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ORIGINAL RESEARCH

# Systemic Immune-Inflammatory Index and Systemic Inflammatory Response Index in the Assessment of Multiple Organ Dysfunction Syndrome Caused by Wasp Stings

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**Objective:** This study aims to assess the prognosis of patients with multiple organ dysfunction syndrome (MODS) caused by wasp stings by analyzing early systemic immune inflammation index (SII) and systemic inflammation response index (SIRI) values.

**Methods:** A retrospective analysis was conducted on 151 patients admitted to the Department of Emergency Medicine, Taihe Hospital, Hubei University of Medicine, from January 2019 to December 2023. Among them, 60 patients developed MODS and 91 patients did not (non-MODS group). Early peripheral blood cell count-derived inflammation indices such as white blood cell count, platelet count, absolute neutrophil value, absolute lymphocyte value, absolute monocyte value, NLR, SII, and SIRI, along with baseline demographics, were compared between the two groups. Logistic regression analyses were performed, and the predictive accuracy of SII and SIRI was evaluated using receiver operating characteristic (ROC) curves, with the area under the curve (AUC) used to quantify sensitivity.

**Results:** Significant differences were observed between the non-MODS and MODS groups in terms of age, hospitalization duration, number of stings, APACHE II score, time to first medical visit, SII, and SIRI ($P < 0.05$). Logistic regression analysis confirmed that both SII and SIRI were significant predictors of prognosis ($P < 0.05$). The AUC for SII and SIRI were 0.776 and 0.853, respectively, indicating their predictive value.

**Conclusion:** Elevations in SII and SIRI are associated with the severity of wasp sting injuries, and early SII and SIRI values can serve as prognostic indicators for predicting MODS development and mortality in wasp sting patients.

**Keywords:** wasp sting, systemic immune-inflammatory index, systemic inflammatory response index, multi-organ failure

## Introduction

There are approximately 6000 species of wasps worldwide, with over 200 species found in China.[1,2] Wasp stings occur sporadically in China, with mortality rates ranging from 5.1% to 21%.[3] Wasp venom contains various allergens and toxins, and clinical symptoms following a sting include pain, swelling at the sting site, skin flushing, or urticaria-like reactions.[4,5] The primary pathogenic mechanisms are allergic reactions and toxin-induced complications.[6] Severe allergic reactions can lead to fatal outcomes, such as Kounis syndrome[7] and stress-induced cardiomyopathy.[8] Moreover, complications of envenoming can affect prognosis and are significantly related to the extent of organ damage,[9] including conditions such as acute kidney injury, rhabdomyolysis, acute respiratory distress syndrome, cerebrovascular accidents, and multi-organ failure.[3,4,10]

Multiple organ dysfunction syndrome (MODS) is a systemic condition triggered by various causes, with a pathological mechanism often involving a severe systemic inflammatory response.[5] Development of MODS is a leading cause of death in victims of wasp sting.[4,11,12] In particular, wasp venom activates the immune system, causing a severe inflammatory reaction.[2]

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Although the 2018 Expert Consensus Statement on the Standardized Diagnosis and Treatment of Wasp Stings in China,[13] along with the Poisoning Severity Score (PSS),[14] developed by the International Programme on Chemical Safety (IPCS) of the United Nations/World Health Organization (UN/WHO) and the European Association of Poison Centres and Clinical Toxicologists (EAPCCT), both determine the severity of wasp stings, neither provides a predictive tool to guide patient care. Moreover, recent eosinophil–basophil to lymphocyte ratios (EB/LR) and eosinophil–basophil platelet to lymphocyte ratios (EBP/LR) have been suggested as useful markers for predicting the severity of allergic reactions in patients with wasp venom allergy.[5] Thus, establishing early predictive models to identify these risk factors and improve patient outcomes is critical in cases of multiple organ failure due to wasp stings.

Wasp stings result from a wasp's tail puncturing the skin and delivering venom into the body.[15] The venom contains multiple bioactive components,[2] including melittin (40–60% of the venom's dry weight), mast cell degranulating peptide, phospholipase $A_2$, and hyaluronidase. Melittin is the primary pain-inducing and cytolytic toxin, capable of disrupting cell membranes,[16] while phospholipase $A_2$ initiates an inflammatory cascade by hydrolyzing membrane phospholipids.[12] Together, these constituents trigger immune activation and tissue injury. Therefore, both the severity of symptoms and the intensity of the inflammatory response are closely related to the number of wasp stings.[3] Each sting injects venom into the body, activating the immune system.[17] As the toxins of wasp venom spread through the bloodstream, they can affect multiple systems and trigger a widespread and sustained systemic inflammatory response resulting in MODS.

In recent years, researchers have paid considerable attention to the systemic immune-inflammation index (SII) and the systemic inflammatory response index (SIRI) as potential predictors of inflammatory reactions. Both indices are calculated from peripheral blood cell counts. Specifically, SII combines neutrophil, lymphocyte, and platelet counts, while SIRI incorporates neutrophil, monocyte, and lymphocyte counts to reflect immune activation following infection, inflammation, or toxin exposure.[18–20] Moreover, studies have demonstrated that these indices can predict severe clinical outcomes, including multiple organ dysfunction syndrome (MODS). Since MODS induced by wasp stings represents a toxin-driven systemic inflammatory response, and because SII reflects the interplay between inflammation and coagulation while SIRI indicates the balance between innate and adaptive immunity—both closely tied to this pathophysiology—these indices may effectively assess disease severity in patients injured by wasp stings.

Therefore, the objective of this study was to assess the prognostic value of SII and SIRI in predicting MODS and mortality in patients with wasp sting. By comparing patients who developed MODS with those who did not, we aimed to evaluate the reliability of SII and SIRI as prognostic markers and to explore their potential as early biomarkers.

# Research Methods

## Inclusion and Exclusion Criteria of the Sample Population

In this retrospective study, 158 wasp sting patients admitted to the Department of Emergency Medicine, Taihe Hospital, Hubei University of Medicine, during January 2019 to December 2023 were included. Nevertheless, seven patients were excluded from final analysis owing to: two patients were over 70 years old, with weakened physical functions and differing immune-inflammatory response manifestations; one patient was a 36-week pregnant woman, excluded due to physiological changes during pregnancy that may affect immune and inflammatory responses; one patient was a 15-year-old girl, and, according to Chinese law, minors under 18 require the informed consent of a legal guardian, which was not obtained due to a disagreement between the guardian and the patient; one patient had a pre-existing serious oncological condition prior to the wasp stings; and finally, two patients refused to participate for personal reasons. These exclusions were made to ensure the accuracy of the study results while respecting the patients' individual rights and ethical considerations.

The study subjects that enrolled into the final analysis included 60 patients who developed MODS and 91 patients who did not (non-MODS group). Based on a 28-day evaluation period, among patients who developed MODS, forty-eight survived (survivor group) and twelve died (non-survivor group). MODS is a clinical syndrome resulting from the failure of multiple organs or systems, with diagnosis based on the guidelines provided by the Surviving Sepsis Campaign.[21] The diagnostic criteria for wasp stings are established according to the Expert Consensus Statement on Standardized Diagnosis and Treatment of Wasp Stings in China.[15] All patient data were approved by the Medical Ethics Committee of Taihe Hospital (reference number: 2024KS88, 12 September 2024), Hubei University of Medicine, and all participants provided written informed consent.

Inclusion criteria: 1. Patients confirmed to have been stung by wasps, verified through patient-provided wasp images upon admission. 2. All laboratory data were available from the first examination conducted upon hospital admission, and the first consultation occurred within 24 hours of the sting. 3. Patients aged between 18 and 70 years. 4. Patients were cooperative with medical care and diagnosis following hospital admission. 5. Complete patient case data were available. Exclusion criteria: 1. Patients and their families explicitly refused participation in this retrospective study. 2. Patients stung by insects other than wasps, such as honeybees or bamboo bees. 3. Patients with pre-existing conditions such as infections, tumors, or multi-organ failure. 4. Patients who had abnormal white blood cell counts, platelet counts, absolute neutrophil counts, absolute lymphocyte counts, and absolute monocyte counts before being stung by a wasp. 5. Recent consumption of drugs that can affect the complete blood count. 6. Case data or laboratory results for were incomplete.

In this retrospective study, a total of seven patients were excluded for the following reasons: Two patients were over 70 years old, with weakened physical functions and differing immune-inflammatory response manifestations; one patient was a 36-week pregnant woman, excluded due to physiological changes during pregnancy that may affect immune and inflammatory responses; one patient was a 15-year-old girl, and, according to Chinese law, minors under 18 require the informed consent of a legal guardian, which was not obtained due to a disagreement between the guardian and the patient; one patient had a pre-existing serious oncological condition prior to the wasp stings; and finally, two patients refused to participate for personal reasons. These exclusions were made to ensure the accuracy of the study results while respecting the patients' individual rights and ethical considerations.

## Data Collection

Basic patient information was collected by accessing the hospital's medical record system. General information included gender, age, hospitalization duration, number of stings, APACHE II score, time of first visit after the sting, site of sting, clinical symptoms, and final outcome. Laboratory tests primarily included white blood cell count, platelet count, absolute neutrophil count, absolute lymphocyte count, and absolute monocyte count. Blood cell counts were performed using a peripheral fully automated blood cell counter (Mindray BC-5800, Shenzhen, China). The following indices were also calculated: NLR (neutrophil-to-lymphocyte ratio), SII (neutrophil count × platelet count/lymphocyte count ratio), and SIRI (neutrophil count × monocyte count/lymphocyte count ratio).

## Data Analysis

Raw data were entered into Microsoft Office 2021 Excel, and statistical analyses were conducted using IBM SPSS Statistics 27. Non-normally distributed data were expressed as median (P25, P75) and compared between groups using the Mann–Whitney *U*-test, and categorical variables were reported as frequency (%) and compared using the chi squared test. The predictive value of SII and SIRI for MODS was assessed through univariate and multivariate logistic regression analyses. Sensitivity and specificity were evaluated using receiver operating characteristic (ROC) curves, and the area under the curve (AUC) was used to quantify predictive performance. A p-value of less than 0.05 was considered statistically significant.

# Results

## Baseline Characteristics of Patients in the Non-MODS and MODS Groups

The analysis of patients with wasp stings revealed statistically significant and clinically relevant differences between the non-MODS and MODS groups, as shown in Table 1. Significant differences were found in age, APACHE II score, time of the first clinic visit after the sting, final outcome, and length of hospitalization, number of stings ($P < 0.05$). However, gender, sting site, clinical symptoms did not show statistically significant differences between the two groups ($P > 0.05$).

## Comparison of Blood Cell Count-Derived Inflammatory Indices Between Non-MODS and MODS Groups

Comparison of data between MODS and non-MODS patients, as shown in Table 2, showed significant differences in WBC (11.58 vs 18.73 $\times 10^9$/L, $P < 0.001$), NEU (9.54 vs 16.54 $\times 10^9$/L, $P < 0.001$), LYM (1.27 vs 0.80 $\times 10^9$/L, $P < 0.001$), MONO

**Table 1** Baseline Characteristics of Patients in the Non-MODS and MODS Groups

| Parameter | Non-MODS (N = 91) | MODS (N = 60) | Statistical Values | *P* |
|---|---|---|---|---|
| Gender, n (%) | | | $\chi^2$=0.53 | 0.465 |
| Male | 43 (47.25) | 32 (53.33) | | |
| Female | 48 (52.75) | 28 (46.67) | | |
| Age, year | 44.00 (30.00, 56.00) | 53.00 (41.00, 63.00) | Z=−2.43 | 0.015 |
| Number of stings, puncture mark | 6.00 (1.00, 11.00) | 24.00 (14.00, 50.00) | Z=−6.80 | <0.001 |
| APACHE II score | 12.00 (11.00, 14.00) | 20.00 (17.00, 24.00) | Z=−8.98 | <0.001 |
| Time to first visit after wasp sting, hour | 3.00 (1.00, 5.00) | 5.00 (3.00, 8.00) | Z=−3.71 | <0.001 |
| Sting site, n (%) | | | | |
| Head | 56 (61.54) | 56 (93.33) | $\chi^2$=19.08 | <0.001 |
| Neck | 20 (21.98) | 8 (13.33) | $\chi^2$=1.79 | 0.181 |
| Torso | 32 (35.16) | 25 (41.67) | $\chi^2$=0.65 | 0.42 |
| Upper limbs | 46 (50.55) | 40 (66.67) | $\chi^2$=3.83 | 0.05 |
| Lower limbs | 28 (30.77) | 18 (30.00) | $\chi^2$=0.01 | 0.92 |
| Clinical symptoms, n (%) | | | | |
| Dizziness, headache | 48 (52.75) | 38 (63.33) | $\chi^2$=1.65 | 0.199 |
| Altered state of mind | 17 (18.68) | 10 (16.67) | $\chi^2$=0.10 | 0.752 |
| Anaphylaxis | 11 (12.09) | 8 (13.33) | $\chi^2$=0.05 | 0.821 |
| Urticaria, erythema | 31 (34.07) | 28 (46.67) | $\chi^2$=2.41 | 0.12 |
| Palpitations, chest tightness | 50 (54.95) | 42 (70.00) | $\chi^2$=3.44 | 0.064 |
| Tightness in the throat | 23 (25.27) | 19 (31.67) | $\chi^2$=0.74 | 0.391 |
| Difficulty in breathing | 20 (21.98) | 17 (28.33) | $\chi^2$=0.79 | 0.374 |
| Abdominal pain | 13 (14.29) | 11 (18.33) | $\chi^2$=0.44 | 0.506 |
| Diarrhoea | 12 (13.19) | 10 (16.67) | $\chi^2$=0.35 | 0.553 |
| Other | 3 (3.30) | 5 (8.33) | $\chi^2$=0.96 | 0.327 |
| Final outcome, n (%) | | | $\chi^2$=17.13 | <0.001 |
| Survival | 91 (100.00) | 48 (80.00) | | |
| Death, n (%) | 0 (0.00) | 12 (20.00) | | |
| Length of hospitalization, day | 2.00 (1.00, 2.00) | 4.00 (2.00, 6.00) | Z=−6.80 | <0.001 |

**Table 2** Comparison of Blood Cell Count-Derived Inflammatory Indices Between Non-MODS and MODS Groups

| Parameter | Non-MODS (N = 91) | MODS (N = 60) | Statistical Values | *P* |
|---|---|---|---|---|
| WBC ($\times10^9$/L) | 11.58 (8.67, 16.73) | 18.73 (14.34, 23.01) | Z=−6.41 | <0.001 |
| PLT ($\times10^9$/L) | 213.00 (178.00, 245.50) | 205.50 (136.00, 238.50) | Z=−1.31 | 0.19 |
| NEU ($\times10^9$/L) | 9.54 (6.93, 15.32) | 16.45 (12.87, 21.33) | Z=−6.22 | <0.001 |
| LYM ($\times10^9$/L) | 1.27 (0.71, 1.89) | 0.80 (0.55, 1.23) | Z=−3.76 | <0.001 |
| MONO ($\times10^9$/L) | 0.36 (0.20, 0.61) | 0.62 (0.32, 0.79) | Z=−3.50 | <0.001 |
| NLR | 8.77 (4.37, 16.28) | 22.05 (15.37, 29.36) | Z=−6.92 | <0.001 |
| SII | 1833.39 (800.01, 3350.52) | 3591.04 (2780.68, 5907.18) | Z=−5.74 | <0.001 |
| SIRI ($\times10^9$/L) | 2.48 (1.12, 4.44) | 11.84 (5.87, 20.20) | Z=−7.32 | <0.001 |

**Abbreviations**: WBC, White Blood Cell Count; PLT, Platelet count; NEU, Neutrophil Count; LYM, Lymphocyte Count; MONO, Monocyte Count; NLR, Neutrophil-to-lymphocyte ratio; SII, Systemic immune-inflammation index; SIRI, Systemic Inflammatory Response Index.

(0.36 vs 0.62 $\times10^9$/L, $P < 0.001$), NLR (8.77 vs 22.05, P = 0.002), SII (1833.39 vs 3591.04, $P < 0.001$), and SIRI (2.48 vs 11.84 $\times10^9$/L, $P < 0.001$) ($P < 0.05$ for all). In contrast, platelet counts (213.00 vs 205.50, $P > 0.19$) did not show a statistically significant difference ($P > 0.05$).

**Table 3** Univariate and Multivariate Logistic Analyses of SII and SIRI in Non-MODS and MODS Groups

| Corresponding Indicators | Single-Factor Logistic | | Multifactor Logistic | |
|---|---|---|---|---|
| | *P* | OR (95% CI) | *P* | OR (95% CI) |
| SII | <0.001 | 1.01 (1.01 ~ 1.01) | <0.001 | 1.01 (1.01 ~ 1.01) |
| SIRI | <0.001 | 1.18 (1.10 ~ 1.26) | 0.02 | 1.09 (1.01 ~ 1.17) |

## Univariate and Multivariate Logistic Analyses of SII and SIRI in Non-MODS and MODS Groups

As shown in Table 3, both univariate and multivariate logistic regression analyses indicated that SII and SIRI were statistically significant prognostic tools and predictors of MODS development in wasp sting patients ($P < 0.05$).

## Area Under the ROC Curve for SII and SIRI in Non-MODS and MODS Groups

ROC curve analysis showed that SIRI had high sensitivity and specificity in predicting MODS, with an AUC of 0.853 (95% CI 0.792–0.914, $P = 0.002$), while the AUC of SII was 0.776 (95% CI 0.704–0.849, $P = 0.003$), as shown in Figure 1.

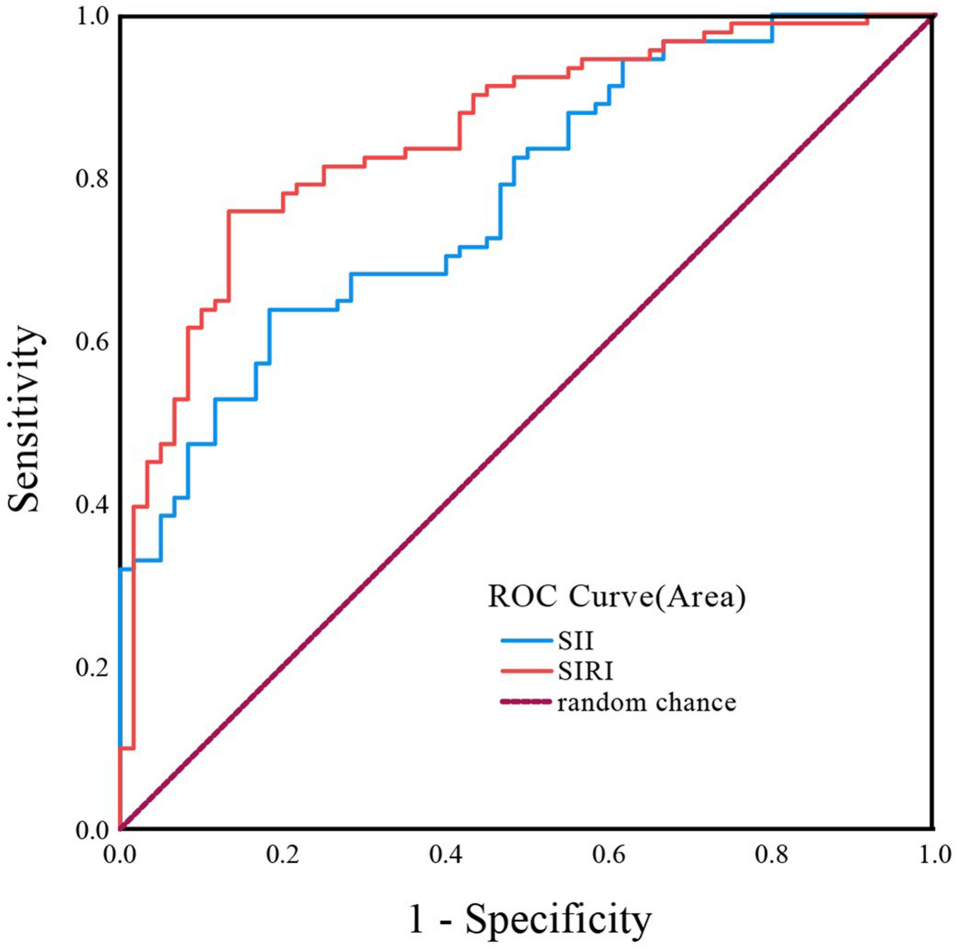


**Figure 1** Area Under the ROC Curve for SII and SIRI in Non-MODS and MODS Groups.


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## Baseline Characteristics of MODS Patients Caused by Wasp Stings in Survivor and Non-Survivor Groups

The analysis of MODS caused by wasp stings revealed statistically significant and clinically relevant differences between the survivor and non-survivor groups, as shown in Table 4. Significant differences were observed in the number of stings, APACHE II score, neck sting site, and clinical symptoms such as throat tightness and difficulty breathing ($P < 0.05$). However, no statistically significant differences were found between the two groups in terms of gender, sting sites (head, torso, upper limbs, and lower limbs), clinical symptoms (dizziness, headache, altered mental state, anaphylaxis, urticaria, erythema, palpitations, chest tightness, abdominal pain, diarrhea), and length of hospitalization ($P > 0.05$).

## Comparison of Blood Cell Count-Derived Inflammatory Indices in MODS Patients Caused by Wasp Stings in Survivor and Non-Survivor Groups

The comparison of data between MODS patients caused by wasp stings in the survivor and non-survivor groups, as shown in Table 5, revealed significant differences in WBC (17.25 vs 26.02 $\times 10^9$/L, $P = 0.014$), NEU (15.12 vs 18.59 $\times 10^9$/L, $P = 0.049$), MONO (0.56 vs 0.72 $\times 10^9$/L, $P = 0.033$), NLR (18.50 vs 24.46, $P = 0.008$), SII (2990.60 vs 5041.17, $P = 0.002$), and SIRI (7.67 vs 18.37 $\times 10^9$/L, $P < 0.001$) ($P < 0.05$ for all). In contrast, platelet counts (209.50 vs 184.50, $P = 0.719$) and LYM (0.82 vs 0.68 $\times 10^9$/L, $P < 0.001$) did not show a statistically significant difference ($P > 0.05$).

**Table 4** Baseline Characteristics of MODS Patients Caused by Wasp Stings in Survivor and Non-Survivor Groups

| Parameter | Survivor Group (N = 48) | Non-Survivor Group (N =12) | Statistical Values | *P* |
|---|---|---|---|---|
| Gender, n (%) | | | $\chi^2$=0.07 | 0.796 |
| Male | 26 (54.17) | 6 (50.00) | | |
| Female | 22 (45.83) | 6 (50.00) | | |
| Age, year | 51.00 (35.00, 63.00) | 57.00 (50.00, 64.00) | Z=−1.12 | 0.263 |
| Number of stings, puncture mark | 22.00 (10.00, 45.00) | 37.00 (29.00, 55.00) | Z=−2.20 | 0.028 |
| APACE II score | 17.00 (14.00, 22.00) | 21.00 (18.00, 23.00) | Z=−2.47 | 0.014 |
| Time to first visit after bee sting, hour | 5.00 (3.00, 8.00) | 4.00 (3.00, 6.00) | Z=−0.09 | 0.926 |
| Sting site, n (%) | | | | |
| Head | 45 (93.75) | 11 (91.67) | | |
| Neck | 3 (6.25) | 5 (41.67) | $\chi^2$=7.58 | 0.006 |
| Torso | 19 (39.58) | 6 (50.00) | $\chi^2$=0.43 | 0.513 |
| Upper limbs | 31 (64.58) | 9 (75.00) | $\chi^2$=0.12 | 0.732 |
| Lower limbs | 12 (25.00) | 6 (50.00) | $\chi^2$=1.79 | 0.181 |
| Clinical symptoms, n (%) | | | | |
| Dizziness, headache | 28 (58.33) | 10 (83.33) | $\chi^2$=1.62 | 0.203 |
| Altered state of mind | 6 (12.50) | 4 (33.33) | $\chi^2$=1.69 | 0.194 |
| Anaphylaxis | 6 (12.50) | 2 (16.67) | | |
| Urticaria, erythema | 22 (45.83) | 6 (50.00) | $\chi^2$=0.07 | 0.796 |
| Palpitations, chest tightness | 31 (64.58) | 11 (91.67) | $\chi^2$=2.19 | 0.139 |
| Tightness in the throat | 10 (20.83) | 9 (75.00) | $\chi^2$=10.63 | 0.001 |
| Difficulty in breathing | 10 (20.83) | 7 (58.33) | $\chi^2$=4.93 | 0.026 |
| Abdominal pain | 6 (12.50) | 5 (41.67) | $\chi^2$=3.68 | 0.055 |
| Diarrhoea | 6 (12.50) | 4 (33.33) | $\chi^2$=1.69 | 0.194 |
| Other | 3 (6.25) | 2 (16.67) | $\chi^2$=0.34 | 0.559 |
| Length of hospitalization, day | 4.00 (2.00, 5.00) | 5.00 (3.00, 6.00) | Z=−1.02 | 0.308 |

**Table 5** Comparison of Blood Cell Count-Derived Inflammatory Indices in MODS Patients Caused by Wasp Stings in Survivor and Non-Survivor Groups

| Parameter | Survivor Group (N = 48) | Non-Survivor Group (N =12) | Statistical Values | *P* |
|---|---|---|---|---|
| WBC ($\times10^9$/L) | 17.25 (13.14, 21.16) | 26.02 (16.77, 35.92) | Z=−2.46 | 0.014 |
| PLT ($\times10^9$/L) | 209.50 (142.75, 235.75) | 184.50 (125.50, 258.50) | Z=−0.36 | 0.719 |
| NEU ($\times10^9$/L) | 15.12 (11.64, 18.64) | 18.59 (13.73, 26.69) | Z=−1.97 | 0.049 |
| LYM ($\times10^9$/L) | 0.82 (0.61, 1.22) | 0.68 (0.47, 1.34) | Z=−0.70 | 0.482 |
| MONO ($\times10^9$/L) | 0.56 (0.29, 0.77) | 0.72 (0.64, 1.20) | Z=−2.14 | 0.033 |
| NLR | 18.50 (14.34, 24.03) | 24.46 (21.54, 28.67) | Z=−2.67 | 0.008 |
| SII | 2990.60 (2449.66, 4444.16) | 5041.17 (3782.19, 7251.76) | Z=−3.08 | 0.002 |
| SIRI ($\times10^9$/L) | 7.67 (4.53, 15.02) | 18.37 (15.43, 23.46) | Z=−3.24 | 0.001 |

**Abbreviations**: WBC, White Blood Cell Count; PLT, Platelet count; NEU, Neutrophil Count; LYM, Lymphocyte Count; MONO, Monocyte Count; NLR, Neutrophil-to-lymphocyte ratio; SII, Systemic immune-inflammation index; SIRI, Systemic Inflammatory Response Index.

**Table 6** Univariate and Multivariate Logistic Analyses of SII and SIRI as Prognostic Indicators in MODS Patients Caused by Wasp Stings in Survivor and Non-Survivor Groups

| Corresponding Indicators | Univariate Logistic | | Multivariate Logistic | |
|---|---|---|---|---|
| | *P* | OR (95% CI) | *P* | OR (95% CI) |
| SII | 0.006 | 1.01 (1.01 ~ 1.01) | 0.037 | 1.01 (1.01 ~ 1.01) |
| SIRI | 0.004 | 1.12 (1.04 ~ 1.21) | 0.016 | 1.12 (1.02 ~ 1.22) |

## Univariate and Multivariate Logistic Analyses of SII and SIRI as Prognostic Indicators in MODS Patients Caused by Wasp Stings in Survivor and Non-Survivor Groups

As shown in Table 6, both univariate and multivariate logistic regression analyses revealed that the SII and SIRI were statistically significant prognostic indicators and predictors for the development of MODS in patients with wasp sting-induced MODS, in both the survivor and non-survivor groups ($P < 0.05$).

## Area Under the ROC Curve for SII and SIRI in MODS Patients Caused by Wasp Stings in Survivor and Non-Survivor Groups

ROC curve analysis showed that SIRI had high sensitivity and specificity in predicting death in patients with wasp sting-induced MODS, in both the survivor and non-survivor groups, with an AUC of 0.806 (95% CI 0.692–0.919, $P = 0.001$), while the AUC of SII was 0.790 (95% CI 0.653–0.927, $P = 0.002$), as shown in Figure 2.

# Discussion

In this retrospective study, we described the clinical profile of a series of patients with wasp stings and assessed early peripheral blood counts, focusing on the SII and SIRI, to predict patient outcomes. We found that elevated SII and SIRI in the early stages of the disease were associated with poor prognosis and an increased likelihood of multiple organ failure. These findings suggest that early SII and SIRI values could serve as prognostic indicators for predicting the development of MODS and final outcome (death or survival) in wasp stings.

Wasp venom contains various active components, including bee venom toxin, mast cell degranulating enzyme, and phospholipase A2. Bee venom toxin, the primary component, constitutes 40–60% of the total venom and is responsible for the pain experienced after a sting.[22,23] These components trigger a cascade of immune responses, leading to tissue damage and systemic inflammation. Recent studies have identified bee venom toxin, phospholipase A2, and

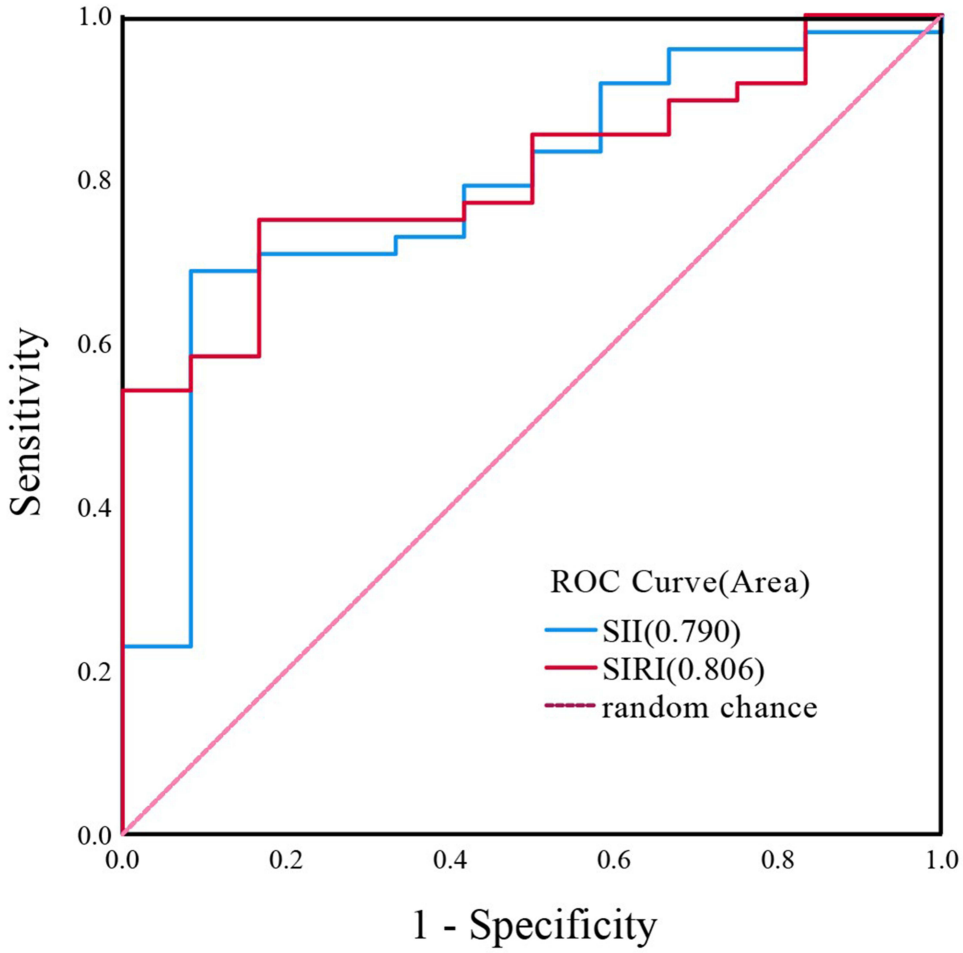


**Figure 2** Area Under the ROC Curve for SII and SIRI in MODS Patients Caused by Wasp Stings in Survivor and Non-Survivor Groups.

hyaluronidase as the key substances responsible for organ damage and lesions.[24] In vivo and in vitro studies revealed that bee toxins can cause dose- and time-dependent cytotoxicity on human peripheral blood lymphocytes (HPBLs). These toxins also regulate the expression of specific genes involved in DNA damage response (TP53, CDKN1A, GADD45α, MDM), oxidative stress (CAT, SOD1, GPX1, GSR, GCLC), and apoptosis (BAX, BCL-2, CAS-3, CAS-7).[25] In acute kidney injury (AKI) models, wasp toxins induce AKI through the TNF-α/NF-κB signaling pathway,[26] and NLRP3 activation is closely linked to renal failure and inflammatory responses.[27] Therefore, early monitoring of the inflammatory response is essential to prevent the development of multi-organ failure.

For patients suffering from wasp stings, organ failure and prognosis are closely related to the early inflammatory response.[28] Studies have shown a positive correlation between elevated levels of serum IL-2, IL-4, IL-6, IFN-γ, IL-17, and leukocyte counts in hornet sting patients.[29] SIRI is derived from routine peripheral blood tests. It evaluates the balance among neutrophils (which initiate inflammation), monocytes (which mediate phagocytosis and cytokine release), and lymphocytes (the core of adaptive immunity), directly reflecting the equilibrium between innate and adaptive immune responses.[30] Similarly, the SII combines neutrophil counts (indicating innate immune activation and inflammatory intensity), platelet counts (involved in coagulation and immune modulation), and lymphocyte counts (reflecting adaptive immunity) to assess the interplay between immune inflammation and coagulation.[31] Both indices rely on cellular parameters that are minimally influenced by pathophysiological variables and are obtained from standard blood counts. This approach offers advantages of low cost and wide accessibility, making SIRI and SII comprehensive and balanced markers for evaluating an individual's overall inflammatory burden and immune status in clinical monitoring.[32] Moreover, these indices have been shown to be associated with sepsis and multi-organ failure.[33] It has been demonstrated

that SIRI is an independent risk factor for MODS in wasp sting patients, with an AUC of 0.886 ($P < 0.001$) for predicting MODS in these patients, an optimal cut-off value of 6.39, a sensitivity of 71.43%, and a specificity of 94.5%.[33] Our study's results showed that the optimal cut-off value of SIRI for predicting MODS in wasp sting patients was 0.853 (95% CI: 0.792–0.914, $P$=0.002), and these findings were largely consistent with those of the previous study, suggesting that SIRI may serve as a reliable predictor for MODS in wasp sting patients. Additionally, the AUC of SII under the ROC curve was 0.776 (95% CI: 0.704–0.849, $P$=0.003). For SIRI, the AUC under the ROC curve was 0.806 (95% CI: 0.692–0.919, $P$=0.001) and 0.790 (95% CI: 0.653–0.927, $P$=0.002) in the survivor and non-survivor groups, respectively. Therefore, combining early SII with SIRI in the assessment of wasp stings may enhance the prediction of MODS development and assist in determining patient survival.

The results of this study have important clinical implications. First, SII and SIRI, as early diagnostic markers, can help clinicians identify patients at high risk of developing MODS after wasp stings. By monitoring these indicators, healthcare professionals can take timely interventions, such as aggressive fluid resuscitation, anti-inflammatory therapy, and close monitoring of organ function, to prevent the progression of MODS, thereby reducing its incidence. Second, the high sensitivity and specificity of SIRI make it a valuable tool in guiding clinical decision-making. In particular, SIRI can help identify patients who require closer monitoring and treatment, while those with lower SIRI values may be at lower risk.

In this study, we found for the first time that the use of early SII and SIRI can be used as prognostic indicators to predict the development and final outcome (death or survival) of MODS in patients with wasp stings. However, it remains to be clarified whether these indices should be applied alongside existing clinical scoring systems or could serve as standalone alternatives. Although this study provides strong evidence for the predictive role of SII and SIRI in MODS, it has several limitations. First, the retrospective nature of the study may introduce biases that could affect the results. Additionally, the study was conducted in a single region and did not encompass the full population of wasp sting cases. Second, the severity of the stings was not considered, which could influence the inflammatory response and the development of MODS. Future studies should stratify patients based on sting severity to better understand the relationship between SII, SIRI, and MODS. Moreover, large-scale, multicenter, and multiregional prospective studies are required to validate the predictive value of SII and SIRI in real-time clinical applications and to facilitate their integration into clinical decision-support tools.

## Conclusion

In conclusion, this study demonstrates that SII and SIRI are important early markers for predicting the development of MODS in wasp sting patients. Elevation of these indicators is closely associated with poor prognosis, underscoring the importance of early monitoring and intervention. Clinicians can use SII and SIRI to identify high-risk patients and implement timely therapeutic measures to prevent the onset of multiple organ failure.

## Data Sharing Statement

In accordance with the regulations and guidelines of the medical Ethics Committee of the institution. The data that support the findings of this study are available from the corresponding author Zhicheng Fang upon reasonable request.

## Informed Consent

The study was conducted in accordance with the Declaration of Helsinki and relevant ethical guidelines. All patient data were approved by the Medical Ethics Committee of Taihe Hospital Affiliated to Hubei University of Medicine (reference number: 2024KS88, September 12, 2024). All participants provided written informed consent, including basic information about the case data, and consent to write and publish the article was obtained from the patient's family.

A total of 151 patients were included in this study, of which 149 were signed by the patients themselves. Among the patients in the MODS death group caused by wasp sting, the informed consent forms of 2 patients were signed by family members (their children) of the patients, mainly because the patients were in a serious state of irritability after wasp sting, and family members were commissioned to sign the informed consent form.

According to the medical ethical principles of the Declaration of Helsinki, when patients are unable to exercise their right to informed consent, their legal representatives can make decisions on their behalf. At the same time, in China, according to Article 1219 of the Civil Code of the People's Republic of China, if the patient is unable to make his own

decision, his close relatives or a written entrusted agent can sign. In addition, most legal systems treat immediate family members as legal representatives. Therefore, our study conformed to the aforementioned medical ethical principles.

## 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. Xiaolin Zhang, Pengfei Liang are equal to this work and share co-first authorship.

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## Disclosure

All authors declare that there is no conflict of interest associated with this study.

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