

Risk Prediction of Severe Complications Caused by Hymenoptera Insect Stings: Development and Validation of a Nomogram Mode

Jiahao Guan^{1,*}, Zhenkai Zhao^{2,*}, Zitong Wang^{1,3}, Mengyao Huang⁴, Jun Wang⁵, Zhenguo Liu⁶, Yajuan Ren⁷, Zifan Lu⁸, Shuling Hu¹, Xianglong Duan⁹

¹Department of Clinical Laboratory, Shaanxi Provincial People's Hospital, Xi'an, Shaanxi, People's Republic of China; ²Department of Burns and Plastic Surgery, Fourth Medical Center of Chinese PLA General Hospital, Beijing, People's Republic of China; ³Medical College, Yan'an University, Yan'an, Shaanxi, People's Republic of China; ⁴Department of Information, Shaanxi Provincial People's Hospital, Xi'an, Shaanxi, People's Republic of China; ⁵Department of Respiratory Medicine, Shaanxi Provincial People's Hospital, Xi'an, Shaanxi, People's Republic of China; ⁶Department of Critical Care Medicine, Shaanxi Provincial People's Hospital, Xi'an, Shaanxi, People's Republic of China; ⁷Department of Respiratory Medicine II, Shaanxi Provincial People's Hospital, Xi'an, Shaanxi, People's Republic of China; ⁸Translational medicine Center of Shaanxi Provincial People's Hospital, Xi'an, Shaanxi, People's Republic of China; ⁹Second Department of General Surgery, Shaanxi Provincial People's Hospital, Xi'an, Shaanxi, People's Republic of China

*These authors contributed equally to this work

Correspondence: Xianglong Duan, Second Department of General Surgery, Shaanxi Provincial People's Hospital, No. 256, Youyi West Road, Xi'an, Shaanxi, 710068, People's Republic of China, Tel +86 029-85251331, Email duanxianglong@nwpu.edu.cn

Background: Hymenopteran stings (Apidae/Vespidae) represent critical emergencies frequently encountered during summer and autumn seasons. These incidents can trigger localized inflammatory responses and severe systemic complications—including anaphylactic shock, acute organ injury, and multi-organ dysfunction—potentially leading to death, especially in resource-limited areas. While honeybee and wasp venom components (melittin/hyaluronidase vs kinins/phospholipase) and effects differ, potentially causing distinct complications, this study develops a universal early risk prediction tool without differentiating bee species. Based on clinical and simple lab indicators, it aims to help frontline providers optimize high-risk patient identification and intervention, reducing mortality and healthcare burden.

Patients and Methods: We retrospectively analyzed 1124 hymenoptera sting patients from Shaanxi Provincial People's Hospital (2014–2023). After screening, 607 eligible patients were randomly divided into training (n=455) and validation (n=152) cohorts (3:1 ratio). Univariate and multivariate logistic regression identified severe complication independent risk factors, enabling nomogram development. Its discriminative ability, calibration, and clinical utility were assessed using ROC curves, calibration plots, and DCA in both cohorts.

Results: Severe complications occurred in 33 patients (5.44%): anaphylactic shock (9, 1.48%), acute kidney injury (4, 0.66%), acute myocardial injury (6, 0.99%), multiple organ dysfunction (13, 2.14%), and coagulation dysfunction (1, 0.16%). Independent predictors were: white blood cell count (OR=1.192, 95% CI: 1.099–1.293), systemic inflammatory response index (OR=1.046, 95% CI: 1.002–1.093), and blood urea nitrogen (OR=1.374, 95% CI: 1.114–1.695). The nomogram achieved AUCs of 0.954 (95% CI: 0.926–0.982) in training and 0.985 (95% CI: 0.965–1.000) in validation cohorts. Calibration showed good agreement (Hosmer-Lemeshow $P > 0.05$). DCA demonstrated significant clinical net benefit.

Conclusion: This study's nomogram effectively predicts severe sting complication risk, serving as a practical tool for primary care providers to identify high-risk patients early and improve decisions.

Keywords: hymenoptera stings, white blood cell count, systemic inflammatory response index, urea nitrogen, nomogram

Introduction

Hymenopteran stings, which are critical and acute conditions prevalent during the summer and autumn months, are primarily caused by the injection of biotoxins through the stingers of insects belonging to the Apidae and Vespidae

families. The clinical manifestations are predominantly local symptoms, characterized by severe pain, edema, and skin necrosis at the sting site. Disease progression can lead to systemic inflammatory response syndrome (SIRS) and may further result in organ dysfunction, including hemolysis, rhabdomyolysis, and acute kidney injury. In severe cases, this condition may even progress to multiple organ failure or death.^{1,2} In China, the majority of hymenopteran stings occur in rural areas where medical resources are comparatively limited.³ Due to a lack of awareness regarding the severity of stings and the associated risk of complications among primary healthcare institutions, patients frequently encounter the risk of delayed diagnosis and treatment, which can exacerbate adverse outcomes.

The clinical management of Hymenoptera stings currently presents a dual challenge. On one hand, there is no globally established consensus on specific diagnostic and therapeutic approaches for these stings. On the other hand, existing assessment tools, such as the Sequential Organ Failure Assessment (SOFA) and the Acute Physiology and Chronic Health Evaluation (APACHE II), while useful for risk stratification in critically ill patients, are primarily designed to identify those at risk of deterioration in the ICU, and they lack early warning efficacy in primary care settings⁴⁻⁶. Consequently, there is an urgent need to develop a practical tool that can promptly assess the condition and accurately predict severe complications arising from stings, enabling early intervention and optimizing treatment strategies. This study aims to develop and validate a visual predictive model grounded in evidence-based medicine. By integrating key clinical indicators, it offers scientific decision-making support for healthcare professionals, particularly primary care workers, thus enhancing diagnostic and treatment efficiency and improving patient prognosis.

Materials and Methods

Study Population

A retrospective analysis was conducted on 1124 patients with hymenopteran stings treated at the Medical Laboratory Center of Shaanxi Provincial People's Hospital (Xi'an, China) from April 2014 to October 2024, all of whom were from the northwestern region of China. The inclusion criteria were as follows: (1) a diagnosis of hymenopteran stings based on patient-reported history, clinical symptoms consistent with envenomation, and identification of the insect by either the patient or the attending physician; (2) age ≥ 18 years. The exclusion criteria were as follows: (1) age < 18 years; (2) a previous history of severe cardiopulmonary disease, severe liver disease, renal insufficiency, malignancy, or immunodeficiency disorders; (3) patients with incomplete clinical data. This study adhered to the principles of the Declaration of Helsinki.

Data Collection

This study primarily focuses on severe systemic complications that arise following Hymenoptera stings, including anaphylactic shock, organ damage, and coagulation disorders. Study data were collected anonymously through the electronic medical record system. To ensure data extraction accuracy, two trained researchers independently performed data entry and verification. The specific workflow included: (1) developing detailed standardized data extraction templates; (2) dual independent entry of clinical information within 24 hours of patient admission; (3) Cross-checking was performed on the entered data; inconsistent entries and outlier data underwent re-verification, with consultation of the original medical records when necessary or arbitration by a third researcher; (4) data locking after confirmation of accuracy. Collected information included demographic information (patient ID, age, gender), number of stings (based on the chief complaints and diagnosis results recorded in the medical records), the time interval from the sting to the visit, and various laboratory indicators, such as white blood cell count (WBC), red blood cell count (RBC), hemoglobin (Hb), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII, calculated as platelet count multiplied by the neutrophil-to-lymphocyte ratio), systemic inflammation response index (SIRI, calculated as the product of neutrophil count and monocyte count divided by lymphocyte count), serum creatinine (Cr), blood urea nitrogen (BUN), thrombin time (TT), prothrombin time (PT), activated partial thromboplastin time (APTT), fibrinogen (Fib), and international normalized ratio (INR).

Predictor Selection and Model Development

Using the R software (caret package), the final selected patients were randomly divided into a training cohort and a validation cohort in a 3:1 ratio. A random seed (seed=123) was set to ensure reproducibility. The training cohort was utilized to develop the nomogram prediction model, while the validation cohort was employed to evaluate this model. Initially, univariate logistic regression analysis was performed to identify indicators associated with clinical endpoints ($P < 0.05$). Subsequently, the results from the univariate logistic regression analysis were integrated into multivariate logistic regression analysis, employing the forward stepwise regression method (Forward: LR) to select variables. Variables with $P < 0.05$ in the multivariate logistic regression were deemed candidate predictive factors for modeling, aimed at predicting the risk of severe complications in patients stung by Hymenoptera insects. Before constructing the model, the collinearity of all candidate predictors was examined using linear regression analysis with variance inflation factors. Based on the respective coefficients of the modeling predictors, a visual predictive model was constructed.

Model Validation and Evaluation

In the training and validation cohorts, we evaluated the discrimination, calibration, and clinical utility of the nomogram prediction model. The receiver operating characteristic (ROC) curve was utilized to analyze the model's discrimination, and the area under the curve (AUC), equivalent to the C-index, was quantified. We calculated sensitivity, specificity, predictive values, and likelihood ratios based on the optimal cutoff value. The Hosmer-Lemeshow goodness-of-fit test was employed to assess calibration, and calibration curves were plotted to demonstrate visually the agreement between predicted and observed outcomes. Given that the use of nomograms for predicting the prognosis of stung patients inevitably involves false positives and false negatives, we employed decision curve analysis (DCA) to determine clinical utility.⁷

Statistical Analysis

Continuous variables exhibiting a nonnormal distribution were presented as median (interquartile range) and analyzed using the nonparametric Mann-Whitney *U*-test. Categorical variables were reported as counts (percentages) and compared using the chi-square test. Variables with more than 25% missing values were excluded, while the remaining missing values were addressed using the multiple imputation method. A bilateral *p*-value of less than 0.05 was deemed statistically significant. All statistical analyses were conducted using R software (version 4.2.3; <https://www.R-project.org>). The R software package and code are available for download at <https://mirrors.tuna.tsinghua.edu.cn/CRAN/>.

Results

Demographic and Clinical Characteristics

The selection of the study population is illustrated in Figure 1. A total of 607 patients who were stung by Hymenoptera were included in this study, with a median age of 45.00 years (interquartile range: 31.00 to 58.00). Among these patients, 368 were male, representing 60.63% of the cohort. Severe complications developed in 33 cases (5.44%) following the sting, which included 9 cases of anaphylactic shock (1.48%), 4 cases of acute kidney injury (0.66%), 6 cases of acute myocardial injury (0.99%), 13 cases of multiple organ dysfunction (2.14%), and 1 case of coagulation dysfunction (0.16%). In the training cohort, 24 patients experienced severe complications, yielding an incidence rate of 5.27%. Conversely, in the validation cohort, 9 patients had severe complications, resulting in an incidence rate of 5.92%. The comparative results of clinical and demographic characteristics between the training group and the validation group are presented in Table 1. No significant differences were observed in the baseline data between the two patient groups ($P > 0.05$).

Screening of Independent Risk Factors and Model Predictors

Univariate logistic regression analysis revealed that age, number, RBC, Hb, WBC, NLR, PLR, SIRI, SII, Cr, BUN, APTT, TT, PT, and INR were associated with severe complications in patients with stings, as shown in Table 2. In contrast, multivariate logistic regression analysis indicated that only WBC (OR=1.192, 95% CI: 1.099–1.293), SIRI (OR=1.046, 95% CI: 1.002–1.093), and BUN (OR=1.374, 95% CI: 1.114–1.695) were independent risk factors for

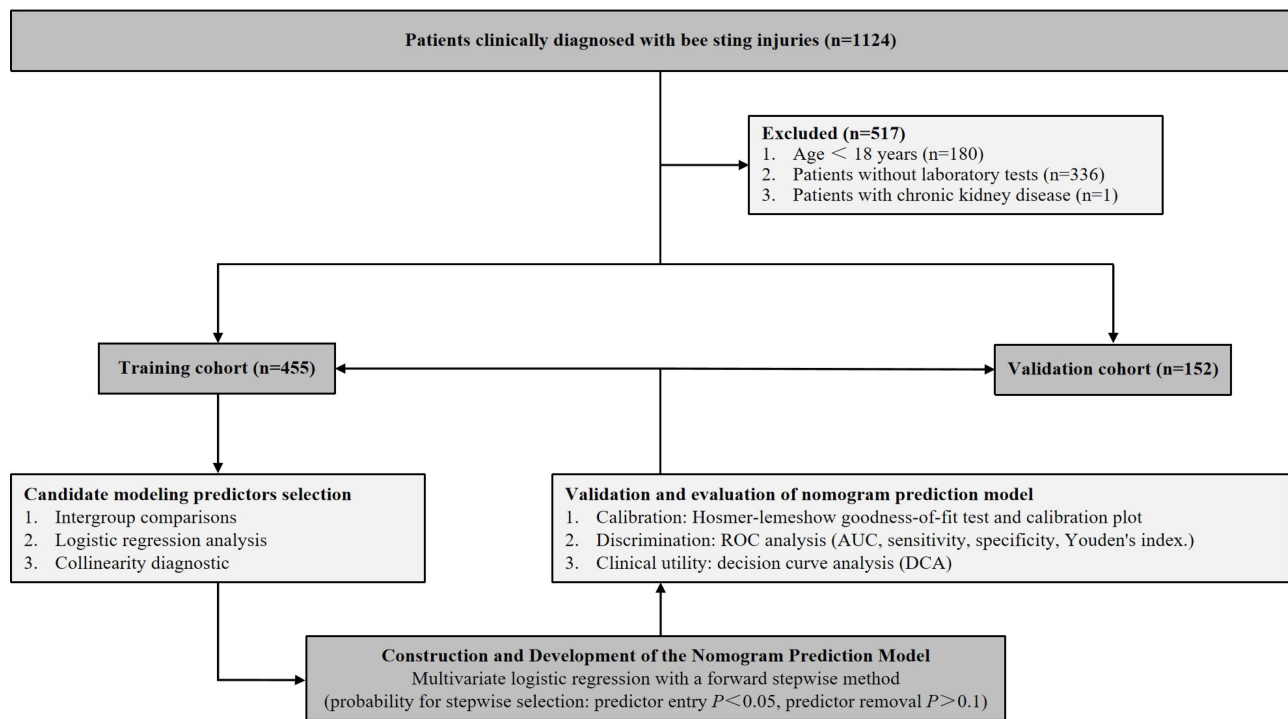


Figure 1 Flow chart of patient enrollment and model development and validation.

severe complications in these patients, as detailed in [Table 3](#). Collinearity diagnostics showed no significant collinearity among WBC, SIRI, and BUN ([Supplementary Table 1](#)); therefore, all three were identified as candidate predictors for the model.

Construction of Traditional and Dynamic Nomograms

The final predictive model was developed based on three independent predictors: WBC, SIRI, and BUN, and it is visualized in the form of a nomogram, as shown in [Figure 2](#). The calculation of the risk of severe complications from hymenopteran stings involves three steps. First, draw a perpendicular line from the axis of each predictor to the “Points”

Table 1 Baseline Characteristics of Patients with Complication in the Training and Validation Cohorts

Baseline Characteristics	Number (%) of Missing Values	Overall Patients (n=607)	Training Cohort (n=455)	Validation Cohort (n=152)	χ^2/Z	P-value
Gender (n, %)	0 (0%)				2.265	0.132
Male		368 (60.63)	268 (58.90)	100 (65.79)		
Female		239 (39.37)	187 (41.10)	52 (34.21)		
Age, years	0 (0%)	45.00 (31.00, 58.00)	46.00 (31.00, 58.00)	43.50 (31.25, 56.00)	-0.785	0.432
Complication (n, %)	0 (0%)				0.093	0.761
Yes		33 (5.44)	24 (5.27)	9 (5.92)		
No		574 (94.56)	431 (94.73)	143 (94.08)		
Time of sting	0 (0%)				0.079	0.779
≤ 24h		523 (86.16)	391 (85.93)	132 (86.84)		
> 24h		84 (13.84)	64 (14.07)	20 (13.16)		
Number of sting	0 (0%)				0.007	0.934
<2		405 (66.72)	304 (66.81)	101 (66.48)		
≥2		202 (33.28)	151 (33.19)	51 (33.52)		

(Continued)

Table 1 (Continued).

Baseline Characteristics	Number (%) of Missing Values	Overall Patients (n=607)	Training Cohort (n=455)	Validation Cohort (n=152)	χ^2/Z	P-value
WBC	23 (3.79%)	8.54 (6.65, 11.77)	8.50 (6.73, 12.11)	8.77 (6.59, 11.33)	-0.215	0.830
RBC	23 (3.79%)	4.71 (4.31, 5.08)	4.73 (4.32, 5.08)	4.68 (4.30, 5.10)	-0.173	0.863
Hb	23 (3.79%)	145.00 (132.00, 158.00)	145.00 (133.00, 157.00)	144.50 (129.25, 159.75)	-0.573	0.567
NLR	23 (3.79%)	3.31 (2.04, 7.07)	3.35 (2.08, 6.90)	3.13 (1.97, 7.57)	-0.048	0.961
PLR	23 (3.79%)	128.67 (95.15, 182.39)	128.68 (94.59, 179.10)	127.95 (97.73, 191.40)	-0.861	0.389
SIRI	23 (3.79%)	1.75 (1.02, 3.69)	1.78 (1.04, 3.70)	1.55 (0.92, 3.69)	-0.798	0.425
SII	23 (3.79%)	721.54 (448.00, 1498.29)	716.84 (454.87, 1447.30)	730.15 (438.18, 1865.06)	-0.477	0.634
Cr	116 (19.11%)	65.00 (54.00, 77.30)	65.00 (54.00, 77.30)	62.95 (53.00, 77.23)	-0.734	0.463
BUN	116 (19.11%)	5.56 (4.47, 6.62)	5.59 (4.58, 6.68)	5.35 (4.19, 6.49)	-1.326	0.185
APTT	145 (23.89%)	28.60 (25.50, 33.40)	28.70 (25.40, 33.60)	28.40 (25.80, 32.60)	-0.286	0.775
TT	144 (23.72%)	18.00 (17.10, 19.10)	18.00 (17.10, 19.10)	18.00 (17.20, 19.20)	-0.229	0.819
PT	144 (23.72%)	12.00 (11.20, 13.10)	12.00 (11.20, 13.10)	12.10 (11.25, 13.18)	-0.570	0.568
Fib	145 (23.89%)	2.62 (2.15, 3.16)	2.61 (2.14, 3.12)	2.63 (2.17, 3.24)	-0.638	0.524
INR	144 (23.72%)	0.99 (0.94, 1.06)	0.99 (0.94, 1.06)	0.97 (0.93, 1.06)	-1.245	0.213

Abbreviations: WBC, White Blood Cell Count; RBC, Red Blood Cell Count; Hb, Hemoglobin; NLR, Neutrophil-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; SIRI, Systemic Inflammation Response Index; SII, Systemic Immune-Inflammation Index; Cr, Creatinine; BUN, Blood Urea Nitrogen; APTT, Activated Partial Thromboplastin Time; TT, Thrombin Time; PT, Prothrombin Time; Fib, Fibrinogen; INR, International Normalized Ratio.

Table 2 Risk Factors Associated with Severe Complications in Patients with Bee Sting Injuries

Variables	B	SE	P-value	OR	95% CI
Sex	0.557	0.421	0.186	1.746	0.764–3.986
Age	0.047	0.015	0.001	1.048	1.019–1.079
Time	0.143	0.632	0.821	1.154	0.334–3.987
Number	2.153	0.513	<0.001	8.608	3.147–23.543
WBC	0.234	0.034	<0.001	1.264	1.182–1.352
RBC	-1.057	0.376	0.005	0.347	0.166–0.726
Hb	-0.026	0.011	0.024	0.975	0.953–0.997
NLR	0.045	0.016	0.004	1.046	1.015–1.079
PLR	0.002	0.001	0.027	1.002	1.000–1.004
SIRI	0.123	0.020	<0.001	1.131	1.088–1.176
SII	0.000	0.000	<0.001	1.000	1.000–1.000
Cr	0.036	0.009	<0.001	1.037	1.019–1.055
BUN	0.514	0.099	<0.001	1.671	1.376–2.029
APTT	0.032	0.008	<0.001	1.033	1.017–1.049
TT	0.589	0.124	<0.001	1.803	1.413–2.301
PT	0.584	0.148	<0.001	1.794	1.342–2.399
Fib	0.283	0.282	0.315	1.327	0.764–2.306
INR	8.424	1.906	<0.001	4555.053	108.609–191,038.179

Abbreviations: WBC, White Blood Cell Count; RBC, Red Blood Cell Count; Hb, Hemoglobin; NLR, Neutrophil-to-Lymphocyte Ratio; PLR, Platelet-to-Lymphocyte Ratio; SIRI, Systemic Inflammation Response Index; SII, Systemic Immune-Inflammation Index; Cr, Creatinine; BUN, Blood Urea Nitrogen; APTT, Activated Partial Thromboplastin Time; TT, Thrombin Time; PT, Prothrombin Time; Fib, Fibrinogen; INR, International Normalized Ratio.

axis to obtain the points for each predictor. Second, sum the points of all predictors to obtain the total score. Third, draw a perpendicular line from the “Total Points” axis to the “Risk” axis to determine the probability of severe complications from hymenopteran stings.

Table 3 Independent Risk Factors for Severe Complications Associated with Bee Sting Injuries

Variables	B	SE	P-value	OR	95% CI
WBC	0.176	0.042	<0.001	1.192	1.099–1.293
SIRI	0.045	0.022	0.042	1.046	1.002–1.093
BUN	0.318	0.107	0.003	1.374	1.114–1.695
Intercept	−8.059	1.019	<0.001	0.000	

Abbreviations: WBC, White Blood Cell Count; SIRI, Systemic Inflammation Response Index; BUN, Blood Urea Nitrogen.

Validation of the Nomogram

In both the training and validation cohorts, the nomogram demonstrated strong agreement between predicted probabilities and observed outcomes, with calibration curves closely approximating the diagonal, as illustrated in Figures 3A and B. The Hosmer-Lemeshow test confirmed acceptable calibration for both cohorts, with all P-values exceeding 0.05 in the aforementioned bidirectional cohorts (training cohort: 0.884, validation cohort: 0.336). The nomogram exhibited excellent discriminative ability, achieving an AUC of 0.954 (0.926–0.982) in the training cohort and 0.985 (0.965–1.000) in the validation cohort, as depicted in Figure 4A and B. The sensitivity and specificity of the nomogram for predicting adverse reactions to hymenopteran stings both exceeded 82% in the training cohort and surpassed 92% in the validation cohort, as shown in Table 4. Furthermore, DCA curves were plotted for both cohorts to evaluate the clinical utility of the predictive model. The DCA results indicated that the nomogram provides a high clinical net benefit, as illustrated in Figure 5A and B.

Discussion

This study utilized real-world data to analyze the clinical characteristics of 607 patients with hymenopteran stings in the northwestern region of China. It identified three independent risk factors, WBC, SIRI, and BUN, to construct

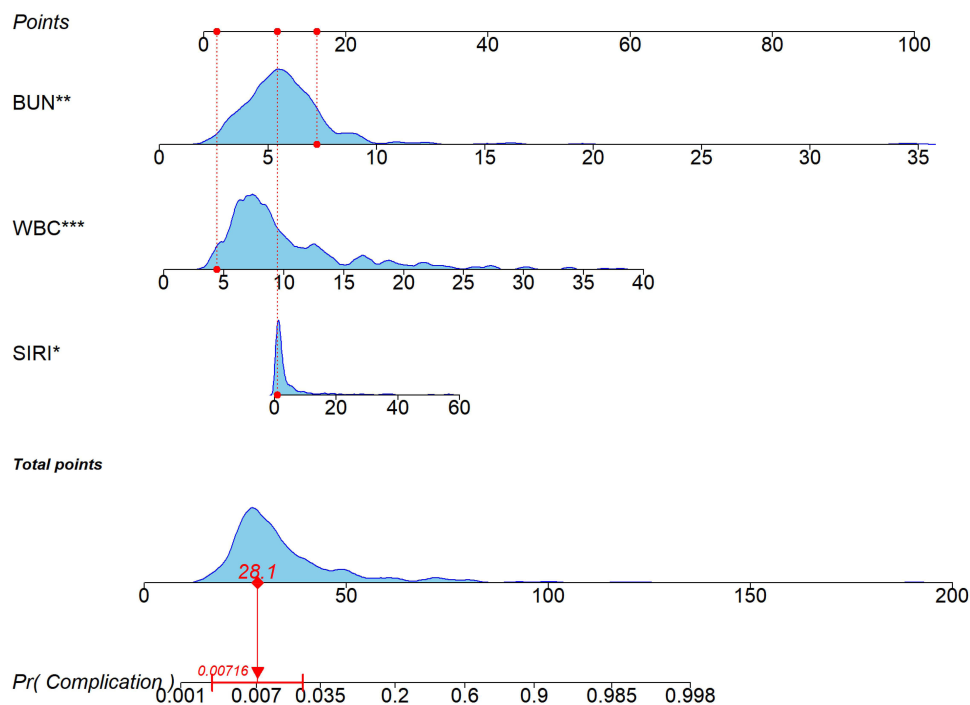


Figure 2 Traditional nomogram prediction model. Asterisks indicate statistical significance levels: * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$; Red-highlighted values on variable axes illustrate an example: A patient with blood urea nitrogen (BUN) of 7, white blood cell (WBC) of 4, and systemic inflammation response index (SIRI) of 2 would receive a total score of 28.1, corresponding to a predicted probability of severe complications of 0.716%.

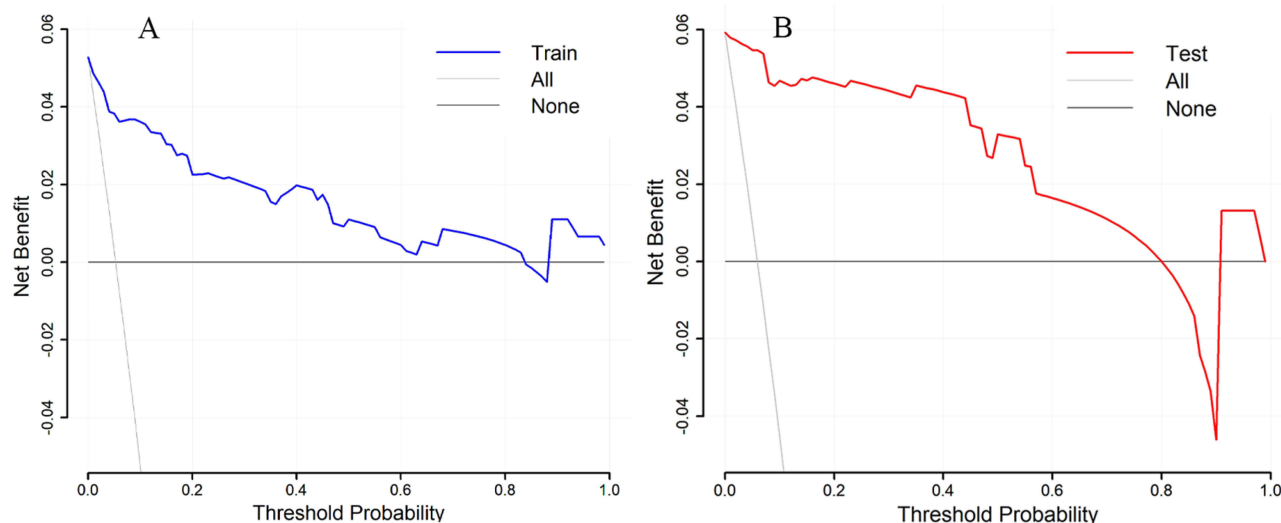


Figure 3 Calibration curves of the predictive model. (A) Training cohort; (B) Validation cohort.

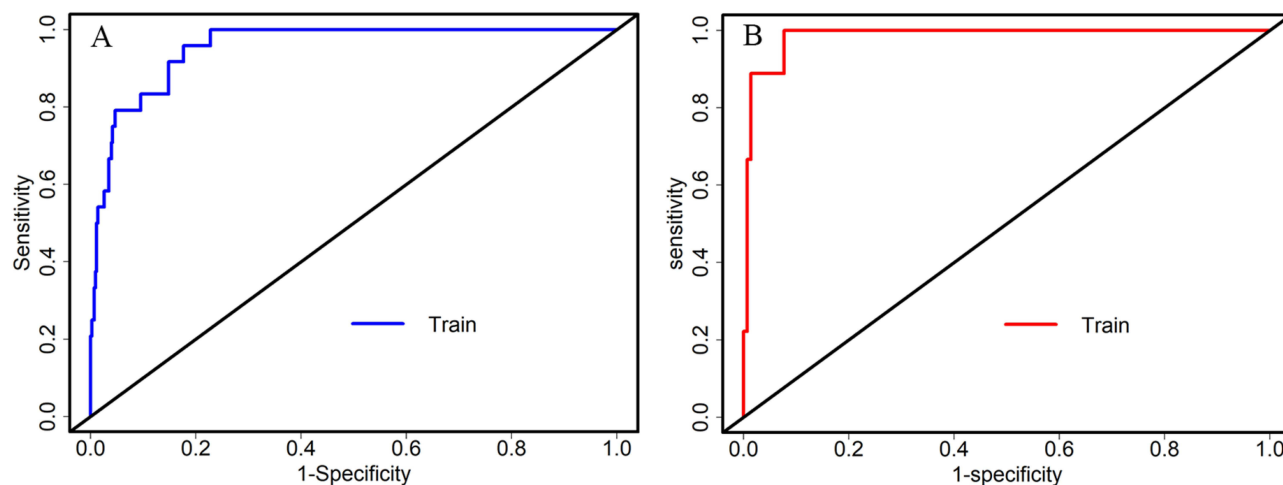


Figure 4 ROC curve of the predictive model. (A) Training cohort; (B) Validation cohort.

a nomogram prediction model for intuitive visualization and clinical application. The nomogram demonstrated excellent discriminative ability for severe complications in both the training and validation cohorts, with AUC values of 0.954 and 0.985, respectively, and showed good calibration, as indicated by Hosmer-Lemeshow test P-values of 0.884 and 0.336. Additionally, DCA further indicated that the nomogram provides a significant clinical net benefit. This model is expected to serve as a tool for early management and decision-making in cases of hymenopteran stings.

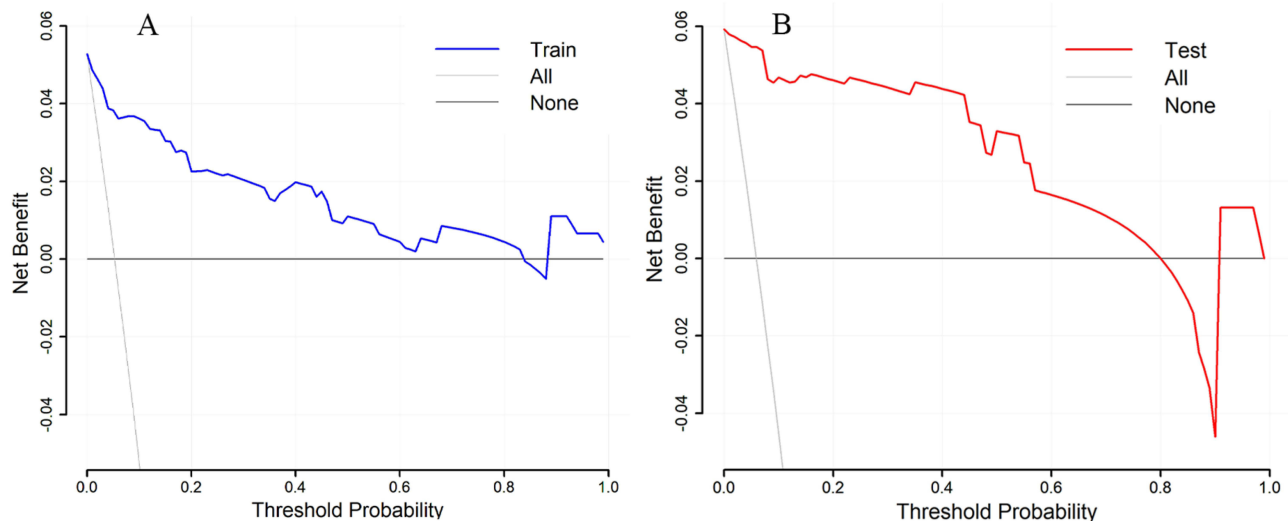
This study reveals that the risk of severe complications following Hymenoptera stings is significantly positively correlated with WBC count and SIRI. Specifically, for each unit increase in WBC and SIRI, the risk of complications rises by 19.2% and 4.6%, respectively. These findings are highly consistent with those of previous studies.^{8,9} Bee venom is a complex toxin composed of various enzymes and bioactive substances, including melittin, phospholipase A2, hyaluronidase, histamine, and apamin.¹⁰ It has been shown to induce a series of pathological changes, such as inflammatory reactions, cell membrane lysis, intravascular hemolysis, and rhabdomyolysis.^{11,12} Additionally, bee venom can activate various inflammatory mediators,¹³ including tumor necrosis factor- α (TNF- α), interleukin-1 (IL-1), interleukin-6 (IL-6), and interleukin-8 (IL-8), thereby promoting the development of systemic inflammatory response syndrome (SIRS).^{14,15} It is noteworthy that substances produced during secondary hemolysis, including heme, ferrous

Table 4 Predictive Performance of the Nomogram

Assessment Indicators	Training Cohort (n=455)	Validation Cohort (n=152)
Hosmer-Lemeshow <i>P</i> -value	0.884	0.336
Cut-off value	-3.604	-2.664
AUC (95% CI)	0.954 (0.926–0.982)	0.985 (0.965–1.000)
Youden's index	0.78	0.92
Sensitivity (%)	95.83	100.00
Specificity (%)	82.37	92.31
Positive predictive value (%)	23.23	45.00
Negative predictive value (%)	99.72	100.00
Positive likelihood ratio	5.43	13.00
Negative likelihood ratio	0.05	0.00

heme, and oxygen free radicals, along with abnormalities in the body's lipid metabolism, can further exacerbate the inflammatory response.¹⁶ However, hymenopteran stings frequently occur in rural areas of developing countries, where primary healthcare resources are limited. Consequently, indicators such as white blood cell (WBC) counts and the Systemic Inflammatory Response Index (SIRI), derived from routine blood tests, are crucial for timely diagnosis and treatment in these resource-constrained regions due to their simplicity, rapidity, cost-effectiveness, and objectivity.

This study further reveals the strong predictive value of BUN for acute kidney injury (AKI) following stings (OR=1.374). Although only four patients met the diagnostic criteria for AKI, it is noteworthy that all 13 patients with multiple organ dysfunction exhibited varying degrees of renal injury, indicating that renal function impairment accounts for 51.5% of severe complications (17/33). This suggests that the kidneys are among the most vulnerable target organs following Hymenoptera stings. Phospholipase A2 (PLA2) in bee venom, as one of the core toxic components, mediates renal injury through multiple pathways. PLA2 can hydrolyze the phospholipid structure in cell membranes, leading to the loss of membrane integrity and exerting toxic effects. When it acts on renal tubular epithelial cells, it can induce direct renal cell toxicity. Furthermore, when it interacts with muscle cells and red blood cells, it can induce rhabdomyolysis and intravascular hemolysis, which leads to the release of myoglobin and free Hb.¹⁷ This, in turn, exacerbates renal injury through mechanisms such as cast obstruction and oxidative stress.^{18,19} The study also found that phospholipase A2 can exert its hemolytic effect and promote erythrocyte lysis only in the presence of melittin; therefore, it is referred to as an "indirect hemolytic toxin".²⁰ Additionally, bee venom triggers a cascade reaction by activating the three pathways of the complement system: the classical pathway, the alternative pathway, and the lectin pathway. This activation exacerbates

**Figure 5** DCA curve of the predictive model. (A) Training cohort; (B) Validation cohort.

the pathological processes in the kidney through a combination of a pro-inflammatory cytokine storm and severe allergic reactions.²¹

Clinicians can utilize three independent risk factors—WBC, SIRI, and BUN—for early risk management in patients. For patients identified with a higher predicted risk, heightened vigilance regarding disease progression is warranted. It is recommended to closely monitor vital signs, urine output, and laboratory parameter changes. Renal replacement therapy (RRT) or transfer to the ICU should be initiated promptly if necessary. Concurrently, considering the mechanisms of inflammatory response and renal injury induced by bee venom, it is advised to proactively administer supportive treatments during the early stages. These include anti-inflammatory therapy, fluid resuscitation, and urine alkalization to mitigate organ damage. Furthermore, other studies have confirmed that^{22,23} factors such as age, gender, number of stings, platelet count, and severity of poisoning scores are closely associated with severe adverse reactions following Hymenoptera stings.^{24,25} However, this study did not observe significant associations among the aforementioned variables, which may be attributed to several factors. Firstly, the heterogeneity of the study population—such as the concentration of this cohort in a specific region, along with variations in genetic background, baseline health status, or the timeliness of medical interventions compared to other studies—may play a role.^{26,27} Secondly, key variables, such as the number of stings, are derived from retrospective medical records, which may introduce information bias. Furthermore, potential confounding factors, including differences in bee species and the timeliness of emergency measures, were not adequately adjusted for.

This study presents several limitations. First, while it included 602 patients, the sample was restricted to a single medical institution in Northwest China. Additionally, subgroup analyses based on bee species (eg, bees versus wasps) or stinging seasons were not performed, which may limit the model's applicability across different populations and seasons. Second, as a retrospective study, certain key variables—such as the site of the sting, specific IgE levels to bee venom, and the patient's immune status—were excluded from the analysis due to incomplete electronic medical records, potentially omitting important predictors. Third, the model did not incorporate dynamic data, such as changes in laboratory indicators over time. Given that the development of complications from Hymenoptera stings is time-dependent, relying on static predictions may underestimate the risk of clinical deterioration. Finally, the ratio of the number of severe complications in the training cohort (24 cases) to the number of final predictor variables was 8:1, which was slightly lower than the ideal standard (10:1). This might to some extent affect the accuracy of the model parameter estimation. Although our model demonstrated excellent performance in internal validation, its clinical applicability still requires external validation in populations from diverse climatic regions (eg, hot and humid southern areas) and healthcare tiers (eg, township health centers, urban tertiary hospitals) to assess its generalizability and robustness. The next step involves developing a web-based dynamic nomogram. This tool will incorporate temporal variations in laboratory parameters (eg, trends in WBC, SIRI, BUN) to enable dynamic tracking of patient status and risk alerting, thereby enhancing the model's accessibility and real-time guidance value in resource-limited settings. Concurrently, basic experimental research will be conducted to investigate the biological mechanisms of WBC, SIRI, and BUN in disease progression, providing a theoretical basis for subsequent targeted interventions.

Conclusion

The nomogram model established in this study, based on WBC, SIRI, and BUN, can effectively predict the risk of severe complications in patients with hymenopteran stings. Its core parameters are derived from routine laboratory tests, providing primary and remote healthcare institutions with a practical early-warning tool to facilitate timely identification and intervention for high-risk patients.

Future research will focus on two key aspects: (1) Mechanistic Exploration: Investigate the biological mechanisms of WBC, SIRI, and BUN in the pathophysiological processes mediated by hymenopteran venom to provide a theoretical basis for developing targeted interventions. (2) Clinical Translation: Assess model robustness through external validation across diverse regions and healthcare settings; Develop a web-based dynamic prediction tool to enhance applicability in remote areas; Strengthen training for primary healthcare providers to promote standardized implementation and clinical adoption of the model.

Ethics Approval

The study protocol was approved by the Ethics Committee of Shaanxi Provincial People's Hospital [Approval No. (2024) Ethics Review No. (R041)], and is a retrospective analysis. In this study, informed consent from patients is not required. The patient data in this research have been anonymized, and sensitive personal information and commercial interests are not involved in the data processing and analysis. According to the relevant legal provisions of the "Notice on Issuing the Measures for Ethical Review of Life Science and Medical Research Involving Humans" (Guwei Kejiaofa [2023] No. 4), this study meets the situation specified in Point (ii) of Article 32, Chapter III of the Measures, and is exempted from ethical review.

Acknowledgments

The authors are grateful to the staff of the microbiology lab for their assistance in identifying bacteria and performing antimicrobial susceptibility testing.

Funding

This study was completed with the support of the following funds: 1, The National Natural Science Foundation of China (Program No. 82460107) 2, Innovation Capability Support Program of Shaanxi (Program No. 2024GH-GHJD-21) 3, Science and Technology Talent Support Program of Shaanxi Provincial People's Hospital (Program No. 2021LJ-05) 4, Science and Technology Development Incubation Fund of Shaanxi Provincial People's Hospital (2023YJY-88).

Disclosure

The authors report no conflicts of interest in this work.

References

- Gkitsaki I, Papachristoforou A, Michailidou S, et al. Correction to: the transmittable through stinging microbiota differs between honeybees and wasps: a potentially greater microbial risk of the wasp sting for humans. *Int Microbiol*. 2023;26(3):691. doi:10.1007/s10123-023-00342-4
- Yu F, Wang L, Yuan H, Gao Z, He L, Hu F. Wasp venom-induced acute kidney injury: current progress and prospects. *Ren Fail*. 2023;45(2):2259230. doi:10.1080/0886022X.2023.2259230
- Yang X, Xiao M, Poisoning HP, Chinese Society Of Toxicology Poisoning And Treatment Of Specialized Committee, Hubei Emergency Medicine Committee Of Chinese Medical Association, Hubei Provincial Poisoning And Occupational Disease Union. Expert consensus statement on standardized diagnosis and treatment of wasp sting in China. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue*. 2018;30(9):819–823. doi:10.3760/cma.j.issn.2095-4352.2018.09.001
- Gong J, Yuan H, Gao Z, Hu F. Wasp venom and acute kidney injury: the mechanisms and therapeutic role of renal replacement therapy. *Toxicon*. 2019;163:1–7. doi:10.1016/j.toxicon.2019.03.008
- Zhang L, Yang Y, Tang Y, et al. Recovery from AKI following multiple wasp stings: a case series. *Clin J Am Soc Nephrol*. 2013;8(11):1850–1856. doi:10.2215/CJN.12081112
- Yuan H, Chen S, Hu F, Zhang Q. Efficacy of two combinations of blood purification techniques for the treatment of multiple organ failure induced by wasp stings. *Blood Purif*. 2016;42(1):49–55. doi:10.1159/000442740
- Zhou ZR, Wang WW, Li Y, et al. In-depth mining of clinical data: the construction of clinical prediction model with R. *Ann Transl Med*. 2019;7(23):796. doi:10.21037/atm.2019.08.63
- Yuan H, Lu L, Gao Z, Hu F. Risk factors of acute kidney injury induced by multiple wasp stings. *Toxicon*. 2020;182:1–6. doi:10.1016/j.toxicon.2020.05.002
- Wu W, Zhang Y, Zhang Y, Qu X, Zhang Z, Zhang R. Machine-learning based prediction model for acute kidney injury induced by multiple wasp stings. *Toxicon*. 2024;250:108112. doi:10.1016/j.toxicon.2024.108112
- Zhang Y, Wu W, Zhang Z. The predictive value of the systemic inflammatory response index for the occurrence of multiple organ dysfunction syndrome in patients with wasp sting injury. *Toxicon*. 2023;234:107269. doi:10.1016/j.toxicon.2023.107269
- Fakhar M, Zakariaei Z, Sharifpour A, Soleymani M, Zakariaei A. Fatal outcome following multiple bee stings: a rare case. *Clin Case Rep*. 2022;10(1):e05303. doi:10.1002/ccr3.5303
- Pucca MB, Cerni FA, Oliveira IS, et al. Bee updated: current knowledge on bee venom and bee envenoming therapy. *Front Immunol*. 2019;10:2090. doi:10.3389/fimmu.2019.02090
- Petricevich VL. Cytokine and nitric oxide production following severe envenomation. *Curr Drug Targets Inflamm Allergy*. 2004;3(3):325–332. doi:10.2174/1568010043343642
- Sun Y, Yang J, Sun Y, et al. Interleukin-6 gene polymorphism and the risk of systemic inflammatory response syndrome caused by wasp sting injury. *DNA Cell Biol*. 2018;37(12):967–972. doi:10.1089/dna.2018.4156
- Yao W, Sun Y, Sun Y, et al. A preliminary report of the relationship between gene polymorphism of IL-8 and its receptors and systemic inflammatory response syndrome caused by wasp stings. *DNA Cell Biol*. 2019;38(12):1512–1518. doi:10.1089/dna.2019.4855

16. Quan Z, Liu M, Zhao J, Yang X. Correlation between early changes of serum lipids and clinical severity in patients with wasp stings. *J Clin Lipidol.* 2022;16(6):878–886. doi:10.1016/j.jacl.2022.09.003
17. Lee SH, Baek JH, Yoon KA. Differential properties of venom peptides and proteins in solitary vs. social hunting wasps. *Toxins.* 2016;8(2):32. doi:10.3390/toxins8020032
18. Perez-Riverol A, Lasa AM, Jra DS-P, Palma MS. Insect venom phospholipases A1 and A2: roles in the envenoming process and allergy. *Insect Biochem Mol Biol.* 2019;105:10–24. doi:10.1016/j.ibmb.2018.12.011
19. Gräler MH, Goetzl EJ. Lysophospholipids and their G protein-coupled receptors in inflammation and immunity. *Biochim Biophys Acta.* 2002;1582(1–3):168–174. doi:10.1016/s1388-1981(02)00152-x
20. Ridolo E, Pellicelli I, Kihlgren P, et al. Immunotherapy and biologicals for the treatment of allergy to Hymenoptera stings. *Expert Opin Biol Ther.* 2019;19(9):919–925. doi:10.1080/14712598.2019.1632286
21. Cheng R, Xu L, Gong J, et al. Complement activation in wasp venom-induced acute kidney injury. *Ren Fail.* 2024;46(1):2344658. doi:10.1080/0886022X.2024.2344658
22. Aurich S, Dölle-Bierke S, Francuzik W, et al. Anaphylaxis in elderly patients-data from the European anaphylaxis registry. *Front Immunol.* 2019;10:750. doi:10.3389/fimmu.2019.00750
23. Ruëff F, Przybilla B, Biló MB, et al. Predictors of severe systemic anaphylactic reactions in patients with hymenoptera venom allergy: importance of baseline serum tryptase-a study of the European Academy of Allergology and Clinical Immunology Interest Group on Insect Venom Hypersensitivity. *J Allergy Clin Immunol.* 2009;124(5):1047–1054. doi:10.1016/j.jaci.2009.08.027
24. Qin M, Wang M, Wang AY, et al. Clinical manifestations and risk factors associated with 14 deaths following swarm wasp stings in a Chinese tertiary grade a general hospital: a retrospective database analysis Study. *J Clin Med.* 2023;12(18):5789. doi:10.3390/jcm12185789
25. Cavalcante JS, Riciopo PM, Pereira AFM, et al. Clinical complications in envenoming by Apis honeybee stings: insights into mechanisms, diagnosis, and pharmacological interventions. *Front Immunol.* 2024;15:1437413. doi:10.3389/fimmu.2024.1437413
26. Mingomataj EÇ, Bakiri AH, Ibranji A, Sturm GJ. Unusual reactions to hymenoptera stings: what should we keep in mind? *Clin Rev Allergy Immunol.* 2014;47(1):91–99. doi:10.1007/s12016-014-8434-y
27. Feás X, Vidal C, Remesar S. What we know about sting-related deaths? Human fatalities caused by hornet, wasp and bee stings in Europe (1994-2016). *Biology.* 2022;11(2):282. doi:10.3390/biology11020282

Journal of Inflammation Research

Publish your work in this journal

The Journal of Inflammation Research is an international, peer-reviewed open-access journal that welcomes laboratory and clinical findings on the molecular basis, cell biology and pharmacology of inflammation including original research, reviews, symposium reports, hypothesis formation and commentaries on: acute/chronic inflammation; mediators of inflammation; cellular processes; molecular mechanisms; pharmacology and novel anti-inflammatory drugs; clinical conditions involving inflammation. The manuscript management system is completely online and includes a very quick and fair peer-review system. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/journal-of-inflammation-research-journal>

Dovepress
Taylor & Francis Group