

## Original Article

# Development and validation of a prediction model for hyperuricemia risk in hypertensive patients

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**Abstract:** Objective: This study aimed to create a predictive model for hyperuricemia (HUA) in patients diagnosed with hypertension and evaluate its predictive accuracy. Methods: Employing a retrospective cohort design, this study investigated HUA incidence and clinical data among 228 patients with essential hypertension selected from the Department of Cardiology at a tertiary A-level hospital in Anhui Province, China, between January 2018 and June 2021. The patients were divided randomly into a training group (168 cases) and a validation group (60 cases) at a 7:3 ratio. The training group underwent univariate and multivariate logistic regression analyses to identify risk factors for HUA. Additionally, an R software-generated nomogram model estimated HUA risk in hypertensive patients. The validation group assessed the nomogram model's discriminatory power and calibration using receiver operating characteristic curve analysis and the Hosmer-Lemeshow goodness-of-fit test. Results: The study found a 29.39% prevalence of HUA among the 228 participants. Logistic regression analyses identified age, body mass index, and concomitant coronary heart disease as independent HUA risk factors (odds ratio [OR] > 1 and P < 0.05). Conversely, high-density lipoprotein cholesterol emerged as an independent protective factor against HUA in hypertensive patients (OR < 1 and P < 0.05). Using these factors, a nomogram model was constructed to assess HUA risk, with an AUC of 0.873 (95% confidence interval [CI]: 0.818-0.928) in the training group and 0.841 (95% CI: 0.735-0.946) in the validation group, indicating a strong discriminatory ability. The Hosmer-Lemeshow goodness-of-fit test showed no significant deviation between predicted and actual HUA frequency in both groups ( $\chi^2 = 5.980, 9.780, P = 0.649, 0.281$ ), supporting the nomogram's reliability. Conclusion: The developed nomogram model, utilizing independent risk factors for HUA in hypertensive patients, exhibits strong discrimination and calibration. It holds promise as a valuable tool for cardiovascular professionals in clinical decision-making.

**Keywords:** Hyperuricemia, hypertension, risk factors, predictive model

## Introduction

Essential hypertension (EH) is a prevalent chronic cardiovascular syndrome characterized by a continual increase in arterial blood pressure within the systemic circulation [1]. Hyperuricemia (HUA) comprises disorders leading to elevated serum uric acid (SUA) levels due to disruptions in purine metabolism. An epidemiological study conducted in Shanghai, China, in 2021 among adults undergoing physical examinations revealed 8,120 cases of HUA among 34,546 individuals, indicating a detection rate of 23.50% [2]. HUA often manifests covertly and frequently coexists with hypertension in clinical settings. The prevalence of HUA among Chinese patients with hyperten-

sion stands at a staggering 38.7% [3]. Prior studies suggest an escalated risk of new-onset hypertension in otherwise healthy individuals with increased blood uric acid (UA) levels [4]. Furthermore, the presence of HUA exacerbates the likelihood of adverse cardiovascular events in hypertensive patients [5]. Individuals experiencing both hypertension and HUA demonstrate heightened damage to vital organs such as the heart, blood vessels, and kidneys [6]. Presently, clinical research predominantly centers on analyzing risk factors contributing to HUA occurrences in primary hypertensive patients [7]. Notably, no efforts have focused on integrating these risk factors in hypertensive patients formulating personalized predictions for HUA occurrences. As a response, this study

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constructed a personalized nomogram model aimed at predicting the likelihood of HUA occurrences among hypertensive patients. The objective of this study was to assist healthcare professionals in identifying hypertensive individuals at high risk of HUA, thereby enhancing clinical screening practices.

## Materials and methods

### *Research subjects*

This retrospective cohort study involved 228 patients diagnosed with EH admitted to a Grade III Grade A hospital in Anhui Province, China, between January 2018 and June 2021. These patients were retrospectively selected as study subjects. Among them, 67 cases belonged to the occurrence group, having HUA during hospitalization, while 161 cases comprised the nonoccurrence group. The incidence rate of HUA was 29.39%. Inclusion criteria for study subjects included meeting hypertension diagnostic criteria according to the Chinese Guidelines for the Prevention and Treatment of Hypertension [8], as well as HUA diagnostic criteria in the Chinese Expert Consensus on the Treatment of Hyperuricemia and Gout [9]. Additionally, subjects should not have recently consumed a high-purine diet. Exclusion criteria included acute or secondary hypertension, malignant tumors, and severe blood system diseases or dysfunction of the heart, liver, or kidneys. Approval for this study was obtained from the Medical Ethics Committee of the First Affiliated Hospital of the University of Science and Technology of China (Approval number: 2021-ky-153). Because of the retrospective nature of the study, the need for informed consent from the study subjects was exempted.

### *Clinical data*

Clinical data during hospitalization were retrospectively gathered through the hospital information system. These data included age, sex, body mass index (BMI), presence of diabetes, cerebrovascular disease, coronary heart disease, atrial fibrillation, smoking and alcohol consumption habits, heart rate, systolic and diastolic blood pressure at admission, as well as various laboratory examination indicators (triglyceride [TG], fasting plasma glucose [FPG], high-density lipoprotein cholesterol [HDL-C],

low-density lipoprotein cholesterol [LDL-C], total cholesterol [TC]).

### *Statistical analysis*

The study utilized SPSS 21.0 and R software (R 3.6.1) for data analysis. Normally distributed continuous data were represented as mean (standard deviation), with comparison between groups conducted using the independent-samples t-test. Categorical data were presented as counts, percentages, and rates, and group comparisons were made using the Pearson chi-square test. Univariate and multivariate logistic regression analyses were employed to identify independent risk factors associated with the occurrence of HUA in hypertensive patients. Following the identification of predictive factors through multivariate logistic regression analysis, a nomogram model was constructed using the “rms” package in R software. To assess the performance of the nomogram, the study utilized the receiver operating characteristic (ROC) curve, decision curve analysis (DCA) curve, and the goodness-of-fit test. These evaluations aimed to assess discrimination, clinical applicability, and calibration, respectively. Statistical significance was determined as  $P < 0.05$ .

## Results

### *Comparison of clinical data between two groups of patients in the training and validation groups*

The comparison of clinical data between the training and validation groups revealed no significant difference ( $P > 0.05$ ), demonstrating comparability between the two patient cohorts, as illustrated in **Table 1**.

### *Univariate and multivariate logistic regression analyses of the occurrence of HUA in the training group*

Both univariate and multivariate logistic regression analyses within the training group indicated age, BMI, and concomitant CHD as independent risk factors for HUA in hypertensive patients (odds ratio [OR]  $> 1$  and  $P < 0.05$ ). Additionally, HDL-C emerged as an independent protective factor for HUA in hypertensive patients (OR  $< 1$  and  $P < 0.05$ ), as shown in **Table 2**.

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**Table 1.** Comparison of clinical data between the training group and the validation group

Variables	Level	Total	Validation group	Training group	$\chi^2/t$	P
n		228	68	160		
Sex (%)	Male	128 (56.1)	39 (57.4)	89 (55.6)	0.058 <sup>a</sup>	0.810
	Female	100 (43.9)	29 (42.6)	71 (44.4)		
Age, mean (SD)		49.29 (8.08)	49.88 (7.13)	49.04 (8.45)	0.722 <sup>b</sup>	0.471
Combined with diabetes (%)	No	160 (70.2)	51 (75.0)	109 (68.1)	1.078 <sup>a</sup>	0.299
	Yes	68 (29.8)	17 (25.0)	51 (31.9)		
Concomitant cerebrovascular disease (%)	No	192 (84.2)	57 (83.8)	135 (84.4)	0.011 <sup>a</sup>	0.917
	Yes	36 (15.8)	11 (16.2)	25 (15.6)		
Combined with atrial fibrillation (%)	No	168 (73.7)	50 (73.5)	118 (73.8)	0.001 <sup>a</sup>	0.972
	Yes	60 (26.3)	18 (26.5)	42 (26.2)		
Combined with CHD (%)	No	149 (65.4)	41 (60.3)	108 (67.5)	1.094 <sup>a</sup>	0.296
	Yes	79 (34.6)	27 (39.7)	52 (32.5)		
BMI, mean (SD)		22.26 (3.91)	22.31 (4.39)	22.24 (3.71)	0.126 <sup>b</sup>	0.900
Smoking (%)	No	172 (75.4)	54 (79.4)	118 (73.8)	0.826 <sup>a</sup>	0.364
	Yes	56 (24.6)	14 (20.6)	42 (26.2)		
Drinking wine/alcohol (%)	No	180 (78.9)	56 (82.4)	124 (77.5)	0.676 <sup>a</sup>	0.411
	Yes	48 (21.1)	12 (17.6)	36 (22.5)		
Heart rate at admission, mean (SD)		87.02 (9.45)	88.13 (8.91)	86.54 (9.66)	1.162 <sup>b</sup>	0.247
Systolic blood pressure at admission, mean (SD)		142.00 (11.05)	141.32 (11.32)	142.29 (10.95)	0.606 <sup>b</sup>	0.545
Diastolic blood pressure at admission, mean (SD)		95.79 (5.24)	95.68 (5.58)	95.83 (5.11)	0.203 <sup>b</sup>	0.839
TC, mean (SD)		4.00 (1.01)	4.06 (1.04)	3.97 (0.99)	0.641 <sup>b</sup>	0.522
TG, mean (SD)		2.81 (0.72)	2.87 (0.81)	2.78 (0.68)	0.813 <sup>b</sup>	0.417
HDL-C, mean (SD)		1.47 (0.32)	1.42 (0.32)	1.49 (0.32)	-1.607 <sup>b</sup>	0.109
LDL-C, mean (SD)		2.67 (0.32)	2.67 (0.34)	2.67 (0.31)	0.099 <sup>b</sup>	0.921
FPG, mean (SD)		4.80 (1.39)	4.78 (1.47)	4.81 (1.35)	-0.157 <sup>b</sup>	0.875
HUA (%)	No	161 (70.6)	48 (70.6)	113 (70.6)	0.001 <sup>a</sup>	0.996
	Yes	67 (29.4)	20 (29.4)	47 (29.4)		

Note: <sup>a</sup> $\chi^2$  value; <sup>b</sup>t value. BMI, body mass index; CHD, coronary heart disease; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein-cholesterol; HUA, hyperuricemia; LDL-C, low-density lipoprotein-cholesterol; SD, standard deviation; TC, total cholesterol; TG, triglyceride.

### Construction of a nomogram model for the occurrence of HUA in hypertensive patients

The nomogram model incorporated the four independent predictive factors identified from the multivariate logistic regression model in **Table 2**. Using the “rms” program package in R software, a nomogram model predicting the occurrence of HUA in hypertensive patients was constructed, as depicted in **Figure 1**.

### Analysis of clinical applicability of the nomogram model

Utilizing the “rmda” program package, DCA curves for the nomogram model were plotted concerning the training and validation groups, illustrated in **Figure 2**. Analysis of the DCA curves revealed that at risk thresholds of 0.01-0.835 for the training group and 0.025-0.835 for the validation group, employing the nomogram yielded a significantly higher net benefit than “full intervention” and “no intervention”

schemes. This underscores the nomogram model's favorable clinical applicability.

### Discrimination analysis of the nomogram model

The discrimination of the nomogram model was evaluated using ROC curves. The areas under the ROC curve (AUC) for the nomogram model in the training group and validation group were 0.873 (95% confidence interval [CI]: 0.818-0.928) and 0.841 (95% CI: 0.735-0.946), respectively, indicating a strong discriminatory ability, as depicted in **Figure 3**.

### Calibration analysis of the nomogram model

Assessment of the nomogram's calibration employed the Hosmer-Lemeshow goodness-of-fit test and calibration curve. The results indicated no significant prediction deviation between the nomogram's prediction probability and the actual frequency of HUA in both the

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**Table 2.** Results of univariate and multivariate regression analyses of the occurrence of HUA in the training group

Variable	Univariate logistic regression analysis		Multivariate logistic regression analysis	
	OR (95% CI)	P	OR (95% CI)	P
Combined with atrial fibrillation	1.995 (0.942, 4.189)	0.068		
Age	1.130 (1.074, 1.199)	< 0.001	1.102 (1.036-1.186)	0.004
BMI	1.246 (1.128, 1.388)	< 0.001	1.238 (1.093-1.418)	0.001
Combined with CHD	3.168 (1.557, 6.524)	0.002	3.090 (1.229-8.030)	0.018
Combined with diabetes	1.150 (0.550, 2.354)	0.704		
Drinking wine/alcohol	0.754 (0.310, 1.708)	0.514		
FPG	1.397 (1.074, 1.846)	0.015	1.218 (0.853-1.770)	0.286
Sex = female (reference: male)	1.149 (0.578, 2.278)	0.69		
HDL-C	0.033 (0.005, 0.149)	< 0.001	0.043 (0.004-0.290)	0.003
Heart rate at admission	1.009 (0.974, 1.046)	0.634		
LDL-C	7.224 (2.279, 24.814)	0.001	3.581 (0.763-18.095)	0.111
Smoking	0.684 (0.293, 1.499)	0.358		
Systolic pressure at admission	1.004 (0.973, 1.036)	0.785		
Combined with cerebrovascular disease	0.724 (0.249, 1.855)	0.522		
Diastolic pressure at admission	1.073 (1.001, 1.155)	0.052		
TC	1.412 (0.994, 2.045)	0.059		
TG	2.515 (1.487, 4.463)	0.001	1.687 (0.881-3.409)	0.125

BMI, body mass index; CHD, coronary heart disease; CI, confidence interval; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein-cholesterol; HUA, hyperuricemia; LDL-C, low-density lipoprotein-cholesterol; OR, odds ratio; TC, total cholesterol; TG, triglyceride.

training and validation groups ( $\chi^2 = 5.980$ , 9.780,  $P = 0.649$ , 0.281). This suggests the nomogram possesses good predictive consistency. Moreover, calibration curves for both groups demonstrated close alignment between the nomogram's fitting curve and the ideal curve, affirming good calibration, as displayed in **Figure 4**.

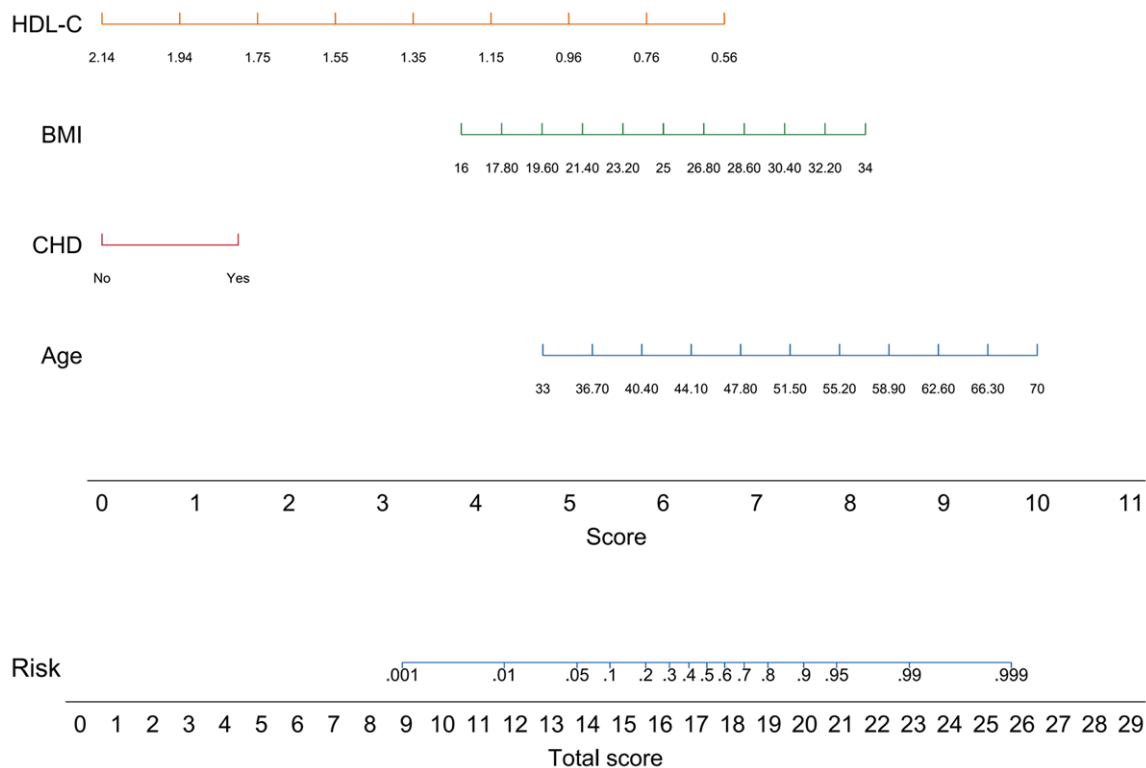
### Discussion

The incidence of HUA in patients with EH ranges between 28.8% and 46.1%. The risk of cardiovascular events and mortality gradually escalates with HUA in hypertensive patients [10, 11]. In this study, the occurrence of HUA among hypertensive patients was 29.39% (67 of 228), aligning with previous research findings. However, it still signifies a notably higher occurrence of HUA in hypertensive individuals. Consequently, early assessment of HUA risk in hypertensive patients becomes essential to proactively address adverse cardiovascular events.

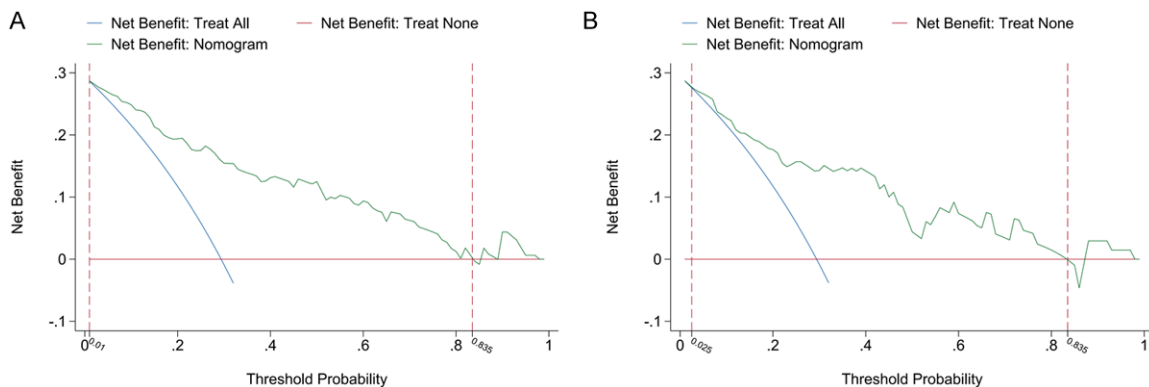
Yu et al. [4] discovered that the prevalence of HUA increased by 1.292, 1.473, and 1.779

times in age groups of 50-59, 60-69, and  $\geq 70$  years, respectively, when compared with those under 50 years old. This study's finding regarding increased HUA risk with advancing age correlates with prior research findings. Wang et al. [12] also highlighted an increasing trend in UA detection rates among the elderly ( $P < 0.05$ ). Considering that UA is the end product of purine metabolism, the decline in purine metabolism ability with age, coupled with weakened renal excretion function, leads to elevated SUA levels and subsequent HUA [13]. Moreover, overweight and obesity have been identified as independent risk factors for HUA onset [14]. A positive association exists between BMI and SUA levels, indicating a higher prevalence of obesity among individuals with HUA [15, 16]. This study reinforces these findings by demonstrating an escalated risk of HUA in hypertensive patients with increasing BMI levels. Studies by Wang et al. [17], Zhu et al. [18], and Kong et al. [19] emphasized the close association between HUA and cardiovascular diseases, aging, and hypertension. Furthermore, this study's findings supported the notion that coronary heart disease stands as an independent

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**Figure 1.** Nomogram model for the occurrence of hyperuricemia in hypertensive patients.



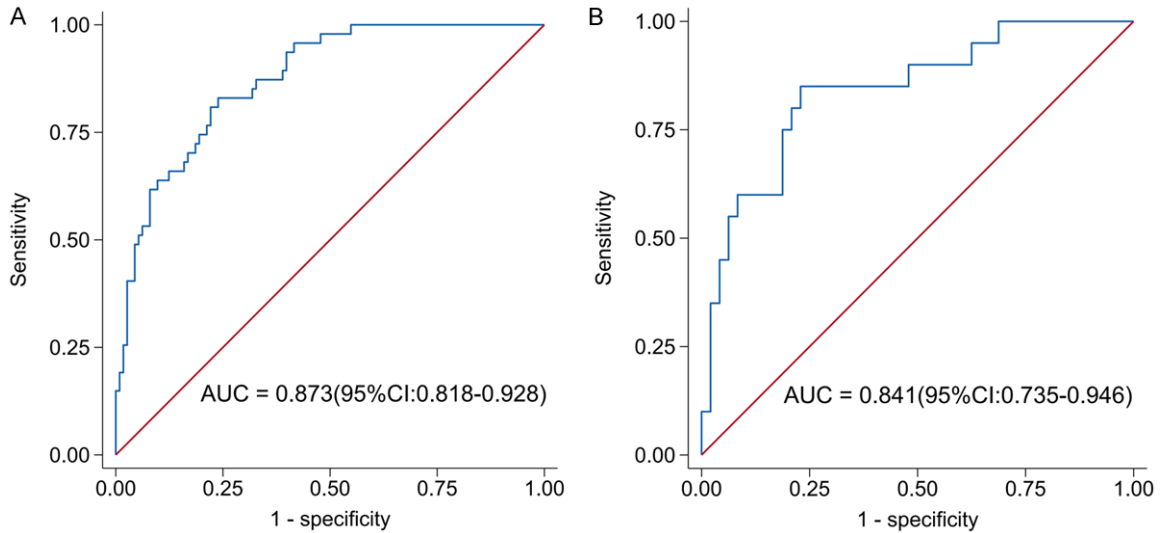
**Figure 2.** Decision curve analysis (DCA) curve of the nomogram model. Note: A. DCA curve in the training group; B. DCA curve in the validation group.

risk factor for HUA occurrence in hypertensive patients. This association might be attributed to endothelial dysfunction, lipid metabolism disorders, and oxidative stress in coronary heart disease patients, heightening the risk of HUA [20]. The study highlighted HDL-C as an independent protective factor against the onset of HUA, aligning with findings from Wang et al.'s investigation [21] on patients with chronic kidney disease. HUA exhibited a correlation with abnormal lipid metabolism [22]. HDL-C's cru-

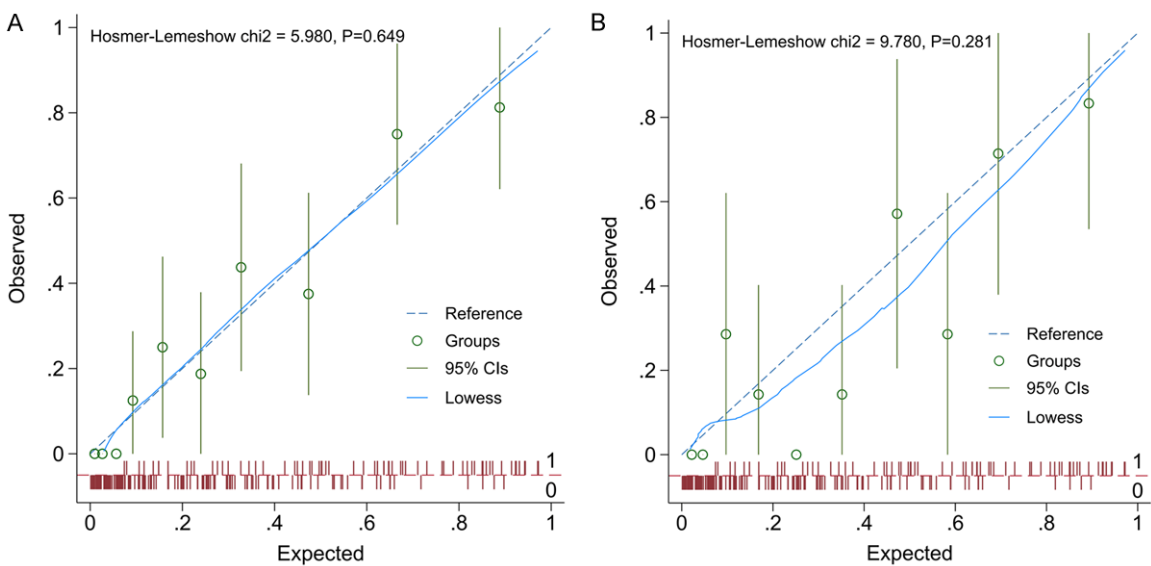
cial role in anti-atherosclerosis stems from its functions such as anti-oxidation, anti-inflammation, anti-apoptosis, and anti-thrombosis [23]. Among these functions, its anti-oxidation ability has been consistently proven to prevent inflammation and oxidative stress, and it is also believed to possess characteristics that reduce UA levels [24].

A nomogram serves as a statistical tool for personalized prediction and clinical event analysis,

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**Figure 3.** Receiver operating characteristic (ROC) curve of the nomogram model. Note: A. ROC curve in the training group; B. ROC curve in the validation group.



**Figure 4.** Calibration curve of the nomogram model. Note: A. Calibration curve in the training group; B. Calibration curve in the validation group.

offering superior personalized risk assessment through intuitive visual representation [25, 26]. Previous studies affirmed the effectiveness of the nomogram model in predicting in-hospital death risk for patients with myocardial infarction complicated with HUA [27], rebleeding risk in elderly hypertensive patients with intracerebral hemorrhage [28], and epilepsy risk secondary to continuous lumbar cistern drainage post-intracerebral hemorrhage surgery in hypertensive patients [29]. However, there is a

lack of research on the nomogram's predictive ability concerning HUA risk in hypertensive patients. Therefore, this study identified four independent predictive factors for HUA occurrence in hypertensive patients - age, BMI, combined with CHD, and HDL-C - through univariate and multivariate logistic regression, constructing a personalized nomogram prediction model. The ROC curve, Hosmer-Lemeshow goodness-of-fit test, and DCA curve confirmed the nomogram model's strong discrimination, calibra-

tion, and clinical applicability, facilitating clinical decision-making.

However, the study has limitations. It is a single-center study that utilized hypertensive patients solely from one research center for training and validation, raising uncertainty about the nomogram's generalizability. Additionally, being retrospective, it might contain selection bias and data quality issues. Moreover, the study's inclusion of limited factors restricts the nomogram's predictive efficacy. Incorporating more risk factors could enhance its predictive efficiency. Thus, future prospective studies involving multiple centers and larger samples should include more risk factors to continually validate the nomogram's generalizability and optimize its predictive performance.

## Conclusion

In summary, this study developed a nomogram model based on four predictive factors - age, BMI, combined with CHD, and HDL-C - that displayed robust calibration, discrimination, and clinical applicability, offering valuable guidance for clinical practice.

## Disclosure of conflict of interest

The authors have declared that there are no commercial or financial affiliations that could be considered a potential conflict of interest in this study.

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