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 mortality1. 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 occur2. Adverse outcomes are decreased when the artery that caused the infarction (IRA) can be revascularized3. Many conditions, especially after myocardial infarction, including arrhythmia, may occur more frequently and faster. High-grade atrioventricular blocks (HG-AVB) may occur after NSTEMI4. 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
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-III1. The definition of HG-A VB includes type-II and type-III AV block. HG-A VB is a pathology that increases the risk of morbidity and mortality and needs to be treated. A significant portion of HG-A VBs 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 guidelines7. Scoring can be done by entering the patients’ variables into the system via software8. 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 patients9.

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-A VB 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 sought10. 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 patients11. 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-A VB 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).

**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. 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.

**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-A VB and PPM, variables with a $p$-value of $\leq 0.25$ 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-A VB 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-A VB 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-A VB group compared to SRG. Hemoglobin levels were significantly lower in the HG-A VB 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-A VB compared to those with SRG ($p=0.006$ and $p=0.014$, respectively), (Table I). The mortality rate was also higher in the HG-A VB 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-A VB group ($p<0.001$).

**HG-A VB Development**

In our study, 111 of the patients (27.5%) developed HG-A VB after NSTEMI. Thirty-three patients died during their hospital stay (5.5%), and 14 of them were in the HG-A VB group ($p=0.001$). Independent predictors of HG-A VB 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-A VB. The GS cut-off value, which predicts the development of HG-A VB, 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-A VB was evaluated. For this purpose, consecutive patients admitted to our hospital were reviewed retrospectively. Those who met the criteria were included in the analyses.
It was determined that high GS on the first day was associated with the development of HG-AV B. The development of HG-AV B 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\(^{19,20}\).

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

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

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

The usefulness of the GRACE risk score to establish the risk of HG-AV B after NSTEMI seems to have significant consequences\(^ {6,21,22}\). After AMI, the patient is at risk of developing HG-AV B\(^ {23}\). Therefore, risk stratification of HG-AV B 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.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>(p)-value</td>
</tr>
<tr>
<td>GRACE score</td>
<td>6.5 (1.9-9.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RCA occlusion</td>
<td>7.1 (2.8-10.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Low hemoglobin</td>
<td>2.7 (1.3-6.3)</td>
<td>0.002</td>
</tr>
<tr>
<td>Creatinine</td>
<td>4.0 (1.8-7.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total Cholesterol</td>
<td>3.4 (1.3-5.8)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

COPD: chronic obstructive pulmonary disease.
GRACE risk score and atrioventricular conduction block after non-st-segment elevation myocardial infarction

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\(^\text{23,24}\). 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 exception of condition of informed consent.

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References


4) Carvalho LSF, Bogniotti LAC, de Almeida OLR, Antman EM, Cohen M, Bernink PJ, McCabe CH, Gore JM, Murray JD. 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.


