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

Pedro Ivo M Moraes,¹ Claudia Rodrigues Alves,¹ Marco Tulio Souza,¹ Suzi Emiko Kawakami,¹ Iran Goncalves Jr,¹ Adriano Henrique Pereira Barbosa,¹ Antonio Celio Moreno,² Adriano Mendes Caixeta,^{1,3} Antonio Carlos Carvalho¹

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¹Discipline of Cardiology - Department of Medicine, Federal University of Sao Paulo, Sao Paulo, Brazil

²Department of Cardiology, Hospital do Servidor Público Municipal, Sao Paulo, Brazil

³Department of Cardiology, Hospital Israelita Albert Einstein, Sao Paulo, Brazil

Correspondence to

Dr Pedro Ivo M Moraes; pedroivo_mm@hotmail.com

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.

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

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

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			P value
	Low (N=94)	Intermediate (N=62)	High (N=62)	
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.

Contributors ACC and PIM conceived of the presented idea. PIM and CRA developed the theory and performed the computations. MTS, SEK, AMC, AHPB, IGJ and ACM contributed to data collect and a critical review of the abstract. All authors discussed the results and contributed to the final manuscript.

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REFERENCES

- Kolte D, Khera S, Aronow WS, *et al.* Trends in incidence, management, and outcomes of cardiogenic shock complicating ST-elevation myocardial infarction in the United States. *J Am Heart Assoc* 2014;3:e000590.
- Goldberg RJ, Spencer FA, Gore JM, *et al.* Thirty-year trends (1975 to 2005) in the magnitude of, management of, and hospital death rates associated with cardiogenic shock in patients with acute myocardial infarction: a population-based perspective. *Circulation* 2009;119:1211–9.
- Aissaoui N, Puymirat E, Tabone X, *et al.* Improved outcome of cardiogenic shock at the acute stage of myocardial infarction: a report from the USIK 1995, USIC 2000, and FAST-MI French nationwide registries. *Eur Heart J* 2012;33:2535–43.
- Katz JN, Stebbins AL, Alexander JH, *et al.* Predictors of 30-day mortality in patients with refractory cardiogenic shock following

- acute myocardial infarction despite a patent infarct artery. *Am Heart J* 2009;158:680–7.
5. Sutton AGC, Finn P, Hall JA, *et al.* Predictors of outcome after percutaneous treatment for cardiogenic shock. *Heart* 2005;91:339–44.
 6. Klein LW, Shaw RE, Krone RJ, *et al.* Mortality after emergent percutaneous coronary intervention in cardiogenic shock secondary to acute myocardial infarction and usefulness of a mortality prediction model. *Am J Cardiol* 2005;96:35–41.
 7. Garcia-Alvarez A, Arzamendi D, Loma-Osorio P, *et al.* Early risk stratification of patients with cardiogenic shock complicating acute myocardial infarction who undergo percutaneous coronary intervention. *Am J Cardiol* 2009;103:1073–7.
 8. Sleeper LA, Reynolds HR, White HD, *et al.* A severity scoring system for risk assessment of patients with cardiogenic shock: a report from the shock trial and registry. *Am Heart J* 2010;160:443–50.
 9. Pöss J, Desch S, Thiele H. Shock management in acute myocardial infarction. *EuroIntervention* 2014;10 Suppl T:T74–T82.
 10. Armstrong PW, Gershlick AH, Goldstein P, *et al.* Fibrinolysis or primary PCI in ST-segment elevation myocardial infarction. *N Engl J Med* 2013;368:1379–87.
 11. Di Mario C, Dudek D, Piscione F, *et al.* Immediate angioplasty versus standard therapy with rescue angioplasty after thrombolysis in the combined abciximab reteplase stent study in acute myocardial infarction (CARESS-in-AMI): an open, prospective, randomised, multicentre trial. *Lancet* 2008;371:559–68.
 12. Danchin N, Coste P, Ferrières J, *et al.* Comparison of thrombolysis followed by broad use of percutaneous coronary intervention with primary percutaneous coronary intervention for ST-segment-elevation acute myocardial infarction: data from the French registry on acute ST-elevation myocardial infarction (FAST-MI). *Circulation* 2008;118:268–76.
 13. Cantor WJ, Fitchett D, Borgundvaag B, *et al.* Routine early angioplasty after fibrinolysis for acute myocardial infarction. *N Engl J Med* 2009;360:2705–18.
 14. Fernández-Avilés F, Alonso JJ, Peña G, *et al.* Primary angioplasty vs. early routine post-fibrinolysis angioplasty for acute myocardial infarction with ST-segment elevation: the GRACIA-2 non-inferiority, randomized, controlled trial. *Eur Heart J* 2007;28:949–60.
 15. Elguindy AM. Lessons from the trials stream and FAST-MI – Pharmacoinvasive therapy: a continued role for fibrinolysis in the primary PCI era.
 16. Caluza ACV, Barbosa AH, Gonçalves I, *et al.* Rede de infarto com supradesnívelamento de ST: sistematização em 205 casos diminui eventos clínicos Na rede pública. *Arq Bras Cardiol* 2012;99:1040–8.
 17. Ferreira GM, Moraes PIM, Carvalho AC, *et al.* ST segment elevation myocardial infarction (STEMI) network sustains low hospital mortality throughout the years in an emerging country location. *Eur Heart J* 2014;35:1173–4.
 18. Ibanez B, James S, Agewall S, *et al.* 2017 ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J* 2018;39:119–77.
 19. Pöss J, Köster J, Fuernau G, *et al.* Risk Stratification for Patients in Cardiogenic Shock After Acute Myocardial Infarction. *J Am Coll Cardiol* 2017;69:1913–20.
 20. Boden WE, Eagle K, Granger CB. Reperfusion strategies in acute ST-segment elevation myocardial infarction. *J Am Coll Cardiol* 2007;50:917–29.
 21. Abbott JD. Pharmacoinvasive strategy for ST-segment elevation myocardial infarction: wading through the treatment options. *Circ Cardiovasc Interv* 2010;3:294–6.
 22. Boersma E, Maas AC, Deckers JW, *et al.* Early thrombolytic treatment in acute myocardial infarction: reappraisal of the golden hour. *Lancet* 1996;348:771–5.