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Predictors of in-hospital mortality among cardiogenic shock patients. Prognostic and therapeutic implications

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ABSTRACT

Background: Cardiogenic shock (CS) has a poor prognosis. The heterogeneity in the mortality through different subgroups suggests that some factors can be useful to perform risk stratification and guide management. We aimed to find predictors of in-hospital mortality in these patients.
Methods: We analyzed all cases of cardiogenic shock due to medical conditions admitted in our intensive acute cardiovascular care unity from November 2010 till November 2015. Clinical, biochemical and hemodynamic variables were registered, as was the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) profile at 24 h of CS diagnosis. From a total of 281 patients, 28 died within the first 24 h and were not included in the analysis.
Results: A total of 253 patients survived the first 24 h, mean age was 68.8 ± 14.4 years, and 174 (68.8%) were men. Etiologies: acute coronary syndrome 146 (57.7%), acute heart failure 60 (23.7%), arrhythmias 35 (13.8%), and others 12 (4.8%). A total of 91 patients (36.0%) died during hospitalization. We found the following independent predictors of in-hospital mortality: age (odds ratio [OR] 1.032, 95% confidence interval [CI] 1.003–1.062), blood glucose (OR 1.004, 95% CI 1.001–1.008), heart rate (OR 1.014, 95% CI 1.001–1.028), and INTERMACS profile (OR 0.168, 95% CI 0.107–0.266).
Conclusions: In patients with CS the INTERMACS profile at 24 h of diagnosis was associated with higher in-hospital mortality. This and other prognostic variables (age, blood glucose, and heart rate) may be useful for risk stratification and to select appropriate medical or invasive interventions.

1. Introduction

Cardiogenic shock (CS) consists a state of end-organ hypoperfusion caused by severe cardiac dysfunction that rapidly progresses to multisystem failure and death of the patient without adequate treatment [1]. The publication of the clinical trial Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock (SHOCK) [2] supposed a radical change in the management of patients with CS due to acute coronary syndrome, adding early coronary revascularization to the standard therapy [3–5]. Partly because of this strategy, the mortality associated with CS, as high as 70% before the 90s [6–8], has shown a significant decrease thereafter, as shown in the Intraaortic Balloon Support for Myocardial Infarction with Cardiogenic Shock (IABP-SHOCK II), that reported a mortality of 40% [9]. However, this means that the prognosis of CS is still poor. The heterogeneity in the mortality, dependent on the clinical profile, suggests that some factors are associated with higher risk [10–12]. Through the last decade, the introduction of ventricular assist devices is causing important change in the management of patients with advanced heart failure. With the appearance of these new therapeutic approaches it is necessary to analyze more contemporary data of patients with CS in search of factors that could help us to stratify the risk in this critical condition and to select patients for advanced therapies.

The Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) scale is a simple and useful tool that is currently used in prognostic stratification in patients with advanced heart failure, classifying these patients into 7 different categories [13] (Table 1). As CS represents the most critical phase of heart failure, we hypothesize that this scale could also be used in these patients. The aims of the present study were to investigate clinical, biochemical and hemodynamic characteristics of patients with CS, as well as its management, in order to find risk predictors of in-hospital mortality.

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Table 1
Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) profiles [13].

Profiles	Definition	Description
INTERMACS 1	Critical cardiogenic shock (Crash and burn)	Patient with life-threatening hypotension despite rapidly escalating inotropic support, critical organ hypoperfusion, often confirmed by worsening acidosis and lactate levels.
INTERMACS 2	Progressive decline (Sliding fast on inotrope)	Patient with declining function despite intravenous inotropic support, that may be manifested by worsening renal function, nutritional depletion, or inability to restore volume balance. Also describes declining status in patients unable to tolerate inotropic therapy.
INTERMACS 3	Stable but inotrope dependent (Dependent stability)	Patient with stable blood pressure, organ function, nutrition, and symptoms on continuous intravenous inotropic support (or a temporary circulatory support device or both), but demonstrating repeated failure to wean from support because of recurrent symptomatic hypotension or renal dysfunction.
INTERMACS 4	Resting symptoms on oral therapy at home	Patient can be stabilized close to normal volume status but experiences daily symptoms of congestion at rest or during activities of daily living. Doses of diuretics generally fluctuate at very high levels. More intensive management and surveillance strategies should be considered, which may in some cases reveal poor compliance that would compromise outcomes with any therapy. Some patients may shuttle between 4 and 5.
INTERMACS 5	Exertion intolerant	Comfortable at rest and with activities of daily living but unable to engage in any other activity, living predominantly within the house. Patients are comfortable at rest without congestive symptoms, but may have underlying refractory elevated volume status, often with renal dysfunction. If underlying nutritional status and organ function are marginal, patient may be more at risk than INTERMACS 4, and require definitive intervention.
INTERMACS 6	Exertion limited (Walking wounded)	Patient without evidence of fluid overload is comfortable at rest, and with activities of daily living and minor activities outside the home but has fatigue after the first few minutes of any meaningful activity. Attribution to cardiac limitation requires careful measurement of peak oxygen consumption, in some cases with hemodynamic monitoring to confirm severity of cardiac impairment.
INTERMACS 7	Advanced NYHA class III (Placeholder)	A placeholder for more precise specification in future. This level includes patients who are without current or recent episodes of unstable fluid balance, living comfortably with meaningful activity limited to mild physical exertion.

NYHA, New York Heart Association.

2. Methods

Monocentric observational study that retrospectively analyzed patients with CS due to medical conditions admitted to the acute cardiovascular care unity in a University Hospital from November 2010 to November 2015. The primary endpoint was all-cause in-hospital mortality.

2.1. Inclusion and exclusion criteria

Patients included in the study had to meet the subsequent criteria: 1) persistent arterial hypotension, with systolic blood pressure <90 mm Hg or a drop of mean blood pressure >30 mm Hg for at least 30 min; 2) signs of systemic hypoperfusion (altered mental state, cold periphery or low urine output <0.5 mL/kg/h or 30 mL/h) and 3) clinical or radiological signs of pulmonary congestion, suggesting adequate o elevated filling pressure. Patients that died within the first 24 h since the diagnosis of CS were excluded.

2.2. Data collection

Clinical history was revised to collect demographic data, medical history, left ventricular ejection fraction and functional class previous to the hospitalization. Patients were considered to have hypertension, diabetes or dyslipidemia when it was a previous diagnosis recorded in medical history or they are treated pharmacologically. Chronic obstructive pulmonary disease was defined when patients had clinical symptoms or they were taking inhalers. Peripheral arterial disease was defined by clinical or echographic signs. We considered chronic renal insufficiency to be present in patients with creatinine level previous to admission >1.5 mg/dL. The etiologies of CS were classified in one of the following: acute coronary syndrome, acute heart failure, myocarditis, stress cardiomyopathy/Tako-tsubo syndrome, bradycardia (complete atrioventricular block/sinus node dysfunction), and arrhythmias (supraventricular/ventricular). Echocardiography was performed at the moment of diagnosis. The need of more advanced therapies during the hospitalization was also recorded: invasive or noninvasive mechanical ventilation, high-flow nasal oxygen delivery system (Optiflow), continuous renal replacement therapies, circulatory support by intraaortic balloon pump counterpulsation, extracorporeal membrane oxygenation or ventricular assist device, as well as heart transplant. Infections and neurological complications were also recorded.

Biochemical parameters were analyzed at diagnosis. The existence of coagulopathy at the diagnosis was defined as activated partial thromboplastin time >40 s, international normalized ratio >1.2 or platelet count <120.000. Hemodynamics parameters as blood pressure and heart rate were also recorded at the moment of CS diagnosis, as well as the number of vasoactive drugs needed at 24 h and 72 h of the diagnosis. The inotrope score (IS) was calculated with Wernovsky formula [14].

The INTERMACS profile at 24 h was assigned by two authors (XL and ISC) independently after checking medical and nurse comments, graphics and all parameters above. In the situation of discrepancy, the case was revised and discussed again.

The ethics committees of our institution approved the study, which conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

2.3. Statistical analysis

Categorical variables are expressed as percentage and continuous variables as median and standard deviation. Comparisons between groups were performed using the chi-squared or Fisher's exact test for categorical variables and Student's t test for continuous variables. Predictors of in-hospital mortality were determined using a multinomial logistic regression model. The modeling process involved forward and backward stepwise methods with a threshold for exit set at P higher than 0.10 and for enter at P lower than 0.10. The aim was a parsimonious model, with the minimum number of variables per logit explaining the greater amount of variability. Results from the regression analyses are presented as odds ratios (ORs) with 95% confidence intervals (CIs). We used SPSS version 16.0 for Windows (SPSS Inc., Chicago, Illinois, USA).

Table 2
Baseline characteristics in survivors and non-survivors.

	Survivors (n = 162)	Non-survivors (n = 91)	P
Age, years	67.0 ± 15.1	71.9 ± 12.4	0.01
Men (%)	112 (69.1)	62 (68.1)	0.87
BMI	27.1 ± 5.0	27.1 ± 3.7	0.91
Medical history (%)			
Smoking	48 (29.6)	21 (23.1)	0.25
Hypertension	112 (69.1)	63 (69.2)	0.99
Diabetes	61 (37.7)	31 (34.1)	0.57
Dyslipidemia	138 (85.2)	65 (71.4)	0.01
COPD	20 (12.3)	15 (16.5)	0.36
Renal insufficiency	38 (23.5)	17 (18.7)	0.38
PAD	15 (9.3)	10 (11.0)	0.66
NYHA III–IV	16 (9.9)	15 (16.5)	0.10

Results are presented as numbers and percentage (%), and mean ± standard deviation.
BMI, body mass index; COPD, chronic obstructive pulmonary disease; PAD, peripheral arterial disease; NYHA, New York Heart Association.