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Original Research

Usefulness of the SYNTAX Score II to Predict In-Hospital and Long-Term Mortality in ST-Segment Elevation Myocardial Infarction Patients Undergoing Primary Percutaneous Coronary Intervention

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Abstract

Objectives: The prognostic significance of SYNTAX Score II (SS-II) is well-known in patients with chronic coronary syndromes. However, its predictive ability for mortality in ST-segment elevation myocardial infarction (STEMI) patients undergoing primary percutaneous coronary intervention (p-PCI) remains unclear. Therefore, we aimed to investigate the prognostic accuracy of SS-II in STEMI patients who underwent p-PCI.

Methods: A total of 743 STEMI patients treated with p-PCI were retrospectively analyzed. Study population was divided into three groups according to SS-II and defined as SS-IILOW ≤22.5 (n=245), 22.5 <SS-II MID ≤31 (n=243) and SS-II HIGH >31 (n=255). In-hospital and long-term mortality at long-term follow-up were defined as clinical endpoints of the study.

Results: The incidence of in-hospital (15% vs. 0.4% vs. 0.8%, p<0.001) and all-cause mortality (32.2% vs. 6.6% vs. 2.9%, p<0.001) were significantly higher in SS-IIHIGH group compared with the other two groups. In addition, Kaplan–Meier analysis showed statistically significantly increased incidence of death in SS-II > 31 group (P [log-rank] <0.001). SS-II >31 was defined as an independent predictor of all-cause mortality (hazard ratio 5.22 95% confidence interval 2.11–12.87 p<0.001). Area under the curve values derived from ROC analysis to evaluate the predictive accuracy of SS-II, anatomical and clinical SS, modified ACEF score, and Global Registry of Acute Coronary Events risk scores for all-cause mortality were 0.82, 0.71, 0.81, 0.82, and 0.82, respectively (p<0.001).

Conclusion: SS-II has an increased predictive ability for in-hospital and long-term mortality in STEMI patients undergoing p-PCI.

Keywords: Primary percutaneous coronary intervention, ST-segment elevation myocardial infarction, SYNTAX score II

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ST-segment elevation myocardial infarction (STEMI) is one of the significant causes of mortality worldwide.[1] Despite widespread use of invasive revascularization therapies such as primary percutaneous coronary intervention (p-PCI) and improvement in medical therapies, STEMI patients still suffer from adverse outcomes.[2]

The early diagnosis of high-risk STEMI patients is essential to reduce following adverse clinical events. In this context, many risk scores have been designed to predict clinical outcomes and determine disease severity. For this purpose, the well-known Global Registry of Acute Coronary Events (GRACE) and Thrombolysis in Myocardial Infarction risk scores had been used.[3,4]

The SYNTAX score (SS), which is a widely used anatomical scoring system, establishes the angiographic properties of coronary lesions and provides prognostic information in patients undergoing PCI.[5] Since the lack of clinical information is the weakness of SS; a novel scoring system consisting of two anatomical and six clinical parameters, the SS-II has been developed. It predicts long-term mortality in patients undergoing PCI or coronary artery bypass grafting (CABG) and strengthens the ability of the SS to predict long-term clinical outcomes through combining anatomical and clinical risk assessment.[6]

Although most recent reports[7,8] suggest that SS gives an important prognostic information, the predictive accuracy of the SS-II for in-hospital and long-term mortality in STEMI patients who have undergone p-PCI remains uncertain.

Therefore, we aimed to investigate the prognostic capability of SS-II for in-hospital and long-term death in STEMI patients undergoing p-PCI.

Methods

A total of 814 STEMI patients who were treated with p-PCI between April 2012 and February 2016 were recruited in our single-center retrospective study. ST-segment elevation more than 1 mm in sequential two electrocardiographic leads or new left bundle-branch block was used to define STEMI. Thrombolytic treatment usage, previous CABG surgery, need for emergency CABG operation, and prior p-PCI for stent or graft thrombosis were defined as exclusion criteria. Of these, 23 patients were excluded due to previous CABG, ten due to stent thrombosis, four due to graft thrombosis, 16 due to emergency CABG operation, and 18 patients due to thrombolytic therapy. Final analysis was conducted with 743 patients. This study was complied with the edicts of the 1975 Declaration of Helsinki and was approved by the Local Ethics Committee (Date: 07/06/2017, no: 215339).

Demographic, laboratory, and clinical information were obtained from the electronic database of the hospital. The demographic, clinical, and laboratory data included age, gender, presence of hypertension (HTN), diabetes mellitus (DM), hyperlipidemia (HL), smoking status, previous MI, prior CABG surgery or PCI, and stroke. Venous blood samples were collected at the time of hospital admission.

All patients were given 600 mg clopidogrel and 300 mg aspirin therapy before the procedure in the emergency department. Experienced interventional cardiologists performed the p-PCI procedures through femoral approach. Patients undergoing PCI were treated with 100 IU/kg heparin. Reduced dose of heparin, 60 IU/kg, was administered if a glycoprotein IIb-IIIa inhibitor (GPI) was used concomitantly. The choice of stent type, thrombus aspiration, or use of GPI is left to the operator's discretion. Lifelong 100 mg aspirin, 75 mg clopidogrel (minimum 12 months), statins, beta blockers, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers were prescribed for all patients at discharge.

The anatomical SS was calculated with SS calculator. SS-II was also determined using www.syntaxscore.com and included additional information about age, gender, glomerular filtration rate levels, left ventricular ejection fraction, the presence of peripheral artery disease (PAD), chronic obstructive pulmonary disease, and left main coronary artery lesion. Two independent interventional cardiologists evaluated the angiographic images. Clinical SS (CSS) was calculated by multiplying SS with ACEF score. Clinical features of the patients at the time of hospital admission were used to determine the GRACE risk score.

The study population was divided into three groups according to SS-II, which was defined as SS-IILOW ≤22.5 (n=245), 22.5< SS-II MID ≤31 (n=243), and SS-II HIGH >31 (n=255). The primary clinical endpoints of the study were determined as in-hospital and long-term mortality during follow-up. Data regarding primary endpoints were obtained from telephone calls or the hospital's electronic database. The median follow-up time of the study group was determined as 48 months (minimum 6 months and maximum 60 months).

Statistical Analysis

SPSS 22 (SPSS Inc., Chicago, Illinois, USA) software was used for statistical analysis. Continuous variables were given as mean±standard deviation, and categorical variables were given as percentages. Continuous variables were compared among groups using the one-way analysis of variance or the Kruskal–Wallis test. Categorical data were compared using the Chi-square test. Cox regression analy-

sis was used to find independent predictors of in hospital and long-term mortality. Kaplan–Meier method was used for event-free survival curves. Differences in survival curves among the groups were assessed using the log-rank test. The performance and predictive accuracy of the SS-II, CSS, SS, GRACE RS, and ACEF scores for all-cause mortality were assessed with ROC analysis. These ROC curves were compared using the De-Long method. P<0.05 was defined as statistically significant.

Results

Demographic and clinical features and the laboratory data of the study population according to SS-II are given in Tables 1 and 2. Significant differences were seen among the groups with respect to age, HTN, DM, COPD, PAD, previous MI, duration of chest pain, Killip class, CI-AKI, SS, CSS, GRACE, and ACEF scores. In addition systolic blood pressure, smoking rate, EF, and male gender were found to decrease from lower SS-II to higher SS-II. Both admission and maximum creatinine, serum glucose, and CK-MB levels tend to be higher in high SS-II tertile.

Procedural and angiographic features of the study population are given in Table 3. Total stent length, contrast volume, and the incidence of 2–3 vessel disease and failed PCI were significantly higher in the high SS-II group. Number of stents implanted, types of stent used, average stent diameter, tirofiban use, and thrombus aspiration were similar among the groups.

Independent predictors of in hospital and long-term mortality, which were defined by multivariate analysis based on the following variables, are given in Tables 4 and 5. These variables were SS-II>31, age, male gender, DM, HTN, smoking, Killip class, failed PCI, duration of chest pain, and 2–3 vessel disease. Among these variables, SS-II >31 age, male gender, Killip class 3–4, and duration of chest pain were found to be independent predictors for long-term mortality. SS-II >31, Killip class 3–4, and failed PCI were found to be independent predictors for in-hospital mortality.

In-hospital mortality (15% vs. 0.4% vs. 0.8%, p<0.001) and long-term mortality at follow-up period (32.2% vs. 6.6% vs. 2.9%, p<0.001) were significantly higher in SS-IIHIGH group compared to other two groups and are shown in Figure 1. Kaplan–Meier analysis is shown in Figure 2 and revealed that the incidence of death was statistically significantly higher in SS-II >31 group (P [log-rank] <0.001).

Table 1. The clinical and demographic characteristics of the study population according to SS-II tertiles

	SS-II ≤22.5 (n=245)	22.5 < SS-II ≤31 (n=243)	SS-II >31 (n=255)	p
Age, years	48±8.2	57.3±8.7	65.1±11.5	<0.001
Male gender	237(96.7%)	217 (89.3%)	176 (69%)	<0.001
Hypertension	60 (24.5%)	83 (34.2%)	123 (48.2%)	<0.001
Diabetes mellitus	51 (20.8%)	69 (28.4%)	98 (38.4%)	<0.001
Hypercholesterolemia	141 (57.6%)	139 (57.2%)	147 (57.6%)	0.99
COPD	18 (7.3%)	46 (18.9%)	43 (16.9%)	0.001
PAD	0	2 (0.8%)	17 (6.7%)	<0.001
Previous MI	29 (11.8%)	38 (15.6%)	60 (23.5%)	0.002
Previous PCI	37 (15.1%)	44 (18.1%)	57 (22.4%)	0.11
Ejection fraction (%)	52.1±4.8	47.9±6.5	41.1±9.6	<0.001
Body mass index (kg/m^2)	23.2±10.7	24.9±10.8	24.6±10.3	0.45
Smoking	185 (75.6%)	161 (66.2%)	102 (40%)	<0.001
Systolic blood pressure (mm Hg)	127.3±22.6	129.8±30.1	121.9±27.4	0.009
Diastolic blood pressure (mm Hg)	79.7±13.1	79.9±15.1	78.3±44.9	0.82
Anterior MI	80 (32.7%)	100 (41.2%)	151 (59.2%)	<0.001
Duration of chest pain, hours	0.96±0.16	1.24±0.27	2.36±1.26	<0.001
Killip class 3 or 4	2 (0.8%)	7 (2.9%)	37 (14.5%)	<0.001
CI-AKI	29 (11.8%)	36 (14.8%)	57 (22.4%)	0.005
Syntax Score	11.9±5.4	16.2±6.8	21.3±8.7	<0.001
Clinical Syntax Score	11.5±5.4	19.9±9.2	50.6±35.2	<0.001
GRACE Score	135±19.8	148.3±22.1	174.9±35.7	<0.001
ACEF score	0.96±0.16	1.24±0.27	2.36±1.26	<0.001

ACEF: Age, creatinine, ejection fraction; CI-AKI: Contrast-induced acute kidney injury; COPD: Chronic obstructive pulmonary disease; GRACE: Global registry of acute coronary events; MI: Myocardial infarction; PAD: Peripheral arterial disease; PCI: Percutaneous coronary intervention; SS-II: Syntax score II.

Table 2. Biochemical values of the study group according to SS-II tertiles

	SS-II ≤22.5 (n=245)	22.5 < SS-II ≤31 (n=243)	SS-II >31 (n=255)	p
Creatinine level on admission (mg/dL)	0.82±0.14	0.90±0.19	1.18±0.85	<0.001
Maximum creatinine level (mg/dL)	0.92±0.36	1.0±0.36	1.52±1.44	<0.001
eGFR (ml/min/1.73 m2)	103.1±25.7	89.1±20.7	69.1±24.2	<0.001
Serum glucose level on admission (mg/dL)	134.3±56.5	140.1±60.6	164.7±91.1	<0.001
Total cholesterol (mg/dL)	195.4±44.5	181.4±43.2	183.2±43.1	0.001
LDL (mg/dL)	134.7±54.4	122.2±37.5	119.6±35.6	<0.001
HDL (mg/dL)	37.9±12.9	39.1±18.3	41.4±11.6	0.03
Triglyceride (mg/dL)	171.5±138.8	143.9±86.5	147.7±123.5	0.04
CK-MB (ng/mL)	138.5±129.1	182.7±178.6	185.1±181.6	0.007

CK-MB: Creatine kinase MB; eGFR: Estimated glomerular filtration rate; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; SS-II: Syntax score II.

Table 3. Angiographic and procedural properties of the study population according to SS-II tertiles

	SS-II ≤22.5 (n=245)	22.5< SS-II ≤31 (n=243)	SS-II >31 (n=255)	p
Number of stents implanted	0.91±0.5	0.93±0.4	0.86±0.5	0.27
Average stent diameter in IRA (mm)	2.94±0.38	2.99±0.38	2.89±0.38	0.79
Total stent length in IRA (mm)	21.6±8.2	22.1±8.1	22.1±8.7	0.04
Contrast volume (mL)	257.1 ±92.1	278.3±103.7	292.9±105.3	<0.001
Tirofiban use	155 (63.5%)	163 (67.1%)	152 (59.6%)	0.22
Thrombus aspiration	126 (51.4%)	146 (60.1%)	129 (50.6%)	0.07
Number of diseased vessels				<0.001
1 vessel	166 (67.8%)	126 (51.9%)	86 (33.7%)	
2 vessels	65 (26.5%)	79 (32.5%)	95 (37.3%)	
3 vessels	14 (5.7%)	38 (15.6%)	74 (29%)	
Infarct related artery				<0.001
LMCA	0	0	4(1.6%)	
LAD	85 (34.7%)	99 (40.7%)	147 (57.6%)	
CX	52 (21.2%)	38 (15.6%)	30 (11.8%)	
RCA	108 (44.1%)	106 (43.6%)	74 (29%)	
Stent type				0.08
DES	216 (88.2%)	201 (82.7%)	217 (85.1%)	
BMS	29 (11.8%)	42 (17.3%)	38 (14.9%)	
Failed PCI	3 (1.2%)	1 (0.4%)	12 (4.7%)	0.002

BMS: Bare metal stent; CX: Circumflex artery; DES: Drug eluting stent; IRA: Infarct related artery; LAD: Left anterior descending; RCA: Right coronary artery; LMCA: Left main coronary artery; PCI: percutaneous coronary intervention; SS-II: Syntax score II.

The ROC analysis comparing the performance and predictive accuracy of SS-II, SS, CSS, ACEF, and GRACE score for all-cause mortality during the follow-up is shown in Figure 3. Based on a 95% confidence interval, the areas under the curve (AUC) for SS-II, SS, CSS, ACEF, and GRACE scores were 0.82, 0.71, 0.81, 0.82, and 0.82 ($p<0.001$ for all). We also performed a pairwise comparison of ROC curves, the predictive accuracy of SS-II with regard to all-cause mortality was superior to SS and similar to ACEF, CSS, and GRACE scores (By de-Long method, AUCss-II vs AUCss z test=2.85 p=0.01, AUCss-II vs. AUCACEF z test = 0.93 p=0.48, AUCss-II vs AUCCSS z test=1.15 p=0.56, and AUCss-II vs. AUCgrace z test = 1.18 p=0.63).

Discussion

The results of our study suggest that SS-II independently predicts in-hospital and long-term mortality in patients undergoing p-PCI for STEMI. In addition, the prognostic performance of SS-II was superior to anatomical SS, whereas similar to CSS, ACEF, and GRACE risk scores in this patient group.

Nowadays, p-PCI is the main treatment strategy for patients with STEMI. Despite extensive usage of p-PCI, STEMI still constitutes one the most significant reason of morbidity and mortality. Hence, the early identification of high risky

Table 4. Univariate and multivariate predictors of in-hospital mortality

	Univariate		Multivariate	
	HR (95%CI)	p	HR (95%CI)	p
SS-II>31	3.22 (1.18–8.78)	0.02	4.14 (1.62–10.59)	0.003
Age	1.01 (0.97–1.06)	0.57		
Male gender	2.22 (0.62–7.97)	0.22		
Diabetes mellitus	1.61 (0.57–4.58)	0.37		
Hypertension	1.86 (0.63–5.47)	0.26		
Smoking	0.63 (0.21–1.91)	0.41		
Previous MI	0.84 (0.27–2.63)	0.76		
Killip class 3–4	4.47 (2.97–6.74)	<0.001	3.97 (2.78–5.65)	<0.001
Failed PCI	5.75 (1.16–28.48)	0.03	6.01 (1.31–27.62)	0.02
Duration of chest pain	1.06 (0.98–1.15)	0.16		
2 or 3 vessel disease	1.32 (0.72–2.41)	0.38		

CI: Confidence interval; HR: Hazard ratio; SS-II: Syntax score II; MI: Myocardial infarction; PCI: Percutaneous coronary intervention.

Table 5. Univariate and multivariate predictors of long-term mortality

	Univariate		Multivariate	
	HR (95%CI)	p	HR (95%CI)	p
SS-II>31	5.25 (2.11–13.09)	<0.001	5.22 (2.12–12.88)	<0.001
Age	1.04 (1.02–1.06)	0.001	1.04 (1.1–1.6)	0.001
Male gender	2.08 (1.14–3.76)	0.02	2.04 (1.17–3.55)	0.01
Diabetes mellitus	1.28 (0.80–2.02)	0.30		
Hypertension	1.29 (0.81–2.10)	0.29		
Smoking	1.21 (0.74–1.97)	0.45		
Previous MI	1.12 (0.66–1.89)	0.68		
Killip class 3–4	9.32 (5.1–17.1)	<0.001	9.2 (5.2–16.4)	<0.001
Failed PCI	1.86 (0.77–4.49)	0.17		
Duration of chest pain	1.06 (1.03–1.09)	<0.001	1.06 (1.02–1.10)	<0.001
2 or 3 vessel disease	1.25 (0.43–1.32)	0.32		

CI: Confidence interval; HR: Hazard ratio; SS-II: Syntax score II; MI: Myocardial infarction; PCI: Percutaneous coronary intervention.

STEMI patients undergoing p-PCI is crucial for follow-up (1). Therefore, SS-II was investigated as a prognostic indicator and compared with the other clinical well-accepted risk scores in STEMI patients in the present study.

Various risk scoring systems have been developed for risk classification of patients with acute coronary syndromes. The most widely-accepted clinical risk score is the GRACE risk score, while the most popular anatomical risk score is SS.[4,8] However, we know that recently validated risk scores increased the prognostic performance of these scoring systems through combining clinical and anatomical parameters.[9-11]

CSS is one of them and it predicts long-term adverse clinical events in STEMI patients whom undergone primary PCI.[9] In addition, a meta-analysis consisted of seven different PCI studies showed that CSS was superior to SS in predicting all-cause mortality during 1-year follow-up. Hence, no superiority was demonstrated in terms of major cardiovascular events.[12]

SS-II, which is a novel reinforced version of the anatomical SS by clinical parameters, was reported to be a predictor of 4-year mortality in patients treated with PCI for complex coronary artery disease[13,14] SS-II was generally investigated in multivessel patients undergoing PCI under elective conditions. Fewer studies conducted in patients with acute coronary syndromes were reflecting the results of shorter follow-up period. A recent study conducted by Wang et al. firstly demonstrated the ability of SS-II to predict 1-year adverse clinical outcomes in STEMI patients whom undergone primary PCI.[15] Furthermore, the predictive ac-

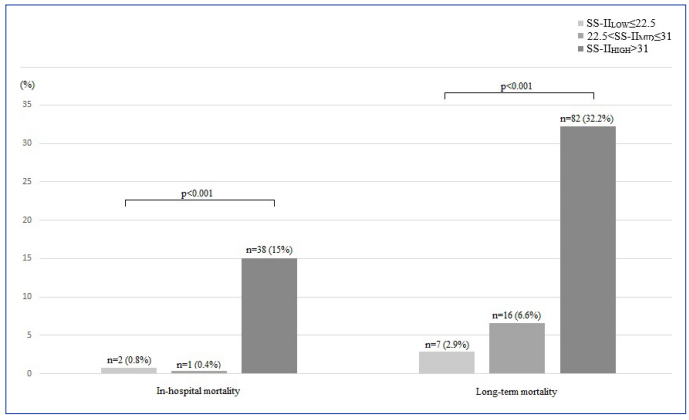

Figure 1. In-hospital mortality and long-term mortality rates of the study groups according to SS-II.

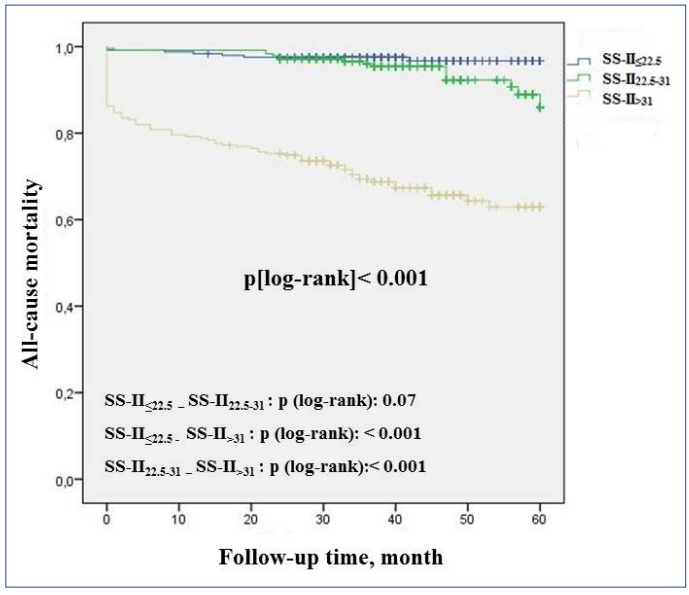

Figure 2. Kaplan–Meier curve for long-term mortality during follow-up.

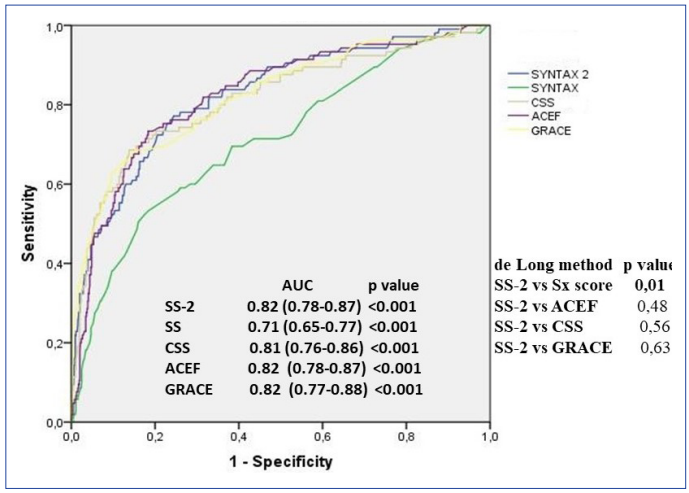

Figure 3. ROC analysis comparing the performance and predictive accuracy of SS-II, SS, CSS, ACEF, and GRACE scores for all-cause mortality.

curacy of SS-II was superior to other risk scores, including anatomical SS. Follow-up time was 1 year that these results may differentiate with much more longer follow-up time. Therefore, we aimed to assess the same population for in-hospital and long-term mortality during a longer follow-up time. Similarly, we demonstrated that the prognostic value of SS-II was better than anatomical SS in terms of adverse clinical events, however similar to other clinical risk scores.

Moreover, SS-II was demonstrated to be an easy and clinically user friendly scoring system for the early risk stratification in STEMI patients complicated with cardiogenic shock and treated with p-PCI.[16] Likewise, SS-II was defined as a strong predictor of in-hospital mortality according to our results, thereby confirming that SS-II has prognostic performance not only for long-term events, but also in-hospital outcomes of STEMI patients.

Our results indicated that higher SS-II level (SS-II>31) was shown to be an independent predictor of in-hospital and all-cause mortality. Patients with higher SS-II were older, more diabetic, hypertensive and had more renal dysfunction with a higher KILLIP class and lower EF. Based on these results, positive relationship was revealed between SS-II and adverse clinical endpoints in patients undergoing p-PCI for STEMI.

There were few limitations to be noted in this study. First of all, it was retrospectively designed, single-center, and modest sample-sized study. Some parameters of the study group may be missing due to the retrospective design of our study. It is unclear whether the outcomes will change with increased usage of novel potent P2Y12 inhibitors (such as prasugrel or ticagrelor) or new generation thin-strut drug eluting stents. Although the predictive accuracy of SS-II was determined to be stronger than anatomical SS, future validation of our findings is needed to determine the clinical usefulness of it in STEMI patients who underwent p-PCI.

Conclusion

Our results demonstrated SS-II as an independent predictor for in-hospital and long-term mortality in STEMI patients who underwent p-PCI. In addition, the prognostic ability of S-II is superior to anatomical SS, whereas similar to CSS, ACEF, and GRACE risk scores. Therefore, widespread use of SS-II may provide benefit in a high-risky patient group such as patients with STEMI.

Disclosures

Ethics Committee Approval: This study was complied with the edicts of the 1975 Declaration of Helsinki and was approved by the Local Ethics Committee (Date: 07/06/2017, no: 215339).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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