Outcome predictors of cardiogenic shock complicating ST-segment elevation myocardial infarction

Facteurs pronostiques du choc cardiogénique compliquant l'infarctus du myocarde avec sus-décalage du segment ST

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RÉSUMÉ

Introduction : Le choc cardiogénique (CC) compliquant l'infarctus du myocarde avec élévation de ST (STEMI) est grevé d'une mortalité élevée. Il existe des preuves limitées pour sa prise en charge, à l'exception de la revascularisation précoce.
Objectif : Nos objectifs étaient d'évaluer le pronostic et les facteurs prédictifs de mortalité précoce du CC compliquant un STEMI.
Méthodes : De janvier 2009 à août 2018, tous les patients se présentant dans les 48 heures suivant un STEMI, compliqué de CC et recevant un traitement invasif, ont été prospectivement inclus.
Résultats : La cohorte d'étude a compris 122 patients consécutifs. L'âge moyen était de 65±12 ans avec 74.5% d'hommes. L'insuffisance ventriculaire gauche était l'étiologie la plus fréquente du CC (72.1%) et des complications mécaniques sont survenues dans 8.2% des cas. Une intervention coronaire percutanée (ICP) a été proposée pour tous les patients et réalisée dans un contexte primaire dans 72.1% des cas. Une prévalence élevée de no reflow a été notée (15.6%). Des lésions multitronculaires ont été notées chez 64.8% et des ICP multitronculaires durant la procédure index ont été réalisées chez 22.1% des cas. Un ballon de contre-pulsion intra-aortique a été utilisé chez 17.2% des patients. La mortalité à 30 jours était de 58.2%. Le seul facteur prédictif de mortalité précoce était l'ICP multitronculaire immédiate (OR=4.1, IC95%: 1.1-14.5; p=0.031).
Conclusion : Malgré des stratégies de prise en charge invasives, la mortalité à 30 jours du CC post-STEMI est restée aussi élevée que 58,2%. L'ICP multitronculaire immédiate était le seul facteur prédictif de mortalité précoce.

Mots-clés
Choc cardiogénique; infarctus du myocarde; intervention coronaire percutanée; mortalité.

SUMMARY

Background: Cardiogenic shock complicating ST elevation myocardial infarction is burdened by a high mortality. There is only limited evidence for the management except for early revascularization and the relative ineffectiveness of intra-aortic balloon pump.
Aim: Our objectives were to evaluate outcome and predictors of early all-cause 30-day mortality in the setting of cardiogenic shock complicating ST elevation myocardial infarction.
Methods: From January 2009 to August 2018, all patients who presented within the first 48 hours of ST elevation myocardial infarction complicated by cardiogenic shock and receiving invasive management were prospectively included.
Results: The study cohort comprised 122 consecutive patients. The mean age was 65±12 years and 74.5% of patients were males. Left ventricular failure was the most common etiology of cardiogenic shock (72.1%) and mechanical complications occurred in 8.2% of cases. Percutaneous coronary interventions were proposed for all patients and performed in a primary setting in 72.1%. A high prevalence of no reflow was noted (15.6%). Multivessel coronary artery disease was noted in 64.8% and multivessel percutaneous coronary interventions at the index procedure were performed in 22.1% of cases. Intra-aortic balloon pump was used in 17.2% of patients. The 30-day mortality was 58.2%. The only predictor of early mortality was the immediate multivessel percutaneous coronary intervention (OR=4.1, 95%CI 1.1–14.5; p=0.031).
Conclusion: Despite invasive management strategies, 30-day mortality of cardiogenic shock complicating ST elevation myocardial infarction remained as high as 58.2%. Immediate multivessel percutaneous coronary intervention was the only predictor of early mortality.

Key-words
Cardiogenic shock; myocardial infarction; percutaneous coronary intervention; mortality.

BACKGROUND

Cardiogenic shock (CS) complicates 6–10% (1) of all ST elevation myocardial infarctions (STEMI). Its in-hospital mortality has been reduced from formerly 80% to 40-50% nowadays, however it remains the leading cause of death following STEMI (1,2), mainly because of a complex physiopathology which implicates both mechanical systole-diastolic dysfunction of cardiac pump and systemic inflammatory response syndrome (3–5).

There is only limited evidence regarding the management of CS (2), except for the proved impact of early revascularization (6,7) and the relative ineffectiveness of routine use of intra-aortic balloon pump (IABP) (8,9). Since SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) trial (6), few therapeutics advances have shown convincing clinical benefit (10).

METHODS

Study population

From January 2009 to August 2018, we prospectively included all patients who presented within the first 48 hours of STEMI complicated by CS and receiving invasive management with percutaneous coronary intervention (PCI) and/or mechanical circulatory support. Transient (<30 min) CS or those from non-cardiac origin were excluded.

Interventional procedure

All patients were transferred to our cathlab for PCI-mediated reperfusion in primary setting, or after fibrinolysis. Fibrinolysis was indicated in patients with a stable hemodynamic status at first medical contact or when primary PCI could not be provided expeditiously (<120 min). In these cases, emergent coronary angiography was performed regardless of the ST resolution and the time from fibrinolysis administration. PCI were performed by six skilled interventional cardiologists and decision to carry out culprit-lesion-only or multivessel-PCI was at the discretion of the operator.

Emergency echocardiography was routinely performed at presentation in cathlab particularly when mechanical complications were suspected.

Patients with mechanical complications of STEMI were discussed for the optimal revascularization and surgical repair strategy by the local “heart-team” on a case by case basis.

IABP use, as the only available percutaneous mechanical circulatory support, was at the discretion of the operator.

Definitions and endpoints

The diagnosis of acute STEMI was defined according to the fourth universal definition of myocardial Infarction (11). Patients were considered in CS in front of persistent hypotension (systolic blood pressure <90 mmHg) despite adequate filling status with signs of low cardiac output and/or pulmonary congestion. CS was also considered if inotropes and/or mechanical circulatory support were needed to maintain systolic blood pressure >90 mmHg (10).

The primary endpoint of our study was to evaluate the 30-day all-cause mortality. The secondary endpoint was to determine predictors this early mortality.

Standardized definitions were used for all-cause deaths, recurrent MI, target vessel revascularization, stroke, stent thrombosis (12), and bleeding events endpoint criteria (13). Angiographic success was defined as a TIMI grade flow 3 with <20% of residual stenosis (14).

Statistical analysis

Independent groups were compared using the Student’s t-test for continuous variables and Mann and Whitney’s test in case of reduced effectives, whereas the chi-square test or Fisher exact test were used to compare the categorical variables. Risk factors were determined by evaluating the Odds ratio. To identify 30-day mortality predictors, a multivariate analysis using logistic regression was performed. At univariate analysis, the following variables were assessed: age, gender, cardiovascular risk factors, myocardial infarction history, chronic kidney disease history, anterior STEMI location, pre-hospital cardiac arrest, left main coronary artery disease involvement, concomitant chronic total occlusion, glycoprotein-IIbIIIa inhibitors, thrombus-aspiration, IABP use, no reflow and performance of multivessel-PCI. Patients with mechanical complications were excluded from analysis. Age, gender and variables with $p<0.1$ were included into a multivariable model. In all cases, p values <0.05 were considered statistically significant.

RESULTS

A total of 122 consecutive patients presented to our center with CS complicating STEMI during the study period. The baseline characteristics are summarized in Table 1.

Table 1: Baseline characteristics.

	N = 122
Age (years)	65 ± 12
Age ≥ 75 years	26 (21.3%)
Males	92 (75.4%)
Cardiovascular risk factors	
Smoker	86 (70.5%)
Diabetes	60 (49.2%)
Arterial hypertension	50 (41.0%)
Dyslipidaemia	22 (18.0%)
History of coronary heart disease	
History of myocardial infarction	18 (14.8%)
History of percutaneous coronary intervention	12 (9.8%)
History of coronary artery bypass graft	0 (0%)
Comorbidities	
History of stroke	11 (9.0%)
History of chronic kidney disease (eGFR < 60 mL/min)	6 (4.9%)
History of lower extremity artery disease	10 (8.2%)
Systolic blood pressure at admission (mmHg)	84.5 ± 18.1
Heart rate at admission (bpm)	100.0 [IQR=73.8-120.0]
Cardiac arrest before cathlab admission	12 (9.8%)
Electrocardiogram findings	
Anterior location	71 (58.2%)
ST elevation in right ventricle leads	22 (18.0%)
Ventricular arrhythmia	6 (4.9%)
Bradycardia < 30 bpm	25 (20.5%)
Atrial fibrillation	2 (1.6%)
Transthoracic echocardiogram findings	
LVEF (%)	31.5 ± 11.1
Ventricular septal defect	7 (5.7%)
Acute severe ischemic mitral regurgitation	3 (2.5%)
Ventricular free wall rupture	0 (0%)

Bpm=beats per minute, eGFR=estimated Glomerular Filtration Rate, LVEF=Left Ventricular Ejection Fraction.

The mean age was 65±12 years and 75.4% were males. Smoking was the most reported cardiovascular risk factor (70.5%) and almost half of patients (49.2%) were diabetic. A median time of 3.0 hours [IQR=1.3-5.6] between chest pain onset and first medical contact was observed in our population. CS was present from the outset in 94 patients (77.0%) and developed early after admission secondary to fibrinolytic therapy failure in 24 patients (19.7%), "no reflow" complicating PCI in three patients (2.5%) and was the consequence of a rapid aggravation of an acute ischemic mitral regurgitation despite a successful primary PCI in one patient (0.8%). Twelve patients experienced cardiac arrest (9.8%) and 13 patients (10.7%) were already intubated and mechanically ventilated before cathlab admission. According to localization, 58.2% of STEMI were anterior. At first medical contact or during transportation, prevalence of rhythm and conduction disturbances was particularly high with 20.5% of patients presenting with severe bradycardia (<30 beats per minute), 4.9% with sustained ventricular arrhythmia and 1.6% with rapid atrial fibrillation.

Fibrinolytic strategy was adopted in 34 patients (27.9%), only in one patient in a prehospital setting, using streptokinase (21.3%) or tenecteplase (6.6%), within a median delay of 52 minutes [IQR=30-125] after first medical contact. Fibrinolysis therapy failed in all cases except the particular situation of one initially hemodynamically stable patient, who developed an electrical storm and CS immediately after successful fibrinolysis, as assessed angiographically, in whom mechanical complications were ruled out, however the issue was fatal.

A median delay of 3.8 hours [IQR=1.5-7.1] was observed between first medical contact and cathlab admission. Interventions were carried out in primary, rescue and emergent setting after successful fibrinolysis in 72.1%, 27.1% and in 0.8% of cases, respectively. Angiographic characteristics as well as procedural techniques and results are summarized in Table 2. Nine patients (6 cases of mechanical complications requiring only IABP support as a bridge for surgery, 2 cases of early per-procedural cardiac arrests and one case with a long lesion and a poor distal vascular bed) did not benefited from PCI. Angiographic success of the coronary PCI of the infarct related artery was achieved in 91 patients for an overall success rate of 74.6%. Except 3 cases with complex coronary anatomy, in whom lesion crossing was impossible, "no reflow" was the main cause of PCI failure, occurring in 19 patients (15.6%) despite the use of glycoprotein IIbIIIa inhibitors and thrombus aspiration in 28.7% and 42.6% of patients respectively. The other minor procedural complications were as follows: coronary dissections (2.5%) and distal embolization (3.3%). All of them were successfully managed.

Table 2: Angiographic characteristics and management strategies.

	N = 122
PCI setting	
Primary	88 (72.1%)
Rescue	33 (27.1%)
Emergency after successful fibrinolysis	1 (0.8%)
Median delay from chest pain onset to	6,5 [IQR=4.0-14.8]
cathlab (hours)	
Femoral access	102 (83.6%)
Angiographic findings	
Culprit lesion	
Left main stem	1 (0.8%)
Left anterior descending artery	70 (57.4%)
Left circumflex artery	15 (12.3%)
Right coronary artery	39 (32.0%)
Multivessel acute occlusion*	3 (2.5%)
Initial TIMI flow	
TIMI 0	75 (61.5%)
TIMI 1	9 (7.4%)
TIMI 2	28 (23.0%)
TIMI 3	10 (8.2%)
Stent thrombosis	8 (6.6%)
Coronary status	
Single vessel disease	43 (35.2%)
2-vessel disease	38 (31.1%)
3-vessel disease	41 (33.6%)
Left main stem significant lesion	21 (17.2%)
Chronic total occlusion	22 (18.0%)
Procedural characteristics and results	
Per-procedural glycoprotein IIbIIIa inhibitors	35 (28.7%)
Thrombus aspiration	52 (42.6%)
Angiographic PCI success in culprit lesion	91 (74.6%)
(<20% residual stenosis, TIMI3)	
No reflow	19 (15.6%)
Lesion crossing failure	3 (2.5%)
PCI not performed†	9 (7.4%)
Multivessel-PCI at the index procedure	27 (22.1%)
IABP	21 (17.2%)
Transvenous temporary cardiac pacing	19 (15.6%)
Median delay from cathlab admission to wire	12.0 [IQR=7.0-17.5]
crossing (min)	
Non-IRA PCI before discharge	4 (3.3%)

*2 cases of multivessel stent thrombosis and one case of multivessel embolic occlusions, †6 cases of mechanical complications requiring only IABP support as a bridge for surgery, 2 cases of per-procedural cardiac arrests, 1 case of poor distal coronary vascular bed. IABP=Intra-aortic balloon pump, IRA=Infarct related artery, PCI=Percutaneous Coronary Intervention, TIMI=Thrombolysis in Myocardial Infarction grade flow.

Multivessel coronary artery disease was present in 79 patients (64.8%) and PCI of non-infarct related artery was performed during the index procedure in 27 patients (22.1%) representing almost the third (34.2%) of patients and before discharge (staged revascularization strategy) in 4 patients (3.3%).

IABP was inserted in 21 patients (17.2%) of patients with a median duration of 43.0 hours [IQR=11.0-56.5].

The mean left ventricular ejection fraction was of 31.5±11.2%.

The considered etiologies of CS complicating STEMI in our series are illustrated in Figure 1. CS resulted from ventricular septal defect in 7 patients (5.7%) and from acute severe ischemic mitral regurgitation in 3 patients (2.5%).

At 30 days, overall mortality was 58.2%. Myocardial infarction recurrence, target vessel revascularization and stroke occurred respectively in 4.1%, 3.5% and 2.5% of cases (Table3). All patients experiencing mechanical complications (n=10) died, despite IAPB use in 7 cases (in whom peripheral vascular anatomy was favorable) and surgical repair in 3 cases (Figures 1,2).

IABP use was associated with non-significant increased 30-day mortality (76.2% vs. 55.4%, p=0.08).

After exclusion of patients with mechanical complications, multivariate analysis revealed that immediate multivessel-PCI during the index procedure was the only predictor of 30-day mortality (OR 4.1; 95% CI 1.1–14.5; p=0.031); while a trend was observed for the presence of a chronic total occlusion in non-infarct related artery (OR 3.5; 95% CI 1.0–12.9; p=0.055).

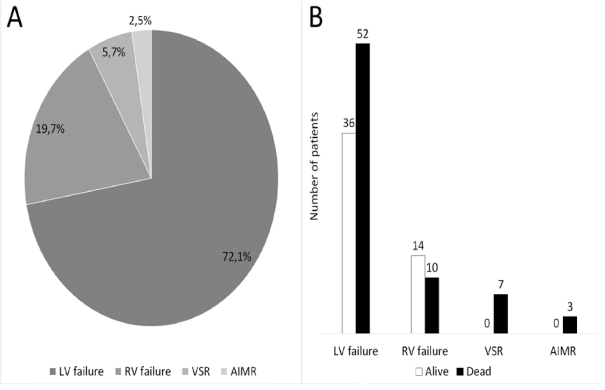

Figure 1: A. Aetiologies of cardiogenic shock after ST elevation myocardial infarction. B. 30-day mortality according to aetiology. LV=Left Ventricle, RV=Right Ventricle, VSR=Ventricular Septal Rupture, AIMR=Acute Ischemic Mitral Regurgitation.

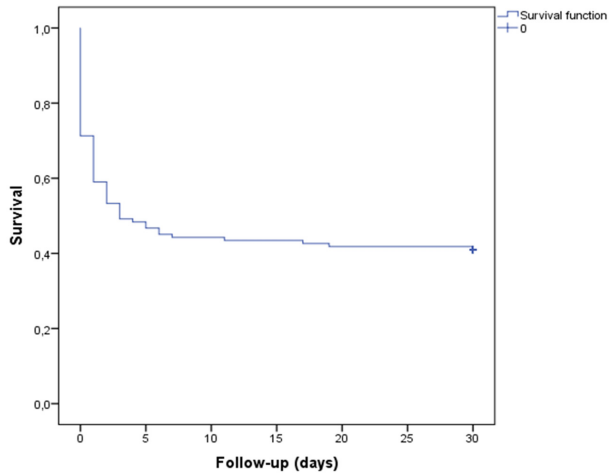

Figure 2: Kaplan Meier cumulative survival analysis at 30-day follow-up in patients with ST elevation myocardial infarction complicated by cardiogenic shock.

Table 3: Cardiac and cerebrovascular events at 30 day follow-up.

	N = 122
MACCE	
Death	71 (58.2%)
Recurrent myocardial infarction	5 (4.1%)
Stroke	4 (3.3%)
Target vessel revascularization	3 (2.5%)
Other events	
Stent thrombosis (ARC)	5 (4.1%)
Acute	3 (2.5%)
Sub-acute	2 (1.6%)
Definite	3 (2.5%)
Probable	2 (1.6%)
Bleeding events (BARC)	4 (3.3%)
BARC 1	0 (0%)
BARC 2	2 (1.6%)
BARC 3	0 (0%)
BARC 4	0 (0%)
BARC 5	2 (1.6%)
Acute lower limb ischemia associated with IABP insertion	2 (1.6%)

MACCE=Major Adverse Cardiac and Cerebrovascular Events, ARC=Academic Research Consortium, BARC=Bleeding Academic Research Consortium.

DISCUSSION

In Tunisia as well as in North Africa, data regarding CS complicating STEMI are scarcely reported.

The major findings of this 10-year prospective cohort-study can be summarized as follows: a) Overall 30-day mortality was 58.2% although a relatively early revascularization proposed to all patients and IABP circulatory support use in 17.2%. b) Analysis of early logistics of care showed mainly a 3.9-hour delay between first medical contact and cathlab admission. c) Left ventricular failure (72.1%) was the main cause of CS, followed by right ventricular failure (19.7%) and mechanical complications (8.2%). d) Multivessel coronary artery disease was present in 64.8% of patients and PCI of non-infarct related artery was performed in almost the third of them (34.2%). e) Immediate multivessel-PCI was associated with increased 30-day mortality in multivariate analysis.

Through this study, the early mortality appeared higher than that reported in recent publications (40 to 50%) (2). This could be due in part to the exclusion of mechanical complications in most of latter studies, which represented 8.2% of CS etiologies in our study population with a fatal outcome in all cases.

In the major CS trials (9,15,16), typical factors associated with higher mortality were older age, anoxic brain damage, lower left-ventricular ejection fraction, lower systolic blood pressure, need for vasopressor support, worse renal function, and higher serum lactate. However according to our multivariate analysis, immediate multivessel-PCI was the main prognostic predictor. Results of several reports (Figure 3) (17–25), pooled in a recent metanalysis, are consistent with this finding and do not support multivessel-PCI in the setting of CS complicating myocardial infarction (26). Previous guidelines, based on pathophysiological considerations, recommended multivessel revascularization in front of a critical or instable non culprit lesion or persistent ischemia despite culprit lesion PCI (10,14,27) and in the setting of persisting CS after revascularization of the presumed culprit lesion (28). The most notable argument was the potential to improve overall myocardial perfusion and function.

Multivessel coronary involvement represents up to 80% of patients with CS (29) and is associated with higher mortality (25,30,31). Despite these considerations, multivessel-PCI was used only in 14 to 39% of patients in a recent metanalysis of the most relevant 10 cohort studies of CS complicating myocardial infarction (26).

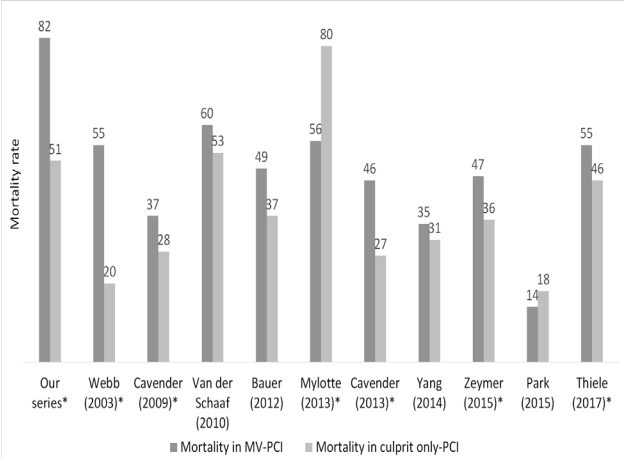

Figure 3: Overview of studies comparing multivessel versus culprit-lesion-only percutaneous coronary interventions in cardiogenic shock with respect to mortality.

The CULPRIT-SHOCK randomized trial was designed to address this controversial problematic. In this trial, among patients with acute myocardial infarction and CS, the risk of death at 30 days was lower with culprit-lesion-only PCI than with immediate multivessel-PCI (32) and mortality did not differ significantly between two groups at 1-year follow-up (33). The given potential reasons for the lack of benefit of immediate multivessel-PCI were the significantly higher dose of contrast load in the second group and consequent decline in renal function although the incidence of renal replacement therapy did not differ significantly between the two groups. Furthermore, the higher dose of contrast load in the multivessel-PCI group may have also led to acute left ventricular volume overload with its potential negative effects on myocardial function and recovery. (32,33). Based on these findings, culprit-lesion-only PCI is currently recommended as the default strategy in patients with CS complicating STEMI in the recent European guidelines on myocardial revascularization (34).

The IABP, as the only available percutaneous mechanical circulatory support in our center, was used in 17.2% of cases. Among patients with mechanical complications, its insertion was possible in 70% of cases. Since 2012 and after the IABP-SHOCK II randomized trial failure to prove a prognostic benefit of IABP implantation in case of CS complicating acute myocardial infarction (8,9), European guidelines do not recommend any more routine IABP implantation, and this device should only be reserved for patients with CS due to mechanical complications as bridge to surgery (35). Among other short-term mechanical circulatory support devices that are currently available, only “extracorporeal membrane oxygenation” showed a potential benefit compared to IABP (36).

The main limitation of this observational study was the potential selection bias. The decision for or against multivessel-PCI was at the discretion of the operator. All confounding factors could not have been ruled out even after multivariate analysis. In fact, patients with refractory shock after culprit-lesion PCI could have been preferentially treated with a multivessel-PCI strategy.

CONCLUSION

In the setting of CS complicating STEMI, mortality remains high despite invasive management strategy. A better collaboration between emergency care providers should be targeted in order to reduce delays. PCI of the culprit-lesion only is actually the recommended revascularization strategy. While IABP use did not improve outcome, “extracorporeal membrane oxygenation” could be of benefit when managing this critical subset of patients.

Conflicts of interest: None

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