ORIGINAL ARTICLE
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UDC: 616.127-005.8-08-037
DOI: https://doi.org/10.2298/VSP200204055D

GRACE, SYNTAX I, and SYNTAX II scores as predictors of one-year MACE in patients with myocardial infarction treated with percutaneous coronary intervention

GRACE, SYNTAX I i SYNTAX II skorovi kao prediktori jednogodišnjeg MACE kod bolesnika lečenih perkutanom koronarnom intervencijom

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Abstract

Background/Aim. The fundamental objective of primary percutaneous coronary intervention (PCI) in myocardial infarction is to provide early, complete, and sustained flow in the occluded artery that has led to myocardial ischemia or necrosis. The aim of this study was to determine the predictive power of a combination of GRACE, SYNTAX I, and SYNTAX II scores in predicting major adverse cardiovascular events (MACE) and one-year mortality in patients with ST-segment elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI) after primary PCI. **Methods.** The study included 400 patients who had their first acute myocardial infarction and underwent PCI. The patients were treated and followed for one year at the Clinical Hospital Center Zvezdara at the Department of Interventional Cardiology. By monitoring the defined clinical parameters, a comparative analysis of risk scores GRACE, SYNTAX I, and SYNTAX II was performed. Their sensitivity, specificity as well as predictive possibilities in predicting adverse outcomes were determined. **Results.** The incidence of MACE in our sample was 12.8%. Patients with STEMI entity had significantly higher values of GRACE, SYNTAX I, and SYNTAX II scores. The highest value for predicting the occurrence of MACE was shown by the SYNTAX II score (score value 29.3), with a sensitivity of 88.2% and a specificity of 76.8%. The GRACE score was a significant predictor of SYNTAX I and SYNTAX II scores. A two-way correlation was observed between the high score values of all three scores. **Conclusion.** The presented scores for the assessment of clinical and angiographic indicators showed good predictive power in assessing the outcome of adverse cardiovascular events in both clinical entities of acute myocardial infarction during one-year follow-up. By using the proposed scores to assess MACE, we can single out high-risk patients in order to prevent adverse events and reduce mortality. This suggests its suitability for clinical use in this patient population.

Key words:
myocardial infarction; percutaneous coronary intervention; prognosis; risk assessment; treatment outcome.

Apstrakt

Uvod/Cilj. Osnovni cilj primarne perkutane koronarne intervencije (PKI) kod infarkta miokarda je da obezbedi rani, potpuni i održivi protok u okludiranoj arteriji koja je dovela do ishemije ili nekroze miokarda. Cilj rada bio je da se utvrdi prediktivna snaga kombinacije GRACE, SYNTAX I i SYNTAX II skorova u predviđanju glavnih kardiovaskularnih neželjenih događaja (MACE) i jednogodišnjeg mortaliteta kod bolesnika sa ST-*segment elevation myocardial infarction* (STEMI) i *non*-STEMI (NSTEMI) nakon primarne PKI. **Metode.** Studijom je bilo obuhvaćeno 400 bolesnika koji su imali prvi akutni infarkt miokarda i bili podvrgnuti PKI. Bolesnici su lečeni i praćeni godinu dana u Kliničko-bolničkom centru Zvezdara na Odeljenju za interventnu kardiologiju. Praćenjem definisnih kliničkih parametara sprovedena je uporedna analiza skorova rizika: GRACE, SYNTAX I i SYNTAX II. Utvrđena je njihova senzitivnost, specifičnost kao i prediktivna vrednost u predviđanju

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neželjenih ishoda. **Rezultati.** Učestalost MACE u našem uzorku je bila 12,8%. Bolesnici sa STEMI entitetom imali su značajno veće vrednosti GRACE, SYNTAX I i SYNTAX II skorova. Najveću vrednost za predviđanje pojava MACE pokazao je SYNTAX II skor (vrednost skora 29,3) sa senzitivnošću 88,2% i specifičnošću 76,8%. Skor GRACE je bio značajan prediktor SYNTAX I i SYNTAX II skora. Zapažena je i dvosmerna korelacija između visokih vrednosti sva tri skora. **Zaključak.** Prikazani skorovi za procenu kliničkih i angiografskih pokazatelja pokazali su dobru prediktivnu moć u proceni pojave neželjenih kardiovaskularnih događaja kod oba klinička entiteta akutnog infarkta miokarda tokom jednogodišnjeg praćenja. Korišćenjem predloženih skorova za procenu MACE možemo izdvojiti visoko rizične bolesnike u cilju prevencije neželjenih događaja i smanjenja mortaliteta. To sugeriše njegovu pogodnost za kliničku upotrebu u ovoj populaciji bolesnika.

Ključne reči:
infarkt miokarda; perkutana koronarna intervencija; prognoza; rizik, procena; lečenje, ishod.

Introduction

The prevalence of cardiovascular disease (CVD) has been steadily increasing in recent decades, and the cause of half of all CVD deaths worldwide is an acute coronary syndrome (ACS). In Serbia, in 2017, CVD was the leading cause of death, with a share of 51.7% of total deaths, and 49.4% were deaths caused by ACS [1].

ACS is a condition of reduced coronary flow that leads to ischemia or necrosis of the corresponding part of the heart muscle [2]. This syndrome encompasses two entities: ACS with ST-segment elevation, which includes vasospastic angina and acute myocardial infarction – (STEMI), and without ST-segment elevation, which includes unstable angina pectoris and acute myocardial infarction (NSTEMI).

The prevalence of NSTEMI, according to research data, ranges from 4% to 13% [3], which is similar to the percentage of data in Serbia, where it is estimated that the number of new patients with acute myocardial infarction (AMI) is 179.8/100,000 [4]. Mortality from STEMI is associated with old age, Killip class, the time delay of treatment, limited capacity of emergency medical networks, care and treatment strategy, history of AMI, diabetes mellitus, renal failure, number of diseased coronary arteries, and left ventricular ejection fraction. Some studies have found that hospital mortality in people with STEMI is slightly higher than in people with NSTEMI (7% : 5%), but this difference decreases over six months by 12%: 13% [5]. The total mortality from AMI in Serbia is 12–13%, with a higher prevalence in patients with STEMI compared to NSTEMI, with a tendency to decrease mortality due to the use of percutaneous coronary intervention (PCI) and pharmacological therapy [4].

The basic mechanism of ischemia is significant occlusion of the coronary artery. Angiograms performed 4 hours after the onset of AMI indicate that STEMI most often has total coronary artery occlusion (84%), while in other cases, subtotal occlusion is present [6]. Pathological substrates differ in two forms of AMI: plaque rupture is present in 72% of STEMI and 32% of NSTEMI, while plaque erosion is present in 28% of STEMI and 48% of NSTEMI. Angiographic studies have shown that multivessel occlusion and culprit lesions in the circumflex artery are more common clinical findings in NSTEMI [7]. The primary goal of primary PCI in AMI is to provide early, complete, and sustained flow in the occluded artery that has led to myocardial ischemia or necrosis. A significant advantage of PCI is the reduction of the risk of intracranial hemorrhage, reduction of the occurrence of undesirable cardiovascular outcomes, improvement of left ventricular myocardial function, and improvement of the clinical outcome. Despite the reduction in mortality within 12 months after PCI by 4 –6% [8], patients remain at risk of adverse events after stent implantation [9].

Clinical experience indicates that in-hospital mortality increases if the "door to balloon" time is greater than 120 min and depends on the size and location of the infarction, age, previous coronary heart disease, risk factors, clinical characteristics, and comorbidities. Intrahospital mortality of patients with AMI-treated PCI is 0% to 13%, while mortality during the first year after PCI is higher (5%) than mortality in subsequent years (1%) [10].

In clinical practice, in order to determine the optimal time for the application of invasive AMI therapy, it is necessary to assess the degree of ischemic risk and determine the predictors of adverse outcomes. Complications after PCI include death, reinfarction, cerebrovascular stroke, emergency coronary artery bypass graft surgery, and various vascular complications (pseudoaneurysm, arteriovenous fistula, retroperitoneal bleeding, etc.) [11].

Numerous scoring systems have been developed with the aim of predicting the short-term and long-term risk of major cardiovascular adverse events (MACE) in patients with STEMI and NSTEMI [12]. In modern cardiology, a combination of scores is usually used to monitor as many significant clinical, angiographic, echocardiographic, and other parameters of clinical outcome in patients as possible in order to implement an optimal therapeutic strategy. The most commonly used predictive scores for short- and long-term risk of MACE in patients with AMI are the Global Registry of Acute Coronary Events (GRACE), the Synergy Between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery (SYNTAX) I, and SYNTAX II score [13, 14].

The aim of this study was to determine the reliability of clinical scores in assessing the risk of MACE in patients with STEMI and NSTEMI. The outcome designated as MACE in the paper refers to cardiac and cerebrovascular events such as mortality, recurrent myocardial infarction, revascularization procedure, and stroke.

Methods

The study was conducted as a prospective, observational study, and it enabled the monitoring of clinical parameters of GRACE, SYNTAX I and II scores in order to determine the short- and long-term risk of MACE in patients with STEMI and NSTEMI.

The study included 400 patients under the diagnosis of AMI, treated with PCI from January 1, 2018, to December 31, 2018, at the Clinical Hospital Center Zvezdara in Belgrade, at the Department of Interventional Cardiology. The diagnosis of AMI (STEMI and NSTEMI) was made based on the criteria for AMI defined by the consensus of the working group of the European Association of Cardiologists. Among patients, 68.5% had STEMI entity, while 31.5% of patients were diagnosed with NSTEMI entity.

Inclusion criteria for the patients in the study were the following: first myocardial infarction, STEMI and NSTEMI presentation, performed coronary arteriography within 12 hrs of diagnosis, and adequate patient compliance (data on regular use of dual antiplatelet therapy with acetylsalicylic acid and P2Y12 receptor inhibitors (clopidogrel/ticagrelor/prasugrel) within 12 months of revascularization (PCI).

Exclusion criteria for the patients from the study were the following: refusal of treatment and follow-up, age of patients < 18 and > 80 years, non-acceptance of the proposed revascularization procedure, the lethal outcome in the inpatient period, cardiogenic shock on admission, severe valvular heart defects, intracerebral tumor/aneurysm, active or recent internal bleeding, known hemorrhagic diathesis, contraindications to heparin and antiplatelet therapy, discontinuation of dual antiplatelet therapy before 12 months of PCI, other conditions leading to inflammatory conditions cardiac troponin values, terminal phase chronic renal failure, previous cerebrovascular stroke, previous myocardial infarction and revascularization procedures, and malignancies.

Instruments used in the research

The GRACE score was designed to stratify the risk in patients with ACS to predict hospital, six-month, and annual deaths [15]. It assesses eight independent variables: age, heart rate, systolic blood pressure, serum creatinine, Killip class on admission, the presence of ST abnormalities, cardiac biomarker values, and cardiac arrest on admission. The categorization of the GRACE score is represented by groups with low (≤ 108; < 1%), intermediate (109–140; 1–3%), and high risk (> 140; > 3%) for intrahospital, and low categories (≤ 88; < 3%), intermediate (89–118; 3–8%), and high risk (> 118; > 8%) for six-month mortality [16].

The SYNTAX I monitors the qualitative and quantitative parameters of coronary arteries in patients with AMI and is important in monitoring patients with stable multivessel coronary disease [17] but also in patients with STEMI, where the SYNTAX is a high score predictor of cardiovascular mortality after PCI [18]. Twelve angiogram parameters were monitored: dominance, number of lesions, localization, total occlusion, bifurcation, trifurcation, thrombosis, lesion length, tortuosity, severe calcification, diffuse disease, and aortic lesions. Scoring categorization is defined as low (≤ 22), intermediate (23–32), and high (> 33) risk.

The SYNTAX II score combines anatomical and clinical factors to predict post-procedural outcomes [19, 20]. It includes angiographic parameters as well as SYNTAX I with the addition of another parameter – "unprotected left main coronary artery" and clinical parameters: sex, age, creatinine clearance, left ventricular ejection fraction, peripheral vascular disease, and chronic obstructive pulmonary disease. The SYNTAX II score is categorized into three groups of mortality risk: low (≤ 22), moderate (23–32), and high (≥ 33) [21]. The SYNTAX risk score includes significant clinical parameters that are not present in the GRACE score and are significant independent predictors of mortality and MACE in patients with AMI.

The research was conducted in accordance with the Declaration of Helsinki. For the purposes of this study, the approval of the Ethics Commission of the Clinical Hospital Center Zvezdara in Belgrade was obtained on December 9th, 2019 (No 09-3174).

Data were analyzed in the SPSS Windows user package, version 19. The level of statistical significance was set to $p < 0.05$. The correlation between scores was examined by Spearman's correlation coefficient test. All variables that showed significant correlation with outcome variables in the univariate regression analysis were included in the multivariate regression analysis.

Linear and COX regression analyses were applied to identify factors associated with outcome variables in our study (SYNTAX I and SYNTAX II, MACE). The Kaplan-Meier test was used to calculate survival time after acute STEMI and NSTEMI entity. Finally, the Receiver Operating Characteristic (ROC) curve analysis was used to examine the validity of the GRACE score in the prediction of significant coronary occlusive disease, as well as the validity of the GRACE, SYNTAX I, and SYNTAX II scores in the prediction of MACE in individuals with STEMI and NSTEMI.

Results

The mean age of patients was 62.6 ± 10.8 years. Patients with NSTEMI were statistically significantly younger (p = 0.01) (60.7 ± 10.2 years) compared with patients with STEMI (63.5 ± 11.0 years). Positive family history was present in 69.0% of patients, and persons with STEMI entity had statistically significantly more associated chronic diseases (p = 0.02). The average body mass index in both groups of patients indicated the absence of obesity without a significant difference between these two groups of subjects (p = 0.8).

The mean value of the GRACE score in patients with NSTEMI entity was 107.9 ± 18.2, while the mean values of the SYNTAX I and SYNTAX II scores were 21.3 ± 4.9 and 22.8 ± 5.0, respectively. In patients with STEMI, the mean value of the GRACE score was 122.7 ± 20.8, while the

values of the SYNTAX I and SYNTAX II scores were 25.8 ± 4.9 and 27.5 ± 4.9, respectively. Statistical significance was observed (p = 0.001), and patients with STEMI entities had higher values of the GRACE, SYNTAX I, and SYNTAX II scores.

Examining the relationship between the GRACE and SYNTAX I and SYNTAX II scores, statistical significance was observed in the correlation of the value of the GRACE score with the SYNTAX I and SYNTAX II scores. In addition, the values of SYNTAX I and SYNTAX II scores in patients in the high-risk group for the development of adverse outcomes statistically significantly correlated (p < 0.01) with the values of the GRACE score.

According to the GRACE score, patients classified in the low-risk group belong to the same group according to the values of SYNTAX I (70.2%) and SYNTAX II (54.3%) scores, with the determining statistical significance. Statistical significance was also observed in the group of patients with medium risk for the development of adverse outcomes estimated according to the values of all three scores. When it comes to high-risk assessment, patients who were by the GRACE score classified into the high-risk group were statistically significantly correlated with the high-risk group according to values of the SYNTAX II score (62.3%), while according to the SYNTAX I score values were statistically significantly correlated with moderate risk group (65.2%) (Figure 1). A significant high degree of correlation was observed between the GRACE score and the SYNTAX I and the SYNTAX II scores (rho > 0.5; p = 0.001).

MACE and survival time of patients with STEMI and NSTEMI were monitored in patients treated with PCI. It was also observed that 51 patients (12.8%) had one of the MACE, namely: revascularization in 75.6% of patients, the fatal outcome in 15.7% of patients, while 3.9% experienced recurrent myocardial infarction and stroke. Among patients, 68.5% had STEMI entity, while 31.5% of patients were diagnosed with NSTEMI entity.

As shown in Table 1, patients with STEMI, the elderly, without a positive family history, with hypertension, Killip class II, cardiac arrest, higher heart rate, more

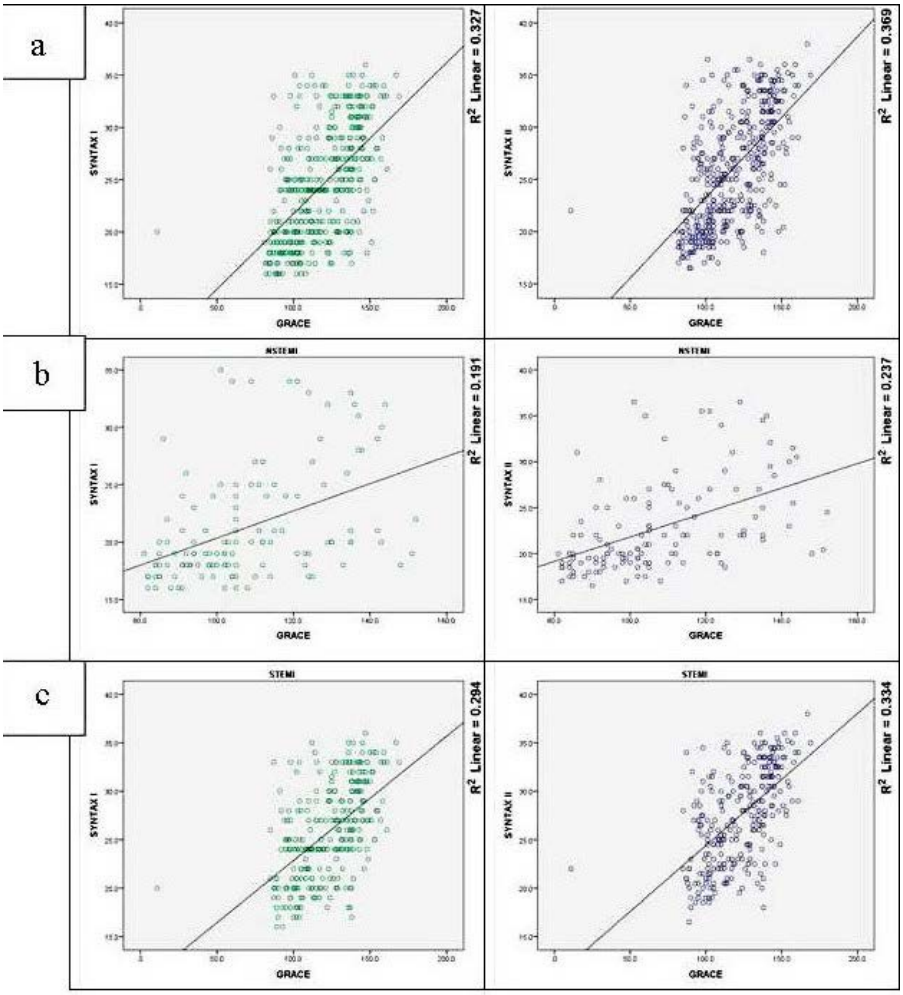


Fig. 1 – Correlation of GRACE score with SYNTAX I and SYNTAX II scores: a) whole sample of patients; b) in patients with NSTEMI entity; c) in patients with STEMI entity.

GRACE – Global Registry of Acute Coronary Events; SYNTAX – Synergy between PCI (percutaneous coronary intervention) with Taxus and Cardiac Surgery; NSTEMI – non-ST-elevation myocardial infarction; STEMI – ST-elevation myocardial infarction.

Table 1

Socio-demographic, clinical, and laboratory characteristics of patients with and without major adverse cardiovascular events (MACE) outcomes during the year

Variables	MACE		*p*
	no	yes	
Myocardial infarction entity, n (%)			
NSTEMI	117 (92.9)	9 (7.1)	0.02
STEMI	232 (84.7)	42 (15.3)	
Gender, n (%)			
male	232 (87.2)	34 (12.8)	0.97
female	117 (87.33)	17 (12.7)	
Smoking status, n (%)			
non-smoker	122 (84.7)	22 (15.3)	0.47
ex-smoker	115 (87.8)	16 (12.2)	
smoker	112 (89.6)	13 (10.4)	
Alcohol consumption, n (%)			
no	333 (87.2)	49 (12.8)	0.83
yes	16 (88.9)	2 (11.1)	
Positive family anamnesis, n (%)			
no	99 (81.8)	23 (18.9)	0.01
yes	250 (89.9)	28 (10.1)	
The presence of chronic diseases, n (%)			
no	44 (93.6)	3 (6.4)	0.007
diabetes	3 (100.0)	0 (0.0)	
hypertension	163 (92.6)	13 (7.4)	
GERBI	2 (100.0)	0 (0.0)	
hypothyroidism	2 (100.0)	0 (0.0)	
COPD	3 (100.0)	0 (0.0)	
more chronic diseases	132 (79.0)	35 (21.0)	
Angina pain or its equivalent, n (%)			
no	52 (85.2)	9 (14.8)	0.61
yes	297 (87.6)	42 (12.4)	
Killip class at the reception, n (%)			
one	331 (89.7)	38 (10.3)	0.001
two	18 (58.1)	13 (41.9)	
Cardiac arrest on admission, n (%)			
no	336 (88.4)	44 (11.6)	0.002
yes	13 (65.0)	7 (35.0)	
Isolated disease of the main tree, n (%)			
no	347 (87.4)	50 (12.6)	0.28
yes	2 (66.7)	1 (33.3)	
Number of diseased coronary arteries, n (%)			
one	172 (99.4)	1 (0.6)	0.001
two	108 (91.5)	10 (8.5)	
three and more	69 (63.3)	40 (36.7)	
Number of stents implanted, n (%)			
one	132 (90.4)	14 (9.6)	0.13
two	110 (88.7)	15 (11.3)	
three	58 (79.5)	15 (205)	
four and more	49 (86.0)	8 (14.0)	
Previous therapy, n (%)			
no	1 (0.3)	0 (0.0)	
antiaggregation	165 (85.5)	28 (14.5)	
antiaggregation + antihypertensive	44 (84.6)	8 (15.4)	
antiaggregation + hypolipidemic	106 (91.4)	10 (8.6)	
triple (antiaggregation, antihypertensive, hypolipidemic)	33 (86.8)	5 (13.2)	
Age (years), mean ± SD	62.17 ± 10.68	65.53 ± 11.26	0.03
Body mass index (kg/m^2), mean ± SD	23.28 ± 2.40	23.20 ± 2.72	0.81
Time from onset of pain to percutaneous coronary intervention (min), mean ± SD	127.53 ± 36.73	138.43 ± 38.44	0.05
Length of hospitalization (days), mean ± SD	7.55 ± 1.88	9.92 ± 3.59	0.001
Heart rate (beat/min), mean ± SD	81.03 ± 17.01	91.35 ± 22.67	0.003
Systolic admission pressure (mmHg), mean ± SD	130.79 ± 20.35	131.76 ± 20.73	0.75
Total cholesterol (mmol/L), mean ± SD	5.22 ± 1.32	5.24 ± 1.50	0.92
Triglycerides (mmol/L), mean ± SD	1.78 ± 1.00	1.95 ± 0.84	0.25
Tnl-ultra Troponin (ng/mL), mean ± SD	20.88 ± 15.38	20.64 ± 18.88	0.001
CRP (mg/L), mean ± SD	15.70 ± 19.15	23.21 ± 22.81	0.01
Glucose (mmol/L), mean ± SD	7.11 ± 2.76	8.57 ± 4.53	0.029
Hemoglobin (g/dL), mean ± SD	13.88 ± 1.65	13.46 ± 1.78	0.09
Leukocytes (x10^9), mean ± SD	9.68 ± 2.81	10.78 ± 2.44	0.008
Neutrophils /lymphocytes, mean ± SD	2.57 ± 0.99	3.03 ± 0.92	0.002
LVEF (%), mean ± SD	44.92 ± 8.99	36.84 ± 9.28	0.001

Note: Clinical and biochemical parameters were defined on patient admission.

NSTEMI – non-ST-elevation myocardial infarction; STEMI – ST-elevation myocardial infarction; GERBI – gastroesophageal reflux disease; COPD – chronic obstructive pulmonary disease; CRP – C-reactive protein; LVEF – left ventricular ejection fraction; SD – standard deviation.

coronary artery disease, longer time from onset of pain to PCI, and longer hospitalization, had higher adverse outcomes, and a statistically significant difference was observed in monitoring the same parameters in the group of patients without MACE. Moreover, statistical significance was observed by monitoring the values of troponin and left ventricle ejection fraction (LVEF), C-reactive protein (CRP), glycemia, and leukocytes, with a higher prevalence in patients with MACE, compared to the group of patients without MACE.

The mean time to onset of MACE in our patients diagnosed with AMI treated with PCI during the one-year follow-up was 334.4 ± 4.3 days. Statistical significance was observed in patients with STEMI in whom the mean time to onset of MACE was shorter (329.0 ± 5.5 days) compared with patients with NSTEMI (346.1 ± 6.2 days) (Log Rank – Mantel-Cox: χ^2 = 5.005, p = 0.02; Breslow: χ^2 = 4.9, p = 0.03; Tarone-Ware: χ^2 = 4.9, p = 0.03) (Figure 2).

Patients recently classified as high-risk of developing MACE based on the values of the GRACE, SYNTAX I, and SYNTAX II scores had significantly more often MACE compared to patients who had a low or moderate risk of developing MACE and those who did not have MACE (Table 2).

In order to analyze the time predictor until the occurrence of the MACE, the COX regression analysis (Enter method) was used (Table 3). Three models (Basic, Score, and Comprehensive model) were created, which included all variables that showed a statistically significant difference in frequency in patients with and without MACE.

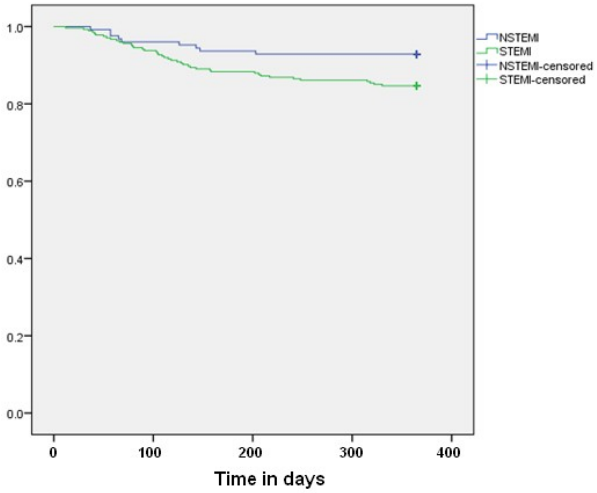


Fig. 2 – Kaplan-Mayer curve of time to onset of major adverse cardiovascular events (MACE) in patients with myocardial infarction treated with percutaneous coronary intervention (PCI) for a period of one year. NSTEMI – non-ST-elevation myocardial infarction; STEMI – ST-elevation myocardial infarction.

Table 2

Differences in values of the GRACE, SYNTAX I, and SYNTAX II scores between patients who developed major adverse cardiovascular events (MACE) during the one-year follow-up and those who did not

Variables	MACE		*p*
	no	yes	
SYNTAX I score, n (%)			
low risk	169 (99.4)	1 (0.6)	
moderate risk	161 (85.6)	27 (14.4)	0.001
high risk	19 (45.2)	23 (54.8)	
SYNTAX II score, n (%)			
low risk	108 (100.0)	0 (0.0	
moderate risk	189 (95.5)	9 (4.5)	0.001
high risk	52 (55.3)	42 (44.7)	
GRACE score, n (%)			
low risk	141 (93.4)	10 (6.6)	0.001
moderate risk	163 (90.6)	17 (9.4)	
high risk	45 (65.2)	24 (34.8)	
SYNTAX I score, mean ± SD	23.37 ± 4.85	31.11 ± 3.32	0.001
SYNTAX II score, mean ± SD	25.04 ± 4.89	32.87 ± 3.08	0.001
GRACE score, mean ± SD	115.78 ± 19.99	133.51 ± 22.73	0.001

GRACE – Global Registry of Acute Coronary Events; SYNTAX – Synergy between PCI (percutaneous coronary intervention) with Taxus and Cardiac Surgery.

All models showed statistical significance (p = 0.001) in examining the prediction of time to onset of MACE.

In the COX regression analysis in the first "Baseline Model", the NSTEMI entity was a significant predictor of the longer time to the onset of MACE. After the inclusion of the GRACE, SYNTAX I, and SYNTAX II scores in the next "Score Model", the NSTEMI entity lost significance in predicting the time to MACE, and only the SYNTAX II score remains a significant predictor of time to MACE onset (Table 3).

Namely, with each increase in the SYNTAX II score by one unit, the risk of shortening the time to the onset of MACE increases by 52.7%.

In the "Comprehensive Model", a higher SYNTAX II score, a long time from disease onset to PCI [95% confidence interval (CI): 1.000−1.017; p = 0.039], and higher age (95% CI: 0.907−0.994; p = 0.027) were the only risk factors that affect the shortening of the time to MACE occurrence (Table 3).

The significance of all three models in the prediction of the occurrence of MACE in the patients of our study was also confirmed in the logistic regression analysis (Enter method): ["GRACE model", χ^2 = 114.8; p = 0.001; B = -1.9; Wald = 164.6; Exp (B) = R2 Nagelkerke = 0.5; classification % = 90.8; "SYNTAX I model", χ^2 = 135.3; p = 0.001; B = -1.9; Wald = 164.6; Exp (B) = 0.1; R^2 Nagelkerke = 0.5; classification % = 89.8; "SYNTAX II model", χ^2 = 143.03; p = 0.001; B = -1.9; Wald = 164.6; Exp (B) = 0.1; R^2 Nagelkerke = 0.6; classification].

To assess the validity of the prediction of the occurrence of MACE using the GRACE, SYNTAX I, and SYNTAX II scores, ROC analysis was used (Figure 3).

Table 3

COX regression analysis of predictors of time of occurrence of major adverse cardiovascular events (MACE)

Variables	Basic model			Score model			Comprehensive model		
	Exp (B)	95% CI	*p*	Exp (B)	95% CI	*p*	Exp (B)	95% CI	*p*
Myocardial infarction entity (NSTEMI/STEMI)	0.449	0.219; 0.923	0.029	1.158	0.528; 2.538	0.715	1.236	0.515; 2.965	0.635
GRACE score				1.001	0.984; 1.020	0.878	0.992	0.968; 1.016	0.496
SYNTAX I score				0.950	0.778; 1.160	0.616	0.887	0.687; 1.146	0.359
SYNTAX II score				1.527	1.208; 1.930	0.001	1.527	1.140; 2.043	0.004
Age							0.949	0.907; 0.994	0.027
Time from disease onset to PCI							1.009	1.000; 1.017	0.039
χ^2/ p (the whole model)	5.003/ 0.025			104,125/ 0.001			162,254/ 0.001		
χ^2/ p (changes from the previous model)	5.572/ 0.018			106,684/ 0.001			25,387/ 0.321		

NSTEMI – non-ST-elevation myocardial infarction; STEMI – ST-elevation myocardial infarction; PCI – percutaneous coronary intervention; GRACE – Global Registry of Acute Coronary Events; SYNTAX – Synergy between PCI with Taxus and Cardiac Surgery.

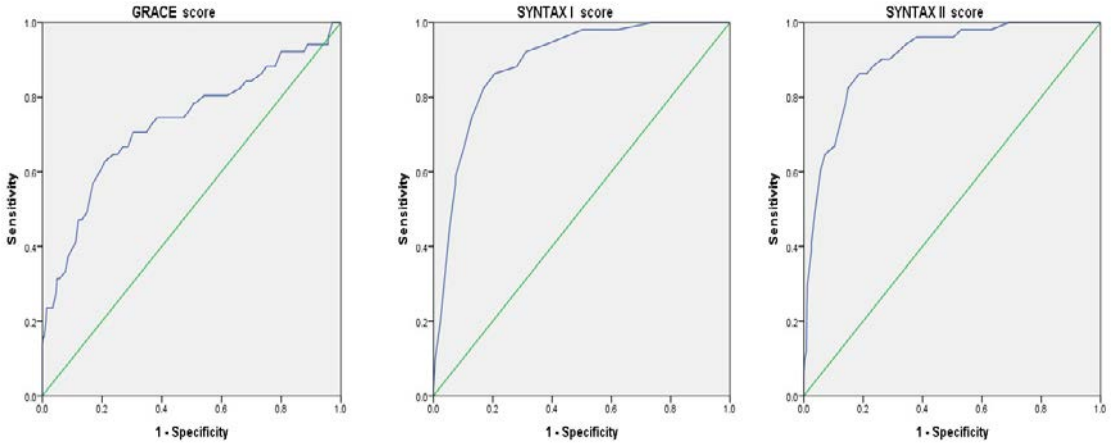


Fig. 3 – Receiver Operating Characteristic (ROC) curve of prediction of major adverse cardiovascular events (MACE) by the GRACE, SYNTAX I and SYNTAX II scores. GRACE – Global Registry of Acute Coronary Events; SYNTAX – Synergy between PCI (percutaneous coronary intervention) with Taxus and Cardiac Surgery.

According to the ROC analysis, the GRACE score explained the occurrence of MACE in 73.0% of patients in our study [AUC (area under curve) = 0.7; 95% CI 0.644 – 0.8; p = 0.001]. The GRACE score of 123.5 was identified as the optimal value for predicting the occurrence of MACE in our patients, with a sensitivity of 74.5% and a specificity of 61.6% (Figure 3).

The SYNTAX I score accurately explained up to 89.1% (AUC = 0.9; 95% CI 0.8–0.9; p = 0.001) of the occurrence of MACE in our patients. The SYNTAX I score of almost 27.5 was identified as the optimal value for predicting the occurrence of MACE in our patients, with a sensitivity of 86.3% and a specificity of 79.4% (Figure 3).

Finally, according to the ROC analysis, the SYNTAX II score explained the occurrence of MACE in 90.5% of the patients in our study (AUC = 0.9; 95% CI 0.9; p = 0.001). The SYNTAX II score of 29.3 was identified as the optimal value for predicting the occurrence of MACE in our patients, with a sensitivity of 88.2% and a specificity of 76.8% (Figure 3).

Discussion

Patients hospitalized for AMI, depending on the severity of the disease, show different values of clinical and laboratory characteristics.

Determining the severity of coronary artery disease and risk stratification is essential for choosing the right therapeutic approach. The GRACE score is a strong, independent predictor of MACE in patients with AMI [20] but is not optimized for patients with PCI due to the lack of angiographic findings in their scoring system, which is consistent with the results of our study.

Moreover, we observed that patients with MACE had statistically significantly higher values of the GRACE, SYNTAX I, and SYNTAX II scores compared with the group of patients who did not have MACE.

In order to analyze the predictors of time to the occurrence of MACE, regression analysis (Enter Method) was used. Three models (Baseline, Score, and Comprehensive models) were created that included all variables that showed a statistically significant difference in incidence in patients with and without MACE. All models showed statistical significance (p = 0.001) in examining the prediction of time to onset of MACE. In general, studies indicate a reduced prognostic value of the GRACE score as a useful tool for the initial classification of patients with NSTEMI – AMI but not for patients with PCI due to lack of angiographic findings in the scoring system, giving preference to the SYNTAX II score [21].

By regression analysis in the first “Basic model”, in NSTEMI entity, we noticed the significance of all three scores as predictors of a long time to the appearance of MACE. After the inclusion of the GRACE, SYNTAX I, and SYNTAX II scores in the next “Score Model”, the NSTEMI entity loses significance in predicting the time to MACE, and only the SYNTAX II score remains as a significant predictor of time to MACE occurrence.

Namely, with each increase in the SYNTAX II score by one unit, the risk of shortening the time to the onset of MACE increases by 52.7%.

In order to analyze the GRACE score as a predictor of the SYNTAX I and SYNTAX II scores, linear regression was used, and all variables that showed a statistically significant correlation with the examined scores were analyzed. All models showed statistical significance (p = 0.001) in the study of assessing the efficiency of predicting the MACE by the SYNTAX I and SYNTAX II scores.

In the regression analysis of the GRACE score as a predictor of SYNTAX I score, it was noticed that a higher GRACE score is a significant predictor of higher values of SYNTAX I score in the whole sample of patients diagnosed with myocardial infarction treated with PCI, in patients with STEMI entity, and in the group of patients with NSTEMI entity. Another study [22] presented the GRACE score as acceptable in the clinical risk stratification of patients with NSTEMI in different age groups. A study conducted in Brazil found that the GRACE score has 50% sensitivity and 98% specificity for predicting a high risk of death in patients with NSTEMI [23].

In addition to the GRACE score, significant predictors of the SYNTAX I score, both in the whole sample and in patients with NSTEMI and STEMI, were a higher number of diseased coronary arteries and the presence of peripheral arterial disease. In addition, a significant predictor of higher SYNTAX I scores in the entire sample of patients diagnosed with myocardial infarction treated with PCI was a long time from the onset of pain to PCI.

Some researchers evaluating the accuracy of the GRACE assessment in predicting the severity and degree of coronary artery stenosis in the correlation with the SYNTAX score found a sensitivity of 73.5% and a specificity of 60% of the GRACE score in predicting coronary artery stenosis in patients with ACS [23, 24].

Analysis of the SYNTAX II score showed that the higher GRACE score is a significant predictor of higher SYNTAX II score values in the entire sample of patients diagnosed with myocardial infarction treated with PCI, as well as in patients with both entities of myocardial infarction. In addition to the GRACE score, significant predictors of the SYNTAX II score in all three models (whole sample, NSTEMI, and STEMI) were a higher number of diseased coronary arteries, the presence of peripheral arterial disease, and lower LVEF values.

In addition, as a significant predictor of higher SYNTAX II scores in the entire sample of patients diagnosed with PCI-treated myocardial infarction, there was a long time from pain to PCI, while in patients with NSTEMI significant predictors of higher SYNTAX II score were lower LVEF and higher HbA1c values.

In the logistic regression analysis in the first GRACE model, the score was not a statistically significant predictor of the occurrence of MACE in patients diagnosed with AMI-treated PCI. Significant risk factors for the occurrence of MACE in the GRACE model were younger age and longer

hospitalizations, while the protective factor was a smaller number of diseased coronary arteries.

In the SYNTAX I model, significant risk factors for the occurrence of MACE were higher SYNTAX I score, younger age, and the presence of hypertension.

In the SYNTAX II model, significant risk factors for the occurrence of MACE were higher SYNTAX II scores and younger life expectancy.

According to the ROC analysis of the value of scores in the prediction of MACE, the sensitivity for the GRACE score was 74.5% and specificity 61.6%; for the SYNTAX I score, sensitivity was 86.3% and specificity 79.4%; for the SYNTAX II score, sensitivity was 88.2% and specificity 76.8%.

The use of clinical and angiographic risk scores in clinical practice in patients with AMI and PCI has provided a powerful clinical stratification tool that can predict MACE more accurately than by applying these scores individually in order to select the best treatment strategy and improve prognosis and the outcome of AMI.

Conclusion

The results of the study indicate that the combination of clinical and anatomical variables in the GRACE and SYNTAX I scores is useful for predicting MACE during hospitalization, but that the SYNTAX II score allows more accurate and individualized mortality assessment over a period of one year after hospitalization, and is, therefore, a clinically more useful tool for predicting MACE occurrence.

Conflict of interest

The authors declare no conflict of interest.

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Received on February 4, 2020
Revised on April 19, 2021
Accepted on May 20, 2021
Online First May 2021