Shock index-based risk indices as prognostic predictor for in-hospital mortality in patients with ST-elevation myocardial infarction, the results from Henan STEMI registry

Shan Wang
Central China Fuwai Hospital of Zhengzhou University, Henan Provincial People's Hospital Heart Center
You Zhang
Central China Fuwai Hospital of Zhengzhou University, Henan Provincial People's Hospital Heart Center
Qianqian Cheng
Henan Key Lab for Prevention and Control of Coronary Heart Disease, Central China Fuwai Hospital of Zhengzhou University, Zhengzhou, China
Datun Qi
Central China Fuwai Hospital of Zhengzhou University, Henan Provincial People's Hospital Heart Center
Xianpei Wang
Central China Fuwai Hospital of Zhengzhou University, Henan Provincial People's Hospital Heart Center
Zhongyu Zhu
Central China Fuwai Hospital of Zhengzhou University, Henan Provincial People's Hospital Heart Center
Muwei Li
Central China Fuwai Hospital of Zhengzhou University, Henan Provincial People's Hospital Heart Center
Junhui Zhang
Henan Institute of Cardiovascular Epidemiology
Dayi Hu
Peking University People's Hospital
Chuanyu Gao (gaocy6802@zzu.edu.cn)
Central China Fuwai Hospital of Zhengzhou University, Henan Provincial People's Hospital Heart Center

Research Article

Keywords: Shock index, thrombolysis in myocardial infarction, ST-elevation myocardial infarction, prognostic performance

Posted Date: April 11th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1512785/v1

Abstract

Background: Shock index-based risk indices predicting in-hospital mortality for ST-elevation myocardial infarction (STEMI) patients have been recently described, debate continues about their accuracy, especially compared with classic scoring system. Thus, we aim to evaluate the predictive value of shock index-based risk indices in STEMI patients and compared with thrombolysis in myocardial infarction (TIMI) risk score.

Method: Consecutive 5063 STEMI patients were divided into 2 groups: non-survivor (392, 7.7%) and survivor (4671, 92.3%). Predictive performance of shock index-based risk indices and TIMI risk score were assessed by C-statistic, Hosmer-Lemeshow test, Nagelkerke-R^2, brier scores, integrated discrimination improvement(IDI) and net reclassification improvement(NRI). Odd ratios (OR) and corresponding 95% confidence intervals of bipartite shock index-based risk indices were estimate by generalized linear mixed model.

Results: The area under the curves (AUC) of shock index-based risk indices were smaller, whereas the sensitivity and specificity of age shock index (age SI) (0.73, 0.69) and age modified shock index (age MSI) (0.70, 0.73) were comparable to TIMI risk score (0.73, 0.77). The Hosmer-Lemeshow *P* values and the Nagelkerke-R^2 of shock index-based risk indices were lower, whereas the brier scores were comparable with TIMI risk score. In-hospital mortality was increasing with the SI based risk indices, when the cut-off value were set, in-hospital mortality in the patients with larger shock index-based risk indices were relatively higher. The prognostic performance of shock index (SI, C-statistic: z=7.944, P<0.001; NRI: 0.749; IDI: 0.067), modified shock index(MSI, C-statistic: z=8.088, P<0.001; NRI: 0.774; IDI: 0.067), age SI(C-statistic: z=3.361, P<0.001; NRI: 0.534; IDI: 0.025), and age MSI(C-statistic: z=3.578, P<0.001; NRI: 0.680; IDI: 0.040) were inferior to TIMI risk score. Univariate and multivariate analysis showed that elevated shock index-based risk indices were associated with a higher rate of in-hospital mortality.

Conclusions: Shock index-based risk indices do not have a significant advantage over TIMI risk score. Age SI and age MSI, with comparable sensitivity, were valuable prognostic tools to identify STEMI patients at high risk of in-hospital death.

Trial registration: [NCT02641262] [29 December, 2015].

Background

ST-elevation myocardial infarction (STEMI) is one of the most urgent and severe coronary artery disease(CAD) threatening life worldwide[1–3], despite thrombolysis, primary percutaneous coronary intervention (PCI), as well as dedicated regional networks have improved the prognosis of patients with STEMI, it remains the leading cause of mortality in China and worldwide. Rapid and accurate risk stratification, timely and effective treatment after medical contact are of great significance to reduce in-hospital mortality [4–8]. Therefore, it is thus indispensable to identify patients at higher risk and to subsequently provide more focused treatment.

Numerous risk scores have been developed and validated to predict mortality in patients with STEMI [9]. One well-known and widely used is the thrombolysis in myocardial infarction (TIMI) risk score, which constituted by eight independent predictors of mortality that collected early after hospital admission (age; history of diabetes, hypertension or angina; systolic blood pressure (SBP); heart rate (HR); Killip class; weight; anterior ST-segment elevation and time to reperfusion therapy)[9]. However, the usefulness of TIMI risk score was limited due to complicated calculation and difficult implementation. Moreover, the lower awareness rate of diabetes, hypertension may decrease the accuracy of TIMI risk score for Chinese STEMI patients [10]. Therefore, a simple risk score for STEMI patients is crucial.

Shock index (SI), which defined as the ratio of HR and SBP, was developed to identify high-risk trauma patients and easily calculated at the bedside. Recent studies found that SI played an important role in quick risk assessment in STEMI [11–13]. In recent years, some derivatives of SI have been created to improve the predictive value of SI, such as modified shock index (MSI), age shock index (age SI) and age modified shock index (age MSI), both indexes could predict the adverse prognosis in patients with STEMI [14–16]. All of these shock index-indices are composed of age, HR, and a parameter of blood pressure. However, it is unknown which index has better predictive value, and whether they are comparable to, or even better than the TIMI risk score for Chinese STEMI patients.

In this study, we aimed to investigate the predictive value of SI, MSI, age SI and age MSI for in-hospital mortality in STEMI patients, and compare with classic TIMI risk score.

Methods

Study population

The data of our study was from *Henan STEMI registry* [17, 18], which is a multicenter, prospective study for STEMI patients and has been registered at URL: https://www.clinicaltrials.gov (NCT 02641262). Form September 2016 to August 2018, patients with definitive diagnosis of STEMI were consecutively enrolled from 66 hospitals from different geographic regions of central China.

STEMI was defined in accordance with the universal definition of Myocardial Infarction (2012) [19], specifically as elevated biomarkers and new or presumed new ST-segment elevation >1mm (0.1mV) in 2 or more contiguous leads or new onset of left bundle branch block. Patients, diagnosed as types 4a and type 5 STEMI and transferred in with prior reperfusion (including intravenous or intracoronary fibrinolytic therapy and PCI) from other hospitals, were excluded**.** Finally, a total of 5063 patients were included in the final analysis.

The central ethics committee at Henan Provincial People's Hospital approved the study with a waiver for informed consent [NO. 2015 (34)], and the other 65 sites were covered by central ethics approval.

Data collection

SBP, DBP and HR of STEMI patients were measured at the first medical contact in hospital, at this time, instruments and drugs such as catecholamine were not applied to patients. The baseline demographic, risk factors and medical histories, clinical characteristics at admission, reperfusion therapy, medications as well as in-hospital outcomes of STEMI patients were prospectively collected through a standardized online reporting platform with automatic checks for invalid values (*Henan STEMI registry platform, Zhao Rui Corporation, Zhengzhou*). We checked consecutiveness of all cases, and a total of 53.84% reported cases were audited for accuracy against medical records for onsite quality control.

Definitions

SI was defined as the ratio of HR and SBP on admission. MSI was defined as the ratio of HR and mean arterial pressure (MAP) on admission, MAP was defined as double the diastolic blood pressure (DBP), the sum then being added to the SBP, then divided by 3. Age SI was defined as age multiplied by SI. Age MSI was defined as age multiplied by MSI. TIMI risk score was calculated according to previous reports [8, 20]. The SBP and DBP were not detectable in 22 patients with cardiogenic shock, we used the maximum value of SI, MSI, age SI and age MSI to impute the missing data of indexes.

Hypertension was defined as having a history of hypertension or receiving antihypertensive therapy. Dyslipidemia was defined according to the guidelines [21]. Diabetes mellitus was defined as having a previous diagnosis of diabetes mellitus, or glycosylated hemoglobin level ≥ 6.5%. Current smoker was defined as smoking within the preceding year. History of coronary heart disease was defined as having a clinical history of myocardial infarction or underwent PCI or coronary artery bypass grafting before the current hospitalization. The wall location of the myocardia infraction was determined by electrocardiogram (ECG).

With the consideration of the actual situation that most patients are reluctant to die in hospital in China, based solely on in-hospital death cannot represent the real outcomes of STEMI patients, for the sake of better reflection of the prognosis, we take death or withdrawal from treatment due to terminal status at discharge (referred to as treatment withdrawal) as the in-hospital mortality, and in-hospital death or treatment withdrawal was used as a quality measure for hospitals by Chinese Government[22], researchers in the coordinating study sites adjudicated the clinical status of patients who withdrew from treatment according medical records. The 5063 STEMI patients were divided into two groups, the non-survivor (in-hospital death or treatment withdrawal) and survivor.

Statistical analysis

We compared the demographic, risk factors, clinical characteristics, treatment therapy, time delay, medicine use during hospitalization between two groups. Categorical variables were presented as number and percentage, Chi-square or Fisher exact tests were used for comparisons as appropriate, whereas continuous variables were reported as means and standard deviation (SD) or median and interquartile range (IQR), *t* test or Mann-Whitney *U* test were used as appropriate.

The C-statistic was calculated and compared using a nonparametric test developed by DeLong with the use of MedCalc software for Windows, version 19.0.4 (MedCalc Software, Mariakerke, Belgium) [23]. Cut-off points of SI, MSI, age SI and age MSI were determined based on the receiver operating curves (ROC). The area under the curve (AUC), the Hosmer-Lemeshow (HL) test and the Nagelkerke-R^2 from the regression modeling were used as indicators of goodness-of-fit of each risk score and to assess the calibration ability of them [24]. In the test, higher HL *P* values and higher Nagelkerke-R^2 indicate better calibration. The brier scores were also calculated, lower brier scores indicate better calibration [25]. We also used the absolute integrated discrimination improvement (IDI) and category-free net reclassification improvement (NRI) to evaluate improvements in risk predictions quantify [26].

Generalized linear mixed models were used to estimate the odd ratios (OR) and corresponding 95% confidence intervals (CI) for in-hospital death or treatment withdrawal over the categorized SI, MSI, age SI, age MSI and TIMI risk score, which account for clustering of patients within hospitals. In the multivariate analysis, the adjusted variable contains age(≥75 years or not), gender(women or man), hospital class(tertiary or second hospital), medical history (hypertension, diabetes, dyslipidemia, current smoker, stroke, coronary heart disease), presenting status (cardiac arrest, anterior myocardial infarction and Killip class(IV vs I II III) at admission), time to present (onset to first medical contact, onset-to-FMC), reperfusion treatment (successful reperfusion, unsuccessful reperfusion or no reperfusion) and medicine use during hospitalization (aspirin, P2Y12 antagonists, statin, β-blocker and Angiotensin Converting Enzyme Inhibitor (ACEI)/Angiotensin Receptor Blockers (ARB)). Two-sided *P* values <0.05 was considered statistically significant. Statistical analyses were performed with SAS 9.4 (SAS Institute Inc., Cary, NC).

Results

Clinical characteristics of survival and in-hospital death group

Among 5063 STEMI patients, 392(7.7%) were died or withdrawal from treatment due to terminal status at discharge. Patients were divided into survivor and non-survivor (in-hospital death or treatment withdrawal). The clinical characteristics of the two groups were summarized in Table 1.

Table 1
Comparison of demographic and clinical characteristics between survivor and non-survivor group

variable	Survivor (N = 4671)	Non-survivor (N = 392)	*P* value
Demographic characteristic			
Age (years)	62.3(52.1–70.1)	73.3(65.9–80.2)	< 0.001
≥ 75years (%)	680(14.6)	174(44.4)	< 0.001
Women (%)	1055(22.6)	179(45.7)	< 0.001
Tertiary hospital (%)	2337(50.0)	173(44.1)	0.025
Risk factors			
Hypertension (%)	2047(43.8)	186(47.5)	0.17
Dyslipidemia (%)	2555(54.7)	166(42.4)	< 0.001
Diabetes (%)	785(16.8)	100(25.5)	< 0.001
Current smoker (%)	1922(41.2)	81(20.7)	< 0.001
Medical history			
Heart failure (%)	41(0.9)	13(3.3)	< 0.001
Coronary heart disease (%)	286(6.1)	28(7.1)	0.42
Stroke (%)	583(12.5)	73(18.6)	< 0.001
CKD (%)	26(0.6)	6(1.5)	0.045
Clinical characteristic			
Cardiac arrest (%)	126(2.7)	28(7.1)	< 0.001
Anterior myocardial infarction (%)	2601(55.7)	274(69.9)	< 0.001
Killip class (%)			< 0.001
I	3487(74.7)	156(39.8)	
II	714(15.3)	72(18.4)	
III	257(5.5)	59(15.1)	
IV	213(4.6)	105(26.8)	
SBP (mmHg)	130 (114–148)	116 (94–135)	< 0.001
DBP(mmHg)	80 (70–92)	73.00(59–85)	< 0.001
HR (BPM)	76 (65–86)	86 (70–104)	< 0.001
eGRF (ml/min/1.73m^2)	103.6(85.2,123.4)	71.3(49.4,99.0)	< 0.001
LVEF (%)	56(48,61)	46(39,56)	< 0.001
Treatment therapy and time delay			

Data are expressed as n (%) or median (IQR), unless otherwise noted.

variable	Survivor (N = 4671)	Non-survivor (N = 392)	*P* value
Reperfusion strategy (%)			
none	1903(40.7)	220(56.1)	< 0.001
PCI	1462(31.3)	55(14.0)	
Fibrinolysis	1306(28.0)	117(29.9)	
Successful reperfusion (%)	2616(56.0)	87(22.2)	< 0.001
Onset-to-FMC (min)	200(105–580)	250(120–949)	< 0.001
Medicine used in hospital			
Aspirin (%)	4536(97.1)	305(77.8)	< 0.001
P2Y12 antagonists (%)	4543(97.3)	304(77.6)	< 0.001
Statin (%)	4450(95.3)	288(73.5)	< 0.001
Beta-blocker (%)	3362(72.0)	149(38.0)	< 0.001
ACEI/ARB (%)	2418(51.8)	87(22.2)	< 0.001
Diuretics (%)	1298(27.8)	110(28.1)	0.908
Digoxin (%)	89(1.9)	14(3.6)	0.025
Heparin (%)	3841(82.2)	244(62.2)	< 0.001
Data are expressed as n (%) or median (IQR), unless otherwise noted.			

Abbreviation: IQR, interquartile range; HR, heart rate; BPM, beat per minute; SBP, systolic blood pressure; Stoke contains ischemic and hemorrhagic. Coronary heart disease contains myocardial infarction, percutaneous coronary intervention and coronary artery bypass graft. CKD, chronic kidney disease. eGRF, estimated glomerular filtration rate. LVEF, left ventricular ejection fraction. PCI, percutaneous coronary intervention. FMC, first medical contact. P2Y12 antagonist, clopidogrel and ticagrelor. ACEI, Angiotensin-Converting Enzyme Inhibitors. ARB, Angiotensin Receptor Blockers.

The median age of the non-survivor group was significantly older than the survivor, and more than two fifths non-survivor were older than 75 years, the non-survivor were more likely admitted to secondary hospital. The non-survivor had a higher percentage of comorbidity such as diabetes, heart failure and stroke. The proportion of cardiac arrest, anterior myocardial infarction and Killip class IV level were higher in non-survivor. The eGRF and LVEF were significantly lower for non-survivor group.

Compared with the survived patients, the non-survivor had a lower proportion of reperfusion therapy, and only 22.2%were successfully reperfusion. The median of Onset-to-FMC time were significantly longer than survived patients. In the terms of medicine used in hospital, the non-survived patients were less likely to receive aspirin, P2Y12 antagonists, statin, beta-blocker, ACEI/ARB and heparin.

Performance For The Prognosis Prediction Of Shock Index-based Risk Indices

As shown in Table2 **and** Fig. 1, the AUCs of SI, MSI, age SI, age MSI were slightly smaller than the TIMI risk score. The sensitivity of SI and MSI at the cut-off value were significantly lower than TIMI risk score, nevertheless, the specificity of SI and MSI at the cut-off value were slightly greater than TIMI risk score. The sensitivity and specificity of age SI and age MSI were in accordance with TIMI risk score.

Table 2
Performance for the prognosis prediction of shock index-based risk indices and TIMI risk score.

	Discrimination						Calibration			
	Cut-off point	AUC	SE	95 CI	Sensitivity	Specificity	HL chi-square	HL P value	Nagelkerke-R^2	Brier score
SI	0.75	0.69	0.02	0.68–0.71	0.47	0.85	38.19	< .0001	0.10	0.07
MSI	1.00	0.70	0.02	0.68–0.71	0.48	0.85	25.51	0.001	0.10	0.07
age SI	40.75	0.78	0.01	0.77–0.79	0.73	0.69	35.12	< .0001	0.15	0.06
age MSI	56.66	0.78	0.01	0.77–0.79	0.70	0.73	54.98	< .0001	0.13	0.06
TIMI risk score	6.00	0.82	0.01	0.81–0.83	0.73	0.77	8.74	0.27	0.23	0.06

Abbreviation: SI, shock index; MSI, modified shock index; TIMI, thrombolysis in myocardial infarction; AUC, area under the curve; SE, standard error; CI, confident interval; HL, Hosmer-Lemeshow.

Figure 2 shows the in-hospital mortality for each quartile of SI, MSI, age SI and age MSI. The in-hospital mortality of STEMI patients was increasing with the shock index-based risk indices. The STEMI patients within the Q4 of SI (Fig. 2A), MSI (Fig. 2B), age SI (Fig. 2C) and age MSI (Fig. 2D) had highest in-hospital mortality, which was significance higher than the other quartile (Q1, Q2 and Q3).

Figure 3 shows when STEMI patients was grouped by the cut-off value of SI, MSI, age SI, age MSI, in-hospital mortality in patients with the larger value were significance higher than the patients with smaller value. In-hospital mortality in STEMI patients with the SI ≥ 0.75 was 20.4%, with the MSI ≥ 1.00 was 20.9%, with age SI ≥ 40.75 was 16.6%, with age MSI ≥ 56.66 was 17.8%, which were relatively higher than the smaller value group.

Univariate And Multivariate Analysis Of Grouped Si Based Risk Indices

The association between SI, MSI, age SI, age MSI, TIMI risk score and in-hospital death was shown utilizing crude and adjusted odds ratio in Fig. 4. In univariate analysis, after accounting for clustering of patients within hospitals, categorized SI, MSI, ag SI, age MSI and TIMI risk score were associated with a higher rate of in-hospital mortality. In the multivariate analysis, categorized SI, MSI, age SI, age MSI and TIMI risk score were revealed to be predictors for in-hospital mortality, after adjusted the clustering of patients within hospitals and potential affecting factors(SI: OR = 2.95, 95% CI:2.25–3.87, P < 0.001; MSI: OR = 3.06, 95% CI:2.33–4.02, P < 0.001; age SI: OR = 3.19, 95% CI:2.39–4.26, P < 0.001; age MSI: OR = 3.03, 95% CI:2.27–4.05, P < 0.001). As for TIMI risk score, the high risk group was 9.19 fold than the low risk group.

Comparisons Of The Prognostic Performance Of Si Based Risk Indices With Timi Risk Score

The calibration of SI, MSI, age SI, and age MSI were not so good, the Hosmer-Lemeshow *P* values were little than 0.05 and the Nagelkerke-R^2 were lower, which indicated bad model calibration. All the parameter of the study had a similar Brier score **(**Table 2**).**

As shown in Table3, the prognostic performance of SI, MSI, age SI, and age MSI were not equivalent to TIMI risk score for predicting in hospital death or treatment withdrawal, the *P* values for C-statistic, *P*values for NRI and P values for IDI were statistical significantly, which indicates SI, MSI, age SI, and age MSI were not comparable to TIMI risk score in predicting in hospital death or treatment withdrawal.

Table 3
Comparisons of the prognostic performance of shock index-based risk indices versus TIMI risk score

	z for C-statistic	*P* for C-statistic	NRI	*P* for NRI	IDI	*P* for IDI
SI vs TIMI risk score	7.94	< 0.001	0.75	< 0.001	0.07	< 0.001
MSI vs TIMI risk score	8.09	< 0.001	0.77	< 0.001	0.07	< 0.001
age SI vs TIMI risk score	3.36	< 0.001	0.53	< 0.001	0.03	0.006
age MSI vs TIMI risk score	3.58	< 0.001	0.68	< 0.001	0.04	< 0.001

Abbreviation: TIMI, thrombolysis in myocardial infarction; SI, shock index; MSI, modified shock index; NRI, net reclassification improvement; IDI, integrated discrimination improvement.

Discussion

This study revealed that elevated SI, MSI, age SI and age MSI were correlates with STEMI patient's prognosis and were independent predictors for in-hospital mortality, age SI and age MSI were stronger independent predictors than SI and MSI. The predictive performance of SI, MSI, age SI and age MSI were inferior to the TIMI risk score, nonetheless, age SI and age MSI, which can be easily calculated using readily available clinical variables and have equivalent sensitivity, were still useful indexes for risk stratification during first contact with STEMI patients in clinical practices.

Identification of the high-risk patients is the best way to prevent complications including death. Reperfusion treatment including thrombolysis and primary percutaneous coronary intervention and the broad uptake of aspirin, P2Y12-inhibitors have improved the prognosis of patients with STEMI[27, 28], whereas the China PEACE revealed that there was no change in the proportion of in-hospital death in 2001–2011[1], and Henan STEMI registry find that the in-hospital death or treatment withdrawal was still higher. There is still much room for improvement in the prognosis of patients with STEMI. TIMI risk score was an efficient index for the predictive of in-hospital outcomes of STEMI patients, however, the complex calculation of the index makes its inconvenient in large-scale clinical practices, a simple index without subjective information, diagnostic blood test results, or complicated algorithm may have wider clinical application, and improve patient's in-hospital outcomes [9, 29].

SI is as a hemodynamic predictor, is usually used to assess the severity of illness and the response to effects of treatment. Previous studies have reported that shock index is associated with the risk of in-hospital cardiogenic shock and more severe myocardial and microvascular damage, and can independently predict in-hospital mortality and 1 year major adverse cardiovascular events (MACE) for STEMI [30, 31]. Bilkova et al identified a shock index of ≥ 0.8 as a

predictor for in-hospital mortality [12]. Ayman El-Menyar found that high SI identified patients at increased risk of in-hospital mortality [14]. SBP and HR are influenced by catecholamine level in the body, insufficiency peripheral perfusion lead the increased secretion of catecholamine to maintain basic tissue metabolism, and thus may results in the inaccuracy assessment of SI for prognosis. Therefore, DBP was included to form the MSI index. Study reported that MSI may be more accurate than SI in prediction of all-cause mortality and MACE rates within 7 days in patients with STEMI [17]. Abreu G reported that MSI was a valuable bedside tool and can rapidly identify high-risk STEMI patients at presentation [32]. Our study demonstrated that SI and MSI correlates with patient's prognosis, even after adjusted for the underlying variables, however, the AUCs of SI and MSI were smaller compared to TIMI risk score, and the sensitivity of the two parameter was small, the prognostic performance of SI and MSI was inferior to TIMI risk score.

Age is an important predictor of in-hospital outcome in STEMI patients [13], age SI and age MSI, which integrate age into risk score, may provide better discriminating power than SI and MSI. Yu T et al demonstrated that age SI, similar to GRACE, can identify patients at high risk of death in AMI patients undergoing PCI [33]. Zhou J reported that age SI and age MSI were stronger predictors than SI and MSI for in-hospital cardiovascular events, 6-month and long-term all-cause mortality in STEMI patients undergoing emergency PCI [15]. In our study, we discovered that age SI and age MSI were independent predictors, which had the similar sensitivity, though the predictive performance of the two parameter were inferior to TIMI risk score.

Various systems have been applied for risk stratification in STEMI patients, including the TIMI risk score and GRACE scores, but the complex calculations make them impractical in daily clinical practice, although there was GRACE 2.0, a revised GRACE algorithm, and "Mini-GRACE" algorithm. What's more, Chinese and Westerners differ in terms of the incidence of coronary spastic angina, physique, and lifestyle, and it is unclear whether the risk scoring systems devised in the Western countries are applicable in Chinese STEMI patients, causing neither Chinese nor the other Asian institutions took part in the stablishing of these system. The in-hospital outcome of STEMI patients is affected by many variables, such as subjective information, patient's medical history or treatment therapy, time delay and diagnostic blood test results, the SI and MSI only take SBP, DBP and HR into account, age SI and age MSI include age, the prediction performance of age SI and age MSI are superior to SI and MSI, however, variables such as myocardial infraction location and cardiogenic shock, which may increase the predictive capacity of risk stratification were excluded [5, 34]. Although the predictive performance of SI, MSI, age SI and age MSI were not equivalent to TIMI risk score, age SI and age MSI, with the similar sensitivity, were still useful indexes for risk stratification during first contact with STEMI patients in emergency.

Limitation

This study had several limitations. Firstly, the data collection burden for investigators may be the greatest barrier to the registry that may lead to some enrollment bias. We have carefully considered each element to limit the burden and have quality control measures in the registry. Secondly, we did not compare the parameter with GRACE score, due to the missing date of some laboratory test results. Thirdly, our data are observational, the information were mainly determined by consulting medical records, and thus some degree of residual confounding cannot be excluded.

Conclusion

SI, MSI, age SI and age MSI were both independent predictors for in-hospital death of STEMI patients. The prognostic performance of SI, MSI, age SI and age MSI were inferior to the TIMI risk score. However, age SI and age MSI, with comparable sensitivity and simple calculation, were valuable prognostic tools to identify STEMI patients at high risk of in-hospital death.

Abbreviations

SI
shock index
MSI
modified shock index
age SI
age shock index
age MSI
age modified shock index
FMC
first medical contact
P2Y12
Clopidogrel and Ticagrelor
ACEI
angiotensin-converting enzyme inhibitor
ARB
angiotensin receptor blocker
CI
confidence intervals
HL
Hosmer-Lemeshow
IDI
integrated discrimination improvement
NRI
net reclassification improvement
OR
odds ratio
CI
confidence intervals.

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Henan Provincial People's Hospital with a waiver for informed consent [NO. 2015 (34)], and the other 65 participating institute were covered by central ethics approval. All treatments applied to participants were in accordance with relevant guidelines and Declaration of Helsinki.

Consent for publication

Not applicable.

Availability of data and materials

The identified participant data are not publicly available, all data generated or analyzed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests.

Funding

This work was supported by the project of Scientific and Technological support plan of Health and Family Planning Commission of Henan province in 2021[grant number: LHGJ20210105], the project of scientific and technological of Science and Technology Department of Henan Province in 2022[grant number: 222102310656], the Project of Scientific and Technological support plan of Health and Family Planning Commission of Henan province in 2016 [grant number: 201602210] and Shanghai Tasly Pharmaceutical Co. Ltd. The sponsors did not involvement in the design and conduct of the study; data collection and analysis; preparation or approval of the manuscript; or the decision to submit the manuscript for publication.

Authors' contribution

SW: conceived the concept of this study, manuscript writing, data analysis and interpretation. YZ, CYG and DYH: conceived the concept of this study, data revising and approval of the version to be published. CQQ, ZJH: Data quality evaluation, data checking and management. DTQ, XPW, ZYZ and MWL: ensuring questions related to the accuracy or integrity of the work are appropriately investigated and resolved. All authors reviewed the manuscript and approved the final version.

Acknowledgments

We would like to thank all of the members of Scientific Committee, and Executive Committee for their contribution to the Henan STEMI registry. We also want to thank all of the study investigators and coordinators for their great work.

References

1. Li J, Li X, Wang Q, Hu S, Wang Y, Masoudi FA, et al. ST-segment elevation myocardial infarction in China from 2001 to 2011 (the China PEACE-Retrospective Acute Myocardial Infarction Study): a retrospective analysis of hospital data. Lancet. 2015; 385: 441–451.
2. GBD 2017 Causes of Death Collaborators. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980–2017: A systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018; 392: 1736–1788.
3. Liu S, Li Y, Zeng X, Wang H, Yin P, Wang L, et al. Burden of Cardiovascular Diseases in China, 1990–2016: Findings From the 2016 Global Burden of Disease Study. JAMA CARDIOL. 2019; 4: 342–352.
4. Chinese Society of Cardiology of Chinese Medical Association, Editorial Board of Chinese Journal of Cardiology. 2019 Chinese Society of Cardiology (CSC) guidelines for the diagnosis and management of patients with ST-segment elevation myocardial infarction. Zhonghua Xin Xue Guan Bing Za Zhi. 2019; 47: 766–783.
5. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). EUR HEART J. 2018; 39: 119–177.
6. Levine GN, Bates ER, Blankenship JC, Bailey SR, Bittl JA, Cercek B, et al. 2015 ACC/AHA/SCAI Focused Update on Primary Percutaneous Coronary Intervention for Patients With ST-Elevation Myocardial Infarction. J AM COLL CARDIOL. 2016; 67: 1235–1250.

7. Fan F, Li Y, Zhang Y, Li J, Liu J, Hao Y, et al. Chest Pain Center Accreditation Is Associated With Improved In-Hospital Outcomes of Acute Myocardial Infarction Patients in China: Findings From the CCC-ACS Project. J AM HEART ASSOC. 2019; 8: e13384.
8. Truong QA, Cannon CP, Zakai NA, Rogers IS, Giugliano RP, Wiviott SD, et al. Thrombolysis in Myocardial Infarction (TIMI) Risk Index predicts long-term mortality and heart failure in patients with ST-elevation myocardial infarction in the TIMI 2 clinical trial. Am Heart J. 2009, 157(4):673–679.
9. 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):1364–1369.
10. Chow CK, Teo KK, Rangarajan S, Islam S, Gupta R, Avezum A, et al. Prevalence, awareness, treatment, and control of hypertension in rural and urban communities in high-, middle-, and low-income countries. J Am Med Assoc. 2013; 310(9): 959–968.
11. 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; 27(6):739–742.
12. 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):270–277.
13. El-Menyar A, Al Habib KF, Zubaid M, Alsheikh-Ali AA, Sulaiman K, Almahmeed W, et al. Utility of shock index in 24,636 patients presenting with acute coronary syndrome. Eur Heart J Acute Cardiovasc Care. 2020; 9(6):546–556.
14. 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.
15. Sankaran P, Kamath AV, Tariq SM, Ruffell H, Smith AC, Prentice P, et al. Are shock index and adjusted shock index useful in predicting mortality and length of stay in community-acquired pneumonia? Eur J Intern Med. 2011; 22(3):282–285.
16. Shangguan Q, Xu JS, Su H, Li JX, Wang WY, Hong K, et al. Modified shock index is a predictor for 7-day outcomes in patients with STEMI. Am J Emerg Med. 2015; 33(8):1072–1075.
17. Zhang Y, Wang S, Yang S, Yin S, Cheng Q, Li M, et al. Rationale and design of the Henan ST-elevation myocardial infarction (STEMI) registry: a regional STEMI project in predominantly rural central China. BMC CARDIOVASC DISOR. 2019; 19(1): 271.
18. Zhang Y, Wang S, Cheng Q, Zhang J, Qi D, Wang X, et al. Reperfusion strategy and in-hospital outcomes for ST elevation myocardial infarction in secondary and tertiary hospitals in predominantly rural central China: a multicentre, prospective and observational study. BMJ Open. 2021; 11(12):e053510.
19. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, et al. Third universal definition of myocardial infarction. CIRCULATION. 2012; 126: 2020–2035.
20. Morrow DA, Antman EM, Charlesworth A, Cairns R, Murphy SA, de Lemos JA, et al. TIMI risk score for ST-elevation myocardial infarction: A convenient, bedside, clinical score for risk assessment at presentation: An intravenous nPA for treatment of infracting myocardium early II trial substudy. CIRCULATION. 2000; 102(17):2031–2037.
21. The joint committee on the revision of guidelines for the prevention and treatment of China adult dyslipidemia. Guidelines for the prevention and treatment of dyslipidemia in Chinese adults (revised in 2016). Zhonghua Xin Xue Guan Bing Za Zhi. 2016; 44: 833–853.
22. Ministry of Health of the People's Republic of China. The qualification standard of secondary General Hospital (version 2012). 2012.

23. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. Biometrics. 1988; 44(3):837–845.
24. Lemeshow S, Hosmer DWJr. A review of goodness of fit statistics for use in the development of logistic regression models. Am J Epidemiol. 1982; 115(1):92–106.
25. Redelmeier DA, Bloch DA, Hickam DH. Assessing predictive accuracy: how to compare Brier scores. J Clin Epidemiol. 1991; 44(11):1141–1146.
26. Pencina MJ, D'Agostino RB Sr, D'Agostino RB Jr, Vasan RS. Evaluating the added predictive ability of a new marker: from area under the ROC curve to reclassification and beyond. Stat Med.2008; 27(2):157–172.
27. Alexander T, Mullasari AS, Joseph G, Kannan K, Veerasekar G, Victor SM, et al. A System of Care for Patients With ST-Segment Elevation Myocardial Infarction in India: The Tamil Nadu-ST-Segment Elevation Myocardial Infarction Program. JAMA CARDIOL. 2017; 2: 498–505.
28. Szummer K, Wallentin L, Lindhagen L, Alfredsson J, Erlinge D, Held C, et al. Improved outcomes in patients with ST-elevation myocardial infarction during the last 20 years are related to implementation of evidence-based treatments: experiences from the SWEDEHEART registry 1995–2014. EUR HEART J. 2017; 38: 3056–3065.
29. Wiśniewski P, Rostoff P, Gajos G, Nessler J, Kruszelnicka O. Predictive value of electrocardiographic STsegment elevation myocardial infarction equivalents for detecting acute coronary artery occlusion in patients with non-STsegment elevation myocardial infarction. Kardiol Pol. 2019; 77(6):624–631.
30. Wei Z, Bai J, Dai Q, Wu H, Qiao S, Xu B. The value of shock index in prediction of cardiogenic shock developed during primary percutaneous coronary intervention. BMC Cardiovasc Disord. 2018;18(1):188.
31. Reinstadler SJ, Fuernau G, Eitel C, de 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):924–930.
32. Abreu G, Azevedo P, Galvão Braga C, Vieira C, Álvares Pereira M, 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):481–488.
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):545–550.
34. Kytö V, Sipilä J, Rautava P. Association of age and gender with anterior location of STEMI. Int J Cardiol. 2014; 176(3):1161–1162.

Figures

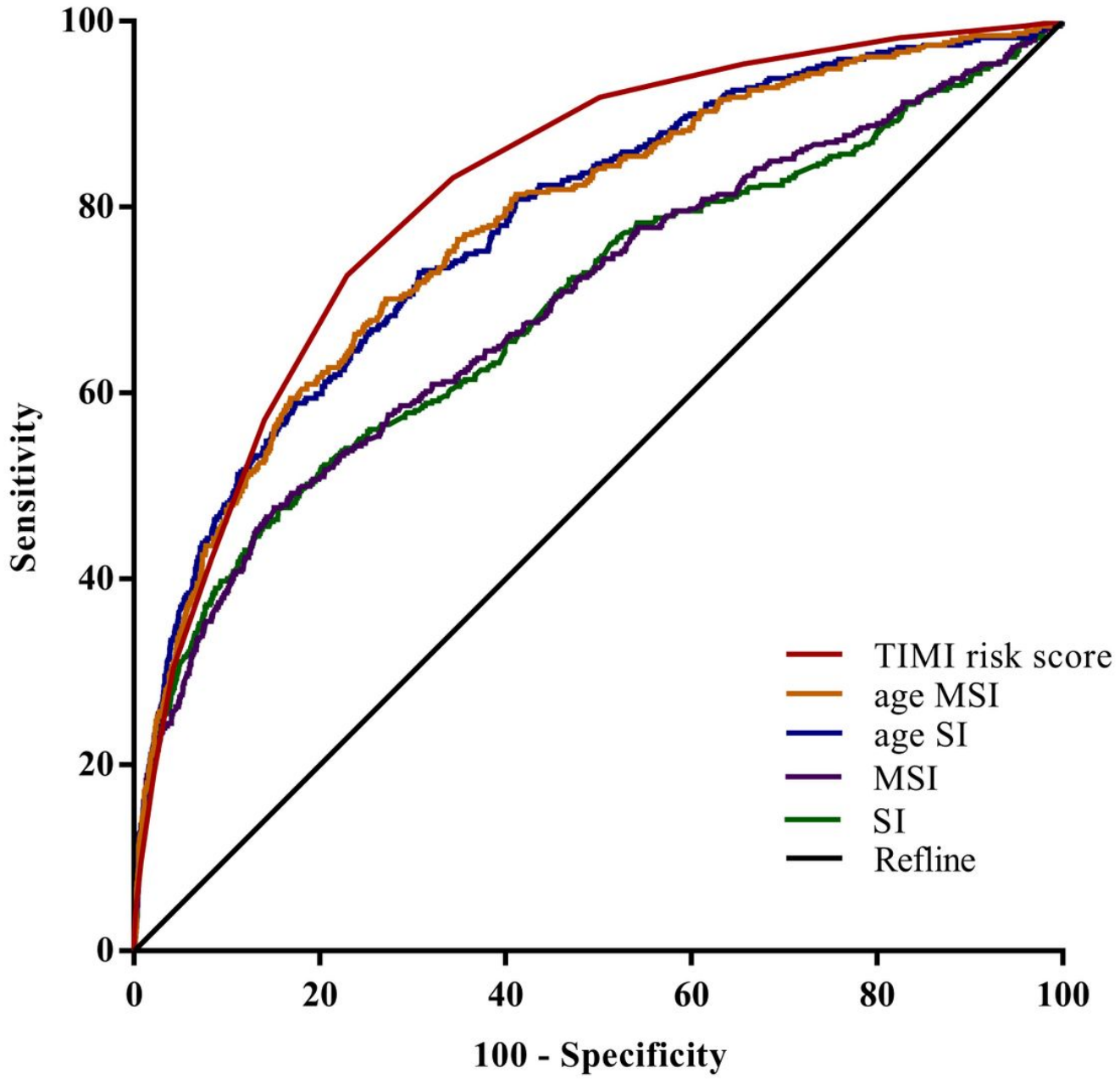

Figure 1

Receiver operating characteristic curves of shock index-based risk indices for in-hospital mortality in STEMI patients.

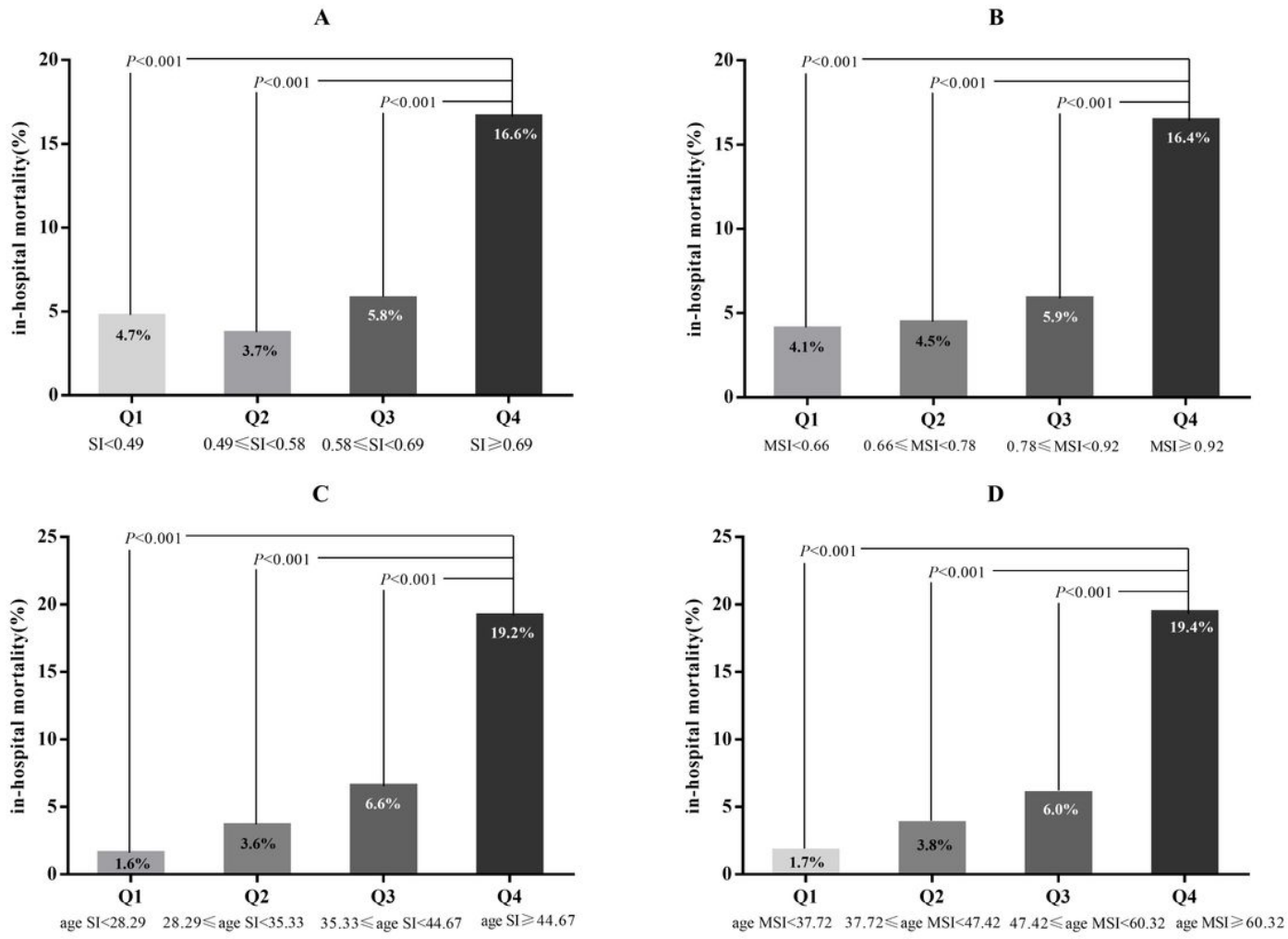

Figure 2

In-hospital mortality according to the quartile of shock index-based risk indices. The in-hospital mortality was increasing with the SI based risk indices, patiens with Q4 had highest in-hospital mortality.

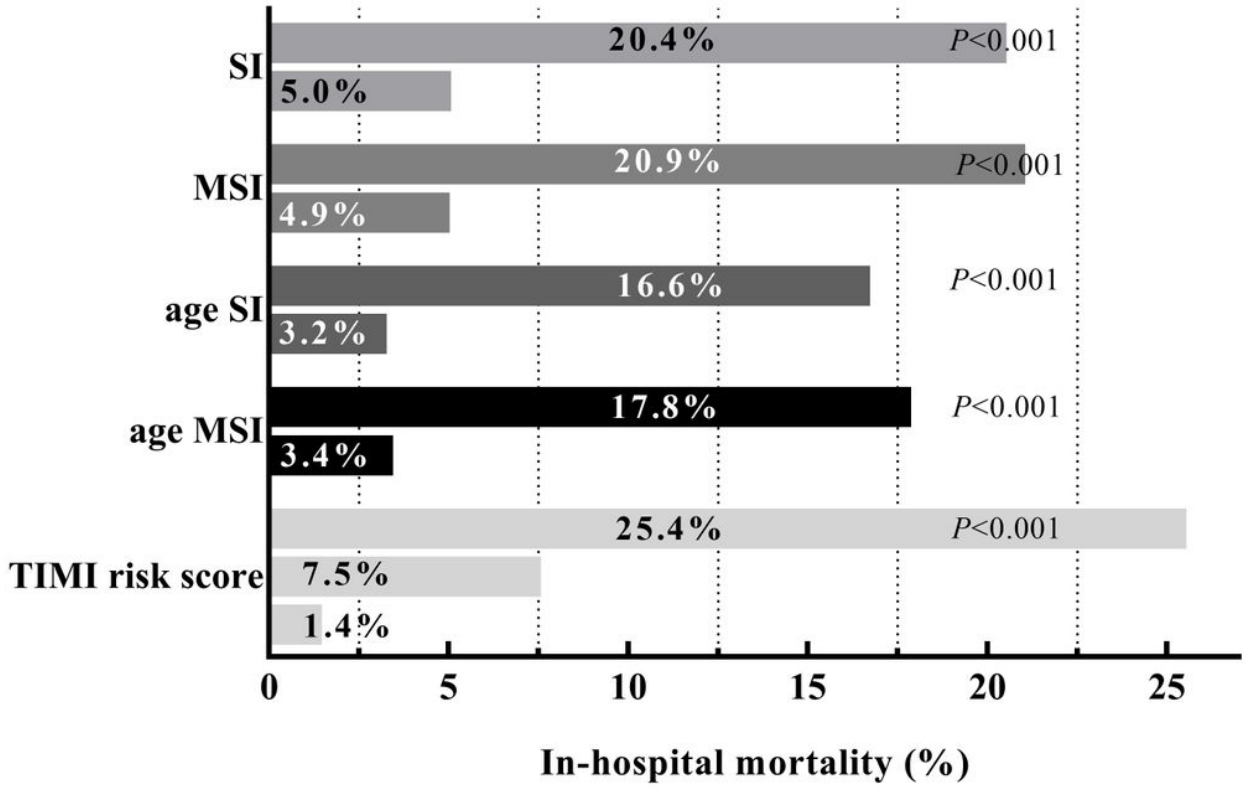

Figure 3

In-hospital mortality according to the cut-off vlaue of shock index-based risk indices.when the cut-off value of shock index-based risk indices were set, in-hospital mortality in the patients with larger shock index-based risk indices were relatively higher than those with smaller value.

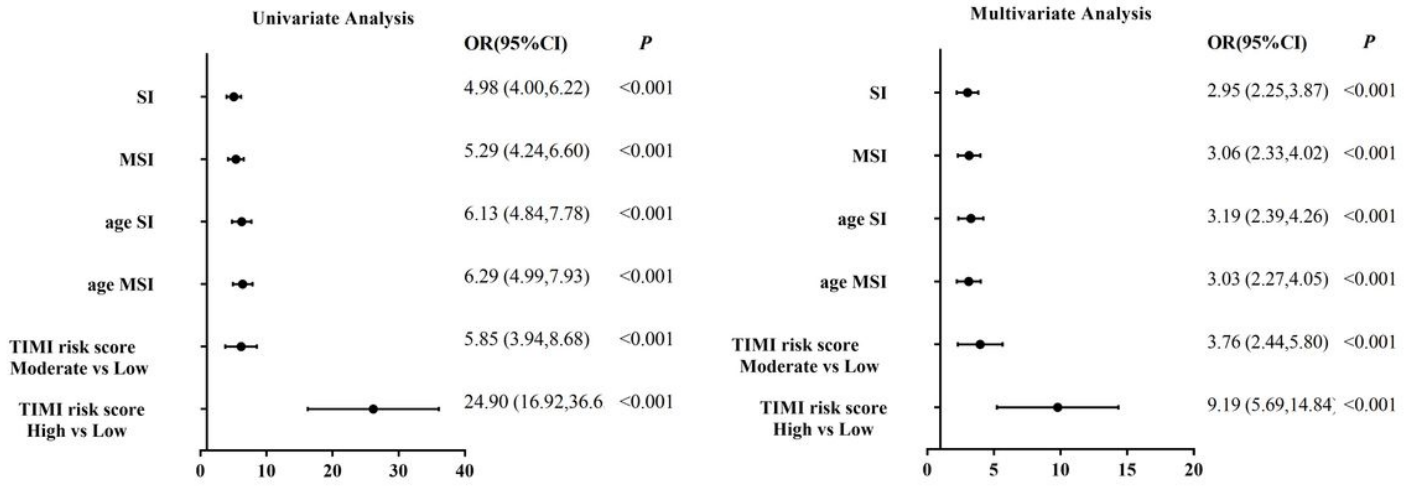

Figure 4

Forrest plot graph. OR and corresponding 95% CI of categorized SI, MSI, age SI, age MSI and TIMI risk score according to univariate and multivariate analysis based on generalized linear mixed model. OR, odds ratio. CI, confidence

intervals. SI, MSI, age SI and age MSI were divided into two groups according to the cutoff point, TIMI risk score classified into three risk groups: low risk(0-3), moderate risk(4-6) and high risk(7-14), the categorized indexes were added into the model to evaluate the OR and 95% CI. In the multivariate analysis, the adjusted variable contains age(≥75 years or not), gender(women or man), hospital class(tertiary or second hospital), medical history (hypertension, diabetes, dyslipidemia, current smoker, stroke, coronary heart disease), presenting status (cardiac arrest, anterior myocardial infarction and Killip class(IV vs I/II/III) at admission), time to present (onset to first medical contact, onset-to-FMC), reperfusion treatment (successful reperfusion, unsuccessful reperfusion or no reperfusion) and medicine use during hospitalization (aspirin, P2Y12 antagonists, statin, β-blocker and ACEI)/ ARB).