Objective. To know the clinical characteristics and determine the related factors to higher in-hospital mortality in patients with cardiogenic shock (CS) due to myocardial infarction in a Peruvian reference hospital.

Materials and methods. We conducted a prospective single-center cohort, to evaluate the clinical characteristics, treatment, and complications of patients with CS due to myocardial infarction from March 2019 to August 2020 at the National Cardiovascular Institute INCOR. Factors related to higher in-hospital mortality and during follow-up were evaluated. Also, the IABP shock II score was applied to stratify the cohort.

Results. Forty patients were included in the study, 75% of cases were due to left ventricular dysfunction, most of them men with an average age of 75 (69-82) years. Fifty percent presented CS after admission to the emergency room. Patients stratified by the IABP shock II score as low, intermediate, and high risk, had in-hospital mortality of 37.5%, 71.4%, and 91.6% respectively. In-hospital mortality was 70%, higher in women, over 75 years old, and in those who developed CS during their hospitalization. Serum lactate > 4 mmol/L in univariate analysis was associated with higher mortality risk (HR: 2.8; IC: 1.6-3.6, p=0.009). Survival to the end of the study was 12.8%.

Conclusions. CS due to myocardial infarction is a clinical entity with high mortality in spite of revascularization and the available treatment in our reality. The highest mortality predictor was the serum lactate at admission > 4 mmol/L. The IABP shock II score showed to be an accurate parameter to stratify the death risk in our population.

Keywords: Cardiogenic shock; Myocardial infarction; Mortality; Peru.
Cardiogenic shock (CS) is a clinical entity characterized by the inability of the heart to carry a sufficient amount of blood to supply the tissue metabolic demands at rest. It requires the presence of low cardiac output and evidence of tissue hypoxia in absence of hypovolemia (1). The definition of CS due to myocardial infarction requires all the following criteria: a) Hypotension > 30 min; b) clinical evidence of tissue hypoperfusion; c) clinical evidence of elevated left ventricular filling pressures and d) cardiac etiology of shock (1).

Worldwide, the incidence of CS due to ST elevation myocardial infarction (STEMI) is estimated at 5-10%, and in non-ST elevation myocardial infarction (NSTEMI) in 2-4% (2). Despite the advances in early reperfusion and treatments for this entity, in-hospital mortality has remained high around 55-60% (3). There are clinical and laboratory parameters, developed from the IABP-SHOCK II trial, that can predict the risk of death in patients with CS (3), including: age > 75 years, prior stroke, glucose at admission > 191 mg/dL, creatinine at admission > 1.5 mg/dL, arterial blood lactate at admission > 5 mmol/L, and Thrombolysis in myocardial infarction (TIMI) flow grade; which classify patients as low, moderate, or high risk of death.

In Peru, it has been reported that CS complicates up to 10.9% of patients with STEMI (4) with an in-hospital mortality of 61% (5). Nevertheless, the risk factors associated with higher mortality in our population have not been defined. Therefore, the objective of the study was to determine the characteristics related to higher mortality (during hospitalization and in the follow-up) in patients with CS due to myocardial infarction in a national referral center.

Materials and methods

In this prospective single-center cohort, we evaluated the clinical, epidemiological and laboratorial characteristics of patients admitted with a diagnosis of CS due to acute coronary syndromes and its relationship with in-hospital mortality and during follow-up (median of eleven months) at the Instituto Nacional Cardiovascular-INCOR, in Lima, Peru. The project was approved by the Institutional Ethics Committee.

The definition of CS was made by the presence of the following criteria: 1) systolic blood pressure (SBP) ≤ 90 mmHg for at least 30 min or vasopressor support to maintain SBP > 90 mmHg; 2) clinical signs of hypoperfusion or pulmonary congestion in the absence of hypovolemia or arrhythmias.

The inclusion criteria were patients aged ≥ 18 years, with CS diagnosed since admission to the hospital or developed during hospitalization and of ischemic etiology (STEMI or NSTEMI). Patients with CS due to valvular disease, obstructive etiology or takotsubo syndrome were excluded. All data were obtained prospectively from the medical records and stored in an electronic database specifically created for this purpose. The variables collected were: sex, age, cardiovascular risk factors, type of infarction, cause of CS (ventricular dysfunction, mechanical complication, cardiac arrest), time from ischemia to reperfusion, time from shock diagnosis to reperfusion, infarct location, strategies and angiographic success of reperfusion, number of vessels with stenosis > 70%, number of vessels treated and moment of treatment, drug therapy, use of mechanical support, use of invasive hemodynamic monitoring, use of mechanical ventilation, laboratory variables on admission and 24 h later, in-hospital death, hospital stay and survival. In addition, in the subgroup of patients with STEMI, who underwent percutaneous coronary intervention (PCI), risk stratification was performed according to the IABP SHOCK II score (6) in low risk (score 0-2), intermediate risk (score 3-4), and high risk (score 5-9).

Frequencies and percentages were used to express qualitative variables and means or medians and their respective dispersion measures in numerical variables. The comparison between both groups was done using Pearson’s chi-square test (categorical variables), Student’s t test (numerical variables with normal distribution) and Mann Whitney’s U (numerical variables with non-normal distribution). Factors related to cardiovascular mortality at one year were evaluated by Cox regression analysis and expressed as HR and their respective confidence intervals. Statistical analysis was performed using the STATA 16 program.

Results

Between March 2019 and August 2020, 52 patients with CS of several etiologies were treated in our hospital. Forty patients (76.9%) had an ischemic etiology (35 STEMI and 5 NSTEMI) and represent our study population (Figure 1).

The characteristics and background of the population according to the type of infarction are presented in Table 1. Twenty patients (50%) arrived with CS at the emergency room and the rest developed it during their hospital stay (in this last group the etiology of CS was: post-cardiac arrest 30%, 25% for left ventricular dysfunction, 20% for unsuccessful post-PCI, 15% for mechanical complication, 5% post-coronary angiography without PCI awaiting surgery, and 5% for NSTEMI).
The etiology of CS in patients with STEMI was left ventricular dysfunction (75%), post-cardiac arrest syndrome (12.5%), mechanical complication (7.5%) (2 free wall rupture and 1 ventricular septum rupture), and right ventricular dysfunction (5%). While in patients with NSTEMI it was left ventricular dysfunction in three cases (60%) and post-cardiac arrest syndrome in two cases (40%).

The time from the onset of ischemic symptoms to reperfusion in STEMI was twelve hours (IQR: 8.1 - 29.5), in the same group the door-to-balloon time was 80 min (IQR: 60-120 min). The time from the beginning of the CS to the placement of mechanical support (in 22 cases where it was placed) was 100 min (IQR: 25 - 660). The time from the diagnosis of cardiogenic shock to admission to our hospital was 4.8 h (IQR:

<table>
<thead>
<tr>
<th>Total (n=40)</th>
<th>STEMI (n=35)</th>
<th>NSTEMI (n=5)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Male</td>
<td>31</td>
<td>77.5</td>
<td>28</td>
</tr>
<tr>
<td>Age (median/IQR)</td>
<td>75</td>
<td>69-82</td>
<td>75</td>
</tr>
<tr>
<td>Hypertension</td>
<td>25</td>
<td>62.5</td>
<td>21</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>14</td>
<td>35</td>
<td>11</td>
</tr>
<tr>
<td>Stroke</td>
<td>7</td>
<td>17.5</td>
<td>7</td>
</tr>
<tr>
<td>CKD</td>
<td>7</td>
<td>17.5</td>
<td>6</td>
</tr>
<tr>
<td>Smoking</td>
<td>8</td>
<td>20</td>
<td>8</td>
</tr>
<tr>
<td>Previous MI</td>
<td>6</td>
<td>15</td>
<td>5</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>1</td>
<td>2.5</td>
<td>0</td>
</tr>
<tr>
<td>Previous PCI</td>
<td>3</td>
<td>7.5</td>
<td>3</td>
</tr>
</tbody>
</table>

2.1 - 13.1), 17.5% of cases had more than 12 hours of CS at the time of admission to our hospital.

Reperfusion

In patients with STEMI, 54% had anterior wall infarction, and 46% other locations. 18 patients (51.4%) were diagnosed with CS at admission to the emergency room. Six patients (17.2%) received fibrinolysis before admission to our hospital, and in 29 cases (83%) percutaneous coronary intervention (PCI) was performed. In 5 patients (14%) PCI could not be done after coronary angiography: 4 due to cardiac surgery indication (2 cases of multivessel disease with surgical indication, one case of interventricular septum rupture and another case due to coronary embolism due to endocarditis), and one patient due to cardiorespiratory arrest (CRA) in the cath lab; in one patient (2.8%) coronary angiography was not performed due to CRA in the emergency room.

In 34 patients with coronary angiography, radial access was the most frequent (44%), follow by femoral access (41%) and finally brachial access (8.8%). The infarct related artery (IRA) was the anterior descending artery in 53%, the right coronary artery in 32.4%, and the circumflex artery in 14.7%. The IRA was occluded in 70.6% of cases at the time of angiography, and the post-PCI flow was: TIMI 0 (10%), TIMI I (13.7%), TIMI II (24%) and TIMI III (51.7%). Twenty two patients (64.7%) had multivessel coronary artery disease and nine of them (40%) were treated with PCI in another vessel in addition to the IRA. Two cases (5.8%) had complications due to the intervention (cardiac tamponade and coronary dissection). Five patients (14%) required cardiac surgery (three due to mechanical complications and two due to multivessel disease).

Sixty percent of NSTEMI patients were in CS at admission to the emergency room, coronary angiography was performed in 100% of cases, multivessel coronary artery disease was found in all of them. The predominant access was the femoral (80%), and there was one complication due to intervention (dissection of the aortic arch). Sixteen percent required coronary artery bypass grafting (CABG) surgery, 20% PCI, and in one case no revascularization was performed due to CRA in the cath lab.

Pharmacological and non-pharmacological support

Eighty percent of patients were assisted with intra-aortic balloon pump (IABP) counterpulsation, the characteristics of this and other supportive therapies are listed in Table 2. IABP use was complicated in one case with lower limb ischemia. Only one case required short-term circulatory mechanical support with extra-corporeal membrane oxygenation (ECMO) due to anterior STEMI after placement of IABP and profound shock. Regarding the medication administered during the first 24h of admission: norepinephrine was used in 100% of cases, with a median dose of 0.3 ug/kg/min (IQR: 0.12 to 0.9 ug/kg/min); dobutamine in 85% of cases with an average dose of 5.9± 2.3 ug/kg/min; 20% dopamine with an average dose of 8.5±3.1 ug/kg/min.

Laboratory

Serum lactate values at admission (median: 2.9 mmol/L, IQR: 1.9-6.2) decreased by 48% at 24 h of treatment (median: 1.5 mmol/L, IQR: 1.1-3.1); creatinine values at admission (median: 1.6 mg/dL, IQR = 0.9 -2.1) increased at 24h by 37.5% (median: 2.2 mg/dL, IQR = 0.9-3.4); the same in the case of transaminases that increased in 9%. There was a decrease of 18% (average 11±3 to 9±2 mg/dL) of hemoglobin at 24h.

Risk stratification and mortality

Risk stratification was performed with the calculation of the IABP shock II score in patients with STEMI who underwent

### Table 2. Cardiac support in patients with CS

<table>
<thead>
<tr>
<th></th>
<th>Total (n=40)</th>
<th>STEMI (n=35)</th>
<th>NSTEMI (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>IABP pre-PCI</td>
<td>7</td>
<td>17.5</td>
<td>4</td>
</tr>
<tr>
<td>IABP post-PCI</td>
<td>25</td>
<td>62.5</td>
<td>23</td>
</tr>
<tr>
<td>No IABP</td>
<td>8</td>
<td>20</td>
<td>8</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>39</td>
<td>97.5</td>
<td>34</td>
</tr>
<tr>
<td>PAC</td>
<td>26</td>
<td>60</td>
<td>24</td>
</tr>
<tr>
<td>ECMO</td>
<td>1</td>
<td>2.5</td>
<td>1</td>
</tr>
</tbody>
</table>

PCI (29 patients), we found 29.6% with low risk, 25.9% with intermediate risk and 44.4% at high risk. In-hospital mortality (IHM) was higher in patients stratified as high risk according to the score ($p = 0.034$) (Figure 2).

Taking into account the classification of the Society for Cardiovascular Angiography and Interventions (SCAI) (7), we found that 30%, 55% and 15% of CS patients at admission were in stage C, D and E respectively, this changed during hospitalization to 5%, 80% and 15% respectively (the increase in stage D cases was characterized by the increase in pharmacological support due to lack of initial response). In-hospital mortality was higher in stage E patients compared to stages C and D ($p = 0.223$) (Figure 3). The summary of all this characteristics, treatments and mortality is presented in the Central Ilustration.

IHM was 70% (71.4% in STEMI and 60% in NSTEMI, $p = 0.627$), higher in women (77% versus 67%). IHM in patients older than 75 years was 71.4% (68.4% in youngers). Women older than 75 years had a mortality of 77% and men older than 75 years of 66% (HR: 1.16, CI: 0.7 - 1.1, $p = 0.44$). Seventy five percent of patients who developed CS during hospitalization died compared to 65% with CS at admission ($p = 0.490$). Mortality in patients with CS with more than 12 hours of evolution was 71.5%, while in CS of less than 12 hours was 68.9% ($p = 0.641$).

At 30-day follow-up, cardiovascular mortality remained similar (70%), but at 16-month follow-up it increased to 79.5% is (82.3% in STEMI and 60% in NSTEMI, $p = 0.268$). Survival to a mean of 11 months of follow-up was only 12.8% (11.8 in STEMI and 20% in NSTEMI, $p = 0.517$) (Figure 4).

The Cox regression analysis of risk factors showed a trend towards higher mortality during follow-up in women older than 75 years, post-PCI TIMI flow < 3, in-hospital CS, and arterial blood lactate greater than 4 mmol/L, only the latter with statistical significance in univariate analysis. However, when performing the multivariate analysis, none of the above, proved to be an independent predictive variable (Table 3).

The hospital stay was around 10.5 days (IQR: 1.5-22) and in the intensive care unit was 7.5 days (IQR: 1-17.5). Six patients (15%) developed infectious complications that led to septic shock and five cases (12.5%) required renal replacement therapy (hemodialysis).
Discussion

In this single-center prospective registry of CS due to myocardial infarction, we found that in-hospital mortality remains high (70%) and is greater than that observed 4 years ago in the PERSTEMI registry (61%) [1]. Among the factors related to higher mortality, only serum lactate > 4 mmol / L at admission was significant (in the univariate analysis). However age > 75 years, female sex, inadequate reperfusion (post-intervention TIMI flow <3) and the appearance of CS during hospitalization were variables probably associated with higher mortality but without statistical significance.

As mentioned in international registries, CS due to STEMI is more common than NSTEMI, and it is more common in older age and males [8,9]. In some studies, age is considered an independent risk factor, patients over 75 years have higher in-hospital mortality and in long-term follow-up, it is also a variable considered in several risk scores [3,6,9], which has been verified with the IABP Shock II score in our study.

The Latin American experience shows that around half of the patients with CS arrive to the emergency room with Killip Kimbal I to III (44% in the Argentine registry) [8], the same study found that one in four cases develops CS within 24 hours of infarction onset. In our study, we found similar data regarding the percentage of cases that arrive to the emergency without CS status (50%). The causes for in-hospital development of CS were ventricular arrhythmia, cardiac arrest and unsuccessful reperfusion (TIMI flow post PCI <3). Some studies found up to 59% of patients with early CS (<48 h after myocardial infarction) [10,11], and patients with intermediate or late CS (after 48 hours) had higher mortality at 30 days (80% vs. 45%, p <0.05) [11].

Clinical practice guidelines recommend early reperfusion in patients with post-infarction CS [12,13]. However, our local times are not optimal yet. Time from the onset of ischemic symptoms to reperfusion in STEMI was 12 hours, longer than the 6 average hours described in the PERSTEMI registry [6]. The longer ischemia time is already a factor that worsens the evolution of the patient and can predispose the appearance of CS. Our data could reflect the delays both in the diagnosis and management of patients with STEMI and should guide us to improve the treatment, prevention and identification of patients at risk of CS.
Cardiogenic shock due to myocardial infarction

Thiele et al. (14) reported approximately 70% to 80% of patients with CS with multivessel coronary disease, similar to our findings (64.7%) and other Latin American registries (8,15). Although the results of the CULPRIT SHOCK (16), that proposes a strategy of treating only the culprit artery and possibly staged revascularization has shown benefit in mortality reduction at 30 days and renal replacement therapy in patients with multivessel disease in CS, we found that up to 40% of patients in our cohort had percutaneous revascularization of the not IRA performed in the same procedure without improving in-hospital mortality.

Currently, in the CS scenario, percutaneous revascularization is more frequent than surgical revascularization. While the IABP SHOCK II clinical trial (16) reported surgical revascularization in 4% of patients, we performed it in 10.4%, which reflects the treatment of patients with mechanical complication of the infarction and cases of patients with multivessel disease with non-reperfused IRA (TIMI <3). It is important to mention that despite more than 80% of patients went to percutaneous revascularization, its success (final TIMI 3 flow) was only achieved in half of the cases. Previous studies show that inadequate TIMI flow after angioplasty is an independent predictor of mortality (15,17), which may explain the high mortality in our cohort.

Due to the pathophysiology of CS, a management strategy is the ventricular unloading with mechanical circulatory support (MCS), which enables a reduction in myocardial oxygen consumption and improve cardiac output, which would increase coronary and systemic perfusion (1,18). In this sense, IABP was placed almost in 80% of cases, which differs considerably from what was found in Argentina (37%) (8) or Chile (16.5%) (15) just to mention neighboring registries, despite the fact that the IABP shock II study did not demonstrate the benefit of its use (16). Of this group of IABP users, almost 22% were placed after a ventricular arrhythmia or mechanical complication of the infarction. Most were placed after PCI and did not improve the patient’s prognosis. Similarly, the use of other devices such as ECMO represented a small percentage (2.5%) similar to that reported in Argentina (2.4%) (8). There is no optimal time to place MCS; it is assumed that by reducing the time to its colocation, the patient status could be optimized before the development of irreversible shock (19). In the DanGer registry (18), the placement of the device was performed immediately after the first confirmation of the CS, so if the patient was in shock before PCI, they recommend placing the device before PCI, considering that they used a support device (Impella®), that we do not possess.

The elevation of serum lactate reflects systemic hypoperfusion and organ dysfunction, but the optimal cut-off point and the ideal time for its measurement is not defined yet. In some studies, it is considered a prognostic factor for mortality (20). Furneau et al. (21) found that a cut-off value of 3.1 mmol/L after 8 hours showed the best discriminating capacity to assess the early prognosis in CS compared to basal lactate value and lactate clearance. For us, the value that correlated with higher mortality was lactate > 4 mmol/L at admission, which may translate the impact of circulatory failure at the peripheral level and therefore the probability of higher mortality.

<table>
<thead>
<tr>
<th>Table 3. Cox regression analysis of characteristics associated to mortality for CS at one-year follow-up.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Univariate analysis</strong></td>
</tr>
<tr>
<td>____________________</td>
</tr>
<tr>
<td>Female sex</td>
</tr>
<tr>
<td>TIMI flow &lt; 3</td>
</tr>
<tr>
<td>Lactate &gt; 4 (at admission)</td>
</tr>
<tr>
<td>Age &gt; 75 years</td>
</tr>
<tr>
<td>IABP use</td>
</tr>
<tr>
<td>CS during hospitalization</td>
</tr>
</tbody>
</table>

IABP: intra-aortic balloon pump. CS: cardiogenic shock. HR: hazard ratio. CI: confidence interval
Despite early revascularization and other treatment strategies, CS has high mortality; in-hospital and 30 days mortality in our study was higher than that from the IABP shock II registry \(^{[6]}\) (40%) and that reported in Argentina (54%) \(^{[6]}\) or Chile (40.8%) \(^{[15]}\) but similar to the what was found in the Mexican study where overall mortality was 80% \(^{[17]}\). The causes of the higher mortality in our cohort may be related to the fact that almost half of the patients with STEMI did not have successful reperfusion (TIMI <3), almost 20% had more than 12 hours of CS at the time of hospital management or delay on average >12 hours in reperfusion of STEMI (generally related to delays in patient transfer). Furthermore, 95% of the study population presented at some point during their hospitalization characteristics of “deteriorating” and “extreme” CS (stage D and E respectively of the SCAI classification), which are related to higher in-hospital mortality \(^{[23]}\). Due to the recentness of the SCAI classification, we do not know the percentage of this group of high-risk patients in the Argentine and Chilean studies \(^{[8,15]}\) for comparison purposes.

The use of the IABP shock II score was able to predict higher mortality with a higher score but we cannot validate its efficacy due to the design of the study. Nonetheless, it is a useful tool to decide more aggressive and earlier management strategies in high-risk patients. Multivariate analysis in some studies found that advanced age, hypotension, deep coma, heart failure, and left coronary artery disease are independent factors for 30-day mortality \(^{[21]}\). In Chile, they found left ventricular ejection fraction <30% and the presence of 2 or more vessels disease as predictors of in-hospital and global mortality \(^{[15]}\). Despite the trend towards higher mortality, we did not find a statistically significant relationship between age, sex, post-intervention TIMI flow, or the use of IABP and mortality, which could be due to our small sample size.

The study has several limitations, the first is that it is a single-center study of a national referral hospital, so it does not reflect the characteristics or the management of CS in Peru. The small number of cases does not allow making adequate statistics inferences such as multivariate logistic regression to know the factors independently related to higher mortality. We did not have adequate hemodynamic registries in this population despite the use of the Swan Ganz catheter; many data were not filled in the clinical history (cardiac index, power heart rate, pulmonary artery pulsatility index, etc.) to be evaluated as mortality risk factors. We had only one case of CS due to myocardial infarction with ECMO support, so it does not allow us to assess whether this device may be related to higher or lower mortality. Some important variables such as bleeding complications were not taken into account due to lack of data.

**Conclusions**

Cardiogenic shock due to myocardial infarction represents a clinical entity with high in-hospital mortality and during follow-up despite revascularization and the treatment available. Serum lactate in the univariate analysis was a factor related to higher in-hospital mortality. The IABP shock II score, was an accurate tool to stratify the death risk in our population.

Strategies should be proposed to optimize the treatment of patients with myocardial infarction: early reperfusion, recognition of the pre shock state (SCAI-B) and the accurate diagnosis and risk stratification of CS patients, so priority can be given in the transfer and reperfusion to centers with higher resolution capacity, which would be optimized with the creation of a nationwide infract network.

**Author contributions**

RGR, GPL, OAT y MChD: design, data collection, writing and corrections; CAL: data collection and writing.

---

**References**


Cardiogenic shock due to myocardial infarction

of ST-elevation myocardial infarction (PERSTEMI), Arch Cardiol Mex. el 1 de diciembre de 2018;88(5):447–53.


