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HEALTH SCIENCES

Correlation Between Early Serum Myoglobin Levels and the Incidence and Prognosis of Intensive Care Unit-Acquired Weakness (ICU-AW) in Septic Shock Patients: A Comparative Study

LING WANG & DENGYAN LONG

Abstract: Intensive Care Unit-acquired weakness (ICU-AW) is a common complication that significantly impedes patient recovery. In the study, we investigated the correlation between early serum myoglobin levels in patients with septic shock due to pneumonia, and the incidence of ICU-AW, duration of mechanical ventilation, and prognosis. Patients were classified based on the development of ICU-AW within the first 10 days of ICU admission. We measured serum myoglobin levels upon ICU entry, and analyzed demographic data, APACHE II scores, use of mechanical ventilation, and clinical outcomes, including mortality and duration of mechanical ventilation. The results indicated significantly elevated serum myoglobin levels in the ICU-AW group, correlated with prolonged mechanical ventilation and increased mortality. ROC analysis revealed myoglobin as a promising biomarker for predicting ICU-AW, with an area under the curve of 0.843 (95% *CI*: 0.819~0.867), demonstrating a sensitivity of 76.00% and specificity of 82.30%. These findings underscored serum myoglobin as a predictive biomarker for early ICU-AW in septic shock patients, highlighting its potential to guide clinical decision-making.

Key words: septic shock, intensive care unit-acquired weakness, myoglobin, prognosis, correlation, biomarker.

INTRODUCTION

Septic shock is a severe disease resulting from infection (Evans et al. 2021, Norse et al. 2021), frequently requiring treatment in the intensive care unit (ICU) and is associated with numerous complications, including ICU-acquired weakness (ICU-AW) (Wang et al. 2020, Panahi et al. 2020). ICU-AW is a common complication in critically ill patients, primarily characterized by significant symmetric limb muscle weakness, potentially leading to prolonged mechanical ventilation, increased medical expenses, and adverse outcomes (Vanhorebeek et al. 2020, Li et al. 2020). While the precise etiology of ICU-AW remains elusive, many scholars believe that neurologic and/or muscular dysfunction plays a pivotal role (Saccheri et al. 2020, Taylor 2021, Siao et al. 2020). Myoglobin, a heme protein present in skeletal and cardiac muscles, is widely recognized as a biomarker for muscle injury. Elevated serum myoglobin levels can indicate muscle damage, thus investigating its correlation with ICU-AW can be crucial for understanding the disease mechanism. The aim of this study was to explore the association between serum myoglobin levels and the incidence and prognosis of ICU-AW in patients with septic shock, providing a reference for clinical diagnosis and treatment.

MATERIALS AND METHODS

Data source

The study selected patients from the general ICU of People's Hospital of Qiandongnan Miao and Dong Autonomous Prefecture admitted between January 1, 2022, and June 1, 2023. Inclusion criteria were patients over 18 years old with pneumonia-induced septic shock. Exclusion criteria included uncertain infection sites, diseases affecting the diagnosis of ICU-AW like spinal fractures, significant central nervous system defects, severe myasthenia gravis, polymyositis, and those who declined treatment or had incomplete data.

Ethical considerations

This research received approval from the Medical Ethics Committee of People's Hospital of Qiandongnan Miao and Dong Autonomous Prefecture (Approval No.: 2021012).

Diagnostic criteria

Diagnosis of ICU-AW was based on the Medical Research Council (MRC) limb muscle strength grading scale, which ranges from 0-5, with a maximum score of 60. A cumulative score below 48 was diagnostic of ICU-AW (Siao et al. 2020). Criteria for septic shock diagnosis aligned with sepsis-3, it involved a confirmed infection causing life-threatening organ dysfunction, with the patient still requiring vasopressor support to maintain a mean arterial pressure > 65 mmHg after adequate fluid resuscitation (Evans et al. 2021).

Treatment protocols

All patients, upon admission, received measures to stabilize vital signs and antibiotic treatments based on disease characteristics and microbiological culture results. When necessary, patients underwent mechanical ventilation, continuous blood purification (CVVH mode), blood transfusions, etc. All patients with septic shock received early bundled care management, vital organ support as needed, and maintenance of nutrition and internal environment stability.

Research methodology

Upon ICU admission, 3ml of venous blood was drawn from patients to test for myoglobin using the centaur XP biochemical analyzer from SIEMENS AG, Germany, employing chemiluminescence as the detection method. 24 hours after ICU admission, daily muscle strength measurements of the limbs were conducted, which included manual evaluations of three functional muscle groups of the upper limbs (shoulder abduction, elbow flexion, and wrist extension) and lower limbs (hip flexion, knee extension, and dorsiflexion of the ankle). Muscle strength was quantified on a scale from 0 (no observed movement) to 5 (normal contraction against full resistance). Patients were observed for ICU-AW coexistence on day 10 (if patient's duration of ICU stay was less than 10 days, the existence of ICU-AW at the time of ICU discharge was recorded), and were categorized into ICU-AW and non-ICU-AW groups. At one month, observations were made for patient mortality and the duration of mechanical ventilation during the ICU stay. Differences between the two groups in terms of gender, age, APACHE II score, proportion of mechanical ventilation, myoglobin, duration of mechanical ventilation, duration of ICU stay, and mortality rate were compared. Statistical methods were employed to analyze the correlation between myoglobin levels and ICU-AW, as well as prognosis. The predictive capability of myoglobin for ICU-AW was also examined.

Statistical methodology

The research employed SPSS 24.0 for data processing and analysis. The

Kolmogorov-Smirnov test was used to verify the normality of the quantitative data. Normally distributed quantitative data were represented by mean ± standard deviation ($\bar{x} \pm s$), and independent sample T-tests were used for inter-group comparisons. Non-normally distributed quantitative data were represented by median (quartile) [$M(Q_{25}, Q_{75})$], and the Mann-Whitney U test was used for inter-group comparisons. Count data were tested using the χ^2 test. Correlation was analyzed using the Spearman correlation analysis. Predictive capability was assessed via the receiver operating characteristic (ROC) curve analysis. A P-value less than 0.05 was considered statistically significant.

RESULTS

Case information

A total of 263 cases were collected, all of which were patients with pneumonia-induced septic shock and simultaneously met the diagnostic criteria for sepsis-3. Among them, 8 cases had spinal fractures, 15 cases had acute cerebral infarction, 3 cases had basal ganglia cerebral hemorrhage, 2 cases had myasthenia gravis, and 2 cases had polymyositis. These cases were excluded as they could impact the diagnosis of ICU-AW. Additionally, 22 cases where treatment was abandoned were also excluded. In the end, 211 patients were included in the study, comprising 130 males and 81 females. Age ranged from 18 to 94 years, with an average age of 62.83 ± 18.45 years. Of these, 129 were diagnosed with ICU-AW, while 82 were not. Within one month, 26 cases died and 185 cases survived. The average myoglobin vilue was 1027.56ng/ml, significantly higher than the normal level (less than 110ng/ml); ICU stay ranged from 2-30 days, averaging 10.21 days; mechanical ventilation duration ranged from 0-720 hours, with an average of 138.41 hours.

General data comparison

Regarding gender distribution, there was no significant difference between the two groups (χ^2=1.716, P>0.05). Compared to the non-ICU-AW group, the ICU-AW group had higher values in age, APACHE II score, proportion of mechanical ventilation, myoglobin, duration of mechanical ventilation, ICU stay duration, and mortality rate ($\chi^2/t/Z$ values were 0.707, 5.654, 10.314, -2.412, -6.780, -9.415, 7.726, with P<0.05 respectively). All these differences were statistically significant, detailed in Table I and Figure 1.

Correlation analysis

Using Spearman correlation analysis, we identified that myoglobin levels exhibited a positive correlation with ICU-AW, duration of mechanical ventilation, and mortality rates (with r-values of 0.166, 0.277, and 0.258 respectively, all P<0.05).

Table I. Comparison of general information between two groups.

Parameter	ICU-AW group(n=129)	Non ICU-AW group(n=82)	$\chi^2/t/Z$	p-value
Gender(Male/Female)	84/45	46/36	1.716	0.195
Age(Years)	65.21±18.98	59.10±17.03	0.707	0.019
APACHEII Score (points)	19.57±2.33	16.42±2.89	5.654	0.000
Mechanical ventilation (n'%)	106(82.17%)	51(62.20%)	10.314	0.002
Myoglobin(ng/ml)	891.00(299.00,1720.00)	648.00(153.00,1212.75)	-2.412	0.016
Mechanical ventilation duration(hours)	120.00(21.50,280.00)	12.00(0,48.00)	-6.780	0.000
Duration of ICU stay(days)	10(7,19)	3(2,5)	-9.415	0.000
Death (n'%)	22(17.05%)	4(4.88%)	7.726	0.009

Predictive capability of myoglobin for ICU-AW

Utilizing myoglobin as the test variable and ICU-AW status as the state variable, an ROC curve was constructed (assigned values: yes=1, no=0). With a cut-off value of 1362.5ng/ml, the area under the ROC curve stood at 0.843 (95% *CI*: 0.819~0.867), boasting a sensitivity of 76.00%, a specificity of 82.30% and Youden's index of 0.583. Refer to Figure 2 for details.

DISCUSSION

In patients with septic shock, elevated levels of myoglobin can be attributed to various factors including neuromuscular damage, ischemia-reperfusion injury, cellular destruction, and metabolic abnormalities (Hosseinpour et al. 2021, Huang et al. 2021). The presence of tissue hypoperfusion and systemic inflammatory response may lead to mitochondrial dysfunction and direct hypoxic injury in neuromuscular tissues. Following fluid resuscitation, ischemia-reperfusion injury may occur. This complex cascade of injuries may subsequently result in cellular dysfunction and metabolic abnormalities, inducing the rupture of muscle fibers and cell death. Consequently, myoglobin is released into the circulation, leading to an elevation in serum creatine kinase levels. This physiological change may represent a critical factor in the development of ICU-AW.

Our study revealed a correlation between elevated serum myoglobin levels and the incidence of ICU-AW and mortality. This offered a new perspective on the association between myoglobin and ICU-AW, suggesting that myoglobin could potentially serve as an early biomarker for predicting the onset of ICU-AW. Furthermore, some clinical studies hade found that myoglobin levels correlate with the duration of mechanical ventilation, length of hospital stay, and prognosis, which were closely tied to the severity and outcome in ICU-AW patients (Yao et al. 2016, Yu et al. 2018, Zhang et al. 2021). This was consistent with our findings.

Monitoring serum myoglobin levels in clinical practice is particularly vital. Firstly, as an indicator of muscle damage, monitoring myoglobin can aid in the timely identification of issues and subsequent interventions (Zhang et al. 2021, Apple et al. 2020). Secondly, due to its correlation with ICU-AW onset, myoglobin can be viewed as a marker for ICU-AW (Wang

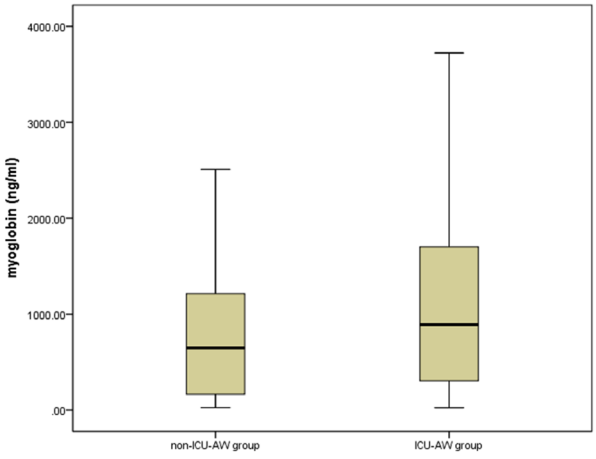

Figure 1. Myoglobin levels in two groups.

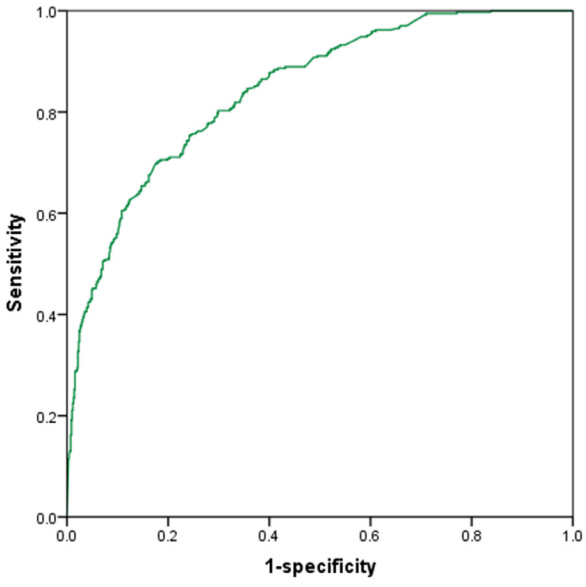

Figure 2. ROC curve illustrating the predictive capability of myoglobin for ICU-AW.

et al. 2020, Chen et al. 2018, Zhang et al. 2020). By monitoring myoglobin levels, physicians can more accurately assess the extent of a patient's muscle damage, speculate on their prognosis, and formulate treatment strategies accordingly (Liu et al. 2024, Aakre et al. 2019).

Nevertheless, research linking myoglobin with ICU-AW remains relatively scarce. While our study indicated an association between serum myoglobin levels and the onset of ICU-AW, the underlying mechanisms were not yet fully elucidated. It's worth noting the limitations of our study: we only selected patients with pneumonia-induced sepsis, and the sample size was small, which may affect result stability. Furthermore, being a single-center study, regional variations might exist. Future research should consider expanding to larger samples and multi-center studies, further confirming and deepening the understanding of the relationship between myoglobin and ICU-AW. Concurrently, combining other clinical indicators will enhance the accuracy of ICU-AW prediction and provide a more profound understanding of its biological mechanisms, potentially aiding the development of therapeutic strategies.

In conclusion, serum myoglobin levels in patients with septic shock have a significant correlation with ICU-AW and its prognosis and can serve as an early biomarker for predicting ICU-AW. However, to better understand the role of myoglobin in ICU-AW, further research is imperative, aiming to offer more strategies for the treatment and improved prognosis of septic patients.

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