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Original Article

ORIGINAL ARTICLE

Development and internal validation of a Wasp Sting Severity Score to assess severity and indicate blood purification in persons with Asian wasp stings

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ABSTRACT

Background. In recent years, the incidence of wasp sting has increased annually in China. Organ damage and high mortality due to mass wasp envenomation remain major challenges. Timely and appropriate medical intervention can improve survival. However, there are currently no normalized tools for early assessment of severity.

Methods. The clinical data of wasp sting patients hospitalized from 2011 to 2019 were used as a training set. Logistic regression was used to explore major risk factors for the development of a severe case of wasp sting (SC). The Wasp Sting Severity Score (WSS) was determined considering these risk factors to identify SCs and was tested in a validation dataset that was prospectively collected in 2020.

Results. The data of 1131 wasp sting patients from 2011 to 2019 were included in the training set. Logistic regression analysis showed that tea-colored urine, number of stings, and lactate dehydrogenase and total bilirubin levels were risk factors for developing an SC. The WSS was developed considering these four risk factors, and the total possible WSS was 20 points. The WSS was tested using the validation dataset, comprising the data of 153 patients, in 2020, and we found that a WSS $\geq$3 points was an important indication for blood purification, with a sensitivity of 71.9%, specificity of 92.6% and an area under the curve of 0.918 (95% confidence interval 0.873–0.962). Among patients with more than 30 stings, mortality in those who underwent plasma exchange (PE) within 24 h after admission was significantly lower than that in those who did not receive PE treatment (14.3% versus 46.9%, P = 0.003). However, continuous venovenous hemofiltration (CVVH) (P = 0.317) and hemoperfusion (HP) (P = 0.869) did not significantly reduce mortality.

Conclusions. Patients with WSS scores $\geq$3 should be considered for blood purification as early as possible in addition to routine treatment. In addition, PE is better than CVVH and HP at reducing mortality in patients suffering from severe wasp stings.

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Keywords: blood purification, continuous venovenous hemofiltration, hemoperfusion, plasma exchange, sting, wasp

INTRODUCTION

Wasp is a general term that usually refers to insects in the family Vespidae, suborder Apocrita, order Hymenoptera. Wasps can be subdivided into two groups: solitary wasps, which live alone and comprise the majority of the family Vespidae, and social wasps, which live in colonies [1–3]. Some species of social wasps present serious health threats to humans, such as *Vespa velutina* and *Vespa mandarinia*; contact with such wasps often leads to accidental stings and even death.

Social wasps usually build their nests in trees, in bushes or underground [4–6]. When the nest is disturbed, the colony may mobilize via an attack pheromone to defend their nest, resulting in intruder mortality due to envenomation [7, 8]. The major components of wasp venom, including phospholipase A_2, hyaluronidase, melittin, kinin, histamine and 5-hydroxytryptamine, can cause allergic reaction, rhabdomyolysis, hemolysis and other biological effects [2, 9]. These biological effects can be classified as allergic reactions and direct toxic effects. The latter have obvious dose–response relationships. Thus, patients stung by a large number of wasps have high mortality.

Wasp sting is a common disease in southern China. Mortality in patients who are stung by a large number of wasps ranges from 30% to 50% unless patients receive timely and appropriate treatment. Although there are many reports on wasp stings, most are case reports from North America [10–15]. Until now, there has been a lack of consensus to guide the clinical treatment of Asian wasp stings. If medical staff fail to implement timely measures, such as blood purification in the early stage, a patient might develop severe complications such as hemolysis, shock or multiple organ failure. The current blood purification options for patients with severe wasp stings mainly include plasma exchange (PE), hemodialysis, hemofiltration and hemoperfusion [16]. However, there is currently no consensus regarding how to evaluate severe cases of wasp stings (SCs) and choose the optimal mode of blood purification. Therefore, we reviewed and analyzed the medical records of wasp sting patients admitted to four hospitals in Sichuan Province from 2011 to 2020 to determine the risk factors for the prognosis of wasp sting and optimize the treatment process.

MATERIALS AND METHODS

Study setting and design

Suining Central Hospital, which is located in the middle of Sichuan Province in southwest China, is a teaching hospital with 2900 beds affiliated with Chongqing Medical University. Our institution treats approximately 100–200 wasp sting patients per year. We included all honeybee and wasp sting patients according to the discharge diagnosis. Data from the first day after admission and at discharge, including main symptoms, signs, laboratory results and blood purification methods within 24 h after admission, from 2011 to 2019 were collected retrospectively. If a medical record did not provide sufficient information, we called the patients or their relatives to obtain the missing information. According to medical records and telephone follow-up, the patients were divided into the honeybee sting group and wasp sting group. If a case could not be determined, the patient was excluded from the study. The data were entered independently by two groups of researchers. Inconsistencies between the two groups were discussed.

We collected data from the other three hospitals, namely, Pengxi County People's Hospital, Shehong People's Hospital and Daying County People's Hospital, using the same methods, but the data of patients stung by bees were excluded during the data collection process to reduce the workload. The data of wasp sting patients from 2011 to 2019 were treated as the training set, and the data of wasp sting patients prospectively collected in 2020 were treated as the validation set. The study was approved by the ethics committees of the four hospitals, and informed consent was exempted (LLSLH20200020).

Routine treatments for honeybee/wasp stings include the following: (i) antiallergic or antishock treatment, including adrenaline, corticosteroids and antihistamines; (ii) local treatment, including removal of stingers and application of dexamethasone and lidocaine to relieve local symptoms; (iii) toxin elimination, including rehydration, diuretic administration (such as furosemide or torasemide) and urine alkalinization—the latter is helpful to prevent or relieve acute renal injury (AKI) caused by rhabdomyolysis and hemolysis and (iv) other treatments, such as analgesia and tetanus antitoxin. Severe patients with multiple stings received blood purification by a Multifiltrate acute therapy machine (Multifiltrate, Fresenius Medical Care, Bad Homburg, Germany), mainly in continuous venovenous hemofiltration (CVVH) mode (Ultraflux AV600S, Fresenius Medical Care, Bad Homburg, Germany) or (plus) hemoperfusion (HA330, Jafron Biomedical Co., Ltd, Zhuhai, China). In 2017, PE (COM. TEC, Fresenius Kabi AG, Bad Homburg, Germany) was initiated at our hospital to improve the prognosis of severe wasp sting patients.

Definitions

Significant pruritus, erythema, urticaria or vascular neuroedema involving nonstung parts of the body or the whole body was defined as an allergic reaction according to the Ring and Messmer Grading Scale [17]. Furthermore, an SC was defined as a case that required blood purification due to hemolysis, rhabdomyolysis or manifested organ dysfunction [Sequential Organ Failure Assessment (SOFA) score $\geq$2] [18].

Tea-colored urine (TCU) is one of the manifestations of severe wasp sting. When a patient's urine was brown, dark brown or reddish brown, we judged that the patient was positive for TCU [19], indicating that there was a large amount of hemoglobin or myoglobin in the urine.

In this study, we defined the time from injury to blood purification (time3) as the time from injury to admission (time1) + time from admission to blood purification (time2). According to our clinical experience, patients with severe wasp stings mainly died within 3 days after admission. When evaluating the impact of different blood purification measures on the prognosis of patients, we used the blood purification measures received by patients within 24 h after admission. In evaluating the effect of the time factor on the prognosis of patients, we used the time from injury to blood purification (time3). Because of the large time span, we mainly compared the difference between patients receiving blood purification within 0–6 h and those receiving blood purification within 6–12 h.

Table 1. Differences between patients with honeybee stings and wasp stings

Variables	Honeybee sting patients	Wasp sting patients in training set	Wasp sting patients in validation set	P-value[a]	P-value[b]
M/F	61/50 (55%)	667/464 (59%)	81/72 (53%)	0.412	0.156
Age (years)	59 (46, 65)	61 (48, 68)	65 (51, 69)	0.162	0.011
Chronic disease	34/111 (31%)	342/1131 (30%)	39/153 (25%)	0.830	0.228
Injury time (h)	3 (2, 4)	3 (1, 5)	4 (3, 6)	0.103	<0.001
Number of stings	10 (4, 20)	10 (5, 18)	14 (7, 26)	0.297	<0.001
Allergy	26/111 (23%)	201/1131 (18%)	24/153 (16%)	0.401	0.524
TCU	2/111 (2%)	122/1131 (11%)	32/153 (21%)	<0.001	<0.001
CK (U/L)	127 (77, 211)	227 (124, 675)	279 (126, 491)	<0.001	0.641
LDH (U/L)	200 (168, 244)	240 (192, 408)	245 (202, 430)	<0.001	0.225
Myoglobin (μg/L)	39 (25, 95)	101 (43, 575)	194 (75, 772)	<0.001	0.003
HBDH (U/L)	160 (136, 193)	184 (149, 267)	197 (170, 335)	<0.001	0.002
TBIL (μmol/L)	12.5 (8.0, 18.6)	17.1 (10.7, 32.8)	18.5 (10.2, 36.4)	<0.001	0.806
Creatinine (μmol/L)	65.5 (54, 79)	70 (58, 84.1)	74 (64, 91)	0.002	0.002
WBCs (10^9/L)	11.4 (7.9, 14.9)	12.2 (8.59, 16.7)	12.1 (8.8, 18.3)	<0.001	0.401
APTT (second)	41 (33.7, 68.1)	43.2 (31.8, 83.1)	63.5 (38.9, 92.2)	0.945	<0.001
Death	1/111 (1%)	67/1131 (6%)	7/153 (5%)	0.006	0.359

Values presented as median (IQR). CK, creatine kinase; HBDH, hydroxybutyrate dehydrogenase; WBCs, white blood cells; APTT, activated partial thromboplastin time.
[a]Comparison between the honeybee sting group and the wasp group in the training set.
[b]Comparison between the wasp sting patients in the training set and the wasp sting patients in the validation set.

Data analysis

Diagnosis of a serious case at discharge was treated as the dependent variable in the logistic regression analysis. Considering that there were major differences among the wasp sting patients' enzymatic indexes, we transformed the indexes into base-10 logarithms to reduce the differences in absolute values, allowing a near linear distribution for further statistical processing. The Box–Tidwell method was used to detect whether there was a linear relationship between the continuous independent variables and the logit conversion value of the dependent variable.

Univariate logistic analysis was used to exclude independent variables without statistical significance. The collinearity among variables was tested. If their tolerance was less than 0.1 or their variance expansion factor was greater than 10, they were excluded. We also used cluster analysis and factor analysis to detect which independent variables were closely related. Variables in the same category with a lower clinical significance were excluded. Finally, the variables without statistical significance in the multivariate logistic regression analysis were also excluded. According to the possibility of an SC of wasp sting, a score was assigned to each independent variable to develop the Wasp Sting Severity Score (WSS). Finally, the receiver operating characteristic curve was used to evaluate the diagnostic value of the WSS score for SCs in the validation set.

The Chi-square test or Fisher's exact test was used for count data [20]. For measurement data, if the data met the homogeneity of variance assumption and had a normal distribution, Student's *t*-test was used to compare the difference between the two groups; otherwise, the rank-sum test was applied. All statistical analyses were performed in SPSS 25.0 and STATA 13.0.

RESULTS

Characteristics of patients in the training set

Excluding 359 pediatric patients and 198 adult patients who were lost to follow-up, a total of 1242 patients, including 111 honeybee sting patients and 1131 wasp sting patients, from 2011 to 2019 were included in the analysis. A total of 153 patients with wasp stings received treatment in our hospital in 2020 (Supplementary data, Figure S1). The differences between the patients stung by honeybees and those injured by wasps are listed in Table 1, and the basic characteristics of the patients stung by wasps are shown in Figure 1. We found that the patients stung by wasps had higher enzymatic indicators and were more prone to organ failure than those stung by honeybees. However, there was no significant difference in the proportion of patients with allergic reactions between the two groups ($P = 0.401$). In recent years, due to the decrease in the number of individuals practicing small-scale honeybee breeding, few patients have visited the hospital for honeybee stings. Through field investigations or pictures provided by family members of patients, we determined the species of wasp responsible for the stings in 20 patients; we found that 17, 2 and 1 patient were stung by common wasps in this area, including *Vespa basalis* (black-bellied hornet), *Vespa velutina nigrithorax* (yellow-legged hornet) and *Vespa mandarinia* (Asian giant hornet), respectively (Figure 2).

Logistic regression of risk factors related to SC

We tested the correlation between the dependent variable, SC and independent variables, including demographic characteristics, symptoms and signs and laboratory results (Table 2). No significant association was found between SC and sex, allergic symptoms or chronic diseases. However, many independent variables had significant correlations with the dependent variable. Therefore, collinearity tests, cluster analysis, factor analysis and multivariate logistic regression analysis were used to further simplify the variables (Supplementary data, Tables S1, S2, Figure S2). Four variables, namely, TCU, number of stings, lactic dehydrogenase (LDH) and total bilirubin (TBIL), were entered into the final model.

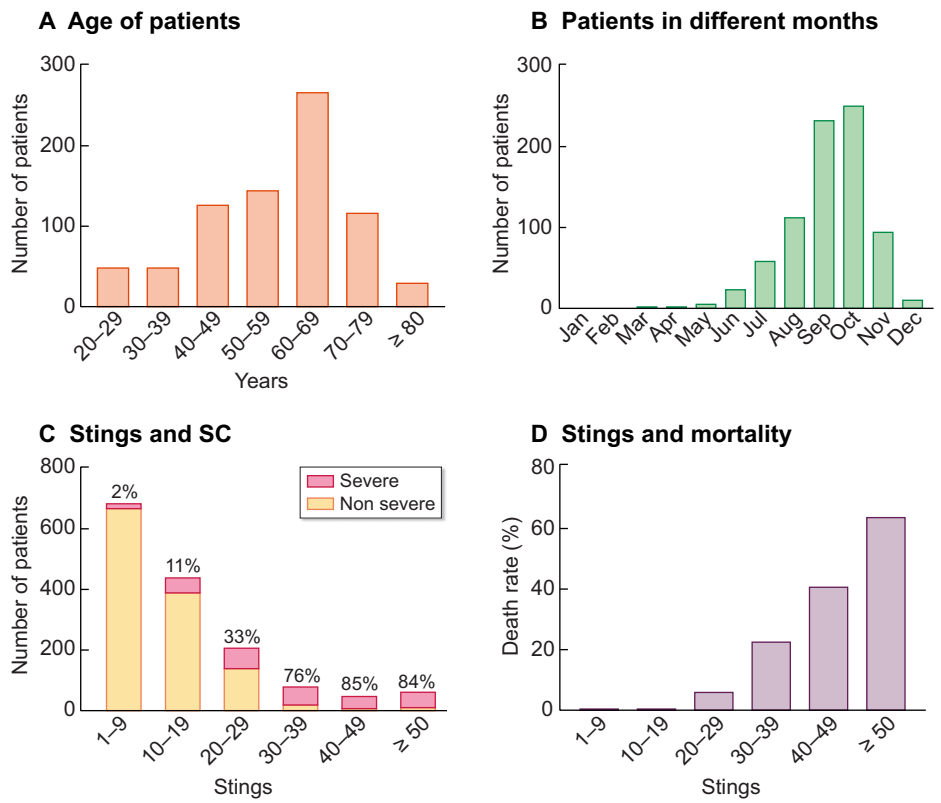

FIGURE 1: Characteristics of the patients stung by wasps. (**A**) The age distribution of wasp sting patients. (**B**) The number of wasp sting patients in different months. (**C**) The relationship between the number of wasp stings and severe cases of wasp stings (SC). (**D**) The relationship between the number of wasp stings and mortality.

Wasp Sting Severity Score

The WSS was developed considering the four significant variables, namely, TCU, number of stings, LDH and TBIL. A score was assigned to each variable, with a total possible score of 20 (Table 3). Each point represents an approximately 20% higher probability of developing an SC requiring blood purification. We applied the WSS to prospective patient data in 2020. The results showed that a score of 3 (WSS $\geq$3) was the cutoff value for predicting SCs, with a sensitivity of 71.88%, specificity of 92.55% and an area under the curve (AUC) of 0.918 [95% confidence interval (CI) 0.873–0.962].

In addition, when the WSS was applied to the training dataset, the results showed an AUC of 0.970 (95% CI 0.956–0.983) when the WSS cutoff was 3, with a sensitivity of 93.18% and a specificity of 89.95% (Supplementary data, Figure S3).

Recommended process for treating patients with wasp stings

We analyzed the effect of blood purification within 24 h after admission on mortality in patients with more than 30 wasp stings. The specific blood purification methods and the severity of disease are shown in Supplementary data, Table S3. In order to evaluate the effectiveness of blood purification, the WSS was used to evaluate the difference in disease severity between the two groups. The WSS for patients who received and did not receive blood purification therapy was 14 (8, 18) and 8 (3, 13), respectively, with $P < 0.001$, which indicated that the condition of patients who received blood purification therapy was more serious at admission. The mortality rate in patients who received blood purification treatment is 35% (41/117); and the mortality rate in patients who did not receive blood purification treatment was 43% (20/47). There was no statistically significant difference between the two groups ($P = 0.368$), which may have been due to the inconsistent impact of different purification methods on mortality. There are many combinations of blood purification methods in clinical practice, but using data for too many groups is not conducive to finding the advantage of a treatment. Therefore, we used another grouping method to compare the effects of different blood purification methods on mortality, as described in the next paragraph.

We divided the patients into a non-PE (Non-PE) treatment group (HP, CVVH, CVVH + HP) and a PE treatment (Yes-PE) group (HP + PE, CVVH + PE, CVVH + HP + PE) according to whether they received PE treatment. Patients were divided into the non-HP (Non-HP) group [PE, CVVH, intermittent hemodialysis (IHD), PE + CVVH] and the HP (Yes-HP) group (PE + HP, CVVH + HP, IHD + HP, PE + CVVH + HP) according to whether they received HP treatment. Patients were divided into the non-CVVH (Non-CVVH) group (PE, HP, PE + HP) and the CVVH (Yes-CVVH) group (PE + CVVH, HP + CVVH, PE + HP + CVVH) according to whether they received CVVH. The results showed that PE was associated with reduced mortality in patients with a similar number of stings (14.3% versus 46.9%, $P = 0.003$), while CVVH and HP did not significantly improve mortality ($P = 0.317$ and 0.869, respectively) (Table 4).

In addition, the mortality rates of patients receiving non-PE treatment (CVVH, CVVH + HP) within 6 h and 6–12 h after having been stung by wasps (time3) were 5/15 (33.3%) and 15/23 (65.2%), respectively, ($P = 0.096$). The number of wasp stings in both

FIGURE 2: Differences between common wasps and honeybees in Sichuan. (**A**) *Apis cerana* (Asian honeybee). (**B**) *Vespa basalis* (black-bellied hornet). (**C**) *Vespa velutina nigrithorax* (yellow-legged hornet). (**D**) *Vespa mandarinia* (Asian giant hornet). (**E**) Comparison between *A. cerana* and several Asian wasps, from left to right: *A. cerana*, *V. basalis*, *V. velutina nigrithorax*, *V. mandarinia*; **A**, **C** and **D** are from the free copyright website www.pixabay.com.

Table 2. Univariate logistic regression analysis relationship between independent variables and the presence of an SC requiring blood purification

Variables	Z Value	OR (95% CI)	P-value
Age	5.15	1.03 (1.02–1.05)	<0.001
Sex	−1.75	0.74 (0.53–1.04)	0.079
Allergy	0.67	1.14 (0.78–1.65)	0.503
Injury time	5.04	1.06 (1.04–1.08)	<0.001
TCU	13.94	57.9 (32.7–102.5)	<0.001
Chronic disease	1.23	1.25 (0.88–1.78)	0.217
Number of stings	11.84	1.14 (1.11–1.16)	<0.001
TBIL	11.87	1.07 (1.06–1.08)	<0.001
Creatinine	7.6	1.02 (1.02–1.03)	<0.001
Albumin	−4.72	0.92 (0.89–0.95)	<0.001
WBCs	11.78	1.26 (1.21–1.31)	<0.001
Platelets	2.47	1 (1.00–1.00)	0.013
Hemoglobin	−5.05	0.98 (0.97–0.99)	<0.001
Lymphocytes	−2.66	0.97 (0.95–0.99)	0.008
Neutrophils	2.82	1.02 (1.01–1.04)	0.005
Basophils	−2.02	0.28 (0.08–0.96)	0.044
Eosinophils	−4.07	0.58 (0.45–0.76)	<0.001
APTT	10.08	1.03 (1.02–1.03)	<0.001
Log_{10} (HBDH)	13.01	471 (187–1192)	<0.001
log_{10} (LDH)	12.62	1127 (379–3357)	<0.001
log_{10} (CK)	9.86	4.56 (3.37–6.16)	<0.001
log_{10} (ALT)	12.04	30.1 (17.3–52.4)	<0.001

OR, odds ratio; WBC, white blood cells; APTT, activated partial thromboplastin time; HBDH, hydroxybutyrate dehydrogenase; CK, creatine kinase; ALT, alanine transaminase.

Table 3. Wasp Sting Severity Score (WSS)

Assigned points	1	3	5
TCU			Positive
Number of stings	15–29	30–49	≥50
LDH (U/L)	400–699	700–999	≥1000
TBIL (μmol/L)	30–49	50–79	≥80

Each point represents an approximately 20% higher probability of developing an SC requiring blood purification.

groups (or the severity degree of two groups) was similar, with 45 (30, 50) versus 42 (35, 50) stings (P = 0.786). The 6-h mortality rate was 11.1% (1/9), and the 6–12 h mortality rate was 23.8% (5/21) in the PE-based treatment group (including PE, PE + HP, PE + CVVH, PE + CVVH + HP), P = 0.637. The numbers of wasp stings in the two groups were 42 (35, 50) and 45 (38, 55) (P = 0.525), respectively. Regardless of whether it was CVVH or PE, the mortality rate in those who received earlier intervention was lower, but due to the small number of included cases, the result did not reach statistical significance. Therefore, the results need to be confirmed in studies with large sample sizes.

Based on the available data, we established a diagnosis and treatment protocol for wasp sting as a reference for medical workers (Figure 3). After admission, patients should undergo timely routine examinations, including blood cell counts, biochemical tests, coagulation function tests and myocardial enzyme spectrum tests, and routine treatment should be initiated. Patients with a WSS score ≥3 should be considered for early

Table 4. Influence of different blood purification methods within 24 h after admission on the prognosis of patients

Groups	Sting (number)	Injury time (h)	LDH (U/L)	TBIL (μmol/L)	WBC (10^9/L)	Death *n*/N(%)
Non-PE	40 (32, 50)	4 (3, 8)	1537 (554, 2645)	53.6 (31.6, 97.9)	22.4 (16, 27.6)	30/64 (46.9)
Yes-PE	42 (35.5, 52.5)	7 (4.5, 12)	1121 (616, 2782)	61.4 (36.9, 85.5)	21.6 (17.6, 26.3)	4/28 (14.3)
Total	41.5 (35, 50)	5 (3, 10)	1366 (614.5, 2751)	56 (32.9, 87.6)	21.8 (16.8, 26.8)	34/92 (37.0)
P	0.246	0.005	0.653	0.852	0.645	0.003
Non-CVVH	40 (32, 50)	4.5 (3, 10)	596 (240, 1896)	36.9 (18.4, 82.5)	19.0 (13.1, 24.1)	7/30 (23.3)
Yes-CVVH	45 (37, 55)	5 (3, 9)	1106 (614, 2450)	56.9 (33.4, 84.9)	21.8 (16.9, 26.8)	16/47 (34.0)
Total	42 (35, 53)	5 (3, 10)	967 (381, 2238)	52.9 (24.2, 84)	19.7 (16.0, 25.4)	23/77 (29.9)
P	0.248	0.834	0.050	0.299	0.072	0.317
Non-HP	39 (32, 50)	4 (3, 10)	1355 (493, 3055)	48.4 (27.9, 77.6)	21.1 (17.2, 25.8)	20/58 (34.5)
Yes-HP	43.5 (35, 52)	5 (3, 10)	1453 (714, 2556)	61.3 (34.4, 90.4)	22.1 (16.7, 27.6)	18/50 (36.0)
Total	40.5 (34, 50)	5 (3, 10)	1436 (615, 2775)	56.8 (30.8, 87.2)	21.3 (16.7, 26.5)	38/108 (35.2)
P	0.078	0.759	0.998	0.231	0.854	0.869

Values in columns 2–7 are presented as median (IQR). Values in columns 27 presented as median (IQR); Disease severity parameters and survival outcomes in patients treated with different blood purification methods.
Non-PE group = HP, CVVH, CVVH + HP; Yes-PE group = HP + PE, CVVH + PE, CVVH + HP + PE; Non-HP group = PE, CVVH, IHD, PE + CVVH; Yes-HP group = PE + HP, CVVH + HP, IHD + HP, PE + CVVH + HP; Non-CVVH group = PE, HP, PE + HP; Yes-CVVH group = PE + CVVH, HP + CVVH, PE + HP + CVVH.

blood purification treatment. We recommend that patients with severe stings be treated with PE initially, followed by other blood purification methods to improve the survive rate in patients.

DISCUSSION

In this study, extensive data review and telephone follow-ups were carried out to obtain detailed and accurate information. The risk factors related to developing an SC were determined by logistic regression analysis. Then, considering the important risk factors, we developed the WSS score to identify severe patients; the WSS will help us determine which patients need early blood purification treatment in future work. This score is also conducive to optimizing the usage of medical resources and improving the treatment success rate in wasp sting patients.

Because the dominant wasp species and races are different between North America and Asia, the clinical symptoms of victims after stings are significantly different. In our hospital, erythema, urticaria, edema and other skin manifestations were common (17.8%), but dyspnea and hypotension were rare occurrences, and few deaths were attributed to severe allergic reaction. In North America, the wasps that pose threats to human health mainly include *Vespula maculifrons* (yellowjackets), *Dolichovespula maculate* (bald-faced hornets) and *Polistes dominula* (paper wasps), whereas in China, they mainly include *V. basalis* (black-bellied hornet), *V. velutina nigrithorax* (yellow-legged hornet) and *V. mandarinia* (Asian giant hornet) [21]. The wasps in North America are less likely to cause death by mass envenomation. Some researchers estimate that the envenomation rate to induce death is approximately 20 stings/kg [22, 23]. Therefore, for a 60 kg adult, the lethal wasp sting dose is 1200 stings. However, this conclusion is substantially different from the results we obtained. From 2011 to 2020, in four Suining hospitals, patients with more than 30 stings had a 37% (61/163) mortality rate, and the mortality rate in those with more than 100 stings was 75% (6/8).

We suggest that patients with wasp stings should receive PE treatment as soon as possible after admission because wasp venom can exert effects on multiple organ systems within 10 min [24, 25]. Our results showed that PE significantly improved the mortality rate in wasp sting patients (14.3% versus 46.9%, P = 0.003), when the severity of the disease was similar between the Yes-PE group and the Non-PE group. Moreover, the mortality rates of patients in the four hospitals before the spring of 2017 and after the introduction of PE (2017–2021) were 7.9% (50/635) and 3.8% (19/505), respectively, with a significant difference (P = 0.004). In addition, among patients with more than 30 wasp stings, patients receiving PE treatment within 6 h since injury had a lower mortality rate than those receiving PE treatment within 6–12 h (11.1% versus 23.8%), but due to the small sample size, we could not draw a definite conclusion. In general, for patients with severe wasp stings, early PE treatment is the most important treatment method to reduce blood toxin concentration and prevent multiple organ failure.

Previous studies have identified some risk factors related to prognosis, such as the level of oliguria, shock and anemia [16, 26, 27]. In this study, we found that these factors were associated with an SC in only the univariate regression analysis. It was confirmed in our clinical practice that oliguria, shock and anemia were not early symptoms of wasp stings in most patients. We identified risk factors considering symptoms, signs and laboratory results at admission mainly to create a scale for identifying severe wasp sting patients and provide appropriate treatment in the early stage. Logistic regression showed that TCU, number of stings, TBIL and LDH were the most important risk factors for poor prognosis. The WSS is a simple scoring table that can identify critical cases in the first day of hospitalization; it is especially suitable for patients with a small number of stings but rapid disease progression. It can also prevent the unnecessary use of medical resources for noncritical patients, such as continuous renal replacement therapy and PE, especially during the peak wasp sting season.

There are some limitations of this study. We assigned points to each risk factor based on the results of logistic regression and an understanding of the clinical situation. Although this may be considered somewhat subjective, the AUC for the WSS score reached 0.918 in the validation set, indicating that the WSS may have good clinical application value. However, since it is difficult for patients and their families to identify species of wasps, we were unable to identify the specific effects of different kinds of hymenopteran venom on patients. We plan to address this in the future.

At present, there is no consensus on the screening and treatment processes for severe wasp stings. We identified the risk fac-

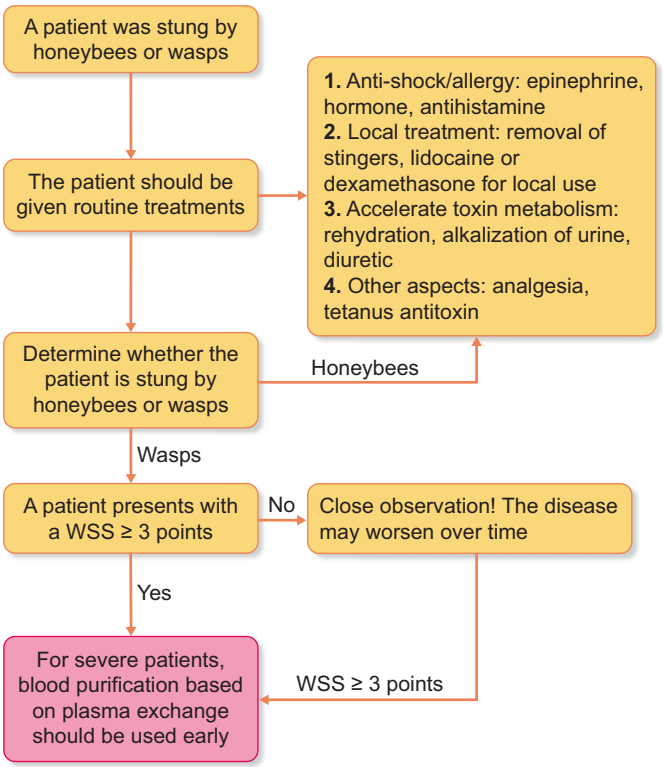

FIGURE 3: Flow chart of the diagnosis and treatment of wasp stings. Note: the vast majority of patients stung by honeybees only need routine treatments, and it is rare for these patients to need blood purification treatment due to organ dysfunction.

tors for development of an SC considering symptoms, signs and laboratory results on the first day of hospitalization. The logistic regression analysis showed that TCU, LDH, number of stings and TBIL were important risk factors for developing an SC, and the WSS was deduced by these variables. The results showed that a WSS $\geq$3 was an indication for blood purification. We recommend that patients with severe stings be treated with PE initially, followed by other blood purification methods.

SUPPLEMENTARY DATA

Supplementary data are available at *ckj* online.

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AUTHORS' CONTRIBUTIONS

Y.Liu and H.X. designed the study and drafted the manuscript; H.S., X.N., H.T., L.T., H.Z., G.Q., D.H., Q.H. and Q.Z. collected the data; Y. Liu, Y. Long performed data reorganization and statistical analysis; and all the listed authors approved the final version of the submitted manuscript.

CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

The data used in this study are available on the Open Science Framework (OSF) data repository [28].

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