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ABSTRACT

Background: Acute coronary syndromes are the leading cause of mortality worldwide. Electrical risk score (ERS) is a novel electrocardiographic risk scoring system. The prognostic importance of ERS in non-ST elevation myocardial infarction (NSTEMI) patients is unknown. We aimed to determine the association of ERS with in-hospital prognosis in NSTEMI patients undergoing coronary angiography (CAG).

Methods: A total of 427 consecutive NSTEMI patients undergoing CAG were enrolled in this study. Six parameters comprised ERS: pulse rate >75, left ventricular hypertrophy according to Sokolow–Lyon criteria, QRS transition zone ≥V4, corrected QT (QTc) interval >450 for men and >460 for women, T peak to T end interval (Tp-e) >89 ms, and frontal QRS-T angle >90°. The ERS was calculated according to the number of abnormal findings in electrocardiogram. The study population was divided into 2 groups as ERS <3 and ≥3.

Results: No significant difference was found between ERS ≥3 and <3 groups in terms of demographic characteristics. However, patients with ERS ≥3 had significantly higher maximum troponin (*P* < .001), thrombolysis in myocardial infarction (*P*=.002), and global registry of acute coronary events (*P* < .001) risk scores and 3-vessel disease frequency (*P*=.001), whereas they had lower left ventricular ejection fraction (*P* < .001). These patients also had higher frequency of in-hospital mortality (*P* < .001) and adverse events. Multiple logistic regression analysis demonstrated that ERS (OR=1.790, 95% CI: 1.036- 3.095, *P*=.037) was an independent predictor of in-hospital mortality.

Conclusion: The frequency of in-hospital adverse events and mortality was significantly higher in NSTEMI patients with an ERS ≥3 at admission. This simple electrocardiographic risk marker may help identify patients at higher cardiac risk in patients presenting with NSTEMI and identify patients who may need early coronary intervention.

Keywords: Electrocardiography, electrical risk score, non-ST elevation myocardial infarction

INTRODUCTION

Acute coronary syndromes (ACSs) are the leading cause of morbidity and mortality worldwide.1 Non-ST-elevation myocardial infarction (NSTEMI) is a type of ACS and commonly defines either complete blockage of a minor coronary artery or incomplete blockage of a major coronary artery.^{2,3} Current guidelines for the management of ACS recommend an immediate invasive strategy for patients at very high risk, while an early (within 24 hours) invasive strategy is recommended for patients with high risk.¹ Identifying patients who would benefit from early percutaneous coronary intervention can be lifesaving; therefore, risk stratification has a very important role in the management of NSTEMI patients.

Despite many technological advances, the 12-lead electrocardiogram (ECG) continues to play a critical role in the diagnosis, risk stratification, and determining the appropriate type of treatment in patients with ACS.⁴ In the 2023 ESC guidelines, dynamic ECG changes are one of the criteria used to determine high risk in patients presenting with NSTEMI. On the other hand, many ECG parameters

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ORIGINAL INVESTIGATION

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have also been used to date to identify high risk in patients with ACS, including heart rate and markers of myocardial depolarization and repolarization.5,6 However, ECG parameters were usually analyzed separately in these studies. This has limited the power of ECG parameters alone and therefore allowed researchers to develop new approaches, such as using ECG as a risk predictor. 7 The most important ECG parameter developed in this context is the electrical risk score (ERS), which an easily obtainable marker from a 12-lead ECG.⁵ It consists of 6 simple ECG parameters, including pulse rate, presence of left ventricular hypertrophy (LVH), QRS transition zone, corrected QT interval (QTc), T peak to T end interval (Tp-e), and frontal QRS-T angle, and has been demonstrated to allow risk assessment in different diseases.5,8-10

To our knowledge, no study has assessed the association of ERS with in-hospital poor outcomes in NSTEMI patients undergoing coronary angiography. In the present study, it was aimed to evaluate the effect of ERS on in-hospital poor outcomes and mortality in patients with NSTEMI.

METHODS

Patient Selection

A total of 427 consecutive NSTEMI patients who underwent coronary angiography between January 2020 and November 2021 were included in this retrospective study. The current guidelines for the management of acute coronary syndromes were used for the diagnosis of NSTEMI.¹ All patients older than 18 years of age and having coronary angiography performed in our clinic were included in this study. Patients with complete bundle branch block, pacemaker rhythm, second or third degree atrioventricular block, and ECG recordings could not be reached were excluded from the study. Harran University Clinical Research Ethic Committee was approved the study design (Approval date: December 13, 2021; Approval no.: HRU/21.22.17).

Electrocardiography

Twelve-lead surface ECG was obtained from all patients on admission in the supine position. Electrical risk score was composed of 6 simple parameters including heart rate, presence of LVH, QTc interval, Tp-e interval, QRS transition zone, and frontal QRS-T angle.⁵ In this score, 1 point was assigned for the presence of an abnormal ECG parameter, and 0 points for a normal ECG parameter. As previously reported, abnormal ECG parameters were defined

HIGHLIGHTS

- Electrical risk score (ERS) is an easily obtainable marker from electrocardiography.
- The ERS consists of 6 simple electrocardiogram parameters.
- No study has assessed the association of ERS with prognosis in patients with non-ST elevation myocardial infarction (NSTEMI).
- We found that NSTEMI patients with a higher ERS had a worse prognosis.

as follows: heart rate >75, presence of LVH according to the Sokolow–Lyon criteria, QRS transition zone ≥V4, QT corrected (QTc) interval >450 ms in men and >460 ms in women, Tp-e interval >89 ms, and frontal QRS-T angle >90° . 11 Presence of LVH was defined as the voltage sum of V1S wave+ V5/6R wave ≥35 mm (3.5 mV), according to the Sokolow–Lyon criteria.12 The QT interval was measured from the beginning of the QRS wave to the end of the T wave, and corrected with the Bazett formula (QTc Bazett: QT/ √RR). The Tp-e interval was measured from the peak of the T wave to the end of the T wave.¹² The QRS transition zone was defined as the precordial lead where the R wave was equal in amplitude or greater than the S wave.13 Frontal QRS-T angle was calculated as the absolute difference between QRS axis and T axis. If this difference exceeded 180 $^{\circ}$, it was calculated by subtracting the angle from 360 $^{\circ}$.14 Some of these parameters are available in the automatic ECG report, while others are calculated by measurement. In the automatic report of the ECG device, heart rate, QTc interval, frontal QRS-T angle, and the Sokolow–Lyon criteria are already available, and these parameters were obtained based on measurements from the ECG device. However, the Tp-e interval and QRS transition zone were calculated from the ECG. An example of the evaluation of ERS from the 12-lead ECG with its automatic report is presented in Figure 1. The inter-observer and intra-observer coefficients were 2.3% and 2.9% for Tp-e interval and 0.8% and 0.4% for QRS transition zone. Scoring was performed for each parameter, and the total score was defined as ERS (lowest score: 0, highest score: 6) (Figure 2).3 Our study population was divided into 2 groups: patients with ERS ≥3 and patients with ERS <3.

Coronary Angiography

Coronary angiography was performed via radial and/or femoral artery using the standard Judkins technique. Digital angiograms and reports were evaluated. Significant stenosis was defined as ≥70% stenosis in the major epicardial coronary arteries and ≥50% stenosis in the left main coronary artery. The number of vessels with critical stenosis and the presence of 3-vessel disease were recorded. The number of implanted stents and stent sizes were also recorded.

Risk Scores

To determine the prognosis of the patients, thrombolysis in myocardial infarction (TIMI) and global registry of acute coronary events (GRACE) risk scores were calculated (1). The synergy between PCI with TAXUS and cardiac surgery (SYNTAX) score was used to determine the anatomical complexity of coronary artery disease.15

Study Outcomes

Contrast-induced acute renal failure was defined as an increase in serum creatinine of ≥25% or 0.5 mg/dL within 72 hours following CAG.16,17 Ventricular arrhythmias were defined as the presence of ventricular tachycardia and/ or ventricular fibrillation during hospitalization. Inotropic requirement was defined as the use of any inotropic drugs due to hypotension (systolic blood pressure <90 mm Hg) and organ perfusion failure during hospitalization. In-hospital

Figure 1. An example of the evaluation of ERS from the 12-lead ECG with its automatic report.

mortality (assessed from the hospital database) was defined as death due to any cause within the hospital, and 6-month mortality (assessed from the death notification system) was defined as death due to any cause within 6 months.

Statistical Analysis

Statistical analysis was performed with the SPSS 22.0 program. The Kolmogorov–Smirnov test was used to determine the normality of continuous data. Normally distributed continuous data were presented as mean ± standard deviation and compared with Student's *t*-test. Continuous data that did not fit the normal distribution were presented as medians (quartiles 25-75) and compared with the Mann–Whitney *U* test. Categorical variables were expressed as numbers (%) and compared with the chi-square test. Pearson or Spearman correlation coefficients were used for correlation analysis. Receiver operating characteristic (ROC) curve analysis was used to determine the best cut-off value for ERS to predict in-hospital mortality. Multiple binary logistic regression analysis was used to identify independent predictors of in-hospital mortality. A *P* value of <.05 was considered significant.

score.

RESULTS

Mean age of the patients was 60.9 ± 11.4 , and 66% were male. Thrombolysis in myocardial infarction and the GRACE risk scores were 4.4 ± 1.4 and 118.5 ± 27.7 at admission, respectively. Three hundred eighty (89%) patients were treated by stent implantation, while 47 (11%) patients underwent coronary artery bypass graft treatment in this study. The ERS distribution of our study population is presented in Figure 3. Electrical risk score was 0 in 48 (11.2%) patients, 1 in 123 (28.8%) patients, 2 in 152 (35.6%) patients, 3 in 65 (15.2%) patients, 4 in 32 (7.5%) patients, and 5 in 7 (1.6%) patients.

The study population was divided into 2 groups: patients with ERS ≥3 (n = 104) and patients with ERS <3 (n = 323). There was no significant difference between the 2 groups in terms of mean age, gender, and frequency of HT and DM. However, patients with ERS ≥3 had a significantly higher TIMI (*P*=.030) and GRACE (*P*< .001) scores, glucose (*P*=.001), urea (*P*=.006), creatinine (*P*=.008), maximum CK-MB (*P* < .001), troponin (*P* < .001), and leukocytes (*P*=.011) compared to patients with ERS <3 (Table 1). Also, when compared to patients with ERS <3, patients with ERS ≥3 had a significantly higher frequency

Figure 3. The electrical risk scores of the patients included in the study.

 BMI, body mass index; BUN, blood urea nitrogen; CAD, coronary artery disease; CRP, C-reactive protein; CVA, cerebrovascular accident; DBP, diastolic blood pressure; DM, diabetes mellitus; GRACE, global registry of acute coronary events; HT, hypertension; SBP, systolic blood pressure; TIMI, thrombolysis in myocardial infarction. Bold values define the statistical significance of P < .05

of 3-vessel disease (*P*=.001) and SYNTAX score (*P* < .001), but lower LVEF (*P* < .001) (Table 2).

A comparison of in-hospital complications is shown in Table 3. Ventricular arrhythmias (*P* < .001), contrast-induced nephropathy (*P* < .001), inotrope requirement (*P* < .001), NIMV requirement (*P* < .001), and in-hospital mortality was significantly higher in patients with ERS ≥3 compared to patients with ERS <3 (Table 3). We also found that, as the number of abnormal ECG parameters increased, the frequency of 3-vessel disease, in-hospital mortality, and ventricular arrhythmia gradually increased (Figure 4).

In correlation analysis, it was observed that ERS was positively correlated with maximum CK-MB (*r*=0.285, *P* < .001), maximum troponin (*r*=0.410, *P* < .001), TIMI (*r*=0.171, *P*=.002), GRACE (*r*=0.243, *P* < .001), and SYNTAX (*r*=0.427, *P* < .001) scores, whereas negatively correlated with LVEF (*r*=−0.363, *P* < .001). Receiver operating characteristic curve analysis was performed to determine the best cut-off value of ERS to predict in-hospital mortality. It was found that ERS ≥2.5 predicted in-hospital death with a sensitivity of 69.2% and specificity of 77.1% (AUC=0.798, 95% CI: 0.675-0.921, *P* < .001) (Figure 5).

LVEF, left ventricular ejection fraction; QTc, corrected QT; SYNTAX, synergy between PCI with TAXUS and cardiac surgery; Tp-e, T peak to T end interval.Bold values define the statistical significance of P < .05

Multiple binary logistic regression analysis was performed to identify independent predictors of in-hospital mortality. ERS (odds ratio (OR)=1.790, 95% CI: 1.036-3.095, *P*=.037), ventricular arrhythmia (OR=7.057, 95% CI: 1.755-28.378, *P*=.006), and GRACE risk score (OR=1.030, 95% CI: 1.010- 1.051, *P*=.004) were determined as the independent predictors of in-hospital mortality (Table 4).

In our study, we also evaluated sixth month mortality of the patients. Patients with an ERS ≥3 had a significantly higher

Figure 4. The frequency of 3-vessel disease, in-hospital mortality, and ventricular arrhythmia according to the number of electrocardiographic abnormalities.

Figure 5. Receiver operating characteristic curve analysis of electrical risk score for predicting in-hospital mortality.

frequency of sixth month mortality (13.5% vs. 4.6%, *P*=.002). In addition, those who died at the sixth month had a higher ERS than those who did not die (2.9 ± 1.3 vs. 1.8 ± 1.1, *P* < .001).

DISCUSSION

In this study, we investigated the clinical and prognostic significance of ERS in NSTEMI patients undergoing coronary angiography. We found that ~25% of our study population had an ERS ≥3. The main findings of our study were as follows: (i) patients with ERS ≥3 had a significantly higher TIMI, GRACE and SYNTAX scores, maximum troponin, leukocytes, and 3-vessels disease frequency whereas lower LVEF compared to patients with ERS <3; (ii) those patients also had significantly higher frequency of in-hospital mortality and adverse events; (iii) ERS was an independent predictor of inhospital mortality. To our knowledge, this is the first study investigating the prognostic importance of ERS in patients presenting with NSTEMI.

The 12-lead ECG continues to play a very important role in diagnosis, risk stratification, and prognosis patients with ACS.4,18,19 The clinical importance of many

hypertension, diabetes mellitus, troponin, 3-vessel disease, electrical risk score, TIMI score, GRACE score, ventricular arrhythmia.

electrocardiographic parameters has been investigated in previous studies.14,18-24 However, these parameters were studied separately in most of the studies. Electrical risk score is a novel cumulative risk score system and was first developed by Aro et al⁵ To obtain this risk score, they included many ECG parameters reflecting different phases of the cardiac electrical cycle in a multivariable model. They reported that the final risk model consists of 6 different electrocardiographic parameters, each of them an expression of electrical and structural cardiac damage.^{5,8} It has been concluded that ECG parameters in this risk score are possibly the predictors of mortality as they show the imbalanced neuro-autonomic control (heart rate, QTc, and Tp-e), the repolarization alterations (QTc, QRS-angle, and Tp-e), and cardiac hypertrophy (QTc, QRS-angle, QRS transition, and Tp-e).8

To date, very few studies have examined the clinical significance of ERS in different populations. Aro et al⁵ found that ERS was associated with sudden cardiac death in patients with a high burden of cardiovascular risk factors. Piccirillo et al⁸ reported that ERS was the strongest predictor of all-cause or cardiovascular mortality in patients undergoing transcatheter aortic valve replacement. Both studies accepted an ERS ≥4 as a high-risk criterion. However, if these studies are investigated, it can be observed that the frequency of ERS \geq 4 is quite low. In the study by Aro et al,⁵ 16% of cases had a high ECG risk score of ≥4. Also, the prevalence of ERS ≥4 was only 13% in the study by Piccirillo et al.⁸ In our study, patients with ERS ≥4 constituted 9.1% of the study population. Due to the small number of patients in this group, our study population was divided into 2 groups: ERS ≥3 and <3 to make better comparisons and avoid possible limitations. Indeed, the fact that we found the best cut-off value of ERS to predict in-hospital mortality was ≥2.5 in ROC curve analysis also supports this idea. We think that comparisons in this way would be more appropriate for our study.

Previous studies performed on patients with ACS demonstrated that each of the ECG parameters, including the ERS, was separately associated with poor prognosis.14,20-24 However, to our knowledge, there is no study examining the clinical significance of ERS in NSTEMI patients. The most important finding of our study was that in-hospital mortality and adverse events rate, and sixth month mortality was significantly higher in NSTEMI patients with ERS ≥3. Also, as the number of abnormal findings on the ECG increased, in-hospital mortality gradually increased. Moreover, ERS was found to be an independent predictor of in-hospital mortality. Similar to our study, previous studies also reported higher mortality rates in patients with higher ERS compared to patients with lower ERS in different patient population.5,8 Our results suggest that ERS is a beneficial marker for detecting NSTEMI patients at high cardiac risk on admission. Moreover, the fact that TIMI and GRACE risk scores were significantly higher in patients with ERS ≥3 at admission in our study strengthens the relationship of increased ERS with mortality. The most likely reason for the increased mortality in patients with ERS ≥3 in our study may be explained by the fact that we found a larger infarct area, a higher GRACE score at admission, and a higher frequency

of ventricular arrhythmias, 3-vessel disease, and acute renal failure in these patients. Therefore, it may be suggested that patients with ERS ≥3 at admission have higher cardiac risk.

Although baseline clinical characteristics were similar, we detected that patients with ERS ≥3 had a significantly higher maximum CK-MB and troponin, 3-vessel disease, SYNTAX score and lower LVEF when compared to patients with ERS <3. Previous studies also reported a significant relationship between ECG markers in ERS and these clinical parameters.14,20-24 We also found that as the number of ECG abnormalities increased, the frequency of 3-vessel disease increased gradually. These results suggest that as the number of vessels with critical stenosis and the extent of myocardial scar increase, the number of depolarization/ repolarization abnormalities detected on the surface ECG also increases, thus increasing the ERS. Moreover, because we found patients with ERS ≥3 had a significantly higher levels of leucocyte counts, we considered that systemic inflammation may be related to the ERS and extent of the scar tissue. It can be concluded that the presence of more scar tissue, increased inflammatory response, and more extensive coronary artery disease may be the causes of increased mortality in patients with ERS ≥3.

Ventricular arrhythmia is a complication that may be seen in ACS patients and is associated with a poor prognosis.²⁵ It has been reported that an increase in parameters indicating myocardial depolarization/repolarization, such as QTc interval, Tp-e interval, and frontal QRS-T angle, is associated with an increased risk of ventricular arrhythmias.^{26,27} In our study, we detected that the frequency of ventricular arrhythmia was significantly higher in patients with ERS ≥3, and as the number of ECG abnormalities increased, the frequency of ventricular arrhythmia also increased gradually. Because the ECG parameters included in the ERS reflect nearly all phases of the cardiac cycle, this parameter can help predict the underlying arrhythmic substrate and probability of experiencing an arrhythmic event with greater accuracy. This finding obtained in our study suggests that in-hospital ventricular arrhythmias will be more frequent in patients admitted with NSTEMI who have higher ERS on admission, and that these patients should be monitored more closely.

Contrast-induced nephropathy is one of the most important complications of coronary angiography. Although the exact mechanism is not clearly understood, direct epithelial toxicity of the contrast agent, inflammation, oxidative stress, apoptosis, and immune regulations may play an important role in the development of contrast induced contrast induced nephropathy.28 We found that patients with ERS ≥3 had a higher frequency of contrast-induced nephropathy in the follow-up. When we investigated the literature, we could not detect such a relationship between ERS and contrast-induced nephropathy. Nevertheless, baseline urea and creatinine values on admission were also higher in patients with ERS ≥3. This may be due to larger infarct size and lower cardiac pump function at presentation in these patients. Similarly, a previous study showed that comorbid conditions

on admission are more common mainly in patients with higher ERS.³ It may be concluded that patients with higher ERS should be followed closely for the development of contrast-induced nephropathy, attention should be paid to the use of opaque substances in these patients when undergoing angiography, and hydration should be provided in these patients after the procedure.

Study Limitations

Our study has some limitations. The most important limitation is its retrospective design and the small number of patients. Second, we could not perform serial ECG monitoring of the patients during hospitalization. Assessing the dynamic changes in ERS score, calculating ERS in the last ECG before discharge, and detecting the relation with long-term adverse events could have increased the value of our study. Third, we did not record the time intervals of in-hospital mortality and the frequency of mortality during the PCI procedure. Fourth, we did not record the cardiac and non-cardiac causes of in-hospital mortality. It would be useful to know the causes of in-hospital mortality. Last, we did not record the medical treatments used by patients. Medications, especially antiplatelet therapy, may affect the prognosis of NSTEMI patients. Recording the medications used by the patients and determining their effects on prognosis may provide additional contributions to our study.

CONCLUSION

The ERS can be easily calculated from surface ECG. It may play an important role in predicting high-risk patients who may develop in-hospital adverse events and mortality in patients presenting with NSTEMI and have an additional contribution in identifying patients who may require early invasive intervention. Further studies with larger participant pools are required to better elucidate the importance of ERS in patients with NSTEMI.

Ethics Committee Approval: The study was approved by Şanlıurfa Harran University Clinical Research Ethics Committee (Approval date: December 13, 2021; Approval no.: HRU/21.22.17). This study was performed in line with the principles of the Declaration of Helsinki.

Informed Consent: Informed consent was obtained from all individual participants included in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – A.N.E., Z.T., R.D.; Design – A.N.E., Z.T., M.B.T., A.B., R.D.; Supervision – A.N.E., Z.T., H.F., K.T., M.B.T., İ.H.A., A.B., R.D.; Resources – A.N.E., Z.T., H.F., K.T.; Materials – A.N.E., Z.T., H.F., K.T., M.B.T., İ.H.A., A.B., R.D.; Data Collection and/or Processing – A.N.E., Z.T.; Analysis and/or Interpretation – A.N.E., Z.T., H.F., K.T., M.B.T., İ.H.A., A.B., R.D.; Literature Search – A.N.E., Z.T., R.D.; Writing – A.N.E., Z.T., R.D.; Critical Review – A.N.E., Z.T., H.F., K.T., M.B.T., İ.H.A., A.B., R.D.

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