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EDITORIAL
Acute coronary syndromes

Predicting the unpredictable: a novel application of artificial intelligence in the cardiac intensive care unit

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This editorial refers to 'Development and external validation of a dynamic risk score for early prediction of cardiogenic shock in cardiac intensive care units using machine learning', by Y. Hu *et al*. https://doi.org/10.1093/ehjacc/zuae037.

Cardiogenic shock (CS) is a common indication for admission to the cardiac intensive care unit (CICU), and patients with shock account for most deaths in the CICU.[1,2] The incidence of CS in patients with acute myocardial infarction (AMI) remains 5–10% despite early reperfusion, being two-fold higher in ST-elevation myocardial infarction (STEMI) vs. non-ST-elevation myocardial infarction (NSTEMI).[2-6] The prevalence of CS among patients with AMI admitted to the CICU is even higher, reflecting selection bias.[1] The majority of patients with AMI-CS develops early CS within 24 h of presentation, but at least one in four may develop late CS.[3,4,7] In recent years, CS due to heart failure (HF) has accounted for a greater proportion of CS cases than AMI, although the prevalence of CS in the broader population of hospitalized patients with HF is not well-described.[1,8] Among CICU patients admitted with HF, approximately one in four carry an admission diagnosis of CS.[9]

Established risk factors for CS in patients with AMI include clinical evidence of HF, older age, higher heart rate, lower blood pressure, and delayed presentation; early aggressive beta-blockade can contribute in at-risk patients.[2,5,6,10,11] The Observatoire Regional Breton sur l'Infarctus (ORBI) risk score was developed in 2018 to include 11 risk factors for CS in patients with STEMI (*Table 1*).[5] This risk score performed well, with a validation AUC of 0.8 that has since been externally replicated; the high-risk group had a one in three incidence of CS.[5,10] More recently, basic machine learning (ML) techniques were applied to develop risk prediction models for CS in patients with STEMI; the LASSO penalized regression technique produced the best model that included eight risk factors (*Table 1*), with an AUC of 0.82 that outperformed the ORBI score.[11] Despite the potential usefulness of these scores for early identification of STEMI patients at elevated risk of CS, similar scoring systems for patients with NSTEMI or decompensated HF do not exist, and only a minority of contemporary CS patients have STEMI.[1] Furthermore, these scores only predict the risk based on static data from the time of admission, and lack any dynamic component to facilitate identification of patients who are clinically deteriorating and at risk of late CS.[13,14]

Regardless of the aetiology, established CS carries a poor prognosis with a short-term mortality of 30–50%.[1,2,4,5,8] Studies vary regarding whether early vs. late onset of CS is associated with worse outcomes, but mortality is high regardless of the time of CS onset.[3,7,14] Delayed recognition of CS can predispose to more severe organ injury from uncorrected hypoperfusion with triggering of a downward spiral of worsening shock, creating strong justification for early identification and stabilization of patients at risk for CS even if they do not meet criteria for CS on CICU admission.[2] This is particularly important because many institutions are shifting low-risk STEMI patients out of the CICU, necessitating effective risk stratification tools to ensure that patients are safely triaged to lower-acuity care environments.[15] Given the dearth of effective therapies for improving survival in established CS, identifying patients early during the clinical course when their CS and organ dysfunction may be reversible is a priority. Accordingly, there is a critical unmet need to develop robust predictive models to identify late-onset CS in CICU patients across the spectrum of AMI and HF. Early recognition of impending CS could facilitate timely escalation of care, adjustment of guideline-directed medical therapies, and haemodynamic stabilization to avoid progression.[2] For example, implementation of temporary mechanical circulatory support in early or mild CS might potentially be effective, while use of these devices later during the disease course has generally failed to improve outcomes.

The manuscript by Hu *et al*.[12] published in this issue of the *European Heart Journal: Acute Cardiovascular Care* is therefore an important step forward in the use of predictive analytics to facilitate early identification of patients at risk of CS. Using ML methods, these authors sought to develop a dynamic prediction algorithm for late-onset CS (including mixed shock but excluding non-cardiogenic shock) in medical CICU patients with AMI or decompensated HF. For model derivation, they used the MIMIC-III database to identify 1500 CICU patients with AMI or HF, of whom 204 (13.6%) had the outcome (i.e. eventually met criteria for CS). They employed a ML method based on a dilated causal convolutional neural network (CNN) to perform time-series modelling, with the model updated every hour to provide dynamic risk stratification.

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Table 1 Risk factors included in predictive scores for cardiogenic shock in STEMI, with the top 10 most important variables from the model by Hu *et al.*[5,11,12]

ORBI risk score[5]	LASSO model[11]	CShock[12]
Older age (>70 years)	Older age	—
Previous stroke or TIA	Chronic kidney disease (eGFR < 60 mL/min)	—
First medical contact to PCI > 90 min	Delayed presentation > 12 h	—
Anterior STEMI	—	STEMI
Heart failure (Killip Class II/III)	—	Acute HF
Cardiac arrest	—	Lower Glasgow coma scale
—	—	Lower Braden scale
Higher heart rate (>90 b.p.m.)	Higher shock index (heart rate/systolic blood pressure ratio)	Higher heart rate
Lower systolic blood pressure (<125 mmHg) with lower pulse pressure (<45 mmHg)	—	Lower systolic blood pressure
Higher blood glucose (>180 mg/dL)	Higher white blood cell count	—
—	Lower haemoglobin	—
—	Higher LDH	—
—	Higher AST (>500 IU/mL)	—
—	—	Higher blood urea nitrogen
—	—	Lower serum chloride
—	—	Lower serum sodium
—	—	Lower arterial pH
Left main culprit artery	—	—
Post-PCI TIMI flow grade < 3	—	—

AST, aspartate aminotransferase; b.p.m., beats per minute; eGFR, estimated glomerular filtration rate; HF, heart failure; LDH, lactate dehydrogenase; PCI, percutaneous coronary syndrome; STEMI, ST-segment elevation myocardial infarction; TIA, transient ischaemic attack.

This model tested 194 input features (182 were time-varying) that were either derived from routinely available measurements in EHR or from chart review of discharge summaries and echocardiogram reports. Convolutional neural network is useful for temporal data because of its chronological principle—the prediction made by the model at one timestep cannot depend on future timesteps. The output of the dilated causal CNN captured the patient's overall physiological state at each hour, producing a time-varying risk score for cardiogenic shock named 'CShock.' The model demonstrated an AUC of 0.82 and could predict the onset of CS more than 36 h ahead of time. A model built using only the top 10 predictors (*Table 1*) performed nearly as well as the full model. The model performed substantially better in patients with STEMI (AUC 0.88), as well as in younger patients and male patients who had a lower risk of CS. Validation in a cohort of 131 institutional CICU patients (19.1% with CS) showed similar performance (AUC 0.80).

This analysis has several strengths that make it an important contribution to the literature. First, the authors included a heterogeneous cohort, with both STEMI and NSTEMI patients as well as decompensated HF, which makes it more representative of the true CICU population and therefore clinically useful. Second, the authors focused on discrete, objective data points (predominantly physiologic measurements) that can be reliably extracted from the electronic health record to allow automation of risk prediction. Third, the authors employed both a multicentre derivation and separate validation cohort, which offers hope of greater external generalizability that has been lacking from many ML risk prediction studies. Fourth, the authors included numerous candidate predictors in the full model, allowing a broad range of potential physiologic processes to be incorporated, and yet were able to build simplified models with equivalent performance and easier clinical use. Finally, the authors employed a more sophisticated ML method than the prior study by Bai *et al.*[11] This enabled creation of a dynamic risk score that could predict late-onset CS in a semi-continuous manner, as opposed to static risk scores based on admission values only.[5,11,13] Heart rate and systolic blood pressure are important risk factors for prediction of CS, and a dynamic score that can incorporate changes or trends in these values would logically be more effective at recognizing early or impending CS (particularly late-onset events) than a single measurement.[5,6,11,12] Identification of at-risk patients > 36 h ahead of time would permit ample time for interventions to be performed in clinical practice.

Despite these strengths, this analysis carries relevant limitations that merit discussion. A key issue is the finding that the admission diagnosis (STEMI vs. HF) was one of the strongest predictors of late CS—knowing that patients with these diagnoses have a different risk of CS is less useful than individualizing the risk prediction in patients according to diagnosis. Model performance was poorer in NSTEMI and HF patients, and when a diagnosis-agnostic model was built. The epidemiology of CS in this CICU cohort is a bit unusual—a late-onset CS incidence of 13–19% is quite high considering the total CS incidence (most of which is early) is often reported less than this.[2-7] This is notable because the observed mortality of patients with late CS in this study was only 15%, dramatically lower than the expected mortality according to previous studies.[1-7,14] The combination of high prevalence and low mortality suggests that the authors' definition of CS, while seemingly appropriate, was identifying patients with borderline or low shock severity. This might have introduced

a bias through 'data leakage,' since the authors pre-trained the ML model using mortality. Additionally, the long lead time involved prior to CS diagnosis raises important questions about who the patients were (i.e. why they were in the CICU for so long if they did not already have CS), and what underlying process may have progressed to the development of CS. Ultimately, this could adversely affect the broad generalizability of the model if the demographic patterns of CICU patients and processes of care differed substantially between centres. This is particularly relevant if the goal is to identify patients outside of the CICU setting who are at risk of CS, recognizing that they may have substantially different pre-test probability and model performance. Finally, the nature of the ML method and model are such that the risk of CS cannot be calculated by hand or using an application, even for the 10-feature model. While this could be overcome using modern electronic health record systems, it limits usefulness in clinical practice. Nonetheless, this analysis represents an important step forward in the development of ML tools for predicting CS in the CICU.

Conflict of interest: None declared.

Data availability

There are no original data in this work.

References

1. Jentzer JC, Ahmed AM, Vallabhajosyula S, Burstein B, Tabi M, Barsness GW, *et al.* Shock in the cardiac intensive care unit: changes in epidemiology and prognosis over time. *Am Heart J* 2020;**232**:94–104.
2. Chioncel O, Parissis J, Mebazaa A, Thiele H, Desch S, Bauersachs J, *et al.* Epidemiology, pathophysiology and contemporary management of cardiogenic shock—a position statement from the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail* 2020;**22**:1315–1341.
3. Lindholm MG, Kober L, Boesgaard S, Torp-Pedersen C, Aldershvile J; Trandolapril Cardiac Evaluation study group. Cardiogenic shock complicating acute myocardial infarction; prognostic impact of early and late shock development. *Eur Heart J* 2003;**24**:258–265.
4. Obling L, Frydland M, Hansen R, Møller-Helgestad OK, Lindholm MG, Holmvang L, *et al.* Risk factors of late cardiogenic shock and mortality in ST-segment elevation myocardial infarction patients. *Eur Heart J Acute Cardiovasc Care* 2018;**7**:7–15.
5. Auffret V, Cottin Y, Leurent G, Gilard M, Beer J-C, Zabalawi A, *et al.* Predicting the development of in-hospital cardiogenic shock in patients with ST-segment elevation myocardial infarction treated by primary percutaneous coronary intervention: the ORBI risk score. *Eur Heart J* 2018;**39**:2090–2102.
6. Kontos MC, Diercks DB, Ho PM, Wang TY, Chen AY, Roe MT. Treatment and outcomes in patients with myocardial infarction treated with acute beta-blocker therapy: results from the American College of Cardiology's NCDR((R)). *Am Heart J* 2011;**161**:864–870.
7. Webb JG, Sleeper LA, Buller CE, Boland J, Palazzo A, Buller E, *et al.* Implications of the timing of onset of cardiogenic shock after acute myocardial infarction: a report from the SHOCK Trial Registry. SHould we emergently revascularize occluded coronaries for cardiogenic shocK? *J Am Coll Cardiol* 2000;**36**:1084–1090.
8. Abraham J, Blumer V, Burkhoff D, Pahuja M, Sinha SS, Rosner C, *et al.* Heart failure-related cardiogenic shock: pathophysiology, evaluation and management considerations: review of heart failure-related cardiogenic shock. *J Card Fail* 2021;**27**:1126–1140.
9. Jentzer JC, Reddy YN, Rosenbaum AN, Dunlay SM, Borlaug BA, Hollenberg SM. Outcomes and predictors of mortality among cardiac intensive care unit patients with heart failure. *J Card Fail* 2022;**28**:1088–1099.
10. Berton F, Polero LD, Candiello A, Rodriguez L, Costabel JP. ORBI score validation as predictor of cardiogenic shock in patients with ST elevation myocardial infarction in two medical centers in Argentina. *Curr Probl Cardiol* 2023;**48**:101136.
11. Bai Z, Hu S, Wang Y, Deng W, Gu N, Zhao R, *et al.* Development of a machine learning model to predict the risk of late cardiogenic shock in patients with ST-segment elevation myocardial infarction. *Ann Transl Med* 2021;**9**:1162.
12. Hu Y, Lui A, Goldstein M, Sudarshan M, Tinsay A, Tsui C, *et al.* Development and external validation of a dynamic risk score for early prediction of cardiogenic shock in cardiac intensive care units using machine learning. *Eur Heart J Acute Cardiovasc Care* 2024:zuae037.
13. Jentzer JC, Rossello X. Past, present, and future of mortality risk scores in the contemporary cardiac intensive care unit. *Eur Heart J Acute Cardiovasc Care* 2021;**10**:940–946.
14. Jentzer JC, Van Diepen S, Patel PC, Henry TD, Morrow DA, Baran DA, *et al.* Serial assessment of shock severity in cardiac intensive care unit patients. *J Am Heart Assoc* 2023;**12**:e032748.
15. Nan JZ, Jentzer JC, Ward RC, Le RJ, Prasad M, Barsness GW, *et al.* Safe triage of STEMI patients to general telemetry units after successful primary percutaneous coronary intervention. *Mayo Clin Proc Innov Qual Outcomes* 2021;**5**:1118–1127.