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The utility of the TIMI risk index on admission for predicting angiographic no-reflow after primary percutaneous coronary intervention in patients with STEMI

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Background/aim: The thrombolysis in myocardial infarction (TIMI) risk score (TRS), and the TIMI risk index (TRI) have been reported in coronary artery disease patients. We investigated whether admission TRI is associated with no-reflow (NRF) in patients undergoing primary percutaneous coronary intervention (p-PCI).

Materials and methods: ST-segment elevation myocardial infarction (STEMI) patients treated with p-PCI were included in the study. TRI was calculated on admission using specified variables. We defined the angiographic NRF phenomenon as a coronary TIMI flow grade of ≤2 after the vessel was recanalized or a TIMI flow grade of 3 together with a final myocardial blush grade (MBG) of <2 in a manner as described in previous studies.

Results: A total of 371 patients (aged 62 ± 14 years; 73/27 men to women ratio) who underwent p-PCI were enrolled in the study. In terms of age, NRF patients were older than reflow patients (P < 0.017 for MBG). Killip class III-IV designations were more common in NRF patients (P = 0.029 for MBG). TRI (P = 0.014 for MBG) values were significantly greater in the NRF group. TRI was an independent predictor of NRF according to MBG flow (P = 0.003, B = –0.035, Exp B = 0966, 95% CI, 0.944–0.988).

Conclusion: Admission TRI may predict the development of NRF phenomenon after p-PCI in patients with acute STEMI.

Key words: ST-segment elevation myocardial infarction, global registry of acute coronary events risk score, thrombolysis in myocardial infarction risk score, thrombolysis in myocardial infarction risk index, no-reflow phenomenon, primary percutaneous coronary intervention

1. Introduction

Coronary artery disease (CAD) and acute myocardial infarction (AMI) are major causes of death and morbidity worldwide (1). Rapid restoration of coronary blood flow to the jeopardized myocardium is the crux of therapy after AMI. The invention and usage of stents have made percutaneous coronary intervention (PCI) a safe, effective, and preferred treatment of ST-segment elevation myocardial infarction (STEMI) (2). However, even after patency of an infarcted artery was successfully achieved via stent implantation, sufficient myocardial reperfusion was not observed in 2.3% to 29% of patients in the setting of AMI, often called the no-reflow (NRF) phenomenon (3–5). Despite the mechanical opening of the infarct-related artery (IRA), early postinfarction complications and in-hospital long-term morbidity and mortality rates increased in patients who developed NRF (6–8). The mechanisms of NRF are complex and multifactorial; the most probable causes include a combination of platelet aggregation, distal embolization, microvascular vasoconstriction, neutrophil plugging, and tissue edema (9). Noninvasive markers of the NRF phenomenon may thus provide important prognostic information. Recently, one of the major issues cardiologists have been working on is risk prediction in patients with STEMI to identify NRF. (6–8,10). A large number of scoring systems and laboratory parameters have been used in clinical practice. Nevertheless, those interested in cardiovascular medicine still need an easily accessible, cost effective, and noninvasive predictor to carry out risk stratification by determining NRF in acute coronary syndrome (ACS) patients. In order to identify high-risk patients with ACS, various risks classification systems and scoring systems are used frequently (11–14). Prediction of early and late mortality in hundreds of thousands of patients has been shown by the in-hospital death global registry of acute coronary events (GRACE) risk score (GRS) and the thrombolysis in myocardial infarction (TIMI) risk score (TRS) (13,14). Recently, the TIMI risk index (TRI) (which

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can predict mortality, may be easier to assess and can be scored with fewer parameters in patients with non-ST-segment elevation ACS (NSTE-ACS) and patients with STEMI) was improved. This index has been shown to be useful and helpful in many studies (15,16). Many studies have investigated the relationship between GRS, TRI, and ACS (1,17–19), but none have addressed the association between TRI, TRS, GRS, and NRF in patients with STEMI. We investigated whether preintervention TRI, TRS, and GRS are related to coronary NRF in patients with STEMI who underwent primary percutaneous coronary intervention (p-PCI).

2. Materials and methods

2.1. Study population

A total of 900 patients who presented with STEMIs and underwent p-PCI within 12 h of symptom onset between January 2012 and February 2014 were included in this retrospective study. STEMI was defined based on the criteria used by the American College of Cardiology and the European Society of Cardiology (20): an increase in troponin I > 1 ng/mL, a new ST elevation as measured from the J-point in 2 or more contiguous leads with leads V1, V2, and V3 measuring at least 0.2 mV or at least 0.1 mV in the remaining leads during the first 12 h after symptom onset, or newly developed left bundle branch block (LBBB) pattern.

Patients with malignancy, bleeding diathesis, hematological disease, severe liver disorder, autoimmune disease, severe valvular disease, and inflammatory or infectious diseases were excluded from the study. In addition, patients on the following medications were not included in the study: corticosteroids, cytotoxic drugs, thrombolytic therapy, glycoprotein IIb/IIIa inhibitors, and diuretics. Patients who were not treated with p-PCI, did not undergo follow-up blood work, or had poor echocardiographic windows were also excluded from the investigation. As a result, a total of 371 patients formed the study group.

All patients underwent physical examination and coronary risk factor assessment through a complete medical history. Additionally, Killip class examinations of all patients were recorded (21).

Demographic data and variables to determine TRS according to age, diabetes mellitus (DM)/hypertension (HT) or angina, heart rate of <100 bpm, systolic blood pressure (SBP) of <100 mmHg, Killip class II-IV, weight of <67 kg, anterior MI or LBBB presentation, and latency of >4 h were recorded (22). Calculation of the TRS was performed with a computer program (http://www.mdcalc.com/timi-risk-score-for-stemi/).

The determination of GRS points including age, creatinine, heart rate, SBP, Killip class, cardiac arrest on admission, elevated cardiac markers, and ST-segment deviation were recorded (14); the calculation of GRS was performed using a computer program (www.outcomesumassmed.org/grace/acs_risk/acs_risk_content.html).

The TRI of patients were calculated by the formula "Heart rate × $(age \div 10)^2 \div SBP$".

During the in-hospital follow-up period patients were monitored for major adverse cardiac events (MACEs). Cardiogenic shock, new advanced heart failure, pulmonary edema, complete atrioventricular block (AVB) requiring a temporary pacemaker, severe ventricular arrhythmia, and in-hospital mortality during the post-PCI follow-up period were regarded as MACEs. An in-hospital mortality was only considered a MACE if the death was caused by myocardial infarction, cardiac arrest, or other cardiac-related causes. Cardiogenic shock was defined as: marked and persistent hypotension lasting more than 30 min with a SBP less than 80 mmHg and signs of hypoperfusion due to left ventricular dysfunction, right ventricular infarction, or cardiac mechanical complications. If the patient qualified for a New York Heart Association functional classification of III or greater, it was considered new-onset advanced heart failure. Severe ventricular arrhythmias (ventricular tachycardia, ventricular fibrillation, or asystole) were considered to be MACEs if they occurred within 48 h of onset.

2.2. Blood samples and echocardiography

Venous blood samples were collected when the patient was admitted to the emergency department or intensive coronary care unit (ICCU) before p-PCI. Hematologic indices were calculated using an automated hematology analyzer system (Abbott Cell-Dyn 3700; Abbott Laboratory). Absolute cell counts were utilized to perform subsequent analyses. The neutrophil to lymphocyte ratio (NLR) was calculated as the ratio of the neutrophils and lymphocytes, both obtained from the same automated blood sample at admission. Total cholesterol, high-density lipoprotein, low-density lipoprotein, triglycerides, and creatinine levels were measured with the Abbott Architect C16000 autoanalyzer (Abbott Laboratory). Fasting lipid panels were obtained after an overnight fast.

Transthoracic two-dimensional echocardiography was performed upon admission to the ICCU to determine left ventricular ejection fraction, left ventricular systolic diameter, left ventricular diastolic diameter, and left atrial diameter (Vivid S6, GE Medical Systems).

2.3. Coronary angiography (TIMI and myocardial blush grade (MBG) flow)

All patients underwent selective coronary angiography using the Judkins technique. PCI procedures were performed with a standard femoral approach using a 7 Fr guiding catheter. Coronary blood flow patterns after

p-PCI were subject to a thorough evaluation on the basis of TIMI flow grade, using grades 0, 1, 2, and 3 (23). The final TIMI flow grade and MBG were assessed using standard methods. Two cardiologists who were blinded to the patients' clinical situations assessed the postprocedural TIMI flow grade of the IRA. We defined the angiographic NRF phenomenon as a coronary TIMI flow grade of ≤2 after the vessel was recanalized or TIMI flow grade 3 together with a final MBG of <2, in the same manner as described in previous studies (24,25). For all study participants, only one artery was identified as the IRA. CAD was defined as greater than 50% stenosis in one of the major coronary arteries.

2.4. Statistical analysis

All analyses were performed with SPSS for Windows version 18.0. Continuous variables were expressed as means ± standard deviation and categorical variables were expressed as percentages. The two-sample Kolmogorov–Smirnov test assessed whether continuous variables followed a normal distribution. Comparisons between categorical and continuous variables between the reflow and NRF groups were performed using the χ^2 or Fischer's exact test and independent samples t-test or Mann–Whitney U-test, respectively. Statistical significance was defined as $P < 0.05$.

Multivariate stepwise forward logistic regression analysis was used to assess independent predictors of postprocedural NRF according to MBG flow. All variables that were significant predictors were included in the logistic regression model; the results were expressed as the odds ratio (OR) with the corresponding 95% confidence interval (CI).

The study protocol was reviewed and approved by the Ethics Committee in accordance with the Declaration of Helsinki.

3. Results

A total of 371 patients were included in the data analysis. Of all the study participants, 17.5% according to MBG flow were in the NRF group, while the remaining were stratified into the reflow group. Baseline demographic characteristics and cardiac risk scores on admission of patients for TIMI and MBG flow after p-PCI results organized according to reflow grouping are shown in Tables 1 and 2. No significant differences regarding known atherogenic risk factors, prehospital medication, location of STEMI, SBP, and heart rate on admission were identified between the groups. NRF patients were older than reflow patients ($P < 0.018$ for TIMI flow, $P < 0.017$ for MBG flow) and Killip class III-IV designations were more common in NRF patients ($P = 0.009$ for TIMI flow, $P = 0.029$ for MBG). TRS ($P = 0.015$ for TIMI flow, $P = 0.043$ for MBG), GRS ($P < 0.001$ for TIMI flow, $P = 0.004$ for MBG), and TRI ($P = 0.002$ for TIMI flow, $P = 0.014$ for MBG) values in the NRF group were significantly greater than those in the reflow group.

Angiographic findings according to reflow grouping are shown in Tables 3 and 4.

In-hospital mortality and MACEs were also significantly higher in the NRF group. Similarly, in-hospital cardiogenic shock, severe ventricular arrhythmia, and cardiopulmonary resuscitations were more common in the NRF patients (Tables 5 and 6).

Multivariate binary forward stepwise logistic regression analysis revealed that a high level of TRI was an independent predictor of NRF according to MBG flow ($P = 0.003$ B = –0.035, Exp B = 0966, 95% CI, 0.944–0.988).

4. Discussion

In the present study we showed that increased TRI, TRS, and GRS on admission were significantly associated with the development of angiographic NRF phenomenon in patients with acute STEMI who underwent p-PCI. Moreover, TRI was a significant and independent predictor of NRF. We also showed the Killip class.

Primary PCI is the recommended treatment for patients with acute STEMI. In 2008 the Stent for Life (SFL) initiative was launched by the European Association of Percutaneous Cardiovascular Interventions and EuroPCR in partnership with the European Society of Cardiology Working Group on Acute Cardiac Care and country-specific national cardiac societies. The aim was to promote the prioritization of PCI treatment for those who will benefit most, namely STEMI patients. The following countries are currently participating: Bulgaria, Egypt, France, Greece, Italy, Portugal, Romania, Serbia, Spain, and Turkey (26). Preliminary reports suggest that major increases have been seen in the numbers of p-PCI treatments performed, with some countries reporting very significant increases in p-PCI use between 2008 and 2010. Improvements in STEMI mortality rates have also been observed. The number of p-PCI treatments performed in Europe has steadily increased over the past decade. However, a European survey from 2007 reported that only 40%–45% of European STEMI patients were treated with p-PCI, with large variations in treatment availability between countries (27). The challenges of introducing new technologies into clinical practice can be substantial and include a complex mix of medical, organizational, patient-related, regulatory, and economic factors (28).

There are 207 PCI capable centers in Turkey, shared among government hospitals, university hospitals, and private hospitals. P-PCI is performed 24/7 in 82 of the 207 centers. In March 2011, the Ministry of Health declared p-PCI as the first choice treatment for STEMI patients nationally, if transport time is less than 90 min. Since

Table 1. Baseline demographic characteristics and cardiac risk scores of patients for TIMI flow after primary PCI.

Variables	Reflow	No-reflow	P value
Age, years	60.8 ± 13.6	65.2 ± 13.4	<0.018*
Males, n (%)	224 (73)	45 (69)	0.515
Previous history			
Hypertension, n (%)	108 (35)	24 (37)	0.803
Diabetes mellitus, n (%)	68 (22)	20 (31)	0.141
Smoking, n (%)	173 (57)	29 (45)	0.080
Hyperlipidemia, n (%)	19 (6)	4 (6)	0.987
Family history, n (%)	60 (20)	12 (19)	0.832
Previous MI or CAD, n (%)	20 (7)	0 (0)	0.034
Previous PCI, n (%)	18 (6)	4 (6)	0.559**
Prehospital medication			
Aspirin use, n (%)	223 (77)	45 (74)	0.634
Clopidogrel, n (%)	154 (53)	24 (40)	0.054
Beta blocker, n (%)	28 (9)	7 (1)	0.691
ACE inhibitors, n (%)	31 (10)	5 (8)	0.546
Statin, n (%)	20 (7)	5 (8)	0.453
Enoxaparine, n (%)	274 (90)	61 (94)	0.287
Killip class on presentation, n (%)			
I-II	274 (94)	51 (83)	0.009**
III-IV	17 (6)	10 (17)	
Admission SBP (mmHg),	127.6 ± 23.9	122.6 ± 25.6	0.128
Admission heart rate (bpm)	83.0 ± 15.9	86.1 ± 20.7	0.264
Duration of chest pain (hour)	5.6 ± 4.1	6.3 ± 3.8	0.210
Location of STEMI			
Anterior, n (%)	131 (45)	30 (49)	0.553
Nonanterior, n (%)	160 (55)	31 (51)	
Cardiac risk scores on admission			
TIMI risk score	3.8 ± 2.2	4.8 ± 2.9	0.015
GRACE risk score	151.7 ± 35.4	177.0 ± 51.4	<0.001*
TIMI risk index	25.6 ± 12.5	32.1 ± 15.8	0.002*

**Fischer Exact; Other Statics Student's *t* -test; χ^2 test; *Mann–Whitney U test; Values are means ± SD or n (%).

Turkey joined the SFL initiative, the number of p-PCI performed has increased significantly in ten pilot cities. In 2010, 85% of STEMI patients were treated with p-PCI. In addition, a STEMI network was created with collaboration between a number of invasive centers, noninvasive hospitals, ambulances, and emergency systems (26).

Rapid restoration of coronary flow to the jeopardized myocardium has become an essential part of therapy after STEMI. P-PCI has also been found to significantly improve the survival of these patients (29). Despite an open IRA, breakdown of obstruction to the coronary microvasculature can markedly decrease blood flow to the

Table 2. Baseline demographic characteristics and cardiac risk scores of patients for MBG after primary PCI.

Variables	Reflow	No-reflow	P value
Age, years	60.9 ± 13.6	66.0 ± 13.8	<0.017*
Males, n (%)	241 (74)	28 (62)	0.099
Previous history			
Hypertension, n (%)	115 (35)	17 (38)	0.742
Diabetes mellitus, n (%)	73 (22)	15 (33)	0.106
Smoking, n (%)	1783 (56)	19 (42)	0.079
Hyperlipidemia, n (%)	20 (7)	3 (6)	0.546**
Family history, n (%)	66 (20)	6 (13)	0.272
Previous MI or CAD, n (%)	20 (6)	0 (0)	0.070**
Previous PCI, n (%)	20 (6)	2 (4)	0.486**
Prehospital medication			
Aspirin use, n (%)	239 (77)	29 (69)	0.251
Clopidogrel, n (%)	160 (52)	18 (43)	0.287
Beta blocker, n (%)	31 (10)	4 (9)	0.574
ACE inhibitors, n (%)	33 (7)	3 (10)	0.338
Statin, n (%)	21 (6)	4 (9)	0.359
Enoxaparine, n (%)	294 (90)	41 (91)	0.551
Killip class on presentation, n (%)			
I-II	290 (93)	35 (83)	0.029**
III-IV	20 (7)	7 (17)	
Admission SBP (mmHg),	127.4 ± 23.9	122.3 ± 26.0	0.193
Admission heart rate (bpm)	83.4 ± 15.9	84.9 ± 23.5	0.686
Duration of chest pain (hour)	5.6 ± 4.1	6.4 ± 3.8	0.255
Location of STEMI			
Anterior, n (%)	144 (47)	17 (41)	0.466
Nonanterior, n (%)	166 (53)	25 (59)	
Cardiac risk scores on admission			
TIMI risk score	3.9 ± 2.2	4.9 ± 3.1	0.043
GRACE risk score	152.9 ± 35.9	178.4 ± 56.0	0.004*
TIMI risk index	25.9 ± 12.6	32.6 ± 17.2	0.014*

**Fischer Exact; Other Statics Student's *t* -test; χ^2 test (%), *Mann–Whitney U test; Values are means ± SD or n (%).

infarct zone. This effect is known as the NRF phenomenon (30,31). Coronary flow decreases in elderly patients, menopausal women, and patients with coronary risk factors (32). This phenomenon is strongly correlated with short- and long-term morbidity and mortality in the settings of STEMI (33). In our study, we showed that NRF was significantly related to in-hospital mortality and MACEs. The pathophysiology of the NRF phenomenon has not been fully clarified and its etiology appears to be multifactorial. Some of the contributing factors in the occurrence of NRF are distal atherothrombotic embolization, mechanical microvascular leukocytes, platelet plugs in situ thrombosis,

Table 3. Angiographic findings of patients for TIMI flow after primary PCI.

	Reflow	No-reflow	P value
Culprit lesion			
LAD, n (%)	139 (46)	37 (57)	0.027
RCA, n (%)	114 (37)	25 (39)	
CX, n (%)	53 (17)	31 (4)	
Number of coronary arteries narrowed			
1 vessel, n (%)	134 (44)	24 (37)	0.299
>1 vessel n, (%)	171 (56)	41 (63)	

CX, circumflex coronary artery; LAD, left descendant coronary artery; RCA, right coronary artery.

Table 4. Angiographic findings of patients for MBG after primary PCI.

	Reflow	No-reflow	P value
Culprit lesion			
LAD, n (%)	153 (87)	23 (13)	0.097
RCA, n (%)	119 (86)	20 (14)	
CX, n (%)	54 (96)	2 (4)	
Number of coronary arteries narrowed			
1 vessel, n (%)	143 (91)	15 (9)	0.175
>1 vessel n, (%)	182 (86)	30 (14)	

CX, circumflex coronary artery; LAD, left descendant coronary artery; RCA, right coronary artery.

Table 5. In-hospital adverse outcomes of patients TIMI flow after primary PCI.

	Reflow	No-reflow	P value
In-hospital MACE**,** n (%)	56 (17)	28 (44)	<0.001
Advanced Heart Failure, n (%)	17 (6)	7 (11)	0.121
Advanced pulmonary edema, n (%)	10 (4)	6 (9)	0.043*
Cardiogenic shock, n (%)	17 (6)	13 (20)	<0.001*
Complete atrioventricular block requiring transient pacemaker	13 (4)	5 (8)	0.193*
Serious ventricular arrhythmia	21 (7)	12 (19)	0.003
Cardiopulmonary resuscitation, n (%)	24 (8)	19 (29)	<0.001
Hospitalization duration (days)	5.3 ± 4.7	6.0 ± 6.2	0.402
In-hospital mortality, n (%)	20(7)	17(26)	<0.001

*: Fischer exact test; MACE: major adverse cardiac event.

Table 6. In-hospital adverse outcomes of patients MBG after primary PCI.

	Reflow	No-reflow	P value
In-hospital MACE, n (%)	62 (19)	22 (50)	<0.001
Advanced Heart Failure, n (%)	20 (6)	4 (9)	0.329*
Advanced pulmonary edema, n (%)	13 (4)	3 (7)	0.305*
Cardiogenic shock, n (%)	19 (6)	11 (24)	<0.001*
Complete atrioventricular block requiring transient pacemaker	13 (4)	5 (11)	0.053
Serious ventricular arrhythmia	23 (7)	10 (22)	0.003*
Cardiopulmonary resuscitation, n (%)	27 (8)	16 (36)	<0.001
Hospitalization duration (days)	5.3 ± 4.6	6.0 ± 7.2	0.543
In-hospital mortality, n (%)	22 (7)	15 (33)	<0.001*

*: Fischer Exact test; MACE: major adverse cardiac event.

ischemic endothelial edema and damage, vasospasm, free oxygen radicals, and susceptibility of the coronary microcirculation to injury (9,34,35). The close interplay between inflammation, coagulation, and atherosclerosis progression has become a field of intensive research. An increased inflammatory activity in the setting of STEMI may be one of the underlying NRF mechanisms. In fact, an elevated leukocyte–platelet interaction at the site of the plaque rupture may play a negative role in distal myocardial reperfusion by activating further inflammation. Botto et al. (36) showed an increased leukocyte–platelet functional interaction in STEMI at the site of plaque rupture relative to the systemic circulation, which may be one of the pathogenic mechanisms liable for NRF phenomenon. Thus, both locally increased inflammatory markers and leukocyte–platelet coaggregates at the site of the plaque rupture may be pathogenic mechanisms responsible for the angiographic NRF phenomenon after p-PCI in STEMI.

Effective risk stratification is integral to the management of patients with ACS (37). Even among patients with STEMI for whom initial therapeutic options are well-defined, patient risk characteristics can affect early therapeutic decision making (38–40). There are few models that have integrated weighing information from multivariate regression in a fashion similar to the TRS, TRI, and GRS. The GRS has been recognized as a validated predictor of adverse cardiovascular disease events (19,41). GRS includes some variables, but does not include the properties of coronary lesion and inflammatory markers. The TRS for STEMI is a clinical stratification calculated with data obtained from hospital presentations that can easily classify low- and high-risk patients (42). The TRS was validated prospectively in various studies. The analysis was subsequently validated in an unselected patient population in the National Registry of Myocardial Infarction (43) and showed a strong predictive value for mortality in patients treated with thrombolytic therapy (44). TRS has been shown to be a predictor of MACEs in patients with STEMI (18). The TRS serves as a prognostic calculator that discriminates high-risk patients with a combination of baseline variables that are part of the routine medical evaluation (22). Moreover, the relationship between TRS and the severity of CAD has been shown in several studies. TRS was compared with the results of coronary angiography in 683 patients with NSTE-ACS; for each increased risk category, the 3-vessel disease was shown to be more frequent (1). In the PRISM-PLUS study of 1491 patients with ACS, it was shown that there were more severe coronary lesions and left main coronary lesions in patients with high TRS compared with those with low TRS (45). The TRS reliably identified patients who were at high risk, while maintaining good discriminatory capacity in the low-risk range, where smaller absolute differences are more likely to impact clinical decisions. The TRS includes some variables, but does not include inflammatory markers and the properties of coronary lesions. Another one of the important scoring systems used in risk stratification in patients with ACS is TRI. It has been shown to be useful and helpful in many studies with large patient populations. It was derived from observed risk relations among 13,253 patients enrolled in the Intravenous NPA for the treatment of infarcting myocardium early (In TIME II) randomized trial of lanoteplase versus alteplase as reperfusion therapy for STEMI (46). The prognostic discriminatory capacity of this index was demonstrated (15,16,46). The TRI was a strong and independent predictor of mortality at

24 h. It was validated in an external data set of STEMI patients from the TIMI-9 trials that showed both a high discriminatory capacity and concordance between the observed 30-day mortality and the predictions based on the In TIME II data (47). Rathore et al. (48) focused on this very point after evaluating the discrimination and calibration performance of the TRI in a community-based cohort of elderly patients taken from the Cooperative Cardiovascular Project. We applied the TRS, TRI, and GRS for STEMI in a group of patients who underwent p-PCI and showed that an increase in these scores was associated with increased frequency of angiographic NRF.

To our knowledge, the relationship of TRI, TRS, and GRS with NRF for STEMI has not been previously investigated. Our results demonstrated for the first time the predictive value of these scores for NRF in patients with STEMI. In the present study, we think that with the help of the calculation of these scores in patients admitted to the emergency department with ACS, information about NRF of the CAD may be obtained.

Some limitations of our study include its retrospective nature and relatively small number of patients. Our study's population was also from a single center. Due to a male dominance in the patients in our study, the results may not be applicable to female patients.

The TRI, GRS, and TRS are routinely used for stratification of patients with ACS. Our study showed that these scores were significantly associated with NRF in patients with STEMI. We think that these findings can guide further clinical practice.

References

1. Santos ES, Aguiar Filho Lde F, Fonseca DM, Londero HJ, Xavier RM, Pereira MP, Minuzzo L, Souza Rd, Timerman A. Correlation of risk scores with coronary anatomy in non-ST-elevation acute coronary syndrome. Arq Bras Cardiol 2013; 100: 511-517.
2. Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC), Steg PG, James SK, Atar D, Badano LP, Blömstrom-Lundqvist C, Borger MA, Di Mario C, Dickstein K, Ducrocq G et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J 2012; 33: 2569-2619.
3. Harrison RW, Aggarwal A, Ou FS, Klein LW, Rumsfeld JS, Roe MT, Wang TY; . Incidence and outcomes of no-reflow phenomenon during percutaneous coronary intervention among patients with acute myocardial infarction. Am J Cardiol 2013; 111: 178-184.
4. Magro M, Nauta ST, Simsek C, Boersma E, van der Heide E, Regar E, van Domburg RT, Zijlstra F, Serruys PW, van Geuns RJ. Usefulness of the SYNTAX score to predict "no reflow" in patients treated with primary percutaneous coronary intervention for ST-segment elevation myocardial infarction. Am J Cardiol 2012; 109: 601-606.
5. Ndrepepa G, Tiroch K, Fusaro M, Keta D, Seyfarth M, Byrne RA, Pache J, Alger P, Mehilli J, Schömig A et al. 5-year prognostic value of no-reflow phenomenon after percutaneous coronary intervention in patients with acute myocardial infarction. J Am Coll Cardiol 2010; 55: 2383-2389.
6. Akpek M, Kaya MG, Lam YY, Sahin O, Elcik D, Celik T, Ergin A, Gibson CM. Relation of neutrophil/lymphocyte ratio to coronary flow to in-hospital major adverse cardiac events in patients with ST-elevated myocardial infarction undergoing primary coronary intervention. Am J Cardiol 2012; 110: 621-627.
7. Celik T, Kaya MG, Akpek M, Yarlioglues M, Sarli B, Topsakal R, Gibson CM. Does serum bilirubin level on admission predict TIMI flow grade and in-hospital MACE in patients with STEMI undergoing primary PCI. Angiology 2014; 65: 198-204.
8. Sen N, Afsar B, Ozcan F, Buyukkaya E, Isleyen A, Akcay AB, Yuzgecer H, Kurt M, Karakas MF, Basar N et al. The neutrophil to lymphocyte ratio was associated with impaired myocardial perfusion and long term adverse outcome in patients with ST-elevated myocardial infarction undergoing primary coronary intervention. Atherosclerosis 2013; 228: 203-210.
9. Rezkalla SH, Kloner RA. Coronary no-reflow phenomenon: from the experimental laboratory to the cardiac catheterization laboratory. Catheter Cardio Inte 2008; 72: 950-957.
10. Yildiz A, Yuksel M, Oylumlu M Polat N, Akyuz A, Acet H, Aydin M, Ülgen MS. The utility of the platelet-lymphocyte ratio for predicting no reflow in patients with ST-segment elevation myocardial infarction. Clin Appl Thromb Hemost 2015; 21: 223-228.
11. Braunwald E, Antman EM, Beasley JW Califf RM, Cheitlin MD, Hochman JS, Jones RH, Kereiakes D, Kupersmith J, Levin TN et al. ACC/AHA 2002 guideline update for the management of patients with unstable angina and non–ST-segment elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients With Unstable Angina) J Am Coll Cardiol 2002; 40: 1366-1374.
12. Boersma E, Pieper KS, Steyerberg EW, Wilcox RG, Chang WC, Lee KL, Akkerhuis KM, Harrington RA, Deckers JW, Armstrong PW et al. Predictors of outcome in patients with acute coronary syndromes without persistent ST-segment elevation. Results from an international trial of 9461 patients. The PURSUITS Investigators. Circulation 2000; 101: 2557-2567.

13. de Araújo Gonçalves P, Ferreira J, Aguiar C, Seabra-Gomes R. TIMI, PURSUIT and GRACE risk scores: sustained prognostic value and interaction with revascularization in NSTE-ACS. Eur Heart J 2005; 26: 865-872.

14. Granger CB, Goldberg RJ, Dabbous O Pieper KS, Eagle KA, Cannon CP, Van De Werf F, Avezum A, Goodman SG, Flather MD et al. Predictors of hospital mortality in the global registry of acute coronary events. Arch Intern Med 2003; 163: 2345-2353.

15. Wiviott SD, Morrow DA, Frederick PD, Giugliano RP, Gibson CM, Mc Cabe CH, Cannon CP, Antman EM, Braunwald E. Performance of the thrombolysis in myocardial infarction risk index in the National Registry of Myocardial Infarction-3 and-4: a simple index that predicts mortality in ST-segment elevation myocardial infarction. J Am Coll Cardiol 2004; 44: 783-789.

16. Bradshaw PJ, Ko DT, Newman AM, Donovan LR, Tu JV. Validation of the Thrombolysis In Myocardial Infarction (TIMI) risk index for predicting early mortality in a population-based cohort of STEMI and non-STEMI patients. Can J Cardiol 2007; 23: 51-56.

17. Garcia S, Canoniero M, Peter A, de Marchena E, Ferreira A. Correlation of TIMI risk score with angiographic severity and extent of coronary artery disease in patients with non-ST-elevation acute coronary syndromes. Am J Cardiol 2004; 93: 813-816.

18. Acet H, Ertaş F, Bilik MZ, Akıl MA, Özyurtlu F, Aydın M, Oylumlu M, Polat N, Yuksel M, Yıldız A et al. The relationship between neutrophil to lymphocyte ratio, platelet to lymphocyte ratio and TIMI risk score in patients with STEMI before primary coronary intervention. Postepy Kardiol Interwencyjnej 2015; 11: 126-135.

19. Acet H, Ertaş F, Akıl MA, Ozyurtlu F, Polat N, Bilik MZ, Aydın M, Oylumlu M, Yüksel M, Yıldız A et al. Relationship between hematologic indices and global registry of acute coronary events risk score in patients with ST-segment elevation myocardial infarction. Clin Appl Thromb Hemost 2016; 22: 60-68.

20. Myocardial infarction redefined: a consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. Eur Heart J 2000; 21: 1502-1513.

21. Killip T, Kimball JT. Treatment of myocardial infarction in a coronary care unit. A two year experience with 250 patients. Am J Cardiol 1967; 20: 457-464.

22. Morrow DA, Antman EM, Charlesworth A, Cairns R, Murphy SA, de Lemos JA, Giugliano RP, McCabe CH, Braunwald E. TIMI risk score for ST-elevation myocardial infarction: a convenient, bedside, clinical score for risk assessment at presentation: an intravenous nPA for treatment of infarcting myocardium early II trial substudy. Circulation 2000; 102: 2031-2037.

23. The Thrombolysis in Myocardial Infarction (TIMI) trial. Phase I findings. TIMI study group. New Engl J Med 1985; 312: 932e6.

24. Sorajja P, Gersh BJ, Costantini C, McLaughlin MG, Zimetbaum P, Cox DA, Garcia E, Tcheng JE, Mehran R, Lansky AJ et al. Combined prognostic utility of ST-segment recovery and myocardial blush after primary percutaneous coronary intervention in acute myocardial infarction. Eur Heart J 2005; 26: 667-674.

25. Gibson CM, Murphy SA, Morrow DA, Aroesty JM, Gibbons RJ, Gourlay SG, Barron HV, Giugliano RP, Antman EM, Braunwald E. Angiographic perfusion score: an angiographic variable that integrates both epicardial and tissue level perfusion before and after facilitated percutaneous coronary intervention in acute myocardial infarction. Am Heart J 2004; 148: 336e40.

26. Kristensen SD, Fajadet J, Di Mario C, Kaifoszova Z, Laut KG, Deleanu D, Gilard M, Guagliumi G, Goktekin O, Jorgova J et al. Implementation of primary angioplasty in Europe: stent for life initiative progress report. EuroIntervention 2012; 8: 35-42.

27. Widimsky P, Wijns W, Fajadet J, de Belder M, Knot J, Aaberge L, Andrikopoulos G, Baz JA, Betriu A, Claeys M et al. Reperfusion therapy for ST-elevation acute myocardial infarction in Europe: description of the current situation in 30 countries. Eur Heart J 2010; 31: 943-957.

28. Laut KG, Pedersen AB, Lash TL, Kristensen SD. Barriers to implementation of primary percutaneous coronary intervention in Europe. European Cardiology 2011; 7: 108-112.

29. Grines CL, Browne KF, Marco J, Rothbaum D, Stone GW, O'Keefe J, Overlie P, Donohue B, Chelliah N, Timmis GC et al. A comparison of immediate angioplasty with thrombolytic therapy for acute myocardial infarction. The primary angioplasty in myocardial infarction study group. New Engl J Med 1993; 328: 673-679.

30. Reffelmann T, Kloner RA. The no-reflow phenomenon: basic science and clinical correlates. Heart 2002; 87: 162-168.

31. Ito H. No-reflow phenomenon and prognosis in patients with acute myocardial infarction. Nat Clin Pract Card 2006; 3: 499-506.

32. Pan W, Liu HW, Wang LF, Li ZQ, Sun XY. Effect of percutaneous thrombectomy on echocardiographic measures of myocardial microcirculation in elderly patients with acute myocardial infarction. Coronary Artery Dis 2010; 21: 121-125.

33. Huczek Z, Kochman J, Filipiak KJ, Horszczaruk GJ, Grabowski M, Piatkowski R, Wilczynska J, Zielinski A, Meier B, Opolski G. Mean platelet volume on admission predicts impaired reperfusion and long-term mortality in acute myocardial infarction treated with primary percutaneous coronary intervention. J Am Coll Cardiol 2005; 46: 284-290.

34. Galasso G, Schiekofer S, D'Anna C, Gioia GD, Piccolo R, Niglio T, Rosa RD, Strisciuglio T, Trimarco B. No-reflow phenomenon: pathophysiology, diagnosis, prevention, and treatment. A review of the current literature and future perspectives. Angiology 2014; 65: 180-189.

35. Niccoli G, Burzotta F, Galiuto L, Crea F. Myocardial no-reflow in humans. J Am Coll Cardiol 2009; 54: 281-292.

36. Botto N, Sbrana S, Trianni G, Andreassi MG, Ravani M, Rizza A, Al-Jabri A, Palmieri C, Berti S. An increased plateletleukocytes interaction at the culprit site of coronary artery occlusion in acute myocardial infarction: a pathogenic role for "no-reflow" phenomenon? Int J Cardiol 2007; 117: 123-130.

37. Maseri A, Rebuzzi AG, Cianflone D. Need for a composite risk stratification of patients with unstable coronary syndromes tailored to clinical practice. Circulation 1997; 96: 4141-4142.

38. Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomized trials of more than 1000 patients. Lancet 1994; 343: 311-322.

39. Becker RC, Burns M, Gore JM, Spencer FA, Ball SP, French W, Lambrew C, Bowlby L, Hilbe J, Rogers WJ. Early assessment and in-hospital management of patients with acute myocardial infarction at increased risk for adverse outcomes: a nationwide perspective of current clinical practice: the National Registry of Myocardial Infarction (NRMI-2) Participants. Am Heart J 1998; 135: 786-796.

40. Hochman JS, Sleeper LA, Webb JG, Sanborn TA, White HD, Talley JD, Buller CE, Jacobs AK, Slater JN, Col J et al. Early revascularization in acute myocardial infarction complicated by cardiogenic shock: SHOCK Investigators: should we emergently revascularize occluded coronaries for cardiogenic shock. New Engl J Med 1999; 341: 625-634.

41. Tang EW, Wong CK, Herbison P. Global registry of acute coronary events (GRACE) hospital discharge risk score accurately predicts long-term mortality post acute coronary syndrome. Am Heart J 2007; 153: 29-35.

42. Morrow DA, Antman EM, Charlesworth A, Cairns R, Murphy SA, de Lemos JA Giugliano RP, McCabe CH, Braunwald E. TIMI risk score for ST-elevation myocardial infarction, a convenient, bedside, clinical score for risk assessment at presentation: an intravenous Npa for treatment of infarcting myocardium early II trial substudy. Circulation 2000; 102: 2031-2037.

43. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. Lancet 2003; 361: 13-20.

44. Morrow DA, Antman EM, Person L, de Lemos JA, Cannon CP, Giugliano RP, McCabe CH, Barron HV, Braunwald E. Application of TIMI risk score for ST elevation myocardial infarction in the National Registry of Myocardial Infarction 3. JAMA 2001; 286: 1356-9135.

45. Mega JL, Morrow DA, Sabatine MS, Zhao XQ, Snapinn SM, Di Battiste PM, Gibson CM, Antman EM, Braunwald E, Théroux P. Correlation between the TIMI risk score and high-risk angiographic findings in non-ST- elevation acute coronary syndromes: observations from the Platelet Receptor Inhibition in Ischemic Syndrome Management in Patients Limited by Unstable Signs and Symptoms (PRISM-PLUS) trial. Am Heart J 2005; 149: 846-850.

46. InTIME-II Investigators. Intravenous NPA for the treatment of infarcting myocardium early; InTIME-II, a double-blind comparison of single-bolus lanoteplase vs accelerated alteplase for the treatment of patients with acute myocardial infarction. Eur Heart J 2000; 21: 2005-2013.

47. Morrow DA, Antman EM, Giugliano RP, Cairns R, Charlesworth A, Murphy SA, de Lemos JA, McCabe CH, Braunwald E. A simple risk index for rapid initial triage of patients with ST-elevation myocardial infarction: an InTIME II substudy. Lancet 2001; 358: 1571-1575.

48. Rathore SS, Weinfurt KP, Gross GP, Krumholz HM. Validity of a simple ST-elevation acute myocardial infarction risk index: are randomized trial prognostic estimates generalizable to elderly patients? Circulation 2003; 107: 811-816.