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Value of syntax score II for predicting in-hospital and long-term survival in octogenarians with ST-segment elevation myocardial infarction: A comparison of six different risk scores

Ibrahim Rencuzogullari[a], Metin Çağdaş[a], Yavuz Karabağ[a], Süleyman Karakoyun[a], Mahmut Yesin[b], Tufan Çinar[c,*], Veysel Ozan Tanik[d], Cengiz Burak[a], İbrahim Halil Tanboğa[e]

[a] Kafkas University Medical Faculty, Department of Cardiology, Kars, Turkey
[b] Kars Harakani State Hospital, Department of Cardiology, Kars, Turkey
[c] Health Science University, Sultan Abdulhamid Han Training and Research Hospital, Department of Cardiology, Istanbul, Turkey
[d] Ankara Diskapi Yildirim Beyazit Training and Research Hospital, Department of Cardiology, Ankara, Turkey
[e] Ataturk University Medical Faculty, Department of Cardiology, Erzurum, Turkey

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ABSTRACT

Background: The aim of this study was to evaluate the usefulness of the Syntax Score II (SSII) in predicting in-hospital and long-term mortality in octogenarians who presented with ST-segment elevation myocardial infarction (STEMI) and were treated with primary percutaneous coronary intervention (pPCI) in addition to compare SS II with other risk-scoring systems.

Methods: We retrospectively enrolled 312 consecutive STEMI patients in the eighth decade of life or older who underwent pPCI. The octogenarians were divided into two groups according to their median SSII (low SSII ≤ 43.6 and high SSII > 43.6), and these groups were compared in terms of mortality. The performance of the SSII in predicting patients' outcomes was further compared with that of other well-known risk-scoring systems.

Results: In the study, the SSII was an independent predictor of long-term mortality (OR: 1.036 95% CI: 1.005–1.068; $p = 0.024$). Both in-hospital (20.8% vs. 1.2%; $p < 0.001$) and long-term mortality (45.0% vs. 11%; $p < 0.001$) were higher among the patients with a high SSII compared to those with a low SSII. An ROC curve comparison showed that SSII was a better predictor (AUC: 0.807; 95% CI: 0.750-0.863) of long-term mortality than SS, PAMI, TIMI, and GRACE risk scores but not CADILLAC.

Conclusions: Based on the study findings, octogenarians with a high SSII had worse in-hospital and long-term survival. The SSII, which includes several clinical and anatomical parameters, may be a better predictor of mortality than other risk-scoring systems in octogenarians.

1. Introduction

Deaths from ischemic heart diseases have decreased in recent years due to an increase in percutaneous coronary intervention (PCI), modern antithrombotic therapy as well as secondary prevention (Hartley et al., 2016; Puymirat et al., 2012). Nevertheless, the mortality of unselected patients with ST-segment elevation myocardial infarction (STEMI) remains high (Ibanez et al., 2018). Primary PCI (pPCI) remains the treatment of choice for STEMI, and there is no identified upper age limit with respect to reperfusion, especially for pPCI (Bueno et al., 2011).

The current guidelines strongly recommend that all patients with STEMI should be assessed in terms of short- and long-term risks because of subsequent adverse events, such as heart failure, recurrent ischemia, residual ischemia, mechanical complications, and death (Ibanez et al., 2018). To date, various scoring systems and scales have been used to predict the prognosis in STEMI patients. These scoring systems include the Primary angioplasty in myocardial infarction (PAMI) risk score (Addala et al., 2004), Thrombolysis in Myocardial Infarction (TIMI) risk score, Global registry of acute coronary events (GRACE), Zwolle, Controlled abciximab and device investigation to lower late angioplasty complications (CADILLAC) (Kozieradzka et al., 2011), Syntax Score (SS) (Magro et al., 2011b), Clinical Syntax Score (Cetinkal et al., 2016),

Abbreviations: ROC, receiver operating curve; SS II, syntax score

* Corresponding author at: Health Sciences University, Sultan Abdulhamid Han Training and Research Hospital, Tibbiye Street, Uskudar, Istanbul.
E-mail address: drtufancinar@gmail.com (T. Çinar).

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and Syntax Score II (SSII) (Wang et al., 2016). However, the majority of these scores are designed for the general population, and their predictive power for octogenarians has not been sufficiently elucidated.

The life expectancy of the population has increased and the ratio of octogenarians in the general population is expected to increase three-fold by 2050 due to improvements in health care (Centers for Disease Control & Prevention, 2003). Therefore, it is expected to encounter more elderly STEMI patients. Although the gold standard treatment of STEMI is pPCI, it may not result in an improved survival in elderly STEMI patients, unlike younger patients with STEMI (Claessen et al., 2010; Oduncu et al., 2013; Yamanaka et al., 2013). Many factors have been put forward to explain the inability of pPCI to achieve desired outcomes in the elderly. These include the presence of atypical symptoms, which result in delayed admission to the hospital (Brieger et al., 2004), in addition to an increased risk of bleeding, a reduction in the organ functions, and the presence of comorbidities (Alexander et al., 2005; Malkin, Prakash, & Chew, 2012). Considering the worse prognosis of elderly STEMI patients, an identifying the most suitable risk scoring system is crucial. This study evaluated the usefulness of SSII in predicting in-hospital and long-term (3.5 years) outcomes in octogenarians who presented with STEMI and were treated with pPCI in addition to compare the SSII with other well-known risk-scoring systems.

2. Materials and methods

2.1. Study population

A total of 325 consecutive STEMI octogenarians, who underwent pPCI between January 2010 and June 2016, at Kafkas University and Ataturk University, Turkey, were retrospectively enrolled in the study. STEMI was defined based on the following criteria: I-) a typical increase or decrease in cardiac biomarkers, II-) ongoing ischemic symptoms (within 12 h of presentation), III-) a newly developed left bundle-branch block pattern, or a new ST elevation in two or more contiguous leads, with readings of at least 0.2 mV in leads V1, V2, and V3 or at least 0.1 mV in the remaining leads (Steg et al., 2012). Of these patients, 33 patients were excluded for the following reasons: the presence of another disease with an expected survival of less than 1 year ($n = 8$), and the need of emergent coronary artery bypasses graft surgery or failed PCI ($n = 14$). Also, patients whose SS II was not calculated due to missing clinical and/or long-term follow-up data from hospital files were excluded from the study ($n = 11$). Thus, the final study consisted of 312 patients. Long-term follow-up data was obtained from hospital records and phone interviews. For patients who could not be reached, information was obtained from the National Institute of Statistics and the Registrar of Birth Records to determine whether they were deceased or not. The study protocol was reviewed and approved by the local ethics committee of Kafkas University, and it was conducted in accordance with the principles of the Declaration of Helsinki.

2.2. Data collection

Patient's medical history, baseline clinical as well as demographic characteristics were obtained from patient files. These files indicated that blood biochemical parameters had been measured, and a complete blood count had been obtained for all patients upon admission to the hospital. Blood samples had been re-tested with an interval of every 6 h for creatine kinase-myocardial band (CK-MB) and troponin T, until the peak levels were obtained. Left ventricular ejection fraction (LVEF) was defined as the postprocedural ejection fraction, and it was assessed using the modified version of Simpson's method. The Cockroft–Gault formula was used to determine the estimated glomerular filtration rate (eGFR) with a using laboratory results of blood samples obtained upon admission.

2.3. Angiographic analysis and calculation of risk scores

All coronary angiograms had been recorded using digital media for quantitative analysis of SS (Dicom-viewer; MedCom GmbH, Darmstadt, Germany). Two independent and experienced interventional cardiologists, who were blinded to all clinical data, analyzed the digital angiograms. In case of any disagreement, the final decision was made through use of a third independent cardiologist as a tie-breaker. Using the online SS calculator, version 2.1, each lesion with ≥ 1.5 mm in diameter, and $\geq 50\%$ stenosis was scored (*SYNTAX score calculator*, 2019; Sianos et al., 2005). The culprit lesions were scored using the angiographic views of the infarct-related artery before the intervention. The total occlusion was accepted as an absence of blood flow more than 3-months duration, as reported in a previous STEMI study (Magro et al., 2011a). SSII was calculated based on the two anatomical variables (SS and left main coronary artery [LMCA] disease) and six clinical variables (age, gender, chronic obstructive pulmonary disease [COPD], peripheral arterial disease [PAD], creatinine clearance, and LVEF), using the online calculator (Farooq et al., 2013). By using the TIMI flow grade, the coronary blood flow patterns before and after pPCI were classified as 0, 1, 2, or 3 (Gibson et al., 1996). TIMI thrombus grading scale, ranging from the grade 0 (no thrombus) to the grade 5 (a very large thrombus, causing vessel occlusion), was used to assess the thrombus burden. Patients with a grade 5 thrombus were reclassified from grade 0 to grade 4 after recanalization with a guide-wire or a small balloon (Gibson et al., 1996). The other clinical risk scores including GRACE (Granger et al., 2003), TIMI (Morrow et al., 2000), CADILLAC (Halkin et al., 2005), and PAMI (Addala et al., 2004) were calculated for each patient using clinical and angiographic characteristics.

2.4. Frailty assessment

In the study, we aimed to determine the potential impact of frailty on long term prognosis by using the FRAIL scale (not frail, pre-frail, and frail) (Abellan van Kan, Rolland, & Bergman, 2008). Additionally, a 5-Item Modified Frailty Index was used to assess comorbidity (Subramaniam, Aalberg, Soriano, & Divino, 2018). This index includes the following items: I-) congestive heart failure, II-) diabetes mellitus, III-) chronic obstructive pulmonary disease or pneumonia, IV-) partial or total dependence in daily living activities, and V-) hypertension requiring medication. The 5-item Modified Frailty Index was calculated for each patient by adding the number of factors present (possible score 0–5). Because of the retrospective design of the study and some missing clinical data, we were able to calculate aforementioned tests only for 221 patients.

2.5. Statistical analysis

The statistical analyses were performed using SPSS version 22.0 (SPSS Inc., Chicago, IL). With respect to data distribution and normality, the mean (± standard deviation) or median (0.25–0.75 percentiles) was used to express continuous variables, and a *t*-test or Mann–Whitney *U*-test was conducted to compare the variables. The categorical variables were presented as numbers (percentages), and compared using Fisher's exact test or a $\chi 2$-test. Multicollinearity between SSII and its components was assessed by the Eigen-value and condition index. Linearity was tested by interacting with the logarithmic transformation of each parameter itself. The Kaplan–Meier method was used to generate event-free survival curves, and the log-rank test was conducted to compare dissimilarities among the SSII groups. Risk factors for all-cause mortality were analyzed and derived using a univariate and multivariate Cox proportional hazard analyses. The association between the incidence of all-cause mortality and SSII was then assessed. A receiver operating curve (ROC) was utilized to derive the cut-off value of the SSII for predicting all-cause mortality. The DeLong method was performed to compare the AUC values of

Table 1
Demographic, clinical, and laboratory characteristics of all patients, patient groups of low and high SSII with P value.

	Total, n:312	Low SS[A] II, n:163	High SS[B] II, n:149	P value
Age, years	85.62 ± 4.57	84.74 ± 4.02	86.58 ± 4.94	0.002
Female gender, n (%)	147 (47.1)	49 (30.1)	98 (65.8)	< 0.001
Diabetes mellitus, n (%)	95 (30.4)	22 (13.5)	73 (49.0)	< 0.001
Hypertension, n (%)	190 (60.9)	86 (52.8)	104 (69.8)	0.002
COPD, n (%)	29 (9.3)	14 (8.6)	15 (10.1)	0.654
Peripheral arterial disease, n (%)	59 (18.9)	6 (3.7)	53 (35.6)	< 0.001
Hyperlipidemia, n (%)	97 (31.1)	45 (27.6)	52 (34.9)	0.165
Family history of CAD, n (%)	38 (12.2)	22 (13.5)	16 (10.7)	0.457
Smoking, n (%)	1 (0.3)	0 (0.0)	1 (0.7)	0.008
Anemia, n (%)	103 (33)	38 (23.3)	65 (43.6)	< 0.001
Acetylsalicylic acid, n (%)	7 (2.2)	2 (1.2)	5 (3.4)	0.205
B-Blocker, n (%)	22 (7.1)	12 (7.4)	10 (6.7)	0.823
ACE-inhibitor/ ARB n, (%)	97 (31.1)	50 (30.7)	47 (31.5)	0.869
Statin, n (%)	48 (15.4)	26 (16.0)	22 (14.8)	0.772
Killip class on admission, n (%) 1	232 (74.4)	135(82.8)	97(65.1)	
2	42 (13.5)	14 (8.6)	28 (18.8)	< 0.001
3	24 (7.7)	11 (6.7)	13 (8.7)	
4	14 (4.5)	3 (1.8)	11 (7.4)	
Systolic blood pressure, mmHg	136 ± 39	139 ± 35	131 ± 43	0.177
Heart rate, bpm	78 ± 19	77 ± 16	79 ± 22	0.118
White blood cell count, $x10^3/mm^3$	11.78 ± 4.01	10.86 ± 3.09	12.79 ± 4.62	< 0.001
Hemoglobin, g/dL	12.5 ± 1.9	12.8 ± 1.8	12.1 ± 1.9	0.001
Plasma glucose, mg/dL	142(114-187)	130 (103-154)	166 (130-222)	< 0.001
C-Reactive protein, mg/dL	13 (7.9-21)	11 (6.7-15.8)	17 (9-25.4)	< 0.001
Creatinine on admission, mg/dL	1.04 ± 0.57	0.88 ± 0.25	1.22 ± 0.75	< 0.001
eGFR, $mL/min/1.73m^2$	71.81 ± 26.27	83.93 ± 23.39	58.56 ± 22.65	< 0.001
CK-MB, ng/mL	174 (98-329)	131(78-209)	288 (144-411)	< 0.001
Left ventricular EF, (%)	45.54 ± 8.73	49.88 ± 6.91	40.78 ± 8.02	< 0.001

Continuous variables are presented with mean ± standard deviation or median, nominal variables are presented with frequency. [A]: SS ≤ 43.6, [B]: SS > 43.6.**Abbreviations**: SS: Syntax Score, COPD: Chronic Obstructive Lung Disease, CAD: Coronary Artery Disease, ACE: Angiotensinogen Converting Enzyme, ARB: Angiotensinogen Receptor Blocker, eGFR: Estimated glomerular filtration rate, CK-MB: Creatinine Kinase Myocardial Band, EF: Ejection Fraction.

different risk scores (DeLong, DeLong, & Clarke-Pearson, 1988). A *p*-value < 0.05 indicated statistical significance.

3. Results

The study population consisted of 312 STEMI patients (mean age: 85 ± 4.5 years; 47.5% female) who underwent pPCI. The SSII of the patients ranged from 22 to 80 (median 43.6). The patients were divided into two groups according to median SSII values: a low SSII group (SSII ≤ 43.6, $n = 163$ patients) and a high SSII group (SSII > 43.6, $n = 149$). Baseline characteristics of all the patients and those with a low and high SSII are shown in Table 1. Patients in a high SSII group were older, and female gender was more common. Patients in a high SSII group also had a higher prevalence of hypertension, anemia, diabetes mellitus, PAD, smoking, and Killip class > 1 as well as higher values of white blood cell (WBC) count, creatinine, plasma glucose, peak CK-MB, and C-reactive protein (CRP) than those in a low SSII group. Furthermore, patients in a high SSII group had lower levels of hemoglobin, eGFR, and LVEF than those in a low SSII group (Table 1).

Angiographic and interventional characteristics of the patients were studied and compared between the high SSII and low SSII groups. The symptom-balloon time was longer in a high SSII group, and this group had more frequent imperfect post-PCI flow findings such as a higher corrected TIMI frame count and higher post-wiring thrombus grade. In addition, the incidence of left anterior descending (LAD) as the infarct-related artery, proximal/ostial localization of the culprit lesion, the implantation of longer stents, and three-vessel disease were more frequent in a high SSII group. The SS was higher in a high SSII group. LMCA lesions, chronic total occlusion, and frequency of drug-eluting stent/bare-metal stent use were similar between two groups. The TIMI, CADILLAC, PAMI, and GRACE risk scoring systems were found to be higher in a high SSII group (Table 2).Besides that, the 5-Item Modified Frailty Index was significantly elevated in patients with a high SS II, while the FRAIL scale, that was defined as not frail, pre-frail, and frail, was not different between the groups.

During an average follow-up of 44.3 months, 85 (27.2%) deaths were occurred. The rate of in-hospital mortality was significantly higher among patients in a high SSII group compared to those in a low SSII group ($n = 31$, 20.8% vs. $n = 2$, 1.2%; $p < 0.001$). The Kaplan–Meier survival curve analysis for in-hospital mortality is shown in Fig. 1. The incidence rate of long-term mortality was significantly higher in patients with a higher SSII than those with a lower SSII ($n = 67$, 45.0% vs. $n = 18$, 11%; $p < 0.001$; Fig. 2).

A Cox regression model was used to determine independent predictors of long-term mortality using parameters found to be associated with mortality in a univariate analysis (age, Killip class > 1, CRP, eGFR, peak CK-MB, COPD, post-pPCI TIMI flow < 3, LVEF, and basal SS and SSII). We noted that there was no multicollinearity between SSII and its continuous parameters (SS, age, LVEF, eGFR); hence they were included into multivariate regression analysis together with SSII. Also, the 5-Item Modified Frailty Index and the FRAIL scale were not included in this model. In the multivariate analysis, independent predictors of long-term mortality were eGFR (hazard ratio [HR]: 0.984, 95% CI: 0.971-0.997; $p = 0.019$), LVEF (HR: 0.924, 95% CI: 0.888-0.962; $p < 0.0001$) and SS II as per point (HR: 1.036; 95% CI: 1.005–1.068; $p = 0.024$), and these variables were shown in Table 3.

Table 4 shows a multivariate Cox regression analysis for long term mortality in patients whose 5-Item Modified Frailty Index and the FRAIL scale were calculated. Notably, SS II remained an independent predictor of long term mortality after inclusion of abovementioned frailty tests (HR: 1.039, 95% CI: 1.002–1.077; $p = 0.039$).

In the ROC curve analysis, the area under the curve (AUC) of SSII was 0.807 ($p < 0.001$, 95% CI: 0.750–0.863). The optimal cut-off value of SSII for all-cause long-term mortality was found to be49.76

Table 2
Coronary angiographic, interventional characteristics and risk score values of all patients, patient groups of low and high Syntax score (SS) II with P value.

	Total, n:312	Low SS[A] II, n:163	High SS[B] II, n:149	P value
Door to balloon time, min	31 ± 7	31 ± 7	32 ± 8	0.093
Total ischemia time, min	209 (131.5-312)	192 (118-262)	245 (162-328)	0.001
Infarct-related artery of LAD, n (%)	146 (46.8)	65 (39.9)	81 (54.4)	0.023
Proximal/ostial lesion for IRA, n (%)	177 (56.7)	74 (45.4)	103 (69.1)	< 0.001
High-grade thrombus burden, n (%)	200 (64.1)	86 (52.8)	114 (76.5)	< 0.001
Stent type BMS, n (%)	280 (94.9)	148 (94.9)	132 (95)	0.960
DES, n (%)	14.0 (4.7)	7 (4.5)	7 (5)	
Stent length, mm	22.55 ± 9.77	21.91 ± 9.64	23.26 ± 9.89	0.040
Stent diameter, mm	3.06 ± 0.39	3.04 ± 0.36	3.08 ± 0.41	0.530
Corrected TIMI frame count	24 (19-33)	21 (17-28)	27 (22-36)	< 0.001
No-reflow, n (%)	63 (20.2)	20 (12.3)	43 (28.9)	< 0.001
Left main coronary artery, n (%)	8 (2.6)	4 (2.5)	4 (2.7)	0.900
Three vessel disease, n (%)	47 (15.1)	17 (10.4)	30 (20.1)	< 0.001
Chronic total occlusion, n (%)	22 (7.1)	10 (6.1)	12 (8.1)	0.510
TIMI risk score	5 ± 2	4 ± 2	5 ± 2	< 0.001
GRACE risk score	190.34 ± 31.94	182.37 ± 23.7	199.06 ± 37.19	< 0.001
CADILLAC risk score	6.41 ± 3.91	4.33 ± 2.56	8.69 ± 3.87	< 0.001
PAMI risk score	9.26 ± 2.2	8.55 ± 1.75	10.05 ± 2.38	< 0.001
Basal SS	17.28 ± 5.36	15.97 ± 5.04	18.71 ± 5.34	< 0.001
Basal SSII	43.64 ± 11.65	34.72 ± 5.02	53.39 ± 8.61	< 0.001
5-Item Modified Frailty Index*	1 ± 0.78	0.78 ± 0.67	1.31 ± 0.83	< 0.001
The FRAIL[#] scale				
Not frail, n (%)	55 (24.9)	28 (21.5)	27 (29.7)	
Pre-frail, n (%)	134 (60.6)	85 (65.4)	49 (53.8)	0.179
Frail, n (%)	32 (14.5)	17 (13.1)	15 (16.5)	
In-hospital mortality, n (%)	33(10.5)	2 (1.2)	31 (20.8)	< 0.001
Long term mortality, n (%)	85 (27.2)	18 (11)	67 (45)	< 0.001

Continuous variables are presented with mean ± standard deviation or median, nominal variables are presented with frequency. [A]: Syntax Score ≤ 43.6, [B]: Syntax Score > 43.6.[*]: 5-Item Modified Frailty Index was calculated only for 221 patients. [#]: The FRAIL[#] scale was calculated only for 221 patients. **Abbreviations**: LAD: Left Anterior Descending; IRA: Infarct Related Artery; BMS: Bare Metal Stent; DES: Drug Eluting Stent, SS: Syntax Score, SS II: Syntax Score II, TIMI: Thrombolysis in Myocardial Infarction, GRACE: Global Registry of Acute Coronary Events, CADILLAC: Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications, PAMI: Primary Angioplasty in Myocardial Infarction.

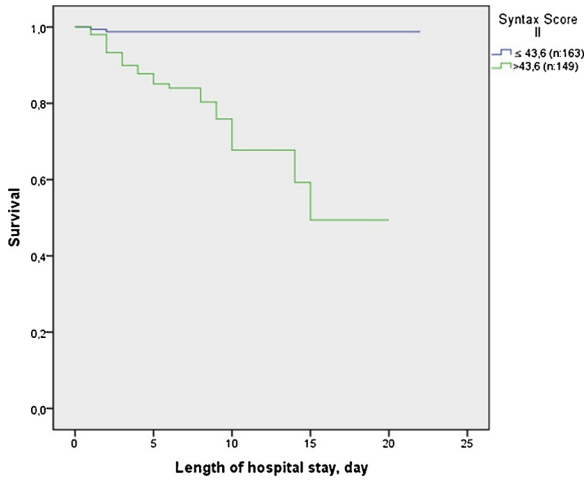

Fig. 1. In-hospital Kaplan–Meier survival curve analysis of patients with a low and high SSII.

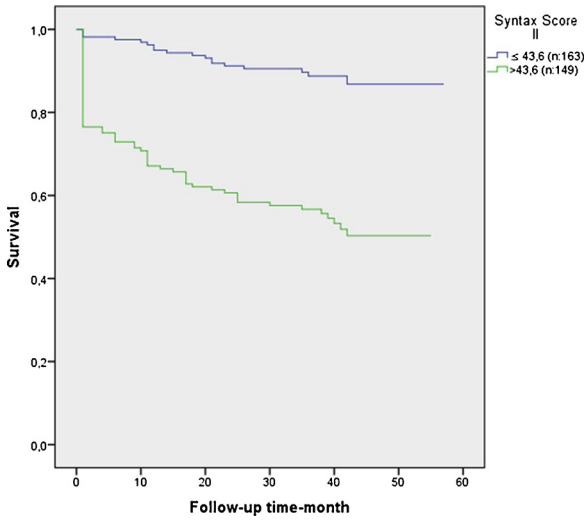

Fig. 2. Long-term Kaplan–Meier survival curve analysis of patients with a low and high SSII.

with 85.5% sensitivity and 61.18% specificity. An ROC curve comparison analysis was performed to compare the different risk scores. The SSII was a better predictor than SS (AUC: 0.644, 95% CI: 0.572–0.716), TIMI risk score (AUC: 0.658, 95%CI: 0.586–0.730), and PAMI risk score (AUC: 0.652, 95%CI: 0.587–0.718) ($p < 0.001$ for each comparison). The SSII was also a better predictor than the GRACE risk score (AUC: 0.689, 95%CI: 0.620–0.788; $p = 0.007$). However, there was no significant difference between the SS II and CADILLAC risk score (AUC: 0.807, 95% CI: 0.750–0.863 vs. AUC: 0.798, 95% CI: 0.741–0.855; $p = 0.975$). In predicting long-term mortality, the CADILLAC risk score was better than the SS, TIMI, PAMI ($p < 0.001$ for each comparison), and GRACE scoring systems ($p = 0.002$), as illustrated in Fig. 3.

4. Discussion

In this study, the association of SSII with in-hospital and long-term mortality was evaluated in octogenarians who presented with STEMI and were treated with pPCI. The main finding of this study was that SSII was an independent predictor of both in-hospital and long-term

Table 3
Adjusted and unadjusted hazards ratios of all patients for long term mortality*.

	Univariate analysis of long term mortality			Multivariate analysis of analysis of long term mortality		
	Hazard ratio	95% C.I.	P value	Hazard ratio	95% C.I.	P value
Age	1.083	1.024-1.145	0.006	–	–	–
COPD	2.260	1.105-4.625	0.026	–	–	–
Killip class	2.145	1.226-3.753	0.007	–	–	–
C-Reactive protein	1.043	1.022-1.064	< 0.001	–	–	–
Peak CK-MB	1.005	1.003-1.007	< 0.001	–	–	–
Post-pPCI TIMI flow < 3	2.141	1.180-3.887	0.012	–	–	–
SS	1.044	1.002-1.087	0.039	–	–	–
eGFR	0.976	0.964-0.988	< 0.001	0.984	0.971-0.997	0.019
Left ventricle EF	0.910	0.880-0.942	< 0.001	0.924	0.888-0.962	< 0.001
SSII	1.081	1.055-1.107	< 0.001	1.036	1.005-1.068	0.024

* 5-Item Modified Frailty Index and the FRAIL scale were not included in this model because of missing clinical data. **Abbreviations**: COPD: Chronic Obstructive Lung Disease, CK-MB: Creatinine Kinase Myocardial Band, pPCI: Primary Percutaneous Coronary Intervention, TIMI: Thrombolysis in Myocardial Infarction, SS: Syntax Score, eGFR: Estimated glomerular filtration rate, EF: Ejection Fraction, SSII: Syntax Score II.

mortality in octogenarians. When compared to the other risk scoring systems, SSII and CADILLAC were superior to other well-known risk scores but not superior to each other.

Octogenarians constitute a fast-growing portion of cardiovascular patients. According to a previously published study, the rate of pPCI in octogenarians has increased from 3.5% in 1997 to 8.8% in 2007 (Claessen et al., 2010). As the life expectancy will further increase in the future, it may be assumed that more elderly people will suffer from STEMI. As it has been shown in previous studies that compared the outcomes of pPCI in older and younger age groups, the STEMI-related mortality rate of elderly patients is significantly higher than that of younger patients, (Claessen et al., 2010; Oduncu et al., 2013; Yamanaka et al., 2013). The in-hospital mortality rate of octogenarians in the present study was 10.5%, and the long-term mortality was 27.2%, which was consistent with the reported mortality rate of the previous studies that included elderly patients (Claessen et al., 2010; Oduncu et al., 2013; Yamanaka et al., 2013). Although many risk scoring systems have been derived from large cohorts and validated in several studies (Gibson et al., 1996; Granger et al., 2003; Halkin et al., 2005; Kozieradzka et al., 2011; Morrow et al., 2000), the prognostic ability of these systems have not been well-studied and validated in octogenarians who represent a high-risk group.

The SS is an anatomical scoring system, which indicates the severity of coronary artery disease (CAD) based on the number of lesions, along with their functional effects, location, and complexity (Sianos et al., 2005). Several studies showed that this scoring system is associated with short- and long-term mortality in STEMI patients (Kul et al., 2012; Magro et al., 2011a). However, a recent study demonstrated that the SSII, which is calculated from six clinical and two angiographic parameters, has a better prognostic accuracy than the SS for unselected elderly patients with CAD (Campos et al., 2012; Kurniawan et al., 2016). Another study reported that SSII was a suitable scale in risk stratifying and predicting long-term outcomes in patients with STEMI (Wang et al., 2016). Based on these study findings, we hypothesized

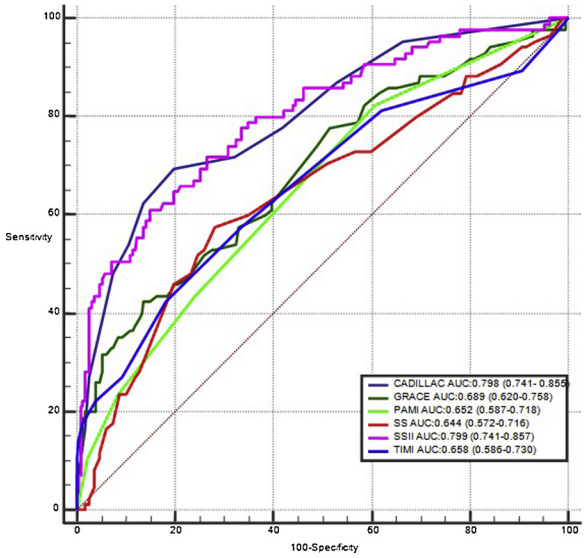

Fig. 3. ROC curves comparison to determine the best scoring system in predicting long-term mortality in octogenarians.

Table 4
Multivariate Cox regression analysis for long term mortality after inclusion of 5-Item Modified Frailty Index and the FRAIL scale&.

	Univariate analysis of long term mortality			Multivariate analysis of analysis of long term mortality		
	Hazard ratio	95% C.I.	P value	Hazard ratio	95% C.I.	P value
COPD	2.414	1.176-4.956	0.016	2.350	1.132-4.880	0.22
Peak CK-MB	1.002	1.001-1.003	0.001	–	–	–
The FRAIL scale	1.448	1.106-1.894	0.007	1.353	1.028-1.782	0.031
Total ischemia time	1.002	1.000-1.004	0.048	–	–	–
eGFR	0.976	0.964-0.988	< 0.001	0.983	0.969-0.996	0.024
Left ventricle EF	0.931	0.900-0.963	< 0.001	0.945	0.904-0.988	0.013
SSII	1.078	1.053-1.104	< 0.001	1.039	1.002-1.077	0.039

& This model included only 221 patients whose 5-Item Modified Frailty Index and the FRAIL scale were calculated. **Abbreviations**: COPD: Chronic Obstructive Lung Disease, CK-MB: Creatinine Kinase Myocardial Band, eGFR: Estimated glomerular filtration rate, EF: Ejection Fraction, SSII: Syntax Score II.

that SSII might be a powerful prognostic tool in determining all-cause mortality among elderly STEMI patients who have potentially different characteristics compared to younger patients. The results of the present study showed that reduced eGFR, LVEF and SSII were independent predictors of long-term all-cause mortality. The role of SSII as an independent predictor of long-term mortality can be attributed largely to its parameters (e.g., advanced age, SS, reduced LVEF, and eGFR) that associated with long-term mortality (Akgun et al., 2015; Kurniawan et al., 2016; Oduncu et al., 2013; Yamanaka et al., 2013; Yazji et al., 2016). In addition, the high SSII group was characterized by higher inflammatory status (increased WBC and CRP), lower hemoglobin levels, longer total ischemia times, higher incidence of no-reflow, greater infarct sizes (increased peak CK-MB), proximal lesion locations, and elevated thrombus grades, all of which have been shown to be associated with a poor prognosis in STEMI patients (Liu et al., 2016; Ndrepepa et al., 2010; Ortolani et al., 2008; Yip et al., 2002).

Even in STEMI patients, where early treatment options are well-defined, an accurate risk classification plays a significant role due to its impact on early and late therapeutic decision-making (Lev et al., 2008). To facilitate the decision making, various risk scores, including TIMI, GRACE, CADILLAC, and PAMI, have been developed. Each of these risk scores has been derived from well-conducted large studies, and the efficacy of each study was proven in other studies. In the present study, we compared the prognostic efficacy of these scoring systems with that of SSII via an ROC curve comparison. The results revealed that the ability of SSII and CADILLAC to predict long-term all-cause mortality was superior to that of the other scoring systems. In addition, prior studies demonstrated that frailty was a strong outcome predictor for cardiovascular diseases in octogenarians (Vicent, Ariza-Sole, & Alegre, 2018; White, Westerhout, & Alexander, 2016). Allying with these previous studies, the FRAIL scale was also found to be an independent predictor of long-term mortality in the study. However, after the adjustment of this factor, SSII was still an independent predictor of long-term mortality in our study.

Our findings may be explained in several ways. First, all the scores predict relatively short-term (a maximum of 12 months) mortality, unlike the SSII, which predicts long-term mortality. Second, TIMI risk score is designed for patients who were treated with a fibrinolytic therapy, whereas the GRACE is designed for non-STEMI patients. Third, TIMI, GRACE, and PAMI do not include variables that reflect CAD severity in which previous studies showed that these variables might have a major effect on the long-term prognosis (Akgun et al., 2015). Finally, CADILLAC and SSII share two powerful common predictors, namely reduced eGFR and LVEF, both of which have been shown to be strongly associated with mortality in STEMI patients. All the aforementioned factors could be the reasons of our study findings.

Evaluating both CAD severity and clinical characteristics may be a good option in the elderly population, as comorbidity is important for this population. Although the current STEMI guidelines appear to emphasize the importance of GRACE and TIMI risk scoring systems, an evaluation of CAD severity may provide additional useful information in terms of prognosis.

4.1. Study limitations

The present study has several limitations. First, the study had a retrospective design, and it was conducted in two centers. Therefore, the data may not be extrapolated to patients from elsewhere; especially the outcomes may be related to the care process and post-discharge case management. Second, CAD severity was based only on a visual assessment and not on the extent of atherosclerosis (i.e., lumen area and plaque size, composition, and distribution). Third, some important outcome predictors such as baseline physical and cognitive functions well as mood status and nutritional status were not evaluated in the study. Finally, symptoms of myocardial infarction among the elderly may be atypical. Thus, some of the patients may not have been diagnosed in the first 12 h of presentation. Some patients may have died and not been admitted to the hospital or may have never been diagnosed. For these reasons, actual mortality may be higher than that observed in the study.

5. Conclusions

To the best of our knowledge, this study is the first in the literature to show that SSII is an independent predictor of in-hospital and long-term mortality in octogenarians who presented with STEMI and treated with pPCI. In this study, SS II and CADILLAC were superior compared to the other risk scoring systems in terms of predicting mortality. The prognostic value of SS II may be due to the inclusion of some clinical parameters, all of which are common in the elderly and have been related with increased mortality.

Compliance with ethical standards

All authors declare that they do not have conflicts of interest. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors. Informed consent was not needed because the study had a retrospective design.

Declaration of conflicting interests

The authors declare they have no conflicts of interest.

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