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Original Research Article

Natural history and risk factors of long-term mortality in acute coronary syndrome patients with cardiogenic shock

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ABSTRACT

Purpose: Cardiogenic shock (CS) is a severe complication of acute coronary syndromes (ACS). Intra-aortic balloon pump (IABP) is considered important mechanical therapy for acute CS. We aimed to analyze the natural history and possible prognostic factors in patients with CS complicating ACS.
Patients/methods: All 126 patients (mean age 65.8 ± 12.5 years), who were hospitalized in single center due to an episode of CS in the course of ACS, had IABP and were scheduled for coronary angiography. The assessed end-point was 5-year death from any cause.
Results: Median left ventricle ejection fraction (LVEF) 28% (interquartile range (IQR) 23–35%), 39 patients (31%) were female, in 91 (72%) the initial diagnosis was ST-elevation myocardial infarction (STEMI). Mean time on the IABP was 3.8 ± 3 days. During index hospitalization there were 56 deaths (44%). Other 27 patients (out of 70 discharged – 38.5%) died during 5-year follow-up. In univariate logistic regression, the significant effect on long term mortality had age, female gender, reduced ejection fraction below 31% and hypotension on admission. The out of hospital survival was also determined by age, gender and hypotension, while LVEF lost its predictive value The multivariate survival analysis both in whole group and in patients discharged from hospital was independently affected by age and hypotension on the admission.
Conclusions: The mortality of patients with CS despite treatment with IABP remains very high, especially during the in-hospital period and early after discharge. Among assessed parameters age and hypotension on the admission are the most important predictors of adverse long term prognosis.

1. Introduction

Without prompt diagnosis and appropriate management cardiogenic shock (CS) is associated with very high mortality [1]. The lowest in-hospital mortality of CS patients in clinical trial exceeds 40% [2]. The therapy consists of rapidly restoring cardiac output and peripheral perfusion by the use of inotropic agents and vasopressors. Intra-aortic balloon counterpulsation (IABP) has been considered the main support in mechanical therapy for acute CS that fails initial stabilization with medical therapy [1], but in the context of very recent Shock II Trial it has become matter of concern [2]. Utilization of IABP improves coronary and peripheral perfusion by improving left ventricular (LV) pumping and by acutely decreasing afterload [3]. According to the previous ESC guidelines regarding the treatment of patients with ST-elevation myocardial infarction (STEMI), IABP implantation was indicated in CS caused by acute coronary syndrome (ACS) together with as early as possible coronary angiography, and revascularization (primary percutaneous coronary intervention – pPCI) as soon as possible – class I, level of evidence C [4]. However, recently even before publication of the results of Shock II Trial, experts changed their consensus and in the current guidelines the use of IABP in CS was downgraded to class IIb [5]. With these changes the treatment of CS in ACS poses a big challenge. Still, single most important variable in treating patients with CS is prompt revascularization [5].

In opposition to the in-hospital survival, there are few reports analyzing long term mortality of patients with cardiogenic shock [6]. It is extremely important for physicians who provide out-patient care for patients after cardiogenic shock to know distant

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mortality and its risk factors, as they may be different from the ones present in general ACS population. Therefore we decided to assess the long term prognosis of CS patients, with additional analysis of survival after the discharge from hospital. The objective of the study was the analysis of long term mortality of consecutive ACS patients with CS and the assessment of its risk factors.

2. Patients and methods

We analyzed 128 patients hospitalized in the Department of Cardiology of University Hospital between 1999 and 2009, in whom IABP was used. All these patients had an episode of ACS, complicated by CS. In order to analyze a homogenous group we excluded patients who died before the implantation of IABP and those in whom implantation of IABP was not possible technically or contraindicated. Patients in whom implantation of IABP was for reason different than CS were also excluded from the study. Basic characteristics of study patients are shown in Table 1. Mean age of the analyzed patients was 65.8 years (±12.5); 31% constituted women. The inclusion criteria was ACS complicated by CS, which was defined as persistent systolic blood pressure (SBP) <90 mmHg, despite either fluids or catecholamine infusion, together with the symptoms of peripheral hypoperfusion [1]. The CS was diagnosed either on admission or any time during hospitalization.

At admission the basic clinical parameters as heart rate (HR), systolic and diastolic blood pressures (SBP, DBP) were assessed. Moreover, parameters related to the infarct size were assessed: localization of MI, the type of the infarct-related artery (IRA), maximal concentrations of serum creatinine and C-reactive protein (CRP) concentration as well as maximal activity of serum creatine kinase myocardial isoenzyme (CK-MB). In some patients from the first years of the study troponin concentration was not available. The majority of patients (n = 112, 88.9%) underwent coronary angiography within first 12 h of the symptom onset. Within first 48 h from admission each of the patients underwent standard transthoracic echocardiography (TTE) with the assessment of left ventricle ejection fraction (LVEF). Before percutaneous coronary intervention (PCI) bolus of weight adjusted unfractionated heparin as well as aspirin at a dose of 300 mg (followed by 75 mg daily) and ticlopidine (500 mg) or clopidogrel (300 mg), after stent or stents (only BMS) implantation, were administered. Antiplatelet treatment with ticlopidine (250 mg twice daily) or clopidogrel (75 mg daily) were continued for at least one month after the procedure.

Table 1
The basic characteristics of the studied patients.

Females *n* (%)	39 (31)
Age, mean (±SD), y	65.8 (±12.5)
Type of ACS, *n* (%)	
STEMI	91 (71)
Non-ST-ACS (NSTEMI, UAP)	37 (29)
In-hospital deaths, *n* (%)	56 (44)
Deaths after hospital discharge during 5 year follow-up, *n* (%)	27 (38.5)
Baseline HR, median (IQR), bpm	100.0 (80.0–110.0)
Baseline blood pressure values:	
SBP, median (IQR), mmHg	103.0 (90.0–130.0)
DBP, median (IQR), mmHg	70.0 (60.0–80.0)
Time from chest pain onset to admission, median (IQR), h	5 (3.0–12.0)
Maximal CKMB, median (IQR), IU/L	246.0 (101.0–498.0)
Maximal serum creatinine, median (IQR), mg/dL	1.3 (0.98–1.98)
LVEF, median (IQR), %	28.0 (23.0–35.0)
CRP, median (IQR), mg/L	121.1 (87.1–153.6)
Coronary angiography, *n* (%)	112 (88.9)
One-vessel disease	33 (25.8)
Two-vessels disease	32 (25)
Three vessel disease	47 (36.7)
IRA, *n* (%)	
LMA	9 (7)
LAD	66 (51.6)
LCx	7 (5.5)
RCA	18 (14)
Localization of MI based on ECG, *n* (%)	
Anterior and anterolateral	87 (67.9)
Inferior and inferiolateral	24 (18.7)
Isolated right ventricle	3 (2.3)

ACS – acute coronary syndrome; STEMI – ST-elevation myocardial infarction; non-ST-ACS – non-ST-elevation acute coronary syndrome; NSTEMI – non-ST-elevation myocardial infarction; UAP – unstable angina pectoris; HR – heart rate; SBP – systolic blood pressure; DBP – diastolic blood pressure; CK-MB – creatine kinase myocardial isoenzyme; CRP – C-reactive protein; LVEF – left ventricle ejection fraction; LMA – left main artery; LAD – left anterior descending artery; LCx – left circumflex artery; RCA – right coronary artery; IQR – interquartile range.

Patients were followed up for 61 months. Only 10 survivors had observation time of less than 5 years (minimum 3.3 years). The analyzed end-point was all-cause mortality. Data concerning out of hospital mortality was obtained from the local population registry run by a Government Office.

The investigation conforms to the principles outlined in Declaration of Helsinki.

2.1. Statistical analysis

Data are presented as median ± interquartile range (IQR: 25th–75th percentile), unless otherwise specified. Distribution of continuous variables was assessed using Shapiro–Wilk test and if the normality hypothesis was rejected non parametric Mann Whitney test was used, otherwise Student's t test was utilized. Categorical data were compared using Chi^2 test. Survival was analyzed using Kaplan–Meier method with F Cox' and log rank tests. Multivariate analysis of factors contributing to patients' prognosis was performed using logistic regression analysis (STATISTICA 10, StatSoft). The level of $p \leq 0.05$ was considered as statistically significant.

3. Results

Median hospitalization time was 7 days (IQR 2–13 days). Median time of IABP support was 3 days (IQR 1–5). In-hospital mortality rate was 44% (56 patients), including 17 (13.3%) patients who died within first 24 h. Time from the symptoms onset to hospitalization was on average 5 h (IQR: 2–12). The most common diagnosis, present in 91 patients (71%), was STEMI; the rest 37 (29%) of patients were hospitalized due to non-ST-elevation acute coronary syndromes (non-ST-elevation myocardial infarction or unstable angina pectoris). The detailed characteristics of patients as well as the revascularization data is shown in Table 1. The majority of the patients suffered from anterior wall myocardial infarction, due to target lesion in left anterior descending or left main stem. The most common complications during hospitalization were arrhythmias and pulmonary edema (Table 2). During long-term follow up period of median 5.1 years, 27 patients died (38.5%), (Table 1).

Among clinical, biochemical, angiographic and echocardiographic parameters, the Kaplan–Meier analysis of survival with log rank and F-Cox' tests identified age, female sex, LVEF ≤ 30% and systolic blood pressure on admission (SBP) ≤ 100 mmHg as variables significantly associated with poor prognosis during 5 year follow up (Fig. 1). Increased mortality in females was associated with older age (79 ± 3.8 years vs 60 ± 10.4 years in males $p < 0.0001$), and gender was not an independent predictor of prognosis in multivariate logistic regression analysis, which identified only age (odds ratio (OR) = 1.09; 95% confidence interval (CI)