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Prognostic value of blood urea nitrogen-to-albumin and C-reactive protein-to-albumin ratios in acute stroke compared with established clinical and radiological predictors: a single-center retrospective cohort study

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Abstract

Background

Blood urea nitrogen-to-albumin ratio (BAR) and C-reactive protein-to-albumin ratio (CAR) are readily available prognostic biomarkers in acute stroke. This study evaluated their associations with in-hospital mortality and compared their discriminatory performance with established clinical and radiological predictors in ischemic and hemorrhagic stroke.

Methods

This single-center retrospective study included 736 adults with acute stroke between January 2020 and January 2025: 582 with ischemic stroke and 154 with hemorrhagic stroke. Admission BAR and CAR were calculated from routine laboratory measurements. Prognostic performance for in-hospital mortality was assessed using receiver operating characteristic analyses, DeLong tests, and multivariable logistic regression. Internal validation used 1,000 bootstrap resamples. Sensitivity analyses assessed interactions by stroke type and adjustment for major comorbidities.

Results

Overall, 148 patients (20.1%) died during hospitalization. CAR showed modest discrimination in the overall cohort (AUC, 0.598) and ischemic stroke subgroup (AUC, 0.648), whereas BAR yielded an AUC of 0.631 in hemorrhagic stroke. Established predictors showed stronger discrimination, including lesion volume (AUC, 0.890 overall and 0.895 in hemorrhagic stroke), National Institutes of Health Stroke Scale (NIHSS) score (AUC, 0.856 overall), and Intracerebral Hemorrhage (ICH) score (AUC, 0.881 in hemorrhagic stroke). CAR remained modestly associated with mortality in the overall cohort (OR, 1.03; 95% CI, 1.00–1.05; p = 0.032) and ischemic stroke subgroup (OR, 1.03; 95% CI, 1.00–1.06; p = 0.047), whereas BAR was not independently associated with mortality. Optimism-corrected AUCs of the primary models were 0.909 overall, 0.884 for ischemic stroke, and 0.931 for hemorrhagic stroke. Biomarker-by-stroke-type interactions were not significant, and more complex sensitivity models did not improve discrimination.

Conclusions

BAR and CAR had limited standalone discriminatory performance compared with established neurological severity scores and imaging-based predictors. CAR retained a modest independent association with in-hospital mortality, whereas BAR did not remain significant after multivariable adjustment. These biomarkers may provide complementary rather than substitutive prognostic information. External validation is required before routine clinical use.

Background

Hemorrhagic and ischemic cerebrovascular diseases are major public health problems because of their substantial mortality and morbidity burden [1, 2]. Accordingly, numerous clinical, radiological, and laboratory markers have been investigated for prognostic assessment. In intracerebral hemorrhage (ICH), impaired level of consciousness reflected by lower Glasgow Coma Scale (GCS) scores and hydrocephalus are recognized markers of disease severity, while faster perihematomal edema expansion has been associated with worse clinical outcomes [3, 4]. The NIHSS has established prognostic value for assessing stroke severity and outcome [5]. Radiologically measured infarct volume is also an important predictor of clinical outcome [6], whereas the ICH score is a validated prognostic tool for mortality and functional outcome in patients with intracerebral hemorrhage [7, 8]. These measures provide early information regarding neurological injury, disease severity, and prognosis.

Inflammation plays an important role in the pathophysiology of both ischemic and hemorrhagic stroke; tissue injury and necrotic cells resulting from cerebrovascular damage contribute to the activation of inflammatory cascades [9–11]. C-reactive protein (CRP) is a positive acute-phase protein whose concentration increases in response to inflammation, whereas albumin, a negative acute-phase reactant, tends to decrease. In addition to CRP and albumin, the CRP-to-albumin ratio (CAR) in particular has been associated with disease severity and adverse clinical outcomes in patients with stroke [12–14]. Other systemic inflammatory indices have also been investigated as prognostic markers in patients with intracerebral hemorrhage [15]. In patients with spontaneous intracerebral hemorrhage, elevated CAR values have also been associated with increased in-hospital mortality [13].

Lower serum albumin concentrations have also been associated with adverse cerebrovascular outcomes [16]. In patients with acute ischemic stroke, elevated BUN-to-albumin ratio (BAR) has been associated with increased mortality [17]. BUN itself has also been reported to have prognostic significance in acute ischemic stroke [18]. More recently, an analysis of the MIMIC-IV database further demonstrated an association between higher BAR and all-cause mortality in critically ill patients with acute ischemic stroke [19]. In patients with spontaneous intracerebral hemorrhage, Bender et al. reported that an elevated urea-to-albumin ratio was independently associated with increased in-hospital mortality [20]. However, because comprehensive multivariable modeling and validation have been limited, it remains uncertain whether these biomarkers provide clinically meaningful prognostic information when evaluated alongside established clinical and radiological tools such as NIHSS, GCS, and lesion volume.

Based on these considerations, this study aimed to comprehensively evaluate the prognostic associations and discriminatory performance of BAR and CAR for in-hospital mortality in patients with ischemic and hemorrhagic stroke, and to determine whether these biomarkers remained independently associated with mortality after accounting for established clinical and radiological predictors, including NIHSS, GCS, ICH score, and lesion volume.

Methods

Study design and setting

This retrospective study reviewed the records of patients diagnosed with hemorrhagic or ischemic cerebrovascular events who presented to the Emergency Department of Necmettin Erbakan University Faculty of Medicine between January 2020 and January 2025. The study was conducted in accordance with the Declaration of Helsinki after approval by the institutional ethics committee (Ethics Committee: T.C. NECMETTİN ERBAKAN ÜNİVERSİTESİ İLAÇ VE TIBBİ CİHAZ DIŞI ARAŞTIRMALAR ETİK KURUL KARARI; Approval No: 2025/5688; Approval Date: April 11, 2025). The requirement for informed consent was waived by the ethics committee because of the retrospective design. Following ethics approval, eligible patients were screened between April 12, 2025 and May 12, 2025.

Patient selection

Adult patients with ischemic or hemorrhagic stroke confirmed by cranial computed tomography (CT) or magnetic resonance imaging (MRI) were eligible for inclusion. Patients with the following characteristics were excluded:

- • Traumatic intracerebral hemorrhage,
- • Cerebrovascular malformations,
- • History of cerebral malignancy,
- • Acute or chronic hepatic failure,
- • Acute or chronic renal failure,
- • Missing data required for the study analyses.

Data collection

Patient data were retrospectively obtained from the hospital electronic medical record system. Demographic variables included age and sex. Recorded comorbidities included hypertension, diabetes mellitus, cardiovascular disease, chronic obstructive pulmonary disease (COPD), malignancy, and previous ischemic or hemorrhagic stroke. Clinical data included admission GCS and NIHSS scores, ICH score, modified Rankin Scale (mRS) score at hospital outcome/discharge, radiologically measured infarct/hemorrhage volume, presence of intraventricular hemorrhage or infratentorial localization, intensive care unit admission, and in-hospital outcome (survival or mortality).

Biochemical parameters

Biochemical parameters measured at emergency department admission were included for all patients. These parameters comprised:

- • Blood urea nitrogen (BUN),
- • Albumin,
- • C-reactive protein (CRP),
- • Lactate,
- • Ionized calcium (iCa).

According to the institutional emergency department protocol, initial blood samples are routinely obtained simultaneously with placement of a peripheral intravenous catheter, either during the initial triage assessment or immediately after transfer to the patient bed, before administration of substantial intravenous fluids or specific medical therapies.

Blood samples were analyzed using a Roche Cobas c702 autoanalyzer (Roche Diagnostics GmbH, Mannheim, Germany). The institutional laboratory reports serum urea rather than direct BUN measurements; therefore, BUN was calculated from serum urea using the standard conversion formula BUN = urea / 2.14. Institutional reference ranges were CRP, 0–5 mg/L; albumin, 3.5–5.2 g/dL; and serum urea, 16.6–48.5 mg/dL. BAR was calculated by dividing BUN (mg/dL) by albumin (g/dL), and CAR was calculated by dividing CRP (mg/L) by albumin (g/dL), using the initial values obtained at emergency department admission. Ionized calcium and lactate were measured simultaneously in admission blood gas samples using a Radiometer ABL800 FLEX analyzer (Radiometer Medical ApS, Copenhagen, Denmark).

Clinical and radiological measurements

For patients with hemorrhagic stroke, admission non-contrast cranial CT scans with a slice thickness of 5 mm were evaluated. Hematoma volume was determined using the established ABC/2 ellipsoid method [21]. The CT slice containing the largest hemorrhage area was identified, and the maximum diameter (A) and its perpendicular diameter (B) were measured. The craniocaudal dimension (C) was calculated by multiplying the number of CT slices containing hemorrhage by the 5-mm slice thickness. Hematoma volume in milliliters was then calculated using the ABC/2 formula. Additional radiological severity parameters, including ICH score, intraventricular extension, and infratentorial localization, were determined from the imaging findings.

For patients with ischemic stroke, infarct volumes were measured on admission cranial CT or MRI. Infarct volume was similarly estimated using the ABC/2 formula, primarily using diffusion-weighted imaging sequences when MRI was available, by identifying the maximum orthogonal diameters (A and B) and craniocaudal extent (C) of the ischemic lesion.

In addition to radiological assessment, admission Glasgow Coma Scale (GCS) and National Institutes of Health Stroke Scale (NIHSS) scores were extracted from the medical records to characterize neurological severity at presentation. The modified Rankin Scale (mRS) was assessed at hospital outcome/discharge as a measure of functional outcome. Because mRS is an outcome measure and incorporates death within its scale, it was not included as a predictor in the multivariable mortality models.

Primary and secondary outcomes

The primary outcome of the study was in-hospital mortality. The primary objective was to evaluate the prognostic associations and discriminatory performance of BAR and CAR for in-hospital mortality in patients with acute ischemic or hemorrhagic stroke. Secondary objectives were to determine whether BAR and CAR remained independently associated with mortality after adjustment for established clinical and radiological prognostic factors, including GCS, NIHSS score, stroke subtype, and lesion volume, and to compare their discriminatory performance with established clinical and radiological predictors, including GCS, NIHSS, ICH score, and lesion volume. Additional sensitivity analyses evaluated whether the associations of BAR and CAR with mortality differed according to stroke subtype and whether adjustment for major comorbidities materially altered the primary findings. The associations of lactate and ionized calcium levels with mortality were also evaluated.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA), and Python version 3.x in the Google Colaboratory (Google Colab) environment, using the statsmodels, scikit-learn, scipy, and pandas libraries. The distribution of continuous variables was assessed using the Kolmogorov-Smirnov test. Because continuous variables did not demonstrate normal distributions, they are presented as medians with interquartile ranges (25th-75th percentiles). Two-group comparisons, including comparisons according to stroke subtype and survival status, were performed using the Mann-Whitney U test. Categorical variables are presented as frequencies and percentages and were compared using the Pearson chi-square test or Fisher's exact test, where appropriate. All statistical tests were two-sided, and a p value < 0.05 was considered statistically significant.

Receiver operating characteristic (ROC) curve analyses were performed to evaluate the discriminatory performance of clinical variables, laboratory parameters, BAR, and CAR for in-hospital mortality. Optimal cut-off values were identified using the maximum Youden index. Internal validation of threshold performance was conducted using 1,000 bootstrap resamples, and apparent sensitivity and specificity estimates were reported together with optimism-corrected estimates. Pairwise comparisons of AUCs between the proposed ratios, their individual components, and established clinical and radiological predictors were performed using DeLong's test. These analyses were interpreted as pairwise comparisons of discriminatory performance rather than as evidence of incremental multivariable model value.

Multivariable binary logistic regression analyses were performed using clinically selected predictors entered simultaneously into the models. Model complexity was constrained according to the number of observed outcome events and the clinical relevance of candidate predictors to reduce the risk of overfitting and numerical instability. In the overall cohort, the primary multivariable model included age, GCS, NIHSS score, stroke/hemorrhage volume, stroke type, BAR, and CAR. Stroke type was entered as a categorical variable, with ischemic stroke as the reference category and hemorrhagic stroke as the index category. The ischemic stroke model included age, GCS, NIHSS score, stroke volume, BAR, and CAR. The hemorrhagic stroke model included age, GCS, NIHSS score, hemorrhage volume, intraventricular hemorrhage, infratentorial hemorrhage, BAR, and CAR. Associations are reported as odds ratios (ORs) with 95% confidence intervals (CIs).

To evaluate the robustness of the primary full-cohort model, three additional sensitivity models were constructed. Model 2 (Interaction Model) extended Model 1 by adding the Stroke Type × BAR and Stroke Type × CAR interaction terms to formally assess potential effect modification by stroke subtype. Model 3 (Comorbidity-Adjusted Model) extended Model 1 by additionally adjusting for hypertension, diabetes mellitus, cardiovascular disease, and previous cerebrovascular disease. Model 4 (Fully Adjusted Model) included the variables from Model 3 together with both interaction terms. For Models 2 and 4, BAR and CAR were mean-centered before construction of the interaction terms to reduce nonessential multicollinearity between the product terms and their constituent main effects. The interaction analyses were used to formally test whether the associations of BAR or CAR with mortality differed between ischemic and hemorrhagic stroke.

Model discrimination was quantified using the area under the ROC curve (AUC), and explanatory performance was additionally summarized using Nagelkerke R^2. Overall prediction error was evaluated using the Brier score. Calibration was assessed using the calibration intercept and calibration slope and was additionally visualized using calibration plots comparing predicted probabilities with observed mortality proportions. The Hosmer-Lemeshow test was used as an additional goodness-of-fit assessment; a p value > 0.05 was interpreted as no statistically significant evidence of lack of fit. Akaike's Information Criterion (AIC) was used to compare relative model fit among models fitted to the same cohort.

Internal validation of the multivariable models was performed using 1,000 bootstrap resamples. Apparent model performance was calculated in the original development dataset, whereas optimism-corrected AUC, Nagelkerke R^2, Brier score, calibration intercept, and calibration slope were obtained from bootstrap validation. Because the apparent calibration intercept and slope are 0 and 1 by construction, respectively, optimism-corrected values were used to assess calibration after internal validation. Graphically presented calibration curves represent apparent performance in the model-development dataset and were not corrected for optimism.

To directly assess whether the additional interaction terms or comorbidity adjustment improved discrimination beyond the primary model, bootstrap-based pairwise differences in AUC (ΔAUC) were

calculated for Model 2 versus Model 1, Model 3 versus Model 1, and Model 4 versus Model 1. Differences were reported with 95% CIs and corresponding two-sided p values.

Multicollinearity was assessed using variance inflation factors (VIFs) in the primary, interaction, comorbidity-adjusted, fully adjusted, and stroke subtype-specific models. A conventional VIF threshold of 5 was used to identify potentially problematic multicollinearity. For Models 2 and 4, BAR and CAR were mean-centered before constructing the corresponding interaction terms.

Use of generative artificial intelligence

During manuscript preparation, ChatGPT (OpenAI) was used to support English-language editing, manuscript organization, and formatting. Gemini (Google) was used to assist with the generation, refinement, and troubleshooting of Python code for selected advanced statistical analyses. All statistical analyses were executed by the authors in the Google Colaboratory environment using the analytical methods and Python libraries described above. AI-generated code was reviewed and adapted as necessary by the authors, and all statistical outputs were reviewed and verified by the authors before inclusion in the manuscript. The generative AI tools did not independently determine the statistical analysis plan, select variables, interpret the results, or draw scientific conclusions. The authors take full responsibility for the statistical analyses and the final content of the manuscript.

Results

Study population and overall characteristics

A total of 736 patients with acute stroke were included in the final analysis, comprising 582 patients (79.1%) with ischemic stroke and 154 patients (20.9%) with hemorrhagic stroke (Fig. 1). The median age of the overall cohort was 72 years (interquartile range [IQR], 63–80 years), and 410 patients (55.7%) were male. The median systolic blood pressure (SBP) was 154 mmHg (IQR, 132–180 mmHg), and the median GCS score was 15 (IQR, 13–15). The median NIHSS score was 6 (IQR, 4–9), the median mRS score at hospital outcome/discharge was 3 (IQR, 2–4), and the median stroke/hemorrhage volume was 4.19 mL (IQR, 1.52–15.54 mL). Among patients with hemorrhagic stroke, the median ICH score was 1 (IQR, 0–2). The overall demographic, clinical, laboratory, and outcome characteristics of the study population are summarized in Table 1.

Table 1
Demographic, Clinical, Laboratory, and Outcome Characteristics of the Overall Cohort (n = 736)

		All Patients (n = 736, 100%)
Age		72 (63–80)
Gender	Male	410 (55.7%)
	Female	326 (44.3%)
Vital Signs	Systolic Blood Pressure (mmHg)	154 (132–180)
	Diastolic Blood Pressure (mmHg)	82 (73–96)
Clinical Scores & Volumes	Glasgow coma scale	15 (13–15)
	NIHSS Score	6 (4–9)
	Modified Rankin Scale at hospital outcome/discharge	3 (2–4)
	Stroke / Hemorrhage Volume (mL)	4.19 (1.52–15.54)
	ICH Score (n = 154)	1 (0–2)
Hemorrhage Characteristics (n = 154)	Intraventricular Hemorrhage	54 (35.1%)
	Infratentorial Hemorrhage	56 (36.4%)
Laboratory Results	BUN (mg/dL)	17.06 (13.44–21.64)
	Albumin (g/dL)	4.06 (3.8–4.25)
	CRP (mg/L)	4.47 (1.91–12.25)
	Lactate (mmol/L)	1.6 (1.2–2.3)
	ICA (mmol/L)	1.18 (1.1–1.22)
	BAR	4.26 (3.34–5.57)
	CAR	1.11 (0.46–2.96)
Medical History	Hypertension	431 (58.6%)
	Diabetes Mellitus	245 (33.3%)
	Cerebrovascular Disease	174 (23.6%)

Data are presented as median (interquartile range, 25th–75th percentile) for continuous variables and as frequency (percentage) for categorical variables. ICH score, intraventricular hemorrhage, and infratentorial hemorrhage were assessed only in the hemorrhagic stroke subgroup (n = 154).

Abbreviations: COPD: Chronic Obstructive Pulmonary Disease; ICU: Intensive Care Unit; BUN: Blood Urea Nitrogen; BAR: BUN/Albumin Ratio; CRP: C-Reactive Protein; CAR: CRP/Albumin Ratio; ICA: Ionized Calcium; NIHSS: National Institutes of Health Stroke Scale; ICH: Intracerebral Hemorrhage.

	Cardiovascular Disease	196 (26.6%)
	Malignancy	48 (6.5%)
	COPD	40 (5.4%)
Emergency Department Disposition	Discharged	15 (2%)
	Ward Unit	376 (51.1%)
	ICU	345 (46.9%)
In-Hospital Mortality	Survivors	588 (79.9%)
	Nonsurvivors	148 (20.1%)
Stroke Type	Ischemic	582 (79.1%)
	Hemorrhagic	154 (20.9%)

Data are presented as median (interquartile range, 25th–75th percentile) for continuous variables and as frequency (percentage) for categorical variables. ICH score, intraventricular hemorrhage, and infratentorial hemorrhage were assessed only in the hemorrhagic stroke subgroup (n = 154).

Abbreviations: COPD: Chronic Obstructive Pulmonary Disease; ICU: Intensive Care Unit; BUN: Blood Urea Nitrogen; BAR: BUN/Albumin Ratio; CRP: C-Reactive Protein; CAR: CRP/Albumin Ratio; ICA: Ionized Calcium; NIHSS: National Institutes of Health Stroke Scale; ICH: Intracerebral Hemorrhage.

The median BUN concentration was 17.06 mg/dL (IQR, 13.44–21.64), and the median serum albumin concentration was 4.06 g/dL (IQR, 3.80–4.25). Median CRP, lactate, and ionized calcium concentrations were 4.47 mg/L (IQR, 1.91–12.25), 1.6 mmol/L (IQR, 1.2–2.3), and 1.18 mmol/L (IQR, 1.10–1.22), respectively. The median BAR was 4.26 (IQR, 3.34–5.57), and the median CAR was 1.11 (IQR, 0.46–2.96). Hypertension was the most common comorbidity (58.6%), followed by diabetes mellitus (33.3%), cardiovascular disease (26.6%), and previous cerebrovascular disease (23.6%). Overall, 345 patients (46.9%) required intensive care unit admission, and 148 patients (20.1%) died during hospitalization.

Comparison of ischemic and hemorrhagic stroke

Several clinically relevant differences were observed between patients with ischemic and hemorrhagic stroke (Table 2). Patients with hemorrhagic stroke were younger than those with ischemic stroke (median, 67 [IQR, 55–77] vs. 73 [IQR, 65–80] years; $p < 0.001$). Neurological severity at presentation was greater in the hemorrhagic group, with lower GCS scores (13 [IQR, 5.75–15] vs. 15 [IQR, 14–15]; $p < 0.001$) and higher NIHSS scores (9.5 [IQR, 3–18] vs. 3 [IQR, 1–8]; $p < 0.001$). Functional outcome at hospital discharge was also poorer in the hemorrhagic group, with higher mRS scores (5 [IQR, 2–6] vs. 1 [IQR, 1–3]; $p < 0.001$).

Table 2
Comparison of Demographic, Clinical, Laboratory, and Outcome Characteristics by Stroke Subtype

Age		**Hemorrhagic (154)**	**Ischemic (582)**	**p value**
		67(55–77)	**73(65–80)**	**< 0.001**
Glasgow coma scale		13(5.75-15)	15(14–15)	< 0.001
NIHSS Score		9.5 (3–18)	3 (1–8)	< 0.001
Modified Rankin Scale		5 (2–6)	1 (1–3)	< 0.001
Stroke/Hemorrhage Volume (mL)		12.49 (4.71–35.48)	1.23 (0.29–7.48)	< 0.001
SBP (mmHg)		170(131.75–190)	152(132.5–175)	0.003
DBP (mmHg)		88(72–100)	81(73–94)	0.037
BUN (mg/dL)		15.75(13.11–20.77)	17.5(13.51-22)	0.039
Albumin (g/dL)		4.1(3.77–4.39)	4.05(3.81–4.23)	0.09
CRP (mg/L)		4(1.69–11.54)	4.57(1.94–12.34)	0.546
Lactate (mmol/L)		1.6(1.18–2.4)	1.6(1.2–2.3)	0.806
ICA (mmol/L)		1.16(1.08–1.21)	1.18(1.11–1.23)	0.002
BAR		3.93(3.18–5.16)	4.36(3.38–5.63)	0.041
CAR		0.95(0.43–2.83)	1.14(0.47–3.06)	0.491
Gender	**Male**	89(57.8%)	321(55.2%)	0.558
	Female	65(42.2%)	261(44.8%)	
Hypertension		89(57.8%)	342(58.8%)	0.828
Diabetes Mellitus		43(27.9%)	202(34.7%)	0.112
Cerebrovascular Disease		35(22.7%)	139(23.9%)	0.764
Cardiovascular Disease		38(24.7%)	158(27.1%)	0.537
Malignancy		11(7.1%)	34(6.4%)	0.726

Continuous variables are presented as median (interquartile range, 25th–75th percentile) and were compared using the Mann–Whitney U test. Categorical variables are presented as frequencies (percentages) and were compared using the Pearson chi-square test. The modified Rankin Scale was assessed at hospital outcome/discharge and is presented as an outcome measure rather than a measure of neurological severity at presentation.

Abbreviations: SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; BUN: Blood Urea Nitrogen; BAR: BUN/Albumin Ratio; CRP: C-Reactive Protein; CAR: CRP/Albumin Ratio; ICA: Ionized Calcium; COPD: Chronic Obstructive Pulmonary Disease; NIHSS: National Institutes of Health Stroke Scale.

Age	Hemorrhagic (154)	Ischemic (582)	p value
	67(55–77)	**73(65–80)**	**< 0.001**
COPD	6(3.9%)	34(5.8%)	0.344
In-Hospital Mortality	74(48.1%)	74(12.7%)	< 0.001
Continuous variables are presented as median (interquartile range, 25th–75th percentile) and were compared using the Mann–Whitney U test. Categorical variables are presented as frequencies (percentages) and were compared using the Pearson chi-square test. The modified Rankin Scale was assessed at hospital outcome/discharge and is presented as an outcome measure rather than a measure of neurological severity at presentation.			
Abbreviations: SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; BUN: Blood Urea Nitrogen; BAR: BUN/Albumin Ratio; CRP: C-Reactive Protein; CAR: CRP/Albumin Ratio; ICA: Ionized Calcium; COPD: Chronic Obstructive Pulmonary Disease; NIHSS: National Institutes of Health Stroke Scale.			

Hemorrhagic stroke was associated with substantially greater lesion volume (12.49 mL [IQR, 4.71–35.48] vs. 1.23 mL [IQR, 0.29–7.48]; p < 0.001). SBP and diastolic blood pressure (DBP) were also higher in the hemorrhagic group (170 vs. 152 mmHg, p = 0.003; and 88 vs. 81 mmHg, p = 0.037, respectively).

Among laboratory variables, BUN was lower in patients with hemorrhagic stroke than in those with ischemic stroke (15.75 vs. 17.50 mg/dL; p = 0.039), as was ionized calcium (1.16 vs. 1.18 mmol/L; p = 0.002). BAR was also lower in the hemorrhagic group (3.93 vs. 4.36; p = 0.041). Albumin, CRP, lactate, and CAR did not differ significantly between stroke subtypes. Sex distribution and recorded comorbidities were similar between groups. In-hospital mortality was substantially higher in hemorrhagic stroke than in ischemic stroke (74/154 [48.1%] vs. 74/582 [12.7%]; p < 0.001).

Comparison of survivors and nonsurvivors in the overall cohort

Of the 736 patients, 148 (20.1%) died during hospitalization and 588 (79.9%) survived to hospital discharge (Table 3). Age did not differ significantly between survivors and nonsurvivors (p = 0.815). Nonsurvivors had lower GCS scores (11 vs. 15; p < 0.001), higher NIHSS scores (13 vs. 3; p < 0.001), and markedly greater stroke/hemorrhage volume (27.17 mL [IQR, 11.15–49.28] vs. 1.07 mL [IQR, 0.28–5.30]; p < 0.001).

Table 3
Baseline Characteristics by In-Hospital Survival Status in the Overall Cohort

Age		**Nonsurvivors (148)**	**Survivors (588)**	**p value**
		72(64–80)	**72(62–80)**	**0.815**
Glasgow coma scale		11(5–15)	15(14–15)	< 0.001
NIHSS Score		13 (9–20)	3 (1–6)	< 0.001
Stroke/Hemorrhage Volume (mL)		27.17 (11.15–49.28)	1.07 (0.28–5.30)	< 0.001
SBP (mmHg)		153.5(130–180)	154(134–180)	0.971
DBP (mmHg)		84(70–100)	81(74–95)	0.871
BUN (mg/dL)		16.89(13.44–24.08)	17.08(13.39–21.19)	0.229
Albumin (g/dL)		3.96(3.42–4.31)	4.06(3.84–4.25)	0.018
CRP (mg/L)		6.59(2.56–19.95)	4.19(1.74–10.16)	0.001
Lactate (mmol/L)		1.8(1.23–2.88)	1.6(1.2–2.2)	0.003
ICA (mmol/L)		1.17(1.1–1.22)	1.18(1.1–1.22)	0.624
BAR		4.51(3.49–6.22)	4.23(3.33–5.39)	0.052
CAR		1.57(0.64–5.59)	1.03(0.43–2.59)	< 0.001
Gender	**Male**	83(56.1%)	327(55.6%)	0.918
	Female	65(43.9%)	261(44.4%)	
Hypertension		84(56.8%)	347(59%)	0.618
Diabetes Mellitus		40(27%)	205(34.9%)	0.071
Cerebrovascular Disease		34(23%)	140(23.8%)	0.830
Cardiovascular Disease		43(29.1%)	153(26%)	0.456
Malignancy		14(9.5%)	34(5.8%)	0.105
COPD		13(8.8%)	27(4.6%)	0.044

Continuous variables are presented as median (interquartile range, 25th–75th percentile) and were compared using the Mann-Whitney U test. Categorical variables are presented as frequencies (percentages) and were compared using the Pearson Chi-Square test, as expected cell counts were ≥ 5 in all categories. A p-value of < 0.05 was considered statistically significant.

Abbreviations: SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; BUN: Blood Urea Nitrogen; BAR: BUN/Albumin Ratio; CRP: C-Reactive Protein; CAR: CRP/Albumin Ratio; ICA: Ionized Calcium; COPD: Chronic Obstructive Pulmonary Disease; NIHSS: National Institutes of Health Stroke Scale.

Serum albumin was lower in nonsurvivors than in survivors (3.96 vs. 4.06 g/dL; p = 0.018), whereas CRP (6.59 vs. 4.19 mg/L; p = 0.001), lactate (1.8 vs. 1.6 mmol/L; p = 0.003), and CAR (1.57 vs. 1.03; p < 0.001) were higher. BUN and ionized calcium did not differ significantly. BAR showed a borderline difference (p = 0.052) but did not reach statistical significance. COPD was more frequent among nonsurvivors (8.8% vs. 4.6%; p = 0.044).

Mortality-related characteristics in ischemic stroke

Within the ischemic stroke subgroup (Table 4), nonsurvivors had lower GCS scores (13 [IQR, 8–15] vs. 15 [IQR, 15–15]; p < 0.001), higher NIHSS scores (12 [IQR, 9–17] vs. 3 [IQR, 1–6]; p < 0.001), and greater stroke volume (22.24 mL [IQR, 5.55–37.45] vs. 0.85 mL [IQR, 0.25–4.41]; p < 0.001).

Table 4
Baseline Characteristics by In-Hospital Survival Status in Ischemic Stroke

Age		**Nonsurvivors (74)**	**Survivors (508)**	**p value**
		73.5(65–84)	**73(65–80)**	**0.224**
Glasgow coma scale		13(8–15)	15(15–15)	< 0.001
NIHSS Score		12 (9–17)	3 (1–6)	< 0.001
Stroke Volume (mL)		22.24 (5.55–37.45)	0.85 (0.25–4.41)	< 0.001
SBP (mmHg)		150(123-165.5)	153(134–176)	0.206
DBP (mmHg)		80(70–94)	81(74–94)	0.377
BUN (mg/dL)		18.34(13.43–24.35)	17.45(13.58–21.56)	0.483
Albumin (g/dL)		3.8(3.23–4.21)	4.05(3.84–4.23)	< 0.001
CRP (mg/L)		8.41(3.01–24.55)	4.3(1.83–10.41)	< 0.001
Lactate (mmol/L)		2(1.38–3.03)	1.6(1.2–2.2)	0.003
ICA (mmol/L)		1.18(1.11–1.22)	1.18(1.11–1.23)	0.832
BAR		4.51(3.42–6.6)	4.31(3.38–5.52)	0.123
CAR		2.39(0.74–7.03)	1.07(0.43–2.65)	< 0.001
Gender	**Male**	38(51.4%)	283(55.7%)	0.496
	Female	36(48.6%)	225(44.3%)	
Hypertension		39(52.7%)	303(59.6%)	0.257
Diabetes Mellitus		22(29.7%)	180(35.4%)	0.336
Cerebrovascular Disease		18(24.3%)	121(23.8%)	0.924
Cardiovascular Disease		24(32.4%)	134(26.4%)	0.274
Malignancy		5(6.8%)	32(6.3%)	0.801*

Continuous variables are presented as median (interquartile range, 25th–75th percentile) and were compared using the Mann-Whitney U test. Categorical variables are presented as frequencies (percentages) and were compared using the Pearson Chi-Square test, except where noted. A p-value of < 0.05 was considered statistically significant.

* Fisher's Exact test was used because the expected cell counts were < 5.

Abbreviations: SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; BUN: Blood Urea Nitrogen; BAR: BUN/Albumin Ratio; CRP: C-Reactive Protein; CAR: CRP/Albumin Ratio; ICA: Ionized Calcium; COPD: Chronic Obstructive Pulmonary Disease; NIHSS: National Institutes of Health Stroke Scale.

Age	Nonsurvivors (74)	Survivors (508)	p value
	73.5(65–84)	**73(65–80)**	**0.224**
COPD	9(12.2%)	25(4.9%)	0.028*
Continuous variables are presented as median (interquartile range, 25th–75th percentile) and were compared using the Mann-Whitney U test. Categorical variables are presented as frequencies (percentages) and were compared using the Pearson Chi-Square test, except where noted. A p-value of < 0.05 was considered statistically significant.			
* Fisher's Exact test was used because the expected cell counts were < 5.			
Abbreviations: SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; BUN: Blood Urea Nitrogen; BAR: BUN/Albumin Ratio; CRP: C-Reactive Protein; CAR: CRP/Albumin Ratio; ICA: Ionized Calcium; COPD: Chronic Obstructive Pulmonary Disease; NIHSS: National Institutes of Health Stroke Scale.			

Albumin was lower in ischemic nonsurvivors (3.80 vs. 4.05 g/dL; p < 0.001), whereas CRP (8.41 vs. 4.30 mg/L; p < 0.001), lactate (2.0 vs. 1.6 mmol/L; p = 0.003), and CAR (2.39 vs. 1.07; p < 0.001) were higher. BAR did not differ significantly between survivors and nonsurvivors (p = 0.123). COPD was more frequent among nonsurvivors (12.2% vs. 4.9%; p = 0.028).

Mortality-related characteristics in hemorrhagic stroke

In the hemorrhagic stroke subgroup (Table 5), nonsurvivors had lower GCS scores (7 [IQR, 3-14.25] vs. 15 [IQR, 12–15]; p < 0.001), higher NIHSS scores (15 [IQR, 9.5–24.5] vs. 4 [IQR, 1–10]; p < 0.001), higher ICH scores (3 vs. 0; p < 0.001), and substantially greater hemorrhage volume (33.57 mL [IQR, 18.04–54.11] vs. 4.76 mL [IQR, 1.44–10.22]; p < 0.001). Intraventricular hemorrhage was present in 62.7% of nonsurvivors compared with 8.9% of survivors (p < 0.001), and infratentorial hemorrhage was present in 58.7% and 15.2%, respectively (p < 0.001).

Table 5
Baseline Characteristics by In-Hospital Survival Status in Hemorrhagic Stroke

Age		**Nonsurvivors (74)**	**Survivors (80)**	**p value**
		70(61.5-77.25)	**65.5(53–75)**	**0.084**
Glasgow coma scale		7(3-14.25)	15(12–15)	< 0.001
NIHSS Score		15 (9.5–24.5)	4 (1–10)	< 0.001
ICH Score		3 (2–4)	0 (0–1)	< 0.001
Hemorrhage Volume (mL)		33.57 (18.04–54.11)	4.76 (1.44–10.22)	< 0.001
Intraventricular Hemorrhage		47 (62.7%)	7 (8.9%)	< 0.001
Infratentorial Hemorrhage		44 (58.7%)	12 (15.2%)	< 0.001
SBP (mmHg)		170(130.75–188.5)	168(134.25-191.75)	0.704
DBP (mmHg)		89(74.75–100.5)	88(72–100)	0.977
BUN (mg/dL)		16.8(13.63–23.75)	14.91(12.76–19.04)	0.009
Albumin (g/dL)		4.09(3.61–4.39)	4.11(3.82–4.39)	0.497
CRP (mg/L)		5.16(2.07–16.26)	2.99(1.6–9.77)	0.143
Lactate (mmol/L)		1.75(1.2–2.58)	1.6(1.1–2.2)	0.207
ICA (mmol/L)		1.16(1.1–1.21)	1.15(1.07–1.2)	0.156
BAR		4.56(3.51–5.77)	3.68(3.03–4.77)	0.007
CAR		1.31(0.51–3.85)	0.74(0.4–2.34)	0.127
Gender	**Male**	45(60.8%)	44(55%)	0.466
	Female	29(39.2%)	36(45%)	
Hypertension		45(60.8%)	44(55%)	0.466
Diabetes Mellitus		18(24.3%)	25(31.3%)	0.338
Cerebrovascular Disease		16(21.6%)	19(23.8%)	0.753

Continuous variables are presented as median (interquartile range, 25th–75th percentile) and were compared using the Mann-Whitney U test. Categorical variables are presented as frequencies (percentages) and were compared using the Pearson Chi-Square test, except where noted. A p-value of < 0.05 was considered statistically significant.

* Fisher's Exact test was used because the expected cell counts were < 5.

Abbreviations: SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; BUN: Blood Urea Nitrogen; BAR: BUN/Albumin Ratio; CRP: C-Reactive Protein; CAR: CRP/Albumin Ratio; ICA: Ionized Calcium; COPD: Chronic Obstructive Pulmonary Disease; NIHSS: National Institutes of Health Stroke Scale; ICH: Intracerebral Hemorrhage.

Age	Nonsurvivors (74)	Survivors (80)	p value
	70(61.5-77.25)	**65.5(53–75)**	**0.084**
Cardiovascular Disease	19(25.7%)	19(23.8%)	0.782
Malignancy	9(12.2%)	2(2.5%)	0.020
COPD	4(5.4%)	2(2.5%)	0.428*
Continuous variables are presented as median (interquartile range, 25th–75th percentile) and were compared using the Mann-Whitney U test. Categorical variables are presented as frequencies (percentages) and were compared using the Pearson Chi-Square test, except where noted. A p-value of < 0.05 was considered statistically significant.			
* Fisher's Exact test was used because the expected cell counts were < 5.			
Abbreviations: SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; BUN: Blood Urea Nitrogen; BAR: BUN/Albumin Ratio; CRP: C-Reactive Protein; CAR: CRP/Albumin Ratio; ICA: Ionized Calcium; COPD: Chronic Obstructive Pulmonary Disease; NIHSS: National Institutes of Health Stroke Scale; ICH: Intracerebral Hemorrhage.			

BUN was higher among hemorrhagic nonsurvivors (16.80 vs. 14.91 mg/dL; p = 0.009), and BAR was similarly elevated (4.56 vs. 3.68; p = 0.007). Albumin, CRP, lactate, ionized calcium, and CAR did not differ significantly between survivors and nonsurvivors. Malignancy was more frequent among nonsurvivors (12.2% vs. 2.5%; p = 0.020).

Discriminatory performance of clinical and laboratory parameters

ROC curve analyses were performed to evaluate discrimination for in-hospital mortality (Table 6). In the overall cohort, stroke/hemorrhage volume showed the highest AUC (0.890; 95% CI, 0.862–0.915), followed by NIHSS (AUC, 0.856; 95% CI, 0.818–0.886) and GCS (AUC, 0.771; 95% CI, 0.723–0.815). CAR showed modest discrimination (AUC, 0.598; 95% CI, 0.545–0.649), while CRP and albumin yielded AUCs of 0.593 and 0.559, respectively (Fig. 2).

Table 6
ROC Analysis and Bootstrap-Validated Threshold Performance for In-Hospital Mortality

Group & Parameter	AUC (95% CI)	Cut-off level	Apparent Sens % (95% CI)	Corrected Sens %	Apparent Spec % (95% CI)	Corrected Spec %
All Patients						
CRP (mg/L)	0.593 (0.540–0.646)	> 9.57	42.3 (29.0-82.7)	39.7	74.4 (33.5–86.5)	73.7
Albumin (g/dL)	0.559 (0.495–0.619)	< 3.66	36.9 (25.0-45.2)	35.8	86.7 (82.8–94.8)	86.5
CAR	0.598 (0.545–0.649)	> 2.28	45.0 (29.3–84.8)	42.4	73.3 (34.0-87.9)	72.6
Lactate (mmol/L)	0.579 (0.523–0.634)	> 2.20	40.9 (15.7–67.1)	38.6	74.1 (50.7–96.9)	73.5
NIHSS Score	0.856 (0.818–0.886)	> 9	76.5 (70.3–88.1)	75.5	81.6 (69.0-85.9)	81.3
GCS	0.771 (0.723–0.815)	< 13	67.1 (52.0-74.3)	66.3	80.1 (75.7–91.9)	79.9
Stroke/Hemorrhage Volume (mL)	0.890 (0.862–0.915)	> 6.11	85.2 (74.7–95.0)	83.5	77.5 (66.9–87.2)	77.1
Ischemic Stroke						
CRP (mg/L)	0.638 (0.566–0.708)	> 15.45	42.7 (33.9–87.5)	39.2	82.0 (34.6–88.5)	81.5
Albumin (g/dL)	0.627 (0.545–0.714)	< 3.66	46.7 (32.9–61.6)	44.9	87.5 (74.4–95.0)	87.3

Receiver operating characteristic (ROC) analysis was performed to assess discrimination for in-hospital mortality. Optimal cut-off values were determined using the maximum Youden index. Apparent sensitivity and specificity were calculated in the original dataset, and optimism-corrected sensitivity and specificity estimates were obtained using 1,000 bootstrap resamples. Apparent estimates are presented with 95% confidence intervals, whereas optimism-corrected estimates are reported as point estimates.

Abbreviations: ROC, Receiver Operating Characteristic; AUC, Area Under the Curve; CI, Confidence Interval; CRP, C-Reactive Protein; CAR, C-Reactive Protein-to-Albumin Ratio; GCS, Glasgow Coma Scale; NIHSS, National Institutes of Health Stroke Scale; BUN, Blood Urea Nitrogen; BAR, Blood Urea Nitrogen-to-Albumin Ratio; ICH, Intracerebral Hemorrhage; Sens, Sensitivity; Spec, Specificity.

Group & Parameter	AUC (95% CI)	Cut-off level	Apparent Sens % (95% CI)	Corrected Sens %	Apparent Spec % (95% CI)	Corrected Spec %
CAR	0.648 (0.578–0.716)	> 4.81	40.0 (33.9–89.9)	36.4	85.9 (34.1–89.2)	85.4
Lactate (mmol/L)	0.609 (0.536–0.681)	> 2.20	45.3 (25.3–80.6)	41.7	74.5 (40.1–91.4)	74.0
NIHSS Score	0.861 (0.819–0.902)	> 7	84.0 (74.7–92.9)	82.1	77.8 (70.6–85.3)	77.6
GCS	0.739 (0.672–0.798)	< 13	60.0 (47.9–73.5)	58.9	82.9 (73.3–90.3)	82.8
Stroke Volume (mL)	0.862 (0.825-0.900)	> 3.32	86.7 (68.7–96.9)	83.5	70.6 (59.4–88.9)	70.1
Hemorrhagic Stroke						
BUN (mg/dL)	0.631 (0.542–0.718)	> 15.35	66.7 (25.6–81.3)	63.8	58.2 (46.4–96.2)	55.6
BAR	0.631 (0.543–0.716)	> 4.83	50.7 (39.8–85.1)	48.6	78.5 (41.4–88.7)	77.1
NIHSS Score	0.812 (0.733–0.877)	> 12	68.0 (58.0-84.9)	66.4	83.5 (65.8–91.4)	82.0
GCS	0.739 (0.658–0.819)	< 10	64.0 (48.6–77.9)	62.1	81.0 (70.1–93.8)	79.4
Hemorrhage Volume (mL)	0.895 (0.840–0.937)	> 13.76	80.0 (69.2–98.7)	77.2	83.5 (62.3–94.4)	81.4

Receiver operating characteristic (ROC) analysis was performed to assess discrimination for in-hospital mortality. Optimal cut-off values were determined using the maximum Youden index. Apparent sensitivity and specificity were calculated in the original dataset, and optimism-corrected sensitivity and specificity estimates were obtained using 1,000 bootstrap resamples. Apparent estimates are presented with 95% confidence intervals, whereas optimism-corrected estimates are reported as point estimates.

Abbreviations: ROC, Receiver Operating Characteristic; AUC, Area Under the Curve; CI, Confidence Interval; CRP, C-Reactive Protein; CAR, C-Reactive Protein-to-Albumin Ratio; GCS, Glasgow Coma Scale; NIHSS, National Institutes of Health Stroke Scale; BUN, Blood Urea Nitrogen; BAR, Blood Urea Nitrogen-to-Albumin Ratio; ICH, Intracerebral Hemorrhage; Sens, Sensitivity; Spec, Specificity.

Group & Parameter	AUC (95% CI)	Cut-off level	Apparent Sens % (95% CI)	Corrected Sens %	Apparent Spec % (95% CI)	Corrected Spec %
ICH Score	0.881 (0.825–0.928)	> 2	81.3 (62.8–100.0)	79.8	75.9 (50.7–92.5)	74.5

Receiver operating characteristic (ROC) analysis was performed to assess discrimination for in-hospital mortality. Optimal cut-off values were determined using the maximum Youden index. Apparent sensitivity and specificity were calculated in the original dataset, and optimism-corrected sensitivity and specificity estimates were obtained using 1,000 bootstrap resamples. Apparent estimates are presented with 95% confidence intervals, whereas optimism-corrected estimates are reported as point estimates.

Abbreviations: ROC, Receiver Operating Characteristic; AUC, Area Under the Curve; CI, Confidence Interval; CRP, C-Reactive Protein; CAR, C-Reactive Protein-to-Albumin Ratio; GCS, Glasgow Coma Scale; NIHSS, National Institutes of Health Stroke Scale; BUN, Blood Urea Nitrogen; BAR, Blood Urea Nitrogen-to-Albumin Ratio; ICH, Intracerebral Hemorrhage; Sens, Sensitivity; Spec, Specificity.

In the ischemic stroke subgroup, stroke volume and NIHSS demonstrated strong discrimination (AUCs, 0.862 and 0.861, respectively). CAR showed modest discrimination (AUC, 0.648; 95% CI, 0.578–0.716), while CRP, albumin, and lactate yielded AUCs of 0.638, 0.627, and 0.609, respectively (Fig. 3).

Within the hemorrhagic stroke subgroup, hemorrhage volume demonstrated the highest discrimination (AUC, 0.895; 95% CI, 0.840–0.937), followed by the ICH score (AUC, 0.881; 95% CI, 0.825–0.928) and NIHSS (AUC, 0.812). BAR and BUN each yielded an AUC of 0.631 (Fig. 4).

ROC thresholds and bootstrap-validated diagnostic performance

Optimal cut-off values were determined using the Youden index and internally validated using 1,000 bootstrap resamples (Table 6). In the overall cohort, the optimal CAR threshold was > 2.28, with an optimism-corrected sensitivity of 42.4% and specificity of 72.6%. For stroke/hemorrhage volume, a threshold > 6.11 mL yielded a corrected sensitivity of 83.5% and specificity of 77.1%.

In ischemic stroke, the optimal CAR threshold was > 4.81, with a corrected sensitivity of 36.4% and specificity of 85.4%. In hemorrhagic stroke, the optimal BAR threshold was > 4.83, with a corrected sensitivity of 48.6% and specificity of 77.1%. An ICH score threshold > 2 yielded a corrected sensitivity of 79.8% and specificity of 74.5%. Apparent and optimism-corrected threshold performance estimates were generally similar.

Comparison of ROC curves using DeLong's test

Pairwise comparisons of AUCs were performed using DeLong's test to compare discriminatory performance (Table 7). In the overall cohort, CAR did not differ significantly from CRP (ΔAUC, 0.005; p =

0.068) or albumin (ΔAUC, 0.039; p = 0.249), whereas NIHSS and stroke/hemorrhage volume had significantly greater AUCs than CAR (both p < 0.001).

Table 7
Pairwise Comparison of AUCs Using DeLong's Test for In-Hospital Mortality

Stroke Subtype	Reference Biomarker (AUC)	Compared Parameter (AUC)	AUC Difference (95% CI)	p value*
All Patients				
Biomarker vs Components	CAR (0.598)	CRP (0.593)	0.005 (-0.000 to 0.010)	0.068
	CAR (0.598)	Albumin (0.559)	0.039 (-0.027 to 0.106)	0.249
Biomarker vs Clinical/Radiological Predictors	CAR (0.598)	NIHSS Score (0.856)	-0.258 (-0.319 to -0.197)	**< 0.001**
	CAR (0.598)	Stroke/Hemorrhage Volume (0.890)	-0.292 (-0.350 to -0.235)	**< 0.001**
Ischemic Stroke				
Biomarker vs Components	CAR (0.648)	CRP (0.638)	0.010 (0.002 to 0.018)	**0.012**
	CAR (0.648)	Albumin (0.627)	0.021 (-0.066 to 0.108)	0.639
Biomarker vs Clinical/Radiological Predictors	CAR (0.648)	NIHSS Score (0.861)	-0.212 (-0.289 to -0.136)	**< 0.001**
	CAR (0.648)	Stroke Volume (0.862)	-0.214 (-0.287 to -0.141)	**< 0.001**
Hemorrhagic Stroke				
Biomarker vs Component	BAR (0.631)	BUN (0.631)	0.000 (-0.031 to 0.031)	0.987
Biomarker vs Clinical/Radiological Predictors	BAR (0.631)	ICH Score (0.881)	-0.251 (-0.353 to -0.148)	**< 0.001**
	BAR (0.631)	Hemorrhage Volume (0.895)	-0.265 (-0.366 to -0.163)	**< 0.001**

DeLong's test was used for pairwise comparison of AUCs between the selected biomarker ratios and their individual components and established clinical or radiological predictors. AUC difference was calculated as the AUC of the reference biomarker minus the AUC of the compared parameter; therefore, a positive value indicates greater discrimination by the reference biomarker.

* $p < 0.05$ indicates a statistically significant difference between the two ROC curves.

Abbreviations: AUC, Area Under the Curve; CI, Confidence Interval; CAR, C-Reactive Protein-to-Albumin Ratio; BAR, Blood Urea Nitrogen-to-Albumin Ratio; CRP, C-Reactive Protein; BUN, Blood Urea Nitrogen; NIHSS, National Institutes of Health Stroke Scale; ICH, Intracerebral Hemorrhage.

In ischemic stroke, CAR had a small but statistically significant AUC advantage over CRP (ΔAUC, 0.010; p = 0.012), but did not differ significantly from albumin (p = 0.639). NIHSS and stroke volume both had significantly greater AUCs than CAR (both p < 0.001). In hemorrhagic stroke, BAR and BUN had equivalent discriminatory performance (ΔAUC, 0.000; p = 0.987), whereas both ICH score and hemorrhage volume significantly outperformed BAR (both p < 0.001).

Multivariable logistic regression analysis

Multivariable logistic regression analyses were performed to evaluate factors independently associated with in-hospital mortality (Table 8). In the overall cohort, lower GCS (OR, 0.91; 95% CI, 0.85–0.98; p = 0.014), higher NIHSS score (OR, 1.12; 95% CI, 1.07–1.17; p < 0.001), greater stroke/hemorrhage volume (OR, 1.04; 95% CI, 1.03–1.05; p < 0.001), and hemorrhagic stroke type (OR, 3.36; 95% CI, 1.92–5.86; p < 0.001) were independently associated with in-hospital mortality. CAR also retained a modest independent association with mortality (OR, 1.03; 95% CI, 1.00-1.05; p = 0.032), whereas BAR did not reach statistical significance (OR, 1.11; 95% CI, 0.99–1.23; p = 0.066).

Table 8
Multivariable Logistic Regression Models and Bootstrap-Validated Performance for In-Hospital Mortality

Predictors	**All Patients (n = 736)**		**Ischemic Stroke (n = 582)**		**Hemorrhagic Stroke (n = 154)**	
	OR (95% CI)	**p value**	**OR (95% CI)**	**p value**	**OR (95% CI)**	**p value**
Age	1.00 (0.98–1.02)	0.853	0.99 (0.96–1.01)	0.275	1.04 (0.99–1.09)	0.085
GCS	0.91 (0.85–0.98)	**0.014**	0.91 (0.82–1.01)	0.077	0.98 (0.85–1.12)	0.722
NIHSS Score	1.12 (1.07–1.17)	**< 0.001**	1.16 (1.09–1.23)	**< 0.001**	1.04 (0.96–1.13)	0.368
Stroke/Hemorrhage Volume	1.04 (1.03–1.05)	**< 0.001**	1.03 (1.02–1.04)	**< 0.001**	1.08 (1.04–1.13)	**< 0.001**
Stroke Type*	3.36 (1.92–5.86)	**< 0.001**	N/A	N/A	N/A	N/A
Intraventricular Hemorrhage	N/A	N/A	N/A	N/A	7.14 (2.05–24.84)	**0.002**
Infratentorial Hemorrhage	N/A	N/A	N/A	N/A	9.95 (3.06–32.37)	**< 0.001**
BAR	1.11 (0.99–1.23)	0.066	1.10 (0.97–1.25)	0.129	1.18 (0.86–1.61)	0.310
CAR	1.03 (1.00–1.05)	**0.032**	1.03 (1.00–1.06)	**0.047**	1.04 (0.95–1.13)	0.401
Model Evaluation Metrics						

Predictors	All Patients (n = 736)		Ischemic Stroke (n = 582)		Hemorrhagic Stroke (n = 154)	
	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value
AUC (Apparent / Corrected)	0.913 / 0.909		0.893 / 0.884		0.949 / 0.931	
Nagelkerke R^2 (Apparent / Corrected)	0.545 / 0.523		0.421 / 0.379		0.737 / 0.634	
Brier Score (Apparent / Corrected)	0.089 / 0.093		0.078 / 0.082		0.093 / 0.116	
Calibration Intercept (Corrected)	-0.039		-0.093		-0.022	
Calibration Slope (Corrected)	0.956		0.932		0.785	
Hosmer-Lemeshow p-value	0.169		0.132		0.231	
AIC	446.2		312.6		107.4	

Multivariable logistic regression analysis was performed using clinically selected predictors entered simultaneously. To estimate and correct for optimism in model performance, internal validation was conducted using 1,000 bootstrap resamples. The 'Apparent' values represent the performance on the original dataset, whereas the 'Corrected' values represent the optimism-adjusted estimates. The apparent calibration intercept and slope are 0 and 1 by construction, respectively; therefore, only their optimism-corrected estimates are presented.

* Stroke type was used as a categorical predictor in the All Patients model (Index category: Hemorrhagic stroke, Reference category: Ischemic stroke).

Abbreviations: OR: Odds Ratio; CI: Confidence Interval; GCS: Glasgow Coma Scale; NIHSS: National Institutes of Health Stroke Scale; BAR: Blood Urea Nitrogen/Albumin Ratio; CAR: C-Reactive Protein/Albumin Ratio; AUC: Area Under the Curve; AIC: Akaike Information Criterion. (A Hosmer–Lemeshow p-value > 0.05 indicates no statistically significant evidence of lack of fit).

In the ischemic stroke subgroup, higher NIHSS score (OR, 1.16; 95% CI, 1.09–1.23; $p < 0.001$), greater stroke volume (OR, 1.03; 95% CI, 1.02–1.04; $p < 0.001$), and CAR (OR, 1.03; 95% CI, 1.00-1.06; $p = 0.047$) remained independently associated with mortality. In the hemorrhagic stroke subgroup, greater hemorrhage volume (OR, 1.08; 95% CI, 1.04–1.13; $p < 0.001$), intraventricular hemorrhage (OR, 7.14; 95% CI, 2.05–24.84; $p = 0.002$), and infratentorial hemorrhage (OR, 9.95; 95% CI, 3.06–32.37; $p < 0.001$) were independently associated with mortality. Neither BAR nor CAR remained statistically significant in the hemorrhagic subgroup. Importantly, the statistical significance of CAR in the ischemic subgroup alone was not interpreted as evidence of a subtype-specific association without formal interaction testing.

Model performance and internal validation

The primary multivariable models demonstrated high apparent discrimination, with AUCs of 0.913 for the overall cohort, 0.893 for ischemic stroke, and 0.949 for hemorrhagic stroke. After 1,000-resample bootstrap internal validation, optimism-corrected AUCs were 0.909, 0.884, and 0.931, respectively. In the ischemic and hemorrhagic subgroup models, apparent/corrected Nagelkerke R^2 values were 0.421/0.379 and 0.737/0.634, whereas apparent/corrected Brier scores were 0.078/0.082 and 0.093/0.116, respectively. Corrected calibration intercepts were − 0.093 and − 0.022, and corrected calibration slopes were 0.932 and 0.785. Hosmer-Lemeshow tests showed no statistically significant evidence of lack of fit in either subgroup model ($p = 0.132$ and $p = 0.231$, respectively). The greater reduction in calibration slope and increase in corrected Brier score in the hemorrhagic model indicated more pronounced optimism than in the ischemic model.

For the overall primary model, the latest bootstrap estimates were an apparent/corrected AUC of 0.913/0.909, apparent/corrected Nagelkerke R^2 of 0.545/0.523, apparent/corrected Brier score of 0.089/0.093, corrected calibration intercept of -0.039, and corrected calibration slope of 0.956. The Hosmer-Lemeshow p value was 0.169 and the AIC was 446.2. The calibration curves are presented in Fig. 5. These curves represent apparent model-development calibration rather than optimism-corrected calibration and should therefore be interpreted together with the bootstrap-corrected calibration metrics reported in Tables 8 and 9.

Table 9
Sensitivity Analyses and Bootstrap-Validated Performance of Multivariable Models in the Overall Cohort

Predictors	Model 1 (Primary Clinical)	Model 2 (Interaction)	Model 3 (Comorbidity-Adjusted)	Model 4 (Fully Adjusted)
Age	1.00 (0.98–1.02) p = 0.853	1.00 (0.98–1.02) p = 0.878	1.00 (0.98–1.02) p = 0.878	1.00 (0.98–1.02) p = 0.890
GCS	0.91 (0.85–0.98) p = 0.014	0.91 (0.85–0.98) p = 0.015	0.91 (0.85–0.98) p = 0.016	0.91 (0.85–0.98) p = 0.017
NIHSS Score	1.12 (1.07–1.17) p < 0.001	1.12 (1.07–1.17) p < 0.001	1.12 (1.07–1.18) p < 0.001	1.12 (1.07–1.18) p < 0.001
Stroke / Hemorrhage Volume	1.04 (1.03–1.05) p < 0.001	1.04 (1.03–1.05) p < 0.001	1.04 (1.03–1.05) p < 0.001	1.04 (1.03–1.05) p < 0.001
Stroke Type (Hemorrhagic)	3.36 (1.92–5.86) p < 0.001	3.46 (1.97–6.07) p < 0.001	3.39 (1.94–5.95) p < 0.001	3.49 (1.98–6.13) p < 0.001
BAR	1.11 (0.99–1.23) p = 0.066	1.09 (0.96–1.23) p = 0.175	1.10 (0.99–1.23) p = 0.084	1.08 (0.96–1.23) p = 0.202
CAR	1.03 (1.00–1.05) p = 0.032	1.03 (1.00–1.06) p = 0.028	1.03 (1.00–1.05) p = 0.037	1.03 (1.00–1.06) p = 0.030
Interaction Terms				
Stroke Type × BAR (Centered)	-	1.10 (0.84–1.45) p = 0.489	-	1.09 (0.83–1.43) p = 0.526
Stroke Type × CAR (Centered)	-	0.98 (0.93–1.03) p = 0.438	-	0.98 (0.92–1.03) p = 0.425
Comorbidities				
Hypertension	-	-	0.85 (0.49–1.48) p = 0.574	0.87 (0.50–1.52) p = 0.628
Diabetes Mellitus	-	-	0.88 (0.49–1.56) p = 0.652	0.86 (0.48–1.54) p = 0.622
Cardiovascular Disease	-	-	1.62 (0.93–2.85) p = 0.091	1.63 (0.93–2.88) p = 0.089

Predictors	Model 1 (Primary Clinical)	Model 2 (Interaction)	Model 3 (Comorbidity-Adjusted)	Model 4 (Fully Adjusted)
Cerebrovascular Disease	-	-	0.73 (0.40–1.35) p = 0.318	0.74 (0.40–1.36) p = 0.330
Model Evaluation Metrics				
AUC (Apparent / Corrected)	0.913 / 0.909	0.914 / 0.908	0.914 / 0.906	0.915 / 0.904
Nagelkerke R^2 (Apparent / Corrected)	0.545 / 0.523	0.546 / 0.516	0.551 / 0.517	0.552 / 0.510
Brier Score (Apparent / Corrected)	0.089 / 0.093	0.089 / 0.094	0.088 / 0.094	0.088 / 0.095
Calibration Intercept (Corrected)	-0.039	-0.052	-0.063	-0.076
Calibration Slope (Corrected)	0.956	0.943	0.932	0.918
Hosmer-Lemeshow p-value	0.169	0.389	0.507	0.392
AIC	446.2	448.3	448.4	451.7

Multivariable logistic regression sensitivity analyses evaluated the robustness of the primary model. Values are presented as odds ratios (ORs) with 95% confidence intervals (CIs) and p values. Model 1 included age, GCS, NIHSS score, stroke/hemorrhage volume, stroke type, BAR, and CAR. Model 2 added the prespecified Stroke Type × BAR and Stroke Type × CAR interaction terms. Model 3 added hypertension, diabetes mellitus, cardiovascular disease, and previous cerebrovascular disease to Model 1. Model 4 included the variables from Model 3 together with both interaction terms. BAR and CAR were mean-centered before construction of the interaction terms. Ischemic stroke was the reference category for stroke type. Internal validation was performed using 1,000 bootstrap resamples. Apparent values represent performance in the original dataset, whereas corrected values represent optimism-adjusted estimates. Only optimism-corrected calibration intercepts and slopes are reported. A Hosmer–Lemeshow p value > 0.05 indicates no statistically significant evidence of lack of fit.

Abbreviations: OR, Odds Ratio; CI, Confidence Interval; GCS, Glasgow Coma Scale; NIHSS, National Institutes of Health Stroke Scale; BAR, Blood Urea Nitrogen-to-Albumin Ratio; CAR, C-Reactive Protein-to-Albumin Ratio; AUC, Area Under the Curve; AIC, Akaike Information Criterion.

Interaction and comorbidity-adjusted sensitivity analyses

Sensitivity analyses were performed in the overall cohort to evaluate whether the primary findings were materially altered by potential stroke subtype-specific biomarker effects or major comorbidities (Table 9). In Model 2, neither the Stroke Type × BAR interaction (OR, 1.10; 95% CI, 0.84–1.45; p = 0.489) nor the Stroke Type × CAR interaction (OR, 0.98; 95% CI, 0.93–1.03; p = 0.438) was statistically significant. The interaction terms also remained nonsignificant in the fully adjusted Model 4 (Stroke Type

× BAR: OR, 1.09; 95% CI, 0.83–1.43; p = 0.526; Stroke Type × CAR: OR, 0.98; 95% CI, 0.92–1.03; p = 0.425). Thus, formal interaction testing provided no statistically significant evidence that the associations of BAR or CAR with in-hospital mortality differed according to stroke subtype.

Adjustment for hypertension, diabetes mellitus, cardiovascular disease, and previous cerebrovascular disease resulted in only minimal changes in the estimated associations of the principal predictors. None of these comorbidities was independently associated with mortality in Models 3 or 4. CAR remained associated with mortality in Model 2 (OR, 1.03; p = 0.028), Model 3 (OR, 1.03; p = 0.037), and Model 4 (OR, 1.03; p = 0.030), whereas BAR remained nonsignificant across all sensitivity models. GCS, NIHSS, stroke/hemorrhage volume, and hemorrhagic stroke type also retained their associations across the sensitivity models.

Increasing model complexity produced only minimal changes in apparent discrimination. Apparent AUCs were 0.913, 0.914, 0.914, and 0.915 for Models 1–4, respectively, whereas optimism-corrected AUCs were 0.909, 0.908, 0.906, and 0.904. Corresponding optimism-corrected Nagelkerke R^2 values were 0.523, 0.516, 0.517, and 0.510; corrected Brier scores were 0.093, 0.094, 0.094, and 0.095; and corrected calibration slopes were 0.956, 0.943, 0.932, and 0.918. AIC increased from 446.2 in Model 1 to 451.7 in Model 4. These findings indicated that increasing model complexity did not improve optimism-corrected discrimination or overall model performance.

Bootstrap-based pairwise comparisons of discrimination further showed no statistically significant improvement in AUC over Model 1. The addition of interaction terms in Model 2 resulted in a ΔAUC of 0.001 (95% CI, -0.0004 to 0.0027; p = 0.158). The addition of major comorbidities in Model 3 yielded a ΔAUC of 0.001 (95% CI, -0.0066 to 0.0077; p = 0.700), whereas the fully adjusted Model 4 yielded a ΔAUC of 0.002 (95% CI, -0.0058 to 0.0086; p = 0.600). Thus, none of the more complex models provided a statistically significant incremental gain in discrimination over the primary Model 1.

Multicollinearity assessment

Multicollinearity diagnostics were performed across the primary, interaction, comorbidity-adjusted, fully adjusted, and stroke subtype-specific models (Table 10). BAR and CAR were mean-centered before construction of the interaction terms in Models 2 and 4. VIF values ranged from 1.02 to 2.31 across all models and remained below the conventional threshold of 5, indicating no evidence of problematic multicollinearity.

Table 10
Variance Inflation Factors Across Multivariable Logistic Regression Models

Predictor Variables	All Patients (Model 1)	Interaction (Model 2)	Comorbidity-Adjusted (Model 3)	Fully Adjusted (Model 4)	Ischemic Stroke	Hemorrhagic Stroke
Age	1.16	1.16	1.24	1.25	1.17	1.11
GCS	1.97	1.98	1.97	1.99	1.61	1.96
NIHSS Score	2.25	2.26	2.30	2.31	1.98	2.28
Stroke / Hemorrhage Volume	1.44	1.44	1.44	1.45	1.29	1.56
Stroke Type (Hemorrhagic)	1.26	1.28	1.26	1.28	N/A	N/A
BAR	1.26	1.62	1.28	1.64	1.23	1.36
CAR	1.14	1.73	1.15	1.73	1.13	1.26
Stroke Type × BAR (Centered)	N/A	1.65	N/A	1.65	N/A	N/A
Stroke Type × CAR (Centered)	N/A	1.87	N/A	1.89	N/A	N/A
Hypertension	N/A	N/A	1.20	1.20	N/A	N/A
Diabetes Mellitus	N/A	N/A	1.14	1.14	N/A	N/A
Cardiovascular Disease	N/A	N/A	1.07	1.08	N/A	N/A
Cerebrovascular Disease	N/A	N/A	1.02	1.02	N/A	N/A
Intraventricular Hemorrhage	N/A	N/A	N/A	N/A	N/A	1.57
Infratentorial Hemorrhage	N/A	N/A	N/A	N/A	N/A	1.29

Variance inflation factors (VIFs) were calculated to assess multicollinearity across the primary, interaction, comorbidity-adjusted, fully adjusted, and stroke subtype-specific logistic regression models. BAR and CAR were mean-centered before constructing interaction terms in Models 2 and 4. The maximum VIF was 2.31, and all values remained below the conventional threshold of 5, indicating no evidence of problematic multicollinearity.

Abbreviations: VIF, Variance Inflation Factor; GCS, Glasgow Coma Scale; NIHSS, National Institutes of Health Stroke Scale; BAR, Blood Urea Nitrogen-to-Albumin Ratio; CAR, C-Reactive Protein-to-Albumin Ratio; N/A, Not Applicable.

Discussion

This study evaluated the prognostic roles of BAR and CAR for in-hospital mortality in a heterogeneous cohort of patients with acute ischemic and hemorrhagic stroke. The principal findings were that CAR was associated with mortality in the overall cohort and in ischemic stroke, while BUN and BAR were associated with mortality in unadjusted comparisons within the hemorrhagic subgroup. Nevertheless, the standalone discriminatory performance of both ratios was modest. In contrast, established clinical and radiological indicators, particularly NIHSS, GCS, lesion volume, and ICH score, demonstrated substantially stronger discrimination. These findings support viewing BAR and CAR as potential complementary biomarkers rather than alternatives to established neurological severity assessment and imaging-based prognostication.

Consistent with previous studies demonstrating the prognostic importance of neurological severity scores and lesion volume [5–8], established clinical and radiological markers showed the strongest discriminatory performance in our cohort. NIHSS and lesion volume achieved AUC values above 0.85 in the overall cohort, while the ICH score and hemorrhage volume yielded AUCs of 0.881 and 0.895, respectively, in patients with hemorrhagic stroke. By comparison, CAR showed an AUC of 0.648 in ischemic stroke and BAR an AUC of 0.631 in hemorrhagic stroke. These findings indicate that neither ratio should be considered a competing prognostic tool to established stroke severity measures. Their potential clinical value is more plausibly related to the fact that they are rapidly available from routine admission blood tests and may provide additional information about systemic inflammatory, nutritional, hydration, and metabolic status.

A notable finding of the multivariable analyses was that CAR retained a modest independent association with in-hospital mortality in the overall cohort and in the ischemic stroke subgroup after adjustment for established clinical and radiological severity indicators. However, this finding should be distinguished from incremental predictive performance. Although CAR remained statistically significant in the multivariable models, its standalone discriminatory ability was modest. Separately, sensitivity analyses showed that adding stroke subtype–biomarker interaction terms and major comorbidities to the primary model did not significantly improve discrimination. Formal interaction analyses also showed that neither the Stroke Type × CAR nor the Stroke Type × BAR interaction term was statistically significant. Therefore, the subgroup findings do not provide evidence that the prognostic associations of CAR or BAR are genuinely modified by stroke subtype, and the observed subgroup-specific patterns should be regarded as descriptive and hypothesis-generating. Taken together, these findings suggest that CAR should not be interpreted as outperforming or substantially improving established clinical and radiological prognostic tools; rather, its potential value may lie in providing complementary information regarding systemic inflammatory and nutritional status using routinely available admission laboratory measurements.

In hemorrhagic stroke, greater hemorrhage volume, intraventricular extension, and infratentorial localization remained the dominant independent predictors of mortality, whereas BAR lost statistical significance after multivariable adjustment. This pattern is clinically plausible because mechanical and

anatomical consequences of hemorrhage, including increased intracranial pressure, herniation, and brainstem involvement, may exert strong effects on early mortality [3, 22]. However, the apparently high discrimination of the hemorrhagic multivariable model should be interpreted cautiously. Although the apparent AUC was 0.949 and the optimism-corrected AUC remained high at 0.931, the corrected calibration slope of 0.785 and corrected Brier score of 0.116 indicated greater optimism than in the overall and ischemic models. These findings underscore the importance of external validation before clinical application.

The present findings can also be considered in the context of previous literature. Li et al. reported an association between elevated BAR and in-hospital mortality in an eICU-derived ischemic stroke cohort [17], while Bender et al. reported prognostic value for the urea-to-albumin ratio in spontaneous ICH [20]. Other studies have similarly associated higher BAR values with adverse outcomes [17, 19, 23]. In the current study, however, the association of BAR with mortality in hemorrhagic stroke was attenuated after adjustment for major anatomical predictors. Conversely, the persistence of the CAR association in ischemic stroke is consistent with literature suggesting that inflammatory burden and nutritional status may contribute to prognosis after stroke [9, 10, 14, 24]. CAR has also been associated with adverse cardiovascular outcomes in coronary and peripheral arterial disease [25–28] and with poor outcomes after thrombolytic treatment for acute ischemic stroke [29]. Nonetheless, the absence of statistically significant biomarker-by-stroke-type interactions in our study indicates that mechanistic explanations for apparent subgroup differences should remain cautious.

Limitations

Several limitations should be considered when interpreting these findings. First, the study had a single-center retrospective design, which may limit generalizability to other institutions and patient populations. Second, biomarker values were based on a single blood sample obtained at emergency department admission. Serial changes in BAR and CAR during hospitalization were not evaluated, and therefore their temporal prognostic behavior could not be assessed.

Third, patients with acute or chronic renal or hepatic failure were excluded. Although this approach reduced the potential influence of major baseline abnormalities in BUN and albumin, it may limit applicability to high-risk real-world populations in whom renal or hepatic dysfunction is common. Fourth, specific post-stroke treatment data, including intravenous thrombolysis, mechanical thrombectomy, and surgical hematoma evacuation, were not available and therefore could not be incorporated into the survival models despite their potential influence on outcome.

Finally, although formal interaction analyses were performed to examine whether the associations of BAR and CAR with mortality differed according to stroke subtype, no statistically significant effect modification was identified. The smaller hemorrhagic stroke subgroup may nevertheless have limited the power to detect modest interaction effects and contributed to greater optimism in the internally validated hemorrhagic model. In addition, several biomarker, subgroup, and ROC analyses were

performed; therefore, findings with borderline p values should be interpreted cautiously. The models and thresholds were internally validated within the same single-center cohort, and external validation in independent, multicenter populations is required before broad clinical application.

Conclusions

In patients with acute stroke, BAR and CAR demonstrated statistically significant associations with in-hospital mortality in selected analyses; however, their standalone discriminatory performance was modest compared with established clinical and radiological predictors. CAR retained a modest independent association with mortality in the overall cohort and ischemic stroke subgroup, whereas BAR was not independently associated with mortality after adjustment for major clinical and anatomical determinants in hemorrhagic stroke. Formal interaction testing did not demonstrate significant effect modification of the associations of BAR or CAR by stroke subtype. Furthermore, the addition of interaction terms and major comorbidities did not significantly improve model discrimination over the primary multivariable model. These findings suggest that BAR and CAR should not be regarded as alternatives to established neurological severity scores or imaging-based predictors, but may provide complementary information regarding systemic inflammatory, nutritional, and metabolic status. External validation in larger, prospective, multicenter cohorts is required before their routine prognostic use can be recommended.

Abbreviations

AIC
Akaike Information Criterion
AUC
Area Under the Receiver Operating Characteristic Curve
BAR
Blood Urea Nitrogen-to-Albumin Ratio
BUN
Blood Urea Nitrogen
CAR
C-Reactive Protein-to-Albumin Ratio
CI
Confidence Interval
COPD
Chronic Obstructive Pulmonary Disease
CRP
C-Reactive Protein
CT
Computed Tomography
DBP

Diastolic Blood Pressure
eICU
eICU Collaborative Research Database
GCS
Glasgow Coma Scale
ICH
Intracerebral Hemorrhage
ICU
Intensive Care Unit
iCa
Ionized Calcium
IQR
Interquartile Range
MIMIC-IV
Medical Information Mart for Intensive Care IV
MRI
Magnetic Resonance Imaging
mRS
modified Rankin Scale
NIHSS
National Institutes of Health Stroke Scale
OR
Odds Ratio
ROC
Receiver Operating Characteristic
SBP
Systolic Blood Pressure
VIF
Variance Inflation Factor
ΔAUC
Difference in Area Under the Receiver Operating Characteristic Curve.

Declarations

Ethics approval and consent to participate: The study was conducted in accordance with the Declaration of Helsinki and approved by the Necmettin Erbakan University Non-Pharmaceutical and Non-Medical Device Research Ethics Committee (Decision number: 2025/5688; approval date: April 11, 2025). The requirement for informed consent was waived by the ethics committee because of the retrospective design of the study.

Consent for publication: Not applicable.

Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Authors' contributions:

M.R.Ö.: Conceptualization, Methodology, Project Administration, Writing – Original Draft, Writing – Review & Editing.
İ.B.B.: Investigation, Data Curation, Writing – Review & Editing.
E.B.: Investigation, Data Curation, Writing – Review & Editing.
K.K.: Methodology, Software, Formal Analysis, Validation, Writing – Review & Editing.
S.A.: Investigation, Supervision, Writing – Review & Editing.
H.H.K.: Methodology, Writing – Review & Editing.
M.A.: Methodology, Writing – Review & Editing.

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Figures

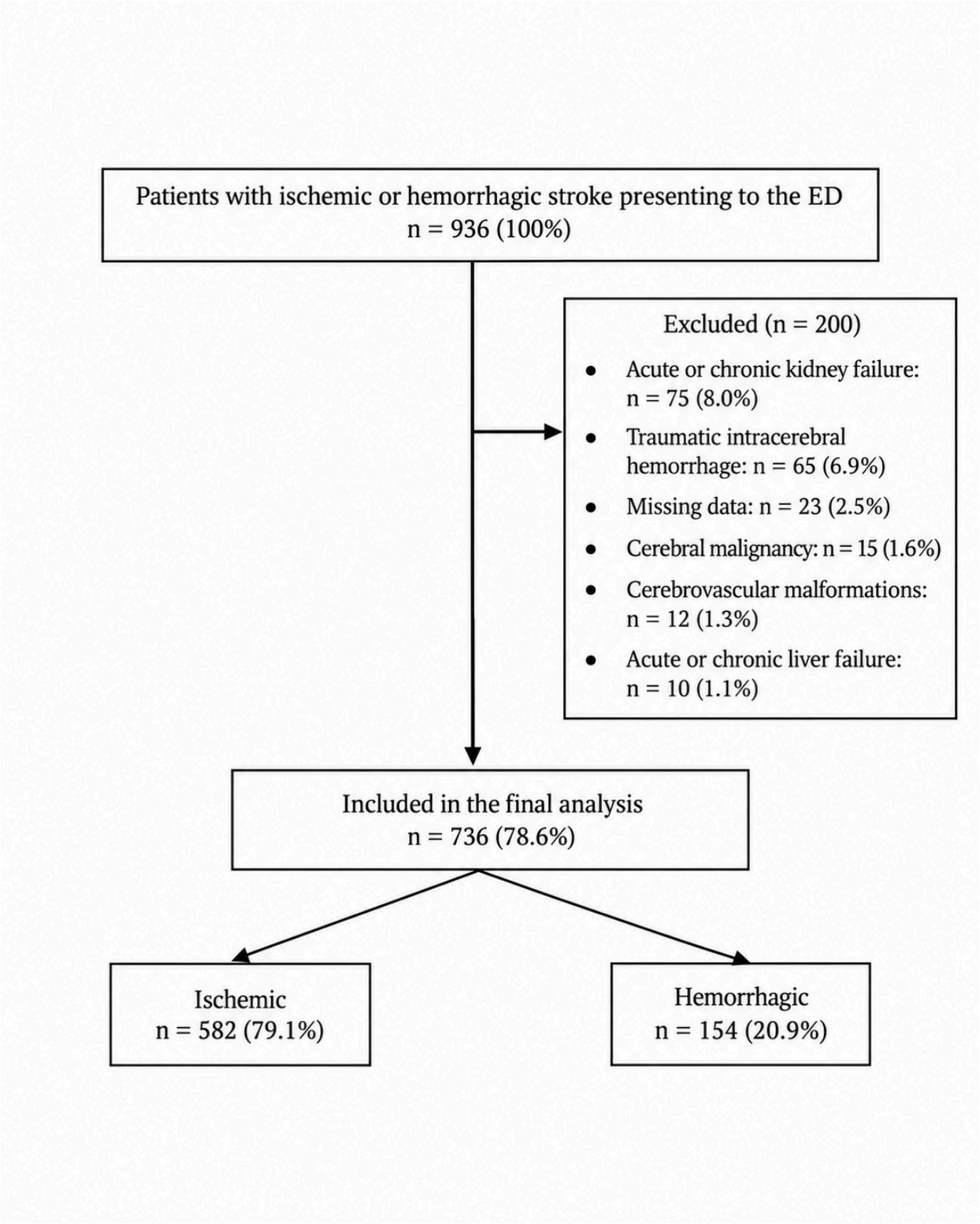


Figure 1

Study flow.

Flow diagram showing patient screening, exclusion criteria, and final inclusion of 736 patients with acute ischemic or hemorrhagic stroke, comprising 582 patients with ischemic stroke and 154 patients with hemorrhagic stroke.

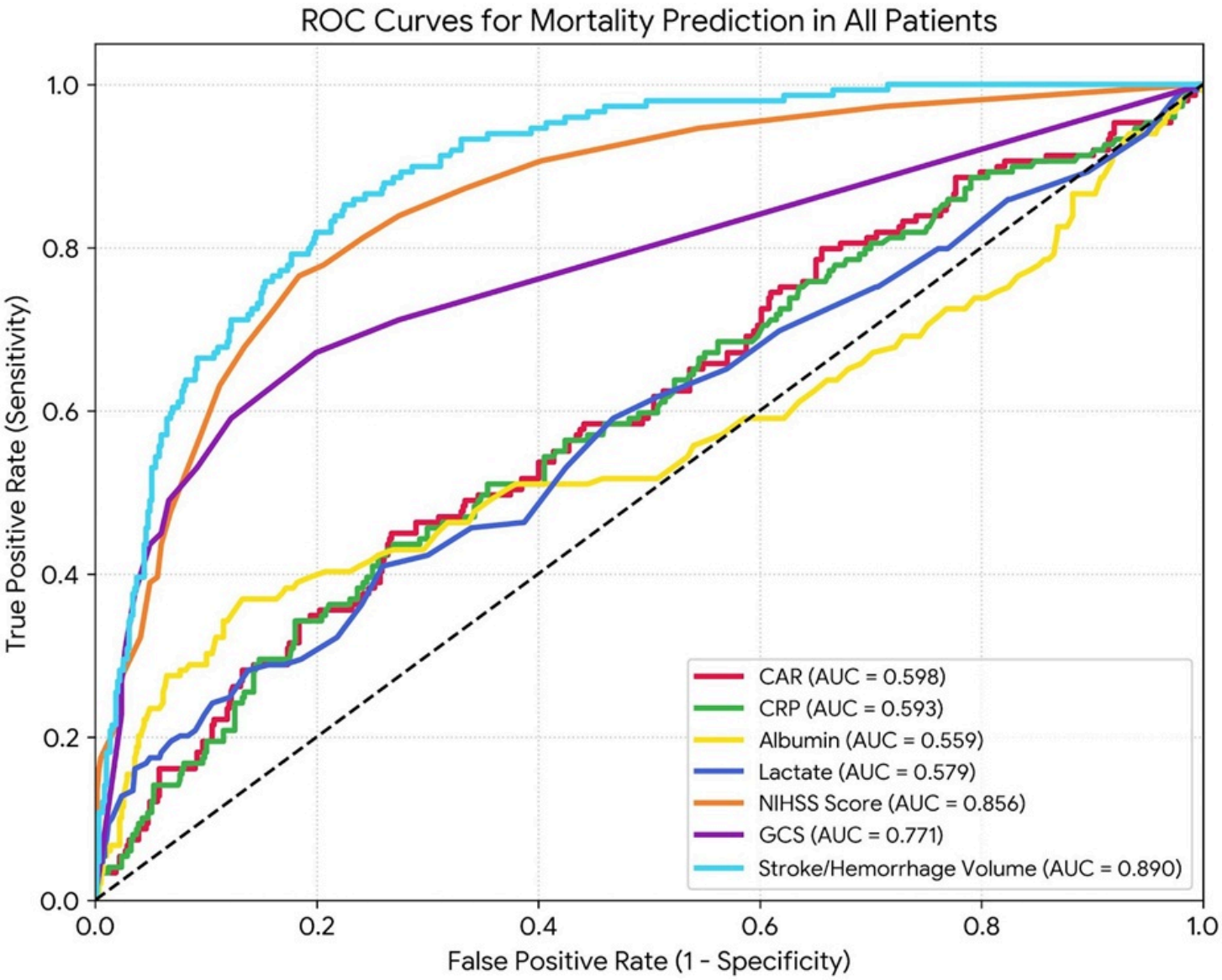


Figure 2

ROC curves for in-hospital mortality in the overall cohort.

Receiver operating characteristic (ROC) curves comparing the discriminatory performance of clinical, radiological, and laboratory parameters for in-hospital mortality in the overall stroke cohort. The corresponding area under the curve (AUC) values are displayed in the figure.

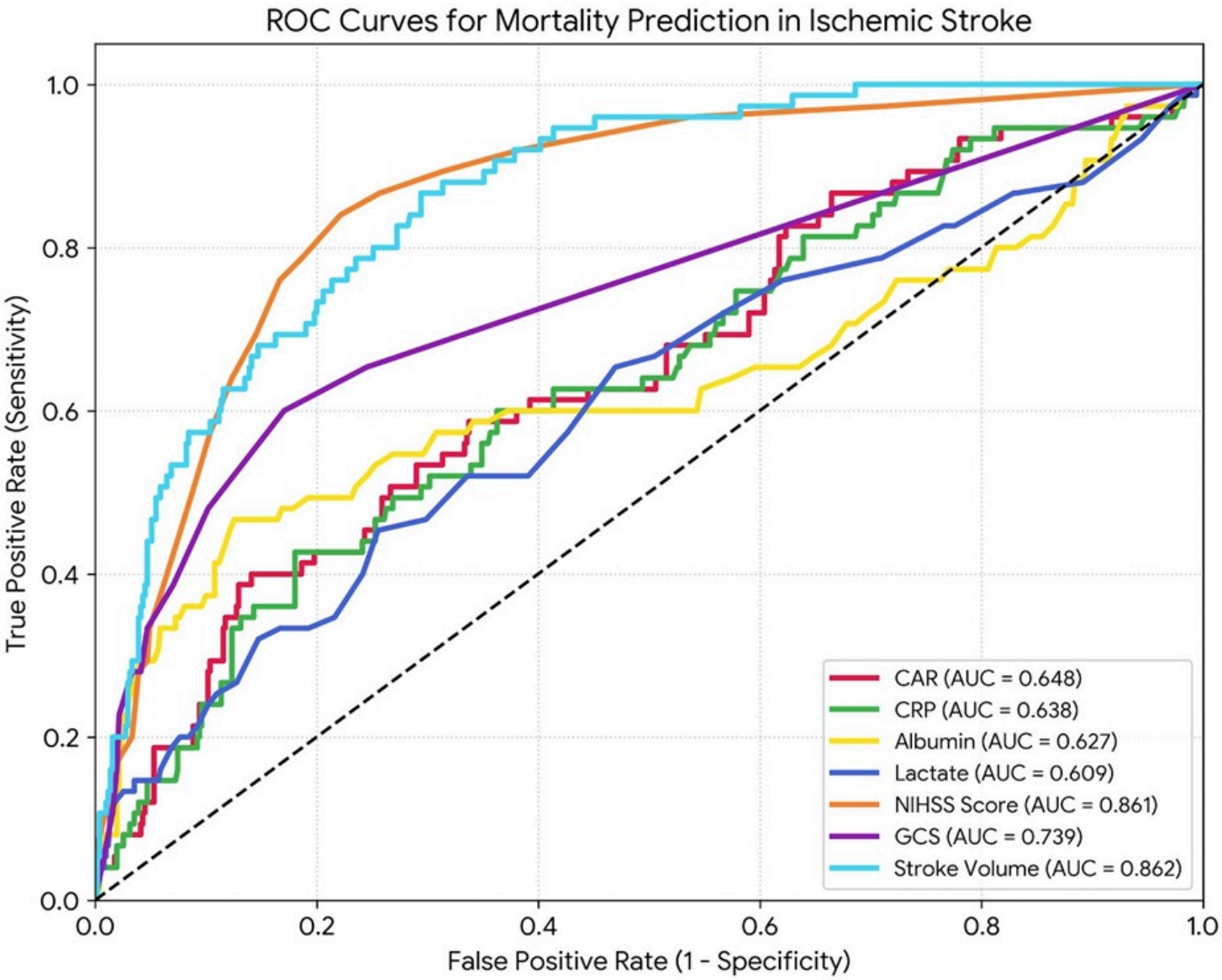


Figure 3

ROC curves for in-hospital mortality in ischemic stroke.

Receiver operating characteristic (ROC) curves comparing the discriminatory performance of clinical, radiological, and laboratory parameters, including the C-reactive protein-to-albumin ratio (CAR) and its components, for in-hospital mortality in the ischemic stroke subgroup.

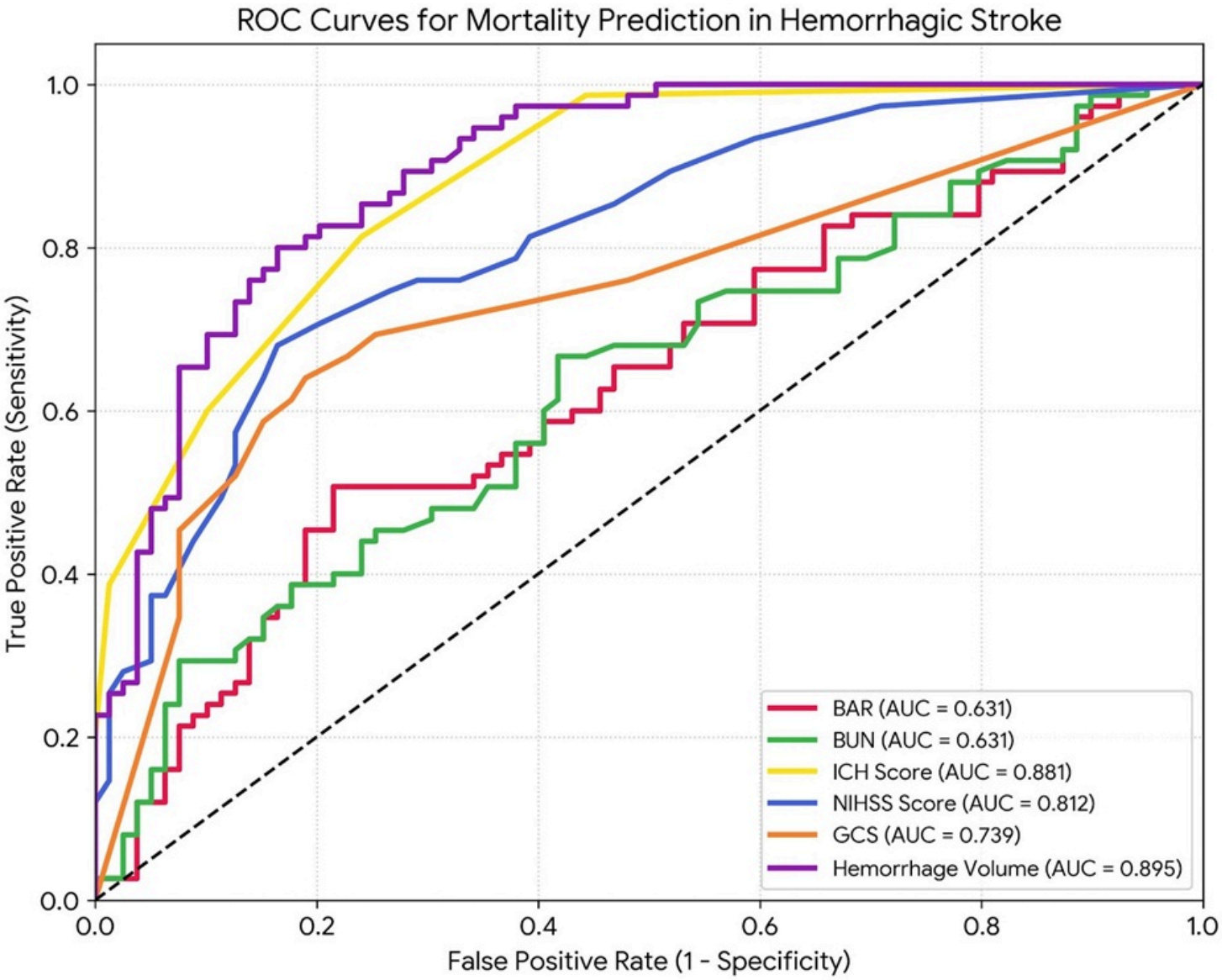


Figure 4

ROC curves for in-hospital mortality in hemorrhagic stroke.

Receiver operating characteristic (ROC) curves comparing the discriminatory performance of clinical, radiological, and laboratory parameters, including the blood urea nitrogen-to-albumin ratio (BAR), for in-hospital mortality in the hemorrhagic stroke subgroup.

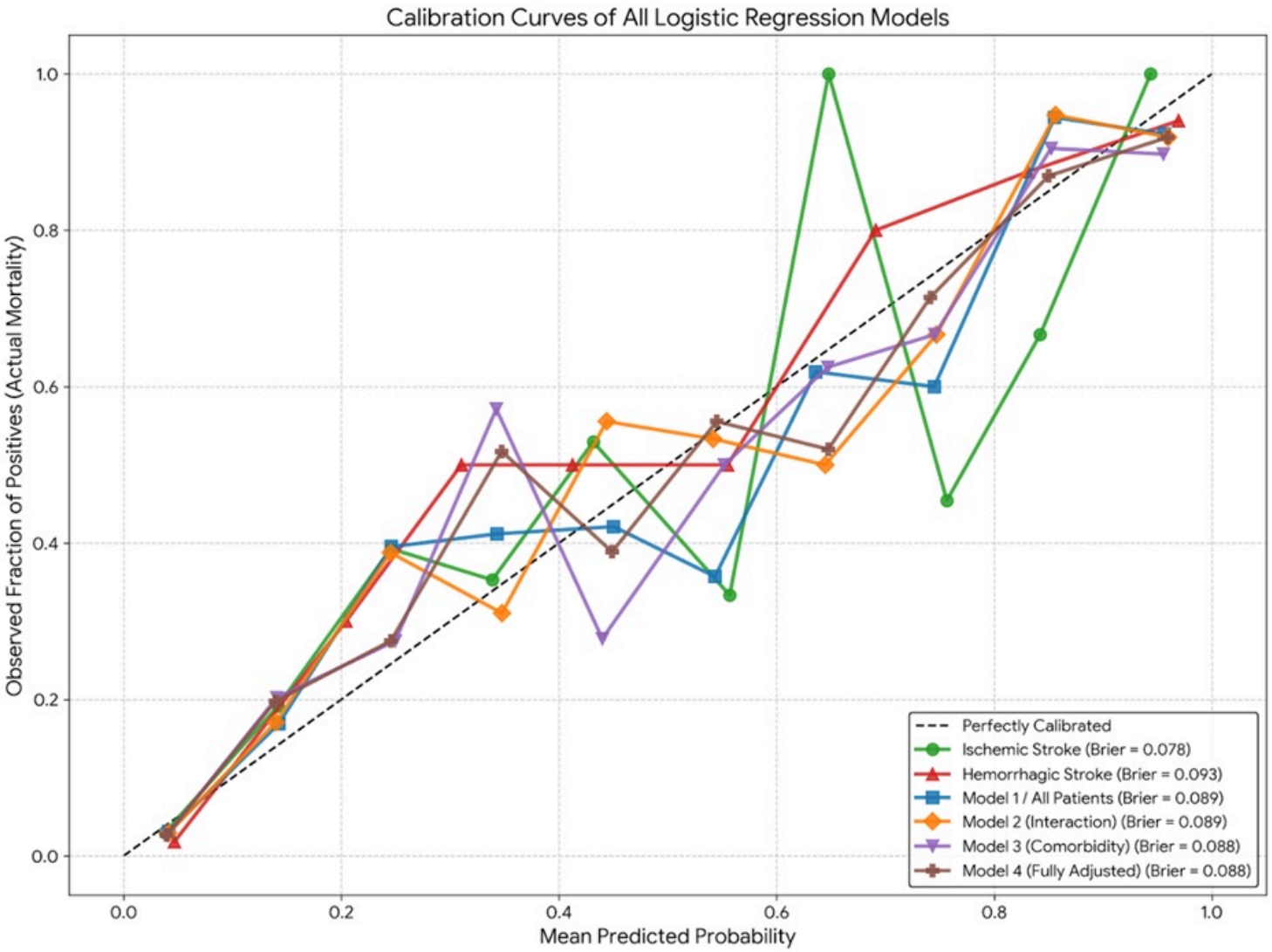


Figure 5

Calibration curves of the multivariable logistic regression models.

Calibration plots show the relationship between predicted probabilities and observed in-hospital mortality for the primary stroke-specific models and the full-cohort sensitivity models. Each marker represents the mean predicted probability and observed mortality proportion within a probability bin, and the dashed diagonal represents ideal calibration. Apparent Brier scores were 0.078 for the ischemic stroke model and 0.093 for the hemorrhagic stroke model. For full-cohort Models 1–4, apparent Brier scores were 0.089, 0.089, 0.088, and 0.088, respectively. The curves and Brier scores represent apparent performance in the model-development dataset and were not corrected for optimism. Bin-specific fluctuations should be interpreted cautiously, particularly in intervals containing few patients.