Int J Cardiovasc Sci. 2024; 37:e20220137

ORIGINAL ARTICLE

Determination of Shock Index and Age Shock Index Cut-Off Points in Patients with ST-Segment Elevation Myocardial Infarction: SEMI-CI Study

Masoumeh Sadeghi,[1] Afsaneh Rahimizad,[2] Mehrbod Vakhshoori,[3] Niloofar Bondariyan,[4] Shima Nasirian,[5] Davood Shafie[6]

Cardiac Rehabilitation Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences,[1] Isfahan - Iran
Heart Failure Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences,[2] Isfahan - Iran
Heart Failure Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences,[3] Isfahan - Iran
Department of Clinical Pharmacy, School of Pharmacy, Shiraz University of Medical Sciences,[4] Shiraz - Iran
Isfahan Cardiovascular Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences,[5] Isfahan - Iran
Heart Failure Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences,[6] Isfahan - Iran

Abstract

Background: Shock index (SI) and age shock index (ASI) are less frequently used for assessment of major adverse cardiovascular events (MACE) among patients with ST-segment elevation myocardial infarction (STEMI), and their reported cut-off points are controversial.

Objectives: We aimed to define proper cut-off value of these indices for MACE prediction among Iranian patients with STEMI.

Methods: This study was in the context of the ST-Elevation Myocardial Infarction Cohort in Isfahan (SEMI-CI) study. SI and ASI were calculated by division of heart rate (HR) over systolic blood pressure (SBP) and age multiplied by SI, respectively, in 818 subjects with STEMI. Receiver operating characteristic (ROC) curve analysis was used to determine optimal SI and ASI cut-off values. Chi-square test, independent t test, and analysis of variance were employed for nominal and numerical variables, as appropriate, with consideration of p values < 0.05. MACE was defined as a composite of non-fatal reinfarction, heart failure (HF), recurrent percutaneous intervention (PCI), rehospitalization for cardiovascular diseases, and all-cause mortality.

Results: Mean age was 60.70 ± 12.79 years (males: 81.7%). Area under curve (AUC) values from ROC curve analysis for SI and ASI were 0.613 (95% confidence interval [CI]: 0.569 to 0.657, p < 0.001) and 0.672 (95% CI: 0.629 to 0.715, p < 0.001), respectively. Optimal SI and ASI cut-offs were 0.61 (sensitivity: 61%, specificity: 56%) and 39.5 (sensitivity: 65%, specificity: 66%), respectively. Individuals with SI ≥ 0.61 or within the highest quartile (SI ≥ 0.75) had significantly higher frequency of one-year MACE compared to the reference group (34.7% versus 22.2%, p < 0.001 and 42.4% versus 20.6%, p < 0.05, respectively). Similar relations were observed in terms of ASI values (ASI ≥ 39.5 versus ASI < 39.5: 43.6% versus 17.3%, p < 0.001, ASI Q4 ≥ 47.5 versus ASI Q1 ≤ 28.8: 49% versus 16.6%, p < 0.05).

Conclusions: SI and ASI cut-off values of 0.61 and 39.5 could reliably predict MACE occurrence among Iranian patients with STEMI.

Keywords: Myocardial Infarction; Sensitivity and Specificity; ROC Curve; Area Under Curve.

Introduction

ST-elevation myocardial infarction (STEMI) mostly happens when complete occlusion occurs in one or more coronary arteries. Family history of coronary artery disease, *increasing age, smoking,* diabetes mellitus (DM), and hypertension are among the top STEMI risk factors.

STEMI leads to symptoms of myocardial ischemia along with elevated cardiac biomarker levels, such as troponin, and electrocardiographic changes.[1,2] Epidemiological data

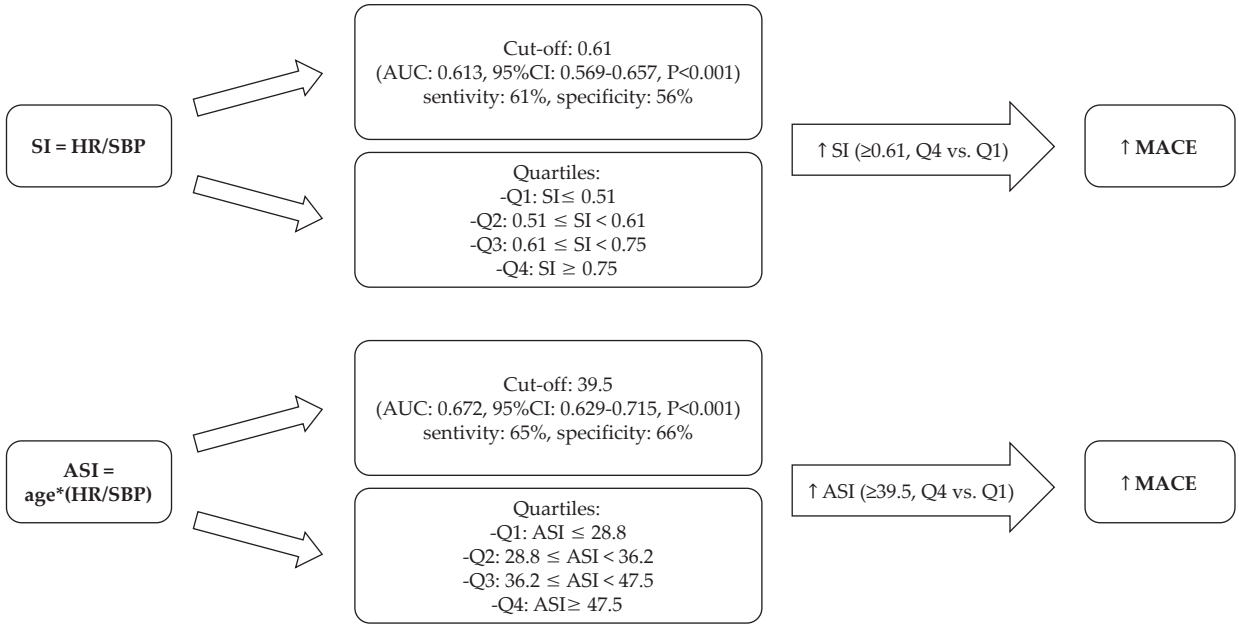
Mailing Address: Davood Shafie
Isfahan University of Medical Sciences. Hezar Jarib Ave. Postal code: 81746-73461. Isfahan – Iran
E-mail: d.shafie87@gmail.com
Editor responsible for the review: Alexandra Arias-Mendoza

DOI: https://doi.org/10.36660/ijcs.20220137

Manuscript received August 29, 2022; revised manuscript January 26, 2024; accepted May 6, 2024.

Central Illustration: Determination of Shock Index and Age Shock Index Cut-Off Points in Patients with ST-Segment Elevation Myocardial Infarction: SEMI-CI Study

INTERNATIONAL JOURNAL OF Cardiovascular SCIENCES



Int J Cardiovasc Sci. 2024; 37:e20220137

Summary characteristics of SI and ASI and their associations with MACEs ASI: age shock index; AUC: area under curve; CI: confidence interval; HR: heart rates; MACE: major adverse cardiovascular events; SBP: systolic blood pressure; SI: shock index.

showed that about one third of all patients with acute coronary syndrome suffered from a STEMI.[3]

Although STEMI incidence and case fatality rate have decreased in recent years,[4] the number of patients living with myocardial infarction (MI) complications is increasing due to population aging.[5,6] These complications, such as *recurrent MI*, frequent rehospitalization, and death, are more common in patients with STEMI than those with non-ST-segment elevation MI. [3] An important factor of morbidity and mortality in STEMI patients is major adverse cardiovascular events (MACE).[7] MACE include non-fatal reinfarction, heart failure (HF), recurrent percutaneous coronary intervention (PCI), rehospitalization for cardiovascular diseases, and all-cause mortality.[1,8-10]

High-risk patient selection and proper risk management should be conducted immediately after patient admission in order to achieve an important reduction in MACE.[11,12] The thrombolysis in myocardial infarction (TIMI) and global registry of acute coronary events (GRACE) scores are risk stratification methods used to identify high-risk patients and evaluate their risk of mortality. However, these scores are complicated to calculate and difficult to use at the bedside.[2,13-15]

The shock index (SI), which is the ratio of heart rate (HR) to systolic blood pressure (SBP), is an easy-to-use bedside tool to estimate prognosis in STEMI.[11] SI has been initially applied in hypovolemic shock, especially in sepsis. Afterwards, its application has been widened in any other critical care conditions.[16-18] The normal *accepted* range of SI is 0.5 to 0.7 in healthy adults.[19] Age shock index (ASI), a derivative of SI, is calculated by multiplying age by SI, and it has been reported to enhance the prognostic value of SI.[20]

Clinical studies have applied different cut-off points for SI to evaluate its predictive power. It has recently been demonstrated that elevated admission SI (SI ≥ 0.7) is related to increased 7-day and 30-day all-cause mortality.[21] SI value ≥ 0.66 has also been reported as an independent prognosticator of MACE.[20] Another study revealed that the value of SI before PCI in STEMI patients can be among the important predictors of long-term mortality.[22]

This study aimed to determine SI and ASI cut-off points in patients presenting with STEMI to evaluate one-year MACE prediction.

Methods

This observational study was in the context of the ST-Elevation Myocardial Infarction Cohort in Isfahan (SEMI-CI) study.[23] Between March 2016 and February 2017, patients presenting with STEMI referred from other affiliated hospitals or directly admitted to a tertiary heart center were eligible to be enrolled. Patients *younger than 18* years old with medical conditions other than STEMI or lack of P waves on their electrocardiogram (ECG) during hospital admission were excluded, and a total of 818 patients with STEMI were finally included in this study.

Before initiating enrollment, the principal investigator fully explained the project in simple terms to all participants, and any questions related to the project were thoroughly answered. Participants were completely free to discontinue the project, and they signed the informed consent forms. This study was conducted in accordance with the *Declaration* of *Helsinki* Ethical Principles.

Baseline data were collected, including male/female sex, age, body mass index (BMI), smoker/non-smoker status, and past medical history including previous cardiovascular diseases, history of treated hypertension, hypercholesterolemia, and DM.

Hypercholesterolemia, as one of the important risk factors for cardiovascular disease, was defined as total cholesterol > 200 mg/dl with normal plasma triglycerides or taking lipid-lowering agents. DM was defined as fasting blood sugar ≥ 126 mg/dl or HbA1c ≥ 6.5% or taking anti-diabetic medications.

HR, SBP, hemoglobin (Hb), and blood sugar levels were measured, and Killip class was registered soon after hospital admission. SI and ASI were obtained from patient's HR, SBP, and age during hospital admission.

The diagnosis of STEMI was established through analysis of ECG findings and troponin levels. Specifically, the presence of new ST elevation at the J point in two contiguous leads, with criteria of > 0.1 mV in all leads except V2-V3, and cut-off points of ≥ 0.25 mV in men < 40 years, ≥ 0.2 mV in men ≥ 40 years, and ≥ 0.15 mV in women for leads V2-V3, indicates STEMI on the ECG of affected patients. Additionally, an elevation in troponin levels up to the 99th percentile of the reference value was utilized as another indicator of STEMI diagnosis.[24,25]

In order to evaluate coronary artery flow, TIMI flow grade was used before and after PCI. In this study, group 1 consisted of patients with TIMI flow grade 0 and 1; patients with partial and complete perfusion who belonged to grades 2 and 3 were included in group 2.

Medical treatment included reperfusion strategies, dual antiplatelet therapy with aspirin and clopidogrel, anticoagulant agents (heparin or low molecular weight heparin, such as enoxaparin or bivalirudin), sublingual or intravenous nitrates, beta-blockers, and morphine. PCI was performed for all recruited patients, regardless of TIMI flow grade.

The length of follow-up period was one year after hospital discharge, and clinical visits and/or phone interviews were conducted accordingly. The endpoint evaluated was incidence of one-year MACE. MACE was defined as a composite of non-fatal reinfarction, heart failure (HF), recurrent percutaneous intervention (PCI), rehospitalization for cardiovascular diseases, and all-cause mortality.

Statistical analysis

Normality of the data was assessed through Kolmogorov–Smirnov test. Categorical and continuous variables were reported as frequency (percentage) and mean ± standard deviation, respectively. Chi-square and independent t test/analysis of variance (ANOVA) with least significant difference post-hoc tests were utilized to analyze nominal and numerical variables across different categories of SI and ASI, respectively. We used receiver operating characteristic (ROC) curves to find the optimal SI and ASI cut-off points using the Youden index. Our data were also analyzed based on SI and ASI quartiles. We evaluated the distribution of MACE based on SI and ASI pre-defined cut-off points and quartiles. No predictive model was used, and their validation was not performed. Statistical Package for Social Sciences (SPSS Inc., version 22.0, Chicago, IL, USA) was used to perform all analyses, and p values < 0.05 were defined as statistically significant.

Results

We enrolled 818 subjects after applying inclusion and exclusion criteria. The total population had a mean age of 60.70 ± 12.79 years. More than 80% of the study sample were males, and 233 (28.5%) patients experienced MACE during the follow-up. The results of the Kolmogorov–Smirnov test were in favor of normal distribution of pre-defined variables. Area under curve (AUC) values from ROC curve analysis

for SI and ASI were 0.613 (95% confidence interval [CI]: 0.569 to 0.657, p < 0.001) and 0.672 (95% CI: 0.629 to 0.715, p < 0.001), respectively (Figure 1 A and B). The optimal SI cut-off value for predicting MACE was 0.61 (sensitivity: 61%, specificity: 56%, positive predictive value: 57%, negative predictive value: 58%, Youden index: 0.17). Likewise, the optimum ASI cut-off was 39.5, with a sensitivity of 65% and specificity of 66%. Positive and negative predictive values were both 66%, with Youden index of 0.32. Characteristics of our study population based on SI cut-off value and quartiles are displayed in Table 1. Patients with SI of at least 0.61 had higher prevalence of DM and untreated hypertension. In terms of para-clinical data, HR and glucose were significantly elevated in the SI ≥ 0.61 group in comparison to the other group, and patients had higher prevalence of Killip class IV. On the other hand, SBP and Hb were significantly lower in patients with higher SI values compared to the lower group.

Further analysis with post-hoc tests stratified by SI quartiles revealed that patients within the highest SI quartile (SI ≥ 0.75) had a significantly higher prevalence of DM, increased glucose levels, and worse Killip class compared to patients with SI ≤ 0.51. In contrast, Hb was lower in the last quartile than in the first one. An increase in SI quartile was associated with a statistically significant decrease in SBP and increase in HR, in each quartile.

Table 2 shows the properties of patients according to ASI cut-off point and quartiles. Participants in the higher ASI category were mostly older females with increased frequency of DM, as well as higher HR and glucose means. Killip class IV was mostly observed among patients with ASI of at least 39.5. Furthermore, worse TIMI flow before PCI was mostly observed among those with higher ASI cut-off values. We also analyzed our data based on ASI quartiles using least significant difference post-hoc test. An increase in each ASI quartile was associated with a significant increase in mean age and HR. On the contrary, SBP decreased significantly as ASI quartiles increased. Individuals within the third and fourth ASI quartiles were mostly nonsmoking females with lower BMI and Hb levels, in comparison to ASI ≤ 28.8. However, they had a higher prevalence of DM history and abnormal blood glucose ranges.

The distribution of MACE according to SI and ASI cut-off values and quartiles is displayed in Table 3. Patients who had SI and ASI values above pre-defined cut-off points experienced more adverse cardiac outcomes in comparison to those with lower ranges. Our further analysis according to SI and ASI quartiles revealed similar outcomes; among subjects within the fourth SI quartile (SI ≥ 0.75) and ASI quartile (ASI ≥ 47.5), MACE was observed more frequently than in those within the respective first quartiles.

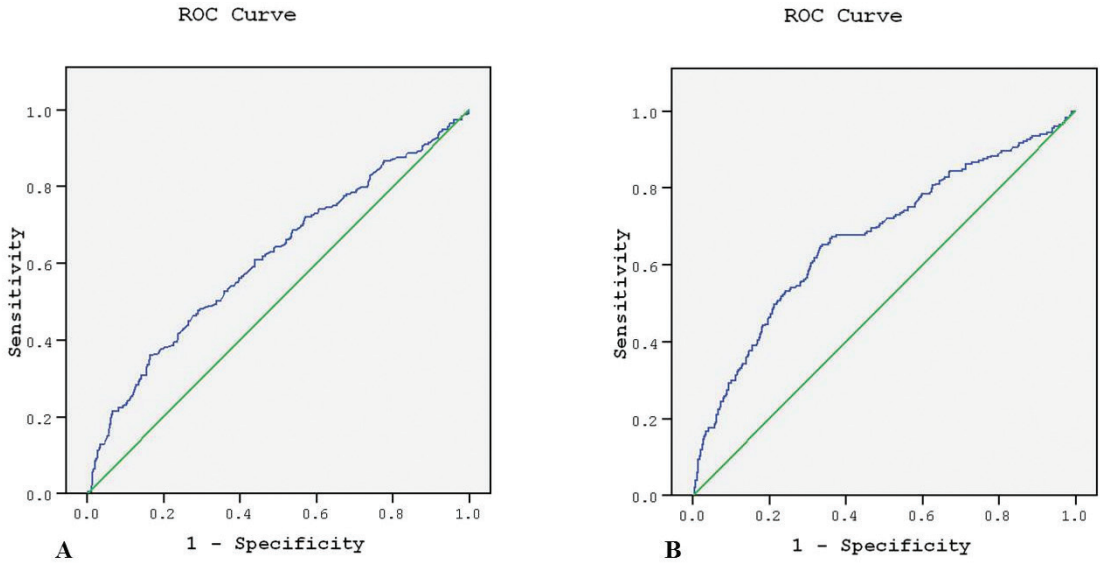


Figure 1 – ROC curve analysis of SI (A) and ASI (B) for prediction of MACE occurrence.
ASI: age shock index; MACE: major adverse cardiovascular events; ROC: receiver operating characteristic; SI: shock index.

Table 1 – General and laboratory characteristics and drug history of the study population according to SI cut-off point and quartiles

Variables		Total (n = 818)	SI cut-off		P	SI quartiles				P
			<0.61 (n = 409)	≥0.61 (n = 409)		Q1 (SI≤0.51) (n = 170)	Q2 (0.51<SI<0.61) (n = 218)	Q3 (0.61≤SI<0.75) (n = 220)	Q4 (SI≥0.75) (n = 210)	
Age (years)		60.70±12.79	61.01±12.66	60.38±12.93	0.485	61.72±12.01	60.38±12.97	58.71±12.83	62.28±12.97	0.021
Male (%)		668(81.7)	338(82.6)	330(80.7)	0.470	143(84.1)	176(80.7)	191(86.8)	158(75.2)	0.015
BMI (kg/m²)		26.30±4.11	26.42±4.08	26.19±4.15	0.468	26.58±4.29	26.25±3.93	26.70±4.07	25.68±4.16	0.105
Previous MI (%)		104(12.7)	49(12)	55(13.4)	0.529	13(7.6)	34(15.6)	24(10.9)	33(15.7)	0.048
Stroke (%)		45(5.5)	27(6.6)	18(4.4)	0.168	12(7.1)	13(6)	10(4.5)	10(4.8)	0.685
Current smoker (%)		326(39)	164(40.1)	162(39.6)	0.886	70(41.2)	86(39.4)	87(39.5)	83(39.5)	0.984
DM (%)		242(29.6)	105(25.7)	137(33.5)	0.014	39(22.9)	59(27.1)	68(30.9)	76(36.2)[C]	0.031
Hypercholesterolemia (%)		241(29.5)	126(30.8)	115(28.1)	0.399	42(24.7)	81(37.2)	55(25)	63(30)	0.017
Treated hypertension (%)		276(33.7)	154(37.7)	122(29.8)	0.018	72(42.4)	76(34.9)	60(27.3)[B]	68(32.4)	0.018
SBP (mmHg)		127.50±26.52	141.53±23.74	113.48±21.22	<0.001	152.77±24.40	134.71±19.74[A]	121.85±17.28[B]	105.49±21.35[C]	<0.001
HR (beats/min)		80.86±19.01	70.02±11.41	91.71±18.92	<0.001	64.98±10.14	73.65±11.11[A]	81.38±11.79[B]	100.67±20.07[C]	<0.001
Killip class (%)	I	758(92.7)	392(95.8)	366(89.5)	<0.001	165(97.1)	208(95.4)	206(93.6)	179(85.2)[C]	<0.001
	II	44(5.4)	16(3.9)	28(6.8)		5(2.9)	9(4.1)	11(5)	19(9)	
	III	3(0.4)	0	3(0.7)		0	0	0	3(1.4)	
	IV	13(1.6)	1(0.2)	12(2.9)		0	1(0.5)	3(1.4)	9(4.3)[C]	
TIMI flow in culprit vessel before PCI (%)	Group 1	555(68.7)	288(70.9)	267(66.4)	0.166	122(72.6)	153(70.5)	137(62.8)	143(69.8)	0.164
	Group 2	253(31.3)	118(29.1)	135(33.6)		46(27.4)	64(29.5)	81(37.2)	62(30.2)	
TIMI flow in culprit vessel after PCI (%)	Group 1	216(26.9)	105(26.1)	111(13.8)	0.573	40(23.8)	59(27.6)	58(26.6)	59(29.2)	0.701
	Group 2	586(73.1)	298(73.9)	288(72.2)		128(76.2)	155(72.4)	160(73.4)	143(70.8)	
Hb (g/dl)		14.32±1.86	14.49±1.70	14.15±2	0.010	14.48±1.71	14.50±1.70	14.43±1.75	13.87±2.18[C]	0.005
Glucose (mg/dl)		168.98±80.8	162.34±73.41	175.79±87.31	0.021	157.40±65	165.97±79.88	162.48±76.31	189.10±94.58[C]	0.002

BMI: body mass index; PCI: percutaneous coronary intervention; TIMI: thrombolysis in myocardial infarction; SI: shock index; DM: diabetes mellitus; MI: myocardial infarction; HR: heart rate; SBP: systolic blood pressure; Hb: hemoglobin. A: P values < 0.05 resulted from the comparison of Q1 versus Q2. B: P values < 0.05 resulted from the comparison of Q1 versus Q3. C: P values < 0.05 resulted from the comparison of Q1 versus Q4.

Table 2 – General and laboratory characteristics and drug history of the study population according to ASI cut-off point and quartiles

Variables		Total (n = 818)	ASI cut-off		P	ASI quartiles				P
			<39.5 (n = 469)	≥39.5 (n = 349)		Q1 (ASI≤28.8) (n = 187)	Q2 (28.8<ASI<36.2) (n = 206)	Q3 (36.2≤ASI<47.5) (n = 215)	Q4 (ASI≥47.5) (n = 210)	
Age (years)		60.70±12.79	55.30±11.35	67.95±10.90	<0.001	49.53±10.48	57.78±9.99[A]	65.04±10.14[B]	69.05±11.36[C]	<0.001
Male (%)		668(81.7)	409(87.2)	259(74.2)	<0.001	167(89.3)	182(88.3)	164(76.3)[B]	155(73.8)[C]	<0.001
BMI (kg/m^2)		26.30±4.11	26.79±4.06	25.56±4.09	<0.001	27.34±4.31	26.52±3.74	25.94±4[B]	25.38±4.18[C]	<0.001
Previous MI (%)		104(12.7)	52(11.1)	52(14.9)	0.112	19(10.2)	24(11.7)	26(12.1)	35(16.7)	0.227
Stroke (%)		45(5.5)	21(4.5)	24(6.9)	0.137	5(2.7)	10(4.9)	17(7.9)	13(6.2)	0.131
Current smoker (%)		326(39.9)	218(46.5)	108(30.9)	<0.001	98(52.4)	98(47.6)	57(26.5)[B]	73(34.8)[C]	<0.001
DM (%)		242(29.6)	117(24.9)	125(35.8)	0.001	36(19.3)	53(25.7)	79(36.7)[B]	74(35.2)[C]	<0.001
Hypercholesterolemia (%)		241(29.5)	137(29.2)	104(28.8)	0.855	48(25.7)	60(29.1)	67(31.2)	66(31.4)	0.573
Treated hypertension (%)		276(33.7)	141(30.1)	135(38.7)	0.011	58(31)	60(29.1)	78(36.3)	80(38.1)	0.173
SBP (mmHg)		127.50±26.52	136.62±24.56	115.26±24.03	<0.001	142.86±26.36	132.46±21.98[A]	128.13±22.79[B]	108.34±22.80[C]	<0.001
HR (beats/min)		80.86±19.01	72.49±12.89	92.12±20.10	<0.001	68.20±11.85	73.70±12.08[A]	81.31±13.78[B]	98.70±20.91[C]	<0.001
Killip class	I	758(92.7)	450(95.9)	308(88.3)	<0.001	182(97.3)	197(95.6)	203(94.4)	176(83.8)[C]	<0.001
	II	44(5.4)	16(3.4)	28(8)		5(2.7)	6(2.9)	11(5.1)	22(10.5)[C]	
	III	3(0.4)	0	3(0.9)		0	0	1(0.5)	2(1)	
	IV	13(1.6)	3(0.6)	10(2.9)		0	3(1.5)	0	10(4.8)[C]	
TIMI flow in culprit vessel before PCI (%)	Group 1	555(68.7)	302(64.9)	253(73.8)	0.008	129(69)	126(62.1)	153(72.2)	147971.4)	0.111
	Group 2	253(31.3)	163(35.1)	90(26.2)		58(31)	77(37.9)	59(27.8)	59(28.6)	
TIMI flow in culprit vessel after PCI (%)	Group 1	216(26.9)	108(23.3)	108(31.9)	0.007	45(24.1)	41(20.4)	62(29.5)	68(33.3)	0.018
	Group 2	586(73.1)	355(76.7)	231(68.1)		142(75.9)	160(79.6)	148(70.5)	136(66.7)	
Hb (g/dl)		14.32±1.86	14.71±1.62	13.78±2.03	<0.001	14.89±1.54	14.67±1.67	14.05±1.90[B]	13.71±2.04[C]	<0.001
Glucose (mg/dl)		168.98±80.80	158.91±74.73	183.30±86.84	<0.001	150.47±63.68	162.49±80.55	172.71±79.32[B]	189.57±92.20[C]	<0.001

BMI: body mass index; PCI: percutaneous coronary intervention; TIMI: thrombolysis in myocardial infarction; SI: shock index; ASI: age shock index; DM: diabetes mellitus; MI: myocardial infarction; HR: heart rate; SBP: systolic blood pressure; Hb: hemoglobin. A: P values < 0.05 resulted from the comparison of Q1 versus Q2. B: P values < 0.05 resulted from the comparison of Q1 versus Q3. C: P values < 0.05 resulted from the comparison of Q1 versus Q4.

Table 3 – Distribution of MACE according to SI and ASI cut-off points and quartiles

Variables	Total (n = 818)	SI cut-off		P	SI quartiles				P
		<0.61 (n = 409)	≥0.61 (n = 409)		Q1 (SI≤0.51) (n = 170)	Q2 (0.51<SI<0.61) (n = 218)	Q3 (0.61≤SI<0.75) (n = 220)	Q4 (SI≥0.75) (n = 210)	
MACE (%)	233(28.5)	91(22.2)	142(34.7)	<0.001	35(20.6)	51(23.4)	58(26.4)	89(42.4)[A]	<0.001
	Total (n = 818)	ASI cut-off		P	ASI quartiles				P
		<39.5 (n = 469)	≥39.5 (n = 349)		Q1 (ASI≤28.8) (n = 187)	Q2 (28.8<ASI<36.2) (n = 206)	Q3 (36.2≤ASI<47.5) (n = 215)	Q4 (ASI≥47.5) (n = 210)	
MACE (%)	233(28.5)	81(17.3)	152(43.6)	<0.001	31(16.6)	43(20.9)	56(26)	103(49)[A]	<0.001

MACE: major adverse cardiovascular events; SI: shock index; ASI: age shock index. A: P values < 0.05 resulted from the comparison of Q1 versus Q4.

Discussion

The current study aimed to evaluate the distribution of MACE according to SI and ASI cut-off points and quartiles. We found SI and ASI cut-off points of 0.61 and 39.5, respectively, for prediction of MACE. Moreover, STEMI patients with SI and ASI values above defined cut-off points and quartiles had increased likelihood of MACE occurrence. Summary characteristics of SI and ASI with their associations with MACE are displayed in the Central Figure.

Early identification of high-risk STEMI patients has a huge impact on prevention of cardiovascular complications. SI is one of the easiest bedside tools applied to evaluate the prognosis of STEMI patients. Due to its objective nature, SI is less susceptible to errors during assessment of patients.[19,21]

Although SI is widely used as a predicting factor in septic shock, pulmonary embolism, and some other critically ill patients,[16-18] only a few studies have considered the prognostic value of SI in patients with STEMI. These studies have applied different cut-off points for predicting STEMI complications. Bilkova et al. reported a significant risk of in-hospital mortality in patients with SI ≥ 0.8 (sensitivity: 75% and specificity: 61%).[26] Another study showed that SI ≥ 1 was directly related to in-hospital mortality and long-term morbidity in patients with STEMI undergoing primary PCI.[22] Huang et al. used SI cut-off value of 0.7 and demonstrated a higher risk of weekly all-cause mortality and MACE in patients with an admission SI ≥ 0.7 (p < 0.001).[21] The threshold for SI was 0.66 in the study by Abe et al., and they reported higher rate of one-year re-hospitalization and MACE in patients presenting with SI ≥ 0.66 (5.7% versus 1.6%, p = 0.011; 8.0% versus 2.8%, p = 0.007, respectively). They also reported higher Killip class in patients with an elevated SI at the time of hospital admission.[20] Reinstadler et al. used a cut-off value of 0.62 and found a higher risk of MACE in patients with SI ≥ 0.62. They also reported a higher Killip class on admission (p = 0.008) and a higher TIMI risk score (p < 0.001) among these patients.[16]

In this study including 818 STEMI patients, the optimal SI cut-off value for predicting MACE was shown to be 0.61 (sensitivity: 61%, specificity: 56%). The difference in MACE between the two groups was shown by a notably higher rate of HF, myocardial reinfarction, unstable angina, and stent thrombosis. Patients with an elevated SI had higher Killip class (2.9% versus 0.2%, p < 0.001). We also observed lower Hb levels in the group with SI ≥ 0.61, which Abe et al. previously reported for patients with SI ≥ 0.66.[20]

On the other hand, Supel et al. utilized a cut-off value of 1.1 for SI and reported no significant difference among the two groups of patients with co-occurrence of DM.[27] While, in our study, the prevalence of DM was higher among patients presenting with an elevated SI (33.5% versus 25.7%, p = 0.014), Boonsom et al. not only reported that a higher proportion of STEMI patients have DM, but they found an increased risk for adverse events including HF, arrhythmia, bleeding, and death among diabetic patients.[28] We also observed higher blood

glucose levels among patients with SI ≥ 0.61. Admission hyperglycemia is highly correlated with in-hospital and long-term mortality rates.[29] Following the acute phase of MI, a hyperadrenergic state results in hyperglycemia. This hyperadrenergic state causes an acute increase in free fatty acids, impaired glucose uptake by the myocardium,[30] and free oxygen radicals,[31] all of which may worsen myocardial ischemia.

The ASI is a more recent index derived from SI used to enhance the prognostic value of SI.[32] In a study by Yu et al., admission ASI ≥ 41 (with a sensitivity of 0.594 and a specificity of 0.722) was used to predict all-cause mortality in STEMI patients undergoing PCI.[33] In another study conducted by Zhou et al., the cut-off values for SI and ASI were 0.87 and 53.20, respectively. In multivariate analyses, they showed that the predictor values of ASI were comparable with GRACE score and superior to SI value for predicting in-hospital cardiovascular events, as well as 6-month and long-term all-cause mortality in STEMI patients undergoing emergency PCI.[32] We determined the ASI cut-off to be 39.5 with a sensitivity of 65% and specificity of 66% for predicting one-year MACE in our patients. Furthermore, patients with elevated ASI in our study had worse TIMI flow before PCI (73.8% versus 64.9%, p = 0.008).

Although this study was the first in the literature to assess appropriate SI and ASI cut-off points for MACE occurrence with adequate follow-up duration, several limitations should be considered. Our sample size was quite small, which might negatively affect our outcomes. Another disadvantage might be associated with the failure to assess the exact TIMI flow of the recruited patients. We implemented this study in a single center, which might be a limiting factor. However, proper time management of SI and ASI calculations in one center compared to multiple centers would probably cover this limitation. Finally, we only investigated SI and ASI cut-off points for MACE incidence, and other complications were not assessed.

Conclusions

This study showed that the optimal SI and ASI cut-off values of 0.61 and 39.5 are useful bedside tools for predicting MACE occurrence among patients with STEMI. They are easy to use, especially in low-income nations with limited sources. Multiple longitudinal studies are still required to clarify our findings.

Author Contributions

Conception and design of the research: Sadeghi M, Rahimizad A, Vakhshoori M, Shafie D; acquisition of data: Rahimizad A; analysis and interpretation of the data, writing of the manuscript and critical revision of the manuscript for intellectual content: Sadeghi M, Vakhshoori M, Bondariyan N, Nasirian S, Shafie D; statistical analysis: Nasirian S. Sadeghi M, Rahimizad A and Vakhshoori M contributed equally.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the Isfahan University of Medical Sciences under the protocol number IR.MUI.MED.REC.1399.1139. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

References

1. Poudel I, Tejpal C, Rashid H, Jahan N. Major Adverse Cardiovascular Events: An Inevitable Outcome of ST-elevation Myocardial Infarction? A Literature Review. Cureus. 2019;11(7):e5280. doi: 10.7759/cureus.5280.
2. O'Gara PT, Kushner FG, Ascheim DD, Casey DE Jr, Chung MK, Lemos JA, et al. 2013 ACCF/AHA Guideline for the Management of ST-elevation Myocardial Infarction: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2013;61(4):78-140. doi: 10.1016/j.jacc.2012.11.019.
3. Alnasser SM, Huang W, Gore JM, Steg PG, Eagle KA, Anderson FA Jr, et al. Late Consequences of Acute Coronary Syndromes: Global Registry of Acute Coronary Events (GRACE) Follow-up. Am J Med. 2015;128(7):766-75. doi: 10.1016/j.amjmed.2014.12.007.
4. Yamashita Y, Shiomi H, Morimoto T, Yaku H, Furukawa Y, Nakagawa Y, et al. Cardiac and Noncardiac Causes of Long-Term Mortality in ST-Segment-Elevation Acute Myocardial Infarction Patients Who Underwent Primary Percutaneous Coronary Intervention. Circ Cardiovasc Qual Outcomes. 2017;10(1):e002790. doi: 10.1161/CIRCOUTCOMES.116.002790.

5. Johansson S, Rosengren A, Young K, Jennings E. Mortality and Morbidity Trends after the First Year in Survivors of Acute Myocardial Infarction: A Systematic Review. BMC Cardiovasc Disord. 2017;17(1):53. doi: 10.1186/s12872-017-0482-9.

6. Moran AE, Forouzanfar MH, Roth GA, Mensah GA, Ezzati M, Flaxman A, et al. The Global Burden of Ischemic Heart Disease in 1990 and 2010: The Global Burden of Disease 2010 Study. Circulation. 2014;129(14):1493-501. doi: 10.1161/CIRCULATIONAHA.113.004046.

7. Wei Z, Bai J, Dai Q, Wu H, Qiao S, Xu B, et al. The Value of Shock Index in Prediction of Cardiogenic Shock Developed During Primary Percutaneous Coronary Intervention. BMC Cardiovasc Disord. 2018;18(1):188. doi: 10.1186/s12872-018-0924-z.

8. Hermans WR, Foley DP, Rensing BJ, Rutsch W, Heyndrickx GR, Danchin N, et al. Usefulness of Quantitative and Qualitative Angiographic Lesion Morphology, and Clinical Characteristics in Predicting Major Adverse Cardiac Events During and after Native Coronary Balloon Angioplasty. CARPORT and MERCATOR Study Groups. Am J Cardiol. 1993;72(1):14-20. doi: 10.1016/0002-9149(93)90211-t.

9. Keane D, Buis B, Reifart N, Plokker TH, Ernst JM, Mast EG, et al. Clinical and Angiographic Outcome Following Implantation of the New Less Shortening Wallstent in Aortocoronary Vein Grafts: Introduction of a Second Generation Stent in the Clinical Arena. J Interv Cardiol. 1994;7(6):557-64. doi: 10.1111/j.1540-8183.1994.tb00496.x.

10. Tsai IT, Wang CP, Lu YC, Hung WC, Wu CC, Lu LF, et al. The Burden of Major Adverse Cardiac Events in Patients with Coronary Artery Disease. BMC Cardiovasc Disord. 2017;17(1):1. doi: 10.1186/s12872-016-0436-7.

11. Abreu G, Azevedo P, Braga CG, Vieira C, Pereira MA, Martins J, et al. Modified Shock Index: A Bedside Clinical Index for Risk Assessment of ST-segment Elevation Myocardial Infarction at Presentation. Rev Port Cardiol. 2018;37(6):481-8. doi: 10.1016/j.repc.2017.07.018.

12. Hasdai D, Holmes DR Jr, Califf RM, Thompson TD, Hochman JS, Pfisterer M, et al. Global Utilization of Streptokinase and Tissue-Plasminogen Activator for Occluded Coronary Arteries. Am Heart J. 1999;138(1):21-31. doi: 10.1016/s0002-8703(99)70241-3.

13. García-Paredes T, Aguilar-Alonso E, Arboleda-Sánchez JA, Vera-Almazán A, Arias-Verdú MD, Oléa-Jiménez V, et al. Evaluation of Prognostic Scale Thrombolysis In Myocardial Infarction and Killip. An ST-elevation Myocardial Infarction New Scale. Am J Emerg Med. 2014;32(11):1364-9. doi: 10.1016/j.ajem.2014.08.026.

14. Fujii T, Suzuki T, Torii S, Murakami T, Nakano M, Nakazawa G, et al. Diagnostic Accuracy of Global Registry of Acute Coronary Events (GRACE) Risk Score in ST-elevation Myocardial Infarction for In-hospital and 360-day Mortality in Japanese Patients. Circ J. 2014;78(12):2950-4. doi: 10.1253/circj.cj-14-0808.

15. Moscucci M, Fox KA, Cannon CP, Klein W, López-Sendón J, Montalescot G, et al. Predictors of Major Bleeding in Acute Coronary Syndromes: The Global Registry of Acute Coronary Events (GRACE). Eur Heart J. 2003;24(20):1815-23. doi: 10.1016/s0195-668x(03)00485-8.

16. Reinstadler SJ, Fuernau G, Eitel C, Waha S, Desch S, Metzler B, et al. Shock Index as a Predictor of Myocardial Damage and Clinical Outcome in ST-Elevation Myocardial Infarction. Circ J. 2016;80(4):924-30. doi: 10.1253/circj.CJ-15-1135.

17. Tseng J, Nugent K. Utility of the Shock Index in Patients with Sepsis. Am J Med Sci. 2015;349(6):531-5. doi: 10.1097/MAJ.0000000000000444.

18. Toosi MS, Merlino JD, Leeper KV. Prognostic Value of the Shock Index Along with Transthoracic Echocardiography in Risk Stratification of Patients with Acute Pulmonary Embolism. Am J Cardiol. 2008;101(5):700-5. doi: 10.1016/j.amjcard.2007.10.038.

19. Berger T, Green J, Horeczko T, Hagar Y, Garg N, Suarez A, et al. Shock Index and Early Recognition of Sepsis in the Emergency Department: Pilot Study. West J Emerg Med. 2013;14(2):168-74. doi: 10.5811/westjem.2012.8.11546.

20. Abe N, Miura T, Miyashita Y, Hashizume N, Ebisawa S, Motoki H, et al. Long-Term Prognostic Implications of the Admission Shock Index in Patients With Acute Myocardial Infarction Who Received Percutaneous Coronary Intervention. Angiology. 2017;68(4):339-45. doi: 10.1177/0003319716653885.

21. Huang B, Yang Y, Zhu J, Liang Y, Tan H, Yu L, et al. Usefulness of the Admission Shock Index for Predicting Short-term Outcomes in Patients with ST-segment Elevation Myocardial Infarction. Am J Cardiol. 2014;114(9):1315-21. doi: 10.1016/j.amjcard.2014.07.062.

22. Spyridopoulos I, Noman A, Ahmed JM, Das R, Edwards R, Purcell I, et al. Shock-index as a Novel Predictor of Long-term Outcome Following Primary Percutaneous Coronary Intervention. Eur Heart J Acute Cardiovasc Care. 2015;4(3):270-7. doi: 10.1177/2048872614561480.

23. Sadeghi M, Soleimani A, Sarrafzadegan N, Askari M, Nouri F, Masoumi G, et al. Background and Design of a 5-year ST Elevation Myocardial Infarction Cohort in Isfahan, Iran: SEMI-CI Study. ARYA Atheroscler. 2021;17(3):1-7. doi: 10.22122/arya.v17i0.2375.

24. Givi M, Sarrafzadegan N, Garakyaraghi M, Yadegarfar G, Sadeghi M, Khosravi A, et al. Persian Registry Of cardioVascular diseasE (PROVE): Design and Methodology. ARYA Atheroscler. 2017;13(5):236-44.

25. Soleimani M, Soleimani A, Roohafza H, Sarrafzadegan N, Taheri M, Yadegarfar G, et al. The Comparison of Procedural and Clinical Outcomes of Thrombolytic-facilitated and Primary Percutaneous Coronary Intervention in Patients with acute ST-elevation Myocardial Infarction (STEMI): Findings from PROVE/ACS Study. ARYA Atheroscler. 2020;16(3):123-9. doi: 10.22122/arya.v16i3.1869.

26. Bilkova D, Motovska Z, Widimsky P, Dvorak J, Lisa L, Budesinsky T. Shock Index: A Simple Clinical Parameter for Quick Mortality Risk Assessment in Acute Myocardial Infarction. Can J Cardiol. 2011 ec;27(6):739-42. doi: 10.1016/j.cjca.2011.07.008.

27. Supeł K, Kacprzak M, Zielińska M. Shock Index and TIMI Risk Index as Valuable Prognostic Tools in Patients with Acute Coronary Syndrome Complicated by Cardiogenic Shock. PLoS One. 2020;15(1):e0227374. doi: 10.1371/journal.pone.0227374.

28. Boonsom W, Ratanasumawong K, Hutayanon P, Tungsabutra W. Implications of Diabetes Mellitus in Patients with STEMI: Data from Thai ACS Registry. J Med Assoc Thai. 2007;90(Suppl 1):12-20.

29. Chioncel V, Mincu D, Anastasiu M, Sinescu C. The Prognostic Value of Blood Glucose Level on Admission in Non-diabetic Patients with Acute Myocardial Infarction. J Med Life. 2009;2(3):271-8.

30. Oliver MF. Metabolic Causes and Prevention of Ventricular Fibrillation During Acute Coronary Syndromes. Am J Med. 2002;112(4):305-11. doi: 10.1016/s0002-9343(01)01104-4.

31. Cai L, Li W, Wang G, Guo L, Jiang Y, Kang YJ. Hyperglycemia-induced Apoptosis in Mouse Myocardium: Mitochondrial Cytochrome C-mediated Caspase-3 Activation Pathway. Diabetes. 2002;51(6):1938-48. doi: 10.2337/diabetes.51.6.1938.

32. Zhou J, Shan PR, Xie QL, Zhou XD, Cai MX, Xu TC, et al. Age Shock Index and Age-modified Shock Index are Strong Predictors of Outcomes in ST-segment Elevation Myocardial Infarction Patients Undergoing Emergency Percutaneous Coronary Intervention. Coron Artery Dis. 2019;30(6):398-405. doi: 10.1097/MCA.0000000000000759.

33. Yu T, Tian C, Song J, He D, Sun Z, Sun Z. Age Shock Index is Superior to Shock Index and Modified Shock Index for Predicting Long-Term Prognosis in Acute Myocardial Infarction. Shock. 2017;48(5):545-50. doi: 10.1097/SHK.0000000000000892.