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Immune Dysregulation Associated with Intracranial Pressure Dynamics and Prognosis in Intracerebral Hemorrhage: Insights from Serum Immunometabolic and Inflammation-resolving Biomarkers

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ABSTRACT

This study examined associations of intracranial pressure (ICP) dynamics and early serum immunometabolic and inflammation-resolving biomarkers with 90-day outcomes after spontaneous intracerebral hemorrhage (ICH).

This single-center observational cohort included 138 patients who underwent clinically indicated ICP monitoring and serum biomarker sampling. Biomarkers were measured within 24 hours after admission, and ICP features were extracted during the first 24 hours after catheter insertion. Patients were classified as having good (modified Rankin Scale [mRS] 0–3; n=82) or poor (mRS 4–6; n=56) outcomes. Logistic regression identified factors associated with poor outcome, while model discrimination and internal stability were assessed using receiver operating characteristic analysis and bootstrap validation.

Patients with poor outcomes had lower admission Glasgow Coma Scale (GCS) scores, larger hematomas, more frequent ventricular involvement, greater ICP burden, higher lactate and interleukin-6 levels, and lower Resolvin D1 (RvD1) and Maresin 1 levels. Admission GCS score (odds ratio [OR]=0.84; 95% confidence interval [CI], 0.74–0.96), peak ICP (OR=1.14; 95% CI, 1.05–1.24), lactate (OR=1.58; 95% CI, 1.12–2.21), and RvD1 (OR=0.97; 95% CI, 0.95–0.99) were independently associated with poor outcome. The combined model achieved an area under the curve of 0.91 (95% CI, 0.86–0.96), with a bootstrap-corrected value of 0.89.

Greater ICP burden and an adverse immunometabolic and inflammation-resolving profile were associated with poor functional outcomes. External validation and calibration are required before clinical application.

Keywords: Biomarkers; Immunometabolism; Intracerebral hemorrhage; Intracranial pressure; Inflammation resolution; Prognosis

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INTRODUCTION

Intracerebral hemorrhage (ICH) represents a major subtype of stroke, often leading to rapid neurological decline within a brief time frame. This condition is associated with elevated risks of mortality and long-term disability.[1] Although advancements in treatment approaches, including blood pressure regulation, neurocritical care, timely surgical interventions, and perioperative support, have been made, a considerable number of patients still face poor functional outcomes following the acute phase.[2] One of the primary challenges in managing ICH is the early identification of high-risk patients and improving the accuracy and timing of prognosis assessments.

Currently, prognosis evaluation largely depends on clinical and imaging data at the time of admission, such as age, consciousness level, hematoma volume, hemorrhage location, and ventricular involvement.[3,4] While these indicators are valuable for assessing the initial degree of injury, they offer limited insights into the dynamic progression of secondary damage during the course of the disease. For severe ICH patients, the deterioration of condition is often not determined by a single structural injury but is a result of various factors, including increased intracranial pressure (ICP),[5] impaired brain perfusion, brain edema progression, systemic stress, and imbalanced immune-inflammatory responses.[6] Therefore, relying solely on static baseline information for risk assessment may not fully capture the patient's true outcome risk.

ICP monitoring provides a continuous window to observe the secondary physiological load following ICH.[7] In clinical practice, increased ICP that is difficult to control often signals limited intracranial compensation,[8] brain tissue compression, and an increased risk of secondary damage.[9–11] It is noteworthy that the clinical significance of ICP is not limited to a single time-point value: dynamic features such as peak pressure, repeated supra-threshold events, and the duration of elevated pressure may more closely reflect the disease progression and the overall pressure load on brain tissue.[12] In other words, the way ICP fluctuates, how long it stays elevated, and how frequently it spikes might provide a more accurate reflection of the patient's pathophysiological status than a single measurement.

Moreover, secondary brain damage following ICH also involves complex immune and metabolic changes. Hematoma and its breakdown products can trigger localized inflammation, oxidative stress, and blood-brain barrier damage, which, in turn, affect peripheral immune responses via the neuro-immune axis.[13] Systemic stress can further alter immune cell metabolism, leading to a coexistence of inflammation activation and immune suppression.[14] The emerging concept of "immunometabolism" has provided a new perspective for understanding these phenomena: the remodeling of immune cell metabolic pathways not only results from inflammatory responses but also influences the intensity, duration, and tissue repair capacity of inflammation.[15]

In addition to inflammation activation, the process of inflammation "termination and resolution" is equally important. Inflammation resolution is not a passive result of the natural decline of inflammation but is an actively regulated biological process.[16] If the resolution process is impaired, persistent inflammation, delayed tissue repair, and limited functional recovery may occur.[17] In the context of severe brain injury, this process may form a feedback loop with prolonged brain edema, difficulties in ICP control, and poor outcomes.[18] However, in ICH patients, especially those with significant ICP dynamic abnormalities, the changes in immune-metabolic and inflammation-resolving biomarkers and their relationship to outcomes are still lacking systematic clinical data.

Given these considerations, this study focused on ICH patients with clinically indicated ICP monitoring and early biomarker sampling. In addition to conventional clinical and imaging indicators, we incorporated ICP dynamic characteristics and serum immunometabolic/inflammation-resolving biomarkers to analyze their relationship with 90-day functional outcome and to develop a combined prognostic model. Compared with prior studies that evaluated ICP variables or inflammatory markers separately, the main novelty of the present work lies in integrating clinical severity, dynamic physiological burden, and inflammation-resolution-related biomarkers within a single early-phase framework. The inclusion of inflammation-resolving biomarkers was intended to extend prognosis assessment beyond injury intensity alone and toward the biological capacity for recovery.

MATERIALS AND METHODS

Study Design and Participants

This research was a single-center, observational cohort study. It included patients with spontaneous intracerebral hemorrhage (ICH) who were admitted to the Department of Neurology, Neurosurgery, and Intensive Care Medicine at our hospital between January 2023 and October 2025. All participants met the diagnostic criteria for ICH and were confirmed via cranial CT imaging.

The main outcome of this study was a poor functional outcome at 90 days, defined as a modified Rankin Scale (mRS) score ranging from 4 to 6. The study protocol involved case screening, collection of clinical and imaging data, monitoring of ICP dynamics, serum sample analysis, and a 90-day follow-up assessment.

Inclusion and Exclusion Criteria

Inclusion Criteria: (1) Age ≥18; (2) diagnosis of spontaneous intracerebral hemorrhage confirmed by cranial CT; (3) admission within a reasonable timeframe after symptom onset and receiving standard treatment and monitoring; (4) availability of continuous or dynamic ICP monitoring data (or continuous recorded data available for extracting ICP dynamic features); (5) completion of serum sample collection and testing of relevant biomarkers within the predefined time window; and (6) relatively complete clinical data and 90-day follow-up outcome data.

Exclusion Criteria: (1) Secondary causes of intracerebral hemorrhage, including aneurysms, vascular malformations, stroke due to tumors, traumatic brain injury, and hemorrhagic transformation, among others; (2) concurrent severe central nervous system infections, autoimmune diseases, active malignancies, or recent immunosuppressive therapy; (3) severe liver or kidney failure or hematological disorders that could significantly affect immunometabolic biomarkers; (4) death or transfer to another facility shortly after admission, preventing completion of key monitoring and sample collection; and (5) missing critical clinical data, making statistical analysis impossible.

Collection of Clinical and Imaging Data

Data on patients' general information, clinical features, laboratory results, imaging findings, and major treatments were gathered. This included details such as age, sex, comorbidities, Glasgow Coma Scale (GCS) score upon admission, hemorrhage location, hematoma size, ventricular involvement, midline shift, initial treatment strategies, and any complications occurring during hospitalization.

Functional outcomes at 90 days were evaluated using the modified Rankin Scale (mRS). Assessments were carried out by trained researchers and follow-up evaluators through phone interviews.

Hematoma volume was calculated using the ABC/2 method and independently assessed by two experienced neurologists specializing in imaging. In case of discrepancies, a senior physician made the final determination.

ICP Dynamic Monitoring and Definition of Indicators

ICP Monitoring: ICP dynamic monitoring was performed in patients who met clinical indications. Catheter insertion was not uniform across patients with respect to symptom onset or admission time, because placement was guided by disease severity and neurosurgical judgment. Monitoring methods included external ventricular drainage (EVD) and/or intraparenchymal probe monitoring, selected according to the clinical scenario. The monitoring system used was the Integra Camino ICP monitoring system (Integra LifeSciences, USA), which continuously recorded ICP changes while major interventions during the monitoring period (eg, sedation/analgesia, hyperosmolar therapy, cerebrospinal fluid drainage, and related surgical treatment) were documented.

To reduce bias caused by differences in monitoring start time and duration, ICP data were standardized to the first 24 hours after catheter insertion for dynamic indicator calculation. Patients monitored for less than 24 hours were excluded from this part of the analysis. Because catheter placement could occur after admission, the ICP observation window was adjacent to—but not necessarily identical with—the biomarker sampling window defined from admission.

ICP Dynamic Features and Indicators

This study extracted the following ICP dynamic indicators for analysis: average ICP; peak ICP; number of ICP>20 mm Hg events; and cumulative duration of ICP>20 mm Hg.

An ICP elevation event was defined as an ICP>20 mm Hg sustained for ≥5 minutes. Events with an interval of less than 5 minutes between them were combined into a single event. ICP data were continuously recorded by the monitoring system and exported as 1-minute average values for analysis.

Serum Sample Collection and Biomarker Testing

Peripheral venous blood samples were obtained within 24 hours after admission and represented a single early-phase measurement. Serum was separated by centrifugation (3000 rpm for 10 minutes) within 30 minutes of collection, aliquoted, and stored at −80°C for later analysis. Repeated freeze-thaw cycles were avoided. In most cases, biomarker sampling and ICP feature extraction reflected the same early in-hospital phase; however, because catheter placement was clinically indicated rather than fixed by protocol, the two windows were not perfectly synchronized in all patients, which may have introduced temporal heterogeneity. Several biomarkers were assessed, including serum lactate, IL-6, Resolvin D1 (RvD1), and Maresin 1 (MaR1). Lactate was measured using an automated biochemical analyzer, whereas IL-6, RvD1, and MaR1 were quantified by enzyme-linked immunosorbent assay (ELISA) according to the manufacturers' instructions. RvD1 was measured using a commercial ELISA kit (Human RvD1 [Resolvin D1] ELISA Kit, ELK Biotechnology Co., Ltd, Wuhan, China; Cat. No. ELK0604; detection range, 15.63–1000 pg/mL), and MaR1 was measured using a commercial ELISA kit (Human MaR1 [Maresin 1] ELISA Kit, ELK Biotechnology CO., LTD, Wuhan, China; Cat. No. ELK0578; detection range, 15.63–1000 pg/mL). Biomarker concentrations were expressed as pg/mL. Laboratory personnel were blinded to outcome grouping.

Outcome Definition and Grouping

The study's primary outcome was the 90-day functional status, measured by the modified Rankin Scale (mRS). Based on the mRS score, patients were classified into two categories: good prognosis group (mRS 0–3) and poor prognosis group (mRS 4–6).

Quality Control

Data collection was carried out using a standardized case report form. Imaging evaluations were conducted by two physicians independently, with any disagreements addressed by a third physician. Laboratory analyses followed established protocols, incorporating internal quality control procedures. Key variables underwent logical checks, and outlier values were verified. Prior to statistical analysis, the data were thoroughly cleaned and consistency checks were completed.

Statistical Analysis

Statistical analysis was conducted using the Statistical Package for the Social Sciences (SPSS) 19.0 (IBM, Armonk, NY, USA) and R software 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria). Continuous variables were first assessed for distribution. Normally distributed data are presented as mean ± standard deviation (SD) and were compared using the independent-samples *t* test. Skewed data are presented as median (interquartile range) and were compared using the Mann-Whitney U test. Categorical data are shown as frequency (percentage) and were compared using the χ^2 test or Fisher exact test. In the ICP comparison, the number of ICP>20 mm Hg events was analyzed as a non-normally distributed variable, whereas the cumulative duration of ICP>20 mm Hg approximated a normal distribution and was therefore analyzed with the *t* test.

The primary outcome (good/poor) at 90 days was treated as a binary dependent variable. Univariate logistic regression was first performed to identify candidate variables associated with prognosis. Variables were not selected for multivariable analysis solely on the basis of univariate *p* values; clinical relevance, collinearity, bedside interpretability, and the number of outcome events were also considered to reduce overfitting. Continuous variables were retained in their original form to avoid information loss from arbitrary categorization. Given 56 poor-outcome events, the final multivariable model was intentionally restricted to a parsimonious set of predictors.

Before modeling, multicollinearity was assessed using variance inflation factor (VIF) and tolerance. Because peak ICP and duration of ICP>20 mm Hg both reflected ICP burden, only one representative ICP dynamic indicator was retained in the final parsimonious model; peak ICP was selected because it was more directly interpretable at the bedside. Model performance was primarily evaluated by receiver operating characteristic (ROC) analysis with the area under the curve (AUC) and 95% confidence intervals (CIs). Internal validation was conducted using Bootstrap resampling (1000 resamples). Formal calibration

analysis, Brier score assessment, and decision-curve analysis were not available from the current manuscript-level summary data and are therefore acknowledged as necessary next steps before clinical implementation.

RESULTS

Study Participants and 90-Day Prognosis Grouping

This study included a total of 138 patients with intracerebral hemorrhage. Based on the 90-day mRS score, participants were categorized into two groups: the good prognosis group (mRS 0–3), which comprised 82 patients (59.4%), and the poor prognosis group (mRS 4–6), consisting of 56 patients (40.6%).

When comparing the two groups based on their 90-day outcomes, the poor prognosis group showed higher-risk features, including older age, lower GCS scores at admission, larger hematoma volumes, and greater ventricular involvement (all $p<0.001$). No significant gender difference was found between the groups ($p=0.580$). The detailed comparison can be seen in Table 1.

Comparison of ICP Dynamic Indicators between Different Prognosis Groups

The poor prognosis group demonstrated significantly higher average ICP and peak ICP values than the good prognosis group (both $p<0.001$). It also showed a higher frequency of ICP>20 mm Hg events and a longer cumulative duration of elevated ICP (both $p<0.001$), supporting the presence of a heavier ICP dynamic burden in patients with worse outcomes. Detailed results are presented in Table 2.

Comparison of Immunometabolic and Inflammation-resolving Biomarkers between Different Prognosis Groups

Patients with poor prognosis had significantly higher lactate and IL-6 levels than those with good prognosis. In contrast, the levels of inflammation-resolving factors A and B were significantly lower in the poor prognosis group. These findings suggest that worse outcomes were accompanied by greater systemic stress and impaired inflammatory resolution in the early stage after ICH. Detailed data are shown in Table 3.

Univariate Logistic Regression Analysis for 90-Day Poor Prognosis

Univariate logistic regression identified older age, peak ICP, cumulative duration of ICP>20 mm Hg, and higher lactate levels as risk factors for 90-day poor prognosis, whereas higher admission GCS and higher Resolvin D1 (RvD1) were associated with lower risk. Because the final model was designed to remain parsimonious and to avoid redundancy among correlated ICP dynamic variables, only peak ICP was taken forward as the representative ICP burden variable for multivariable analysis. The detailed results are shown in Table 4.

Table 1. Comparison of general information between different 90-day prognosis groups (n=138)

Variables	Good prognosis group (mRS 0–3, n=82)	Poor prognosis group (mRS 4–6, n=56)	Statistic	*p*
Age, y	58.3±11.2	66.8±10.5	$t=-4.50$	<0.001
Male, No. (%)	52 (63.4)	38 (67.9)	$\chi^2=0.30$	0.580
GCS on admission, median (IQR)	12 (10–14)	7 (5–9)	$Z=-7.32$	<0.001
Hematoma volume, mL	18.6±8.9	36.2±14.3	$t=-8.76$	<0.001
Ventricular involvement, No. (%)	18 (22.0)	34 (60.7)	$\chi^2=21.40$	<0.001

GCS: Glasgow Coma Scale; IQR: interquartile range; mRS: modified Rankin Scale.

Table 2. Comparison of ICP dynamic indicators between different 90-day prognosis groups

Variables	Good prognosis group (mRS 0–3, n=82)	Poor prognosis group (mRS 4–6, n=56)	Statistic	*p*
Mean ICP, mm Hg	15.2±3.4	21.8±5.6	$t=-8.60$	<0.001
Peak ICP, mm Hg	22.5±4.8	32.6±6.9	$t=-9.47$	<0.001
Times of ICP>20 mm Hg, median (IQR)	2 (1–4)	8 (5–12)	$Z=-8.12$	<0.001
Duration of ICP>20 mm Hg, h	3.1±1.8	12.4±5.2	$t=-13.40$	<0.001

ICP: intracranial pressure; IQR: interquartile range; mRS: modified Rankin Scale.

Table 3. Comparison of immunometabolic and inflammation-resolving biomarkers between different 90-day prognosis groups

Variables	Good prognosis group (mRS 0–3, n=82)	Poor prognosis group (mRS 4–6, n=56)	Statistic	*p*
Lactate, mmol/L	2.1±0.6	3.8±1.1	$t=-11.10$	<0.001
IL-6, pg/mL	18.4±6.2	42.7±12.3	$t=-13.90$	<0.001
Resolvin D1 (RvD1), pg/mL	210±55	132±47	$t=8.80$	<0.001
Maresin 1 (MaR1), pg/mL	98±24	61±19	$t=9.74$	<0.001

IL: interleukin; MaR1: Maresin 1; mRS: modified Rankin Scale; RvD1: Resolvin D1.

Table 4. Univariate logistic regression analysis for 90-day poor prognosis

Variables	OR	95% CI	*p*
Age (for each additional year)	1.07	1.03–1.11	0.001
Admission GCS (for each 1-point increase)	0.78	0.70–0.87	<0.001
Peak ICP (per 1-mm Hg increase)	1.18	1.10–1.27	<0.001
Duration of ICP>20 mm Hg (every additional hour)	1.25	1.15–1.36	<0.001
Lactate (per 1-mmol/L increase)	1.92	1.40–2.63	<0.001
Resolvin D1 (RvD1) (per 1-pg/mL increase)	0.96	0.94–0.98	<0.001

CI: confidence interval; GCS: Glasgow Coma Scale; ICP: intracranial pressure; OR: odds ratio; RvD1: Resolvin D1.

Multicollinearity Diagnosis for Multivariate Logistic Regression Candidate Variables

A multicollinearity diagnosis was performed for the candidate variables included in the multivariable analysis. The VIF values for age, admission GCS score, peak ICP, lactate, and Resolvin D1 (RvD1) were all <5 and tolerance values were all >0.2, indicating no significant multicollinearity among the final candidate predictors. The detailed results are shown in Table 5.

Multivariate Logistic Regression Analysis for 90-day Poor Prognosis

Age, admission GCS score, peak ICP, lactate, and Resolvin D1 (RvD1) were included in the multivariable model. Given 56 poor-outcome events, this corresponded to 11.2 events per variable at model entry. After adjustment, admission GCS score, peak ICP, lactate, and Resolvin D1 (RvD1) remained independently associated with poor 90-day prognosis

(all $p<0.05$), whereas age did not retain statistical significance ($p=0.14$). Maresin 1 (MaR1) was not entered into the final parsimonious model because the primary aim was to limit model complexity and prioritize the more clinically interpretable inflammation-resolution variable in the main analysis. Full results are shown in Table 6.

ROC Analysis for Single Indicators and Combined Model in Predicting 90-day Poor Prognosis

ROC analysis showed that peak ICP, lactate, and Resolvin D1 (RvD1) each had moderate discriminative ability for predicting 90-day poor prognosis, with AUCs of 0.82, 0.79, and 0.77, respectively. The combined model incorporating admission GCS score, peak ICP, lactate, and Resolvin D1 (RvD1) achieved an AUC of 0.91 (95% CI, 0.86–0.96), and the Bootstrap-corrected AUC was 0.89. These results support good discrimination, but calibration assessment and external validation remain necessary before clinical use. Detailed results are shown in Table 7.

Table 5. Multicollinearity diagnosis for multivariate logistic regression candidate variables

Variables	VIF	Degree of tolerance
Age	1.31	0.76
GCS on admission	2.18	0.46
Peak ICP	2.74	0.36
Lactate	1.93	0.52
Resolvin D1 (RvD1)	1.58	0.63

GCS: Glasgow Coma Scale; ICP: intracranial pressure; RvD1: Resolvin D1; VIF: variance inflation factor.

Table 6. Multivariate logistic regression analysis for 90-day poor prognosis

Variables	OR	95% CI	*p*
Age	1.03	0.99–1.08	0.14
GCS on admission	0.84	0.74–0.96	0.01
Peak ICP	1.14	1.05–1.24	0.002
Lactate	1.58	1.12–2.21	0.008
Resolvin D1 (RvD1)	0.97	0.95–0.99	0.01

CI: confidence interval; GCS: Glasgow Coma Scale; ICP: intracranial pressure; OR: odds ratio; RvD1: Resolvin D1.

Table 7. ROC analysis for single indicators and combined model in predicting 90-day poor prognosis

Indicator/model	AUC	95% CI	Bootstrap-corrected AUC
Peak ICP	0.82	0.75–0.89	0.80
Lactate	0.79	0.72–0.86	0.77
Resolvin D1 (RvD1)	0.77	0.69–0.85	0.75
Combined model (GCS + peak ICP + lactate + RvD1)	0.91	0.86–0.96	0.89

AUC: area under the curve; CI: confidence interval; GCS: Glasgow Coma Scale; ICP: intracranial pressure; ROC: receiver operating characteristic; RvD1: Resolvin D1.

Summary of Results

In this cohort, 90-day poor prognosis after ICH was associated with heavier ICP dynamic burden—particularly higher peak ICP—as well as greater immunometabolic stress and weaker inflammation-resolution capacity. Admission GCS score, peak ICP, lactate, and Resolvin D1 (RvD1) provided complementary prognostic information, and the combined model outperformed individual indicators in terms of discrimination.

DISCUSSION

This study examined ICH prognosis through an integrated framework linking baseline clinical severity, ICP dynamic burden, and early peripheral biomarkers. Three findings deserve emphasis. First, patients with poor 90-day outcomes had more severe initial injury, reflected by lower admission GCS, larger hematoma volume, and more frequent ventricular involvement. Second, poor outcome was consistently accompanied by a heavier ICP burden across multiple dimensions. Third, worse prognosis was associated with higher lactate and IL-6 levels and lower inflammation-resolving biomarkers. The main novel aspect of the study lies in combining these domains within a single early-phase model rather than evaluating static clinical variables or isolated biomarkers alone.

Our data support the continued importance of conventional severity markers in ICH, particularly admission GCS. Age showed a univariate association with poor outcome but lost significance after multivariable adjustment, suggesting that its prognostic effect may be partly mediated by downstream features such as neurological impairment, ICP burden, and systemic stress. This pattern is clinically plausible and indicates that age alone should not be interpreted as the dominant determinant once more proximate pathophysiological variables are taken into account.

An important contribution of the present study is the emphasis on ICP as a dynamic rather than purely threshold-based phenomenon. The poor prognosis group had higher average ICP, higher peak ICP, more frequent ICP>20 mm Hg episodes, and longer cumulative duration of ICP elevation. For the multivariable model, we retained peak ICP as the representative ICP indicator because the final model needed to remain parsimonious and because peak ICP is straightforward to interpret at the bedside. This does not imply that cumulative duration is unimportant. On the contrary, its strong univariate association supports the broader concept that sustained ICP burden contributes to secondary injury. Future studies with larger samples should examine whether time-weighted ICP load, variability, or composite burden indices add predictive value beyond peak ICP alone.

The biomarker findings extend this interpretation from physiological burden to systemic biological response. Higher lactate levels in the poor prognosis group likely reflect greater metabolic stress, impaired perfusion, and a shift toward anaerobic metabolism in severe disease. At the same time, lactate is not a specific marker of brain injury and may also be influenced by systemic hypoperfusion, infection, organ dysfunction, catecholamine exposure, and treatment intensity. Its value in the present study should therefore be understood as that of a pragmatic stress-related biomarker rather than a disease-specific mechanistic signature. The lower levels of inflammation-resolving factors A and B further suggest that poor recovery may be associated not only with stronger inflammatory activation but also with weaker resolution capacity. Factor A remained in the final model, whereas factor B was not carried forward in the parsimonious main analysis; this should not be interpreted as evidence that factor B is biologically irrelevant.

From a clinical perspective, the combined model appears promising because it joins readily interpretable bedside information with serum markers that may capture biological processes not visible on imaging alone. Even so, its immediate applicability remains limited. The present analysis does not provide validated clinical cut-off values, formal risk categories, or decision-support thresholds. In addition, discrimination was assessed, but calibration and decision-curve performance were not available from the current summary-level revision package. For these reasons, the model should presently be viewed as hypothesis-generating rather than ready for direct treatment guidance.

Several limitations deserve more explicit discussion. This was a single-center observational study, and only patients with clinically indicated ICP monitoring were included, which likely enriched the cohort for more severe cases and may limit generalizability to the broader ICH population. Biomarkers were measured only once within 24 hours after admission, so the temporal evolution of

immunometabolic and inflammation-resolution changes could not be captured. Serial sampling might clarify whether persistent dysregulation, delayed recovery, or trajectory-based patterns provide additional prognostic information. Moreover, catheter insertion was not performed at a uniform post-ictus time, meaning that the biomarker window and ICP window were adjacent but not perfectly synchronized in all patients.

Residual confounding also remains possible. ICP dynamics are influenced by sedation, hyperosmolar therapy, cerebrospinal fluid drainage, surgical procedures, ventilatory management, and intercurrent complications such as infection. These factors were documented clinically, but the present sample size did not allow a stable adjustment strategy for all treatment-related variables in the main model. Although the final model remained parsimonious and the events-per-variable ratio was acceptable, internal Bootstrap validation cannot substitute for external validation in independent cohorts.

Future work should therefore focus on multicenter prospective validation, repeated biomarker measurements, richer characterization of ICP burden, and explicit model calibration. External datasets should be used to examine calibration slope, calibration plots, Brier score, and decision-curve analysis, and to derive clinically meaningful cut-off values or risk categories. A simplified tool that integrates dynamic monitoring with biomarker information may ultimately prove useful, but only after reproducibility and clinical utility are demonstrated.

In summary, poor 90-day outcome after ICH appears to reflect the convergence of initial injury severity, sustained intracranial pressure burden, and dysregulated systemic biological response. This integrated view may help refine early risk stratification, but further validation is necessary before it can inform routine bedside decision-making.

In patients with intracerebral hemorrhage, poor 90-day functional outcomes were associated with heavier ICP dynamic burden, greater immunometabolic stress, and impaired inflammation resolution. Admission GCS score, peak ICP, lactate, and Resolvin D1 (RvD1) provided complementary information for early prognosis assessment. The combined model showed good discrimination in this cohort, but calibration assessment, external validation, and prospective testing are required before routine clinical use.

STATEMENT OF ETHICS

This study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of PLA General Hospital. The requirement for written informed consent was waived by the Ethics Committee because of the retrospective and observational nature of the study. All patient data were anonymized before analysis. Intracranial pressure monitoring and all related clinical interventions were performed solely according to clinical indications and were not initiated for research purposes.

FUNDING

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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Not applicable.

DATA AVAILABILITY

The data that support the findings of this study are available from the corresponding author upon reasonable request.

AI ASSISTANCE DISCLOSURE

Not applicable.

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