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AGE-MODIFIED SHOCK INDEX INSTEAD OF GRACE SCORE IN PATIENTS WITH NON-ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION

ST-SEGMENT YÜKSEKLİĞİ OLMAYAN MİYOKARD ENFARKTÜSÜ OLAN HASTALARDA GRACE SKORU YERİNE YAŞ-MODİFİYE ŞOK İNDEKSİ

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ABSTRACT

Introduction: Measures such as blood pressure, heart rate, shock index (SI), and the derived modified shock index (MSI) have been extensively evaluated for their potential to forecast negative outcomes in acute myocardial infarction patients. Newly proposed parameters include Age-SI and Age-MSI. This research aimed to determine if Age-MSI could be a more manageable alternative to the challenging GRACE score in patients presenting with NSTEMI.

Methods: A retrospective study was conducted at a single facility, which comprised 495 patients diagnosed with NSTEMI, who did not present with cardiogenic shock upon admission, from July 2019 to December 2022. The Age-MSI and GRACE scores of all patients in the study were collected and scrutinized.

Results: There was a significant relationship between the GRACE risk score and initial Age-MSI (p<0.001; r:0.752, AUC:0.865, CI95%:0.831-0.901, cutoff: 51.0, Sensitivity 88%, Specificity 89%).

Conclusion: Age-MSI alone could identify patients with a high GRACE in NSTEMI undergoing PCI. It is better than SI, MSI, and Age-SI at predicting patients with high GRACE scores, although Age-MSI is more straightforward to calculate than GRACE.

Keywords: Age-modified-shock-index, GRACE, NonST elevation, myocardial infarction

ÖZET

Giriş: Kan basıncı ve kalp hızı ile bu parametrelerden türetilen şok indeksi (SI) ve modifiye şok indeksi (MSI), akut miyokard enfarktüsü geçiren hastalarda olumsuz sonuçları tahmin etmek için kapsamlı bir şekilde incelenmiştir. Yaş-SI ve özellikle yaş-MSI yeni tanımlanan parametrelerdir. NSTEMI ile başvuran hastalarda yaş-MSI'nın, kullanımı zor olan GRACE skoru yerine yatak tercih edilip edilemeyeceğini değerlendirmeyi amaçladık.

Gereç ve Yöntemler: Bu retrospektif çalışma, Temmuz 2019 ile Aralık 2022 tarihleri arasında, başvuru sırasında kardiyojenik şokta olmayan NSTEMI tanısı alan 495 hastayı içeren tek bir merkezde gerçekleştirildi. Tüm hastaların yaş-MSI ve GRACE skoru kaydedildi ve analiz edildi.

Bulgular: NSTEMI hastalarında, GRACE skoru ile başvuru yaş-MSI arasında iyi bir korelasyon bulundu (r: 0,752, p<0,001; AUC:0,865, p<0,001 GA %95: 0,831-0,901, cutoff : 51,0, Sensitivite %88, Spesifisite %89).

Sonuçlar: Tek başına yaş-MSI, NSTEMI hastalarında yüksek GRACE skoru olan hastaları belirleyebilir. Yüksek GRACE skorlu hastaları öngörmede yaş-MSI; SI, MSI ve yaş-SI'dan daha iyi korelasyona sahiptir. Ayrıca, yaş-MSI'ın hesaplanması GRACE skorundan daha kolay ve pratiktir.

Anahtar kelimeler: GRACE, ST-segment yüksekliği olmayan miyokard enfarktüsü, Yaş-modifiye şok indeksi

INTRODUCTION

World Health Organization data indicate that around eighteen million people worldwide die from cardiovascular diseases yearly (1). These deaths represent about thirty-one percent of all deaths worldwide (1). Approximately eighty-five percent of all cardiovascular diseases are due to acute myocardial infarction and cerebrovascular events (1). Elevated cardiac troponin levels, surpassing the 99th percentile of the upper reference limit, indicate myocardial damage (2). An upsurge followed by a downswing in cardiac troponin concentrations signifies acute myocardial injury (2). In the context of signs pointing towards acute myocardial ischemia, an acute myocardial infarction (AMI) is clinically defined by the detection of acute myocardial injury through abnormal cardiac biomarkers, specifically troponin (2). The GRACE (Global Registry of Acute Coronary Events) score serves as a predictive tool for the prognosis of patients with AMI (3-5). The purpose of developing the GRACE score was to assist healthcare providers in pinpointing patients who are more likely to face complications during and post-AMI. This scoring system includes eight parameters in total, including clinical, hemodynamic, and laboratory data. The factors considered in this context are age, systolic blood pressure (BP), heart rate (HR), the assignment of Killip class from I to IV, occurrence of cardiac arrest, serum creatinine levels, presence of ST segment deviation, and elevated cardiac parameters (3-5). Calculating the GRACE score is quite time-consuming because it contains many parameters. It is complex and challenging to apply routinely at the bedside.

HR and systolic BP are considered essential parameters in determining the prognosis of AMI (6, 7). Incorporating

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these vital sign components together, rather than leaning on a single essential parameter like HR or BP individually, might offer more reliable results in forecasting unfavorable outcomes in AMI. The shock-index (SI), known as the ratio between HR (beats per minute) and systolic BP (mmHg), is an easily obtained bedside index. It is formulated as follows: SI = HR / Systolic BP. SI provides reliable data about the hemodynamic instability of the patient. In addition, SI is better than using HR alone, systolic BP alone, or even some risk classification systems (8). Several observational studies involving patients with AMI have suggested that elevated admission SI (9-14). Its three derivatives, the Modified (MSI), the Age (age-SI), and the Age-Modified(age-MSI), are introduced to enhance its prognostic value (18). The MSI is the proportion of the Heart-Rate (HR) to the Blood-Pressure (BP). It is formulated as follows: MSI = HR / mean BP (15). The Age-SI is calculated by multiplying age with the SI (16-18). The prognostic value of them in AMI has been shown in many studies, however they have not been adequately examined whether the use of these parameters instead of GRACE risk assessment is used for Non-ST-Elevation Myocardial Infarct (NSTEMI) is beneficial.

The objective of this study is to explore the correlation between the GRACE and SI and its variants at the time of hospital admission for who have undergone PCI following a NSTEMI.

MATERIAL AND METHOD

The study's design was granted approval by the Institutional Review Board of Adana City Training and Research Hospital, aligning with the guidelines set out in the Declaration of Helsinki (IRB no: 2347, 2022). Furthermore, the IRB of our hospital approved a waiver of informed consent owing to the retrospective design. The retrospective study consisted of 847 consecutive patients admitted to the Emergency Department between February-2021 and December-2022 and subsequently underwent PCI. In all of them, 352 were excluded as follows: (a) STEMI (225), (b) noncoronary heart disease patients (27), (c) obvious arrhythmia at BP and HR measurements (36), (d) patients with cardiogenic shock (16), (e) deaths within 24h of admission (8), and (f) no follow-up (40). AMI is classified as either STEMI or NSTEMI. A diagnosis of NSTEMI was assigned to patients who presented with intense chest pain, exhibited no ST-segment elevation on an electrocardiogram, and showed elevated levels of enzymes. All data of the remaining 495 NSTEMI patients aged 40-75 years who underwent percutaneous coronary intervention were recorded. The study excluded individuals presenting with cardiogenic shock, persistent hypotension (systolic BP less than 90 mmHg) unresponsive to fluid balance adjustments and necessitating intra-aortic balloon pump or intravenous inotropic therapy. Also excluded were patients with arrhythmias causing irregular heart rate, such as atrial fibrillation and atrial flutter, those with a history of coronary artery bypass grafting or PCI, patients with 2nd or 3rd degree atrioventricular heart block and sinus bradycardia, patients with diabetes or chronic kidney disease, and those with malignancies or bleeding disorders. SI calculation was performed in every patient at presentation using the ratio between the HR and systolic BP (Shock Index = HR / Systolic BP).

Data Analysis

Data analysis was performed using SPSS-v21. The Kolmogrov-Smeirnov was selected for the normality analysis of continuous parameters. Such variables were represented as the average ± standard deviation (SD) or as the middle value with the interquartile range (IQR). For categorical variables, representation was done using both percentages (%) and raw counts. To observe the indices and GRACE-scoring, correlation coefficients were deployed. The ROC curve analysis was utilized to explore the connection between the GRACE and the shock-index along with its derivatives. The study maintained a 95%confidence-interval, and a p-value under 0.05 was deemed as representing a significance in this investigation.

RESULTS

Of 847 patients, 352 were excluded due to incomplete data, the presence of atrial fibrillation, ventricular premature extrasystole, or other apparent arrhythmias at admission. Ultimately 495 remaining patients were analyzed. Upon comprehensive examination of their medical records, it

Table 1. Baseline characteristics of the study population.

Variables	Results
Age (years) (mean±ss)	57.7±10.6
Sex (male), n (%)	60 (60%)
Body mass index, kg/m2 (mean±ss)	28±4.5
Low density lipoprotein - cholesterol, mg/dl (mean±ss)	123.8±30.6
Triglyceride, mg/dl (mean±ss)	180.4±76.3
Urea, mg/dl (mean±ss)	34.1±10.2
Creatinine, mg/dl (mean±ss)	0.83±0.25
Left ventricular ejection fraction, % (mean±ss)	51.8±7.8
GRACE score (mean±ss)	126.2±29.9
Heart rate, beats/min (mean±ss)	73.8±10.8
Systolic BP, mmHg (mean±ss)	120.6±17
Diastolic BP, mmHg (mean±ss)	71±10.6
SI (mean±ss)	0.62±0.11
Age_SI (mean±ss)	35.7±8.3
MSI (mean±ss)	0.85±0.14
Age MSI (mean±ss)	49±7.16

BP: Blood pressure; GRACE: Global registry of acute coronary events; MSI: Modified shock index; NSTEMI: Non-ST-eegment elevation myocardial infarction; SI, shock index.

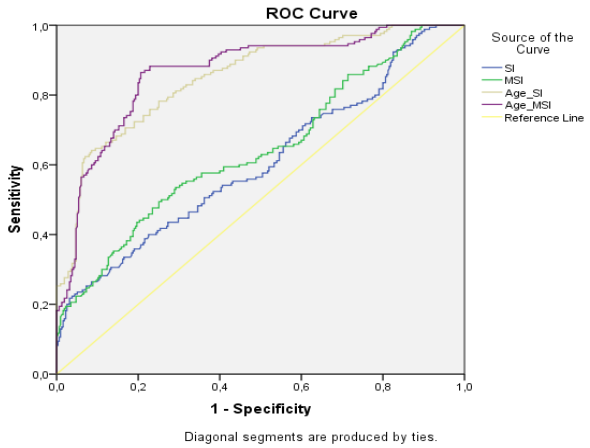

Figure 1. Receiver operating characteristic curves of admission SI, modified SI, age SI, modified age SI and GRACE score. GRACE indicates Global Registry of Acute Coronary Events; SI, shock index. (AUC:0.865, p<0.001 CI 95%: 0.831-0.901, cutoff: 51.0, Sensitivity 88%, Specificity 89%)

was determined that these patients met the criteria for a confirmed NSTEMI diagnosis based on the parameters set forth in the current study. Of these patients, 60 (60%) were male, 198 (40%) were female (mean age:57.7±10.6). Demographic, clinical characteristics and laboratory findings of all study patients are shown in Table 1. These patients were divided into the low-risk (<109), intermediate-risk (109-140), and the high-risk (>140) categories according to GRACE scores. Correlation between GRACE and admission SI (r:0.12; p=0.24), MSI (r:0.23; p=0.023), age-SI (r:0.679; p<0.001), age-MSI (r:0.752; p<0.001) are shown in Table 2. ROC curve (Figure 1) between GRACE risk score and admission SI, MSI (AUC:0.642, p<0.001 CI 95%: 0.589-0.695, cutoff: 0.88, sensitivity 56%, specificity 71%), age-SI (AUC:0.850, p<0.001 CI 95%: 0.814-0.886, cutoff: 39.0, sensitivity 68%, specificity 82%), age-MSI (AUC:0.865, p<0.001 CI 95%: 0.831-0.901, cutoff: 51.0, sensitivity 88%, specificity 89%) (Table 3). There was a significant correlation between GRACE score and age-MSI. In addition, age-MSI was found to have a significantly higher sensitivity and specificity to predict a high GRACE (>140), scheduled for early invasive intervention.

DISCUSSION

Early revascularization is the most important strategy for healing outcomes in NSTEMI patients with high-risk features (19). Thus, rapid identification of NSTEMI with higher risk characteristics is an essential stone of their management. This pioneering research not only explores the link between age-MSI and the GRACE in NSTEMI undergoing PCI but also uniquely compares the admission age-MSI with variables such as admission MSI, age-SI, SI, and the GRACE itself. Age-MSI was highly correlated with the GRACE scoring system compared to others (admission SI, age-SI, and MSI). Moreover, further ROC analysis showed that the admission age-MSI had significantly

Table 2. Correlation values between GRACE score and admission SI, modified SI, age SI, modified age SI in patients with NSTEMI who underwent right/left selective coronary angiography.

GRACE score		
Parameters	**r value**	**p value**
Heart rate	0.11	0.29
Systolic blood pressure	-0.05	0.62
Diastolic blood pressure	-0.29	0.004
Mean blood pressure	-0.22	0.035
SI	0.12	0.24
Age-SI	0.679	<0.001
Modified SI	0.23	0.023
Modified age SI	0.752	<0.001

Notes: GRACE: Global registry of acute coronary events; NSTEMI: Non-ST-segment elevation myocardial infarction; SI, shock index. p value (<0.05) is statistically significant.

Table 3. ROC values between GRACE score and admission SI, modified SI, age SI, modified age SI in patients with NSTEMI who underwent right/left selective coronary angiography.

Variables	AUC	p	CI 95%	cutoff	Sensitivity	Specificity
SI	0.605	0.028	0.550-0.659	-	-	-
Age_SI	0.850	<0.001	0.814-0.886	39	68%	92%
Modified SI	0.642	<0.001	0.589-0.695	0.88	56%	71%
Modified age SI	0.865	<0.001	0.831-0.901	51	88%	89%

Notes: GRACE indicates Global Registry of Acute Coronary Events; SI, shock index.; p value (<0.05) is statistically significant.

highersensitivity and specificity than the admission SI, age-SI, and MSI (20).

In 1967, SI was improved for assessing the level of hemodynamic-stability was proposed as an accurately and practically evaluable risk index for circulatory failure in trauma patients. Bilkova and colleagues demonstrated that SI forecasts the mortality among patients suffering from STEMI. (9). Considering that coronary perfusion mostly occurs in the diastolic phase, MSI has been used instead of SI after a while since diastolic blood pressure is undeniably important in determining clinical severity in patients with AMI (13, 21). It is a comfortably computable simple index not containing subjective details. It does not require previous patient history. It is not an index dependent on blood tests (13). It has been demonstrated that, for patients experiencing trauma, the MSI serves as a more effective prognostic tool than the SI. (21, 22). Both SI and

MSI presented useful prognostic device in this population (13, 21, 22). Neumann and colleagues revealed that Age-SI serves as a predictor of the mortality of hospitalization of geriatric trauma better than SI-MSI (19). Prior studies have highlighted the significance of age as a prognostic factor for unfavorable outcomes among individuals diagnosed with Acute Coronary Syndrome (23). In research conducted by Jian Zhou et al., it was observed that an elevated age-SI independently predicts the occurrence of cardiovascular events during hospitalization as well as all-cause mortality in patients with STEMI. Intriguingly, the predictive ability of age-SI surpassed that of both SI and MSI in the study (18). Age-MSI is a new index derived from SI. It includes several parameters such as age, HR, systolic BP, and diastolic BP. In patients with STEMI, Jian Zhou and their colleagues discovered that age-MSI plays a crucial role in predicting unfavorable outcomes independently (18). Their findings demonstrated that age-MSI's predictive capability is on par with the GRACE score when it comes to in-hospital cardiovascular events and overall mortality. Age-MSI surpasses SI-MSI in terms of its strength in predicting events of STEMI (18). However, clinicians need to acknowledge the consequences of both false positive or negative when evaluating SI, MSI, and age-SI.

Our study showed that age-MSI had a good correlation with GRACE in NSTEMI. Therefore, age-MSI can be a useful indice that can be found quickly and can quickly distinguish higher risk NSTEMI. It requires complex calculations to obtain these risk scores. This limits their use in routine clinical practice. Age-MSI has the advantage that it can be calculated quickly. Therefore, it can be considered a valuable prognostic tool. Age-MSI can support clinicians in applying different strategies in the ACS population to improve their outcomes. One possible approach is to implement strategies aimed at providing hemodynamic support and delivering timely interventions that can potentially impact the prognosis. Previous studies have demonstrated the effectiveness of utilizing the GRACE to identify individuals with a higher likelihood of experiencing negative outcomes in populations affected by ACS (24, 25). Each patient's detailed demographic, hemodynamic data, electrocardiographic findings and troponin values are required for calculating the GRACE. It is challenging to gain all of these parameters as soon as patients with ACS apply to hospitals. Therefore, the implementation of a risk-stratification tool like age-MSI, which efficiently identifies high-risk patients, holds significant clinical value. In comparison to the GRACE risk score, age-MSI is a simpler calculation and can serve as a readily accessible tool for stratifying patients with non-ST-segment elevation myocardial infarction (NSTEMI), providing valuable guidance for their clinical care.

Study limitations

It is important to note that the study had a retrospective nature, without randomization, and relied on observational data. Furthermore, the study was limited to a single center, which increases the likelihood of potential confounding factors and selection bias not being fully accounted for. Secondly, it is worth mentioning that heart rate (HR) and blood pressure (BP) were only measured at a single time point, which may not fully capture the dynamic nature of these physiological variables. Subsequent repeated measurements may be affected by later interventions. These data may still be the most reliable indicator. Third, patients with obvious arrhythmias such as ventricular early extrasystole, atrial fibrillation (AF) were not included in this study. These arrhythmias can cause inaccurate BP measurements. In addition, Lopes et al. showed that there is a relationship between mortality and AF in AMI (26). Finally, data on medical treatment such as beta-blockers, calcium channel blocker, digoxin, and amiodarone affecting admission HR or BP were incomplete.

CONCLUSIONS

In NSTEMI, age-MSI at presentation has stronger sensitivity and specificity than presentation SI, MSI, and age-SI compared with the GRACE risk score. Age-MSI appears to offer a practical and straightforward bedside tool for rapid identification of valuable patients with NSTEMI with high-risk features at presentation. It can be useful for risk stratification in emergency settings.

Ethics Committee Approval: The study's design was granted approval by the Institutional Review Board of Adana City Training and Research Hospital, aligning with the guidelines set out in the Declaration of Helsinki (IRB no: 2347, 2022).

Informed Consent: This study was retrospectively.

Authorship Contributions: Idea/Concept: ME, Design: ME, Supervision: ME, Data Collection or Processing: ME, Analysis or Interpretation: ME, Literature Search: ME, Writing: ME, Critical Review: ME, References And Fundings: -, Materials: ME.

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