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Journal of Cardiovascular Emergencies 2016;2(3):114-121
DOI: 10.1515/jce-2016-0018

ORIGINAL RESEARCH

Integrated ST Segment Elevation Scores and In-hospital Mortality in STEMI Patients Undergoing Primary PCI

Diana Opincariu, Monica Chițu, Nora Rat, Imre Benedek

University of Medicine and Pharmacy, Tîrgu Mureș, Romania

ABSTRACT

The **objective** of this study was to study the integrated score of ST-segment resolution (ISSTE) and in-hospital death in patients undergoing primary percutaneous intervention (pPCI) for ST-segment elevation myocardial infarction (STEMI). **Material and Methods:** This prospective study included 586 consecutive patients admitted with STEMI to the Cardiology Clinic of the County Emergency Clinical Hospital of Tîrgu Mureș, between January 1st, 2013 and December 31, 2014, who underwent pPCI in less than twelve hours after the onset of symptoms. Clinical and demographic data were analyzed in 539 (91.9%) survivors (Group 1) and 47 (8.1%) nonsurvivors (Group 2). The Integrated Score of ST elevation (ISSTE) was calculated by summing the amplitude of the ST segment elevation in all the 12 leads, before and at 2 hours after revascularization. **Results:** The ISSTE score calculated at baseline, immediately before the primary percutaneous coronary intervention, was significantly higher in Group 2 as compared to Group 1 (13.9 ± 1.2 vs. 11.0 ± 0.2, p = 0.026). At the same time, the ISSTE score calculated at 2 hours after the coronary intervention was significantly higher for patients in Group 2 (7.36 ± 1.12 vs. 2.9 ± 0.1, p <0.0001). Analysis of the dynamics of the ISSTE score indicated that patients who survived presented a more expressed reduction in the ISSTE score following pPCI, as compared to those who subsequently died (73.5% reduction in Group 1 compared to 47.2% reduction in Group 2, p <0.0001). In-hospital mortality was significantly higher in the group of patients with >50% reduction in the ISSTE score. The in-hospital death rate was 5.4% in patients with >50% reduction in the ISSTE score, compared to 19.4% for those who presented less than 50% reduction in the ISSTE score following pPCI (p <0.0001). The rate of successful reperfusion rate, expressed by the reduction in ISSTE score, was 83.8% in Group 1, compared to 55.3% in Group 2 (p <0.0001), indicating that the absence of an efficient reperfusion after pPCI is associated with a higher mortality in STEMI patients, and could be evaluated using regression of the ISSTE score, which proved to be directly associated with mortality. **Conclusion:** The ISSTE score is shown to be an effective ECG-derived marker of myocardial damage in STEMI patients. A high ISSTE score is associated with higher mortality, while a reduction in the ISSTE score after pPCI may indicate an efficient reperfusion and a decrease in mortality in the first days after infarction.

Keywords: ISSTE score, STEMI, mortality, ST segment resolution

ARTICLE HISTORY

Received: 10 May, 2016
Accepted: 11 August, 2016

CORRESPONDENCE

Monica Chițu
Str. Gheorghe Marinescu nr. 38
540139 Tîrgu Mureș, Romania
Tel: +40 265 215 551
E-mail: iuliachitu@yahoo.com

Diana Opincariu: Str. Gheorghe Marinescu nr. 38, 540139 Tîrgu Mureș, Romania. Tel: +40 265 215 551. E-mail: diana.opincariu@yahoo.ro
Nora Rat: Str. Gheorghe Marinescu nr. 38, 540139 Tîrgu Mureș, Romania. Tel: +40 265 215 551. E-mail: ratnora@gmail.com
Imre Benedek: Str. Gheorghe Marinescu nr. 38, 540139 Tîrgu Mureș, Romania. Tel: +40 265 215 551. E-mail: imrebenedek@yahoo.com

INTRODUCTION

Early reperfusion with primary percutaneous coronary intervention (pPCI) has substantially improved outcomes for ST-elevation myocardial infarction (STEMI) patients. However, despite the efficiency of pPCI, in-hospital mortality after acute myocardial infarction (AMI) remains high.[1]

Detecting patients with an elevated risk for further events such as re-infarction or death, is necessary to initiate appropriate therapy and to reduce the risk of adverse events.

Prognostic evaluation for STEMI is far from ideal. Therefore, an ongoing search for markers to complete the currently applied risk scores is essential. ST segment resolution after pPCI or thrombolysis is indicative for efficient reperfusion at the level of the myocardial tissue. Several studies demonstrated that in STEMI patients, reversal of ST segment elevation is a good predictor for the patency of an infarct-related artery (IRA), and is inversely correlated with subsequent death.[2–4] On the other hand, the persistence of ST segment elevation is specific for either an obstructed IRA or a patent artery, but with no myocardial and microvascular reperfusion (no-reflow phenomenon).[4]

The objective of this study was to study the integrated score of ST segment resolution (ISSTE) as an indicator of ECG-based score and in-hospital death in patients undergoing pPCI for STEMI.

The null hypothesis is that there is no statistical difference between patients who die during hospitalization and those discharged alive, for integrated score of ST segment resolution.

MATERIAL AND METHODS

This prospective study included all consecutive patients admitted to the Cardiology Clinic of the County Emergency Clinical Hospital of Tîrgu Mureș between January 1st, 2013 and December 31, 2014, with ST segment elevation myocardial infarction who underwent pPCI in less than twelve hours after the onset of symptoms. This resulted in 586 patients being enrolled in the study.

The inclusion criteria were:

- typical chest pain lasting for more than 10 minutes, with the onset less than 12 hours before presentation;
- troponin elevation;
- ST segment elevation of more than 1 mm in two or more consecutive leads, with reciprocal ST segment depression in opposite leads;
- pPCI performed in less than 12 hours from the onset of symptoms.

The exclusion criteria were:

- patients presenting with left bundle branch block (LBBB), which precluded the correct assessment of ST elevation on the surface ECG;
- the lack of any ST segment elevation on the ECG.

All patients underwent angiographic evaluation and revascularization via pPCI.

The study protocol was approved by the ethics committee of the institution, and all patients gave written informed consent before being enrolled in the study. The study was conducted by the principles stipulated in the Declaration of Helsinki.

Demographic data, medical history, clinical presentation, Killip class, serum biomarkers and angiographic recordings were recorded and analyzed in 539 (91.9%) survivors (Group 1) and 47 (8.1%) nonsurvivors (Group 2).

Twelve-lead electrocardiograms (ECGs) were obtained at presentation, immediately after pPCI and two hours after revascularization. The Integrated Score of ST Elevation (ISSTE) was calculated by summing the amplitude of the ST segment elevation in all twelve leads, before and at two hours after revascularization.

STUDY ENDPOINTS

The primary endpoint of the study was the all-cause mortality during hospitalization. The duration of stay in the hospital for the study population was 8.3 days (maximum), with an average of 6.5 days. All-cause mortality was recorded during this period. Only deaths that occurred during the hospitalization were included in the analysis.

The secondary endpoint of the study was the rate of successful reperfusion following pPCI, as defined by a reduction of >50% of the ISSTE at two hours after pPCI.

STATISTICAL ANALYSIS

The data was statistically analyzed using GraphPad Prism 6.0. Quantitative values were expressed as mean ± standard deviation, and categorical variables as frequencies and percentage values.

Statistical comparisons between the two study groups were performed using the Chi^2 test or Fisher's exact test when suitable, for qualitative data.

For continuous values, the two groups were compared using the two-tailed Student t-test or the two-tailed Mann-Whitney test when suitable.

The relative performance of each test was evaluated with a 95% confidence interval (CI).

TABLE 1. Patient demographics

	Group 1 Survivors	Group 2 Deceased	p value
Age (mean, y)	61.4 ± 11.7	70.5 ± 10.7	<0.0001
Gender (female)	226 (41.9%)	19 (40.42%)	0.8411

The level of significance was set at alpha = 0.05, against which the p values of each test are compared.

RESULTS

The null hypothesis of the study was rejected, as there was a significant statistical difference between the study groups in relation to the stated parameter (ISSTE resolution).

BASELINE AND CLINICAL CHARACTERISTICS

The mean population age was significantly higher in the nonsurvivor group compared to survivors (61.4 ± 11.7 years in Group 1 vs. 70.5 ± 10.7 years in Group 2, p <0.0001) (Table 1). There was no significant difference between the study groups in respect to gender (p = 0.8), the presence of hypertension (p = 0.9), smoking status (p = 0.4), obesity (p = 0.1) and previous myocardial infarction (p = 0.6). However, compared to Group 1, Group 2 presented a significantly higher incidence of diabetes (48.9% vs. 21.5%, p <0.0001), previous stroke (19.1% vs. 6.1%, p = 0.0009), or left ventricular dysfunction (85.0% vs. 49.0%, p <0.0001) (Table 2).

Interestingly, higher rates of hypercholesterolemia and hypertriglyceridemia were recorded in the survivor group (Table 2).

Serum biomarkers characterizing myocardial necrosis and renal function were significantly elevated in the survivor group compared to the nonsurvivors (creatinkinase 3,035 ± 385 mg/dl vs. 2,103 ± 89.6 mg/dl, p = 0.006, creatinine 1.4 ± 0.8 vs. 0.9 ± 0.6, p <0.0001) (Table 3).

The clinical status at presentation was significantly more altered in patients who died during hospitalization compared to the survivor group, as expressed by: (1) the significantly higher incidence of Killip III and IV class in Group 2 (14.8% Killip III and 36.1% Killip IV in Group 2, compared to 2.8% Killip III and 4.6% Killip IV in Group 1, p<0.0001), and (2) the lower values of mean systolic arterial pressure in Group 2 (104.7 ± 31.13 mmHg vs. 129.6 ± 23.93 mmHg, p <0.0001), indicating haemodynamic compromise in this group (Table 4).

ANGIOGRAPHIC ANALYSIS

The most frequent infarct-related artery was the left anterior descending coronary artery (LAD) in both groups, the difference between the groups being not statistically significant.

At the same time, angiographic analysis indicated a significantly higher number of cases with multi-vessel coronary disease among deceased patients (46.8% vs. 26.2%, p = 0.003, OR = 2.47, 95% CI = 1.3–4.5). Post-procedural angiographic analysis indicated a significantly higher incidence of TIMI 3 flow following pPCI in the survivor group, as compared to the nonsurvivors (92.5% vs. 80.8%, p = 0.0054, OR = 2.94, 95% CI = 1.3–6.5), indicating a superior rate of successful reperfusion in the survivor group (Table 5).

TABLE 2. Risk factors and comorbidities in the study population

	Group 1 Survivors n = 539 (91.9%)	Group 2 Deceased n = 47 (8.1%)	OR (95% CI)	p value
Diabetes	116 (21.5%)	23 (48.9%)	3.4 (1.8-6.4)	<0.0001
Hypertension	461 (85.6%)	40 (85.1%)	0.9 (0.4-2.2)	0.913
Smoking	216 (40.1%)	16 (34.0%)	0.7 (0.4-1.4)	0.411
Obesity	211 (39.2%)	13 (27.6%)	0.5 (0.3-1.1)	0.117
History of stroke or TIA	33 (6.1%)	9 (19.1%)	3.6 (1.6-8.1)	0.0009
History of angina pectoris	257 (47.7%)	23 (48.9%)	1.0 (0.5-1.9)	0.878
Previous MI	48 (8.9%)	5(10.6%)	1.2 (0.4-3.2)	0.694
Peripheral artery disease	22 (4.0%)	6 (12.7%)	3.4 (1.3-8.9)	0.0075
Left ventricular failure	264 (49.0%)	40 (85.0%)	5.9 (2.6-13.4)	<0.0001
Hiper-cholesterolemia	243 (45.1%)	8 (17.0%)	0.2 (0.1-0.5)	0.0002
Hiper-triglyceridemia	111 (20.6%)	1 (2.1%)	0.08 (0.01-0.6)	0.002

TABLE 3. Baseline clinical and biological characteristics of the study groups

	Survivors	Deceased	p value
Heart rate (bpm)	80.7 ± 46.9	89.4 ± 25.8	0.001
SBP (mmHg)	129.6 ± 23.9	104.7 ± 31.1	<0.0001
DBP (mmHg)	76.2 ± 13.1	64.3 ± 19.6	<0.0001
Troponin (ng/ml)	3.7 ± 1.05	5.5 ± 2.0	0.4551
CK (mg/dl)	2,103 ± 89.6	3,035 ± 385	0.006
LDH (u/l)	824.9 ± 37.9	1,385 ± 223.2	0.0066
ASAT (u/l)	232.9 ± 9.8	253.5 ± 33.6	0.7135
ALAT (u/l)	87.7 ± 13.4	110.1 ± 21.5	0.0361
Glycemia (mg/dl)	138.9 ± 52.2	201.5 ± 105.6	<0.0001
Hemoglobin (mg/dl)	15.1 ± 8.1	13.9 ± 2.7	0.089
Hematocrit (%)	42.0 ± 16.4	39.5 ± 5.4	0.051
Creatinine (mg/dl)	0.9 ± 0.6	1.4 ± 0.8	<0.0001
Urea (mg/dl)	38.6 ± 17.2	70.1 ± 57.9	<0.0001
WBC count/ ml	11,420 ± 7,101	14,274 ± 4,868	0.0002
Platelet count/ml	225,754 ± 62,403	235,590 ± 82,418	0.7679

TABLE 4. Killip class on admission

Killip class	Survivors	Deceased	p value, OR, 95% CI
I	366 (68.2%)	11 (23.4%)	p <0.0001, OR = 0.14 [0.07–0.28]
II	132 (24.5%)	12 (25.5%)	p = 0.8791, OR = 1.05 [0.53–2.09]
III	15 (2.7%)	7 (14.8%)	p <0.0001, OR = 6.10 [2.35–15.83]
IV	25 (4.6%)	17 (36.1%)	p <0.0001, OR = 11.63 [5.67–23.84]

TABLE 5. Angiographic analysis

	Survivors	Deceased	p value, OR, 95% CI
LAD	257 (47.76%)	28 (55.3%)	p = 0.1, OR = 1.6 [0.87–2.95]
Three vessel disease	141 (26.20%)	22 (46.80%)	p = 0.003 , OR = 2.4 [1.35–4.53]
TIMI 3 flow post pPCI	498 (92.56%)	38 (80.85%)	p = 0.005, OR = 2.94 [1.33–6.53]

TABLE 6. Angiographic analysis

	Survivors	Deceased	p value
ISSTE before pPCI (mm)	11.08 ± 0.29	13.96 ± 1.25	<0.0001
ISSTE after pPCI (mm)	2.93 ± 0.16	7.36 ± 1.12	<0.0001
>50% decrease in ISSTE	26 (55.31%)	451 (83.82%)	<0.0001
<50% decrease in ISSTE	21 (44.68%)	87 (16.17%)	< 0.0001

THE INTEGRATED SCORE OF ST SEGMENT ELEVATION

The ISSTE score calculated at baseline, immediately before the primary percutaneous coronary intervention, was significantly higher in Group 2 compared to Group 1 (13.9 ± 1.2 vs. 11.0 ± 0.2, p = 0.026). At the same time, the ISSTE score calculated at two hours after the coronary intervention was significantly higher for patients in Group 2 (7.36 ± 1.12 vs. 2.9 ± 0.1, p <0.0001) (Figure 1). Analysis of the dynamics of the ISSTE score indicated that patients who survived presented a greater reduction in the ISSTE score following pPCI, compared to those who subsequently died (73.5% reduction in Group 1 compared to 47.2% reduction in Group 2, p <0.0001) (Table 6).

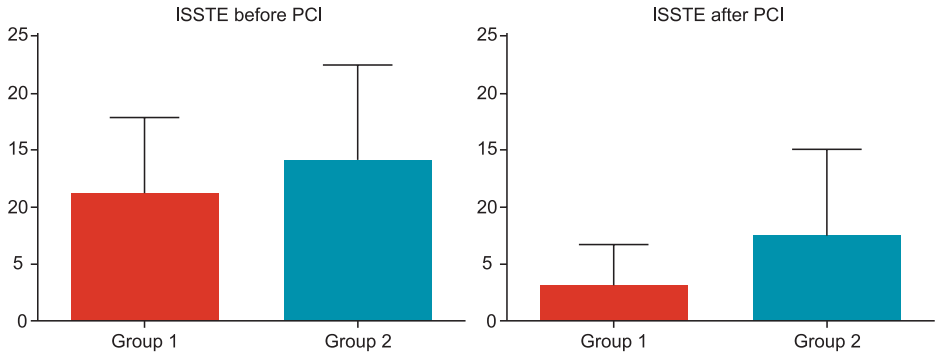

FIGURE 1. ISSTE score before and after revascularization (ISSTE in mm)

STUDY ENDPOINTS

In-hospital mortality

In-hospital mortality was significantly higher in the group of patients with >50% reduction in the ISSTE score. The in-hospital death rate was 5.4% in patients with >50% reduction in the ISSTE score, compared to 19.4% for those who presented less than 50% reduction in the ISSTE score following pPCI (p <0.0001) (Figure 2).

The mean duration of hospitalization was 6.4 days for those who survived, while in the group of patients who died, cardiac arrest occurred on average after 2.3 days following admission and pPCI.

Reperfusion rate

The rate of successful reperfusion, expressed by the reduction in the ISSTE score, was 83.8% in Group 1 compared to 55.3% in Group 2 (p <0.0001), indicating that the absence of an efficient reperfusion after pPCI is associated with a higher mortality in STEMI patients, and could be evaluated using regression of the ISSTE score.

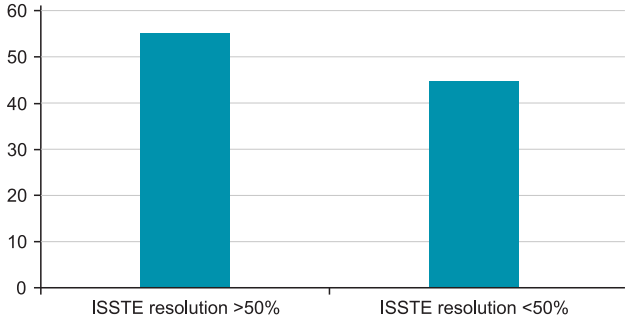

FIGURE 2. Mortality rates according to the ISSTE score decrease after PCI

DISCUSSIONS

STEMI MORTALITY IN THE STUDY POPULATION

Widimsky *et al.* studied the reperfusion therapy for STEMI in 30 European countries, and found that the in-hospital mortality for pPCI-treated MI patients varied between 2.7% and 8%.[1] Similarly, in the present study population, 8.03% of patients died during hospitalization.

Early risk assessment is essential for STEMI patients. Therefore, there is a clear need to develop effective tools for assessing the risk of immediate fatal events in this patient population. This has generated the reevaluation of the prognostic usefulness of ST segment elevation decrease after STEMI.

ECG SCORES FOR PREDICTING MORTALITY IN STEMI PATIENTS

Previous studies have evaluated the predictive ability of early ST segment resolution after thrombolytic therapy. Schröder *et al.*, in a substudy of the International Joint Efficacy Comparison of Thrombolytics (INJECT) trial, divided patients into three groups, based on ST segment resolution (STR) following thrombolytic administration. They defined the groups as (1) complete resolution (≥70 STR), (2) partial resolution (70–30%) and (3) no resolution (<30% STR), and concluded that a complete STR (≥70%) is associated with a lower mortality, while no STR (<30%) predicts a very high early mortality.[5] An analysis derived from Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico (GISSI-2) trial, performed on 7,426 patients, evaluated the correlation between ST segment changes after fibrinolysis for myocardial infarction and the composed endpoint of in-hospital mortality plus congestive heart failure (CHF). In this study, the patients were categorized into two groups, the

ECG cut-off for predicting coronary artery patency being ≥50% decrease in the ST segment elevation, after four hours of alteplase or streptokinase therapy. Their results showed that patients with ≥50% STR after thrombolytic administration, had a lower occurrence of the endpoint than patients with <50% ST segment decrease (16.2% vs. 22.9% respectively).[6] Furthermore, in 2004, McLaughlin *et al*. evaluated the predictive power of various techniques for assessing ST segment resolution, after primary percutaneous coronary intervention performed for MI. Five methods were used to quantify STR, the thirty-day mortality rates being strongly associated with three of the five methods: ΣSTR (total % STR across multiple leads), MaxSTR (% STR in the lead with the highest ST elevation at baseline), MaxSTPost (absolute highest ST elevation after the intervention), and concluded that there was a strong correlation between mortality and ST segment resolution after pPCI.[7]

The present study proposes a method for measuring ST segment elevation, via mapping the ST segment elevation in all leads on the surface ECG. Based on this method, the Integrated Score of ST segment Elevation (ISSTE) is shown to be an effective tool that provides valuable prognostic information for post-MI early mortality, and allows easy stratification of patients into low- and high-risk groups. The ISSTE score was obtained by summing the amplitude of ST segment elevation in all leads, using the standard 12-lead ECG. ISSTE was calculated and then compared for both the pre- and two hours post-revascularization electrocardiograms. In line with previous studies, this method demonstrated that patients with ≥50% decrease in the ISSTE have a lower risk for mortality.

CLINICAL PRESENTATION AND STEMI MORTALITY

A study published in 2009 concluded that after pPCI, female gender is an independent predictor of death during hospitalization.[8] However, in the current study, it was observed that there was a lower number of women in the deceased group (40.42%) than in the survival group (41.92%), though the difference was not statistically significant. An increased glycaemia can increase the mortality risk and negatively influence prognosis in post-MI patients. Capes *et al.* concluded in a meta-analysis that an acute increase in blood glucose concentrations is related to a higher risk of in-hospital death in both diabetic and nondiabetic patients.[9] Also, Hsu PH *et al.* concluded, in a study comparing in-hospital outcome of STEMI patients with and without diabetes, that in-hospital mortality rate is higher for diabetic than nondiabetic patients.[10]

There was a larger number of diabetics among deceased patients (48.93%), whereas only 21.56% of the survivors were diabetics (p <0.0001). The deceased patients also had higher blood glucose levels on admission when compared to survivors.

A study performed on 3,076 patients undergoing PCI for AMI, assessed the influence of the body mass index (BMI) on outcome, and concluded that BMI itself did not affect mortality during the hospital stay.[11] However, another study, performed on 10,534 patients from the German MITRA PLUS Registry, showed that STEMI occur at a younger age in obese individuals, and that obesity cases showed, paradoxically, the lowest in-hospital mortality from all body mass index groups (obese >30 kg/m^2, overweight 25–29.9 kg/m^2, average weight 18.5–24.9 kg/m^2).[12] Furthermore, a study that analyzed the in-hospital prognosis of percutaneous coronary interventions in extremely obese and normal weight patients, found that extreme obesity is an independent factor for assessing in-patient mortality.[13] Das SR *et al.* showed, in a study on 50,149 patients, that morbidly obese patients suffering from STEMI are younger, and have less severe coronary atherosclerotic disease, better systolic function of the left ventricle and higher mortality rates compared to class I obese individuals.[14]

In the present study, there was a lower rate of obesity among the deceased (27.65%) compared to survivors (39.20%), although the difference was not significant (p = 0.1179). Wang W *et al*. studied the correlation between cardiovascular risk factors and death rates in STEMI complicated with ventricular fibrillation, and one of their results revealed a strong correlation connecting smoking and mortality.[15] The results of the present study showed that patients who died during hospitalization were less likely to have been active smokers.

A previous study, which aimed to determine the influence of hypertension on mortality rates after AMI, concluded that hypertension at the time of the acute coronary event is associated with higher in-hospital mortality.[16] In the present study, we found an increased incidence of hypertension in the deceased group, compared to survivors.

In the present study, in the deceased group, there was a higher percentage of patients who had a history of angina pectoris (48.93% vs. 47.76%), and a higher rate of patients who had previously suffered an MI (10.63% vs. 8.92%) when compared to the survivor group, in agreement with previously published results.

When analyzing the effects of prior stroke on in-hospital outcomes in MI patients, Abtahian *et al.* concluded that STEMI patients with previous stroke have an increased

risk of death during hospitalization.[17] In the current study cohort, when analyzing the deceased versus the survivor groups, 19.14% of patients who died had a positive history of stroke in comparison with survivors, where only 6.13% had a previous stroke (p = 0.0009).

A study of early risk stratification in STEMI patients treated with pPCI based on leucocytes count, glycaemia and creatinine on admission showed that higher death rates were noted in cases with increased creatinine (cut-off value of 1.2 mg/dl).[18] In the present study patients who died had higher levels of creatinine compared to patients who survived (1.4 ± 0.8 vs. 0.9 ± 0.6, p <0.0001).

Lipšic *et al*. sought to find a relation between hemoglobin (Hb) levels on admission and thirty-day mortality in MI. Their research, which included 1,841 patients admitted for MI, concluded that lower hemoglobin levels (<10 g/dl) on admission were associated with higher mortality rates.[19] Although in the present study the mean hemoglobin on admission was not lower than 10 g/dl, the deceased patients had a lower Hb level (13.97 ± 2.774) compared to survivors (15.11 ± 8.165) (p = 0.089).

Shiraishi J *et al.* studied the predictive relevance of systolic blood pressure (SBP) on presentation, on the in-hospital prognosis for STEMI patients who underwent pPCI. Their results showed that patients with an SBP of 141.158 mmHg have better outcome, whereas an SBP <105 mmHg is associated with high death rates during hospitalization.[20] In our study, patients who deceased had lower SBP values on admission than survivors (104.7 mmHg vs. 129.6 mmHg, p <0.0001). Furthermore, the deceased patients also recorded lower diastolic blood pressure values upon admission (64.38 mmHg vs. 76.27 mmHg, p <0.0001).

Another result of Shiraishi *et al.* was that Killip class >III on presentation and multi-vessel coronary disease were independent factors in predicting the risk of death during hospital admission.[20] In our results, from the total number of subjects that had deceased, 46.80% presented with three-vessel CAD, whereas, out of the survivors, only 26.20% were diagnosed with multivessel coronary disease. Regarding the Killip class of heart failure, we found that a higher percentage of patients who died had a Killip class IV score (36.17%) compared to patients who survived (4.64%). Killip class III was also better represented in the deceased group with 14.89% compared to 2.78% among patients who survived. Moreover, the majority (68.29%) of the survivors were categorized as Killip class I, compared to only 23.40% in the deceased group.

CONCLUSIONS

The ISSTE score is a useful ECG-derived marker of myocardial damage in STEMI patients. A high ISSTE score is associated with higher mortality, while the regression of ISSTE after pPCI could indicate an adequate reperfusion and decreased mortality in the first days after infarction. Therefore, ISSTE could represent a simple, quick, inexpensive and effective method for categorizing patients into high and low risk of death during hospital stay following an acute myocardial infarction.

CLINICAL IMPLICATIONS

The Integrated Score of ST segment Elevation is a simple electrocardiographic tool, which can be used to stratify patients into low- and high-risk groups, according to the cut-off value of 50% ST segment resolution after revascularization. Risk stratification is essential in the management of STEMI patients, as it optimizes patient triage for appropriate treatment, and improves monitoring during hospitalization and follow-up after discharge. Furthermore, the ISSTE should be used in addition to other risk scores that include clinical, laboratory and angiographic variables, in order to best predict in-hospital events for STEMI patients following revascularization.

CONFLICT OF INTEREST

None declared.

ACKNOWLEDGEMENT

This research was supported by the Cardio Med Medical Center, project no. CAM/2015/RD/17.

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