European Review for Medical and Pharmacological Sciences 2023; 27: 9773-9780

The importance of GRACE risk score in the development of high-grade atrioventricular conduction blocks after non-st-segment elevation myocardial infarction

U. UYAN[1], C. AYDIN[2], İ. GÜL[3]

[1]Department of Cardiology, Ödemis State Hospital, Izmir, Turkey
[2]Department of Cardiology, Faculty of Medicine, Tekirdag Namik Kemal University, Tekirdag, Turkey
[3]Bakirçay University, Çigli Training and Research Hospital, Izmir, Turkey

Abstract. – OBJECTIVE: The development of high-grade atrioventricular block (HG-AVB) after acute coronary syndrome (ACS) increases morbidity and mortality rates. A significant portion of HG-AVBs resolve spontaneously after revascularization. We aimed to evaluate the power of the GRACE scoring system in predicting the development of HG-AVB and its importance in determining the need for cardiac pacemakers.

PATIENTS AND METHODS: Patients who applied to our center between July 2020 and February 2023 were included in the study. 600 patients [340 (56.6%) male, mean age 65.4±13.6] without ST-segment elevation (NSTEMI) and who underwent revascularization were evaluated within the scope of the study. The heart rhythms of the patients were evaluated from the electrocardiograms (ECG) at admission. Patients with HG-AVB and other patients were divided into two groups. The heart rhythms of these patients were evaluated during their hospitalization. Then, HG-AVB patients were also divided into two groups (with and without PPM need). Demographic, laboratory, angiographic, and echocardiographic characteristics of these patients were evaluated.

RESULTS: Morbidity and mortality were higher in the HG-AVB group. These patients had longer intensive care and hospital stays. The mean age, creatinine value, GRACE score (GS), total cholesterol (TC), and RCA lesion rates were higher in the HG-AVB group; hemoglobin level was found to be lower. As a result of regression analysis, RCA lesion, hemoglobin value, GRACE score, creatinine, and TC levels were predictors of HG-AVB development. In determining the need for PPM, these variables were found to be effective. ROC analysis was performed for GS, which predicted the development of HG-AVB, and the cut-off value was found to be 185.5.

CONCLUSIONS: The development of HG-AVB after NSTEMI is an important health problem. By detecting these patients and those who may need PPM beforehand, various complications can be prevented, and the length of stay in the hospital can be shortened. Calculation of GS is an important parameter that can be used to predict the development and course of HG-AVB.

Key Words:
Non-ST segment elevation myocardial infarction, High-grade atrioventricular conduction block, GRACE risk score, Permanent pacemaker.

Introduction

Today, Coronary Artery Disease (CAD) is one of the leading causes of morbidity and mortality[1]. Recent technological developments have helped to reduce the problems associated with this condition. Due to CAD, the blood supply of the myocardial tissue is impaired, and ischemic and arrhythmic pathologies may occur[2]. Adverse outcomes are decreased when the artery that caused the infarction (IRA) can be revascularized[3]. Many conditions, especially after myocardial infarction, including arrhythmia, may occur more frequently and faster. High-grade atrioventricular blocks (HG-AVB) may occur after NSTEMI[4]. HG-AVB can occur at any level of the conduction system in the atrioventricular (AV) node and His-Purkinje system. According to the level and severity of the block, different appearances can be detected in the electrocardiography (ECG). The relationship between the "p" wave, which indicates atrial activity, and the QRS complexes, which indicates ventricular activity, may deteriorate at various rates, and even in some patients, the

Corresponding Author: Cihan Aydin, MD; e-mail: drcihanaydin@hotmail.com

conduction may be completely interrupted (Total AV-Block). The level and type of block can be understood by evaluating the region known as the PR segment on the ECG. AVBs are divided into three types. Type-I defines the delay in atrioventricular conduction. Diagnosis is made if the PR time is more than 200 milliseconds. Type-I AV block can be seen normally in athletes and some special groups. Beginning with the type-II block, the relationship between the p wave and the QRS complex deteriorates to a certain extent, and a QRS response does not occur to some p waves. In type-III block, there is no relationship between p waves and QRS complexes. Cardiac electrical conduction propagates independently within the atria and ventricles. Generally, QRS complexes due to an ectopic focus originating from the ventricle are observed in type-III[5]. The definition of HG-AVB includes type-II and type-III AV block. HG-AVB is a pathology that increases the risk of morbidity and mortality and needs to be treated. A significant portion of HG-AVBs caused by CAD can recover after revascularization. A small number of them need a permanent pacemaker (PPM)[6]. The GRACE risk score has been known for many years. It is a scoring system whose calculation is emphasized to be of prognostic importance in current guidelines[7]. Scoring can be done by entering the patients' variables into the system *via* software[8]. It has been stated that the GRACE score calculated at the time of admission >140 may be related to the morbidity and mortality that may develop in the patient. Early revascularization is recommended for these patients[9].

Within the scope of our study, the GRACE risk scores of the patients who applied to our emergency department with the diagnosis of NSTEMI were calculated. It was aimed to determine the relationship between GRACE risk score, HG-AVB and PPM implantation.

Patients and Methods

The center where the study was carried out was a tertiary center with a 24/7 catheter laboratory. The study was conducted by following the Helsinki Declaration and its latest amendments. The study protocol was approved by the ethics committee. 745 patients diagnosed with NSTEMI who applied to our center between July 2020 and February 2023 were evaluated within the scope of the study. For the diagnosis of NSTEMI during coronary angiography, the detection of a significant critical lesion in a coronary artery that may be responsible for infarction and a significant elevation in cardiac enzymes was sought[10]. Patients diagnosed with NSTEMI, according to the 2020 NSTEMI European Society of Cardiology guidelines, were included in the study.

600 patients who met the study criteria were included in the analysis. Chronic renal failure (at admission creatinine >2.5 mg/dl, reference potassium >5.5 mmol/L) and active infection, cerebral dysfunction, chronic lung disease, chronic liver disease, post-revascularization TIMI those with ≤2 flow, congenital heart disease, coronary artery bypass grafting (CABG), other pathologies that may cause cardiac enzyme elevation, advanced heart valve disease, previously known cardiac arrhythmia, using any antiarrhythmic drug, and patients with permanent pacemakers were excluded from the study. Electrocardiographs, blood tests, treatments, and hemodynamic parameters of all patients at the time of admission to the emergency department were evaluated. Echocardiography was required for all patients within the first 24 hours. Patients who did not meet this criterion were excluded from the study. It was determined that intravenous or subcutaneous heparin, dual antiplatelets, proton pump inhibitors, and statins were started at the first contact in all patients by the guideline recommendations. It was observed that treatments such as RAAS blocker and Beta-Blocker started when necessary according to the hemodynamic status of the patients[11]. It was determined that diuretic treatments were administered intravenously to patients with pulmonary edema.

Patients with type-II and type-III atrioventricular block were included in the HG-AVB group, and those without it were included in the Sinus Rhythm Group (SRG). Then, two subgroups were determined as those who need PPM and those who do not within the HG-AVB.

Biochemical and hematological parameters were evaluated in blood samples collected during hospitalization. Cardiac Troponin-I (cTnI) and CK-MB levels were identified during the cardiac enzyme follow-up.

Echocardiography

Echocardiographic analysis was performed in the left lateral decubitus position according to the American Society of Echocardiography guidelines within the first 24 hours of admission in emergency service or coronary care unit by Philips HD11

XE ultrasound system with a 3.2 MHz transducer (Philips Healthcare, Best, the Netherland)[12].

GRACE Score

The GS was calculated using a computer program (www.outcomes-umassmed.org/grace/acs_risk). Age, heart rate, systolic blood pressure, serum creatinine level, and Killip class were determined for GS[13]. ST-segment deviation and data about cardiac enzymes were entered into the computer program as appropriate.

Coronary Angiography

Patients with successful percutaneous coronary intervention (PCI) procedure (TIMI flow >2 after stenting) within the first 24 hours were considered in the cohort. The intervention was based on the discretion of the primary operator. Elective PCI was recommended for other lesions according to the judgment of the primary operator. All implanted stents were drug-eluting stents (DES) in the cohort. Patients were followed during the hospital period after NSTEMI. 1-vessel disease (VD) indicated that there was one vessel with >70% stenosis; 2-VD showed that there were two vessels with >70% stenosis; and 3-VD indicated that there were three vessels with >70% stenosis[14].

Statistical Analysis

SPSS 22.0 statistical software (IBM Corp., Armonk, NY, USA) was used for statistical analysis. Continuous variables were expressed as mean ± Standard deviation (SD) or median and interquartile range as appropriate. Categorical variables were expressed as percentages. The Kolmogorov-Smirnov test was used to test the normality of the distribution of continuous variables. Group means for continuous variables were compared with the Student's *t*-test or the Mann-Whitney U test, as appropriate. A two-tailed $p<0.05$ was considered statistically significant. The Chi-square test or Fisher exact test examined the correlation between categorical variables. To find independent associates of HG-AVB and PPM, variables with a *p*-value of ≤ 0.25 at the univariate analysis were selected for backward stepwise multiple regression analyses. The patients were divided into two groups for a Receiver Operating Characteristic (ROC) analysis: those with HG-AVB and those with SRG. The area under the ROC curve analysis, cut-off value for GS, 95% confidence intervals, and sensitivity and specificity values were determined. The calculated *p*-values less than 0.05 were considered statistically significant.

Results

Demographic and Laboratory Findings

There were 600 patients with NSTEMI at admission, and the mean age of patients with Hg-AVB was older than those with SRG (Table I). Baseline characteristics were presented in Table I. There were no differences between groups regarding previous CAD, diabetes, and hypertension prevalence. GRACE score on the first day, CK-MB, creatinine, and total cholesterol levels were higher in the HG-AVB group compared to SRG. Hemoglobin levels were significantly lower in the HG-AVB group, whereas platelets and potassium levels were similar in both groups. Appropriate therapy was initiated immediately in all patients as per hospital protocol. The average length of stay in the intensive care unit and the ward was significantly longer in patients with HG-AVB compared to those with SRG ($p=0.006$ and $p=0.014$, respectively), (Table I). The mortality rate was also higher in the HG-AVB group.

Echocardiography and Coronary Angiography Findings

Echocardiographic left ventricular ejection fractions were similar between groups (44.9±9.0 *vs.* 44.1±9.1%, $p=0.383$). SYNTAX score averages were similar. RCA disease was more frequently seen in the HG-AVB group ($p<0.001$).

HG-AVB Development

In our study, 111 of the patients (27.5%) developed HG-AVB after NSTEMI. Thirty-three patients died during their hospital stay (5.5%), and 14 of them were in the HG-AVB group ($p=0.001$). Independent predictors of HG-AVB are shown in Table II. In multivariate regression analysis, RCA lesion, GS, low hemoglobin, creatinine, and total cholesterol were found to be independent predictors of HG-AVB. The GS cut-off value, which predicts the development of HG-AVB, was calculated as 185.5 (AUC: 0.711; $p<0.001$; 95%CI: 0.646-0.776; sensitivity, 68%; specificity, 71%) (Figure 1).

Discussion

Within the scope of our study, the effectiveness of the GRACE score calculated during the first admission to the hospital after NSTEMI in predicting the development of HG-AVB was evaluated. For this purpose, consecutive patients admitted to our hospital were reviewed retrospectively. Those who met the criteria were included in the analyses.

Table I. Baseline characteristics of the patients. The differences between the groups of High Grade AV Block (HG-AVB) and Sinus Rythm (SR).

Variable	HG-AVB (n=111)	SR (n=489)	*p*-value
Age (years)	66.6 ± 11.8	63.2 ± 13.3	0.014
Hypertension, n (%)	67 (60.4)	276 (56.4)	0.259
Diabetes Mellitus, n (%)	25 (22.5)	83 (17.0%)	0.110
Troponin-I (ng/ml)	77.1 ± 6.9	69.1 ± 3.1	0.273
CK-MB	1376.1 ± 377.1	910.2 ± 268.8	0.048
Admission creatinine (mg/dl)	1.13 ± 0.51	0.91 ± 0.44	<0.001
GFR (mg/dl/1.73 m^2)	81.1± 36.1	87.7 ± 32.9	0.168
Potassium	4.4 ± 1.1	4.2 ± 0.7	0.602
Admission hemoglobin (g/dl)	12.9 ± 3.1	13.9 ± 3.9	<0.001
Platelets (x1000)	232.8 ± 71.4	241.5 ± 69.1	0.239
GRACE score at day 1	176.1± 46.6	150.4 ± 41.6	<0.001
SYNTAX score	20.2 ± 9.4	18.8 ± 8.9	0.682
LV-Ejection Fraction, before PCI, (%)	44.9 ± 9.0	44.1 ± 9.1	0.383
Total cholesterol (mg/dl)	197.8 ± 48.7	180.4 ± 43.3	0.002
LDL-cholesterol (mg/dl)	127.5 ± 47.1	119.4 ± 44.4	0.088
Intensive care unit stay (days)	4.3 ± 3.2	3.6 ± 1.6	0.006
Total hospital stay (days)	7.2 ± 4.6	6.3 ± 2.7	0.014
Previous CAD n (%)	26 (23.4)	80 (16.4)	0.055
Permanent pacemaker implantation, n (%)	12 (10.8)	0	<0.001
Mortality, n (%)	14 (12.6)	19 (3.9)	0.001
RCA, n (%)	73(65.8)	126 (25.8)	<0.001

CAD; Coronary artery disease, CK-MB; Creatinine kinase-myocardial band, LDL; Low density lipoprotein, LV; Left ventricle, RCA; Right coronary artery

It was determined that high GS on the first day was associated with the development of HG-AVB. The development of HG-AVB after NSTEMI significantly increases the morbidity and mortality rates[15,17]. On the other hand, GS began to be used as a scoring system for prognostic evaluation in ACS patients after the GRACE study conducted in 2003[18]. Its calculation is recommended in NSTEMI patients according to recent AHA and ESC guidelines[19,20].

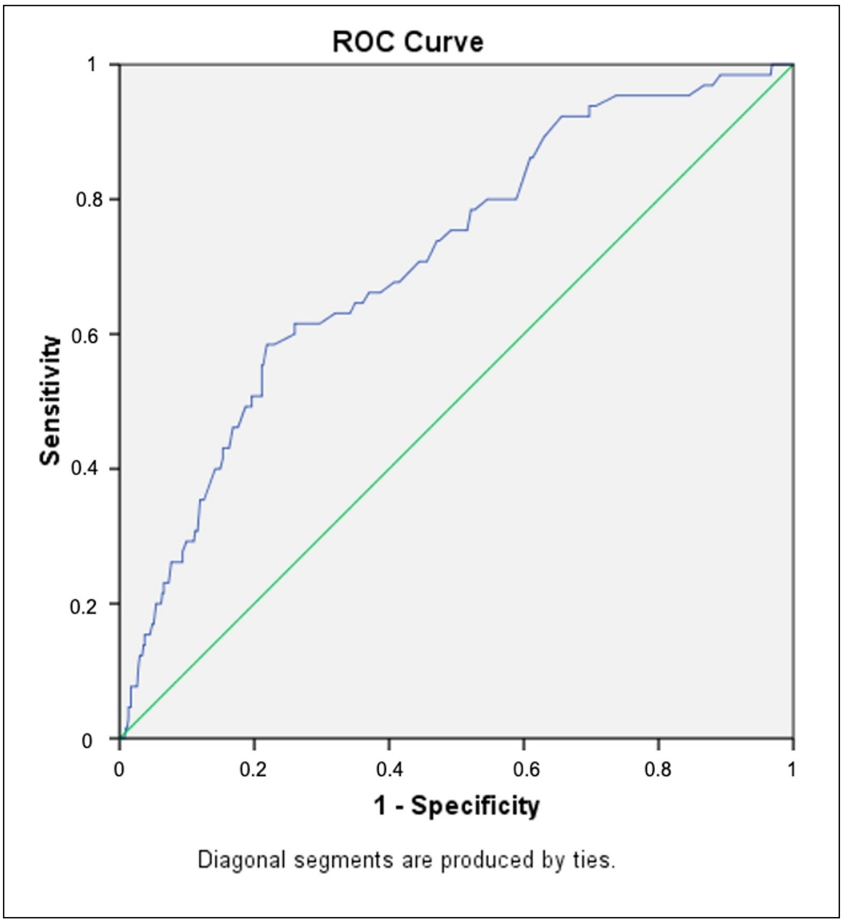
The usefulness of the GRACE risk score to establish the risk of HG-AVB after NSTEMI seems to have significant consequences[6,21,22]. After AMI, the patient is at risk of developing HG-AVB[23]. Therefore, risk stratification of HG-AVB patients to predict HF is important. However, in-hospital prognosis has rarely been evaluated in high-risk patients with NSTEMI. In our study, on the first day, GS was able to predict

Table II. Univariate and multivariate analysis of risk factors determining High Grade Atrioventricular block.

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
GRACE score	6.5 (1.9-9.4)	<0.001	2.8 (1.3-4.4)	<0.001
RCA occlusion	7.1 (2.8-10.3)	<0.001	3,1 (1.6-5.1)	<0.001
Low hemoglobine	2.7 (1.3-6.3)	0.002	1.4(0.7-2.3)	0.044
Creatinine	4,0 (1.8-7.1)	<0.001	2.1(1.1-3.1)	0.002
Total Cholesterole	3.4 (1.3-5.8)	<0.001	1.9 (0.9-2.8)	0.012

COPD: chronic obstructive pulmonary disease.

Figure 1. Receiver operating characteristic (ROC) curve. The GRACE risk score cut-off value, which predicts the development of HG-AVB, was calculated as 185.5 (AUC: 0.711; (p<0.001; 95% CI: 0.646-0.776; sensitivity, 69%; specificity, 73%). (AUC: Area Under the Curve; CI: Confidence Interval; HG-AVB: High-Grade Atrioventricular Block).



those patients who develop HG-AVB in the hospital, hence widening the indication of GRACE in NSTEMI patient cohorts.

As it is well established, the KC (Killip classification) is used to assess the severity of ischemic heart failure. Depending on KC, patients can get a score between 0-59 points in GS. However, only patients with KC-I at admission were included in this study. Therefore, the Killip classification was KC-I for scoring all of the patients, and its contribution to the score was zero. The presence of cardiac arrest during the admission period is represented by 39 points. However, in our study, the patients who were brought to the hospital with cardiac arrest were not included. Of note, some patients who were admitted to the hospital with KC-I developed cardiac arrest during the follow-up period. In-hospital cardiac arrest rate was higher in the HG-AVB group. The other two components of GS are cardiac enzyme elevation (14 points) and ST segment change (28 points). In our study, cardiac enzymes and ST segment change ratios were similar between groups.

Of note, other than GS, RCA lesion, low hemoglobin, creatinine, and total cholesterol were found to be independent predictors of HG-AVB. In our study, PCI was performed in all patients. As known, the severity of CAD and cardiac complication rates increase as well[23,24]. Nonetheless, in our study, there were not differences between groups according to the CAD burden. SYNTAX scores were similar before revascularization. This suggests that there is no linear relationship between CAD prevalence and the development of HG-AVB. The blood supply of structures such as the sinus node and AV node is mostly provided by RCA and less frequently by Cx. In this case, it shows that CAD is related to which artery is the lesion rather than the extent and severity. In our study, RCA is the most common IRA in HG-AVB patients. (Table I). During PCI, only the culprit lesions were intervened. Despite this, it was observed that PCI was applied to other lesions in the same session when necessary, depending on the hemodynamic status of the patients. Kidney functions, hemoglobin, and cholesterol levels are other predictors of HG-AVB development.

During the study period, 33 (5.5%) patients died. Most of them were in the HG-AVB group (p=0.001). The mortality rates were reported between 4-9% in previous studies[23,24]. Our results were in agreement with the previous data.

In many studies, it has been determined that the decrease in hemoglobin levels is associated with cardiac complications. Adverse events, including mortality, occur more frequently in hemorrhage or chronic anemia. In our study, there were lower hemoglobin levels in the HG-AVB group. Ischemia occurs in two ways, as is well known. These are the increase in need and the lack of resources. Poor presentation can be caused by anemia as well as by CAD. According to the results of our study, HG-AVB rates seem to increase when these two factors coexist in NSTEMI patients.

In addition, the heart and kidney are two organs that are directly related to each other. The pathology that occurs in one causes a regression in the functions of the other. Creatinine is the most commonly used functional indicator of kidney function. It has been determined that one of the factors facilitating the development of HG-AVB is high creatinine. This result once again emphasizes the cardiological importance of healthy kidneys.

Total cholesterol is a general indicator of blood lipids. Hyperlipidemia is the main cause of the atherosclerotic process. Hyperlipidemia is one of the important risk factors for the development of CAD. In our study, it was determined that low-density lipoprotein (LDL) cholesterol levels were not directly related to the development of HG-AVB. This supports the relationship with the location of the lesion in the RCA vessel rather than the extent and severity of CAD discussed above. The results of our study support the importance of the concept of non-LDL cholesterol and residual risk. High total cholesterol increases the development of HG-AVB after NSTEMI.

Morbidity and mortality were found to be higher in the HG-AVB group. The need for permanent pacemaker implantation arose in 12 (2%) patients. In our study, we aimed to evaluate the predictors of the need for a permanent pacemaker. However, we could not make this evaluation because the need for PM after NSTEMI was very low. The reasons for the need for PPM after NSTEMI can be investigated with a larger number of patients.

Limitations

First of all, this is a retrospective analysis of the data of a single tertiary care center. Several potentially missing data remain as confounders of the study results. Additionally, in accordance with the study protocol, only the in-hospital period was evaluated.

On the other hand, by longer follow-ups, particularly in the vulnerable phase after discharge, additional information can be obtained. Therefore, the findings should be supported by larger studies.

Conclusions

Calculation of GS is an important parameter that can be used to predict the development and course of HG-AVB. The duration of time in the hospital can be decreased, and complications can be avoided by identifying these individuals and those who could require PPM earlier.

Conflict of Interest
The authors declare that they have no conflict of interest.

Informed Consent
Patients and their families signed informed consent forms.

Authors' Contributions
CA, UU designed this study. İG, CA provided funding. CA and UU revised the manuscript. İG, CA, and UU finished the manuscript and analyzed the data. UU, CA, and İG collected the clinical data. CA contributed to the literature search.

Data Availability
The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics Approval
This study was approved by the International University of Kyrenia Medical Ethics Committee with the decision numbered GU/ETK 22.16 on 24.06.2022, with the expection of condition of informed consent.

Funding
None.

ORCID ID
UU: 0000-0002-3799-4470
CA: 0000-0002-1401-5727
İG: 0000-0001-8312-310X

References

1) Rogers WJ, Frederick PD, Stoehr E, Canto JG, Ornato JP, Gibson CM, Pollack CV Jr, Gore JM, Chandra-Strobos N, Peterson ED, French WJ. Trends in presenting characteristics and hospital mortality among patients with ST elevation and non-ST elevation myocardial infarction in the National Registry of Myocardial Infarction from 1990 to 2006. Am Heart J 2008; 156: 1026-1034.
2) Antman EM, Cohen M, Bernink PJ, McCabe CH, Horacek T, Papuchis G, Mautner B, Corbalan R, Radley D, Braunwald E. The TIMI risk score for unstable angina/non-ST elevation MI: A method for prognostication and therapeutic decision making. JAMA 2000; 284: 835-842.
3) Spencer FA, Meyer TE, Goldberg RJ, Yarzebski J, Hatton M, Lessard D, Gore JM. Twenty-year trends (1975-1995) in the incidence, in-hospital and long-term death rates associated with heart failure complicating acute myocardial infarction: a community-wide perspective. J Am Coll Cardiol 1999; 34: 1378-1387.
4) Carvalho LSF, Bogniotti LAC, de Almeida OLR, E Silva JCQ, Nadruz W, Coelho OR, Sposito AC. Change of BNP between admission and discharge after ST-elevation myocardial infarction (Killip I) improves risk prediction of heart failure, death, and recurrent myocardial infarction compared to single isolated measurement in addition to the GRACE score. Eur Heart J Acute Cardiovasc Care 2019; 8: 643-651.
5) Gheorghiade M, Sopko G, De Luca L, Velazquez EJ, Parker JD, Binkley PF, Sadowski Z, Golba KS, Prior DL, Rouleau JL, Bonow RO. Navigating the crossroads of coronary artery disease and heart failure. Circulation 2006; 114: 1202-1213.
6) Eagle KA, Lim MJ, Dabbous OH, Pieper KS, Goldberg RJ, Van de Werf F, Goodman SG, Granger CB, Steg PG, Gore JM, Budaj A, Avezum A, Flather MD, Fox KA; GRACE Investigators. A validated prediction model for all forms of acute coronary syndrome: estimating the risk of 6-month postdischarge death in an international registry. JAMA 2004; 291: 2727-2733.
7) McAllister DA, Halbesma N, Carruthers K, Denvir M, Fox KA. GRACE score predicts heart failure admission following acute coronary syndrome. Eur Heart J Acute Cardiovasc Care 2015; 4: 165-171.
8) Littnerova S, Kala P, Jarkovsky J, Kubkova L, Prymusova K, Kubena P, Tesak M, Toman O, Poloczek M, Spinar J, Dusek L, Parenica J. GRACE Score among Six Risk Scoring Systems (CADILLAC, PAMI, TIMI, Dynamic TIMI, Zwolle) Demonstrated the Best Predictive Value for Prediction of Long-Term Mortality in Patients with ST-Elevation Myocardial Infarction. PLoS One 2015; 10: e0123215.
9) Brieger D, Fox KA, Fitzgerald G, Eagle KA, Budaj A, Avezum A, Granger CB, Costa B, Anderson FA Jr, Steg PG; Global Registry of Acute Coronary Events Investigators. Predicting freedom from clinical events in non-ST-elevation acute coronary syndromes: the Global Registry of Acute Coronary Events. Heart 2009; 95: 888-894.
10) Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, White HD; ESC Scientific Document Group. Fourth universal definition of myocardial infarction (2018). Eur Heart J 2019; 40: 237-269.
11) Lee KL, Woodlief LH, Topol EJ, Weaver WD, Betriu A, Col J, Simoons M, Aylward P, Van de Werf F, Califf RM. Predictors of 30-day mortality in the era of reperfusion for acute myocardial infarction. Results from an international trial of 41,021 patients. GUSTO-I Investigators. Circulation 1995; 91: 1659-1668.
12) Gottdiener JS, Bednarz J, Devereux R, Gardin J, Klein A, Manning WJ, Morehead A, Kitzman D, Oh J, Quinones M, Schiller NB, Stein JH, Weissman NJ; American Society of Echocardiography. American Society of Echocardiography recommendations for use of echocardiography in clinical trials. J Am Soc Echocardiogr 2004; 17: 1086-1119.
13) DeGeare VS, Boura JA, Grines LL, O'Neill WW, Grines CL. Predictive value of the Killip classification in patients undergoing primary percutaneous coronary intervention for acute myocardial infarction. Am J Cardiol 2001; 87: 1035-1038.
14) Neeland IJ, Patel RS, Eshtehardi P, Dhawan S, McDaniel MC, Rab ST, Vaccarino V, Zafari AM, Samady H, Quyyumi AA. Coronary angiographic scoring systems: an evaluation of their equivalence and validity. Am Heart J 2012; 164: 547-552.e1.
15) Gheorghiade M, Zannad F, Sopko G, Klein L, Piña IL, Konstam MA, Massie BM, Roland E, Targum S, Collins SP, Filippatos G, Tavazzi L; International Working Group on Acute Heart Failure Syndromes. Acute heart failure syndromes: current state and framework for future research. Circulation 2005; 112: 3958-3968.
16) Juillière Y, Cambou JP, Bataille V, Mulak G, Galinier M, Gibelin P, Benamer H, Bouvaist H, Méneveau N, Tabone X, Simon T, Danchin N; FAST-MI Investigators. Heart failure in acute myocardial infarction: a comparison between patients with or without heart failure criteria from the FAST-MI registry. Rev Esp Cardiol (Engl Ed) 2012; 65: 326-333.
17) Judge KW, Pawitan Y, Caldwell J, Gersh BJ, Kennedy JW. Congestive heart failure symptoms in patients with preserved left ventricular systolic function: analysis of the CASS registry. J Am Coll Cardiol 1991; 18: 377-382.
18) Granger CB, Goldberg RJ, Dabbous O, Pieper KS, Eagle KA, Cannon CP, Van De Werf F, Avezum A, Goodman SG, Flather MD, Fox KA; Global Registry of Acute Coronary Events Investigators. Predictors of hospital mortality in the global registry of acute coronary events. Arch Intern Med 2003; 163: 2345-2353.
19) Amsterdam EA, Wenger NK, Brindis RG, Casey DE Jr, Ganiats TG, Holmes DR Jr, Jaffe AS, Jneid H, Kelly RF, Kontos MC, Levine GN, Liebson PR, Mukherjee D, Peterson ED, Sabatine MS, Smalling RW, Zieman SJ. 2014 AHA/ACC Guideline for the Management of Patients with Non-ST-Elevation Acute Coronary Syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014; 64: e139-e228.

20) Roffi M, Patrono C, Collet JP, Mueller C, Valgimigli M, Andreotti F, Bax JJ, Borger MA, Brotons C, Chew DP, Gencer B, Hasenfuss G, Kjeldsen K, Lancellotti P, Landmesser U, Mehilli J, Mukherjee D, Storey RF, Windecker S; ESC Scientific Document Group. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). Eur Heart J 2016; 37: 267-315.
21) Abu-Assi E, Ferreira-González I, Ribera A, Marsal JR, Cascant P, Heras M, Bueno H, Sánchez PL, Arós F, Marrugat J, García-Dorado D, Peña-Gil C, González-Juanatey JR, Permanyer-Miralda G. “Do GRACE (Global Registry of Acute Coronary events) risk scores still maintain their performance for predicting mortality in the era of contemporary management of acute coronary syndromes?”. Am Heart J 2010; 160: 826-834.e1-3.
22) Cakar MA, Sahinkus S, Aydin E, Vatan MB, Keser N, Akdemir R, Gunduz H. Relation between the GRACE score and severity of atherosclerosis in acute coronary syndrome. J Cardiol 2014; 63: 24-28.
23) Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Drazner MH, Fonarow GC, Geraci SA, Horwich T, Januzzi JL, Johnson MR, Kasper EK, Levy WC, Masoudi FA, McBride PE, McMurray JJ, Mitchell JE, Peterson PN, Riegel B, Sam F, Stevenson LW, Tang WH, Tsai EJ, Wilkoff BL; American College of Cardiology Foundation; American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for managing heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2013; 62: e147-239.
24) Sianos G, Morel MA, Kappetein AP, Morice MC, Colombo A, Dawkins K, van den Brand M, Van Dyck N, Russell ME, Mohr FW, Serruys PW. The SYNTAX Score: an angiographic tool grading the complexity of coronary artery disease. EuroIntervention 2005; 1: 219-227.
25) Serruys PW, Onuma Y, Garg S, Sarno G, van den Brand M, Kappetein AP, Van Dyck N, Mack M, Holmes D, Feldman T, Morice MC, Colombo A, Bass E, Leadley K, Dawkins KD, van Es GA, Morel MA, Mohr FW. Assessment of the SYNTAX score in the Syntax study. EuroIntervention 2009; 5: 50-56.