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SUMMARY OF PHD THESIS

PREDICTIVE FACTORS OF IN-HOSPITAL MORTALITY IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION TREATED BY PRIMARY PCI, IN THE WESTERN REGION OF ROMANIA

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INTRODUCTION

In Romania, cardiovascular diseases account for 63% of all deaths, while in Europe the percentage is 37% (1). Acute myocardial infarction (AMI) is by far the leading cause of death in patients with ischemic heart disease. In our country, ~13,000 people annually suffer from AMI, with mortality rates reaching worrying levels. The risk of death is maximum within the first 2 hours of onset of the disease. According to the data from some studies, 52% of deaths occur before the patient reaches the hospital. The mortality rate drops dramatically after admission: 19% in the first 24 hours and only 8% on the second day. Finally, 21% of deaths occur later, up to 30 days (1).

Studies published over the past 20 years have undoubtedly demonstrated that early coronary reperfusion significantly reduces mortality, reduces the infarct area, and leads to a better preservation of contractile heart function (3). Furthermore, reperfusion significantly reduces the risk of ventricular fibrillation. A prompt intervention in these patients, according to existing resuscitation protocols (basic support and advanced support of life), triple their survival chances and can reduce the risk of developing post-resuscitation neurological sequel by more than 50% (2).

In the last decade, the treatment of patients with myocardial infarction has improved as a result of the efforts made by the Romanian Society of Cardiology to implement progress in the field, in accordance with international guidelines. The reperfusion strategies performed in the first hours after the onset of acute myocardial infarction with ST-segment elevation contributed to a significant reduction in the mortality rate. There was a transition in reperfusion strategy, from fibrinolytic therapy to primary percutaneous coronary interventions (PCI).

In Romania, no predictors of mortality have been established in patients with acute myocardial infarction with ST-segment elevation treated with intervention. This is an important issue, because Romanian patients may have some differences in terms of clinical aspects, coronary risk factors, compared to patients with acute myocardial infarction with ST-segment elevation in other European countries.

In this context, for the diagnosis and treatment of patients with acute myocardial infarction, it is necessary to approach as soon as possible and promptly establish the diagnosis together with possible complications.

Therefore, the aim of our study was to evaluate the prognostic impact of heart rate and systolic blood pressure on admission on mortality in patients with acute myocardial infarction with ST-segment elevation treated by percutaneous coronary interventions.

The three themes covered in the paper are the association between coronary risk factors and acute myocardial infarction treated by acute PCI, the impact of heart

rate and systolic blood pressure on mortality, and last but not least in-hospital and one-year mortality. elderly patients.

The three topics will be briefly presented below, in terms of research purpose, study design, results.

CANADA ACUTE CORONARY SYNDROME SCORE WAS A STRONGER BASELINE PREDICTOR THAN AGE ≥75 YEARS OF IN-HOSPITAL MORTALITY IN ACUTE CORONARY SYNDROME PATIENTS IN WESTERN ROMANIA

The aim of this study was to identify the clinical variables associated with in-hospital mortality in patients with acute coronary syndrome, using a simple risk assessment tool, the new Canadian risk score for patients with ACS.

The study population consists of all consecutive ACS patients admitted to the Cardiology Clinic of Timisoara Clinical Emergency City Hospital from January 2000 to December 2015. The patients with unstable angina and non-ST-segment elevation myocardial infarction formed the non-ST-segment elevation acute coronary syndrome (NSTE-ACS) subgroup, while the patients with ST-segment elevation myocardial infarction (STEMI) were included in the STEMI subgroup.

The study population included 960 ACS patients, 22% being women. The mean age was 68±11 years (range 35–85 years), 22.7% having an age ≥75 years. Of the total ACS cohort, 42.6% presented with STEMI and 57.4% with NSTE-ACS. Comorbid conditions were common.

We observed that STEMI patients tended to be younger, of male sex, with current or recent smoking history, with lower SBP, and higher HR at presentation. The C-ACS score for all ACS patients was 0.62±0.78, being significantly higher in STEMI vs NSTE-ACS patients ($P<0.001$). In-hospital mortality was 11.8% in the study group, significantly higher in the STEMI subgroup (14.9%) than in the NSTE subgroup (9.6%), $P<0.02$. The mortality rate was also significantly higher in patients aged ≥75 years vs those <75 years in the study group (OR =1.71, 95% CI: 1.16–2.54, $P=0.006$) and in the STEMI subgroup (OR =4.25, 95% CI: 2.57–7.01, $P<0.0001$).

We observed a progressive increase in intrasiptical mortality correlated with increased C-SCA risk score in all hospitalized patients with acute coronary syndrome. The predicted mortality was slightly higher than the mortality observed in the hospital in patients with acute coronary syndrome, but the difference was not statistically significant.

The ACS patients who died were more frequently older, females, smokers, with a Killip class >1, and were more likely to have at presentation an SBP <100 mmHg and an HR >100 bpm. The mean C-ACS score was significantly higher among the dead ACS patients (3.02 vs 0.54, $P<0.0001$). The STEMI patients who died were also more likely to be older, hypertensive, smokers, with a Killip class >1, dyslipidemia, and presented more frequently with SBP <100 mmHg and an HR >100 bpm. Their mean C-ACS score was 2.80 vs 0.61 in the STEMI survivors

(P<0.0001). The NSTE-ACS patients who did not survive were more frequent females, with diabetes mellitus, a Killip class >1, and had lower SBP and higher HRs at admission. Their mean C-ACS score was 3.3, comparative to 0.48 in the NSTE-ACS survivors (P<0.0001).

At multivariate logistic regression, we found two independent predictors of in-hospital mortality in the total ACS cohort: the C-ACS score (P<0.0001) and the age ≥75 years (P=0.016). The C-ACS score had the greatest power of discrimination in the whole ACS group, with a C-statistic of 0.94 (95% CI: 0.92–0.95). The C-statistic for age ≥75 years was 0.70 (95% CI: 0.67–0.73).

In the STEMI cohort, multivariate logistic regression also retained two independent predictors of in-hospital mortality: C-ACS score (P<0.0001) and the presence of dyslipidemia (P=0.005). The best discriminative value was observed for C-ACS score, with a C-statistic of 0.92 (95% CI: 0.89–0.94). Dyslipidemia had a C-statistic of 0.59, 95% CI: 0.54–0.63)

In the NSTE-ACS subgroup, multivariate logistic regression identified two independent predictors of in-hospital mortality: C-ACS score (P<0.0001) and female sex (P=0.016). Discriminative power had both the C-ACS score, with a C-statistic of 0.97 (95% CI: 0.95–0.98) and the female sex, with a C-statistic of 0.75 (95% CI: 0.73–0.78).

Our study showed that the C-ACS risk score performed well when used to evaluate the ACS patients using exclusively clinical data at first medical examination. Despite its simplicity, this risk-assessment tool was useful in all types of ACS. Age ≥75 years was associated with in-hospital mortality in the total ACS cohort and in the STEMI subgroup while female sex was associated with in-hospital mortality in the NSTE-ACS subgroup. Future studies are necessary to evaluate prospectively the C-ACS score regarding its impact on ACS therapy and subsequently on hospital mortality. We believe that the C-ACS risk score is satisfactory to guide routine clinical practice and to perform research activities concerning ACS treatment strategies.

PROGNOSTIC IMPACT OF BLOOD PRESSURE AND HEART RATE AT ADMISSION ON IN-HOSPITAL MORTALITY AFTER PRIMARY PERCUTANEOUS INTERVENTION FOR ACUTE MYOCARDIAL INFARCTION WITH ST-SEGMENT ELEVATION IN WESTERN ROMANIA

The present study aims to investigate the prognostic impact of BP and HR at admission on intrahospital prognosis of STEMI patients treated with primary percutaneous coronary intervention (PCI).

Between January and April 2017, 326 patients with STEMI were admitted to the Cardiology Clinic of the Timisoara Institute of Cardio-Vascular Diseases. The hospitalization was done within the first 12 hours of the onset of the symptoms. Among them, 294 patients underwent primary PCI and were included in this study.

Of the 294 patients with STEMI subjected to primary PCI, 218 (74%) were men. The average age was 62±17 years (33–95 years).

According to the SBP at admission, STEMI patients were divided into five groups.

Compared to the other groups, group I patients (with SBP <105 mmHg at admission) were more often elderly (P=0.033), smokers (P=0.026), with a history of old MI (P=0.003), systemic hypertension (P=0.023), diabetes (P=0.041), or chronic kidney disease (P=0.0200). They had more often a HR ≥80 bpm (P=0.028) and a Killip class 3 or 4 at admission (P=0.020). Group V patients, with SBP ≥159 mmHg at admission, were more frequently hypertensive and diabetic.

For patients in group I, the most common lesions responsible for the AMI were located in the right coronary artery, the left coronary artery trunk, or on more than two vessels, and the peak CPK-MB values were significantly higher.

Patients in group I had much higher concentrations of CK-MB and a higher mortality rate in the hospital, compared to patients in group V who had a lower CK-MB value.

It is known that total occlusion of the right coronary artery, which vascularizes mostly the right ventricle, leads to hypotension, which could be observed in patients in our study.

In over 50% of patients with occlusion on the right coronary artery, blood pressure was below 105 mmHg.

During the hospitalization, 18 deaths (6%) occurred, 11 of them having a cardiac cause (3.7%) and the other seven having noncardiac causes (3.3%).

The main cardiac causes of in-hospital death were cardiogenic shock, acute pulmonary edema, myocardial rupture and atrial fibrillation, the most common causes in group I patients.

It is known that stroke is often fatal in elderly patients, however there are other more common causes that lead to the death of a patient with acute myocardial infarction.

As we can see in our study, the appearance of cardiogenic shock and rupture of the free myocardial wall led to the death of patients with myocardial infarction in group I.

The patients in group I (n=60) had an intrahospital mortality rate of 15%, significantly higher than the rest of the groups (P=0.018). Between the other groups, the differences in mortality rates were not significant.

Cardiac deaths occurred significantly more frequently in group I (P=0.032), whereas noncardiac events had a similar distribution in the five groups.

In patients who had SBP <105 mmHg at admission, the RR of death due to any cause was 4.9 (95% CI 1.977–12.205, P=0.006), and the RR of cardiac death was 5.4 (95% CI 1.723–17.249, P=0.003). HR ≥80 bpm is another predictive parameter of the increased risk of death in patients with STEMI.

The multivariate logistic regression analysis selected those variables with independent predictive power for the risk of intrahospital death.

We compared the predictive power of the selected independent variables using the ROC curves, analyzing the area under the curve (AUC).

Regarding the risk of death in post-PCI STEMI patients, the best predictor was SBP ≤105 mmHg (AUC =0.804, 95% CI 0.712–0.896, P<0.0001), followed by diabetes mellitus (AUC =0.697, 95% CI 0.582–0.813, P=0.0013), HR ≥80 bpm (AUC =0.664, 95% CI 0.541–0.747, P=0.0272), and history of hypertension (AUC =0.554, 95% CI 0.439–0.670, P=0.0009).

Significant differences between areas under the ROC curves, which indicate significant differences between predictive capacities, were also observed for diabetes mellitus and history of hypertension (0.143, 95% CI 0.0033–0.283, P=0.044).

In the case of post-PCI STEMI cardiac death risk, the strongest predictor was Killip class ≥3 at admission (AUC =0.896, 95% CI 0.872–0.919, P=0.0429), followed by SBP ≤105 mmHg (AUC =0.791, 95% CI 0.669–0.913, P=0.0057), HR ≥80 bpm (AUC =0.756, 95% CI 0.727–0.785, P=0.0023), and multivascular CAD (AUC =0.648, 95% CI 0.498–0.798, P=0.0015).

Significant differences between the areas under the ROC curves were observed for HR ≥80 bpm versus the Killip class ≥3 (0.140, 95% CI 0.106–0.173, P<0.0001) and for the Killip class ≥3 versus multivessel CAD (0.248, 95% CI 0.0955–0.399, P=0.0014).

Our retrospective study is the first study in Romania addressing the prognostic impact of HR and SBP at admission on STEMI patients undergoing primary PCI. The results show that these easily determinable clinical parameters are independent predictors of intrahospital mortality.

In our study, the mean HR was 75±18 bpm in post-PCI STEMI survivors, 89±15 in the case of in-hospital deaths of all causes (P=0.0423), and 92±12 bpm in the patients with cardiac deaths (P=0.0021).

An even stronger predictor was SBP at admission. It had an average value of 136±24 mmHg for the entire group of STEMI patients. The mean SBP was 139±22 mmHg in survivors and 110±35 mmHg in those who died (P<0.0001). SBP at admission <105 mmHg increased 4.9 times the risk of all-cause death (P=0.0060) and 5.4 times the risk of cardiac death (P=0.0039).

In our study, mortality was significantly higher in group I, which included STEMI patients with SBP <105 mmHg, compared to the other four subsets of SBP values. Patients in group I (n=60), with the highest mortality (15%), were more frequently elderly (≥65 years), with a history of MI and chronic kidney disease. They had admission HR ≥80 bpm, Killip classes ≥3, and high CPK values more often. Angiographic data in these patients revealed more frequently involvement of the left main trunk or multivessel CAD.

The lowest mortality (3.3%) was recorded in group V (SBP ≥159 mmHg), in which STEMI patients were younger, nonsmokers, and more often hypertensive and diabetic. They had lower CPK-MB values, and the culprit lesion was found more frequently on the left anterior descending coronary artery.

In group I, cardiac deaths were twice as common as non-cardiac causes (10% vs 5%, P=0.3), whereas in group V, the two types of deaths had equal frequencies (1, 6%).

In our study, HR ≥80 bpm and SBP <105 mmHg were the only variables that predicted both all-cause and cardiac-related death risk in STEMI patients after primary PCI. Systemic hypertension and diabetes mellitus were independent predictors only for all-cause deaths, while Killip ≥3 class at admission and multivessel CAD were independent predictors for cardiac-related deaths.

Our study suggests that vital signs (HR and SBP) reported on admission of STEMI patients can provide valuable information on the risk of in-hospital death after primary PCI.

IN-HOSPITAL AND 1-YEAR MORTALITY AFTER PRIMARY PCI FOR ACUTE MYOCARDIAL INFARCTION IN ELDERLY PATIENTS, IN WESTERN ROMANIA

Advances in drug treatment and early myocardial revascularization have led in recent years to improved clinical outcomes in patients with acute myocardial infarction.

However, it has been suggested that, compared to younger subjects, elderly patients with acute myocardial infarction are less likely to receive evidence-based treatment, including myocardial revascularization therapy.

In this study, we aimed to fill the gaps in knowledge, by a detailed description of a cohort of 264 patients aged ≥ 65 years as part of the 476 patients treated with primary angioplasty for ACS at the Institute of Cardiovascular Diseases of Timisoara, from 1st January to 31st of December 2018.

In hospital and 1-year mortality of the elderly with ACS was compared with the mortality rates of the patients aged 65 years. With a twice as high in-hospital mortality and three times higher one-year mortality, it is obvious that there is a large potential for improvement of the ACS care in the elderly.

Of the 522 admitted with ACS, 476 were enrolled in the study. The mean age was 67.38 13.4 years (32-95 years). 294 (61,7%) were men. According to the age at admission, AMI patients were divided into two groups: group I (65 years, n=264), and group II (65 years, n=212).

Compared to Group II, the Group I patients were more often women (P 0.0001), less often current smokers (P 0.0001), with a history of systemic hypertension (P=0.01), diabetes (P=0.041), stroke (P =0.02), congestive heart failure (P 0.002), and chronic kidney disease (P=0.01). The values of serum creatinine and brain natriuretic peptide were higher in Group I patients (P 0.0001, respectively P=0.04). The elderly patients presented more often NSTEMI (P=0.003), a higher functional class Killip (P 0.001), atrial fibrillation (P 0.001), 3rd atrioventricular block (P 0.0001), left ventricular ejection fraction 40% (P=0.0002), and left ventricular diastolic dysfunction (P =0.003).

No angiography could be done in 5 (1.9%) of group I patients and 2 (0.09%) patients of group II (P=0.66), because of severe kindney failure. Group II patients had a significantly higher proportion of monovascular coronary disease (P =0.0001), a significantly lower proportion of triple vessel disease (P=0.03), and had a significantly higher rate of interventional revascularization by PCI (79% vs. 65%, (P=0.0008). The rate of coronary artery bypass graft was 2.6% in group II and 2% in group I (P=0.66). Regarding the concomitant medication, diuretics were more often administered in Group I patients (P=0.02).

Total all-cause mortality rate, including in-hospital and 1-year mortality, was 14.3% (n=67). The number of deaths was 50 (18.9%) for the Group I and 17 (8%) for the Group II, P=0.0004.

Due to the fact that the overall mortality is much higher in group I, these patients require prolonged surveillance, as this group of patients also associates other comorbidities. Among the most important, we mention hypertension, COPD, diabetes, stroke, acute renal failure. Due to the association of these comorbidities, the clinical symptoms that may indicate an unfavorable evolution may be masked.

During the hospitalization for AMI, 53 patients (12.3%) died, 39 being from group I (20%), and 14 from group II (6%), P□0.0001. The cardiac causes of death (n=44, 9.2%) were more frequent in group I patients (n=32, 12%), P=0.016, while the noncardiac causes had similar frequencies in the two groups.

As we can see, the main causes of in-hospital mortality are malignant arrhythmias, respectively ventricular fibrillation, and cardiogenic shock.

The relative risk for in-hospital death for Group I patients was 2.5 (95% CI , 1.12 - 5.77), P=0.001,and 0.39 for Group II patients (95% CI 0.17 to 0.88)

The multivariate logistic regression selected two variables as independent predictors for the risk of in-hospital death. These variables were age □ 65 years (P=0.017, 95% CI 0.512 - 0.626) and Killip class at admission (P□0.0001, 95% CI 0.738 - 0.835). When comparing the receiver operating characteristic (ROC) curves for these parameters, the Killip class at admission was a more powerful predictor (AUC=0.786) than age □ 65 years (AUC=0.569), P□ 0.0001.

423 AMI patients were discharged alive (88.8%). Group I patients received at discharge more often oral anticoagulants (P=0.0003) and diuretics (P=0.045). and less often beta-blockers (P=0.04).

During the follow-up period, further 14 patients died, the 1-year mortality is 3.3%. 1-year mortality was slightly higher in group I patients (4.8% vs. 1.5%, P=0.05), with no significant differences among the causes of death.

During the 1-year follow-up period, 22 patients (5.2%) were rehospitalized. The readmission rate was lower in group I patients, but the difference was not significant (P=0.24). The causes of readmissions had similar frequencies in the two groups

The main causes of hospitalization were recurrent myocardial infarction, grade 3 atrioventricular block, congestive heart failure, stroke and hemorrhage.

As we can see, in group I the main cause was congestive heart failure, while group II had several causes: recurrent myocardial infarction, grade 3 atrioventricular block, hemorrhage.

Patients> 65 years of age suffer from a much more severe acute myocardial infarction and a much wider coronary artery disease.

Compared to the group of younger patients, they have a much higher mortality rate. Age> 65 years and Killip classification at the time of admission were indicators of in-hospital mortality.

Due to the fact that there are many diseases in the elderly (ischemic heart disease, hypertension, diabetes, COPD, chronic renal failure), this may cause the clinical picture of acute coronary syndrome to be uncharacteristic.

The focus for the elderly population should be better on better control of hypertension, dyslipidemia and diabetes, while for the young population, in addition to hypertension and diabetes, smoking and obesity should be controlled.

It is very important to use a score to help clinicians evaluate the patient with an acute myocardial infarction in order to get an idea of the possible evolution of the patient's condition.

In our study, the assessment of risk factors revealed that young patients with acute myocardial infarction, compared to elderly patients, were smokers, most of them male.

There were no significant differences between the two age groups in the presence of hypertension, diabetes and hypercholesterolemia. Elderly patients presented more frequently, Killip class 2-3, had ventricular arrhythmias, ventricular fibrillations and the presence of grade 3 atrio-ventricular block was observed.

Coronary angiography could be performed in most patients, only a small percentage of patients could not perform, because they had chronic renal failure.

Comparing the data from angiography, we can see that patients in group I have a higher percentage for trivascular lesions.

The overall mortality, including mortality in hospital and one year after discharge, was 14.3%. In-hospital mortality was higher in group I patients. Cardiac death was more present in patients> 65 years of age, and noncardiac death was similar in both groups.

GENERAL CONCLUSIONS

As it is known, acute myocardial infarction is one of the main causes of death, so it is very important to identify the risk factors associated with in-hospital mortality.

As we can see, age is a risk factor for the evolution of patients with acute coronary syndrome, because this category of patients is associated with other comorbidities (COPD, acute renal failure, diabetes, etc.).

In the first part of the study, we showed that the use of a risk score to help the attending physician in assessing the patient with acute coronary syndrome, has the advantage of an overview of the evolution of the patient's condition. Consequently, the C-sca risk score correctly assessed patients with acute coronary syndrome. This assessment was also possible using only clinical data from the first medical contact with the patient.

It is known that the main treatment of patients with acute coronary syndrome is coronary revascularization, or percutaneous coronary angioplasty, because it has reduced the rate of mortality and reinfarction in recent decades. This invasive exploration has an important role especially if it can be performed as soon as possible from the onset of clinical symptoms.

After performing the routine medical examination, the main parameters, namely heart rate and systolic blood pressure help to quantify the prognosis of patients with acute myocardial infarction.

In our study, we showed that an HR≥80 bpm in patients with acute myocardial infarction with ST-segment elevation at hospitalization is associated with a higher risk of in-hospital death even in patients with primary PCI.

Also TAS <105mmHg indicated an increased risk of death in patients with acute myocardial infarction, this parameter increased the risk of cardiac death by 5.4 times.

A heart rate lower than 80 bpm, and a systolic blood pressure above 150mmHg, are associated with a better prognosis.

The elderly represent a significantly increased percentage of the population. Old age is a negative prognostic parameter in patients with acute coronary syndrome and causes significant morbidity and mortality.

In the last part of the study we highlighted the fact that patients over the age of 65 suffer from a much more severe acute myocardial infarction.

Most studies have shown that the risk of cardiovascular events in patients with acute myocardial infarction was much higher in the first year after MI, so prolonged surveillance is required in this group of patients.

Compared to the general population, patients who survive an acute myocardial infarction remain at higher risk, especially the elderly, patients with high blood pressure, diabetes or a history of stroke.