

Factors Associated with In-Hospital Mortality in Acute Coronary Syndromes

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Introduction

Acute coronary syndromes continue to be a major healthcare problem worldwide, being the major cause of cardiovascular mortality despite the ongoing developments in the diagnostic and therapeutic management of these patients.

Recent development in the treatment of acute myocardial infarction, from interventional revascularization to therapeutic hypothermia and stem cell therapies have led to a substantial improvement in these patients' outcomes and prognosis.

Cardiac arrest is one of the major complications of acute myocardial infarction, which can take place out of the hospital, or during admission. Out of hospital cardiac arrest (OHCA) can be one of the initial presentations of the acute coronary event, or it may happen during patient transfer to a PCI center. The electrical instability of the heart is at its peak during the 4-6 hours from symptom onset, leading to malignant arrhythmias, including ventricular fibrillation.

Acute myocardial infarction associated with out of hospital cardiac arrest is linked to high mortality rates both during hospitalization, or with long term death rates. Patients that present cardiac arrest during hospital admission (IHCA – In-Hospital Cardiac Arrest) present a significantly higher chance of survival and better prognosis in terms of neurological sequelae due to prompt initiation of resuscitation protocols and ease of access to intensive care measures.

Furthermore, OHCA patients with acute coronary syndromes present a reserved prognosis due to a delayed resuscitation, having higher rates of neurological damage and risk for further complications.

The aim of this study was to identify clinical and angiographical predictors of in-hospital mortality in patient that have presented either out-of-hospital or in-hospital cardiac arrest, as a complication of an acute coronary syndrome.

Material and methods

This was a retrospective study that included 154 deceased patients that were admitted in the hospital with the following diagnoses: STEMI, NSTEMI or acute myocardial infarction presenting in more than 12h from onset, all complicated with either OHCA or IHCA, during 1st of January to 31st of December 2013. The analyzed information includes the patients' medical history, clinical, electrocardiographical, and laboratory data, as well as the required time for intensive care unit admission, of mechanical ventilation, as well as the location where the patients had presented the cardiac arrest and where they died. The angiographical and interventional cardiology data included the location of the culprit lesion, the level of coronary atherosclerotic involvement, the STEMI times, the time from the onset of the cardiac arrest to revascularization).

The study was approved by the Ethical Committee of the Tirgu Mures Emergency Clinical County Hospital and the Ethics Committee of the University of Medicine and Pharmacy of Tirgu Mures.

The study population comprised of 154 patients that were analyzed within three substudies.

First substudy - Factors associated with mortality in patients with OHCA versus IHCA in acute myocardial infarction patients

Second substudy - Mortality predictors in STEMI patients with resuscitated OHCA

Third substudy - Factors associated with increased mortality in patients with acute coronary syndromes

The statistical analysis was performed by using GraphPad Prism 6, GraphPad InStat and JMP 10 (SAS Institute Inc, North Carolina) respectively, and the level of statistical significance was set at an alpha coefficient of 0.05.

Results

The first substudy included 50 patients with OHCA and 104 with IHCA. There were no statistically significant differences between the two groups regarding gender ($p=0.887$), but the IHCA group had a significantly higher number of patients aged over 65 years (79.8% vs. 42%, $p<0.0001$). The patients with OHCA were more likely to die in the ICU department (78% vs. 39.42%, $p<0.0001$), whereas IHCA subjects presented higher mortality during the revascularization procedure (12% vs. 6.73%, $p=0.335$) as well as during admission in the Clinical Cardiology department (4% for OHCA vs. 40.38% for IHCA, $p<0.001$). Cardiogenic shock was higher among OHCA patients (62% vs. 46.15%, $p=0.033$), and in total 10 patients from the total study population required the use of the intra-aortic balloon pump (6% for OHCA vs. 6.73% for IHCA, $p=1.000$). Angiographic results showed that patient IHCA had a higher incidence of multivessel coronary artery disease (28% for OHCA vs. 31.73% for IHCA, $p=0.64$) as well as left main significant stenosis (6.73% for OHCA vs. 21.15% for IHCA, $p=0.007$). Regarding the type of cardiac arrest, OHCA patients presented significantly higher rates of ventricular fibrillation 94.0% vs. 8.56%, $p<0.0001$), whereas IHCA subjects presented a higher number of left ventricular free wall rupture ($p<0.005$).

The second substudy has aimed to compare factors associated with mortality in 22 patients that had deceased and 50 that had survived after OHCA as a complication of acute myocardial infarction. There were no statistically significant differences between the two groups regarding the cardiovascular risk factors (old age – $p<0.06$; hypertension – $p=0.4$; dyslipidemia – $p=0.09$; diabetes – $p=0.2$). Factors associated with higher death rates in patient with OHCA included cardiogenic shock at presentation ($p=0.02$), renal failure ($p=0.004$) and anemia ($p=0.02$). The angiographical results revealed that the presence of multivessel coronary artery disease ($p=0.03$) and an impaired postprocedural TIMI flow <3 ($p=0.03$) were significantly associated with a higher death rate. The time from symptom onset to revascularization and the time from cardiac arrest to revascularization were significantly higher among patients that had deceased during hospitalization ($p=0.004$ and $p=0.002$ respectively). The most significant mortality predictor however, were the need for mechanical ventilation for more than 48h ($p=0.002$) and admission in the ICU for more than 5 days ($p=0.002$).

Third substudy aimed to identify factors associated with the overall mortality during hospitalization, for acute coronary syndrome patients. The results showed that from the 684 patients, 60.3% presented STEMI <12 h from onset of symptoms, 8.3% STEMI >12 h from onset, 17.9% with NSTEMI, and 13.3% with unstable angina respectively. The overall in-hospital mortality rate was 11% ($n=78$). Angiographical risk factors include the presence of multivessel coronary artery disease (56.4% of cases in the deceased population). IMA STEMI presented the culprit lesion at the level of the left anterior descendant artery, which led to higher rates of cardiogenic shock in these patients (44.4% LAD lesions vs. 21.7% non-LAD lesions in cardiogenic shock, $p=0.038$). In NSTEMI subjects, the culprit lesion that was associated with the development of the cardiogenic shock was located in the left main coronary artery (LM lesion – 47.0% vs. non-LM lesion 28.5%, $p=0.046$, in patients with cardiogenic shock). Regarding the hospitalization period in the ICU department, the study found that those that required more than 24h of intensive care unit observation were significantly younger (73.0 ± 8.5 - <24 h of ICU, vs. 64.4 ± 11.2 years of ICU, $p=0.007$).

Discussions and Conclusions

The present study has identified, according to the location in which the cardiac arrest has occurred (OHCA versus IHCA) two independent profiles of risk factors that are associated with an increased mortality rate.

First patient profile, with higher risk of OHCA, includes younger patients, with univascular coronary artery disease, with no myocardial ischemic preconditioning, in which AMI is the first

presentation of the coronary artery disease. The risk factors identified in these patients include the presence of cardiogenic shock, impaired renal function at presentation, the need for a longer admission period in the intensive care unit, and also sepsis as a main complication occurring during hospitalization. One of the modifiable risk factor is the presence of ventricular fibrillation or ventricular tachycardia which are shockable rhythms that allow a faster recovery during resuscitation, thus leading to lower death rates and less neurological damage due to prolonged hypoxia.

The second patient profile, associated with a higher risk of IHCA includes the old age, with extended coronary atherosclerosis and ischemic preconditioning of the myocardium, with a less severe clinical aspect upon presentation, but with several associated an increased number of comorbidities. The risk factors in this patient category includes severe coronary artery disease, left main stenoses, age higher than 65 years, as well as multiple associated pathologies.

Among patients with STEMI and successfully resuscitated OHCA, the present study has identified several independent mortality risk factors including the use of vasopressor agents, the use of intra-aortic balloon pump and anemia. The culprit lesions were identified at the level of the left descending artery, being correlated with a more severe clinical status and higher death rates. Moreover, an increased time frame from the onset of the cardiac arrest to the revascularization, named "arrest-to-balloon time", which is a new nomenclature in the literature, has been proven to be a factor linked to increased death rates, therefore indicating that STEMI networks should be used to decrease this time frame by implementing appropriate logistic measures in the healthcare system.

Among patients with non-ST elevation myocardial infarction, the present thesis has identified several predictive factors for in-hospital mortality that include the increased average age, severe coronary atherosclerotic involvement, and associated comorbidities. Culprit lesions located in the left main and the left anterior descending artery, in association with multivessel coronary artery disease have been correlated to a higher rate of cardiogenic shock, and subsequent higher mortality in these subjects.

All in all, the most important predictor for in-hospital mortality in patients with acute coronary syndromes with OHCA or IHCA, was the intensive care unit admission and the requirement for mechanical ventilation of more than 48 hours, in patients with acute coronary syndromes.