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Cardiogenic shock after ST elevation myocardial infarction and IABP-SHOCK II risk score validation in a cohort treated with pharmacoinvasive strategy

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ABSTRACT

Objective To validate the Intra-aortic Balloon Pump in Cardiogenic Shock II (IABP-SHOCK II) score in patients with cardiogenic shock after ST elevation myocardial infarction (STEMI) treated with pharmacoinvasive strategy (PhIS) and to analyse the influence of ischaemia time on different risk strata.

Methods We analysed 2143 patients with STEMI who underwent reperfusion with tenecteplase in primary health services between May 2010 and April 2017 and were transferred to a tertiary hospital for cardiac catheterisation and continuity of care. Those who evolved to cardiogenic shock were scored as low (0–2), moderate (3–4) or high (5–9) risk of death in 30 days and pairwise-log-rank test was used to compare strata. Time intervals between symptoms onset and lytic (pain-to-needle) and fibrinolytic-catheterisation were also compared.

Results Cardiogenic shock occurred in 212 (9.9%) individuals. The 30-day mortality using the IABP-SHOCK II score was 26.6% for low-risk (n=94), 53.2% for moderate-risk (n=62) and 76% for high-risk (n=25) analysed patients (p<0.001). Validation of the score showed good discrimination for death, area under the curve of 0.73 (CI: 0.66 to 0.81; p<0.001). The median intervals of pain-to-needle and fibrinolytic-catheterisation showed no association with the group stratification (220 vs 251 vs 200 min; p=0.22 and 390 vs 435 vs 315 min; p=0.18, respectively).

Conclusions In patients with cardiogenic shock after STEMI treated with PhIS, risk stratification using IABP-SHOCK II score was adequate. There was no influence of pain-to-needle and fibrinolytic-catheterisation times on the ability to the score model stratification.

Key questions

What is already known about this subject?
► Risk stratification models in patients with cardiogenic shock after ST elevation myocardial infarction (STEMI) are well recognised in the literature, particularly in patients undergoing primary percutaneous coronary intervention.

What does this study add?
► The study contributes to the validation of a risk stratification model in the specific setting of pharmacoinvasive strategy (PhIS), a scenario that is relatively underexplored. The results also incorporate an epidemiological knowledge about cardiogenic shock.

How might this impact on clinical practice?
► In a high-severity scenario such as cardiogenic shock after STEMI, risk stratification offers important prognostic information and may aid to selection of patients for advanced therapies. Our findings reveal that, particularly in a population treated with PhIS, the simple-to-use Intra-aortic Balloon Pump in Cardiogenic Shock II score is suitable.

important prognostic information and may direct the selection of patients for advanced therapies such as mechanical ventricular assistance and cardiac transplantation.[4–9]

Although primary percutaneous coronary intervention (PPCI) is the ideal strategy for reperfusion, the similarity between pharmacoinvasive strategy (PhIS) and PPCI has been recently demonstrated in patients without shock up to 3 hours after the onset of symptoms.[10] Based on multiple data, PhIS has been considered a valuable and effective alternative in patients who cannot reach early access to a cardiac catheterisation laboratory and it was incorporated into

INTRODUCTION

In a high-severity scenario such as cardiogenic shock after acute ST elevation myocardial infarction (STEMI), hospital mortality rates reach 50%, even after adequate reperfusion.[1–3] Immediate risk stratification offers

Table 1 Variables of the Intra-aortic Balloon Pump in Cardiogenic Shock II score

Variable	Points
Age >73 years	1
History of stroke	2
TIMI flow grade <3 after PCI	2
Glucose >191 mg/dL	1
Arterial lactate >45 mg/dL (>5 mmol/L)	2
Creatinine >1.5 mg/dL	1
Maximum	9

PCI, percutaneous coronary intervention; TIMI, Thrombolysis In Myocardial Infarction.

guidelines.[10–18] On the other hand, PhIS in cardiogenic shock has only recently been formally considered when PPCI is not available.[18] In developing countries, PhIS to patients with cardiogenic shock has been applied more often and the analysis of this population may fill gaps of knowledge on this subject.

A new and simple risk score (table 1), derived from the Intra-aortic Balloon Pump in Cardiogenic Shock II (IABP-SHOCK II Trial),[19] was developed and validated for 30-day risk of death stratification in patients with cardiogenic shock secondary to STEMI who undergo PPCI. Several demographic characteristics and the metrics of STEMI care differentiate patients receiving PPCI or PhIS.[20 21]

This study aimed to validate the IABP-SHOCK II score in a cohort of patients with cardiogenic shock secondary to STEMI treated according to a PhIS and examined the influence of ischaemia time on the different risk strata.

METHODS

A total of 2143 patients with STEMI who underwent reperfusion with tenecteplase (TNK) between May 2010 and April 2017 in primary health services and were transferred to a tertiary hospital (hub-and-spoke model), as previously reported.[16 17] Patients who progressed to cardiogenic shock due to primary ventricular failure within the first 12 hours of symptom onset, including those with signs of circulatory collapse prior to TNK administration, were included in this report. Cardiogenic shock was defined by the presence of classic clinical signs of organ hypoperfusion, sustained systolic blood pressure <90 mm Hg or need for vasoactive drugs.

In the development of the IABP-SHOCK II score, six variables were identified for stratification of the groups: age >73 years, history of stroke, blood glucose >191 mg/dL, creatinine >1.5 mg/dL, arterial lactate >45 mg/dL and Thrombolysis in Myocardial Infarction (TIMI) flow after coronary angioplasty <3. The scoring system gave one or two points for each variable based on the observed HR ranging from 0 to 9 points (table 1).[19] Patients were scored as low (0–2 points), moderate (3–4 points) and high risk (5–9 points) of death in 30 days, and the pairwise-log-rank test was used to compare death rates among strata. The area under the curve (AUC) was used to analyse the accuracy of the score, and the receiver operating characteristic curve was used to evaluate the efficiency of the variables for discrimination of death.

Time between onset of symptoms and administration of a fibrinolytic agent (pain-to-needle time) and time between thrombolytic infusion and cardiac catheterisation (fibrinolytic-catheterisation time) were compared in relation to the different strata.
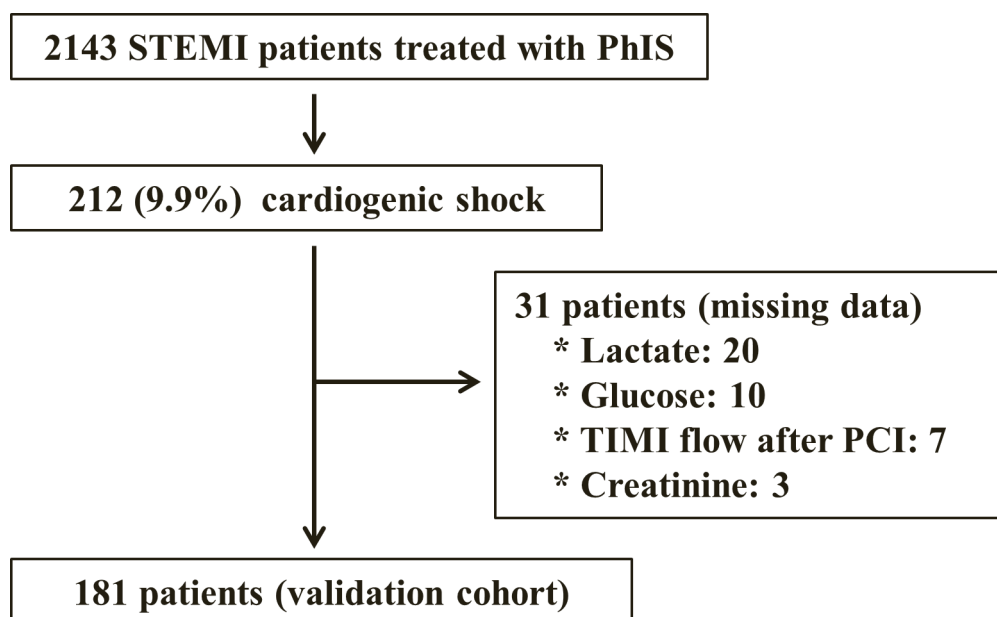

Figure 1 Validation cohort of patients with cardiogenic shock after STEMI treated with PhIS. PCI, percutaneous coronary intervention; PhIS, pharmacoinvasive strategy; STEMI, ST elevation myocardial infarction; TIMI, Thrombolysis In Myocardial Infarction.
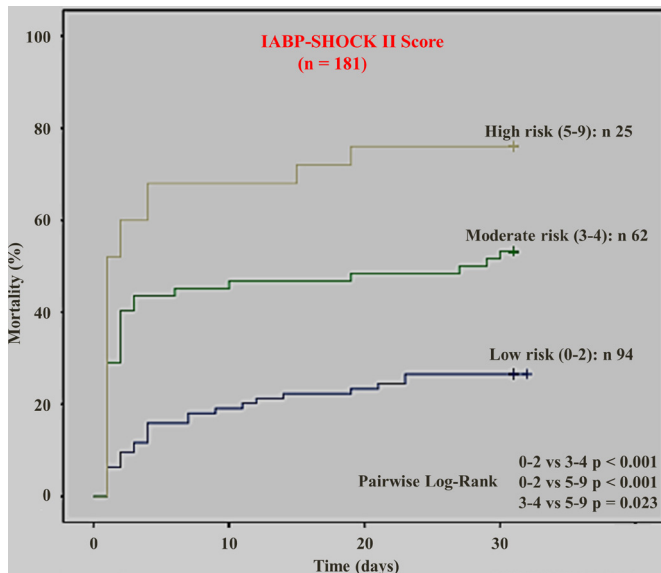
Figure 2 Kaplan-Meier analysis for 30-day mortality according to the score stratification in patients with cardiogenic shock after ST elevation myocardial infarction treated with pharmacoinvasive strategy. IABP-SHOCK II, Intra-aortic Balloon Pump in Cardiogenic Shock II.

The categorical variables were compared with the χ^2 test and the continuous variables with Student's t-test and the Mann-Whitney test. The Kruskal-Wallis test was used to compare continuous variables in three distinct groups when the normality assumption was not met. SPSS V.22.0 was used for statistical analysis. A value of $p<0.05$ was considered statistically significant.
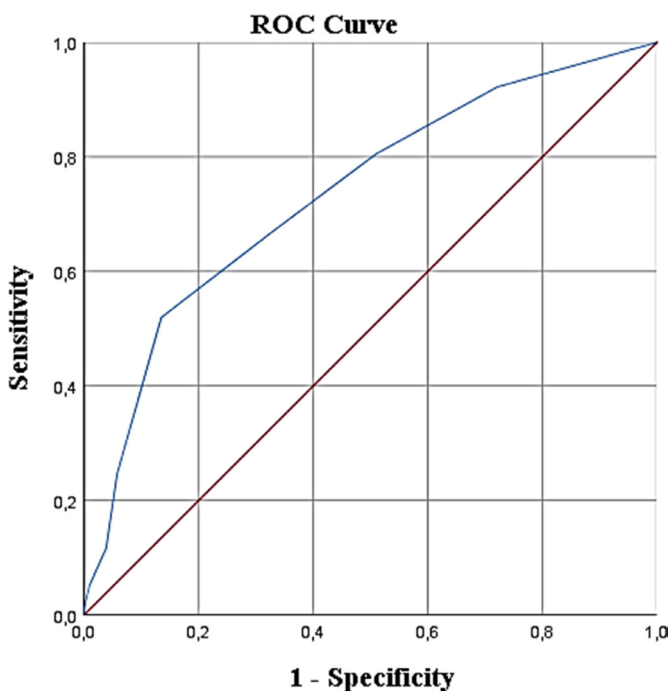

Figure 3 ROC curve Intra-aortic Balloon Pump in Cardiogenic Shock II score. ROC, receiver operating characteristic.

RESULTS

Out of 2143 patients diagnosed with STEMI treated with PhIS, 212 (9.9%) developed cardiogenic shock. In all, 31 patients (14.6%) with incomplete data were excluded from the analysis, and the validation cohort included remaining 181 patients. Mortality rates were similar between the analysed and excluded patients (42.5% and 45.1%, respectively, p=0.77) (figure 1).

The median age was 61 years, with IQR 53–71 years, 134 (63.2%) were men, 144 (67.9%) had systemic arterial hypertension, 111 (52.3%) were current or previous smokers, 106 (50%) had hypercholesterolaemia, 87 (41%) had diabetes mellitus and 14 (6.6%) had a previous stroke. The mean ejection fraction by echocardiogram was 38% and the overall use of IABP was 55.2%.

In this validation cohort, 94 (51.9%) were classified as low risk, 62 (34.2%) as moderate risk and 25 (13.9%) as high risk. The 30-day mortality in the three strata using the IABP-SHOCK II score was 26.6%, 53.2% and 76%, respectively. Comparison between groups using a Kaplan-Meier curve (figure 2) with the pairwise log-rank test showed good discrimination (low vs moderate risk, p<0.001 and moderate vs high risk, p=0.029).

The overall 30-day mortality was 42.5% (N=77), showing adequate predictive value of the score with an AUC of 0.73 (95% CI: 0.66 to 0.81; p<0.001) (figure 3).

Pain-to-needle time was significantly longer in patients who died (251 min IQR 140–528 vs 210 min, IQR 130–343 min, p=0.032). However, there was no difference between group stratification with the IABP-SHOCK II score and the median pain-to-needle time and fibrinolytic-catheterisation time according to (p=0.22 and p=0.18, respectively) table 2.

Furthermore, the AUC showed adequate accuracy for TIMI coronary flow <3 after angioplasty in the differentiation between low-risk (AUC 0.76, 95% CI: 0.66 to 0.83, p<0.001), moderate-risk (AUC 0.65, 95% CI: 0.56 to 0.73, p<0.001) and high-risk groups (AUC 0.76, 95% CI: 0.67 to 0.86, p<0.001), indicating that this variable maintained discriminatory scoring capacity despite the use of fibrinolytic agents.

DISCUSSION

Our study demonstrated the validity of the IABP-SHOCK II score in a population of patients with cardiogenic shock after STEMI treated with a PhIS. Both the mortality rate and the ability to predict risk of death in this cohort were equivalent to those in the original cohort of patients treated with PPCI from which the score was derived.[19]

PPCI treatment is the most effective reperfusion method for myocardial salvage in patients with STEMI, especially in the most severe cases, allowing faster and more complete reperfusion in late comers or in the presence of cardiogenic shock.[18] However, PhIS in cardiogenic shock is a reality in patients without immediate haemodynamic instability or places with a delay in access to a cardiac catheterisation laboratory, especially

Table 2 Comparison of pain-to-needle and fibrinolytic-catheterisation intervals in relation to groups stratified by the score

| | Intra-aortic Balloon Pump in Cardiogenic Shock II score | | | |
| | Low | Intermediate | High | |
	(N=94)	(N=62)	(N=62)	P value
Pain-to-needle	220	251	200	0.22
(Median in minutes)	IQR 135–392	IQR 150–495	IQR 120–378	
Pain-to-needle<3 hours	40 (42.5%)	23 (37.1%)	11 (44.0%)	0.85
Fibrinolytic-catheterisation	390	435	315	0.18
(Median in minutes)	IQR 280–713	IQR 280–820	IQR 232–557	

in developing countries and rural areas. The experience of previous randomised trials including only patients with short pain-to-needle times is hardly transferred to clinical practice where the same socioeconomic factors that hamper access to PPCI increase ischaemic times.[15 17]

Clearly, as the time for administration increases, the efficacy of fibrinolytic agents in PhIS is reduced, and this fact may affect not only mortality rates but also TIMI 3 coronary flow rates after angioplasty.[22] However, the AUC in the different strata of our population showed adequate accuracy of TIMI coronary flow <3 after angioplasty, indicating that this variable maintains adequate discriminatory capacity for scoring mechanical reperfusion and was not influenced by pre-PCI flow or by the delay in reaching the catheterisation laboratory (more than 6 hours).

As expected, the time between onset of symptoms and administration of a fibrinolytic agent (pain-to-needle time) was significantly longer in patients who died. However, pain-to-needle and fibrinolytic-catheterisation times were not associated with the group stratification using the IABP-SHOCK II score. This finding may be explained by the potential of these variables to be more closely associated with the development of cardiogenic shock in patients with STEMI treated with PhIS, and to be less associated with progression to death when the patient is already in shock.

The need for early identification of patients with cardiogenic shock and a higher risk of death than usual is obvious, since early intervention could prevent an unfavourable outcome. In addition, the validation of an easy-to-use risk score has the potential to become a very useful tool for emergency physicians and intensivists, especially when delays in standard ideal treatments may impact outcomes.

CONCLUSIONS
The IABP-SHOCK II score is suitable for 30-day risk-of-death stratification in patients with cardiogenic shock secondary to STEMI treated with PhIS. Although prolonged pain-to-needle time was associated with higher mortality, there was no influence of pain-to-needle and fibrinolytic-catheterisation times on the ability to the score model stratification.

Limitations of the study
Although data were collected prospectively, this was a retrospective analysis of a cohort that originated from a single tertiary STEMI (online supplementary file 1) treatment centre. Since all patients received TNK, our results do not necessarily apply to populations using other types of fibrinolytic agents or different PhIS models (non-systematic cardiac catheterisation or different time intervals for cardiac catheterisation or fibrinolytic infusion). The exclusion of 31 of the 212 patients (14.6%) with cardiogenic shock is a limitation mitigated by the fact that mortality was not significantly different between the excluded group and the validation cohort used for scoring.

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