0	52.8 ± 5.2	48.9 ± 7.8	0.005
LVEF <50%, n (%)	35 (35)	11 (23.4)	24 (45.3)	0.018
Clinical presentation				0.196
STEMI, n (%)	39 (39)	22 (46.8)	17 (32.1)	
NSTEMI, n (%)	58 (58)	23 (48.9)	35 (66.0)	
Unstable angina, n (%)	3 (3)	2 (4.1)	1 (1.9)	
Dual antiplatelet therapy				0.661
Aspirin + clopidogrel, n (%)	33 (33)	14 (29.8)	19 (35.8)	
Aspirin + prasugrel, n (%)	18 (18)	8 (17.0)	10 (18.8)	
Aspirin + ticagrelor, n (%)	49 (49)	25 (53.1)	24 (45.3)	

COPD = chronic obstructive pulmonary disease; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NSTEMI = non ST-elevation myocardial infarction; PCI = percutaneous coronary intervention; SD = standard deviation; SS = Syntax score; STEMI = ST-elevation myocardial infarction.

Table 2. Angiographic characteristics and procedural details.

	Total patients (n = 100)	SSII <29 (n = 47)	SS ⩾29 (n = 53)	p
Baseline SS, median (ranges)	26 (7–47)	23 (10–43)	28.5 (7–51)	0.006
Number of treated vessels, mean ± SD	2.7 ± 0.5	2.7 ± 0.4	2.7 ± 0.6	0.889
Treated vessels				
ULM, n(%)	19 (19)	4	15	0.01
LAD, n(%)	94 (94)	45 (95.7)	49 (92.4)	0.398
LCx, n(%)	72 (72)	39 (82.9)	33 (62.2)	0.02
RCA, n(%)	85 (85)	41 (87.2)	44 (83.0)	0.297
Number of treated lesions, mean ± SD	3.3 ± 0.9	3.4 ± 0.8	3.3 ± 1.0	0.730
Number of implanted stents, mean ± SD	3.8 ± 1.4	4.0 ± 1.3	3.7 ± 1.5	0.322
Total stent length, mm, mean ± SD	86.3 ± 35.7	91.3 ± 33.7	82.0 ± 37.1	0.193
Complete revascularization, %	67 (67)	33 (70.2)	34 (64.1)	0.334
ΔSS, median (ranges)	23.5 (5–46)	18 (5–41)	27 (7–46)	0.007
Angiographic success, %	100 (100)	47 (100)	53 (100)	1
Procedural success, %	98 (98)	46 (97.8)	52 (98.1)	0.961

LAD = left anterior descending; LCx = left circumflex; RCA = right coronary artery; SD = standard deviation; SS = SYNTAX score; ULM = unprotected left main.

Statistical analysis

Continuous variables were expressed as mean ± standard deviations, except SS, SS II, rSS, and ΔSS which were expressed as median and ranges, as they did not follow a normal distribution. One-year clinical outcome analyses were based on SS median value. Survival analysis based on Kaplan–Meier curves and log-rank tests were used to assess the event free-survival between ACS patients with SS II ⩾29 and ACS patients with SS II <29. Cox proportional hazards regression analysis was applied to identify the variables associated with MACCE occurrence at 1-year follow-up. All univariate variables with $p < 0.1$ were included in the multivariate model. Discrimination of SS II was tested using c statistic, while calibration was appraised with Hosmer-Lemeshow Goodness of fit test. The additive prognostic value of SS II in comparison with SS was assessed using the net reclassification improvement and the integrated discrimination improvement. In all cases, p values <0.05 were considered statistically significant. Statistical analysis was performed with SPSS 21.0 software (SPSS, Inc., Chicago, IL, USA).

Table 3. In-hospital and 1-year clinical outcome of the study population.

	Total patients (n = 100)
In-hospital outcome	
Death, %	1
Nonfatal MI, %	1
Repeat revascularization, %	0
Stroke, %	0
MACCE, %	2
At 1-year follow-up	
Death, %	4
Nonfatal MI, %	4
TLR, %	12
TVR nonTLR, %	5
Repeat revascularisation, %	17
Stroke, %	0
MACCE, %	25

MACCE = major adverse cardiac and cerebrovascular events; MI = myocardial infarction; TLR = target lesion revascularization; TVR = target vessel revascularization.

Results

Patients' characteristics and procedural results

Among 1591 consecutive patients admitted for ACS in our tertiary referral hospital during the study period, 217 (13.6%) had severe CAD. Among the latter, 100 patients (46.1%) underwent PCI and were enrolled into the study (Fig. 1).

The mean age was 66.3 ± 10.6 years; 81% were men; and diabetes mellitus was observed in 33% of cases. Baseline clinical characteristics according to SS II are shown in Table 1. The median of SS and SS II were 26 (range, 7–47) and 29 (range, 14–59), respectively. Of note, the interobserver agreement (κ statistic) for anatomical SS in our study was κ = 0.88, 95% confidence interval (CI)

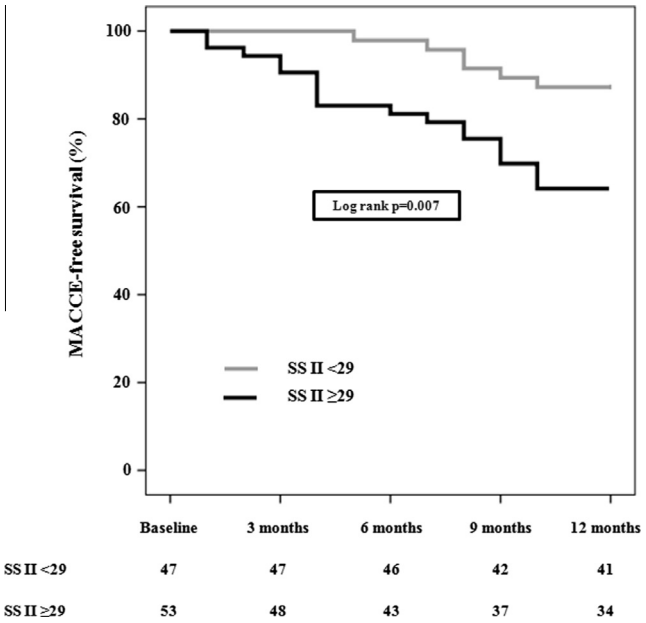

Figure 2. Kaplan–Meier survival curve for major adverse cardiac and cerebrovascular events at 1-year follow-up. MACCE = major adverse cardiac and cerebrovascular events; SS II = Syntax score II.

(0.79, 1.00). Left anterior descending was the most commonly revascularized vessel; the number of treated vessels and lesions were 2.7 ± 0.5 and 3.3 ± 0.9 per patient, respectively. A mean of 3.5 ± 1.4 stents were implanted for a mean total stent length of 86.3 ± 35.7 mm. Second or third generation drug eluting stents were employed in all cases. Angiographic success was achieved in all patients, while procedural success rate was 98%. Incomplete anatomical revascularization was obtained in 33% of cases with a median rSS of 4 (range, 2–18.5). Despite a similar rate of complete revascularization (64.1% vs. 70.2%; $p = 0.334$), ΔSS was higher in patients with SS II ⩾29, compared with those with SS <29 [27 (range, 7–46) vs. 18 (range, 5–41), respectively; $p = 0.007$]. Angiographic characteristics and procedural details are summarized in Table 2.

Clinical outcome

Overall, at 1-year clinical follow-up, 25% of patients experienced MACCE. Table 3 shows the clinical outcome of the study population. A total of four deaths were observed; all of them were cardiac deaths. One patient died during the index hospitalization: he was a 70-year-old man

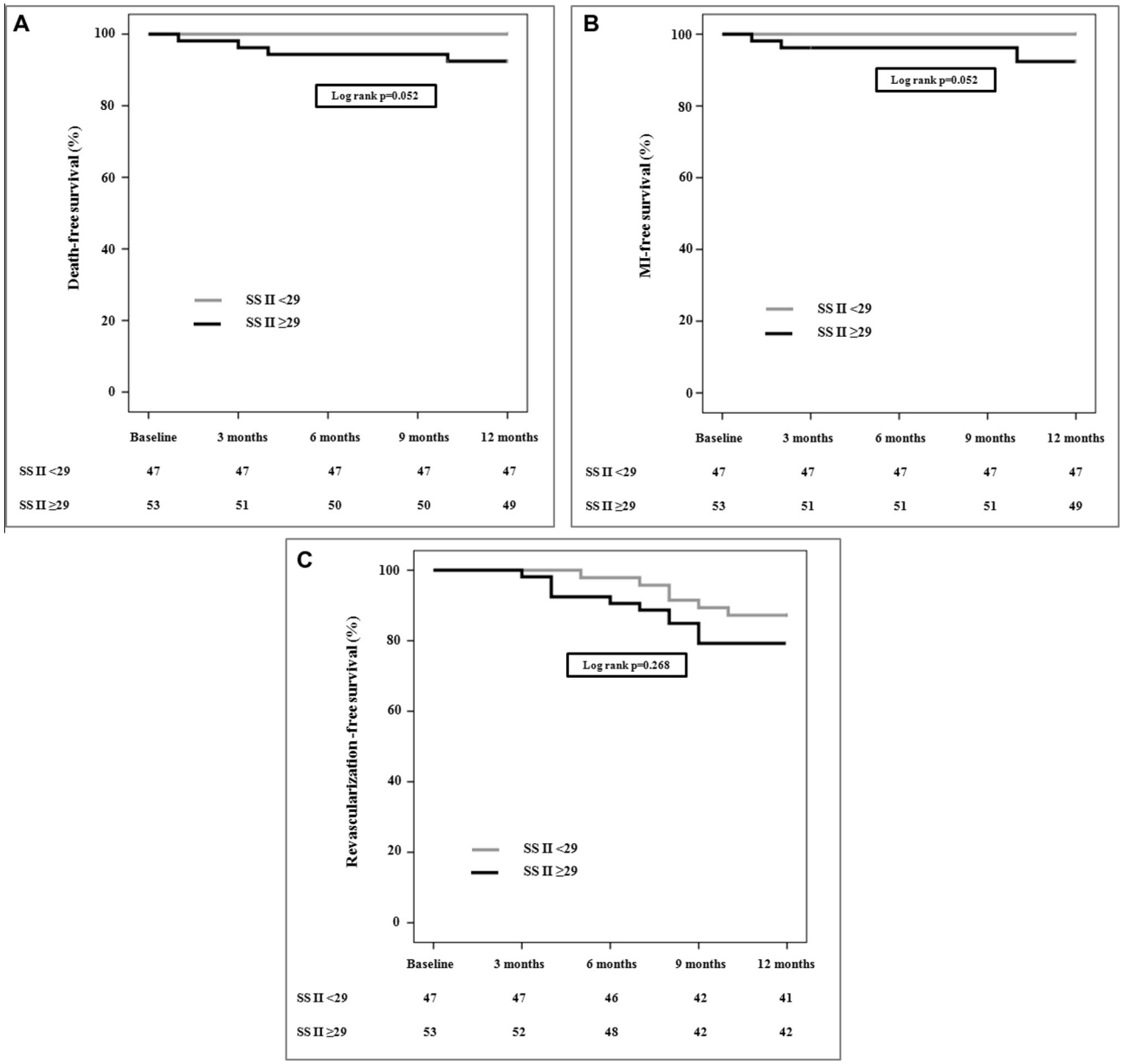

Figure 3. Kaplan–Meier survival curve for cardiac death, myocardial infarction and for repeat revascularization at 1-year follow-up. SS II = Syntax score II.

admitted with an anterior ST-elevation MI (STEMI) complicated by cardiac arrest due to ventricular fibrillation. Angiographic analysis showed ULM thrombosis and right coronary artery chronic total occlusion. An 87-year-old man with diabetes, previous MI, and impaired LVEF, who underwent ULM, left anterior descending (LAD), and left circumflex PCI, with untreated right coronary artery chronic total occlusion, had a sudden cardiac death 3 months after the index PCI. A 75-year-old diabetic man who underwent ULM, LAD, and left circumflex PCI, had a fatal acute MI due to late ST (angiographically demonstrated) 4 months after the index PCI. The last cardiac death occurred 10 months after the index PCI, due to MI in an 82-year-old female who underwent ULM and LAD PCI.

A total of four nonfatal acute MI occurred. One patient had a troponin I elevation more than five times the upper reference limit and transient ischemic electrocardiographic changes immediately after LAD PCI, with a diagonal occlusion at control angiogram, medically treated; this patient was alive and asymptomatic at 1 year follow-up. The second nonfatal acute MI was a NSTEMI attributable to late ST occurring 2 months after the index procedure, and successfully treated with balloon dilatation. The two remaining nonfatal acute MI occurred both after 10 months from the index PCI, and were NSTEMI attributable to a nonpreviously treated small coronary arteries, managed with medical therapy. Repeat revascularization PCI was performed in 17 patients (12 TLR and 5 TVR nonTLR) after a mean delay of 6.9 ± 2.2 months; while no patient underwent CABG. Of note, all patients were compliant to dual antiplatelet therapy during follow-up period; a switch of P2Y12 receptor antagonist was performed in two patients (one from ticagrelor to clopidogrel for dyspnea, and one from prasugrel to clopidogrel for a new onset of AF requiring an oral anticoagulation).

Patients with incomplete revascularization did not show worse cardiovascular outcome, compared with those who underwent complete revascularisation (74.6% vs. 75.8%, respectively; $p = 0.554$). Similar MACCE rates were also observed in STE-ACS versus NSTE-ACS patients either in all cohort (26.2% vs. 23.1%, respectively; $p = 0.398$) or in patients' group of SS II $\geqslant 29$ (41.2% vs. 33.3%, respectively; $p = 0.398$).

Prognostic value of SS II

The 1-year MACCE-free survival was significantly lower in patients with SS $\geqslant 29$ than in those with SS <29 (64.2% vs. 87.2%, respectively; $p = 0.007$) (Fig. 2). Similarly, the 1-year death-free

Table 4. Univariate and multivariate Cox regression.

Variables	HR	95% CI	*p*
Univariate analysis			
Age (10 y increase)	1.33	0.93–1.93	0.097
Female gender	1.13	0.42–3.01	0.805
Diabetes	1.46	0.65–3.25	0.355
Chronic kidney disease	2.05	0.97–5.10	0.08
COPD	0.89	0.29–3.55	0.810
Peripheral vascular disease	2.1	1.4.1–6.1	0.01
Prior MI	0.60	0.17–1.95	0.379
Prior PCI	1.38	0.52–3.7	0.515
STEMI	0.85	0.38–1.93	0.701
LVEF <50%	0.83	0.36–1.93	0.672
ULM stenosis	3.2	1.42–7.31	0.005
SS $\geqslant 26$[a]	1.4	0.63–3.12	0.407
SSII $\geqslant 29$[a]	3.3	1.3–8.2	0.011
Incomplete revascularization	0.93	0.40–2.16	0.875
ΔSS $\geqslant 23.5$[a]	1.6	0.72–3.57	0.245
Multivariate analysis			
Age (10 y increase)	1.04	0.56–2.39	0.762
Chronic kidney disease	1.1	0.60–2.72	0.741
Peripheral vascular disease	1.43	0.92–1.87	0.107
ULM stenosis	2.52	1.02–5.85	0.031
SSII $\geqslant 29$	2.74	1.30–8.21	0.011

CI = confidence interval; COPD = chronic obstructive pulmonary disease; HR = hazard ratio; LVEF = left ejection fraction; MI = myocardial infarction; PCI = percutaneous coronary intervention; SS = Syntax score; STEMI = ST-elevation myocardial infarction; ULM = unprotected left main.

[a] The used cut-off represents the median value of the variable observed in our cohort.

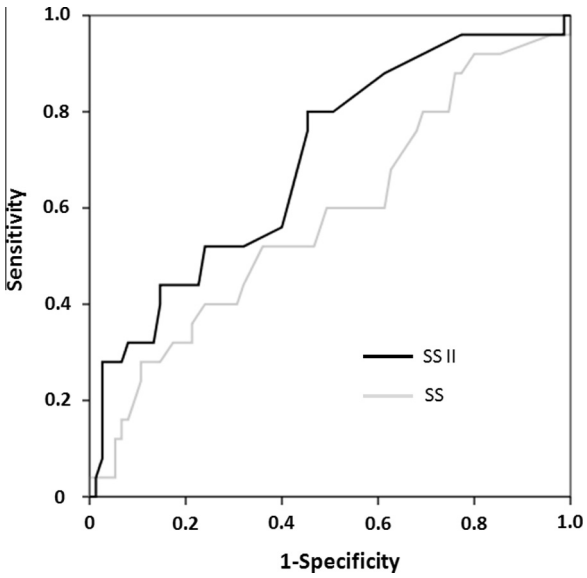

Figure 4. Receiver operating characteristic curve of Syntax score and Syntax score II. Area under the curve of SS II was 0.70 (95% confidence interval: 0.58–0.81), while that of SS was 0.58 (95% confidence interval: 0.45–0.71) (p = 0.11). SS II = Syntax score II.

survival (92.5% vs. 100%; $p = 0.052$), and MI-free survival (92.5% vs. 100%; $p = 0.052$) were lower in patients with SS II $\geqslant$29, as compared with those with SS <29, with a strong trend. No significant difference was found regarding repeat revascularization-free survival between patients with SSII $\geqslant$29 and those with SS II <29 (79.2% vs. 87.2%, respectively; $p = 0.268$) (Fig. 3). In Cox proportional hazards regression analysis, the presence of ULM stenosis [hazard ratio (HR) 2.52, 95% CI: 1.02–5.85; $p = 0.031$) and SS II $\geqslant$29 (HR 2.74, 95% CI: 1.30–8.21; $p = 0.011$) were the only predictors of MACCE at 1-year clinical follow-up (Table 4).

The c-index of SS II was 0.70 (95% CI: 0.58–0.81) (Fig. 4), and Hosmer-Lemeshow goodness-of-fit test was $p = 0.308$. For patients who experienced MACCE, the SS II reclassification improved by 36%, whereas in nonevent patients the reclassification improved by 22%. The net reclassification index was 0.24 ($p = 0.09$).

Discussion

Our study represents a real world experience of unrestricted use of PCI to treat complex CAD in the setting of ACS. We also investigated the ability of SS II as a new tool to predict clinical outcome at 1-year follow-up.

The main findings of our study can be summarized as follows: (1) PCI in high anatomical and clinical risk patients admitted for ACS was associated with high rates of MACCE; and (2) SS II, combining clinical and anatomical features might have a prognostic value in such a subset of patients.

As regards the safety and efficiency of PCI in high risk patients, it is worth highlighting the high rate of angiographic success achieved in our cohort (100%). Moreover, the in-hospital outcome was uneventful in 98% of cases. In EARLY ACS trial PCI subgroup, at 96 hours after the index procedure, Hess et al. [12] showed a rate of cardiac events as low as 2% (cardiac death 0.4%, MI 1.1%, and ischemia requiring emergent revascularization 0.5%). However, the majority of patients enrolled in the latter study presented one or two-vessel disease without ULM involvement [12]. In a cohort of 903 patients with severe CAD assigned to PCI, in-hospital MACCE occurred in 4% patients; notably, PCI was performed in ACS setting in less than 30% of cases [13]. The in-hospital outcome of PCI subgroup of the Multicenter Registry Evaluating Percutaneous Coronary Intervention Versus Coronary Artery Bypass Grafting for Left Main Treatment (the Delta registry) showed a MACCE rate of 7.9% [14]. This latter registry only included patients with ULM, while this lesion subset was shown in only 19% of our patients.

In our cohort, repeat revascularization was required in a relatively high percentage of cases (17%). Latib et al. [15] and Serruys et al. [13] reported revascularization rates of 12.7 % and 14.2%, respectively, in such a patients subset after 12 months from the index procedures. In the PCI subgroup of DELTA registry enrolling patients with ULM stenosis, TLR at 2-years was 15.5%, while the overall MACCE was 34.9% [14].

However, achieving complete revascularization remains challenging in multivessel disease patients. Despite the relatively high rate of incomplete revascularization in our cohort (33%), this fact was not associated with a higher MACCE rate. Conversely, Tamburino et al. [16] revealed a protective effect of complete revascularization at 2-year follow-up for MACE (HR 0.37, 95% CI 0.15–0.92; $p = 0.03$) and for repeat revascularization (HR 0.45, 95% CI 0.29–0.69; $p < 0.001$). Similarly, Farooq et al [17] demonstrated that rSS was a powerful indicator of 5-year mortality in the SYNTAX Trial. Interestingly in our study, although higher ΔSS was achieved in presence of SS II $\geqslant$29, this subset of patients showed a worse cardiovascular prognosis. Higher reduction in CAD burden was not reported to predict a better outcome [18,19]. This latter finding is in accordance with a recent report by Witberg et al. [20], who demonstrated that ''reasonable'' incomplete revascularization carries better clinical outcome versus more aggressive strategy in patients with three-vessel disease or ULM treated by PCI [20].

However, according to both European and US guidelines of myocardial revascularization, CABG remains the gold standard in term of severe CAD with better long-term outcome [1,21]. Furthermore, in high risk patients such as diabetics, clear evidence has been demonstrated in favor of CABG, in the setting of multivessel disease [22].

The decision making process to establish the optimum revascularization strategy passes through the concept of ''heart team approach'' and the evaluation of expected benefits and procedural (interventional or surgical) risk. In this respect, anatomical SS represents an important instrument able to predict the outcome of both strategies; thus, a capital tool to propose the optimal therapeutic method [23]. Indeed, in the ACUITY trial, the authors showed that the SS is an independent predictor of the 1-year rates of

death, cardiac death, MI, and TVR in patients with NSTE-ACS undergoing PCI [3]. In case of ULM disease, SS <33 was recognized to have the same clinical outcomes regardless the adopted strategy, while a SS ⩾33 goes in favor of CABG; in three-vessel disease patients, the recommended cut-off is 23 [1,21].

In addition, the prevailing guidelines advise to take also into account important clinical variables, particularly those with an impact on prognosis [1,2,21,23]. Therefore, scores combining both anatomical and clinical parameters have emerged. The SS II has been recently developed by applying a Cox proportional hazards model to the results of the SYNTAX trial [4]. This latter score had a significantly higher accuracy compared with anatomical SS for all-cause death measured by the c-statistic [24]. In our study, differently in addition to the presence of ULM stenosis, SS II was independently related to 1-year clinical outcome. Similarly, SS II was able to provide reliable predictions of 4-year mortality for patients with ULM disease undergoing PCI [4]. At 4-year follow, according to low-, medium-, and high-risk tertiles, Campos et al. [6] revealed the following mortality rates in severe CAD patients who underwent: 95.4%, 88.9%, and 68.1%, respectively. Furthermore, the authors demonstrated that SS II surpassed SS in discriminating both CABG and PCI groups [6].

In a large cohort of 1528 consecutive patients undergoing ULM PCI, Xu et al. [25] found that the SS II for PCI was able to risk-stratify patients and predict long-term adverse ischemic events, including mortality. Moreover, this scoring system demonstrated better predictability for long-term mortality compared with the strictly anatomic SS among this patients' subset. Importantly, in the latter study, a third of patients had a stable angina [25]. In the setting of ACS, Obeid et al. [26] have recently demonstrated that SS II provided incremental predictive value for risk stratification, showing that patients with high SS II (>32) had a 10 and 13-fold high risk for MACE and MACCE, respectively.

The ultimate objective of the SS II is not only the isolated risk prediction for PCI or CABG; indeed, this latter score was developed to evaluate the interactions of risk factors that could help in the decision making process between these revascularization strategies. In a patient-level pooled analysis of a large cohort of patients enrolled in contemporary coronary stent trials, Compos et al. [27] demonstrated the capability to help in stratifying PCI procedures.

The originality of our study concerns the fact that all severe CAD patients enrolled showed ongoing ischemia. ACS setting is a condition able to modify some clinical features such as LVEF or renal function. Indeed, our findings reinforce the interest of SSII in predicting outcome, surpassing the anatomical static SS, as it represents a dynamic risk score able to follow the clinical presentation.

Study limitations

Our study had some limitations common to the similar single center studies. First of all is the limited number of patients. Secondly, the time course of a clinical tool as SS II was not assessed (i.e., changes in creatinine clearance or in LVEF), and therefore we cannot correlate the occurrence of major adverse events during the follow-up period with changes in SS II.

Conclusion

As a risk score combining both anatomical and clinical variables, the SS II might represent a useful tool to predict the risk of adverse clinical events in not only ideal stable patients, but also an unrestricted, real-world population of patients with ACS and severe CAD undergoing PCI.

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