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Predictors Of Mortality In Patients With ST-Segment Elevation Acute Myocardial Infarction And Resuscitated Out-Of-Hospital Cardiac Arrest

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Abstract

Introduction: In patients with out-of-hospital cardiac arrest (OHCA) complicating an ST-segment elevation myocardial infarction (STEMI), the survival depends largely on the restoration of coronary flow in the infarct related artery. The aim of this study was to determine clinical and angiographic predictors of in-hospital mortality in patients with OHCA and STEMI, successfully resuscitated and undergoing primary percutaneous intervention (PCI).

Methods: From January 2013 to July 2015, 78 patients with STEMI presenting OHCA, successfully resuscitated, transferred immediately to the catheterization unit and treated with primary PCI, were analyzed. Clinical, laboratory and angiographic data were compared in 28 non-survivors and 50 survivors.

Results: The clinical baseline characteristics of the study population showed no significant differences between the survivors and non-survivors in respect to age (p=0.06), gender (p=0.8), the presence of hypertension (p=0.4), dyslipidemia (p=0.09) obesity (p=1), smoking status (p=0.2), presence of diabetes (p=0.2), a clinical history of acute myocardial infarction (p=0.7) or stroke (p=0.17). Compared to survivors, the non-survivor group exhibited a significantly higher incidence of cardiogenic shock (50% vs 24%, p=0.02), renal failure (64.3% vs 30.0%, p=0.004) and anaemia (35.7% vs 12.0%, p=0.02). Three-vessel disease was significantly higher in the non-survivor group (42.8% vs. 20.0%, p=0.03), while there was a significantly higher percentage of TIMI 3 flow postPCI in the infarct-related artery in the survivor group (80.% vs. 57.1%, p=0.03). The time from the onset of symptoms to revascularization was significantly higher in patients who died compared to those who survived (387.5 +/- 211.3 minutes vs 300.8 +/- 166.1 minutes, p=0.04), as was the time from the onset of cardiac arrest to revascularization (103.0 +/- 56.34 minutes vs 67.0 +/- 44.4 minutes, p=0.002). Multivariate analysis identified the presence of cardiogenic shock (odds ratio [OR]: 3.17, p=0.02), multivessel disease (OR: 3.0, p=0.03), renal failure (OR: 4.2, p=0.004), anaemia (OR: 4.07, p=0.02), need for mechanical ventilation >48 hours (OR: 8.07, p=0.0002) and a duration of stay in the ICU longer than 5 days (OR: 9.96, p=0.0002) as the most significant independent predictors for mortality in patients with OHCA and STEMI.

Conclusion: In patients surviving an OHCA in the early phase of a myocardial infarction, the presence of cardiogenic shock, renal failure, anaemia or multivessel disease, as well as a longer time from the onset of symptoms or of cardiac arrest to revascularization, are independent predictors of mortality. However, the most powerful predictor of death is the duration of stay in the ICU and the requirement of mechanical ventilation for more than forty-eight hours.

Keywords: cardiac arrest, acute myocardial infarction, mechanical ventilation, cardiogenic shock

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Introduction

Coronary artery disease continues to represent the leading cause of death worldwide and acute myocardial infarction remains one of its most severe forms, being associated with high mortality rates and other complications. In patients with ST-segment elevation myocardial infarction (STEMI), survival is directly correlated with the timely initiation of reperfusion therapy. Proper network organization is crucial in getting the patient to the catheterization unit expeditious. Large data registries indicate a decrease in mortality from 25% to 5%, following efficient initiation of reperfusion therapy in STEMI cases [1]. Landmark trials such as GUSTO (The Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries) [2] or PRAGUE (PRimary Angioplasty in patients transferred from General community hospitals to specialized PTCA Units with or without Emergency thrombolysis) [3] demonstrate that STEMI associated mortality is directly correlated with the time from the onset of symptoms to the initiation of reperfusion therapy, and that a significant improvement in survival can be achieved if the patient arrives in the catheterization unit within twelve hours from the onset of symptoms. However, a significant number of patients present cardiac arrest as the first manifestation of the acute event [4]. Many patients may not be admitted to a hospital immediately after the onset of symptoms, and suffer a cardiac arrest before reaching the hospital. In many cases the cardiac arrest complicating the acute coronary event could have been successfully resuscitated if specialized care is delivered in time. Survival, after the acute event, depends largely on the restoration of the coronary flow in the infarct-related artery [3], following successful resuscitation. Despite progresses in the last years in the logistics related to delivering health care to this complex cases, (including better organization of ambulance services, availability of external defibrillators in highly populated areas or development of STEMI networks), out-of- hospital cardiac arrest (OHCA) continues to be associated with high mortality rates in STEMI patients, especially in severe cases complicated by cardiogenic shock (CS) [4-7].

The aim of this study was to determine clinical and angiographic predictors of in-hospital mortality in successfully resuscitated patients who had had a pre-hospital cardiac arrest as a complication of STEMI, and who underwent primary percutaneous intervention (PCI).

Methods

From January 2013 to July 2015, seventy-eight successfully resuscitated patients with STEMI presenting OHCA, transferred immediately to the catheterization unit and treated with primary PCI, were included in the study. All patients underwent immediate coronary angiography and revascularization of the infarct related artery. Clinical, laboratory and angiographic data (including age, weight, gender, history, risk factors, smoking status, cholesterol values, creatinine values, blood sugar, NYHA class, blood pressure, location of culprit lesion and the presence of multivessel disease) were collected and compared in twenty-eight non-survivors (Group 1) and fifty survivors (Group 2). The following critical time intervals were determined and analyzed in survivors and non-survivors:

1. The time from the onset of symptoms to revascularization (calculated as the time from the onset of symptoms to balloon inflation and stent deployment), representing the ischemic time;
2. The time from the onset of the cardiac arrest to revascularization.
3. The duration of stay in the intensive care unit or coronary care unit.
4. The length of mechanical ventilation.

The study was approved by the ethics committee of both the University of Medicine and Pharmacy of Tirgu Mures, Romania and of the County Clinical Emergency Hospital Tirgu Mures, Romania, and all the investigations were in accordance with the Declaration of Helsinki.

Statistical analysis

The Fisher's exact test (or the Student's t-test for age) was used to compare the baseline characteristics of patients in Group1 and Group 2. Continuous values were expressed as the mean and standard deviation, and statistical significance was determined using the Mann-Whitney test. Logistic regression analysis was used to identify independent predictors of death in the study population. Statistical significance was considered for p values <0.05, and all p values were 2-sided.

All the statistical analyzes were performed using the InStat Graph Pad software.

Results

Baseline and clinical characteristics

The population mean age was 64.8 +/- 11.2 in Group 1 and 68.8 +/- 7.5 in Group 2. The clinical baseline characteristics of the study population showed no significant differences between Groups 1 and 2, with respect to age (p=0.06), gender (p=0.8), the presence of hypertension (p=0.4), dyslipidemia (p=0.09) obesity (p=1), smoking status (p=0.2), presence of diabetes (p=0.2), and clinical history of acute myocardial infarction (p=0.7) or stroke (p=0.17) (table 1).

Mortality in patients with OHCA was positively associated with a worse clinical status at presentation. Compared to Group 2, Group 1 had a significantly higher incidence of cardiogenic shock as a complication of myocardial infarction (50% vs 24%, p=0.02), renal failure (64.3% vs 30.0%, p=0.004) and anaemia (35.7% vs 12.0%, p=0.02) (table 2).

Angiographic analysis

Angiographic analysis indicated the presence of a three-vessel disease to a significantly higher extent in Group 1 (42.8% vs. 20.0%, p=0.03), while the complete restoration of coronary flow, expressed by a TIMI 3 flow post-PCI in the infarct-related artery, was significantly higher in Group 2 (80.% vs 57.1%, p=0.03).

Angiographic analysis of the location of the culprit lesion, indicated that in Group 1, the left anterior descending artery (LAD) or the left main (LM) were the

Table 1. Baseline characteristics of study population

	Group 1 OHCA non-survivors n=28 (35.9%)	Group 2 OHCA survivors n=50 (64.1%)	P value
Age, years	64.8 +/- 11.2	68.8 +/- 7.5	0.06
Gender, male	13 (46.4%)	21 (42.0%)	0.8
Hypertension	13 (46.4%)	18 (36.0%)	0.4
Hyperlipidemia	16 (63.3%)	18 (36.0%)	0.09
Obesity (BMS>25 km/m2)	7 (25.0%)	12 (24.0%)	1
Smoker *	16 (57.1%)	21 (42.0%)	0.2
Diabetes	10 (35.7%)	11 (22.0%)	0.2
History of AMI	6 (21.4%)	9 (18.0%)	0.7
History of stroke	4 (14.3%)	5 (10.0%)	0.7

*past or present

OHCA = out of hospital cardiac arrest

Table 2. Clinical and angiographic characteristics of the study population

	Group 1 OHCA non-survivors n=28 (35.9%)	Group 2 OHCA survivors n=50 (64.1%)	P value
Clinical status at presentation			
Cardiogenic shock	14 (50.0%)	12 (24.0%)	0.02
Anemia	10 (35.7%)	6 (12.0%)	0.02
Renal failure	18 (64.3%)	15 (30.0%)	0.004
Angiographic characteristics			
Three-vessel disease	12 (42.8%)	10 (20.0%)	0.03
TIMI 3 flow in the infarct related artery following PCI	16 (57.1%)	40 (80.0%)	0.03
Condition severity			
Need for mechanical ventilation for >48 hours	15 (53.5%)	6 (12.0%)	0.0002
Stay in the ICU for >5 days	13 (46.4%)	4 (8.0%)	0.0002

OHCA = out of hospital cardiac arrest
ICU – intensive care unit

two most infarct-related arteries (61% vs 36%, p=0.05 for LAD, and 21% vs 4%, p=0.02 for LM, respectively), while in the Group 2 the infarct-related artery was more frequent the circumflex artery (Cx) or the right coronary artery (RCA) (11% vs. 30%, p=0.09 for Cx and 7% vs. 30%, p=0.02 for RCA, respectively) (Figure 1).

Condition severity

Condition severity and the degree of deterioration of haemodynamic status were significantly associated with a higher mortality in patients with OHCA. Both the need for mechanical ventilation for more than 48 hours and the stay in the ICU for more than five days were significantly higher in the Group 1 compared to Group 2 (Table 2).

The duration of stay in the ICU was significantly higher in Group 1 compared to Group 2 (5.9 +/- 6.0 days vs. 1.5 +/- 1.4 days, p<0.0001).

Group 1 patients were transferred to the coronary care unit (CCU), where the average stay was 2.4 +/- 0.8 days, after which they were transferred to the cardiology ward and then discharged (Figure 2).

Only a few patients from the Group 1 were transferred to the CCU, as most of them died in the ICU.

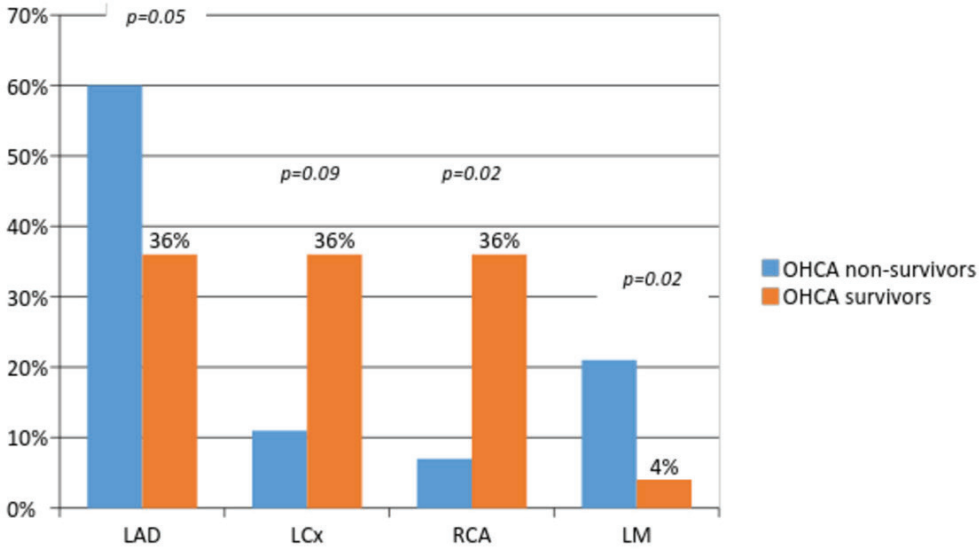

Fig. 1. Location of the culprit lesion (infarct related artery)

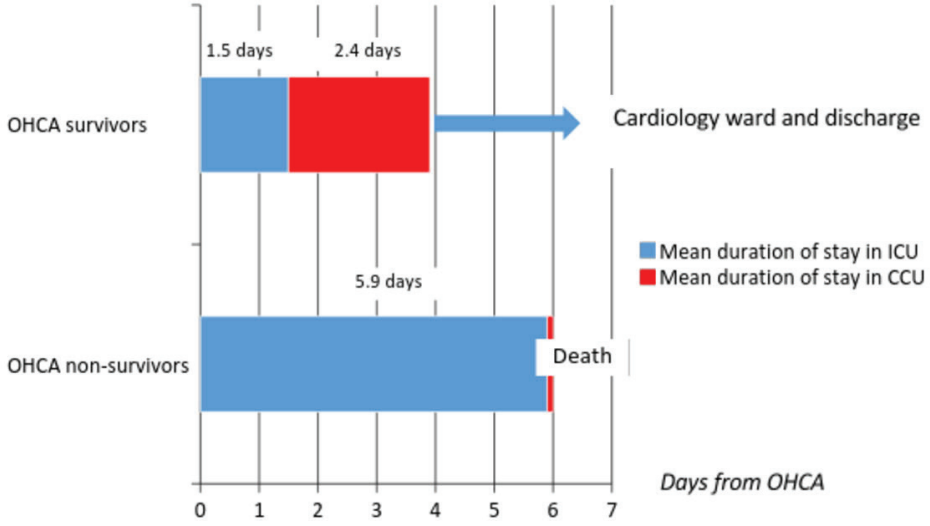

Fig. 2. Duration of stay in intensive care facilities in patients with OHCA

Table 3. Critical time intervals and duration of stay in intensive care facilities in patients with OHCA

	Group 1 OHCA non-survivors n=28 (35.9%)	Group 2 OHCA survivors n=50 (64.1%)	p value
Time from symptoms onset to balloon (minutes)			0.04
Mean +/- SD	387.5 +/- 211.3	300.8 +/- 166.1	
95% confidence interval	305.6 –469.4	253.5- 348.0	
Time from OHCA to balloon (minutes)			0.002
Mean +/- SD	103.0 +/- 56.34	67.0 +/- 44.4	
95% confidence interval	81.2-124.9	54.4-79.6	
Duration of stay in the ICU (days)			<0.0001
Mean +/- SD	5.9 +/- 6.0	1.5 +/- 1.4	
95% confidence interval	3.6- 8.25	1.0 – 1.9	
Duration of stay in the CCU (days)			<0.0001
Mean +/- SD	0.1 +/- 0.4	2.4 +/- 0.8	
95% confidence interval	-0.03 – 0.3	2.1 – 2.6	

OHCA = out of hospital cardiac arrest; ICU = intensive care unit; CCU = coronary care unit

Critical time intervals in patients with OHCA

The time from the onset of symptoms to revascularization was significantly higher in patients who died (group 1) as compared to those who survived (group 2) (387.5 +/- 211.3 minutes vs 300.8 +/- 166.1 minutes, p=0.04), as was the time from the onset of cardiac arrest to revascularization (103.0 +/- 56.34 minutes vs 67.0 +/- 44.4 minutes, p=0.002). (Table 3, Figure 3).

Predictors for mortality in patients with OHCA and STEMI

The most significant independent predictors of mortality in patients with OHCA and STEMI, were the presence of cardiogenic shock (odds ratio [OR]: 3.17, p=0.02), multi-vessel disease (OR: 3.0, p=0.03), renal failure (OR: 4.2, p=0.004), anaemia (OR: 4.07, p=0.02), need for mechanical ventilation >48 hours (OR: 8.07,

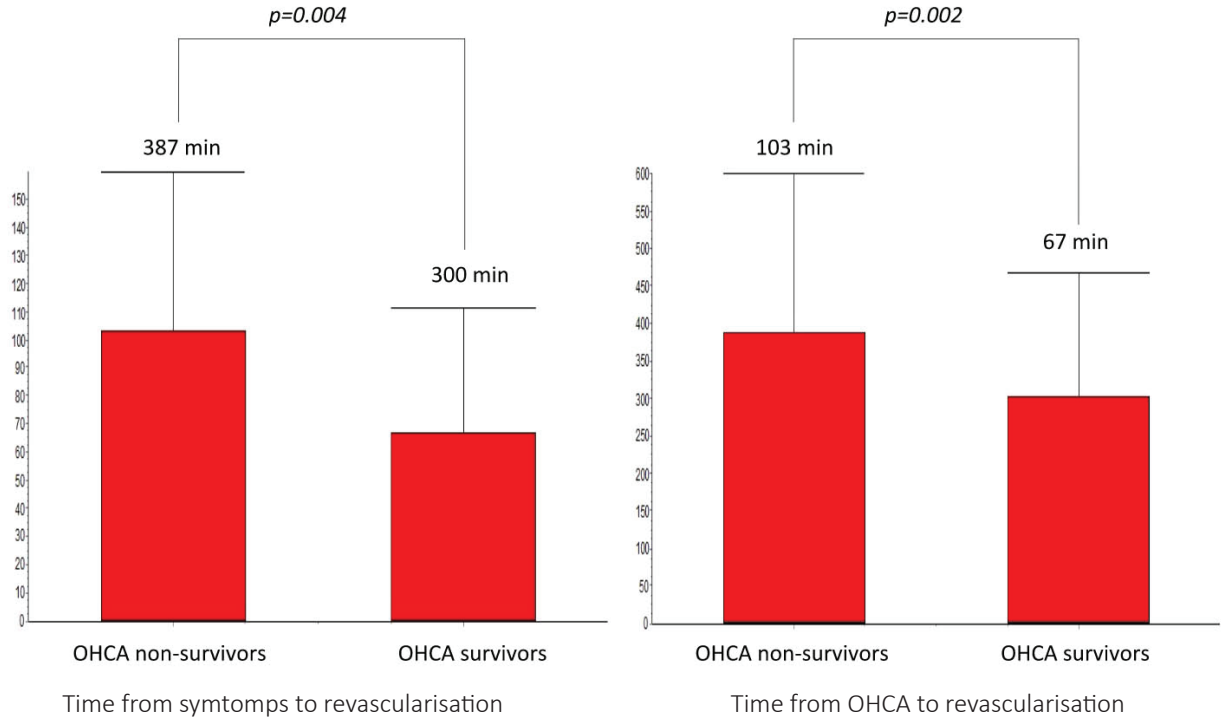

Fig. 3. Critical time intervals in patients with OHCA

p=0.0002) and a duration of stay in the ICU longer than 5 days (OR: 9.96, p=0.0002) (Table 4).

Discussions

The results of the present study show that in patients with successfully resuscitated OHCA in the early phase of STEMI, following an urgent coronary revascularization procedure, the outcomes depend largely on the condition of the coronary circulation, the existing comorbidities and the time intervals from the onset of symptoms or of cardiac arrest to revascularization.

Cardiogenic shock has been shown to represent the most serious complication in STEMI patients [8]. In patients with myocardial infarction and cardiogenic shock, the use of vasopressor agents, age, cardiac arrest, renal failure and counterpulsation balloon insertion, have been proved to represent independent predictors of in-hospital mortality [8,9]. A study reporting on 572 consecutive patients with cardiogenic shock and AMI, indicated that a more severe clinical profile and serious arrhythmia are associated with a higher mortality [9].

In the present study, non-surviving patients exhibited a higher incidence of multi-vessel disease. It is important to note that a recent study reported significantly better outcomes in cases of multivessel revascularization as compared with revascularization of the culprit lesion alone in patients with cardiogenic shock [10]. Another study showed that in STEMI patients with cardiogenic shock and cardiac arrest, multi-vessel revascularization during primary PCI significantly improved the clinical outcome and survival rate [11]. Therefore, taking into consideration the significant correlation between the presence of multi-vessel disease and mortality in patients with OHCA, as shown in the present study, multi-vessel revascularization may be the treatment of choice instead of revascularization of the infarct related artery alone, in these complex cases.

However, in a study on 248 consecutive patients with acute myocardial infarction and cardiogenic shock, OHCA was not an independent predictor of death [12], while in another 5-year follow-up study on 3670 STEMI patients, cardiogenic shock at the initial stage was associated with a higher mortality risk at one year [13]. These studies prove that the high mortality associated with CS and cardiac arrest is mainly caused by the deterioration of the clinical status leading to CS and not by the cardiac arrest, which once resuscitated, is not associated with a significantly higher risk in the long term [14].

Similar to other studies, which indicated the involvement of LAD and LM in OAHC cases [14], the present study recorded a higher incidence of LAD and LM involvement in the non-survivor group. This suggests that culprit lesions located in the LAD or LM, are responsible for more severe myocardial infarctions, these arteries supplying a larger myocardial region. These lesions are more often associated with cardiogenic shock, and their urgent revascularization proves to be life-saving in many clinical conditions [15].

Other studies confirmed that anaemia on admission, and a TIMI 3 flow postPCI in the infarct-related artery, are critical determinants of in-hospital mortality. Similarly, in the present study, anaemia, renal failure, and a lower TIMI flow were powerful predictors of death in patients with OHCA, though the need for mechanical ventilation and a longer duration of stay in the ICU remained the most powerful predictors of death. In accord with other studies, patients who required mechan-

Table 4. Multivariate predictors of death in patients with out of hospital cardiac arrest and ST elevation acute myocardial infarction undergoing primary PCI

	Odds Ratio (95% CI)	p value
Gender (male)	1.19 (0.47- 3.03)	0.8
Age >65 years	0.4 (0.16- 1.16)	0.09
Cardiogenic shock	3.17 (1.18- 8.48)	0.02
Multivessel disease	3.0 (1.08- 8.3)	0.03
Renal failure	4.2 (1.57- 11.21)	0.004
Anemia	4.07 (1.28- 12.8)	0.019
Mechanical ventilation >48 h	8.07 (2.6 – 25.08)	0.0002
Duration of stay in ICU >5 days	9.96 (2.81 – 35.25)	0.0002
TIMI 3 flow post-PCI	0.33 (0.12 – 0.92)	0.03

ical ventilation presented a higher in-hospital mortality (44.3% vs. 1.5%, p<0.0001) [16]. Patients who spent a longer period in the ICU had a lower chance of survival compared to patients who were transferred to a coronary care unit within fort-eight hours. The duration of stay in the ICU was significantly higher in non-survivors, who spent a longer period intubated and developed specific complications such as sepsis. Once in the CCU, the duration of stay was relatively low, patients being transferred to the cardiology ward within two and a half days.

The time between the onset of symptoms and revascularization was shown to be directly correlated with mortality in STEMI population and corroborates the correlation between the respective time and mortality in OHCA patients, detailed in the current study. Different time intervals have been suggested as being associated with mortality in STEMI population, including the first contact with balloon time for PCI, first contact to needle time in case of thrombolysis, or ischemic time, i.e., from the onset of symptoms to the opening of the coronary artery.

According to authors`s knowledge, this is the first study to report a correlation between the arrest-to-balloon time, proving that a longer arrest-to-balloon time may be associated with a higher mortality. Therefore, STEMI networks should take steps to reduce this critical period by employing appropriate logistic measures.

Conclusions

The present study demonstrates that in patients surviving an OHCA in the early phase of a myocardial infarction, the presence of cardiogenic shock, renal failure, anaemia or multi-vessel disease, as well as a longer time from the onset of symptoms or of cardiac arrest to revascularization, are independent predictors of mortality. These data underline the need for a proper network organization in order to reduce the time intervals from the onset of cardiac arrest to revascularization. However, the most powerful predictor of death is the duration of stay in the ICU and the need for mechanical ventilation for more than 48 hours. Assessment of all these data could play a considerable role in risk stratification in OHCA patients with AMI, and may help to identify subsets of patients at increased risk for death following resuscitated cardiac arrest in the prehospital phase.

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