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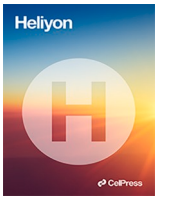

Research article

Development of a nomogram to predict the incidence of acute kidney injury among ischemic stroke individuals during ICU hospitalization

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ABSTRACT

Background: Limited clinical prediction models exist to assess the likelihood of acute kidney injury (AKI) occurrence in ischemic stroke individuals. In this retrospective study, our aim was to construct a nomogram that utilizes commonly available clinical features to predict the occurrence of AKI during intensive care unit hospitalization among this patient population.

Methods: In this study, the MIMIC-IV database was utilized to investigate potential risk factors associated with the incidence of AKI among ischemic stroke individuals. A predictive nomogram was developed based on these identified risk factors. The discriminative performance of the constructed nomogram was assessed. Calibration analysis was utilized to evaluate the calibration performance of the constructed model, assessing the agreement between predicted probabilities and actual outcomes. Furthermore, decision curve analysis (DCA) was employed to assess the clinical net benefit, taking into account the potential risks and benefits associated with different decision thresholds.

Results: A total of 2089 ischemic stroke individuals were included and randomly allocated into developing (n = 1452) and verification cohorts (n = 637). Risk factors for AKI incidence in ischemic stroke individuals, determined through LASSO and logistic regression. The constructed nomogram had good performance in predicting the occurrence of AKI among ischemic stroke patients and provided significant improvement compared to existing scoring systems. DCA demonstrated satisfactory clinical net benefit of the constructed nomogram in both the validation and development cohorts.

Conclusions: The developed nomogram exhibits robust predictive performance in forecasting AKI occurrence in ischemic stroke individuals.

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1. Introduction

Ischemic stroke is a significant global health concern, with an estimated lifetime risk of approximately 25 % among individuals aged 25 and above [1], making it the second leading cause of mortality worldwide. The substantial burden it places on healthcare systems and the associated economic implications are profound [2]. Patients with chronic kidney disease have an increased susceptibility to cerebrovascular diseases [3,4]. However, a growing body of evidence has elucidated a close link between ischemic stroke and subsequent acute kidney injury (AKI) [5–7], prompting researchers to investigate the intricate interplay of the "brain-kidney axis" [8]. In a comprehensive dataset comprising 5,751,601 cases of acute ischemic stroke, acute renal dysfunction emerged as the second most prevalent post-stroke complication, with an incidence rate of 10.1 % [9]. Significantly, the prevalence of acute renal function impairment exhibited a notable threefold surge, rising from 4.8 % to 14 % over the span of 2007–2019 [9].

Prior studies have endeavored to construct a nomogram for AKI incidence in ischemic stroke patients using the Medical Information Mart for Intensive Care (MIMIC) III database [10]. Regrettably, this model relies on the Oxford Acute Severity of Illness Score (OASIS), which introduces clinical intricacy and restricts its broader applicability. Moreover, the existing model solely forecast AKI within 48 h of ICU admission, lacking the ability to accurately predict AKI throughout the entire ICU stay [10]. Therefore, it is imperative to devise a simplified nomogram based on readily accessible clinical features, enabling prompt and effective assessment of the risk of AKI incidence during the ICU hospitalization of individuals with ischemic stroke. This research endeavor represents a pivotal focus in the realm of clinical science.

To the best of our knowledge, this study represents the first endeavor to construct an intuitive and efficient nomogram, tailored for clinical use, to predict the risk of AKI incidence during the ICU hospitalization of individuals with ischemic stroke, utilizing commonly available clinical features collected on the first day after transfer to the ICU from ischemic stroke individuals in the MIMIC-IV database.

2. Methods

2.1. Source of data

The study data were obtained from a comprehensive critical care database called MIMIC-IV (version 2.1), which encompasses multi-parameter intelligent monitoring. MIMIC-IV is an openly accessible and freely available database that includes intensive care data from more than forty thousand patients from 2008 to 2019 [11]. The establishment of this database was conducted in compliance with the ethical guidelines and regulations, receiving approval from both the Massachusetts Institute of Technology (MIT) and the Beth Israel Deaconess Medical Center (BIDMC). The main researcher has duly fulfilled the requirements of the Human Subject Research

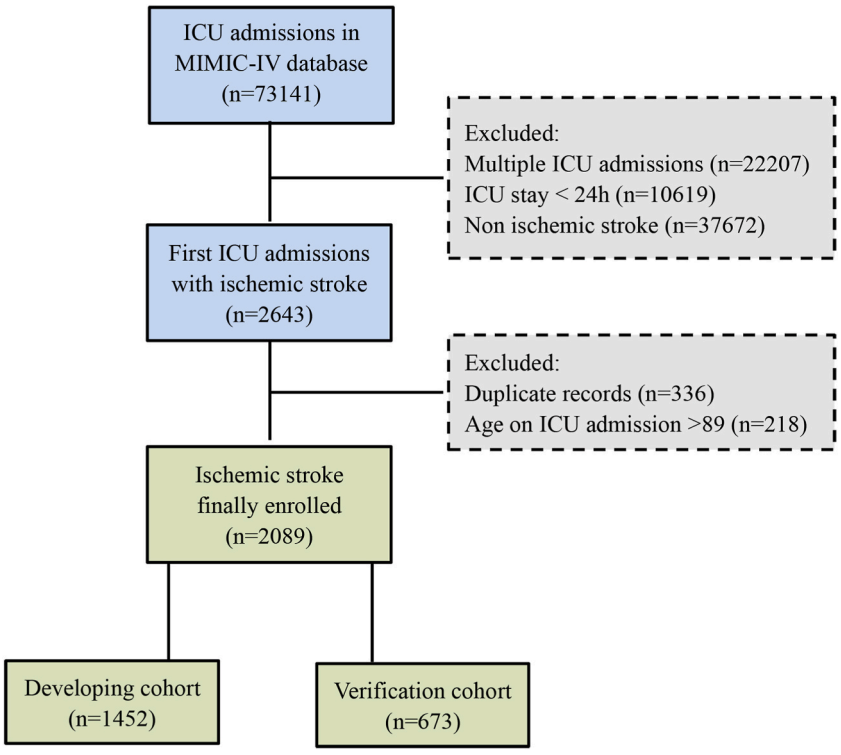

Fig. 1. Diagram illustrating the process of participant inclusion in the study. MIMIC-IV, medical information mart for intensive care IV; ICU, intensive care unit.

Table 1
Clinical features of ischemic stroke individuals categorized based on randomization allocation.

Characteristics	All patients (N = 2089)	Developing cohort (n = 1452)	Verification cohort (n = 637)	P value
Age, median (IQR)	68.92 (57.33, 78.86)	68.74 (57.36, 78.78)	69.26 (57.29, 79.25)	0.836
Female, No. (%)	993 (47.53)	693 (47.73)	300 (47.10)	0.790
Weight, median (IQR) (kg)	78.10 (66.50, 93.50)	77.95 (66.30, 93.55)	79.40 (67.00, 93.20)	0.685
Race, No. (%)				
White	1242 (59.45)	836 (59.44)	379 (59.50)	0.724
Hispanic	74 (3.54)	52 (3.58)	22 (3.45)	
Black	223 (10.67)	154 (10.61)	69 (10.83)	
ASIAN	60 (2.87)	37 (2.55)	23 (3.61)	
Other	490 (23.46)	346 (23.83)	144 (22.61)	
Marital Status, No. (%)				
Married	894 (42.80)	635 (43.73)	259 (40.66)	0.676
Single	516 (24.70)	349 (24.04)	167 (26.22)	
Widowed	217 (10.39)	153 (10.54)	64 (10.05)	
Divorced	146 (6.99)	100 (6.89)	46 (7.22)	
Other	316 (15.13)	215 (14.81)	101 (15.86)	
Underlying Diseases, No. (%)				
Myocardial Infarct	327 (15.65)	238 (16.39)	89 (13.97)	0.161
Congestive Heart Failure	467 (22.36)	320 (22.04)	147 (23.08)	0.600
Chronic Pulmonary Disease	377 (18.05)	255 (17.56)	122 (19.15)	0.384
Mild Liver Disease	111 (5.31)	79 (5.44)	32 (5.02)	0.696
Severe Liver Disease	35 (1.68)	27 (1.86)	8 (1.26)	0.322
Diabetes without chronic complication	573 (27.43)	399 (27.48)	174 (27.32)	0.938
Diabetes with chronic complication	175 (8.38)	126 (8.68)	49 (7.69)	0.454
Malignant Cancer	181 (8.66)	134 (9.23)	47 (7.38)	0.166
Charlson Comorbidity Index, median (IQR)	7.00 (5.00, 8.00)	7.00 (5.00, 9.00)	7.00 (5.00, 8.00)	0.397
Disease severity Scoring System, median (IQR)				
Firstday GCS[a]	12.00 (8.00, 14.00)	12.00 (8.00, 14.00)	11.00 (8.00, 14.00)	0.510
Firstday SOFA	4.00 (2.00, 6.00)	4.00 (2.00, 6.00)	4.00 (2.00, 7.00)	0.332
Firstday LODS	4.00 (2.00, 7.00)	4.00 (2.00, 7.00)	4.00 (2.00, 7.00)	0.684
Firstday OASIS	33.00 (26.00, 40.00)	33.00 (26.00, 39.50)	33.00 (26.00, 40.00)	0.348
Firstday APS III	42.00 (30.00, 61.00)	42.00 (30.00, 61.00)	43.00 (31.00, 63.00)	0.355
Firstday SAPS II	32.00 (25.00, 41.00)	32.00 (25.00, 41.00)	32.00 (26.00, 42.00)	0.310
Vital Indicators, median (IQR)				
Temperature (°C)[b]	37.28 (37.06, 37.83)	37.28 (37.06, 37.83)	37.28 (37.00, 37.83)	0.847
Heart Rate (beats/min)[c]	80.00 (70.15, 90.96)	79.72 (70.48, 90.47)	80.72 (69.58, 92.27)	0.870
Respiratory Rate (breaths/min)[b]	27.00 (24.00, 31.00)	27.00 (24.00, 31.00)	27.00 (23.00, 31.00)	0.701
MBP (mmHg)[a]	65.00 (56.00, 75.00)	65.00 (57.00, 75.00)	65.00 (56.00, 74.00)	0.506
Glucose (mmol/L)[b]	8.50 (6.83, 11.33)	8.50 (6.83, 11.44)	8.44 (6.83, 10.94)	0.513
Firstday Urine Output (L)	1.60 (1.04, 2.35)	1.62 (1.05, 2.36)	1.55 (1.00, 2.31)	0.243
Laboratory Indicators, median (IQR)				
White Blood Cells (K/uL)[b]	11.90 (8.80, 15.90)	11.75 (8.70, 15.90)	12.10 (9.00, 15.80)	0.327
Creatinine (μmmol/L)[b]	88.40 (70.72, 114.92)	88.40 (70.72, 114.92)	88.40 (70.72, 114.92)	0.410
Potassium (mEq/L)[b]	4.30 (3.90, 4.70)	4.30 (3.90, 4.70)	4.20 (3.90, 4.70)	0.637
Calcium (mEq/L)[a]	2.13 (1.98, 2.23)	2.13 (1.98, 2.23)	2.10 (1.98, 2.23)	0.128
Medications and Interventions, No. (%)				
Endovascular Obstruction Removal	192 (9.19)	139 (9.57)	53 (8.32)	0.362
Alteplase	38 (1.82)	23 (1.58)	15 (2.35)	0.225
Furosemide	93 (4.45)	60 (4.13)	33 (5.18)	0.285
Vasoactive Agent	515 (24.65)	368 (25.34)	147 (23.08)	0.268
Invasive Mechanical Ventilation	756 (36.19)	526 (36.23)	230 (36.11)	0.958
Supplemental Oxygen	794 (38.01)	556 (38.29)	238 (37.36)	0.687
Outcomes				
28-Day Mortality (%)	457 (21.88)	314 (21.63)	143 (22.45)	0.675
ICU Mortality (%)	269 (12.88)	192 (13.22)	77 (12.09)	0.476
Hospital Mortality (%)	378 (18.09)	261 (17.98)	117 (18.37)	0.830
AKI Incidence (%)	1342 (64.24)	930 (64.05)	412 (64.68)	0.783
AKI Stage				
AKI Stage 0 (%)	747 (35.76)	522 (35.95)	225 (35.32)	0.950
AKI Stage 1 (%)	267 (12.78)	187 (12.88)	80 (12.56)	
AKI Stage 2 (%)	699 (33.46)	480 (33.06)	219 (34.38)	
AKI Stage 3 (%)	376 (18.00)	263 (18.11)	113 (17.74)	

AKI, acute kidney injury; ICU, Intensive Care Unit; IQR, Interquartile Range; GCS, Glasgow Coma Scale; APS III, Acute Physiology Score III; SOFA, Sequential Organ Failure Assessment; LODS, Logistic Organ Dysfunction System; SAPS II, Simplified Acute Physiology Score II; OASIS, Oxford Acute Severity of Illness Score; MBP, Mean Blood Pressure; [a]: the min value of indicators on the firstday of ICU stay; [b]: the max value of indicators on the firstday of ICU stay; [c]: the mean value of indicators on the firstday of ICU stay. The administration of vasoactive agents was characterized by the use of specific medications such as norepinephrine, epinephrine, phenylephrine, dopamine, dobutamine, vasopressin, or milrinone within the initial 24 h after admission to the ICU. Within the same timeframe, disease severity scoring systems, vital signs, laboratory markers, and interventions were evaluated. Notably, during the random assignment process, a seed value of 222 was utilized.

Course, receiving certification (Certification Number: 46141344), and has obtained official authorization to access this database.

2.2. Population selection criteria

The study cohort encompassed individuals who had a length of stay exceeding one day when admitted to ICU for the primary admission. We identified ischemic stroke patients using international classification of disease (ICD) codes, similar to our previous research [12]. It is noteworthy that patient data for those aged 89 years or older were excluded, as the database categorized them as 91 years old. Ultimately, a total of 2089 cases of ischemic stroke patients were selected and randomly allocated in a 7:3 ratio to the developing dataset or the verification dataset (Fig. 1). The randomization seed for this study was set as 222, which differs from our previous research [12], thus resulting in different randomization outcomes.

3. Outcome and predictions

Our aim was to develop a user-friendly and clinically applicable nomogram to predict the risk of AKI during ICU hospitalization in individuals with ischemic stroke. The primary outcome was the occurrence of AKI during the ICU stay. We extracted AKI stage information using the MIMIC-IV concept. AKI was characterized based on the Kidney Disease Improving Global Outcomes (KDIGO) criteria [3], which encompassed the following indicators: a rise in serum creatinine (sCr) levels by $\geq$ 50 % within one week, an increase in sCr of $\geq$26.5 μmol/l within 2 days, or a sustained decrease in urine output below 0.5 ml/kg/hr for a duration exceeding 6 h. AKI status was determined each time a measurement of creatinine or urine output was recorded. The baseline creatinine level was defined as the lowest sCr value within the previous one week.

All predictive variables were extracted from the database using the PostgreSQL tool (version 14.2.1). The study encompassed a cohort of ICU-admitted individuals, and their demographic attributes were documented. Additionally, on the initial day of ICU admission, a comprehensive assessment of pertinent factors was conducted utilizing the database concept, including the evaluation of underlying comorbidities, the calculation of the Charlson Comorbidity Index (CCI), vital signs, oxygen saturation, blood glucose, urine output, complete blood count, biochemical markers, electrolytes, coagulation function, medication or non-medication interventions, common severity scores, and were consistent with our previous research [12].

3.1. Statistical analysis

A thorough examination of potential outliers was conducted using Stata software (version 17.0) through the application of histogram analysis, and Winsorization (replacing values beyond the 0.5th and 99.5th percentiles) was applied to address the outliers. Multiple imputation techniques were utilized to handle missing data. Initially, a LASSO regression was employed to identify potential variables from the development cohort. Logistic regression analysis was then conducted with AKI occurrence during ICU hospitalization as the dependent variable, aiming to determine independent risk factors for AKI among individuals with ischemic stroke. To evaluate the presence of multicollinearity among the variables, an analysis of variance inflation factor was conducted. This statistical technique was employed to examine the degree of correlation between predictor variables in the model. By assessing the variance inflation factor, we were able to ascertain the extent to which multicollinearity could potentially affect the reliability and interpretability of the regression results. Subsequently, a nomogram was constructed to predict the probability of AKI occurrence among individuals with ischemic stroke. The discriminatory performance of the predictive model was assessed using several statistical measures, including the net reclassification improvement (NRI), integrated discrimination improvement (IDI), and concordance index (C-index). To evaluate the calibration and clinical utility of the model, calibration curve analysis was performed to assess the agreement between observed and predicted probabilities. Furthermore, decision curve analysis (DCA) was employed to assess the clinical net benefit of the model by examining the balance between potential harms and benefits.

The following procedures were primarily implemented using R software (version 4.2.1): LASSO regression was performed using the "glmnet" package, "car" package was libraried to test variance inflation factor, and the nomogram for predicting AKI in patients with ischemic stroke was constructed using the "rms" package. The C-index for the development and validation cohorts was obtained using the "pROC" package. The predictive performance improvement of different models was evaluated using IDI and NRI through the "PredictABEL" package. Following the inclusion of the "rms" package, the calibration curves were constructed utilizing the "val.prob" function. The clinical value of the developed nomogram was assessed through DCA using the "rmda" package.

4. Results

4.1. Participants

Table 1 provides an overview of the demographic and clinical features among the whole individuals. There were no significantly statistical differences ($P > 0.050$) observed in the baseline characteristics, including demographic factors, clinical features, and available predictive factors, between the development and validation cohorts. This finding indicates that the random allocation of study participants into the respective cohorts was scientifically sound.

4.2. Model development

The clinical factors associated with the occurrence of AKI in ischemic stroke individuals were identified, as shown in Fig. 2a and b. A total of 18 relevant features were selected, including weight, history of congestive heart failure, history of renal disease, CCI, average heart rate, minimum diastolic blood pressure, minimum mean arterial pressure, highest blood glucose level, first-day urine output, maximum white blood cell count (WBC), minimum calcium ion level, maximum creatinine level, maximum potassium level, use of vasoactive medications, use of furosemide, initiation of mechanical ventilation, administration of supplemental oxygen, and minimum Glasgow Coma Scale (GCS) score on the first day. Furthermore, these features underwent additional binary multivariable logistic regression analysis, resulting in the identification of 12 independent risk factors ($P < 0.05$) for AKI occurrence in ischemic stroke patients, as presented in Table 2. Based on these findings, we developed the nomogram (Fig. 3).

4.3. Model performance and specification

The nomogram demonstrated high predictive performance for AKI occurrence in ischemic stroke patients, as indicated by the C-index of 0.837 (95 % Confidence Interval, 95 % CI: 0.817–0.858) in the development cohort and 0.848 (95 % CI: 0.818–0.878) in the validation cohort. These values suggest that our model outperforms commonly used clinical scoring systems (Table 3).

The results of IDI and NRI revealed significant improvements in predictive performance compared to models based on other commonly used scores ($P < 0.001$) (Table 4). The actual incidence of AKI in ischemic stroke patients corresponded closely to the predicted probabilities generated by our nomogram in both datasets (Fig. 4a and b). Furthermore, DCA demonstrated superior clinical net benefit compared to commonly employed severity scoring systems in both the validation and development cohorts (Fig. 5a and b).

5. Discussion

This study pioneers the development of a user-friendly nomogram for clinical use, utilizing easily accessible clinical features collected within one day after ICU admission from ischemic stroke population in the MIMIC-IV database. LASSO regression and logistic regression identified independent risk factors, including weight, prior congestive heart failure, GCS score, urine output, heart rate, blood glucose level, WBC, blood calcium concentration, use of vasoactive drugs, furosemide, invasive mechanical ventilation, and supplemental oxygen. The nomogram demonstrates superior predictive performance, as evidenced by C-index, NRI, and IDI analyses. The model aligns well with the actual occurrence of AKI. DCA assessment confirms its significant clinical value in both validation and development cohorts. The nomogram accurately predicts the occurrence of AKI during ICU stay. There is a constructed model to predict the risk of stroke recurrence among young individuals after ischemic stroke [13], demonstrating the remarkable predictive

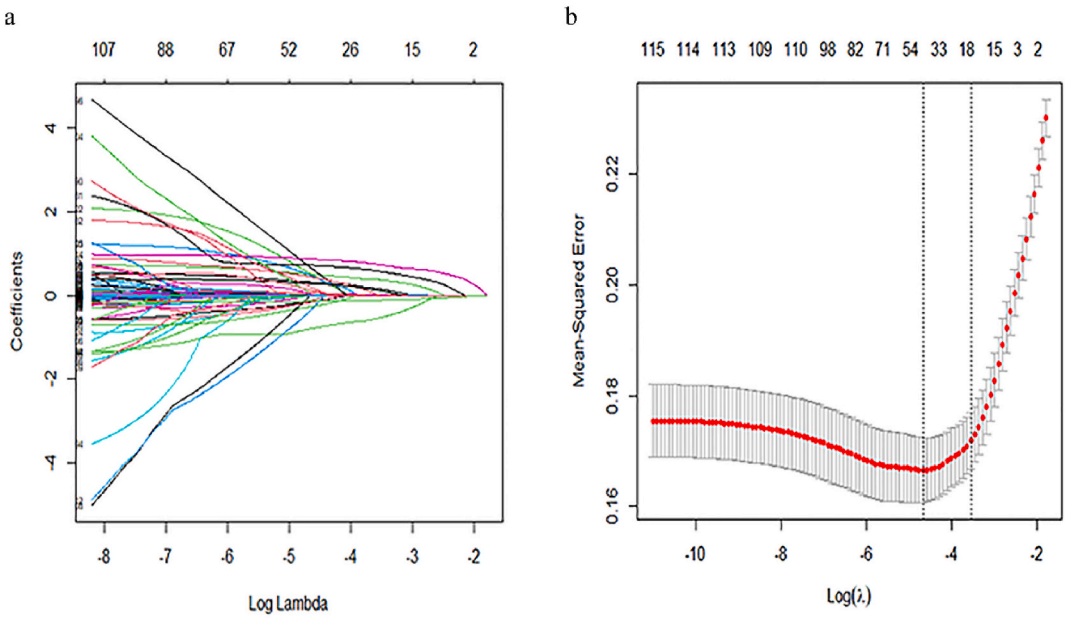

Fig. 2. Schematic representation depicting the selection of clinical features. **a** Plot demonstrating the association between feature coefficients and lambda values. The coefficients for each feature exhibited a gradual convergence towards zero with increasing lambda values. **b** The graph presents the 10-fold cross-validation curve of the LASSO regression. The left dotted vertical line represents the number of features and the optimal logarithm (lambda) value associated with the smallest mean squared error ($\lambda = 0.009380591$). Using the one standard error criterion for determining the optimal logarithm (lambda), the right dotted vertical line indicates that the model, consisting of 18 variables, achieved a satisfactory balance between accuracy and simplicity ($\lambda = 0.02864697$). λ, lambda.

Table 2
Multivariable logistic regression analysis of independent predictors associated with AKI occurrence among ischemic stroke patients.

Variables	OR	95 % CI	P-value	VIF
Weight	1.024	1.017–1.031	<0.001	1.100
Underlying Congestive Heart Failure (Yes)	2.034	1.423–2.936	<0.001	1.074
Heart Rate (beats/min)[c]	1.017	1.007–1.026	<0.001	1.095
Blood Glucose (mmol/L)[b]	1.058	1.020–1.099	<0.001	1.065
Firstday Urine Output (mL)	0.9995	0.9994–0.9996	<0.001	1.120
White Blood Cells (K/uL)[b]	1.027	1.002–1.053	0.003	1.114
Blood Calcium (mmol/L)[a]	0.320	0.156–0.643	<0.001	1.136
Vasoactive agents administration (Yes)	2.765	1.837–4.229	<0.001	1.171
Use of Furosemide (Yes)	2.700	1.172–7.067	0.003	1.033
Invasive Mechanical Ventilation (Yes)	2.815	1.979–4.031	<0.001	1.300
Supplemental Oxygen (Yes)	1.570	1.188–2.077	<0.001	1.107
Firstday GCS[a]	0.844	0.809–0.880	<0.001	1.114

AKI, acute kidney injury; OR, odd ratio; CI, confidence interval; GCS, Glasgow Coma Scale; VIF, variance inflation factor. [a]: the min value of indicators on the firstday of ICU stay; [b]: the max value of indicators on the firstday of ICU stay; [c]: the mean value of indicators on the firstday of ICU stay. The administration of vasoactive agents was characterized by the use of specific medications such as norepinephrine, epinephrine, phenylephrine, dopamine, dobutamine, vasopressin, or milrinone within the initial 24 h after admission to the ICU.

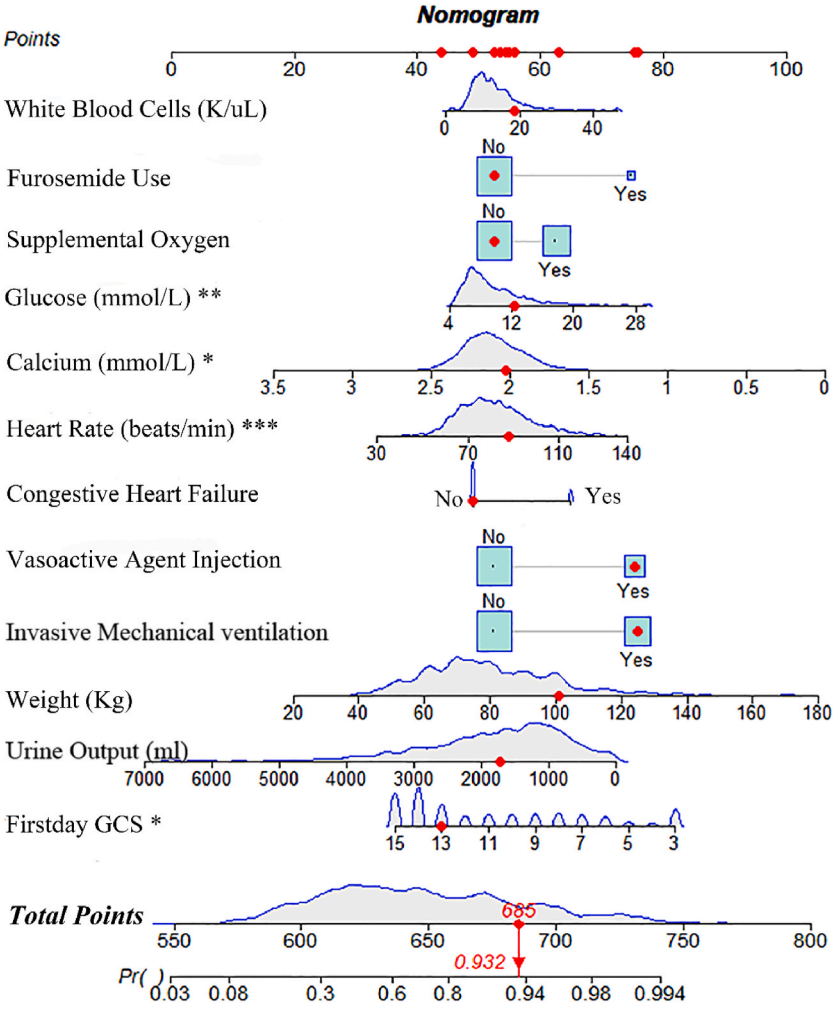

Fig. 3. Nomogram developed for the prediction of AKI incidence in patients with ischemic stroke. The nomogram assigns scores to each variable, enabling the assessment of AKI probability by summing the scores associated with the patient's specific values. The red dot denotes a selected patient within the cohort, with a cumulative score of 685 (P = 0.932), signifying a 93.2 % probability of AKI occurrence. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Table 3
Comparison of C-index between models for prediction of AKI occurrence in patients with ischemic stroke.

Models	Developing cohort		Verification cohort	
	C-index	95 % CI	C-index	95 % CI
Nomogram	0.837	0.817–0.858	0.848	0.818–0.878
GCS	0.695	0.668–0.723	0.723	0.684–0.761
SOFA	0.780	0.756–0.804	0.789	0.754–0.824
APS III	0.765	0.741–0.790	0.796	0.762–0.831
LODS	0.776	0.752–0.800	0.798	0.764–0.832
SAPS II	0.701	0.676–0.7303	0.746	0.707–0.786
OASIS	0.754	0.7282–0.779	0.775	0.739–0.812

AKI, acute kidney injury; C-index, concordance index; CI, confidence interval; GCS, Glasgow coma score; SOFA, sequential organ failure assessment; APS III, acute physiology score III; LODS, logistic organ dysfunction system; SAPS II, simplified acute physiology score II; OASIS, oxford acute severity of illness score.

Table 4
Comparison of NRI and IDI among models for the prediction of AKI among ischemic stroke.

Index	Developing cohort			Verification cohort		
	Estimate	95 % CI	P value	Estimate	95 % CI	P value
NRI (vs. GCS)	0.410	0.364–0.457	<0.001	0.412	0.342–0.483	<0.001
NRI (vs. SOFA)	0.216	0.159–0.274	<0.001	0.229	0.144–0.314	<0.001
NRI (vs. APS III)	0.269	0.214–0.325	<0.001	0.219	0.131–0.308	<0.001
NRI (vs. LODS)	0.234	0.178–0.291	<0.001	0.237	0.147–0.327	<0.001
NRI (vs. SAPS II)	0.3611	0.309–0.413	<0.001	0.256	0.170–0.342	<0.001
NRI (vs. OASIS)	0.283	0.228–0.338	<0.001	0.278	0.185–0.370	<0.001
IDI (vs. GCS)	0.213	0.192–0.234	<0.001	0.1894	0.156–0.223	<0.001
IDI (vs. SOFA)	0.108	0.089–0.128	<0.001	0.101	0.068–0.133	<0.001
IDI (vs. APS III)	0.129	0.109–0.150	<0.001	0.092	0.058–0.125	<0.001
IDI (vs. LODS)	0.112	0.092–0.131	<0.001	0.086	0.052–0.119	<0.001
IDI (vs. SAPS II)	0.205	0.184–0.227	<0.001	0.167	0.132–0.202	<0.001
IDI (vs. OASIS)	0.144	0.124–0.163	<0.001	0.124	0.092–0.156	<0.001

AKI, acute kidney injury; NRI, net reclassification index; IDI, integrated discrimination improvement; CI, confidence interval; GCS, Glasgow coma score; SOFA, sequential organ failure assessment; APS III, acute physiology score III; LODS, logistic organ dysfunction system; SAPS II, simplified acute physiology score II; OASIS, oxford acute severity of illness score. Cutoff: 0, 0.2, 0.4, 1.

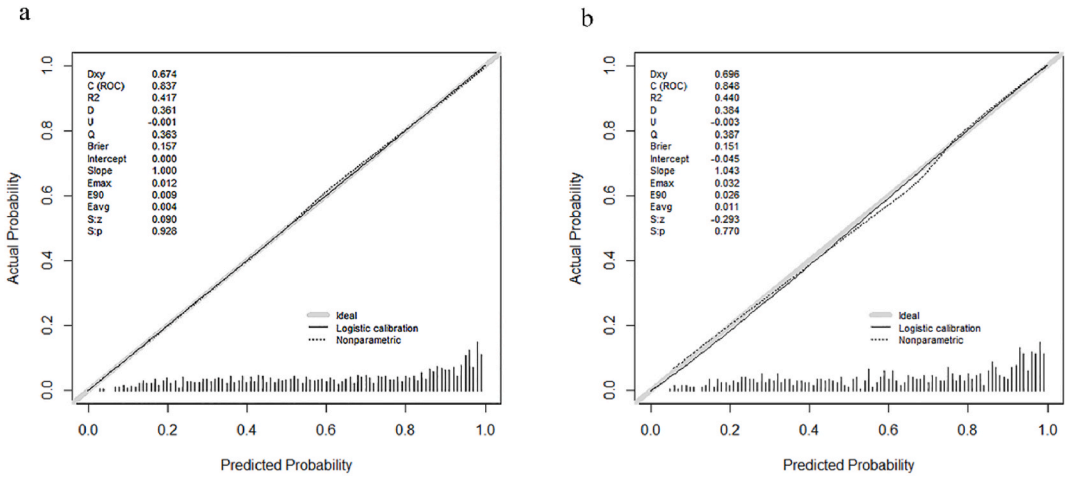

Fig. 4. Calibration curves were constructed for the nomogram in the development cohort **(a)** and validation cohort **(b)**, depicting the concordance between the observed and predicted rates of AKI occurrence in both groups (P > 0.050).

performance of the nomogram. Furthermore, other researchers have successfully established nomograms for predicting ischemic stroke long-term prognosis [12,14], providing valuable guidance for related clinical practices.

Certain demographic characteristics and medical history variables are fundamental components within predictive models. Weight has emerged as a notable contributor to the development of ischemic stroke, exhibiting a direct association with its occurrence [15]. The presence of the "obesity paradox" further substantiates obesity as an independent risk factor for ischemic stroke [16], wherein

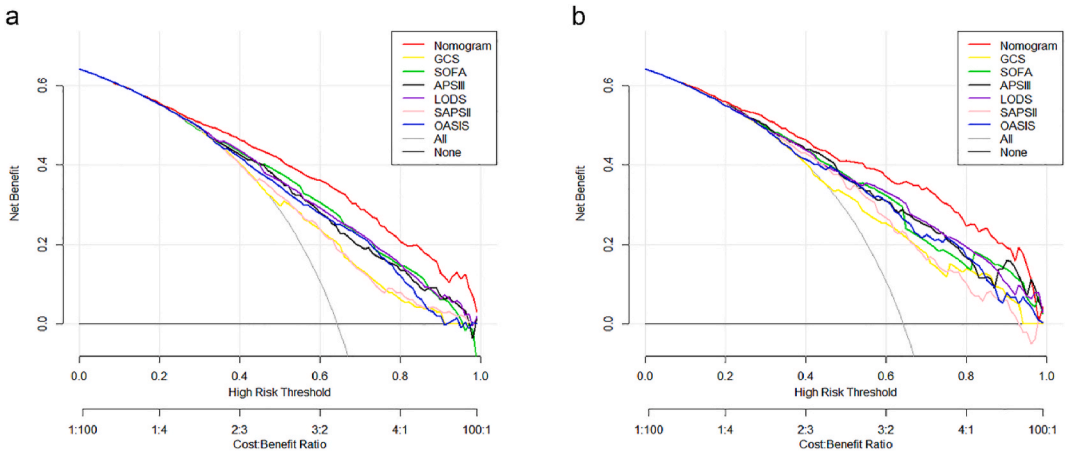

Fig. 5. DCA was performed in the development **(a)** and validation **(b)** cohorts. The red line represents our developed nomogram, demonstrating superior performance compared to the conventional scoring systems. DCA, decision curve analysis GCS, Glasgow coma score; SOFA, sequential organ failure assessment; APS III, acute physiology score III; LODS, logistic organ dysfunction system; SAPS II, simplified acute physiology score II; OASIS, oxford acute severity of illness score. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

obese individuals demonstrate heightened rates and severity of AKI compared to their leaner counterparts [17]. The pathophysiology underlying obesity-related AKI is likely multifaceted, involving intricate interplay among various factors, including glomerular pathology, metabolic syndrome, hypertension, cardiovascular disorders, endothelial dysfunction and so on [18]. Heart failure patients are frequently predisposed to an increased susceptibility to ischemic stroke, and a reciprocal cause-and-effect relationship exists between these two conditions [19]. Within the heart failure population, a decline in glomerular filtration rate commonly manifests as an inevitable consequence, and the occurrence of AKI functions as an autonomous predictive indicator for mortality estimation in this patient population [20]. The principal underlying pathophysiological mechanisms entail perturbations in hemodynamics arising from diminished cardiac output and/or venous return, and so on [21].

Clinical presentations are frequently incorporated as predictive variables in clinical prediction models. Acute-phase heart rate in stroke patients predicts significant clinical events [22]and targeting heart rate control may prevent subsequent cardiovascular events, as demonstrated in a prospective study [23]. Heart rate is associated with AKI and serves as a reliable biomarker, as evidenced by reduced AKI occurrence in mice with focal cerebral ischemia treated with metoprolol [24]. While GCS has garnered substantial recognition as a significant and independent prognostic indicator among acute stroke [25], it is unfortunate that no literature has been found to elucidate the association between GCS or the extent of impaired consciousness and the incidence of AKI among ischemic stroke.

Multiple ancillary examination outcomes function as surrogate markers within the prognostic model. A meta-analysis involving 9766 patients indicates the reliability of the neutrophil-to-lymphocyte ratio as a biomarker for detecting AKI [26], with retrospective studies providing support for its correlation with the risk of postoperative AKI [27]. However, the relationship between WBC and AKI occurrence in ischemic stroke remains insufficiently understood. In patients with AKI, elevated inflammatory markers may be attributed to mechanisms mediated by neurohormones or inflammation [28]. The relationship between blood calcium levels and the occurrence of AKI in ischemic stroke has received limited research attention. Prior investigations have examined the influence of elevated calcium levels on the glomerular filtration rate in rats with normal physiological conditions, revealing a reversible decrease in renal filtration rate in response to elevated blood calcium levels [29], potentially due to the direct vasoconstrictive effects of increased calcium ions on renal blood vessels [30]. However, the specific association between blood calcium levels and AKI in ischemic stroke remains incompletely understood. Patients with inadequate glycemic control are at increased risk of both stroke and AKI [31,32]. Notably, among individuals with ischemic stroke, the presence of diabetes is independently associated with the occurrence of AKI subsequent to endovascular therapy [33].

The inclusion of specific intervention measures as predictive variables in clinical prediction models is also a valuable consideration. In the latest KDIGO Conference findings [34], oliguria remains a diagnostic criterion for AKI, and decreased urine output is a significant factor linked to the 28-day mortality in AKI patients [35]. A multicenter study revealed that furosemide solely enhances urine output without substantial prognostic improvement in AKI patients [36]. Furthermore, a comprehensive meta-analysis encompassing over 800 studies indicated the absence of any clinical benefits associated with furosemide administration for the treatment of AKI among adult individuals [37]. Sympathetic nervous system activation and subsequent catecholamine release in ischemic stroke patients induce excessive vasoconstriction of renal blood vessels upon vasoactive drug administration, resulting in inadequate renal perfusion and an elevated risk of AKI [38]. Chiu et al. [39], in a multicenter study, demonstrated a significant association between the use of vasopressor agents and increased AKI occurrence. Moreover, the KDIGO summary discourages early administration of vasoactive drugs like dopamine in the initial stages of AKI [31]. Supplemental oxygen, specifically high-pressure oxygen therapy [40], shows potential neuroprotective benefits for stroke patients. Timely administration of oxygen therapy can effectively prevent

contrast-induced AKI in certain individuals [41], and preclinical studies have indicated potential advantages of high-pressure oxygen therapy in mice with AKI [42]. Nevertheless, stroke patients undergoing mechanical ventilation are susceptible to infections such as pneumonia and sepsis, which can exacerbate renal dysfunction and contribute to the development of AKI [43,44].

To illustrate the clinical application of the nomogram, a specific case was presented from the development cohort, as depicted in Fig. 3. The red dot represents an individual patient. This patient exhibited certain characteristics, including a weight of 100.9 kg, absence of congestive heart failure history, a GCS score of 13, an average heart rate of 87.59 beats per minute, a urine output of 1719 ml, a maximum white blood cell count of 18.4 K/μL, a peak blood glucose level of 12.33 mmol/L, a minimum blood calcium level of 2.03 mmol/L, no use of furosemide or supplemental oxygen, and the administration of vasoactive agents and invasive mechanical ventilation. Each variable contributed to a corresponding score. The cumulative score of these variables (685) was located on the total points line, and a solid red line was drawn downward to the axis to determine the risk probability of AKI incidence (93.2 %).

This study has several inherent limitations. Firstly, despite the vast clinical data available in the MIMIC-IV database, its susceptibility to data errors and biases cannot be overlooked. Hence, meticulous data cleansing procedures were diligently implemented, encompassing thorough detection and appropriate management of outliers and missing values. Secondly, the retrospective design of this study underscores the need for future prospective investigations to establish the clinical applicability and validity of our developed nomogram. Thirdly, our study did not systematically address the variation in AKI incidence following stroke among patients from diverse geographic regions. The reported rates of AKI subsequent to stroke exhibit considerable disparities, attributed to the inherent heterogeneity of patient populations and the divergence in defining AKI through the use of distinct diagnostic criteria and ICD codes [45]. Lastly, it is important to note that the nomogram's validation was confined to internal assessment, emphasizing the necessity for external validation to ascertain its performance and reliability.

6. Conclusion

In conclusion, this study identified independent risk factors associated with AKI occurrence in ischemic stroke patients admitted to the ICU. These factors included weight, prior congestive heart failure, GCS score, urine output, heart rate, blood glucose level, WBC, blood calcium concentration, vasoactive drugs injection, furosemide administration, invasive mechanical ventilation, and supplemental oxygen. The developed nomogram, based on these variables, showed promising predictive performance and clinical utility for assessing AKI risk in ICU-admitted ischemic stroke patients. However, external validation and prospective investigations are crucial to further validate the effectiveness of the nomogram.

Author Contributions

Study design: GJ, MZ, XC. Data extraction: GJ, FM. Data curation: MZ, YL, XC. Statistical analysis: YL, FM. Writing—original draft preparation: GJ, FM, YL. Writing—review and editing: BM, WH, XC. Supervision and project administration: GJ, BM, WH. Resources and funding acquisition: GJ, MZ, WH. All authors contributed to the article and approved the submitted version.

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Ethical standards

Ethical approval for the inclusion of human participants was obtained from the Institutional Review Boards of MIT and BIDMC. In accordance with national regulations and agency guidelines, the need for informed consent was waived given the retrospective design of the study.

Data availability statement

The entirety of the raw data employed in this study originates from the MIMIC IV (version 2.1) database, a publicly accessible repository. The specific dataset accessed for this investigation can be retrieved from the designated URL: https://physionet.org/content/mimiciv/2.1/

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the author(s) used ChatGPT in order to improve language and readability. After using this tool/service, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the publication.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Abbreviations

ICU, intensive care unit; AKI, acute kidney injury; KDIGO: Kidney Disease Improving Global Outcomes; C-index, concordance index; NRI, net reclassification index; IDI, integrated discrimination improvement; DCA, decision curves analysis; LASSO, least absolute shrinkage and selection operator; MIMIC, medical information mart for intensive care; ICD, international classification of disease; CCI, Charlson comorbidity index; WBC, white blood cells; GCS, Glasgow Coma Scale; OASIS, Oxford Acute Severity of Illness Score; BIDMC, Beth Israel Deaconess Medical Center; MIT: Massachusetts Institute of Technology.

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