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Prognostic impact of the SYNTAX score II in patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention: analysis of a four-year all-comers registry

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KEYWORDS

- multiple vessel disease
- risk stratification
- STEMI

Abstract

Aims: This study aimed to investigate the prognostic impact of the SYNTAX score II (SS-II) on ST-segment elevation myocardial infarction (STEMI) patients undergoing a primary percutaneous coronary intervention (pPCI).

Methods and results: This retrospective cohort study included 1,689 patients with STEMI who underwent pPCI between January 2008 and December 2016. The patients were categorised into three groups based on SS-II tertiles (SS-II low tertile <24 [n=585], SS-II intermediate tertile ≥24 and ≤34 [n=567], and SS-II high tertile >34 [n=537]). In-hospital mortality was significantly lower in patients with low and mid SS-II when compared with high SS-II (0.7% vs 0.5% vs 16.4%, p=0.001). During follow-up (median 2.35 years), a high SS-II was positively correlated with MACE (12.3% for low SS-II vs 18.3% for mid SS-II vs 43.2% for high SS-II, p=0.001), all-cause mortality (1.5% vs 3.9% vs 14.2%, p=0.001) and heart failure (0.3% vs 2.7% vs 8.2%, p=0.001). The SS-II showed additive value on top of GRACE, anatomical SYNTAX score and residual SYNTAX score.

Conclusions: The SS-II in patients with STEMI undergoing pPCI adds important prognostic information regarding midterm adverse outcomes, being an independent and powerful predictor of MACE, heart failure and all-cause mortality during follow-up.

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Abbreviations

AIC	Akaike information criterion
BIC	Bayesian information criterion
CABG	coronary artery bypass grafting
LVEF	left ventricular ejection fraction
MACE	major adverse cardiovascular events
MVD	multivessel coronary artery disease
NRI	net reclassification improvement
PCI	percutaneous coronary intervention
pPCI	primary percutaneous coronary intervention
rSS	residual SYNTAX score
SS	SYNTAX score
SS-II	SYNTAX score II
STEMI	ST-elevation myocardial infarction

Introduction

The SYNTAX score II (SS-II) was developed within the SYNTAX trial as a strategy to improve the ability of the anatomical (only) SYNTAX score (SS)[1], by integrating relevant clinical variables (left main coronary artery disease, age, creatinine clearance, gender, left ventricular ejection fraction [LVEF], chronic obstructive pulmonary disease, and peripheral vascular disease), to identify patients with high cardiovascular risk among a population with complex artery disease, and favouring individualised decision making between coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI)[2].

Patients with ST-elevation myocardial infarction (STEMI) are susceptible to significant morbidity and mortality, even when an early revascularisation strategy such as primary percutaneous coronary intervention (pPCI) is performed[3]. Thus, an appropriate risk stratification after pPCI is essential to estimate the short- and long-term prognosis for these patients[3-5].

SS-II has been used as a tool for the assessment of prognostic value for outcomes of patients with stable ischaemic heart disease, multivessel or left main coronary artery disease and complex coronary artery disease, as well as for those with acute coronary syndrome with cardiogenic shock[5-9]. Nonetheless, it has not been tested in terms of long-term major adverse cardiovascular events (MACE) and all-cause mortality outcome evaluation in a population of non-selected STEMI patients undergoing pPCI.

The aim of this study was to assess the prognostic impact and clinical value of SS-II in a large cohort of real-life STEMI patients undergoing pPCI.

Methods

STUDY POPULATION

This was a single-centre, observational cohort study that enrolled consecutive patients with STEMI who underwent pPCI at the University Clinical Hospital of Santiago de Compostela between January 2008 and December 2016. A total of 1,723 patients were screened for inclusion in our study, of whom 34 were excluded, either because of unavailability of a complete coronary angiogram, or because they had a prior history of CABG or planned CABG after primary PCI, or it was not possible to follow them because they belonged to another community. Accordingly, the final cohort was composed of 1,689 patients.

Primary PCI was undertaken according to the European Society of Cardiology guidelines[10,11] and operators' routine practice.

Digitally archived diagnostic and procedural coronary angiograms were reviewed by two interventional cardiologists to calculate the anatomical SS, using an online calculator (www.syntaxscore.com).

As patients with STEMI were excluded from the SYNTAX trial[12], we calculated the SS using the current algorithm, scoring the culprit lesion as a totally occluded artery (not considering the possible distal lesions), as observed before any intervention, and defined the duration of the occluded infarct artery as less than three months, as performed in studies of patients with STEMI[4,13]. The residual SYNTAX score (rSS) comprised the score accumulated by any untreated lesions, a value of 0 indicating complete revascularisation[13].

Demographic, clinical, echocardiographic and laboratory data at admission were collected from an electronic database. Individual SS-II was calculated using the SS-II nomogram, as previously described[2]. To calculate SS-II, the anatomical SS was combined with the above-mentioned clinical variables[2]. Patients were stratified and compared according to SS-II tertiles.

DEFINITIONS

The diagnosis of STEMI was made according to current guidelines[10,11]. Ischaemia time was defined as the time between symptom onset and reperfusion (guidewire passage in culprit artery during pPCI). Multivessel coronary artery disease (MVD) was defined as at least one lesion in a non-infarct-related artery deemed angiographically significant (more than 50% luminal narrowing diameter). MACE during follow-up comprised all-cause mortality, myocardial infarction (MI), heart failure requiring hospitalisation and unplanned repeat revascularisation (uRR).

Heart failure (HF) was defined as the presence of signs or symptoms of congestion, mainly shortness of breath and signs of fluid retention, that are consistent with that diagnosis and led to hospitalisation. Criteria for left ventricular systolic dysfunction (LVSD) were LVEF <40% or a qualitative report of moderate or severe LVSD.

AIMS AND FOLLOW-UP

Our primary objective was to calculate the SS-II in our real-life STEMI patients who underwent pPCI and assess its clinical impact during follow-up. Additionally, we evaluated the additive prognostic value of the SS-II over control variables, SS, rSS and GRACE risk score, the latter being the preferred tool to stratify the risk of acute coronary syndrome patients and to predict their mortality.

Follow-up was carried out by consulting the electronic registries available in the autonomic community of Galicia, Spain (IANUS, the Galician Electronic Medical Record system); all medical evaluations and hospital registries were reviewed. Median follow-up was 2.35 (interquartile range 1-4.59) years.

STATISTICAL ANALYSIS

Univariate analysis of categorical variables was accomplished using the chi-square test, with results expressed as percentages, and of continuous variables using the ANOVA test, with results expressed as means±standard deviation. All variables were stratified according to the three SS-II groups. Survival curves were constructed for time-to-event variables (MACE and all-cause mortality) with Kaplan-Meier estimates.

To evaluate the additive prognostic value of SS-II (as a continuous variable), three Cox survival models were created as follows: univariate model, multivariate model using control variables that were statistically significant as predictors of events (body mass index, hypertension, diabetes, dyslipidaemia, smoking, ischaemic cardiomyopathy, ischaemia time, STEMI localisation [anterior versus other], infarct-related artery, use of drug-eluting stents, use of GP IIb/IIIa inhibitors, troponin I peak, haemoglobin, glucose, heart rate, systolic blood pressure, Killip class, CRUSADE score and medication at discharge), and multivariate models using as control variables the GRACE, SYNTAX and rSS scores separately. In order to check the robustness of the results against the temporal influence, all models were estimated considering temporal dummies. Results were also compared using the Harrell C-statistic, Akaike information criterion (AIC) and the Bayesian information criterion (BIC). Harrell's C-statistic is a natural extension of the receiver operating characteristic (ROC) curve which can vary between 0.5 (aleatory assignation for the different groups) and one (perfect model assignation), while AIC and BIC measure the goodness of fit and the complexity of a model (lower values translate into higher goodness of fit and lower complexity). Models with a higher Harrell C-statistic and lower AIC and BIC are preferred. To evaluate the additional prognostic value of SS-II on top of GRACE, the increase of the area under the ROC curve and the net reclassification improvement (NRI) were calculated in a logit model. NRI indicates the number of patients who are reclassified after adding SS-II to the model. All analyses were two-tailed, and differences were considered significant if the p-value was <0.05. The statistical analysis was performed using SPSS, Version 22.0 (IBM Corp., Armonk, NY, USA) and Stata 13.0 (StataCorp, College Station, TX, USA).

Results

BASELINE CHARACTERISTICS

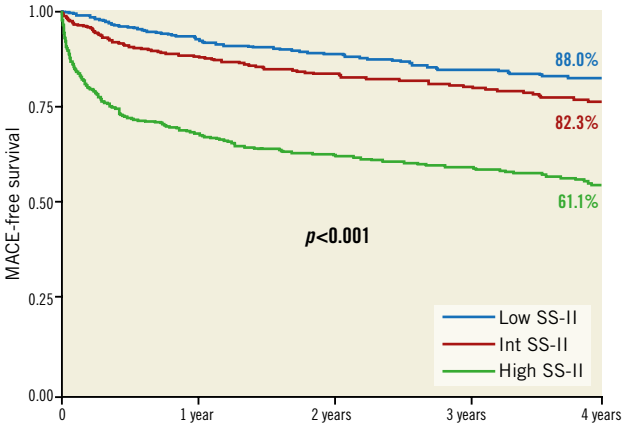
The cohort was composed of 1,689 patients with STEMI who underwent pPCI as the invasive management strategy and was divided into three groups determined by SS-II: the low-tertile group: <24 (n=585, 34.6%), the intermediate-tertile group: ≥24 and <34 (n=567, 33.5%), and the high-tertile group: ≥34 (n=537, 31.7%). Amongst the total cohort, the mean SS-II was 30.43 and the median SS-II 28.1.

We compared the baseline characteristics according to the three SS-II groups. The results are shown in **Table 1**. Male gender was more frequent in the low and intermediate SS-II tertiles. Patients in the high SS-II tertile were older and had a significantly higher prevalence of hypertension, diabetes mellitus 2, history of ischaemic heart disease and MVD (p=<0.001); interestingly, however, fewer smokers were found in this group. The left anterior descending artery (LAD) was the most frequent infarct-related artery (IRA) for the high SS-II tertile group, and the left main (LM) was involved in 2.24% of patients in this group. Mean ischaemia time before PCI was 275 minutes, with no statistical difference among groups. The average number of patients in Killip class IV was 18.4% for the high-tertile group, and 1.54% for the low-tertile group. Mean glomerular filtration rate (GFR) in the high SS-II group was 57 mL/min.

Clopidogrel was more frequently used in patients with high SS-II, whilst ticagrelor and prasugrel were more frequently used in low SS-II patients.

CLINICAL OUTCOMES

The clinical adverse events during follow-up are displayed in **Table 2**. In-hospital mortality was significantly higher in patients in the high SS-II tertile group when compared with the SS-II intermediate and low tertile groups (16.4% vs 0.5% vs 0.7%, p=<0.001). During follow-up, the MACE-free survival rate was positively correlated with the SS-II, with the highest MACE-free survival rate in the low SS-II tertile group and the lowest MACE-free rate in the high SS-II tertile group (87.7% vs 81.7% vs 56.8%; p=<0.001) **(Figure 1)**. All-cause mortality was significantly higher in the high SS-II tertile group compared with the intermediate and low tertile groups (14.2% vs 3.9% vs 1.5%,



Follow-up (years)		SS-II <24	SS-II 24-<34	SS-II ≥34	p-value
1 year	At risk	583	563	545	<0.001
	Events	39	63	167	
2 years	At risk	424	401	304	<0.001
	Events	15	18	22	
3 years	At risk	289	290	229	<0.001
	Events	11	10	11	
4 years	At risk	205	215	176	<0.001
	Events	5	9	12	

Figure 1. *Kaplan-Meier curves for MACE. MACE: major adverse cardiovascular events*

Table 1. Baseline characteristics.

Characteristics		Low SS-II (n=585)	Int SS-II (n=567)	High SS-II (n=537)	*p*-value
Demographics					
Age (years)		53.7 (9.0)	64.2 (11.4)	74.3 (11.2)	<0.001
Male sex		95.73%	80.95%	54.00%	<0.001
BMI (kg/m^2)		28.7 (4.0)	28.5 (4.21)	28.3 (4.48)	0.333
Past history					
Hypertension		31.62%	52.03%	86.67%	<0.001
Diabetes		12.82%	22.75%	83.78%	<0.001
Dyslipidaemia		48.89%	48.15%	97.30%	0.873
Smoking		73.33%	49.21%	23.65%	<0.001
IHD		7.52%	11.46%	14.71%	<0.001
Primary PCI data					
Ischaemia time (min)		275 (253)	279 (245)	272 (218)	0.894
Infarct-related artery	LAD	30.96%	45.45%	49.16%	<0.001
	CX	19.83%	14.62%	12.90%	
	RCA	49.22%	38.68%	33.27%	
	LM	0.00%	0.71%	2.24%	
	SV	0.00%	0.53%	0.56%	
Use of GP IIb/IIIa inhibitors		36.92%	36.33%	25.51%	<0.001
MVD		7.69%	14.64%	23.84%	<0.001
Laboratory data					
GFR (mL/min)		116.1 (33.1)	87.3 (30.7)	57.0 (26.0)	<0.001
Creatinine (mg/dL)		0.88 (0.31)	0.98 (0.29)	1.30 (0.91)	<0.001
Troponin I peak (ng/mL)		70.7 (70.5)	100.0 (106.5)	143.0 (187.6)	<0.001
Haemoglobin (g/dL)		14.8 (1.4)	14.3 (1.6)	13.5 (1.9)	<0.001
Glucose (mg/dL)		147.0 (62.1)	161.4 (65.8)	198.6 (100.0)	<0.001
Clinical data					
Heart rate (bpm)		73.0 (16.2)	74.7 (19.5)	81.6 (23.5)	<0.001
SBP (mmHg)		131.9 (23.6)	130.6 (27.3)	122.1 (30.8)	<0.001
Killip class	Class I	96.41%	90.48%	61.45%	<0.001
	Class II	1.54%	4.59%	13.78%	
	Class III	0.51%	1.41%	5.77%	
	Class IV	1.54%	3.53%	18.99%	
LVEF (%)		57.5 (6.5)	52.1 (9.6)	42.9 (12.8)	0.000
GRACE score		131.0 (25.0)	152.0 (31.8)	195.0 (47.4)	0.000
CRUSADE score		12.8 (8.0)	22.8 (10.5)	40.0 (14.3)	<0.001
Radial access		95.5%	92.7%	80.2%	<0.001
Thrombectomy		73.3%	70.2%	61.5%	<0.001
TIMI flow post pPCI	0	1.2%	1.4%	3.4%	0.020
	1	0.5%	0.9%	1.7%	
	2	1.5%	3.0%	2.4%	
	3	96.8%	94.7%	95.6%	
Medication at discharge					
Aspirin		99%	99%	95%	<0.001
$P2Y_{12}$ receptor inhibitor	Clopidogrel	63.87%	71.99%	84.80%	<0.001
	Prasugrel	14.21%	13.11%	4.71%	
	Ticagrelor	20.38%	12.75%	4.07%	
Beta-blocker		87.84%	86.67%	73.61%	<0.001
ACE-I		80.99%	83.78%	76.61%	0.015
Statin		97.60%	97.30%	94.42%	<0.001

ACE-I: angiotensin-converting enzyme inhibitor; BMI: body mass index; CX: circumflex artery; GFR: glomerular filtration rate; GP: glycoprotein; IHD: ischaemic heart disease; Int: intermediate; LAD: left anterior descending artery; LM: left main artery; LVEF: left ventricular ejection fraction; MVD: multivessel disease; pPCI: primary percutaneous coronary intervention; RCA: right coronary artery; SBP: systolic blood pressure; SV: saphenous vein; TIMI: Thrombolysis In Myocardial Infarction

p=<0.001) **(Figure 2)**. HF during follow-up was significantly higher in the high SS-II tertile group compared to the intermediate and low tertile groups (8.2% vs 2.7% vs 0.3%, p=<0.001). Nonetheless, the rates of MI and uRR during follow-up were not different among the groups (4.5% vs 4.6% vs 3.9%, p=0.844, and 7.1% vs 6.5% vs 7.0%, p=0.923, respectively). Stent thrombosis during follow-up was also higher in the high SS-II tertile group compared with the intermediate and low tertile groups (1.2% vs 1.4% vs 3%, p<0.001).

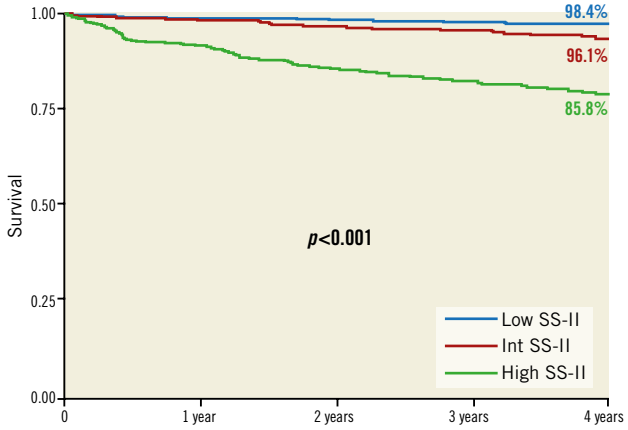
Table 2. Adverse events.

Adverse event	Low SS-II (n=585)	Int SS-II (n=567)	High SS-II (n=537)	*p*-value
In-hospital mortality	0.7%	0.5%	16.4%	<0.001
MACE during follow-up	12.3%	18.3%	43.2%	<0.001
All-cause mortality	1.5%	3.9%	14.2%	<0.001
Myocardial infarction	3.9%	4.6%	4.5%	0.844
Heart failure	0.3%	2.7%	8.2%	<0.001
Repeat revascularisation	7.0%	6.5%	7.1%	0.924
Stent thrombosis	1.2%	1.4%	3.0%	0.048

Int: intermediate; MACE: major adverse cardiovascular events

ADDITIVE VALUE OF SS-II

The Cox survival models for MACE and all-cause mortality are depicted in **Table 3**. In our population, the SS-II was also an independent predictor of MACE and all-cause mortality during follow-up, adding prognostic value over control variables and GRACE, anatomical SS and rSS. Additional independent predictor variables for mortality were heart rate, smoking, Killip class, diabetes mellitus, haemoglobin on admission, beta-blockers and ACE inhibitors at discharge and stent type. Models that consider SS-II are preferred according to the C-statistic, AIC and BIC values. When compared with patients with a low SS-II, intermediate-risk and high-risk SS-II patients have a 2.5 and 10.5 times higher risk of MACE, respectively. Regarding all-cause



Follow-up (years)		SS-II <24	SS-II 24-<34	SS-II ≥34	*p*-value
1 year	At risk	585	564	547	<0.001
	Events	4	8	38	
2 years	At risk	457	443	372	<0.001
	Events	2	6	22	
3 years	At risk	322	333	285	<0.001
	Events	2	3	10	
4 years	At risk	239	254	224	<0.001
	Events	1	5	8	

Figure 2. *Kaplan-Meier curves for all-cause mortality.*

mortality, intermediate-risk and high-risk SS-II patients have a 1.496 and 4.041 times higher risk of an event compared to the low-risk SS-II group.

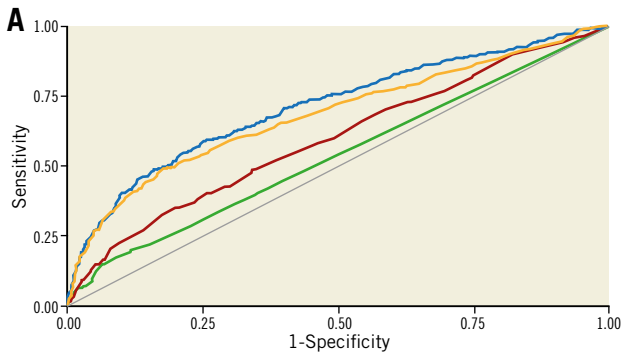
The additive value of SS-II on top of GRACE, SS and rSS is also supported by the increase of the area under the ROC curve **(Figure 3)** and the correct reclassification of patients after the addition of SS-II to GRACE, anatomical SS and rSS regarding in-hospital mortality, MACE, all-cause mortality and the development of HF during follow-up **(Supplementary Table 1-Supplementary Table 3)**.

Discussion

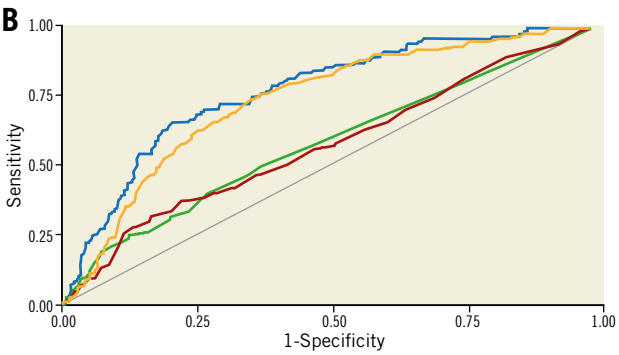
In this study, we aimed to assess the midterm prognostic value of the SS-II in a real-life population of consecutive patients with STEMI who underwent pPCI. The main findings are the following: 1) a high SS-II was associated with adverse outcomes in STEMI patients after pPCI; 2) SS-II was shown to be a strong independent predictor of midterm all-cause mortality, MACE and HF, but not of MI or uRR; 3) SS-II adds prognostic value on top of the traditional GRACE score, anatomical SYNTAX score and residual SYNTAX score.

Risk stratification in patients with STEMI is a major feature in real clinical practice, as it provides a broad perspective of patient outcomes based on patient characteristics and optimal treatment. In this regard, plenty of clinical risk scores for determining prognosis in STEMI patients, such as the GRACE risk score, TIMI score, PAMI score, Zwolle risk score, CADILLAC score, ALPHA score[14-19] have been tested to provide an optimal management. The GRACE risk score is considered the most robust score for evaluating the risk in patients with STEMI/NSTEMI at initial presentation[14], although it is a classic score which was developed in an era of less effective pharmacological and interventional treatment and it does not consider the impact of the angiographic severity of the disease, the history of peripheral vascular disease and the effect of pulmonary disease on cardiovascular outcomes. In our study, the SS-II was demonstrated to add prognostic value for all-cause mortality and MACE better than a clinical score such as the GRACE risk score.

The SYNTAX score II considers angiographic and clinical variables, which are widely known to affect long-term outcomes of PCI[2]. The SS-II has been tested in different challenging clinical scenarios such as in complex coronary artery disease (CAD) in patients undergoing PCI[6], where it was superior to the anatomical SS in predicting two-year mortality. In acute coronary syndromes with severe CAD, the SS-II has proved to be a good tool for predicting MACE after one-year



MACE	AUC	IC	*p*-value
SYNTAX-II	0.7133	0.683-0.7436	<0.001
SYNTAX	0.5978	0.5653-0.6303	<0.001
rSS	0.5390	0.5095-0.5684	0.001
GRACE	0.6847	0.6527-0.7167	<0.001



All-cause mortality	AUC	IC	*p*-value
SYNTAX-II	0.7694	0.7253-0.8135	<0.001
SYNTAX	0.5722	0.5126-0.6317	0.014
rSS	0.5777	0.5235-0.6319	0.005
GRACE	0.7361	0.6907-0.7814	<0.001

Figure 3. *ROC curves for MACE and all-cause mortality. A) MACE. B) All-cause mortality. MACE: major adverse cardiovascular events*

Table 3. Cox survival models for MACE and all-cause mortality.

Cox survival model for MACE							
Variable		**Model**	**HR**	**HR (95%)**	**Harrell's C-statistic**	**AIC**	**BIC**
SYNTAX-II		Univariate	1.060	1.051-1.070	0.709	5,167	5,215
SYNTAX-II (groups)	Low risk	Univariate	1.480	1.096-1.997	0.6893	5,223	5,277
	High risk		3.909	2.979-5.129			
SYNTAX-II		Multivariate	1.026	1.009-1.043	0.712	4,007	4,241
SYNTAX-II (groups)	Low risk	Multivariate	1.065	0.746-1.520	0.712	4,014	4,258
	High risk		1.615	1.013-2.573			
SYNTAX-II		GRACE	1.047	1.036-1.057	0.711	5,151	5,206
SYNTAX-II (groups)	Low risk	GRACE	1.176	0.858-1.612	0.707	5,187	5,247
	High risk		2.348	1.711-3.221			
SYNTAX-II		SYNTAX	1.060	1.051-1.070	0.709	5,169	5,223
SYNTAX-II (groups)	Low risk	SYNTAX	1.434	1.055-1.951	0.695	4,223	5,282
	High risk		3.694	2.790-4.893			
SYNTAX-II		rSS	1.059	1.050-1.068	0.710	5,137	5,191
SYNTAX-II (groups)	Low risk	rSS	1.428	1.050-1.942	0.695	5,188	5,247
	High risk		3.677	2.783-4.857			
Cox survival model for all-cause mortality							
Variable		**Model**	**HR**	**HR (95%)**	**Harrell's C-statistic**	**AIC**	**BIC**
SYNTAX-II		Univariate	1.095	1.079-1.112	0.790	1,393	1,442
SYNTAX-II (groups)	Low risk	Univariate	2.479	1.142-5.384	0.766	1,428	1,482
	High risk		11.060	5.483-22.310			
SYNTAX-II		Multivariate	1.059	1.031-1.088	0.865	1,151	1,389
SYNTAX-II (groups)	Low risk	Multivariate	1.035	0.434-2.469	0.863	1,161	1,405
	High risk		2.334	0.968-5.623			
SYNTAX-II		GRACE	1.076	1.058-1.095	0.799	1,384	1,438
SYNTAX-II (groups)	Low risk	GRACE	1.863	0.852-4.074	0.794	1,408	1,468
	High risk		5.735	2.766-11.891			
SYNTAX-II		SYNTAX	1.101	1.082-1.119	0.788	1,392	1,446
SYNTAX-II (groups)	Low risk	SYNTAX	2.495	1.144-5.441	0.767	1,430	1,490
	High risk		11.186	5.515-22.691			
SYNTAX-II		rSS	1.092	1.074-1.110	0.786	1,382	1,436
SYNTAX-II (groups)	Low risk	rSS	2.344	1.077-5.103	0.771	1,411	1,471
	High risk		9.992	4.958-20.140			

HR: hazard ratio; rSS: residual SYNTAX score

follow-up. A single study has assessed the prognostic ability of SS-II in a real-life STEMI population of 477 patients undergoing pPCI with a one-year follow-up. It did not show superiority to other scores in predicting MACE, but it did in predicting target vessel revascularisation (TVR) after pPCI[20]. Our study is the first to show a long-term prognostic value for SS-II in terms of all-cause mortality and MACE in a cohort of a significant number of patients; nonetheless, it did not show any difference in ischaemic soft outcomes such as MI and repeat revascularisation, probably due to the high index of complete revascularisation among MVD patients.

The anatomical SYNTAX score has proved to be useful in the risk stratification of non-STEMI and STEMI patients who underwent urgent PCI as an independent predictor of mortality, MACE, and stent thrombosis up to one-year follow-up, albeit the ability of this score would have been reinforced by adding a combination of angiographical and clinical variables[1,4,21,22]. On the other hand, the rSS showed it was also an independent predictor of MACE and all-cause mortality during follow-up (OR 2.9 for reasonable incomplete and 3.9 for incomplete revascularisation), adding prognostic value over control variables and GRACE[13]. In our study, the SS-II improved the predictive accuracy of long-term all-cause

mortality, MACE and HF when compared with the anatomical SYNTAX score and the residual SYNTAX score, demonstrating that the addition of clinical variables to purely angiographic scores enables better prediction of the long-term prognosis of the patients with STEMI undergoing pPCI. Nonetheless, the rate of MI and uRR during follow-up was not different between groups.

In addition, our study provides important information regarding the prediction of developing HF after a pPCI. This is a very relevant issue since HF after a STEMI event has been shown to be a predictor of late mortality even after successful revascularisation[23]. In our total cohort, 17% of patients were classified as Killip class II to IV at the time of presentation, of whom 12.6% were in the high SS-II tertile group. Of this group, 6.4% of patients developed HF in the first year, with a yearly downward trend to 0.6% after four years. HF has been shown to have a significant impact in patients after an acute coronary syndrome (ACS)[3] or after a pPCI[24]; nevertheless, HF has not been properly assessed among real-life cohorts after a STEMI and pPCI. None of the trials assessing the anatomical SYNTAX score, or the residual SS in this set of patients, has provided information on predicting the development of HF[4,13]. Other MI trials have focused predominantly on thrombosis, bleeding and MACE, rather than HF events specifically[25].

In our study, the SS-II improved the predictive accuracy of intermediate-term all-cause mortality, MACE and HF when compared with the anatomical SYNTAX score, the residual SYNTAX score and the GRACE risk score. Analysing the results, we consider that the strongest characteristic of the SS-II is the integration of the anatomical characteristics of the SYNTAX score and clinical variables.

Although it is necessary to analyse the anatomical coronary lesions to obtain the SS-II score, it provides a good stratification profile that makes it worth employing on a routine basis.

Limitations

This was a retrospective observational and non-randomised study conducted at a single hospital and, as such, has the inherent limitations and bias related to retrospective single-centre studies. Interpretation of angiograms and assessment of the SS were not adjudicated by a core laboratory; although each interventional cardiologist was experienced and well trained to calculate this score, different results might have been obtained if they had been carried out by consensus. We did not collect data on functional assessment of coronary stenosis in patients who underwent multivessel PCI; it is likely that in most patients the assessment of non-culprit lesion significance was made only on coronary angiography.

Conclusions

The present study shows that the SS-II in patients with STEMI undergoing pPCI adds important prognostic information regarding intermediate-term adverse outcomes, being an independent and powerful predictor of MACE, heart failure and all-cause mortality during follow-up.

Impact on daily practice

Risk stratification in patients with STEMI is a major feature in real clinical practice, as it provides a broad perspective of patient outcomes based on patient characteristics and optimal treatment. Our results may have several clinical implications and implications for the health-system organisation. We describe for the first time the intermediate-term prognostic value of SS-II in terms of all-cause mortality and MACE from a large, contemporary real-world cohort of STEMI patients submitted to pPCI. Our results also suggest that this score may be used for improvements in the "network care system" for STEMI patients, with implications for risk stratification and hospital and long-term care organisation.

Conflict of interest statement

The authors have no conflicts of interest to declare.

References

1. Sianos G, Morel MA, Kappetein AP, Morice MC, Colombo A, Dawkins K, van den Brand M, Van Dyck N, Russell ME, Mohr FW, Serruys PW. The SYNTAX Score: an angiographic tool grading the complexity of coronary artery disease. *EuroIntervention.* 2005;1:219-27.

2. Farooq V, Van Klaveren D, Steyerberg EW, Meliga E, Vergouwe Y, Chieffo A, Kappetein AP, Colombo A, Holmes DR Jr, Mack M, Feldman T, Morice MC, Ståhle E, Onuma Y, Morel MA, Garcia-Garcia HM, van Es GA, Dawkins KD, Mohr FW, Serruys PW. Anatomical and clinical characteristics to guide decision making between coronary artery bypass surgery and percutaneous coronary intervention for individual patients: development and validation of SYNTAX score II. *Lancet.* 2013;381:639-50.

3. Steg PG, Dabbous OH, Feldman LJ, Cohen-Solal A, Aumont MC, López-Sendón J, Budaj A, Goldberg RJ, Klein W, Anderson FA Jr; Global Registry of Acute Coronary Events Investigators. Determinants and prognostic impact of heart failure complicating acute coronary syndromes: observations from the Global Registry of Acute Coronary Events (GRACE). *Circulation.* 2004;109:494-9.

4. Garg S, Sarno G, Serruys PW, Rodriguez AE, Bolognese L, Anselmi M, De Cesare N, Colangelo S, Moreno R, Gambetti S, Monti M, Bristol L, Bressers M, Garcia-Garcia HM, Parrinello G, Campo G, Valgimigli M; STRATEGY and MULTISTRATEGY Investigators. Prediction of 1-year clinical outcomes using the SYNTAX score in patients with acute ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention: a substudy of the STRATEGY (Single High-Dose Bolus Tirofiban and Sirolimus-Eluting Stent Versus Abciximab and Bare-Metal Stent in Acute Myocardial Infarction) and MULTISTRATEGY (Multicenter Evaluation of Single High-Dose Bolus Tirofiban Versus Abciximab With Sirolimus-Eluting Stent or Bare-Metal Stent in Acute Myocardial Infarction Study) trials. *JACC Cardiovasc Interv.* 2011;4:66-75.

5. Salvatore A, Boukhris M, Giubilato S, Tomasello SD, Castaing M, Giunta R, Marzà F, Abdelbasset HM, Khamis H, Galassi AR. Usefulness of SYNTAX score II in complex percutaneous coronary interventions in the setting of acute coronary syndrome. *J Saudi Heart Assoc.* 2016;28:63-72.

6. Song Y, Gao Z, Tang X, Ma Y, Jiang P, Xu J, Yao Y, Zhao X, Qiao S, Yang Y, Gao R, Xu B, Yuan J. Usefulness of the SYNTAX score II to validate 2-year outcomes in patients with complex coronary artery disease undergoing percutaneous coronary intervention: A large single-center study. *Catheter Cardiovasc Interv.* 2018;92:40-7.

7. Galvão Braga C, Cid-Álvarez AB, Redondo Diéguez A, Trillo-Nouche R, Álvarez Álvarez B, López Otero D, Ocaranza Sánchez R, Gestal Romaní S,

González Ferreiro R, González-Juanatey JR. Multivessel Versus Culprit-only Percutaneous Coronary Intervention in ST-segment Elevation Acute Myocardial Infarction: Analysis of an 8-year Registry. *Rev Esp Cardiol (Engl Ed).* 2017;70:425-32.

8. Hayıroğlu Mİ, Keskin M, Uzun AO, Bozbeyoğlu E, Yıldırımtürk Ö, Kozan Ö, Pehlivanoğlu S. Predictive value of SYNTAX score II for clinical outcomes in cardiogenic shock underwent primary percutaneous coronary intervention; a pilot study. *Int J Cardiovasc Imaging.* 2018;34:329-36.

9. Campos CM, Van Klaveren D, Farooq V, Simonton CA, Kappetein AP, Sabik JF 3rd, Steyerberg EW, Stone GW, Serruys PW; EXCEL Trial Investigators. Long-term forecasting and comparison of mortality in the Evaluation of the Xience Everolimus Eluting Stent vs Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization (EXCEL) trial: prospective validation of the SYNTAX Score II. *Eur Heart J.* 2015;36:1231-41.

10. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, Caforio ALP, Crea F, Goudevenos JA, Halvorsen S, Hindricks G, Kastrati A, Lenzen MJ, Prescott E, Roffi M, Valgimigli M, Varenhorst C, Vranckx P, Widimský P; ESC Scientific Document Group. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J.* 2018;39:119-77.

11. Authors/Task Force members, Windecker S, Kolh P, Alfonso F, Collet JP, Cremer J, Falk V, Filippatos G, Hamm C, Head SJ, Jüni P, Kappetein AP, Kastrati A, Knuuti J, Landmesser U, Laufer G, Neumann FJ, Richter DJ, Schauerte P, Sousa Uva M, Stefanini GG, Taggart DP, Torracca L, Valgimigli M, Wijns W, Witkowski A. 2014 ESC/EACTS Guidelines on myocardial revascularization: The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). *Eur Heart J.* 2014;35:2541-619.

12. Serruys PW, Morice MC, Kappetein AP, Colombo A, Holmes DR, Mack MJ, Ståhle E, Feldman TE, van den Brand M, Bass EJ, Van Dyck N, Leadley K, Dawkins KD, Mohr FW; SYNTAX Investigators. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *N Engl J Med.* 2009;360:961-72.

13. Braga CG, Cid-Alvarez AB, Diéguez AR, Alvarez BA, Otero DL, Sánchez RO, Pena XS, Salvado VG, Trillo-Nouche R, González-Juanatey JR. Prognostic impact of residual SYNTAX score in patients with ST-elevation myocardial infarction and multivessel disease: Analysis of an 8-year all-comers registry. *Int J Cardiol.* 2017;243:21-6.

14. Tang EW, Wong CK, Herbison P. Global Registry of Acute Coronary Events (GRACE) hospital discharge risk score accurately predicts long-term mortality post acute coronary syndrome. *Am Heart J.* 2007;153:29-35.

15. Morrow DA, Antman EM, Charlesworth A, Cairns R, Murphy SA, de Lemos JA, Giugliano RP, McCabe CH, Braunwald E. TIMI risk score for ST-elevation myocardial infarction: a convenient, bedside, clinical score for risk assessment at presentation: An intravenous nPA for treatment of infarcting myocardium early II trial substudy. *Circulation.* 2000;102:2031-7.

16. Addala S, Grines CL, Dixon SR, Stone GW, Boura JA, Ochoa AB, Pellizzon G, O'Neill WW, Kahn JK. Predicting mortality in patients with ST-elevation myocardial infarction treated with primary percutaneous coronary intervention (PAMI risk score). *Am J Cardiol.* 2004;93:629-32.

17. De Luca G. Prognostic assessment of patients with acute myocardial infarction treated with primary angioplasty: implications for early discharge. *Circulation.* 2004;109:2737-43.

18. Halkin A, Singh M, Nikolsky E, Grines CL, Tcheng JE, Garcia E, Cox DA, Turco M, Stuckey TD, Na Y, Lansky AJ, Gersh BJ, O'Neill WW, Mehran R, Stone GW. Prediction of mortality after primary percutaneous coronary intervention for acute myocardial infarction: the CADILLAC risk score. *J Am Coll Cardiol.* 2005;45:1397-405.

19. Hizoh I, Gulyas Z, Domokos D, Banhegyi G, Majoros Z, Major L, Ratkai T, Kiss RG. A novel risk model including vascular access site for predicting 30-day mortality after primary PCI: The ALPHA score. *Cardiovasc Revasc Med.* 2017;18:33-9.

20. Wang G, Wang C, Zhang Y, Wang P, Ran C, Zhao L, Han L. Usefulness of the SYNTAX score II to predict 1-year outcome in patients with primary percutaneous coronary intervention. *Coron Artery Dis.* 2016;27:483-9.

21. Yang CH, Hsieh MJ, Chen CC, Wang CY, Chang SH, Lee CH, Hsieh IC. The prognostic significance of SYNTAX score after early percutaneous transluminal coronary angioplasty for acute ST elevation myocardial infarction. *Heart Lung Circ.* 2013;22:341-5.

22. Yang CH, Hsieh MJ, Chen CC, Chang SH, Wang CY, Lee CH, Hsieh IC. SYNTAX score: an independent predictor of long-term cardiac mortality in patients with acute ST-elevation myocardial infarction. *Coron Artery Dis.* 2012;23:445-9.

23. Cahill TJ, Kharbhanda RK. Heart failure after myocardial infarction in the era of primary percutaneous coronary intervention: Mechanisms, incidence and identification of patients at risk. *World J Cardiol.* 2017;9:407-15.

24. DeGeare VS, Boura JA, Grines LL, O'Neill WW, Grines CL. Predictive value of the Killip classification in patients undergoing primary percutaneous coronary intervention for acute myocardial infarction. *Am J Cardiol.* 2001;87:1035-8.

25. Magro M, Räber L, Heg D, Taniwaki M, Kelbaek H, Ostojić M, Baumbach A, Tüller D, von Birgelen C, Roffi M, Pedrazzini G, Kornowski R, Weber K, Meier B, Lüscher TF, Serruys PW, Jüni P, Windecker S. The MI SYNTAX score for risk stratification in patients undergoing primary percutaneous coronary intervention for treatment of acute myocardial infarction: a substudy of the COMFORTABLE AMI trial. *Int J Cardiol.* 2014;175:314-22.

Supplementary data

Supplementary Table 1. Additive value of SS-II over GRACE risk score.

Supplementary Table 2. Additive value of SS-II over residual SYNTAX score.

Supplementary Table 3. Additive value of SS-II over SYNTAX score.

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Supplementary data

Supplementary Table 1. Additive value of SS-II over GRACE risk score.

Characteristics	***p*-value** SS-II	**Δ ROC (%)** [χ^2 *p*-value]	**NRI event**	**NRI no event**	**NRI global**
In-hospital mortality	**<0.001**	**3.35 [0.05]**	**0**	**4.0**	**4.0**
MACE during follow-up	**<0.001**	**2.96 [0.01]**	**-1.5**	**4.6**	**3.1**
All-cause mortality	**<0.001**	**0.01 [0.99]**	**1.9**	**2.4**	**4.2**
Heart failure	**0.001**	**3.60 [0.14]**	**6.6**	**2.8**	**9.4**
Myocardial infarction	0.469	Non-significant variable			
Repeat revascularisation	0.052	Non-significant variable			
Stent thrombosis	0.393	Non-significant variable			

MACE: major adverse cardiovascular events; NRI: net reclassification improvement; ROC curve: receiver operating characteristic curve; SS-II: SYNTAX score II

Supplementary Table 2. Additive value of SS-II over residual SYNTAX score.

Characteristics	*p*-value SS-II	Δ ROC (%) [χ^2 *p*-value]	NRI event	NRI no event	NRI global
In-hospital mortality	**<0.001**	**19.17 [<0.001]**	**34.0**	**-1.2**	**32.8**
MACE during follow-up	**<0.001**	**17.43 [<0.001]**	**26.6**	**-1.2**	**25.4**
All-cause mortality	**<0.001**	**26.76 [<0.001]**	**37.2**	**3.2**	**40.4**
Heart failure	**<0.001**	**24.89 [<0.001]**	**45.9**	**4.9**	**50.8**
Myocardial infarction	0.475	Non-significant variable			
Repeat revascularisation	0.454	Non-significant variable			
Stent thrombosis	0.162	Non-significant variable			

MACE: major adverse cardiovascular events; NRI: net reclassification improvement; ROC curve: receiver operating characteristic curve; SS-II: SYNTAX score II

Supplementary Table 3. Additive value of SS-II over SYNTAX score.

Characteristics	***p*-value** SS-II	**Δ ROC (%)** [χ^2 *p*-value]	**NRI event**	**NRI no event**	**NRI global**
In-hospital mortality	**<0.001**	**19.61 [<0.001]**	**20.6**	**10.8**	**31.4**
MACE during follow-up	**<0.001**	**11.51 [<0.001]**	**7.1**	**11.1**	**18.2**
All-cause mortality	**<0.001**	**22.19 [<0.001]**	**21.3**	**13.6**	**34.9**
Heart failure	**<0.001**	**25.09 [<0.001]**	**26.2**	**13.3**	**39.5**
Myocardial infarction	0.487	Non-significant variable			
Repeat revascularisation	0.183	Non-significant variable			
Stent thrombosis	0.502	Non-significant variable			

MACE: major adverse cardiovascular events; NRI: net reclassification improvement; ROC curve: receiver operating characteristic curve; SS-II: SYNTAX score II