

## ORIGINAL RESEARCH



# Myocardial infarction with cardiogenic shock---the experience of a primary PCI centre from North-East Romania

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## Abstract

**Objectives:** To evaluate the severity of acute myocardial infarction (AMI) complicated with cardiogenic shock (CS), by comparison with inferior and right ventricular AMI, which is also considered a severe form of myocardial infarction.

**Methods:** In an observational study, from 774 patients with STEMI hospitalized in our Cardiology Institute, over one year and a half, only 120 patients met the inclusion and exclusion criteria (60 patients with CS and 60 patients with right ventricular AMI). Data collected included age, sex, vital signs, oxygen saturation, respiratory rate, left ventricular ejection fraction, right ventricular dysfunction, complications during hospitalization and coronarography results.

**Results:** Patients with CS had a more severe systolic dysfunction (median ejection fraction  $22.72 \pm 12.30\%$  vs.  $41.93 \pm 10.50\%$ ,  $P < 0.0001$ ). Single-vessel disease was the most common in both groups, left anterior descending artery being the culprit artery in most patients with cardiogenic shock, 25% of them having residual lesions with a severity  $>75\%$ . Using a multivariate analysis, we observed that for patients with CS, delayed coronary angiography evaluation, as well as the presence of severe triple-vessel disease, were associated with a higher risk of death. In-hospital mortality ( $53.33\%$  vs.  $8.33\%$ ,  $P < 0.0001$ ) and ventricular arrhythmia were significantly higher in patients with CS ( $48.3\%$  vs.  $11.3\%$ ,  $P < 0.0001$ ).

**Conclusions:** Our study suggests that patients with AMI and CS can be considered the most severe form of myocardial infarction and should, therefore, benefit of prompt and appropriate treatment, to improve the outcome.

## Keywords

Cardiogenic shock; Ischaemic heart disease; Mortality; Right ventricular myocardial infarction

## 1. Introduction

Cardiogenic shock (CS) is a major challenge in acute cardiovascular care [1, 2], being one of the important causes of death worldwide [3, 4]. CS complicates 5% to 10% of cases of acute myocardial infarction (AMI) [1, 4–8]. Recently, the Society of Cardiovascular Angiography and Interventions (SCAI) has proposed a new classification of cardiogenic shock. They divided patients into five subgroups: patients at risk of developing CS (A), patients with beginning CS (B), classic CS (C), deteriorating patients (D) or patients presenting in extremis (E) [9]. In a recent study, Schrage *et al.* [10] applied this classification in a broad real-world cohort of patients with cardiogenic shock and demonstrated that higher SCAI classification was significantly associated with lower 30-day survival.

Right ventricular myocardial infarction (RVMI) complicates one third to one half of patients with inferior myocardial infarction

[11, 12], less than 10% of patients with anterior myocardial infarction, though isolated RVMI is rare ( $<3\%$  of all cases of fatal infarction) [13–17]. The short-term prognosis of RVMI is reserved due to hemodynamic and electrophysiological complications [18], and timely identification and treatment of these patients is very important for reducing mortality [19, 20].

The present study aimed to investigate the severity of acute myocardial infarction with cardiogenic shock in the contemporary primary percutaneous coronary intervention (PCI) era. We also evaluated whether the presence of an old myocardial infarction, ventricular arrhythmia, the interval from the onset of symptoms to coronary angiography or the number and severity of coronary lesions, are associated with a higher risk of death in patients with cardiogenic shock.

## 2. Methods

Data acquisition and analysis was performed in compliance with protocols approved by the Ethical Committee of the Cardiovascular Diseases Institute “Prof. Dr. George I. M. Georgescu”, Iasi, Romania (ethical approval number 197/27.12.2017). Written informed consent was obtained from all participants included in the study. The research is in accordance with the Helsinki Declaration of 1975, as revised in 2010.

### 2.1 Study population

We included patients with acute myocardial infarction with ST-segment elevation admitted to the Cardiology Clinic of Cardiovascular Diseases Institute “Prof. Dr. George I.M. Georgescu”, Iasi, Romania, between January 1, 2018 and June 30, 2019. During the study period, 774 patients diagnosed with STEMI were hospitalized. We manually reviewed all the digital case files of these patients, and only 123 patients met the inclusion and exclusion criteria. Patients were then stratified in two groups: the first group included patients with acute inferior myocardial infarction and RVMI, without shock signs (60 patients) and the second included patients with acute myocardial infarction and cardiogenic shock (63 patients). Because three of the patients in the second group died within the first 30 minutes of admission, and we did not have sufficient paraclinical investigations available, we excluded these patients from the study. Each participant was examined according to good clinical practice guidelines.

### 2.2 Data collection

Data collected included basic demographic information: age, gender, body mass index (BMI) calculated by weight in kilograms divided by height in square metres; characteristics of chest pain and associated symptoms; cardiac history and risk factors including smoking status, hypertension, dyslipidemia and diabetes mellitus; laboratory parameters. The shock was defined by the presence of systolic blood pressure <90 mmHg with appropriate fluid resuscitation with clinical and laboratory evidence of end-organ damage (cold extremities, oliguria, altered mental status, narrow pulse pressure, metabolic acidosis, elevated serum lactate, elevated serum creatinine) [21].

Electrocardiographic, echocardiographic and angiographic data were also collected. Considering that the echocardiographic evaluation was performed in emergency conditions, we evaluated only the most important parameters. Coronary artery disease was defined as a 50% reduction in the internal diameter of the left anterior descending artery, right or circumflex coronary arteries, or their primary branches. The extension of coronary artery disease was classified according to the standard method into uniconary, biconary and triconary lesions [22]. The datasets used and analysed during the current study are available from the corresponding author on a reasonable request.

## 2.3 Statistics

Statistical analysis was performed using the Statistical Package for the Social Sciences (version 26.0 IBM SPSS). Data were labelled as nominal or quantitative variables. Continuous variables are expressed as the means with the standard deviation, whereas categorical variables are expressed as the numbers and percentages. The independent *t*-test or one-way ANOVA and Chi-square test (categorized variables between the groups) were used for the analysis of general characteristics. All statistical tests were two-sided, and a *P*-value of < 0.05 was considered statistically significant.

## 3. Results

### 3.1 Baseline characteristics

Over one-and-a-half-year study period, a total of 120 patients were included in this study. Of these patients, 60 patients (50%) were stratified as acute inferior myocardial infarction with RVMI, and 60 patients (50%) were stratified as acute myocardial infarction with cardiogenic shock. Patients included in the study were between 32 and 86 years, and the global median age was  $66.86 \pm 11.15$  years. Most of the patients included in the study were male, a higher percentage being found in patients with CS (68.3% vs. 60%,  $\chi^2 = 0.906$ ;  $P = 0.341$ ).

Another important aspect was the evaluation of the presence of cardiovascular risk factors. Diabetes mellitus and obesity were more frequent in patients with STEMI and cardiogenic shock (63.3% vs. 33.3%,  $\chi^2 = 10.81$ ;  $P = 0.001$  in case of diabetes; 63.3% vs. 30.1%,  $\chi^2 = 14.41$ ;  $P = 0.001$  in case of obesity). Also, more than half of the patients with RVMI had a chronic heart failure (53.3% vs. 26.7%,  $\chi^2 = 18.91$ ;  $P = 0.001$ ).

### 3.2 Clinical exam

The most frequent symptom of addressing patients at the hospital was the presence of angina, which was found in 98.3% of patients with RVMI, compared to 73.3% of patients with CS ( $P < 0.0001$ ). The other symptoms, in order of their frequency, were syncope and dyspnoea, both of them being more common in patients with inferior and RVMI. It should be noted that none of the patients included in the study had palpitations.

Monitoring the blood pressure values at admission, we observed a difference of about 33 mmHg in systolic blood pressure, higher in patients with RVMI, with a *P*-value < 0.0001. A statistically significant difference was also observed in cardiac frequency, patients with cardiogenic shock having a heart rate with 24 beats/minute higher than those with RVMI (Table 1).

### 3.3 Paraclinical tests

Laboratory analyses showed higher values of cardiac enzymes in patients with cardiogenic shock, the median difference between the two groups being more than 100 U/L for creatine kinase MB (CK-MB), more than 300 U/L for aspartate transaminase (AST) and more than 1000 U/L for lactate dehydrogenase (LDH), with a *P*-value < 0.0001 for all of these parameters.

Most of the patients with inferior myocardial infarction and RVMI had a mild or moderate systolic dysfunction, the median

**TABLE 1. Baseline characteristics of patients included in the study.**

	Inferior STEMI with RVMI (N = 60)	STEMI with cardiogenic shock (N = 60)	P value
Demographics			
Median age (years)	64.05 ± 11.73	69.68 ± 10.58	-
Male	60.0%	68.3%	0.341
Urban area	63.3%	60.0%	0.707
Cardiovascular risk factors			
Diabetes mellitus	33.3%	63.3%	<b>0.001</b>
Obesity	30.1%	63.3%	<b>0.001</b>
Arterial hypertension	83.3%	73.3%	0.094
Smoking	48.3%	26.7%	0.014
Chronic heart failure	53.3%	26.7%	0.001
Symptoms at admission			
Angina	98.3%	73.3%	< <b>0.0001</b>
Syncope	11.7%	1.7%	<b>0.028</b>
Dyspnea	10.0%	8.3%	0.752
Hemodynamics			
Median SBP (mmHg)	138.77 ± 28.83	105.77 ± 27.08	< <b>0.0001</b>
Median DBP (mmHg)	85.57 ± 17.38	72.78 ± 18.35	<b>0.023</b>
Median HR (bpm)	72.78 ± 18.35	96.88 ± 27.90	< <b>0.0001</b>

Abbreviations: DBP, diastolic blood pressure; HR, heart rate; RVMI, right ventricular myocardial infarction; SBP, systolic blood pressure; STEMI, myocardial infarction with ST-segment elevation.

ejection fraction for these patients being  $41.93 \pm 10.50\%$ , compared with a moderate and severe systolic dysfunction in patients with CS, who had a median ejection fraction of  $22.72 \pm 12.30\%$  ( $P < 0.0001$ ) (Table 2).

Assessing the interval from the onset of symptoms to coronary angiography, we observed that almost half of the patients with cardiogenic shock (46.7%) were evaluated by coronary angiography within the first two hours after the onset of symptoms. In patients with RVMI, coronary angiography was performed, in most of the cases, between 2 and 6 hours after the onset of symptoms ( $P = 0.673$ ). In both groups, the single-vessel disease was the most common (45% vs. 53.3%,  $P = 0.187$ ), followed by two-vessel disease in patients with RVMI (36.7%) and triple-vessel disease in those with CS (25%). In patients with cardiogenic shock, the culprit artery was the left anterior descending, in most of the cases (38.3%), followed by the circumflex and right coronary artery. Assessment of the severity of residual coronary lesions showed that most of the patients had insignificant ( $<50$ ) residual coronary lesions (75% vs. 41.7%,  $\chi^2 = 13.74$ ;  $P = 0.001$ ), only 10% of patients with right ventricular myocardial infarction having residual lesions with a severity  $>75\%$ , compared with 25% of patients with cardiogenic shock.

### 3.4 Outcome

The median period of hospitalization was  $7.10 \pm 7.34$  days for patients with RVMI and  $6.30 \pm 9.31$  days for patients with CS ( $P = 0.001$ ). During hospitalization, mortality was higher in patients with CS (53.33% vs. 8.33%,  $P < 0.0001$ ).

Ventricular arrhythmia was more common in patients with CS (48.3% vs. 11.3%,  $P < 0.0001$ ), whereas total atrioventricular block appeared mainly in patients with RVMI (18.3% vs. 11.7%,  $P = 0.306$ ). None of the patients with RVMI had right or left bundle branch block. On the contrary, the left and right bundle branch block appeared with equal frequency in patients with cardiogenic shock (16.7%).

In a one-way multivariate analysis of variance, we evaluated whether there are any relationships between death, as an independent variable, and the presence of an old myocardial infarction, the presence of ventricular arrhythmia, the interval from the onset of symptoms to coronary angiography and the number and severity of coronary lesions in patients with CS. Death appeared to be associated with the number ( $P = 0.043$ ) and severity of coronary lesions ( $P = 0.048$ ), and also with the time from the onset of symptoms to coronary angiography (0.025) (Table 3).

Therefore, from our study, it appears that for patients with acute myocardial infarction and cardiogenic shock, delayed coronary angiography evaluation as well as the presence of severe triple-vessel disease, are associated with a higher risk of death.

## 4. Discussion

In this clinical study, we investigated the severity of AMI complicated with CS, by comparison with inferior and RVMI, and we observed some novel findings. First, the mortality (53.33% vs. 8.33%,  $P < 0.0001$ ) and ventricular arrhythmia (48.3% vs. 11.3%,  $P < 0.0001$ ) were significantly higher in

**TABLE 2. Paraclinical tests of patients included in the study.**

	Inferior STEMI with RVMI (N = 60)	STEMI with cardiogenic shock (N = 60)	P value
Laboratory (median values)			
CK-MB (U/L)	101.03 ± 84.50	207.55 ± 118.75	< <b>0.0001</b>
AST (U/L)	110.65 ± 99.64	428.65 ± 214.98	< <b>0.0001</b>
LDH (U/L)	203.92 ± 90.68	1607.40 ± 135.37	< <b>0.0001</b>
Total cholesterol (mg/dL)	203.82 ± 54.45	162.15 ± 50.62	< <b>0.0001</b>
LDLc (mg/dL)	135.48 ± 55.25	101.68 ± 41.05	< <b>0.0001</b>
Triglycerides (mg/dL)	146.90 ± 67.50	130.60 ± 84.16	0.079
Fasting blood glucose (mg/dL)	146.37 ± 79.33	207.62 ± 85.69	< <b>0.0001</b>
Hemoglobin (g%)	13.72 ± 1.93	12.92 ± 2.51	0.053
Echocardiography (median values)			
Volumetric LVEF (%)	41.93 ± 10.50	22.72 ± 12.30	< <b>0.0001</b>
TAPSE (mm)	17.38 ± 5.46	16.58 ± 9.82	0.201
LVEDD (mm)	49.50 ± 7.59	50.75 ± 7.92	0.744
LVESD (mm)	36.53 ± 7.27	41.97 ± 8.10	< <b>0.0001</b>
LVEDV (mL)	126.60 ± 35.66	138.37 ± 34.54	0.044
LVESV (mL)	74.75 ± 27.82	102.40 ± 34.12	< <b>0.0001</b>
LAVI (mL/m <sup>2</sup> )	31.05 ± 5.12	39.40 ± 4.19	< <b>0.0001</b>
Coronarography			
PTCA LAD	8.3%	38.3%	< <b>0.0001</b>
PTCA RCA	85%	6.7%	< <b>0.0001</b>
PTCA LCX	3.3%	15%	< <b>0.0001</b>
The severity of residual coronary lesions			
<50%	75%	41.7%	<b>0.001</b>
50–75%	15%	33.3%	<b>0.001</b>
>75%	10%	25%	<b>0.001</b>

Abbreviations: AST, aspartate aminotransferase; CK-MB, creatine-kinase-MB; LAD, left anterior descending artery; LAVI, left atrial volume index; LCX, left circumflex artery; LDLc, low-density lipoproteins cholesterol; LHD, lactate dehydrogenase; LVEDD, left ventricular end-diastolic diameter; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; LVESV, left ventricular end-systolic volume; PTCA, percutaneous transluminal coronary angioplasty; RCA, right coronary artery; RVMI, right ventricular myocardial infarction; STEMI, myocardial infarction with ST-segment elevation; TAPSE, tricuspid annular plane systolic excursion.

**TABLE 3. Results of one-way multivariate analysis of variance for death, as an independent variable.**

	F <sup>a</sup>	Partial Eta Squared <sup>b</sup>	P value
Old myocardial infarction	0.541	0.009	0.456
Ventricular arrhythmia	0.010	0.001	0.368
The interval from the onset of symptoms to coronary angiography	1.321	0.022	<b>0.025</b>
Number of coronary lesions	1.850	0.032	<b>0.043</b>
Severity of coronary lesions	0.791	0.037	<b>0.048</b>

<sup>a</sup> F-statistics for Wilks' lambda.

<sup>b</sup> Partial Eta Squared, a standard measure of effect size.

patients with CS, whereas atrioventricular blocks were more common in patients with RVMI. Second, in order of their frequency, angina, syncope and dyspnoea, were more common in patients with RVMI. Third, we observed statistically significant differences in terms of left ventricular ejection fraction

values, patients with CS having a moderate to severe systolic dysfunction ( $P < 0.0001$ ). Fourth, in both groups, the single-vessel disease was the most common, left anterior descending artery being the culprit artery in most of the patients with CS, 25% of them having residual lesions with a severity >75%.

Fifth, diabetes mellitus and obesity were more frequent in patients with STEMI and CS ( $P = 0.001$ ). Also, it appears that for patients with CS, delayed coronary angiography evaluation as well as the presence of severe triple-vessel disease, are significantly associated with a higher risk of death.

The incidence of cardiogenic shock has increased in recent years [9, 23–25], being higher in women and patients aged >75 years [2, 26]. In our study, we observed that most of the patients with CS were male (68.3%), and the patients were younger than those reported in the literature, the median age being  $69.68 \pm 10.58$  years (limits 38–86 years).

Usually, patients with CS present with signs of pulmonary congestion and cold extremities, secondary to a reduced cardiac index, increased systemic vascular resistance and increased pulmonary capillary wedge pressure [27]. Our findings showed a statistically significant difference ( $P < 0.0001$ ) of about 33 mmHg in systolic blood pressure, lower in patients with CS and also for cardiac frequency, higher on average by 24 beats/minute in patients with CS. Instead, only 8.3% of patients with cardiogenic shock had dyspnoea, 18.3% presented cool extremities, and none of them had palpitations.

Echocardiography is an essential investigation in patients with CS, but it should not delay cardiac catheterization. It is used especially for the assessment of ventricular function and also to evaluate the possible MI-related mechanical complication precipitating CS. Evaluation of left ventricular ejection fraction in our study pointed out that patients with CS had a moderate to severe systolic dysfunction, with a median ejection fraction of  $22.72 \pm 12.30\%$  ( $P < 0.0001$ ). Instead, no statistically significant difference was observed in terms of the systolic function of the right ventricle, assessed through TAPSE ( $P = 0.201$ ). It is known that TAPSE is an echocardiographic measurement of right ventricular function and has prognostic implications in the context of AMI. In a recent study, Alhamshari *et al.* [16] found that subjects with better RV function as measured by TAPSE at the time of AMI, were less likely to develop new-onset heart failure after two years follow up and obese patients were less likely to develop new-onset heart failure after AMI.

About 40% to 60% of patients with AMI have multivessel disease and this proportion approaches 80% in patients with CS [28, 29]. We observed that 53.3% of patients with CS had single-vessel disease and 25% triple-vessel disease.

The SYNTAX (SYNergy between PCI with TAXUS and Cardiac Surgery) score, an angiographic grading system that evaluates the complexity of coronary artery disease in patients with left main or multivessel disease, has recently demonstrated its prognostic value in patients with infarct-related cardiogenic shock. The SYNTAX score has been found to be strongly associated with 30 days and 1-year all-cause death; all-cause death or renal replacement therapy; and all-cause death, MI, or stroke. Thus, the choice of coronary revascularization strategy in this setting should not depend on the complexity of coronary artery disease, and a culprit lesion-only percutaneous coronary intervention should remain the preferred strategy [30].

In the last years, the in-hospital mortality has improved [1, 9, 11], but the 6 to 12-month mortality in patients with CS has remained unchanged at about 50% over the last two decades

[1, 9, 24]. In our study, we also observed a higher mortality rate in patients with CS (53.33% vs. 8.33%,  $P < 0.0001$ ).

Using one-way multivariate analysis of variance, from our study it appears that for patients with acute myocardial infarction and cardiogenic shock, delayed coronary angiography evaluation as well as the presence of severe triple-vessel disease, are associated with a higher risk of death. On the other hand, the presence of an old myocardial infarction or ventricular arrhythmia was not associated with a higher risk of death. In a subgroup analysis of the SHOCK trial, it was also observed that early revascularization approach had been associated with lower short- (54.5% vs. 72.1%) and medium-term (60.4% vs. 80.1%) mortality [27].

Many observational studies have shown the importance of high-sensitivity troponin T (hs-TnT) and red cell distribution width as predictors of cardiogenic shock [31]. It has also been described that hs-Troponin T values measured immediately after surgery is an independent predictor of postoperative cardiogenic shock requiring mechanical circulatory support [32].

Acute kidney injury is one of the common complications of cardiogenic shock, which leads to the appearance of cardiorenal syndrome. The diagnosis of acute kidney injury is made by at least one of the following criteria: increase in serum creatinine  $\geq 0.3$  mg/dL within 48 hours; increase in basal serum creatinine by  $\geq 1.5$  times within the previous 7 days; urine volume  $< 0.5$  mL/kg/h for 6 hours. Regarding the possible strategies to improve the outcome of patients with cardiogenic shock and acute kidney injury, Ghionzoli and coworkers mentioned that patients' and emergency medical system's delays should be as reduced as possible, because the longer they persist, the higher is the likelihood of developing irreversible organ damages and to require mechanical support devices [33].

Another important parameter with significant prognostic implication among patients with CS undergoing primary percutaneous coronary intervention is Thrombolysis In Myocardial Infarction (TIMI) flow. Mehta and coworkers demonstrated that post-procedural TIMI flow grades 0 to 2 in the infarct-related artery after primary percutaneous coronary intervention for STEMI among patients with cardiogenic shock is associated with higher mortality [34]. Unfortunately, in our study we didn't succeed to evaluate these parameters in all the patients, which is why we could not include them in our statistical analysis.

There are some limitations of the current study that should be acknowledged. First of all, this is a retrospective study, and many inherent biases could influence our results. However, findings from our study provided insight into the baseline characteristics and in-hospital outcomes of patients with acute myocardial infarction and cardiogenic shock, compared to patients with acute inferior myocardial infarction and RVMI. Second, although we analysed 774 patients with AMI, hospitalized for one year and a half in our clinic, the final number of patients included in the study is reduced, considering also the reduced incidence of CS. Third, we didn't succeed to evaluate some important parameters with clinical significance in patients with CS, such as high-sensitivity troponin T, red cell distribution width values, acute kidney injury or TIMI flow. Also, we only evaluated the in-hospital outcomes, and

future studies are needed to evaluate the long-term outcomes of patients with AMI and cardiogenic shock.

Despite these limitations, this study is the first, to our knowledge, to highlight that acute myocardial infarction with cardiogenic shock is a severe form of AMI, considering the severity of left ventricular systolic dysfunction, the severity of the coronary lesions and ventricular arrhythmia, and also the higher rate of deaths during hospitalization.

## 5. Conclusions

Our main finding is that patients with acute myocardial infarction and CS have a more severe left ventricular systolic dysfunction, more frequent severe coronary lesions and ventricular arrhythmia, and also a higher rate of deaths during hospitalization. These patients should, therefore, benefit of prompt and appropriate treatment, to improve the short- and long-term outcome.

## AUTHOR CONTRIBUTIONS

LA contributed to the study conception and design. LA, RS and CS performed data collection and analysis. The first draft of the manuscript was written by Larisa Anghel and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Data acquisition and analysis was performed in compliance with protocols approved by the Ethical Committee of the Cardiovascular Diseases Institute “Prof. Dr. George I. M. Georgescu”, Iasi, Romania (ethical approval number 197/27.12.2017). Written informed consent was obtained from all participants included in the study. The research is in accordance with the Helsinki Declaration of 1975, as revised in 2010.

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## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this article. Larisa Anghel, Radu Sascău, and Cristian Stătescu are co-Guest Editors of this journal.

## DATA AVAILABILITY

The data used to support the findings of this study are available from the corresponding author upon request.

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