

Multiple Organ Dysfunction Syndrome Caused by Sepsis: Risk Factor Analysis

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Purpose: To analyze the risk factors of multiple organ dysfunction syndromes (MODS) caused by sepsis.

Patients and Methods: A total of 180 patients with sepsis admitted to The First Affiliated Hospital of Harbin Medical University (No. 23, Post Street, Nangang District, Harbin 150001, Heilongjiang province, China) from July 2018 to June 2019 were selected and divided into a non-MODS group and a MODS group, with 90 cases in each group. Clinical data of the patients were retrospectively analyzed, and univariable and multivariable analyses were performed.

Results: The univariable analysis showed that there were no significant differences in terms of age, body temperature, heart rate, respiration, mean arterial pressure, RBC specific volume, blood sodium, serum potassium, and infection site ($P > 0.05$). Whereas significant differences were found between the groups in terms of gender, arterial blood pH, WBC count, Apache II score, blood glucose, creatinine, chronic medical history, surgery, and ventilator usage ($P < 0.05$). The growth of bacterial culture, the increase of creatinine level, chronic diseases and Apache II score were discovered to have significant effects on the occurrence of MODS through the multivariable logistic regression analysis.

Conclusion: Bacterial culture, serum creatinine level, history of chronic disease and Apache II score may be risk factors of MODS in sepsis patients.

Keywords: sepsis, multiple organ dysfunction syndrome, risk factors, systemic inflammatory response syndrome, sepsis patients, multivariable logistic regression analysis

Introduction

Sepsis is a systemic inflammatory response syndrome (SIRS) caused by either infectious or non-infectious factors.¹⁻³ It can easily develop into septic shock and multiple organ dysfunction syndromes (MODS) if not treated in a timely manner, and its fatality rate can be as high as 28–56%.⁴ Clinically, MODS can be categorized into Phase I immediate type and Phase II delayed type. To date, the preferred medical examination for MODS includes the examination of hemogram, blood, pathogenic bacteria and urine.^{5,6} Systemic inflammatory response syndrome may be viewed as the systemic expression of cytokine signals that normally function on an autocrine or paracrine level. Sepsis is defined as systemic inflammatory response syndrome caused by an infection. MODS may represent the end stage of severe systemic inflammatory response syndrome or sepsis. Many cells are involved, including endothelial cells and leukocytes and multiple proinflammatory and anti-inflammatory mediators (cytokines, oxygen free radicals, coagulation factors, and so forth). Various pathophysiological mechanisms have been postulated. The most

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popular theory is that the inflammatory process loses its autoregulatory capacity.^{5,6} Existing studies recognize that immune dysfunction caused by uncontrolled systemic inflammatory response is the main pathophysiological mechanism of sepsis, while the underlying pathogenesis is poorly understood.⁵ Involving multiple organs and pathophysiological systems, these diseases are closely related to the systemic inflammatory network, bacterial endotoxin, inflammatory mediators, immune dysfunction, intestinal bacterial and endotoxin translocation, coagulation dysfunction, and gene polymorphism. The pathogenesis of sepsis needs further clarification.⁷ This study was undertaken with an attempt to further elucidate the risk factors related to MODS caused by sepsis, and to take targeted prevention and treatment measures.

Patients and Methods

General Material

A total of 180 patients presenting to The First Affiliated Hospital of Harbin Medical University (No. 23, Post Street, Nangang District, Harbin 150001, Heilongjiang province, China) due to sepsis from July 2018 to June 2019 were selected for this research. Among them, there were 113 males and 67 females, who aged between 18–79 years (mean, 41.23±7.27) years old. There were 117 cases of acute abdominal disease (including suppurative cholangitis, acute severe pancreatitis, etc.), 6 cases of systemic infection, 19 cases of multiple injuries, 22 cases of abdominal trauma, and 16 other cases. Patients who were admitted to the intensive care unit (ICU) and then left or died in the ICU were included, while those who died within 24 hours after being sent to the ICU were excluded. The primary infection in patients with sepsis and diseases distribution were observed. The studies involving human participants were reviewed and approved by First Affiliated Hospital of Harbin Medical University. The patients provided their written informed consent to participate in this study. This study has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

Diagnostic Criteria

Sepsis is defined in accordance with the diagnostic criteria in the Guidelines for Emergency Treatment of Sepsis/Septic Shock in China (2018) issued by the Emergency Physicians Branch of the Chinese Physicians Association.

When the sequential organ failure assessment (SOFA) score rises by over 2 points from baseline, it is considered as sepsis. See Table 1. The criteria for organ dysfunction lie with the MODS score developed by Marshall, a Canadian scholar. See Table 2.

Methods

Patients were equally divided into a non-MODS group and a MODS group means according to their conditions. MODS standard was interpreted by the kidney, lung, heart, blood, liver and brain. Each organ is associated with several indicators. For instance, creatinine is considered the indicator for kidney, respiration for lung, heart rate for heart, concentration for sodium ion, serum potassium ion and blood glucose the indicators for blood. Each clinical indicator of the patient was recorded, and the worst value of each indicator was input into the database.

Predictor Variables

- (1) General items: gender, age, history of chronic diseases.
- (2) Post-inoculation (HPI): body temperature, heart rate, respiration, mean arterial pressure, arterial blood pH value, infection site, red blood cell (RBC), white blood cell (WBC) count, APACHE II score, surgery, blood sodium, blood serum potassium, blood glucose, serum creatinine, bacteria growth, ventilator usage.

Statistical Methods

SPSS22.0 statistical software was used for univariable analysis. Measurement data were represented by ($\bar{x}\pm s$) and the differences between groups were analyzed by *t*-test. Enumeration data were expressed as n(%) and the differences between groups were analyzed by χ^2 test. Logistic regression was used for multivariable analysis. $P < 0.05$ was considered statistically significant.

Results

Comparison of Measurement Index Between the Groups

No statistically significant difference was found in terms of age, body temperature, heart rate, respiration, mean arterial pressure, RBC hematocrit, blood sodium, serum potassium between the two groups ($P > 0.05$). The arterial blood pH value, the WBC count, APACHE II score, blood glucose, and creatinine were statistically different between the groups ($P < 0.05$). See Table 3 for details.

Table 1 SOFA Scoring Criteria

| System | Score/Points | | | | |
|---|--------------|------------------|--------------------------------------|--|--|
| | 0 | 1 | 2 | 3 | 4 |
| Respiratory system PaO ₂ /FiO ₂ /mmHg(kPa) | ≥400(53.3) | <400(53.3) | <300(40.0) | <200(26.7) + Mechanical ventilation | <100(13.3) + Mechanical ventilation |
| Coagulation system Blood platelet/ (10 ³ ·μL ⁻¹) | ≥150 | <150 | <100 | <50 | <20 |
| Liver Bilirubin / [mg·dL ⁻¹ (μmol·L ⁻¹)] | <1.2(20) | 1.2–1.9(20–32) | 2.0–5.9(33–101) | <6.0–11.9(102–204) | ≥12.0(204) |
| Cardiovascular system | MAP≥70mmHg | MAP<70mmHg | Dopamine <5 or dobutamine (any dose) | Dopamine 5.1–15.0 or epinephrine ≤0.1 or norepinephrine >0.1 | Dopamine >15 or adrenaline >0.1 or norepinephrine >0.1 |
| Central nerve system (GCS) | 15 | 13–14 | 10–12 | 6–9 | <6 |
| Kidney Creatinine / [mg·dL ⁻¹ (μmol·L ⁻¹)] | <1.2(110) | 1.2–1.9(110–170) | 2.0–3.4(171–299) | 3.5–4.9(300–400) | >4.9(440) |
| Urine Volume (mL·d ⁻¹) | – | – | – | <500 | <200 |

Table 2 MODS Score (Marshall Standard)

| Organ | Score | | | | |
|--|-------|-----------|-----------|-----------|-------|
| | 0 | 1 | 2 | 3 | 4 |
| Respiratory system (PaO ₂ /FiO ₂) | >300 | 226–300 | 151–225 | 76–150 | ≤75 |
| Kidney (Blood Cr μmol·L ⁻¹) | ≤100 | 101–200 | 201–350 | 351–500 | >500 |
| Liver (hemobilirubin μmol·L ⁻¹) | ≤20 | 21–60 | 61–120 | 121–240 | >240 |
| Cardiovascular system (PAR=HR×CVP/MAP) | ≤10.0 | 10.1–15.0 | 15.1–20.0 | 20.1–30.0 | >30.0 |
| Blood (platelet count 10 ⁹ ·L ⁻¹) | >120 | 81–120 | 51–80 | 21–50 | ≤20 |
| Nerve system (Glasgow Coma score) | 15 | 13–14 | 10–12 | 7–9 | ≤6 |

Comparison of Enumeration Indexes Between the Groups

There was no statistically significant difference between the two groups in the site of infection ($P > 0.05$), but significant differences were found in terms of frequencies of gender, history of chronic disease, surgery, bacterial culture and growth, and ventilator usage ($P < 0.05$). See [Table 4](#) for details.

Logistic Regression Analysis of Risk Factors for MODS in Sepsis Patients

The univariable analysis preliminarily screened out gender, arterial blood pH value, the WBC count, APACHE II

score, blood glucose, creatinine, chronic disease, bacterial culture growth, surgery, and ventilator usage, totaling 10 variables for binary logistic regression analysis. The result showed that the growth of bacterial culture, increased creatinine level, combined chronic diseases, a higher score of APACHE II are risk factors for MODS occurrence. See [Table 5](#) for details.

Site Composition of Primary Infection in Patients with Sepsis

Compared with the incidence of respiratory tract infection, the incidence of digestive tract, abdominal cavity,

Table 3 Comparison of Measurement Data Between the Two Groups ($\bar{x}\pm s$)

| Observation Index | MODS Group (n=90) | Non-MODS Group (n=90) | P |
|--|-------------------|-----------------------|--------|
| Age (year old) | 46.04±17.42 | 43.83±15.21 | 0.366 |
| Body temperature (°C) | 38.53±0.91 | 38.58±0.94 | 0.717 |
| Heart rate (times/min) | 113.80±18.07 | 110.92±16.81 | 0.269 |
| Respiration (times/min) | 29.44±6.42 | 27.84±5.05 | 0.065 |
| MAP (mmHg) | 88.15±19.35 | 90.42±18.01 | 0.416 |
| Arterial blood Ph value | 8.42±0.23 | 7.45±0.08 | <0.001 |
| RBC specific volume (%) | 34.42±9.95 | 36.76±9.28 | 0.105 |
| WBC count ($\times 10^9 \cdot L^{-1}$) | 19.88±5.34 | 16.86±5.91 | <0.001 |
| APACHE II Score (points) | 26.14±11.36 | 16.13±6.86 | <0.001 |
| Blood sodium ($mmol \cdot L^{-1}$) | 138.88±8.67 | 138.05±7.11 | 0.483 |
| Serum kalium ($mmol \cdot L^{-1}$) | 5.38±0.92 | 5.35±0.64 | 0.799 |
| Blood glucose ($mmol \cdot L^{-1}$) | 21.33±6.30 | 10.65±3.92 | <0.001 |
| Creatinine ($\mu mol \cdot L^{-1}$) | 185.46±235.16 | 84.03±94.51 | <0.001 |

Table 4 Comparison of Enumeration Data Between the Two Groups [n (%)]

| Observation Index | MODS Group (n = 90) | Non-MODS Group (n = 90) | P |
|---|---------------------|-------------------------|-------|
| Gender (Male/Female) | 71/19 | 58/32 | 0.032 |
| History of chronic disease (Yes/No) | 36/54 | 17/73 | 0.002 |
| Infection site (Respiration system/Other than Respiration system) | 73/17 | 81/9 | 0.090 |
| Surgery (Surgery/Non-surgery) | 39/51 | 54/36 | 0.025 |
| Bacteria culture growth (Yes/No) | 35/55 | 53/37 | 0.007 |
| Ventilator usage (Applied/Not applied) | 76/14 | 85/5 | 0.029 |

nervous system and other infections was significantly lower ($\chi^2=34.844$, $P < 0.05$). See [Figure 1](#) for details.

Disease Distribution in the Two Groups

The diseases of the patients are mainly diffuse peritonitis, pancreatitis, hepatobiliary diseases, multiple injuries,

intestinal obstruction, chest diseases, limb diseases, etc. No significant difference was observed in the disease distribution between the two groups ($P > 0.05$). See [Figure 2](#) for details.

Discussion

Sepsis serves as the organ dysfunction syndrome caused by the imbalance of the human body's response to infection.⁸ After infection, inflammatory response cells are activated by bacterial toxins and will release inflammatory mediators such as interleukin-6 (IL-6), interleukin-1 (IL-1) and tumor necrosis factor- α (TNF- α), triggering systemic or local inflammatory responses.⁹⁻¹¹ Its clinical manifestations include changes in mental state, shortness of breath, palpitation, fever, chills and other symptoms, and in severe cases, MODS will develop.¹² MODS refers to the clinical syndrome in which at least two systems or organs suffer from simultaneous or sequential dysfunction during major surgery, infection, shock, poisoning and severe trauma, thus undermining the stability of the internal environment.¹³⁻¹⁵ Early Goal-Directed Therapy (EGDT) regimen, early monitoring of risk factors and active fluid resuscitation can reduce the incidence and mortality of MODS, and plays a key role in early control of sepsis.¹⁶

Table 5 Logistic Regression Analysis of Risk Factors for MODS in Sepsis Patients

| Factors | Estimated Parameter | P value | OR Value | 95% CI |
|----------------------------|---------------------|---------|----------|--------------|
| Bacterial culture growth | -1.776 | 0.032 | 0.275 | 0.045, 0.787 |
| Increased creatinine level | 0.061 | <0.001 | 1.062 | 1.028, 1.075 |
| Combined chronic diseases | -1.758 | 0.029 | 0.204 | 0.049, 0.768 |
| Increased APACHE II score | 0.339 | <0.001 | 1.367 | 1.132, 1.394 |

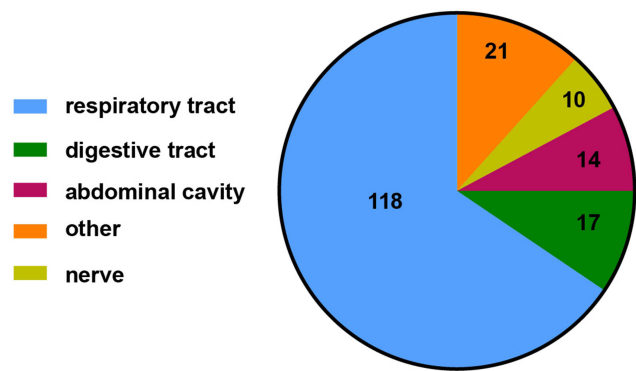


Figure 1 Site composition of primary infection in patients with sepsis.

The univariable analysis of this research showed that the two groups of patients had significant differences in gender, arterial blood pH value, WBC count, APACHE II score, blood glucose, serum creatinine, chronic disease, bacterial culture growth, surgery, ventilation treatment. Additionally, it is documented that patients with sepsis caused by shock, infection, trauma and other factors will have pathophysiological changes in their circulatory, respiratory and nervous systems, including tissue and organ ischemia and hypoxia, renal function decline, electrolyte disturbance, shortness of breath, blood pressure drop, and acid-base imbalance.¹⁷ On account of these, MODS and even death may arise if early symptoms are not treated in time.

The multivariable logistic stepwise regression analysis showed that the growth of bacterial culture, increased creatinine level, combined chronic diseases, a higher score of APACHE II are risk factors for the occurrence of MODS. As a vital index for evaluating sepsis patients, APACHE II score reflects the association between the

body's physiological disorders and the severity of sepsis, which is positively correlated with MODS.¹⁸ Moreover, it has been pointed out by a prior trial that patients with sepsis combined with cardiopulmonary diseases, diabetes, hypertension and other chronic diseases have a higher risk of developing MODS than others.¹⁹ Serum creatinine is also an important indicator to observe the development of sepsis. Systemic inflammatory reactions owing to infection can easily cause changes in the circulatory system. It in turn dilates blood vessels, slows down blood flow and lowers blood pressure, and subsequently further decreases renal blood flow, impairs renal function and increases serum creatinine. Our study demonstrated that serum creatinine in the MODS group was significantly higher than that in the non-MODS group. Taken together, early protection of renal function and improvement of microcirculation are of paramount importance for the treatment of MODS.²⁰

Hence, we suggest that gender, arterial blood pH value, the WBC count, APACHE II score, blood glucose, serum creatinine, chronic disease, surgery, bacterial growth, ventilator usage and other factors were relevant to the development of MODS in patients with sepsis in the Emergency Department in The First Affiliated Hospital of Harbin Medical University (No. 23, Post Street, Nangang District, Harbin 150001, Heilongjiang province, China.). Among them, bacteria culture growth, increased creatinine level, combined chronic diseases, a higher score of APACHE II appear to be risk factors for the occurrence of MODS. Therefore, early monitoring of these factors and timely control measures can improve the

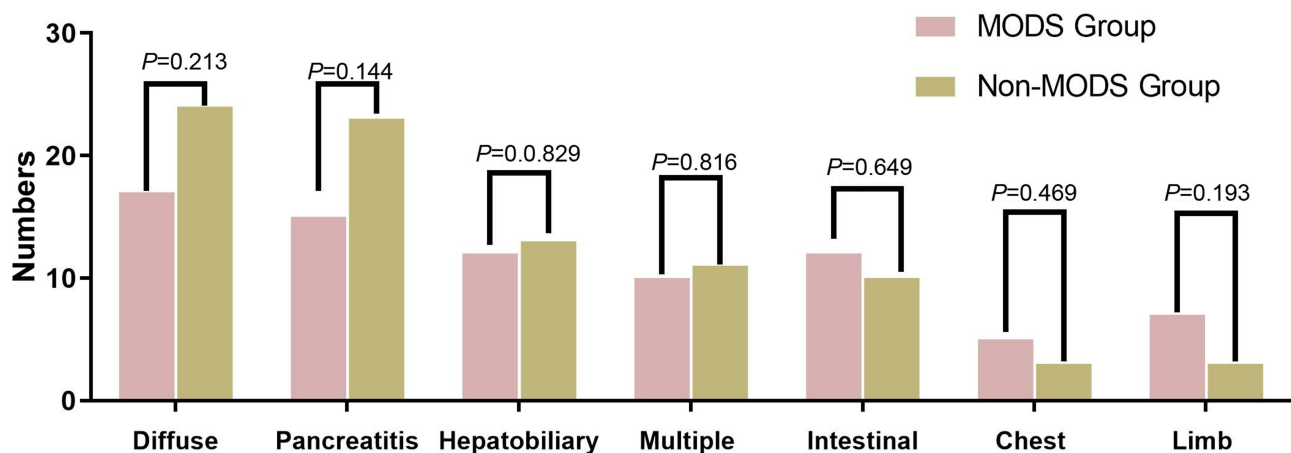


Figure 2 Disease distribution.

cure rate and reduce the fatality rate of sepsis patients. Moreover, the confounding and omitted variables of the results were critical and should be emphasized in future. Meanwhile, a multivariable model with a less selective set of explanatory variables should be performed in future studies.

Thus, we concluded that Bacterial culture, serum creatinine level, history of chronic disease and Apache II score might be risk factors of MODS in sepsis patients.

Disclosure

The authors report no conflicts of interest in this work.

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