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ORIGINAL RESEARCH

Development and Validation of the Systemic Inflammatory Response Index-Based Nomogram for Predicting Short-Term Adverse Events in Patients With Acute Uncomplicated Type B Aortic Intramural Hematoma

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Purpose: This study aims to develop and validate a nomogram based on the Systemic Inflammatory Response Index (SIRI) to predict short-term aortic-related adverse events (ARAEs) in patients with acute uncomplicated Type B intramural hematoma (IMH).

Patients and methods: We retrospectively analyzed 332 patients diagnosed with acute uncomplicated Type B IMH between April 2018 and April 2024. Patients were categorized into the stable group (N=225) and the exacerbation group (N=107) based on the occurrence of ARAEs within 30-day observation period. SIRI was calculated using neutrophil, monocyte, and lymphocyte counts. ARAEs were defined as death related to aortic disease, and the progression of IMH to aortic dissection or penetrating aortic ulcer. The nomogram was developed incorporating SIRI and other significant clinical variables. The model's performance was evaluated using the area under the curve (AUC), calibration curves, decision curve analysis (DCA), and net reclassification index (NRI).

Results: Among the 332 patients, 217 were male (65.4%), with a mean age of 64.3±9.4 years. Multivariate logistic regression and LASSO regression analyses identified SIRI, anemia, diabetes, maximum diameter of aortic diameter (MDAD), and ulcer like projection (ULP) as independent predictors of ARAEs. Two nomogram models were developed: the Clinical model, including anemia, diabetes, MDAD, and ULP; and the Clinical-SIRI model, incorporating SIRI to the Clinical model. The Clinical-SIRI model demonstrated higher predictive accuracy, with an AUC of 0.788 (95% CI: 0.740–0.831), compared to the Clinical model's AUC of 0.742 (95% CI: 0.691–0.788, P = 0.012). SIRI improved predictive accuracy, as shown by a continuous NRI of 0.521 (95% CI: 0.301–0.743). Calibration curves and DCA further supported the clinical utility of the Clinical-SIRI model.

Conclusion: The SIRI-based nomogram is a valuable prognostic tool for predicting short-term ARAEs in patients with acute uncomplicated Type B IMH.

Plain Language Summary: This study introduces a novel nomogram that integrates the Systemic Inflammatory Response Index with clinical variables to enhance the prediction of adverse events in patients with Type B aortic intramural hematoma, a condition marked by highly variable clinical outcomes. The inclusion of this biomarker not only optimizes patient management but also aligns with the growing emphasis on precision in medical interventions.

Keywords: Systemic inflammatory response Index, Type B aortic intramural hematoma, biomarkers, nomogram, prognosis

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Introduction

Aortic intramural hematoma (IMH) presents serious clinical challenges due to its potential for rapid progression to severe complications.[1] According to the Stanford classification, Type B IMH does not involve the ascending aorta,[2] and more commonly affects the descending thoracic aorta (60%) than the ascending aorta (30%) or aortic arch (10%).[3,4] The European Society of Cardiology guidelines strongly recommend initial optimal medical therapy (OMT) and regular imaging follow-up for acute uncomplicated Type B IMH (Class I).[5] However, despite receiving standardized medical management, 35% to 50% of patients experience rapid disease progression.[6] Progression to aortic dissection (AD) or penetrating aortic ulcer (PAU) indicates worsening and necessitates increased vigilance. The prognosis of Type B IMH remains unpredictable, requiring continuous monitoring and timely intervention.

Inflammatory responses and immune activation are known to play significant roles in cardiovascular disease development.[7] But individual inflammatory markers may not fully capture systemic inflammation.[8] The Systemic Inflammatory Response Index (SIRI), which combines neutrophil, monocyte, and lymphocyte counts, provides a comprehensive measure of inflammation and shows promise in predicting outcomes in various diseases, including cancer and cardiovascular conditions.[9] In 2013, Qi et al first reported that SIRI could predict survival in patients with pancreatic adenocarcinoma undergoing gemcitabine-based chemotherapy.[10] Compared to other inflammatory markers, such as interleukin-2, interleukin-6, and C-reactive protein (CRP), SIRI is more accessible through routine medical records and is available for most patients. Given the role of inflammation in IMH pathogenesis, we hypothesize that SIRI could serve as an effective adjunctive prognostic tool for patients with Type B IMH. Additionally, neglecting other clinical characteristics could compromise the accuracy and applicability of the prediction model.[11] Effective risk stratification and timely intervention are for improving patient outcomes. Traditionally, clinical decisions have relied on imaging findings and symptoms, which often fail to accurately predict short-term adverse outcomes. Therefore, developing reliable biomarkers and predictive models is crucial.

This study aims to develop and validate a SIRI-based nomogram to estimate the short-term risk of exacerbation in patients with acute uncomplicated Type B IMH. By integrating SIRI with other clinical variables, we aim to provide a practical and accurate tool for risk stratification, ultimately enhancing patient management and outcomes.

Methods

Study Population and Enrollment Criteria

This retrospective study included 562 patients diagnosed with Type B IMH via computed tomography angiography (CTA) at the General Hospital of Northern Theater Command between April 2018 and April 2024. Inclusion criteria were: (I) age ≥18 years; and (II) confirmed diagnosis of Type B IMH. Exclusion criteria were: (I) subacute or chronic Type B IMH with onset of more than 15 days; (II) complicated Type B IMH; (III) TEVAR or surgery after initial medical contact; (IV) traumatic aortic injury; (V) Marfan syndrome or other genetic/connective tissue diseases; (VI) incomplete clinical or imaging data; (VII) loss to follow-up within 30-day observation period. Additionally, patients with diseases affecting the number of inflammatory cells were excluded, including autoimmune diseases or the use of immunosuppressants within the previous month(n=8), active malignant tumors(n=3), and the use of anti-inflammatory drugs within the previous month(n=3). Finally, a total of 332 patients with acute uncomplicated Type B IMH were included in this study. These patients were divided into two groups: stable group (N=225) and exacerbation group (N=107).The exacerbation group comprised patients who experienced aortic-related adverse events (ARAEs) within 30-day observation period. The stable group consisted of patients who did not experience any ARAEs during the observation period (Figure 1).

This study strictly adhered to the Declaration of Helsinki. The study was approved by the Ethics Committee of the General Hospital of Northern Theater Command [Number Y(2024)234]. Given the retrospective nature of the study, the Committee waived the requirement for patients' written informed consent. The privacy of all medical records and individually identifiable health information in this study was ensured at all times.

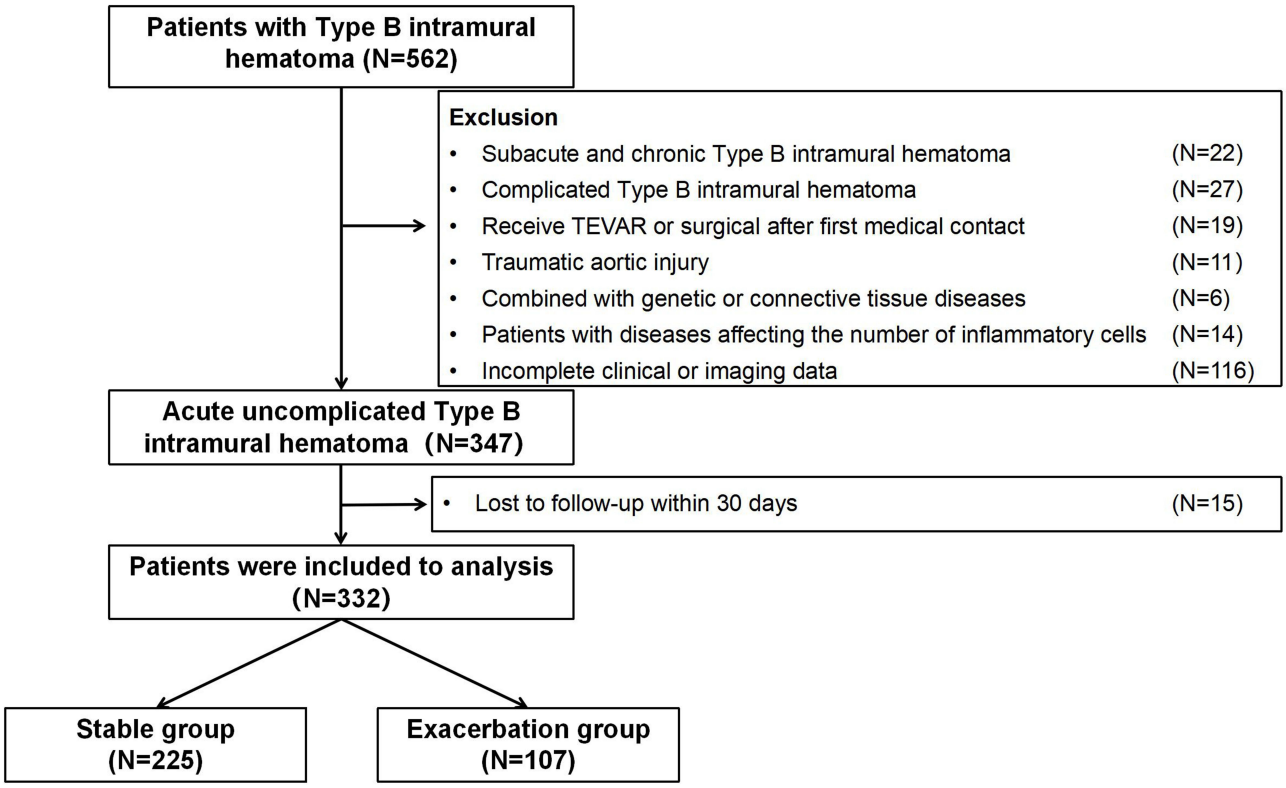

Figure 1 Flow chart of research.
Abbreviations: TEVAR, thoracic endovascular aortic repair.

Treatment and Management

All patients received OMT, including sedation, pain relief, and cardiovascular monitoring (blood pressure and heart rate). The primary treatment objectives were pain alleviation and regulation of blood pressure. Medications were administered to maintain systolic blood pressure at 100–120 mmHg and diastolic blood pressure at 70–80 mmHg. Heart rate targets were set at 60–70 beats per minute. Blood pressure management primarily involved oral antihypertensive drugs tailored to each patient's specific needs.The objective was to reduce aortic wall stress and prevent further extension of dissection, which could lead to rupture or malperfusion.[12]β-blockers were used to maintain heart rate, with dosage adjustments or cessation if the rate fell below 55 beats per minute.

CTA Measurement

CTA images from the institutional Picture Archiving and Communication Systems facilitated detailed analysis. This analysis included the location and extent of the aortic lesion, aortic atherosclerosis, ulcer like projections (ULP), hematoma shape, and pleural effusions. Aortic measurements were taken from first CTA on presentation to hospital. Measurements included the maximum diameter of descending aorta (MDAD, mm) and the maximum diameter of hematoma thickness (MDHT, mm). The standard scanning protocol involved confirming the diagnosis with the first imaging examination after onset, followed by CTA scans at 14 days and 30 days. If imaging revealed Type B IMH progression to AD, PAU, or other high-risk conditions like impending rupture, patients were considered for preventive invasive interventions to avert rupture or death. All diagnoses and measurements in Type B IMH patients were confirmed by at least two experienced clinicians.

Data Collection and Definitions

Patient baseline characteristics, laboratory results, and follow-up information were obtained from our electronic medical record database. Follow-up information was gathered from the most recent medical records or through telephone

interviews. A complete blood collection was performed upon admission and immediately analyzed using an automated hematology analyzer. When multiple blood samples were available, the first analysis report was selected.

The primary outcome of this study was the occurrence of ARAEs within 30-day observation period.[13,14] ARAEs were defined as death related to aortic disease, or the progression of IMH to AD and PAU. The SIRI was calculated as follows: SIRI = (neutrophil count × monocyte count)/lymphocyte count.[15] The criteria for complicated IMH included expansion despite pharmacological management, impending rupture, uncontrolled hypertension, end-organ damage, refractory pain, or an intimal tear evident on CTA.[16] ARAEs were defined as death related to aortic disease, or the progression of IMH to AD and PAU. AD is characterized by an intimal tear that separates the aorta into true and false lumens, which may be variably filled with contrast medium. PAU involves penetration of an atherosclerotic plaque through the internal elastic layer into the media, forming a contrast-filled pocket on the aortic wall, leading to intimal destruction and possible hematoma formation. ULP refers to contrast-filled pouches protruding from the aorta, with a breach diameter greater than 3 mm. Unlike PAU, ULPs do not penetrate the internal elastic membrane and may occur without atherosclerosis.[17]

Statistical Analysis

Statistical analyses were performed using RStudio (version 4.4.0; R Foundation for Statistical Computing, Vienna, Austria) and GraphPad Prism (version 8.0; GraphPad Software, San Diego, CA, USA). Continuous variables were presented as mean ± SD or median (quartile 1 to quartile 3). Data normality was assessed using the Shapiro–Wilk test and Quantile-Quantile(Q-Q) plots. Student's *t*-test were conducted for normally distributed variables, while the Mann–Whitney *U*-test was applied to non-normally distributed variables. Categorical variables were reported as frequencies and percentages and analyzed using the chi-square or Fisher's exact test.

Multivariate logistic regression was used to investigate the association between the SIRI (independent variable) and the risk of ARAEs (dependent variable) through five distinct models for statistical inference, such as demographic characteristics, comorbidities, CTA characteristics, and laboratory results. The proportional hazards assumption was tested using Schoenfeld residuals, and no potential violation was observed. The receiver operating characteristic (ROC) curve was used to explore the predictive value of SIRI for ARAEs.

Logistic regression analyses were used to identify odds ratios (OR) with 95% confidence intervals (CI). Variables with $P < 0.05$ in the univariate analysis were included in the multivariate analysis, using the enter method to determine independent risk factors associated with ARAEs. In the univariate logistic regression analyses, nine features were significantly related to ARAEs. Additionally, sex, age, body mass index, MDHT, hypertension, and prothrombin time, all with $P > 0.05$, were included. These 15 features were considered potential predictors. Feature selection was performed using the "glmnet" package, and the LASSO regression algorithm was applied based on these features, with the optimal penalty coefficient λ determined using the 10-fold cross-validation method and the 1-SE criterion.

The rms' package was used to construct the nomogram, while the 'pROC' package was used to draw the ROC curve, plot the area under the curve (AUC), and evaluate the models diagnostic performance. Internal validation was performed using the bootstrap method. The calibration curve assessed the consistency between the predicted survival probability of the nomogram and the bootstrap resamples. Decision curve analysis (DCA) and clinical impact curves (CIC) were used to evaluate the net benefit of the nomogram.The effectiveness of SIRI in predicting risk was assessed using DeLong's test. The continuous net reclassification improvement (NRI) was also used to quantify the added predictive value of SIRI. Statistical significance was determined using a two-sided test with a $P < 0.05$.

Result

Baseline Characteristics

This study included 332 patients with acute uncomplicated Type B IMH, comprising 217 men (65.4%) and 115 women (34.6%), with a mean age of 64.3±9.4 years. Among these patients, 89 developed PAU, 16 developed AD, and 10 cases resulted in death related to aortic disease. Baseline demographics are presented in Table 1. No significant differences were observed between the exacerbation and stable group in terms of age, gender, body mass index, admission blood pressure, heart rate, drinking history, smoking history, comorbidities, medications, or clinical symptoms. However, the

Table 1 Clinical Characteristics

Variables	Overall N = 332	Stable group N = 225	Exacerbation group N = 107	P-value
Age, year	64.3 ± 9.4	64.6 ± 9.7	63.7 ± 8.6	0.434
Male, n (%)	217 (65.4%)	146 (64.9%)	71 (66.4%)	0.793
Body mass index, kg/m^2	24.6 (22.5, 27.7)	24.7 (22.5, 27.7)	24.6 (22.6, 27.7)	0.727
Systolic blood pressure, mmHg	140.0 (125.0, 156.0)	141.0 (125.0, 157.0)	139.0 (124.0, 153.0)	0.297
Heart rate, BPM	84.0 (74.0, 93.0)	82 (72.0, 93.0)	85 (76.0, 94.0)	0.277
Smoking, n (%)	151 (45.5%)	102 (45.3%)	49 (45.8%)	0.937
Drinking, n (%)	175 (52.7%)	123 (54.7%)	52 (48.6%)	0.301
Hypertension, n (%)	236 (71.1%)	166 (73.8%)	70 (65.4%)	0.116
Diabetes, n (%)	37 (11.1%)	32 (14.2%)	5 (4.7%)	0.010
Coronary artery disease, n (%)	12 (3.6%)	8 (3.6%)	4 (3.7%)	>0.999
Anaemia, n (%)	23 (6.9%)	10 (4.4%)	13 (12.1%)	0.010
Cerebrovascular disease, n (%)	38 (11.4%)	29 (12.9%)	9 (8.4%)	0.231
Peripheral vascular disease, n (%	1 (0.3%)	0 (0.0%)	1 (0.9%)	0.322
Clinical symptoms				
Tachycardia, n (%)	2 (0.6%)	2 (0.9%)	0 (0.0%)	>0.999
Chest distress, n (%)	23 (6.9%)	14 (6.2%)	9 (8.4%)	0.463
Chest or back pain, n (%)	301 (90.7%)	205 (91.1%)	96 (89.7%)	0.667
Abdominal pain, n (%)	38 (11.4%)	26 (11.6%)	12 (11.2%)	0.927
Dyspnea, n (%)	50 (15.1%)	29 (12.9%)	21 (19.6%)	0.109

Notes: Data presented as as mean ± SD, median (quartile 1 to quartile 3) or number (percentage). Abbreviations: BPM, beat per minute. Anemia is defined as a hemoglobin level of <120 g/L in adult men and <110 g/L in adult women.

prevalence of diabetes was significantly lower in exacerbation group than the stable group (5.7% vs 14.2%, P = 0.010), whereas the prevalence of anemia was significantly higher in the exacerbation group (12.1% vs 4.4%, P = 0.010).

Laboratory results indicated that WBC count, neutrophil count, monocyte count, and SIRI were significantly higher in the exacerbation group (P < 0.05). In contrast, the stable group had a higher lymphocyte count (P < 0.001). There were no significant differences between the two groups in other variables (Table 2).

Imaging examination results showed that the MDAD (35.0±4.4 mm vs 33.1±4.8 mm, P < 0.001) and the proportion of patients with ULP (49.5% vs 17.8%, P < 0.001) were significantly higher in the exacerbation group compared to the stable group. No significant differences were observed between the two groups in other variables (Table 3).

Sensitivity Analysis

Furthermore, analyzing SIRI as a continuous variable consistently showed independent associations between SIRI and clinical exacerbation in Type B IMH patients across all five models, regardless of the adjustment model used. To further evaluate the prognostic significance of SIRI in predicting clinical exacerbation, we constructed five logistic regression models (Figure 2). In models 1–3, a higher likelihood of experiencing ARAEs was observed in patients with elevated SIRI levels after accounting for demographic variables (P<0.001). In model 4, after adjusting for the covariates from models 1–3 and incorporating CTA characteristics, the association between high SIRI levels and clinical exacerbation remained statistically significant (P<0.001). Model 5, which included full covariate adjustment, yielded similar results (OR = 1.169, 95% CI 1.016–1.288, P<0.001).

Logistic Regression Analysis and LASSO Regression Analysis

Univariable logistic regression analysis identified associations between ARAEs within 30-day observation period and diabetes, anemia, ULP, MDAD, white blood cell count, neutrophil count, lymphocyte count, monocyte count, and SIRI. To further investigate the independent risk factors for ARAEs in acute uncomplicated Type B IMH, two multivariate logistic regression models were developed, referred to as Multivariate Analysis 1 and Multivariate Analysis 2. In Multivariate Analysis 1, variables with P<0.05 in the univariable analysis were included. The results indicated that

Table 2 Laboratory Results

Variables	Overall N = 332	Stable group N = 225	Exacerbation group N = 107	P-value
WBC, 10^9/L	10.3 (8.3, 12.4)	10.3 (8.2, 12.0)	10.6 (8.8, 13.5)	0.034
NBC, 10^9/L	8.6 (6.7, 10.8)	8.5 (6.4, 10.1)	8.9 (6.8, 12.1)	0.038
LBC, 10^9/L	1.0 (0.7, 1.4)	1.13 (0.7, 1.5)	1.0 (0.9, 1.2)	0.030
MBC, 10^9/L	0.5 (0.4, 0.7)	0.4 (0.3, 0.6)	0.5 (0.4, 0.8)	0.002
RBC, 10^12/L	4.4 ± 0.5	4.4 ± 0.5	4.4 ± 0.6	0.731
PLT, 10^9/L	204.5 (169.0, 246.0)	204.0 (167.0, 247.5)	206.0 (177.0, 245.0)	0.825
NT-proBNP, pg/mL	209.9 (101.0, 447.9)	202.7 (97.4, 439.2)	214.6 (106.4, 503.0)	0.383
GLU, mmol/L	7.42 (6.41, 8.55)	7.36 (6.52, 8.50)	7.50 (6.21, 8.65)	0.791
ALT, U/L	16.8 (12.5, 24.0)	16.5 (12.3, 24.2)	17.6 (13.4, 23.7)	0.250
AST, U/L	19.7 (16.8, 24.9)	19.8 (17.0, 25.4)	19.4 (16.8, 23.7)	0.541
LDH, U/L	207.5 (177.0, 243.0)	208 (179, 245)	203 (175, 237)	0.360
UA, umol/L	5.77 (4.7, 7.2)	5.83 (4.8, 7.3)	5.7 (4.7, 6.9)	0.872
TBiL, umol/L	10.2 (7.4, 14.7)	10.1 (7.0, 14.7)	10.5 (7.6, 14.6)	0.313
SCr, umol/L	67.2 (54.3, 79.9)	67.3 (54.7, 80.0)	67.2 (52.8, 79.6)	0.998
TNT, ng/L	9.0 (6.0, 15.8)	9.0 (6.0, 15.0)	8.5 (6.0, 17.0)	0.844
APTT, s	33.6 (30.3, 37.3)	33.6 (30.1, 37.2)	33.5 (30.6, 37.7)	0.391
FIB, g/L	3.29 (2.7, 4.2)	3.25 (2.7, 4.2)	3.62 (2.8, 4.4)	0.202
TT, s	13.2 (12.7, 13.8)	13.10 (12.7, 13.7)	13.4 (12.9, 13.9)	0.037
D-Dimer, mg/L	1.7 (0.8, 3.9)	1.7 (0.9, 3.9)	1.9 (0.7, 4.2)	0.802
SIRI	4.1 (2.6, 6.6)	3.9 (2.5, 5.6)	5.4 (2.9, 9.4)	<0.001

Notes: Data presented as mean ± SD, or median (quartile 1 to quartile 3).
Abbreviations: WBC, white blood cells; NBC, neutrophil count; LBC, lymphocyte count; MBC, monocyte count; RBC, red blood cells; PLT, platelets; NT-proBNP, N-terminal pro b-type natriuretic peptide; GLU, glucose; ALT, alanine transaminase; AST, aspartate transaminase; LDH, lactate dehydrogenase; UA, uric acid; TBiL, total bilirubin; SCr, serum creatinine; TNT, troponin-T; APTT, activated partial thromboplastin time; FIB, fibrinogen; TT, thrombin time; SIRI, systemic inflammatory response index.

Table 3 CTA Characteristics

Variables	Overall N = 332	Stable group N = 225	Exacerbation group N = 107	P-value
MAAD, mm	41.8 (39.4, 45.0)	41.6 (39.0, 44.8)	42.3 (39.7, 45.2)	0.373
MDAD, mm	33.8 ± 4.8	33.1 ± 4.8	35.0 ± 4.4	<0.001
MDHT, mm	8.5 (7.0, 11.0)	8.4 (6.7, 11.0)	8.6 (7.6, 11.1)	0.210
ULP, n (%)	93 (28.0%)	40 (17.8%)	53 (49.5%)	<0.001
Pleural effusion, n (%)	56 (16.9%)	34 (15.1%)	22 (20.6%)	0.215
Circular hematoma, n (%)	125 (37.7%)	84 (37.3%)	41 (38.3%)	0.863
Crescent hematoma, n (%)	207 (62.3%)	141 (62.7%)	66 (61.7%)	0.863
IMH passing abdominal cavity, n (%)	234 (70.5%)	153 (68.0%)	81 (75.7%)	0.151
IMH passing diaphragm, n (%)	226 (68.1%)	148 (65.8%)	78 (72.9%)	0.193
IMH passing iliac artery, n (%)	50 (15.1%)	32 (14.2%)	18 (16.8%)	0.536

Notes: Data are expressed as mean ± SD, or number (percentage).
Abbreviations: CTA, computed tomography angiography; MAAD, maximum ascending aorta diameter; MDAD, maximum descending of aorta diameter; MDHT, maximum descending of aorta hematoma thickness; ULP, ulcer like projection; IMH, intramural hematoma.

diabetes (OR = 0.27, 95% CI: 0.09–0.82, P = 0.021), anemia (OR = 3.54, 95% CI: 1.30–9.62, P = 0.013), MDAD (OR = 1.08, 95% CI: 1.02–1.14, P = 0.013), and ULP (OR = 4.24, 95% CI: 2.36–7.61, P < 0.001) were independent predictors of ARAEs for patients with acute uncomplicated Type B IMH. In Multivariate Analysis 2, SIRI was included while neutrophil count, monocyte count, and lymphocyte count were excluded. The results showed that diabetes (OR= 0.23, 95% CI: 0.07–0.74, P = 0.014), anemia (OR = 3.52, 95% CI: 1.33–9.35, P = 0.011), MDAD (OR = 1.08, 95% CI: 1.02–1.15, P = 0.007), ULP (OR = 3.83, 95% CI: 2.19–6.71, P < 0.001), and SIRI (OR = 1.16, 95% CI: 1.06–1.27, P <

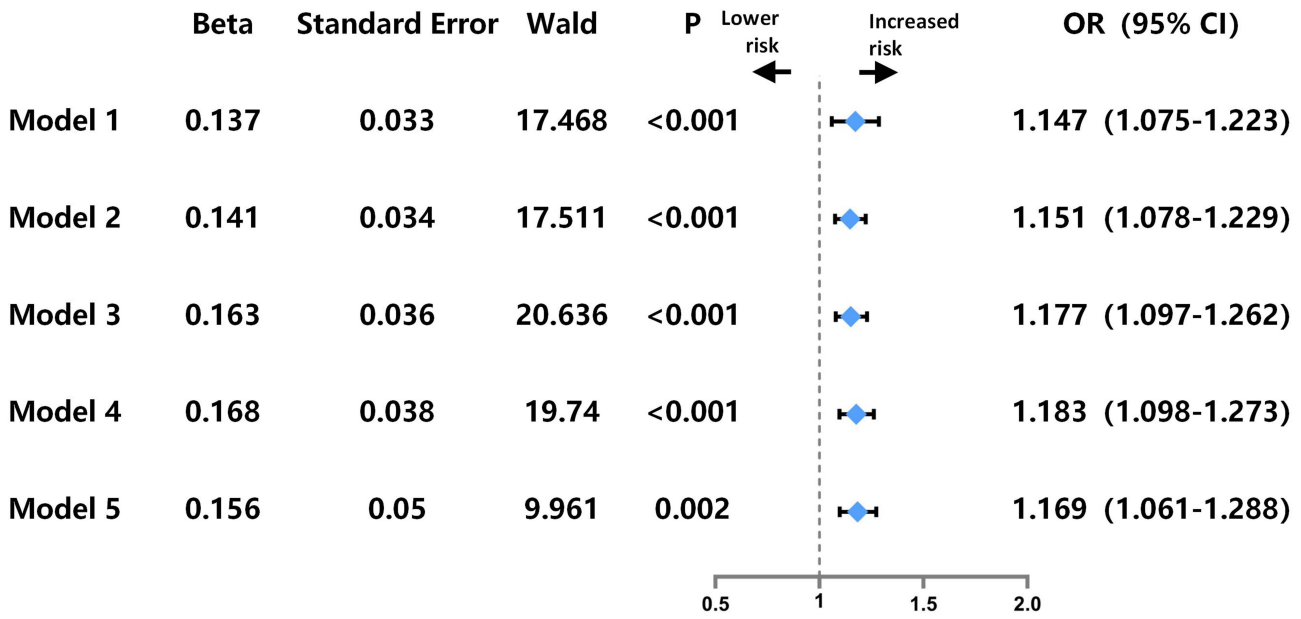

Figure 2 Forest plot of adverse related aortic events hazard ratios by multivariable logistic regression analyses for the association between systemic inflammatory response index and adverse related aortic events. Model 1: unadjusted. Model 2: adjusted for age, gender, and body mass index. Model 3: adjusted for age, gender, body mass index, and previous comorbidities. Model 4: adjusted for age, gender, body mass index, previous comorbidities, and imaging characteristics. Model 5: adjusted for age, gender, body mass index, previous comorbidities, imaging characteristics, and laboratory results.
Abbreviations: OR, odds ratio; CI, confidence interval.

0.001) remained independent predictors of ARAEs. These findings are summarized in Table 4. To further validate these predictors, LASSO regression analysis was also performed, which confirmed the same five predictors as in the Multivariate Analysis 2, thereby strengthening the results of Multivariate Analysis 2 (Figure 3).

Establishment and Application of Nomogram Model

To quantitatively predict the risk of ARAEs in patients with acute uncomplicated Type B IMH undergoing OMT, we developed two nomograms incorporating significant predictors (Figure 4A and B). Clinical predictors were used to construct the Clinical model based on the proportional hazards analysis from Multivariate Analysis 1, with regression coefficients. Similarly, the Clinical-SIRI model was constructed by integrating clinical risk predictors with SIRI. This nomogram showed that SIRI contributed the most to prognosis. Each variable was assigned a score on the points scale,

Table 4 Independent Predictors of AREAs by Univariate and Multivariate Logistic Regression Analysis

Variables	Univariate analysis			Multivariate analysis 1			Multivariate analysis 2		
	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value
Diabetes	0.30	0.11, 0.78	0.014	0.27	0.09, 0.82	0.021	0.23	0.07, 0.74	0.014
Anaemia	2.97	1.26, 7.02	0.013	3.54	1.30, 9.62	0.013	3.52	1.33, 9.35	0.011
ULP	4.54	2.73, 7.56	<0.001	1.08	1.02, 1.14	0.013	1.08	1.02, 1.15	0.007
MDAD	1.09	1.04, 1.15	<0.001	4.24	2.36, 7.61	<0.001	3.83	2.19, 6.71	<0.001
WBC	1.10	1.03, 1.18	0.007	1.04	0.04, 27.78	0.981	1.03	0.92, 1.15	0.653
NBC	1.10	1.03, 1.18	0.005	1.07	0.04, 28.00	0.968	-	-	-
LBC	0.57	0.36, 0.88	0.012	0.38	0.01, 14.03	0.600	-	-	-
MBC	4.04	1.79, 9.12	<0.001	6.13	0.18, 206.51	0.312	-	-	-
SIRI	1.15	1.08, 1.22	<0.001	-	-	-	1.16	1.06, 1.27	0.001

Abbreviations: OR, odds ratio; CI, confidence interval. ULP, ulcer like projection; MDAD, maximum descending of aorta diameter; WBC, white blood cells; NBC, neutrophil count; LBC, lymphocyte count; MBC, monocyte count; SIRI, systemic inflammatory response index; ARAEs, adverse related aortic events.

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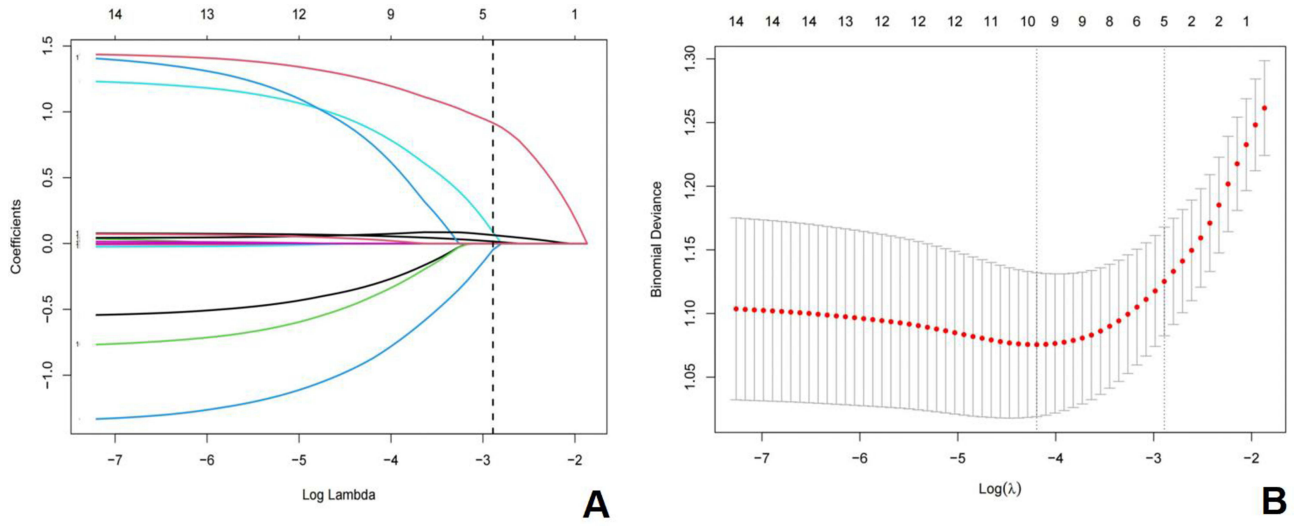

Figure 3 Short-term exacerbation predictors in patients with acute uncomplicated Type B IMH identified using LASSO regression. (**A**) LASSO coefficient distribution for each clinical feature. (**B**) The optimal penalty coefficient λ for the LASSO model determined by 10-fold cross-validation and the 1-SE criterion.
Abbreviations: SE, standard error; LASSO, least absolute shrinkage and selection operator.

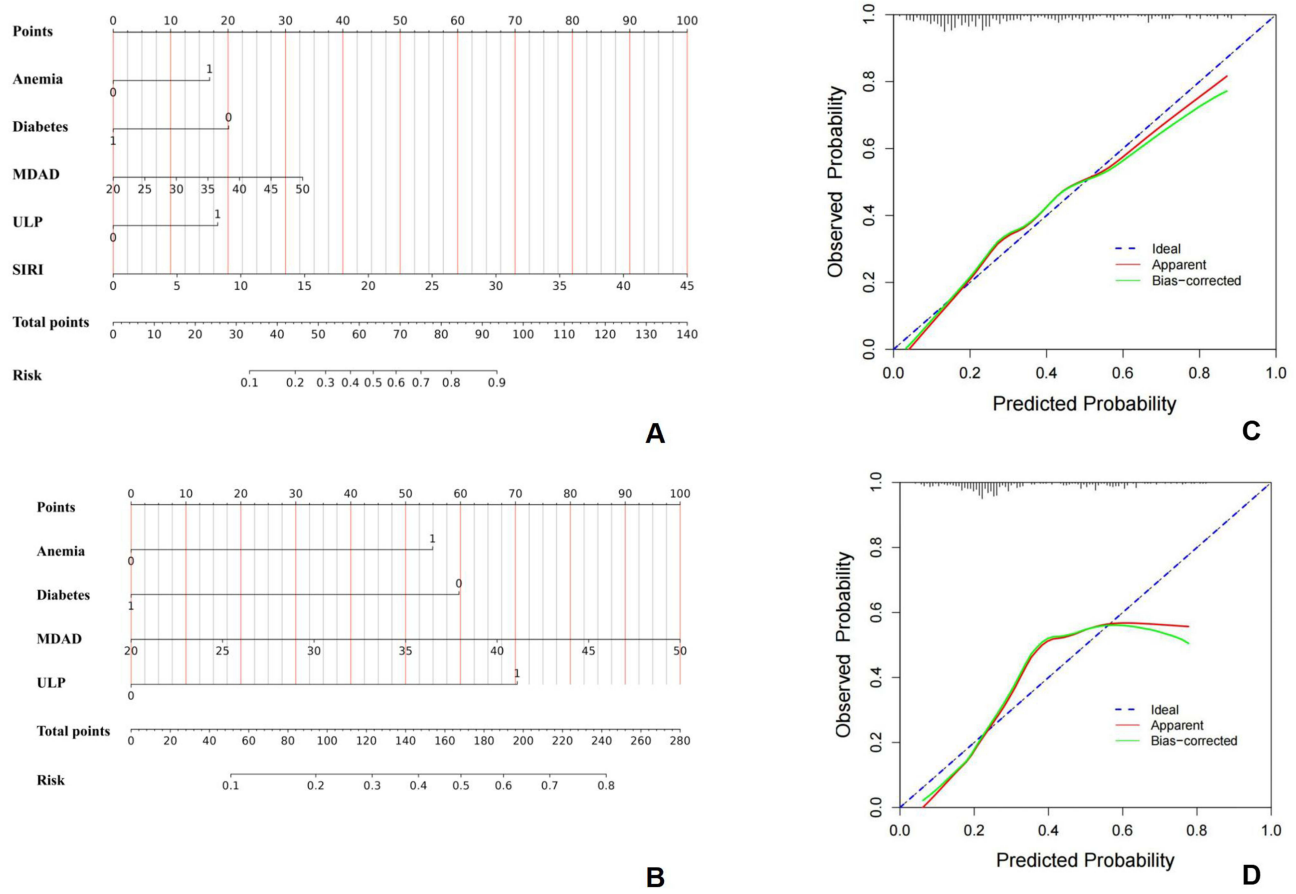

Figure 4 Constructed nomograms and their calibration curves. (**A**) and (**B**) show the nomograms for the Clinical-SIRI model and the Clinical model, respectively, predicting the incidence of ARAEs in patients with acute uncomplicated Type B IMH within a 30-day follow-up period. Calibration curves for the Clinical-SIRI model (**C**) and the Clinical model (**D**) illustrate the agreement between the nomogram-predicted probabilities of 30-day ARAEs and the actual observed probabilities. The "Ideal" line represents a perfect prediction model. The "Apparent" line shows the prediction probability from the original development dataset. The "bias-corrected" line shows the prediction probability obtained through Bootstrap resampling, which involved 1000 iterations. The x-axis represents the nomogram-estimated probabilities of 30-day ARAEs, and the y-axis represents the actual observed incidence of 30-day ARAEs.
Abbreviations: IMH, aortic intramural hematoma; SIRI, systemic inflammation response index; ARAEs, adverse related aortic events.

Table 5 Incremental Predict Value of the SIRI

Prediction	AUC(95% CI)	P-value		
		Model 1 vs.	Model 2 vs.	Model 3 vs.
Model 1: Clinical-SIRI model	0.788(0.740–0.831)	-	0.012	<0.001
Model 2: Clinical model	0.742(0.691–0.788)	0.012	-	0.044
Model 3: SIRI model	0.643(0.589–0.694)	<0.001	0.044	-

Abbreviations: SIRI, systemic inflammation response index; AUC, area under the curve; CI, confidence interval.

and these scores were summed to obtain a total score, which was then located on the total points scale. A line was drawn straight down to determine the risk of ARAEs and the estimated survival probability at each time point.

To validate the model, the bootstrap method was employed with 1000 repetitions (Supplemental Figure 1), resulting in an AUC of 0.788 (95% CI: 0.738–0.838). To enhance the model's usability for clinicians, we developed an online calculator based on the nomogram, available at https://aorticresearch.shinyapps.io/imhprognosis/."

Clinical Application of Nomogram Model

The ROC curve analysis was performed to assess the predictive value of SIRI for ARAEs, revealing an AUC of 0.643 (95% CI, 0.589–0.694). The incremental prognostic value of the model was assessed using the AUC, revealing that the Clinical-SIRI model had an improved goodness of fit compared to the Clinical model[0.788 (95% CI: 0.740–0.831) vs 0.742 (95% CI: 0.691–0.788), P=0.012] (Table 5 and Figure 5). Incorporating SIRI to the Clinical-SIRI model

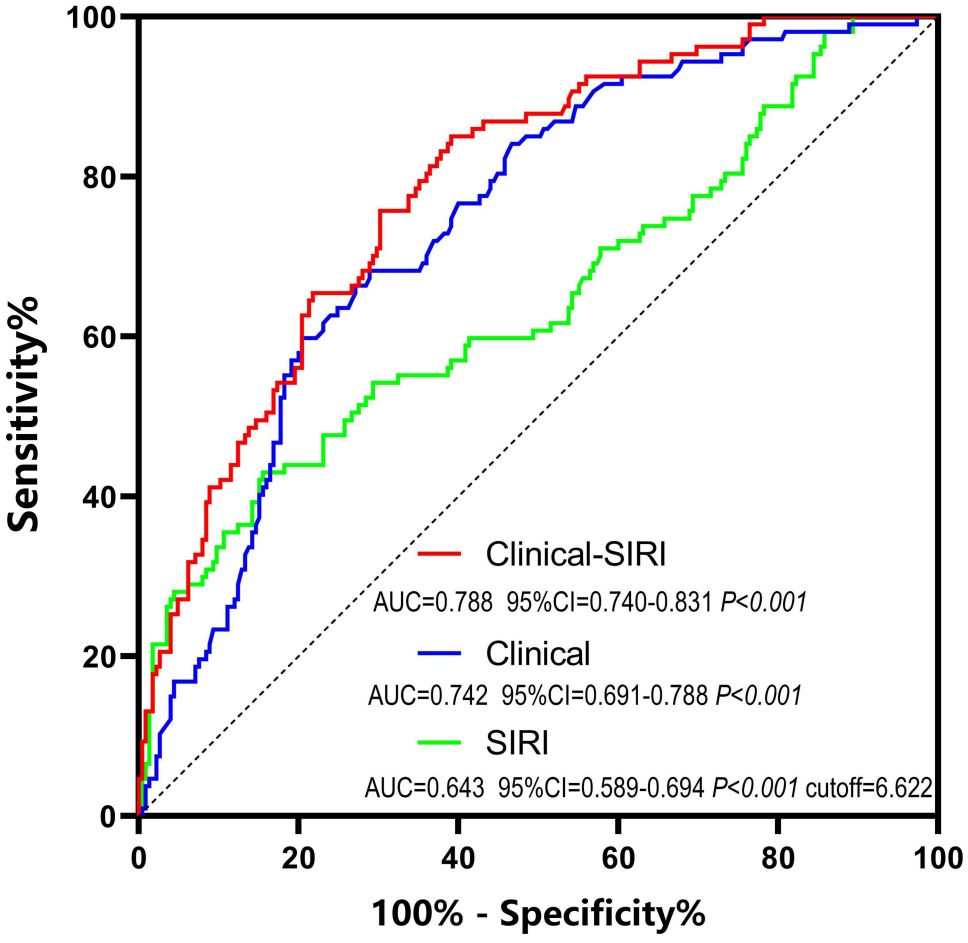

Figure 5 Receiver operating characteristic curves of Clinical-SIRI model, Clinical model, and SIRI model for the incidence of AREAs. SIRI, systemic inflammation response index.

Abbreviations: ARAEs, adverse related aortic events. AUC, area under the curve; CI, confidence interval.

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significantly enhanced predictive accuracy over the clinical model, with a continuous NRI of 0.521 (95% CI: 0.301–0.743). Additionally, the calibration curve demonstrated strong agreement between the predicted and observed probabilities for the short-term exacerbation risk model in acute uncomplicated Type B IMH patients. The calibration curve for the Clinical-SIRI model showed better alignment between predictions and observations than the Clinical model alone (Figure 4C and Figure 4D).

DCA was used to examine the clinical usefulness of the three models (Figure 6). The DCA showed that the Clinical-SIRI model had a higher net benefit than either the SIRI model or the Clinical model across the ARAEs' incidence of the threshold probabilities. SIRI model has greater benefit than Clinical model at higher risk thresholds. CIC plots illustrated the number of high-risk patients and the number of truly high-risk cases at each high-risk threshold, demonstrating the model's favorable predictability and clinical applicability(Supplemental Figure 2). These findings suggest that the Clinical-SIRI model may play a significant role in identifying patients likely to experience ARAEs.

Discussion

Current research on inflammatory markers and predictive models in IMH remains limited. This study is the first to establish an association between SIRI and poor prognosis in patients with acute uncomplicated Type B IMH. It introduces a novel nomogram-based prediction model that leverages SIRI to evaluate short-term prognosis in these patients. The combination of SIRI with four additional clinical variables offers a comprehensive approach to risk assessment, supporting timely and personalized clinical decision-making.

IMH is related to, but pathologically distinct from, AD and PAU. It is characterized by hemorrhage within the media layer of the aortic wall, potentially with or without intimal disruption.[18] Radiographically, IMH presents as high-

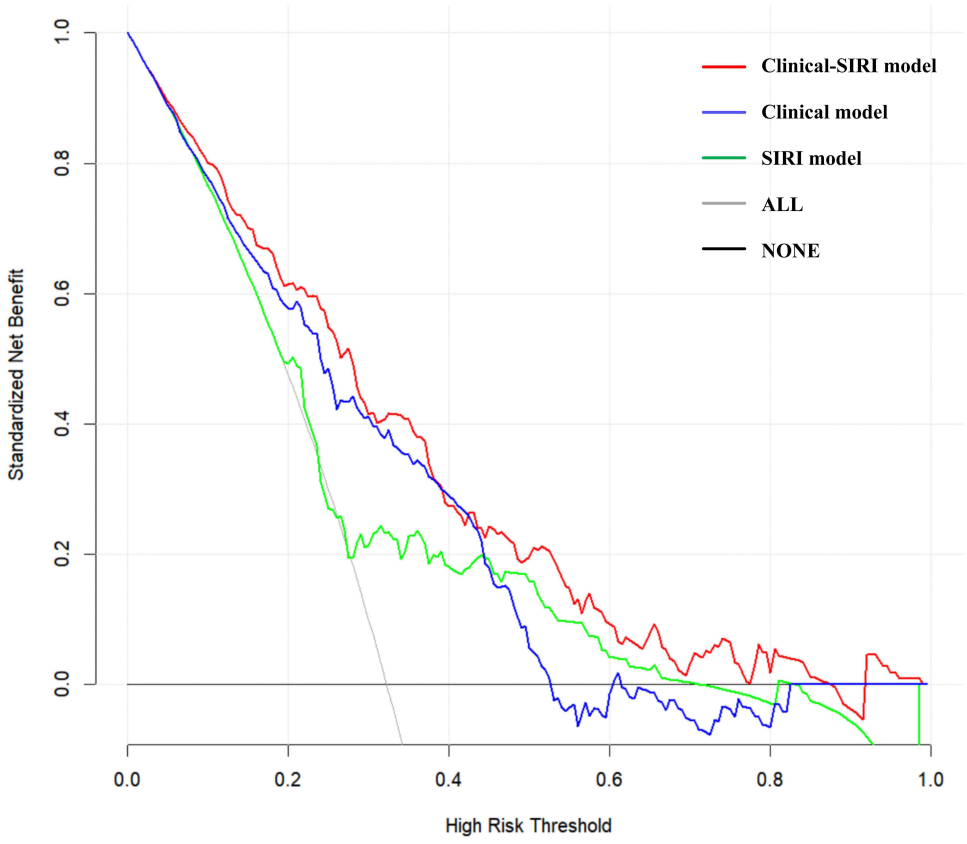

Figure 6 Decision curve analysis for the Clinical-SIRI model, Clinical model, and SIRI model. The x-axis represents the threshold probability. The y-axis represents the net benefits in comprehensive consideration of insufficient treatment (false negative) and excessive treatment (false positive) across the threshold probability of 0–1.0. Decision curve analysis reveals that Clinical-SIRI model had a higher net benefit than Clinical model or SIRI model in clinical practice.
Abbreviations: SIRI, systemic inflammation response index.

attenuation crescentic or circumferential thickening of the aortic wall on noncontrast imaging, with no evidence of blood flow through a false lumen on contrast-enhanced imaging.[16] Prospective studies suggest that within 30 days post-admission, IMH may resolve, progress to classical AD or PAU, result in contained rupture, or lead to aneurysm formation.[19] Most adverse events occur within the first 30 days post-diagnosis.[20] Therefore, vigilant medical surveillance and timely intervention during the early stages of IMH are essential for improving patient outcomes.

The Correlation Between SIRI and IMH: SIRI quantifies systemic inflammation by incorporating the ratios of neutrophil, monocyte, and lymphocyte counts.[21] Inflammatory markers may play a significant role in the progression of IMH, and the SIRI may provide a more comprehensive assessment of a patient's systemic inflammatory status compared to other individual biomarkers. However, there are few studies on other inflammatory markers in this field. Chen et al demonstrated that higher levels of CPR was associated with increased aortic-related mortality in patients with acute uncomplicated Type B IMH.[22] Other studies have shown that serum CRP levels rise rapidly after the onset of the acute phase response, peaking within 24 to 48 hours before decreasing. In contrast, SIRI levels remained relatively stable during the acute phase(less than 14 days).[23] Since SIRI measurement is not time-dependent, it offers a more stable reflection of the inflammatory status in acute phase.

Neutrophils are key mediators of acute inflammatory responses, rapidly migrating to sites of inflammation and releasing various mediators such as reactive oxygen species and proteases, which can cause tissue damage and exacerbate pathological changes.[24] In acute Type B IMH, elevated neutrophil counts may indicate significant aortic wall damage and an intensified inflammatory response, thereby increasing the risk of ARAEs.[25]

Monocytes, upon reaching the lesion site, differentiate into macrophages and dendritic cells, both crucial for inflammation and tissue repair. Macrophages engulf damaged cells and tissue debris, releasing a variety of cytokines and growth factors that modulate inflammation and facilitate repair.[26] However, excessive macrophage activity can lead to fibrosis and scarring, which further compromise the structural integrity of the aortic wall.[27,28] Elevated monocyte levels in acute Type B IMH may indicate a sustained inflammatory response and an imbalance in tissue repair, potentially exacerbating the lesion.

Lymphocytes, particularly T cells, play a central role in regulating immune responses. A reduced lymphocyte count may indicate impaired immune regulation, leading to inadequate control of inflammation.[29,30] In acute Type B IMH, decreased lymphocyte counts may reflect disrupted immune regulation, resulting in uncontrolled inflammation and an increased risk of ARAEs.

SIRI provides a robust method for evaluating systemic inflammation. Elevated SIRI values typically correlate with increased neutrophil and monocyte counts and decreased lymphocyte counts, indicating an intensified acute inflammatory response and diminished immune regulatory capacity. In aortic diseases, such inflammatory and immune dysregulation may contribute to further damage and instability of the aortic wall, thereby increasing the risk of ARAEs in patients with Type B IMH during short-term follow-up. Based on the results, patients with acute uncomplicated Type B IMH and elevated SIRI (>6.622) may be at higher risk for short-term deterioration. Clinicians can implement more aggressive management strategies for patients with high-risk ARAEs, including intensified blood pressure control, increased follow-up frequency, or early intervention.

Additional Clinical Risk Factors: Beyond SIRI, other high-risk clinical factors also must be considered. Through logistic and LASSO regression analysis, we identified four additional independent clinical predictors of ARAEs: diabetes, anemia, MDAD, and ULP. Hyperglycemia reduces inflammatory cell infiltration into the aortic media and inhibits neovascularization in the aortic adventitia, decreasing vascular smooth muscle cell death and extracellular matrix degradation, ultimately inhibiting disease progression.[31] Anemia reduces oxygen-carrying capacity, leading to inadequate tissue oxygenation and impaired aortic function.[32] Previous research by Shao et al, and Zhang et al highlighted the prognostic value of an MDAD over 40 mm in predicting IMH progression. The prognostic value of MDAD in IMH evolution likely stems from the increased stress on a dilated aortic wall, which implies a higher risk of rupture compared to a non-dilated aorta.[17,33] ULP, defined as focal outpouchings of contrast from the aortic lumen in IMH without associated atherosclerotic plaque and characterized by a communicating orifice >3 mm, are present in 32% of Type B IMH cases and significantly predict aorta-related mortality and adverse events, particularly in the acute phase.[34]

Limitations

This study has several limitations. First, while SIRI shows potential as a prognostic biomarker, it is not specific to IMH and may be influenced by other inflammatory conditions. Additionally, the study did not explore the underlying mechanisms behind elevated SIRI levels and poor outcomes. Future studies into inflammation mechanisms and IMH prognosis are needed. The study also focused on short-term outcomes, and although which are critical for patient prognosis, but did not evaluate long-term outcomes. Finally, although internal validation was conducted, the study lacks external validation across multiple centers. Future research should aim to validate this model in larger, multicenter cohorts and further investigate its role in clinical decision-making for poor prognosis.

Conclusion

Our study highlights the potential of SIRI as a valuable prognostic marker. The SIRI-based nomogram provides a practical and effective tool for predicting short-term outcomes in patients with acute, uncomplicated Type B IMH. By facilitating the early identification of high-risk patients, this model can guide clinical management and ultimately improve patient prognosis.

Abbreviations

IMH, Aortic intramural hematoma; OMT, Optimal medical therapy; AD, Aortic dissection; PAU, Penetrating aortic ulcer, SIRI, Systemic inflammatory response index; CRP, C-reactive protein; CTA, Computed tomography angiography; ARAEs, Aortic-related adverse events; ULP, Ulcer like projections; Maximum diameter of descending aorta; MDAD MDHT, Maximum diameter of hematoma thickness; ROC, Receiver operating characteristic; OR, Odds ratio; CI, Confidence intervals; AUC, Area under the curve; DCA, Decision curve analysis; CIC, Clinical impact curves; NRI, Net reclassification improvement.

Data Sharing Statement

The data underlying this article will be shared on reasonable request to the corresponding author.

Ethics Approval and Informed Consent

The studies involving humans were approved by the Ethics Committee of General Hospital of Northern Theater Command(Number Y(2024)234). The studies were conducted in accordance with the local legislation and institutional requirements. The ethics committee/institutional review board waived the requirement of written informed consent for participation from the participants or the participants' legal guardians/next of kin because the study was a retrospective study.

Consent for Publication

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

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