# scientific reports



## **OPEN**

# The association between Oxford Acute Severity of Illness Score and mortality in critical hemorrhagic stroke patients: a retrospective cohort study

Yuan Jiang¹, Shuying Qiu², Qianyi Peng¹, Li Huang¹™ & Lina Zhang¹™

Hemorrhagic stroke is a kind of disastrous cerebrovascular disease, Oxford Acute Severity of Illness Score (OASIS) was only evaluated among mixed critically ill patients, its predictive value in hemorrhagic stroke patients remains undiscovered. Evaluate the association between Oxford Acute Severity of Illness Score (OASIS) and mortality in critical hemorrhagic stroke patients. A retrospective cohort study. Data were extracted from a public database named Medical Information Mart for Intensive Care III (MIMIC-III). 1838 critical hemorrhagic stroke patients were included, multivariable logistic regression and receiver operating characteristic (ROC) curves were mainly used to analyze data. ROC curve analyses were also conducted in hemorrhagic stroke patients stratified by Glasgow Coma Scale (GCS) as subgroup analyses. The primary outcome was 30-day mortality. The sample size of this study is 1838 patients. The OASIS was significantly correlated with 30-day mortality (Odds ratio (OR) 1.125 per one-point increase, 95% confidence interval (CI) [1.107–1.144], p < 0.0001), the area under the ROC curve (AUC) of OASIS was comparable to that of Simplified Acute Physiology Score II (SAPSII) for predicting 30-day mortality (AUC: 0.7702 vs. 0.788, P = 0.096). Sensitivity analyses showed the results were stable. In subgroup analyses OASIS also has the similar discriminatory power to predict 30-day mortality for the severe (GCS 3-8) and mild (13-15) hemorrhagic stroke patients, but it has lower discriminatory power to predict 30-day mortality for the moderate (9-12) patients. The OASIS might serve as an alternative choice to predict outcomes of severe and mild hemorrhagic stroke patients in consideration of the practicality. Selection bias was unavoidable because this study was a retrospective observational study.

Keywords OASIS, Hemorrhagic stroke, Prognosis, Intensive care unit

Hemorrhagic stroke is a disastrous cerebrovascular accident with high morbidity and mortality<sup>1</sup>. Hemorrhagic stroke patients generally require critical care in intensive care unit (ICU), mechanical ventilation is the major risk factor for the death of hemorrhagic stroke patients, the mortality ranges from 40 to 80% in previous literatures<sup>2,3</sup>.

Scoring systems have been designed to predict prognosis for ages, some of scoring systems have been extensively used in ICU for critical illness, for example, the Simplified Acute Physiology Score II (SAPS II)<sup>4</sup>. SAPSII was developed to assess the severity of critically ill patients primordially, including hemorrhagic stroke patients in ICU. With the application of SAPSII, patients under threat of dying from hemorrhagic stroke patients was identified. The SAPSII contains complex laboratory results, while clinicians usually prefer a score system which is easy to perform without lots of laboratory parameters. The Oxford Acute Severity of Illness Score (OASIS) was raised by Johnson, Kramer & Clifford in 2013, it is a new critical illness score based on machine-learning algorithms with no laboratory parameter, which possessed comparable discrimination and standard than other complex scores<sup>5,6</sup>. In consideration of the predictive value of the OASIS was mainly evaluated among mixed critical ill patients, its predictive value in hemorrhagic stroke patients remains undiscovered. So we

<sup>1</sup>Department of Critical Care Medicine, Xiangya Hospital, Central South University, Changsha 410008, Hunan, People's Republic of China. <sup>2</sup>Department of Critical Care Medicine, Third Xiangya Hospital, Central South University, Changsha 410013, Hunan, People's Republic of China. <sup>™</sup>email: huang|200903@126.com; 2675283030@qq.com

assessed the correlation between OASIS and the prognosis of hemorrhagic stroke patients in ICU, and compared its predictive value with the SAPS II.

### Methods

### Database and criteria

The MIMIC-III is a freely-available database, consists of clinical data of more than 40,000 patients who was hospitalized in the Beth Israel Deaconess Medical Center from 2001 to 2012<sup>7</sup>. It contains detailed data including clinical outcomes, lab results, scoring systems and so on<sup>8</sup>. The data in MIMIC-III underwent de-identification, and the utilization of the database for research purposes was granted approval by the Institutional Review Boards of Massachusetts Institute of Technology and Beth Israel Deaconess Medical Center. As a result, the informed consent and approval of the Institutional Review Board were waived.

Inclusion criteria were: (1) patients were diagnosed as hemorrhagic stroke, namely either subarachnoid hemorrhage (SAH; ICD-9 430) or intracerebral hemorrhage (ICH; ICD-9 431)<sup>9</sup>; (2) patients were more than 18 years old; (3)Patients were admitted to ICU, if the same patient was admitted to ICU repeatedly, first admission was chosen. Exclusion criteria were: (1) patients who stayed ICU for less than 24 h; (2) clerical error, such as the ICU stay was longer than hospital stay. Because the patients are de-identified, no informed consent was required.

### Data extraction

Transact-SQL and related MIMIC-III codes were applied to extract data<sup>10</sup>. General information including age, sex was extracted from the MIMIC-III database, so was the inspection result including white blood cell count, blood platelet and hemoglobin on admission. Data on hemorrhagic stroke severity score systems were also extracted including OASIS, SAPSII and Glasgow Coma Scale (GCS) on admission. For comorbidity evaluation, we extracted the Elixhauser score, chronic obstructive pulmonary disease, coronary heart disease, hypertension and diabetes. Length of ICU stay and hospital stay were computed according to the extracted data. Patients whose ages were more than 89 years old shifted to 300 years for privacy, before analyses we corrected them by this formula: age-300+89.

### **Outcomes**

The primary research outcome was 30-day mortality, while ICU mortality and hospital mortality were considered as secondary outcomes. The length of ICU stay and hospital stay were excluded from the analysis, serving only for statistical description.

### Statistical analysis

The descriptive statistics for continuous variables included the median, 25th percentile, and 75th percentile. Categorical variables were presented as frequencies and percentages. Mann-Whitney U tests were used to analyze continuous variables, while Chi-squared tests were employed for comparing categorical variables, if the values of categorical variables were below 10, Fisher's exact tests were applied instead of Chi-squared tests. A multivariable logistic regression was performed for assessing the associations of OASIS and ICU outcomes. The determinants of the primary outcome were evaluated by univariable logistic analyses, the variables with p value<0.2 were applied for the multiple analyses. The AUC was used to comparing the discriminatory power between two score system, the statistical significance of the discriminative difference was tested with the DeLong test for correlated ROC curves. The most appropriate threshold of each scoring system was determined by Youden's index, Kaplan–Meier curves was applied to assess the survival of patients grouped by threshold. we performed sensitive analyses by excluding patients more than 80 years old to test the stableness of the results. Different subgroups stratified by GCS score were analyses by logistic regression analyses to evaluate association between OASIS and the primary outcome. Software Stata V.11.2All was used to statistical analyses. All tests were two sided, the significance level was identified as p = 0.05.

### Use of experimental animals, and human participants

The present study was a retrospective analysis utilizing openly accessible datasets and did not deal with human participants or cohorts. Consequently, the requirement for consent was inapplicable. Solely computational methodologies were employed, with no implementation of clinical or experimental approaches. All procedures adhered to pertinent guidelines and regulations.

### Results

### Baseline characteristics of patients

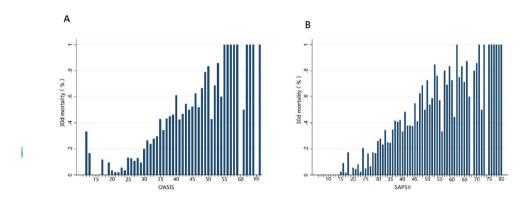
A total of 1838 hemorrhagic stroke patients in ICU were included in this analysis, comprising 1279 survivors and 559 non-survivors, the median of OASIS on admission is 33 (27–39). The median age of the patients was 66.57 years (54.08–78.56), 942 patients (52.64%) were male. The Comorbidities of chronic obstructive pulmonary disease, coronary heart disease, hypertension and diabetes were 0.54%, 10.34%, 58.43% and 19.04% respectively. The 30-day mortality was 30.41% (559 non-survivors and 1279 survivors). The hospital mortality and ICU mortality were 25.57% and 20.02% respectively. The length of ICU stay was 3.21(1.67–8.42), and the length of hospital stay was 8.67(4.5-15.58). More details are presented in Table 1.

### OASIS and clinical outcomes of hemorrhagic stroke patients

The OASIS on admission of non-survivors was significantly higher than that of survivors (39 (34–44) vs. 30 (25–36), p < 0.001), the distributions of OASIS and SAPSII with relevant 30-day mortality were showed in Fig. 1. The 30-day mortality increased as OASIS increased to a first approximation, so was the 30-day mortality and SAPSII.

Variable	All patients (n = 1838)	Survivors ( <i>n</i> = 1279)	Non-survivors (n = 559)	p
Age (years)	65.79 (54.08–78.56)	62.91 (51.79-74.83)	74.49 (60.37–82.13)	< 0.001
Male	942 (51.25%)	657 (51.37%)	285 (50.98%)	0.879
Hospital mortality	470 (25.57%)	0 (0%)	470 (84.08%)	< 0.001
ICU mortality	368 (20.02%)	0 (0%)	368 (65.83%)	< 0.001
Length of ICU stay (days)	3.21 (1.67-8.42)	3.5 (1.71-10)	2.88 (1.54-6.33)	< 0.001
Length of hospital stay (days)	8.67 (4.5-15.58)	10.5 (5.92-17.67)	4.58 (1.71-9.75)	< 0.001
OASIS on admission	33 (27–39)	30 (25–36)	39 (34–44)	< 0.001
SAPS II on admission	33 (25-42)	37 (22–37)	42 (34–52)	< 0.001
GCS score on admission	14 (11–15)	14 (12–15)	15 (7–15)	0.385
White blood cell count on admission (k/uL)	10.8 (8.2–14)	10.3 (7.9–13.1)	12.3 (9-15.7)	< 0.001
Blood platelet (k/μL)	223 (178–281)	226 (183–280)	217 (163–282)	0.004
Hemoglobin (g/dL)	12.1 (10.8-13.3)	12.2 (11.1-13.4)	11.8 (10.2-13.1)	< 0.001
Elixhauser Comorbidity Index (SID30)	8 (0-14)	5 (0-13)	8 (0-17)	< 0.001
Comorbidities				
Chronic obstructive pulmonary disease	10 (0.54%)	5 (0.39%)	5 (0.89%)	0.183
Coronary heart disease	190 (10.34%)	123 (9.62%)	67 (11.99%)	0.125
Hypertension	1074 (58.43%)	743 (58.09%)	331 (59.21%)	0.654
Diabetes	350 (19.04%)	225 (17.59)	125 (22.36%)	0.017

**Table 1.** Characteristics and comparison between survivors and non-survivors determined by 30-day mortality. Patients were grouped as survivors and non-survivors determined by 30-day mortality. Data are expressed as median (25th–75th percentiles) or n (%) unless otherwise stated. Mann–Whitney U and Chisquare (or Fisher's exact if values in any of the cells of a contingency table are below 10) tests were used to analyze continuous and categorical variables, respectively. Statistical significance (p<0.05) is shown in bold. The asterisk indicated that the Fisher's exact test was used instead of the Chi-squared test. ICU, intensive care unit; OASIS, Oxford Acute Severity of Illness Score; SAPS II, Simplified Acute Physiology Score II; GCS, Glascow coma score.



**Fig. 1.** Association between different severity scores on admission and 30-day mortality. (**A**) 30-day mortality by OASIS on admission among critical patients with hemorrhagic stroke; (**B**) 30-day mortality by SAPSII on admission among critical patients with hemorrhagic stroke. OASIS, Oxford Acute Severity of Illness Score; SAPSII, Simplified Acute Physiology Score II.

The age, initial white blood cell count, initial platelet count, initial hemoglobin concentration, GCS and the Elixhauser Comorbidity Index were used in the multivariable regression analyses according to the univariable logistic regression analyses (presented in Table S5). By the adjusted multivariable regression analyses, the OASIS demonstrated a significant association with 30-day mortality (OR 1.125 per one-point increase, 95% CI [1.107–1.144], p < 0.0001), ICU mortality (OR 1.150 per one-point increase, 95% CI [1.128–1.172], p < 0.001), and hospital mortality (OR 1.140 per one-point increase, 95% CI [1.121–1.161], p < 0.001), more details were showed in Table 2. Results of analyses of the SAPS II are presented in Table S6.

### Discriminatory power of the OASIS in hemorrhagic stroke patients

The AUC of OASIS for predicting 30-day mortality was 0.7702 (95% CI [0.748-0.793]), which demonstrated comparable performance to the SAPSII score (AUC 0.788, 95% CI [0.766-0.810], P=0.096) (Figure S3). The best threshold of OASIS was 35, the specificity and sensitivity were 72.45% and 69.43% respectively, positive

Outcomes	OR	95%CI	p		
30-day mortality					
Non-adjusted	1.132	[ 1.116–1.149 ]	< 0.001		
Adjusted	1.125	[ 1.107-1.144 ]	< 0.001		
ICU mortality					
Non-adjusted	1.132	[ 1.114–1.151 ]	< 0.001		
Adjusted	1.150	[ 1.128–1.172 ]	< 0.001		
Hospital mortality					
Non-adjusted	1.138	[ 1.121–1.156 ]	< 0.001		
Adjusted	1.140	[ 1.121–1.161 ]	< 0.001		

**Table 2.** Association of OASIS with 30-day mortality, ICU mortality and hospital mortality. Associations of OASIS with 30-day mortality, ICU mortality and hospital mortality and were analyzed using logistic regression models. Model was adjusted for age, initial white blood cell count, initial platelet count, initial hemoglobin concentration, GCS and the Elixhauser Comorbidity Index (SID30). Statistical significance (p < 0.05) is shown in bold. OASIS, the Oxford Acute Severity of Illness Score; ICU, intensive care unit; OR, odds ratio; CI, confidence interval.

likelihood ratio was 2.3699 and negative likelihood ratio was 0.3968 (Table S7). The AUC of OASIS for predicting ICU mortality and hospital mortality were similar to that of SAPSII, as presented in Figure S3. The Kaplan–Meier curves showed that higher OASIS score predicted shorter survival time for hemorrhagic stroke patients, so was the SAPSII (Figure S4).

We further evaluated the performance of the OASIS and SAPSII scales in predicting 30-day mortality in ICU patients(including hemorrhagic stroke and non-hemorrhagic stroke patients in ICU, in total 53423 patients), and found that SAPSII had a significantly higher AUC for predicting 30-day mortality rate compared to OASIS (AUC 0.793, 95%CI[0.787–0.798] vs. AUC 0.760, 95%CI[0.754–0.767], p=0.000). This suggests that the predictive efficacy of the OASIS and SAPSII scales for prognosis differs between hemorrhagic stroke patients and ICU patients (Figure S5).

### Sensitive analyses

We performed sensitive analyses to evaluate the stableness of results by excluded hemorrhagic stroke patients who are more than 80 years old (> 80 years old). The OASIS was still significantly correlated with 30-day mortality (OR = 1.125, 95% CI [1.103–1.146], p < 0.001), ICU mortality (OR = 1.156, 95% CI [1.131–1.182, p < 0.001), and hospital mortality (OR = 1.144, 95% CI [1.121–1.168, p < 0.001) by the multivariable regression analyses, the results were showed in Table S3. Association of SAPSII scores with outcomes were showed in Tables S8.

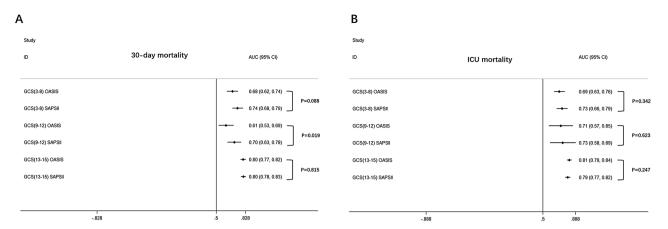
### Subgroup analyses

The severity of hemorrhagic stroke patients was stratified by GCS, subgroup analysis was performed to evaluate the association of OASIS with 30-day mortality across different patients grouped by GCS. The results were showed in Table S4 and Fig. 2, indicated that the OASIS had similar discriminatory power to the SAPSII for predicting 30-day mortality and ICU mortality expect for predicting 30-day mortality of moderate hemorrhagic stroke patients (GCS 9–12 subgroup), OASIS had lower discriminatory abilities to predict 30-day mortality of GCS 9–12 subgroup than SAPSII (AUC 0.61 with 95% CI [0.53–0.69] vs. AUC 0.70 with 95% CI [0.63–0.78], P=0.019).

### Discussion

In this study, we retrospected 1838 hemorrhagic stroke patients from MIMIC-III database and revealed that OASIS on admission was significantly correlated with the prognosis of hemorrhagic stroke patients, the 30-day mortality, ICU mortality and hospital mortality increased as the OASIS of patients increased. When comparing to SAPSII, we found that OASIS had the comparable discriminatory power to predict ICU mortality for hemorrhagic stroke patients, OASIS also had the comparable discriminatory power to predict 30-day mortality for the severe (GCS 3–8) and mild (13–15) hemorrhagic stroke patients, but it had lower discriminatory power to predict 30-day mortality for the moderate (9–12) patients, which might be attributed to that OASIS relied on gross physiological derangements with limits discriminative power in moderate patients. In contrast, SAPSII's multi-organ profiling captures incipient metabolic disturbances (e.g., hypokalemia, respiratory alkalosis), enabling finer risk stratification within this heterogeneous subgroup. For all we know, this was the first time to evaluate the prediction value of OASIS for critical hemorrhagic stroke patients, so was the first time to comparing the discriminatory power between OASIS and SAPSII for predicting the prognosis of hemorrhagic stroke patients.

There are several scoring systems used in ICU that designed to predict the prognosis of critical patients<sup>11</sup>. Patients in ICU consist of different spectrums of critical disease, conflicting conclusions have been reported when evaluating the predictability of various scoring systems<sup>12,13</sup>, indicates that appropriate scoring system should be chosen for specific critical disease. SAPSII is usually applied to predict the prognosis of critical patients in ICU, which includes 17 types of clinical data about physiological data, main organ systems and other



**Fig. 2.** Comparison the discriminatory ability of OASIS and SAPSII on admission for predicting 30-day mortality and ICU mortality stratified by GCS. (**A**) Comparing AUCs for 30-day mortality by OASIS and SAPSII stratified by GCS; (**B**) Comparing AUCs for ICU mortality by OASIS and SAPSII stratified by GCS. OASIS, the Oxford Acute Severity of Illness Score; ICU, intensive care unit; SAPS II, Simplified Acute Physiology Score II; AUC, area under the ROC curve; ROC, receiver operating characteristic.

parameters<sup>14</sup>. OASIS is a new critical illness score designed in 2013, which comprising 10 convenient parameters including age, length of hospital stay prior ICU admission, heart rate, mean arterial pressure, respiratory rate, core body temperature, Glasgow Coma Scale, urine volume, respiratory support and datechosen operation<sup>5</sup>. OASIS is more easy-to-use than SAPSII in daily assessment for ICU patients on account of simple components which contains few laboratory results. Previous studies found that SAPSII had higher discriminatory abilities than OASIS for predicting the mortality of sepsis patients<sup>6</sup>, but the predictive value of OASIS for the prognosis of hemorrhagic stroke patients, and which scoring system is the better choice, still remains unknown. Our study may provide some help for clinicians to make decision, OASIS was significantly correlated with clinical outcomes of hemorrhagic stroke patients, and OASIS may be a better choice than SAPSII when evaluating the prognosis of severe and mild patients because of its' convenience. To evaluate the stability, we performed sensitive analyses by excluding the patients who were more than 80 years old. Our conclusions were stability because the results of sensitive analyses were consistent.

There were some limitations for this study. First, selection bias was unavoidable because this study was a retrospective observational study. Second, we did not take several variables into consideration because the missing data was large, such as body mass index. Third, the performance of the OASIS might be overestimated because we ignored that the data in the study was from different ICUs. Fourth, this study included a total of 1,838 patients, which is considered a relatively small sample size. Therefore, future multicenter studies with larger-scale cohorts are required to validate the conclusions.

### Conclusion

In conclusion, the admission OASIS was found to have a significant association with the short-term outcomes of patients with hemorrhagic stroke, it had comparable discriminatory power for prognosis prediction of severe and mild patients and had lower discriminatory power for prognosis prediction of moderate patients, which suggesting that the OASIS might serve as an alternative choice to predict outcomes of severe and mild hemorrhagic stroke patients considering the practicability.

### Data availability

No datasets were generated or analysed during the current study.

Received: 13 December 2023; Accepted: 2 May 2025

Published online: 15 May 2025

### References

- van Asch, C. J. et al. Incidence, case fatality, and functional outcome of intracerebral haemorrhage over time, according to age, sex, and ethnic origin: a systematic review and meta-analysis. Lancet Neurol. 9(2), 167–176 (2010).
- Schonenberger, S., Al-Suwaidan, F., Kieser, M., Uhlmann, L. & Bosel, J. The setscore to predict tracheostomy need in cerebrovascular neurocritical care patients. Neurocrit Care. 25(1), 94–104 (2016).
- 3. Schonenberger, S. et al. Early tracheostomy in ventilated stroke patients: study protocol of the international multicentre randomized trial SETPOINT2 (Stroke-related early tracheostomy vs. prolonged orotracheal intubation in neurocritical care trial 2). *Int. J. Stroke.* 11(3), 368–379 (2016).
- 4. Le Gall, J. R., Lemeshow, S. & Saulnier, F. A new simplified acute physiology score (SAPS II) based on a European/North American multicenter study. *JAMA* 270(24), 2957–2963 (1993).
- Johnson, A. E., Kramer, A. A. & Clifford, G. D. A new severity of illness scale using a subset of acute physiology and chronic health evaluation data elements shows comparable predictive accuracy. Crit. Care Med. 41(7), 1711–1718 (2013).

- 6. Chen, Q., Zhang, L., Ge, S., He, W. & Zeng, M. Prognosis predictive value of the Oxford Acute Severity of Illness Score for sepsis: a retrospective cohort study. *PeerJ* 7, e7083 (2019).
- 7. Zhou, Y et al. Outcomes for patients with sepsis following admission to the intensive care unit based on health insurance status: A study from the medical information Mart for intensive care-III (MIMIC-III) database. *Med. Sci. Monit.* 26, e924954 (2020).
- 8. Kurniati, A. P., Rojas, E., Hogg, D., Hall, G. & Johnson, O. A. The assessment of data quality issues for process mining in healthcare using medical information Mart for intensive care III, a freely available e-health record database. *Health Inf. J.* **25**(4), 1878–1893 (2019).
- 9. McCann, M. R., Hatton, K. W., Vsevolozhskaya, O. A. & Fraser, J. F. Earlier tracheostomy and percutaneous endoscopic gastrostomy in patients with hemorrhagic stroke: associated factors and effects on hospitalization. *J. Neurosurg.* 132(1), 87–93 (2019).
- 10. Johnson, A. E., Stone, D. J., Celi, L. A. & Pollard, T. J. The MIMIC code repository: enabling reproducibility in critical care research. J. Am. Med. Inf. Assoc. 25(1), 32–39 (2018).
- 11. Evran, T., Serin, S., Gurses, E. & Sungurtekin, H. Various scoring systems for predicting mortality in intensive care unit. *Niger J. Clin. Pract.* 19(4), 530–534 (2016).
- 12. Strand, K. & Flaatten, H. Severity scoring in the ICU: a review. Acta Anaesthesiol. Scand. 52(4), 467-478 (2008).
- 13. Balkan, B., Essay, P. & Subbian, V. Evaluating ICU clinical severity scoring systems and machine learning applications: APACHE IV/IVa case study. *Annu. Int. Conf. IEEE Eng. Med. Biol. Soc.* **2018**, 4073–4076 (2018).
- 14. Singh, P., Pathak, S. & Sharma, R. M. A comparison of acute physiology and chronic health evaluation III and simplified acute physiology score II in predicting sepsis outcome in intensive care unit. *Anesth. Essays Res.* 12(2), 592–597 (2018).

### **Author contributions**

YJ designed the research, extracted and analyzed data, drafted this manuscript. SQ and QP contributed to analyzing data and graph. LH and LZ designed and supervised the research and amended the manuscript. All authors have read and approved the final manuscript. All authors reviewed the manuscript.

### **Funding**

This work was supported by the National Natural Science Foundation of China (Grant no.82202421), National Outstanding Young Physician Program, Central South University Sublimation Scholars Program (2024), Hunan Provincial Health Commission Leading Talent Support Program (No. 20230486) and Youth Science Fund Project of Hunan Provincial Natural Science Foundation (Category C) (No. 2025JJ60725).

### **Declarations**

### Ethics approval and consent to participate

The study was performed according to the guidelines of the Helsinki. The use of the MIMIC-III database was approved by the review committee of Massachusetts Institute of Technology and Beth Israel Deaconess Medical Center. The data is publicly available (in the MIMIC-III database), therefore, the ethical approval statement and the requirement for informed consent were waived for this study.

### Competing interests

The authors declare no competing interests.

### Additional information

**Supplementary Information** The online version contains supplementary material available at https://doi.org/1 0.1038/s41598-025-00959-7.

Correspondence and requests for materials should be addressed to L.H. or L.Z.

Reprints and permissions information is available at www.nature.com/reprints.

**Publisher's note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

**Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <a href="http://creativecommons.org/licenses/by-nc-nd/4.0/">http://creativecommons.org/licenses/by-nc-nd/4.0/</a>.

© The Author(s) 2025