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Rhabdomyolysis in intensive care unit—distinctive clinical indicators and prognosis

Zhen Wang[1*], Qing Wang[2], Jinghan Chen[1] and Leiming Cai[3]

Abstract

Background Rhabdomyolysis is commonly encountered in intensive care unit (ICU), yet its clinical features and prognostic indicators have not been comprehensively defined. This study aims to identify clinical characteristics and outcomes of ICU patients with rhabdomyolysis, and assess if rhabdomyolysis predicts outcomes.

Methods This retrospective study investigated patients admitted to the ICU of Shanghai Baoshan District Wusong Central Hospital from 2022 to 2023. Clinical and laboratory indices, along with discharge outcomes, were analyzed.

Results The study included 151 patients, divided into Control group (CK ≤ 1000 U/L, $n=117$) and RML group (CK > 1000 U/L, $n=34$) groups. The RML group showed higher proportions of male gender (76.5% vs. 56.4%, $p=0.035$), infection (88.2% vs. 68.4%, $p=0.022$), muscle weakness (41.2% vs. 13.7%, $p=0.035$), and myoglobin > 1000 U/L (55.9% vs. 14.5%, $p<0.001$), but lower incidence of malignant tumors (0% vs. 17.9%, $p=0.017$). The poor outcome rate (POR, the combined rate of death and cessation of treatment) was significantly higher in the RML group (52.9% vs. 33.3%, $p=0.038$). Multivariate logistic regression analysis identified male gender [OR, 1.120–7.147; $p=0.028$], sepsis [OR, 1.234–10.949; $p=0.019$], and mechanical ventilation [OR, 1.489–8.478; $p=0.004$] as independent risk factors for poor outcome in ICU patients. Rhabdomyolysis was not an independent risk factor.

Conclusions ICU patients with rhabdomyolysis experienced a significantly higher rate of poor outcomes. Male gender, sepsis, and mechanical ventilation were identified as independent risk factors for poor outcomes, while rhabdomyolysis itself was not found to be an independent risk factor. Prospective research is needed to validate these findings in diverse ICU populations.

Keywords Intensive care unit, Creatine kinase, Rhabdomyolysis, Prognosis

Background

Rhabdomyolysis is a serious medical condition characterized by the rapid breakdown of skeletal muscle tissue. This process leads to the release of various cellular components into the bloodstream and surrounding tissues, including proteins such as myoglobin and enzymes like creatine kinase (CK), as well as electrolytes. The severity of rhabdomyolysis can vary significantly, ranging from mild cases with minimal symptoms and slightly elevated CK levels to severe, life-threatening cases [1]. Although traumatic injury is a common cause, a wide range of other factors can also trigger this condition. Previous

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studies and our research have confirmed that factors such as infection, certain medications, pancreatitis, alcohol consumption, electrolyte imbalance, excessive physical exertion, and heatstroke can also lead to elevated CK [2–4]. The diverse range of potential causes underscores the complexity of this condition and the importance of considering rhabdomyolysis in various clinical scenarios.

Given the diverse etiology of rhabdomyolysis, patients admitted to the intensive care units (ICUs) with critical illnesses are particularly susceptible to developing rhabdomyolysis. This condition can lead to severe complications, including acute kidney injury (AKI) and multiple organ dysfunction syndrome(MODS) [5]. Previous studies have demonstrated a positive correlation between elevated creatine kinase (CK) levels and the incidence of AKI [6]. Despite its clinical significance, the specific characteristics and risk factors contributing to mortality or adverse outcomes in ICU patients with rhabdomyolysis are not fully understood. Moreover, the relationship between elevated serum CK levels and increased patient mortality remains controversial [5, 7]. In light of these uncertainties, the objective of this study is to investigate the clinical characteristics and outcomes of ICU patients diagnosed with rhabdomyolysis and to determine whether rhabdomyolysis constitutes a risk factor for outcomes within this patient population.

Methods

A retrospective study was conducted on ICU patients admitted to Shanghai Baoshan District Wusong Central Hospital from January 2022 to December 2023. The study adhered to the principles of the Declaration of Helsinki and received approval from the Ethics Committee of Shanghai Baoshan District Wusong Central Hospital (Project No. 2024-P-01).

Patient data, including medical history, laboratory test results, hospitalization expenses, clinical outcomes, and other relevant information, were extracted from the patients' medical records. The inclusion criteria consisted of ICU patients aged 18 years and older who underwent CK testing. Patients with elevated CK levels due to myocardial infarction or acute coronary syndrome were excluded. The ICU patients were stratified into two groups based on peak serum creatine kinase (CK) levels: the control group (CK ≤ 1000 U/L) and the rhabdomyolysis (RML) group (CK > 1000 U/L). This stratification was based on the established diagnostic threshold for rhabdomyolysis, where a CK level exceeding 1000 U/L is considered diagnostic of the condition [1]. Our diagnosis of muscle weakness is based on the documentation of weakness symptoms in the patient's medical history and/or confirmation through physical examination, which reveals decreased muscle strength.

The Acute Physiology and Chronic Health Evaluation II (APACHE II) system is derived from data collected from patients in the intensive care unit (ICU) and is frequently associated with the severity of disease and patient prognosis [8]. Previous studies have shown that average APACHE II scores are generally higher in non-surgical patients [9]. We compared APACHE II scores between the control group and the rhabdomyolysis group. Additionally, we conducted a subgroup analysis stratifying patients by surgical versus non-surgical status.

AKI is commonly observed in ICU patients and is associated with reduced survival rates [10]. The diagnostic criteria for AKI follow the definition established by Kidney Disease: Improving Global Outcomes (KDIGO) [11]. To investigate the effect of rhabdomyolysis and acute AKI on poor outcomes in patients, we categorized ICU patients using three distinct grouping methods. First, patients were divided into a control group and a rhabdomyolysis group based on the presence or absence of rhabdomyolysis. Second, patients were classified into non-AKI and AKI groups based on the presence or absence of acute kidney injury. Finally, for the third grouping, patients were categorized into four subgroups based on all possible combinations of rhabdomyolysis and AKI: rhabdomyolysis alone, AKI alone, both rhabdomyolysis and AKI, and neither condition.

Categorical data were presented as frequencies and percentages [n (%)], with statistical analyses conducted using the Pearson chi-square test or Fisher's exact test, as appropriate. Descriptive statistics for non-normally distributed data were summarized using the median and interquartile range (IQR). The Mann-Whitney U test, a non-parametric statistical method, was employed to assess potential differences between two independent samples. Factors with p-values less than 0.1 in the univariate analysis were included in the logistic regression analysis to assess potential predictors [12]. Multivariate logistic regression analysis was used to identify potential predictors of clinical outcomes, with a p-value of < 0.05 considered statistically significant. All statistical analyses were performed using SPSS software version 27.0 (IBM Corporation, Armonk, NY, USA).

Results

Clinical characteristics of ICU patients with and without rhabdomyolysis

As shown in Fig. 1, of the 175 patients admitted to the ICU at Wusong Central Hospital (Baoshan District, Shanghai) between January 2022 and December 2023, 24 patients did not undergo CK testing.The study included a total of 151 patients, with 117 patients in the control group and 34 in the rhabdomyolysis (RML) group. Table 1 presents the clinical characteristics of these patients. Among all subjects, 60.9% were male, with a significantly

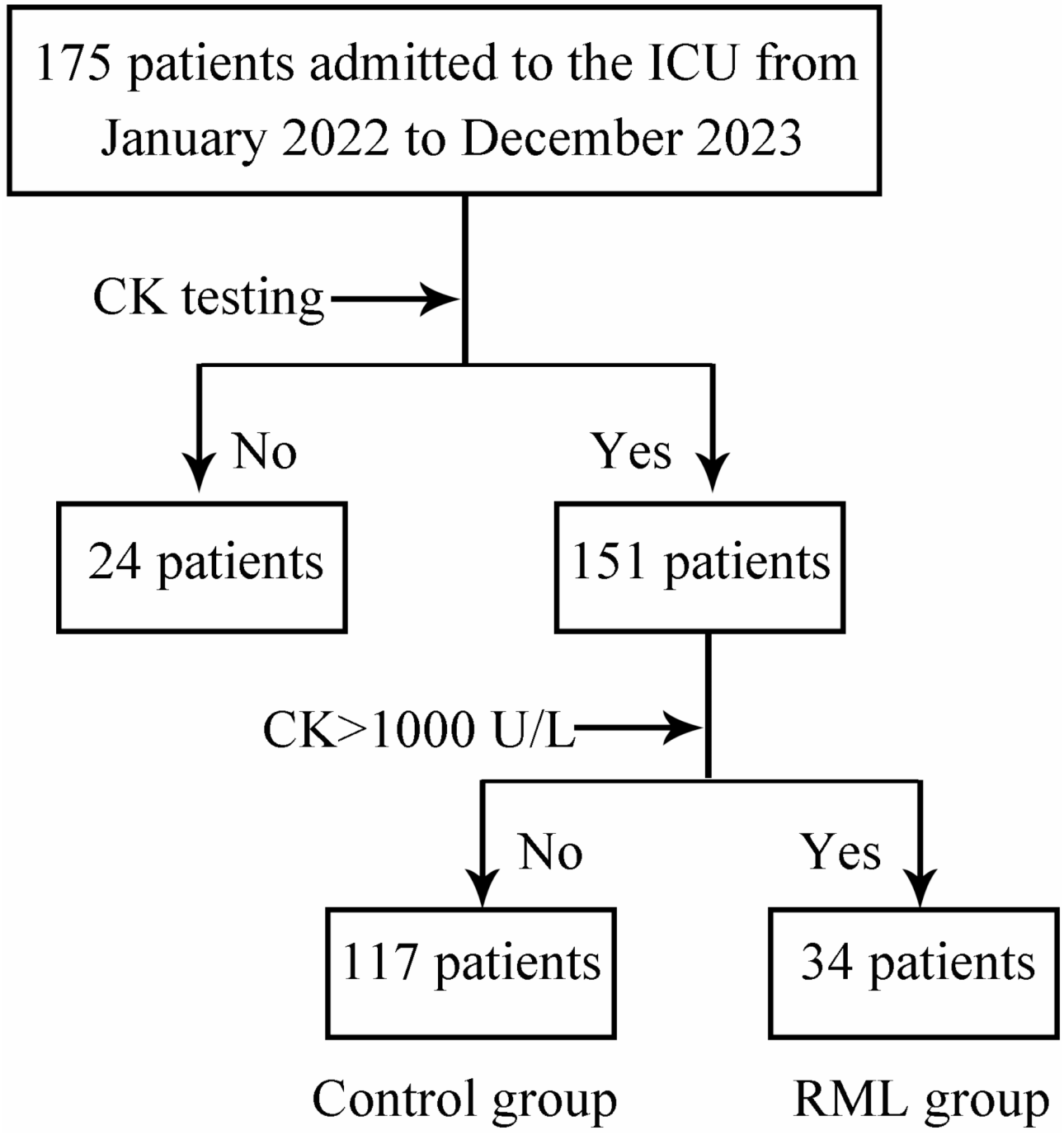

Fig. 1 Flowchart of patient selection process. ICU: Intensive Care Unit. CK: creatine kinase. RML group: Rhabdomyolysis group

higher proportion of males in the RML group compared to the control group (76.5% vs. 56.4%, $p = 0.035$). The median age of the patients was 73 years, with an interquartile range (IQR) of 62 to 81 years. As shown in Table 1; Fig. 2A, the length of hospital stay before ICU admission(pre-ICU LOS) was significantly shorter in the RML group (0.0 [0.0–2.25] days) compared to the control group (2.0 [0.0–6.0] days; $p = 0.026$). Patients with rhabdomyolysis had a significantly lower rate of pre-ICU stays > 2 days compared to the control group (23.5% vs. 47.9%, $p = 0.011$). As illustrated in Fig. 2B, among the 34 patients with rhabdomyolysis, 4 met the diagnostic criteria while in the general ward prior to ICU admission, whereas the remaining 30 met the criteria after admission to the ICU.

Table 1 Clinical characteristics of ICU patients without and with Rhabdomyolysis

	Total ($n=151$)	Control group ($n=117$)	RML group ($n=34$)	*p* value
General Condition and Status Before Admission to the ICU				
Population information				
Male gender	92(60.9)	66(56.4)	26(76.5)	0.035
Age(years)	73(62–81)	74(64-82.5)	70(52.5–80)	0.110
pre-ICU LOS (days)	2.0(0.0–5.0)	2.0(0.0–6.0)	0.0(0.0-2.25)	0.026
pre-ICU LOS (> 2 days)	64(42.4)	56(47.9)	8(23.5)	0.011
Reason for hospitalization				
Cerebrovascular Accident	54(35.8)	38(32.5)	16(47.1)	0.118
Fracture	28(18.5)	25(21.4)	3(8.8)	0.098
Infectious Disease	18(11.9)	13(11.1)	5(14.7)	0.788
Malignant Tumor	21(13.9)	21(17.9)	0(0.0)	0.017
other	30(19.9)	20(17.1)	10(29.4)	0.113
Past medical history				
Hypertension	83(55.0)	61(52.1)	22(64.7)	0.195
Diabetes	43(28.5)	31(26.5)	12(35.2)	0.317
Coronary artery disease	35(23.2)	26(22.2)	9(26.4)	0.605
Trauma	53(35.1)	42(35.9)	11(32.4)	0.703
Fall	33(21.9)	22(18.8)	11(32.4)	0.092
Conditions during ICU stay				
Apache II score*				
Apache II	14(10-20.5)	14(10–20)	14.5(10–24)	0.536
Apache II(≥ 15)	70(46.9)	53(46.1)	17(50.0)	0.688
Surgery($n=89$)	37(41.6)	29(38.7)	8(57.1)	0.198
Non-surgery($n=60$)	33(55.0)	24(60.0)	9(45.0)	0.271
Comorbidities and complications				
Cumulative infection #	110(72.8)	80(68.4)	30(88.2)	0.022
Acidosis	23(15.2)	17(14.5)	6(17.6)	0.656
Shock	47(31.1)	34(29.1)	13(38.2)	0.309
MODS	21(13.9)	14(12.0)	7(20.6)	0.319
Sepsis	31(20.5)	20(17.1)	11(32.4)	0.053
Acute Kidney Injury	70(46.4)	50(42.7)	20(58.8)	0.098
Manifestations of rhabdomyolysis				
Muscle pain	58(38.4)	45(38.5)	13(38.2)	0.981
Muscle weakness	30(19.9)	16(13.7)	14(41.2)	< 0.001
Dark-colored urine	0(0.0)	0(0.0)	0(0.0)	1.000
Treatment				
Surgery	90(59.6)	76(65.0)	14(41.2)	0.013
Mechanical ventilation	73(48.3)	52(44.4)	19(55.9)	0.075
Lipid-Lowering	20(13.2)	14(12.0)	6(17.6)	0.567
Blood Purification Therapy	15(9.9)	10(8.5)	5(14.7)	0.465

Categorical data are presented as frequencies and percentages [n (%)]. Non-normal distributions are summarized using the median and interquartile range (IQR). pre-ICU LOS: the length of hospital stay before ICU admission. MODS: Multiple Organ Dysfunction Syndrome. Apache II(≥ 15) *: Due to the unavailability of APACHE II data for certain cases, the actual number of APACHE II score for the control group and RML group was 115/34(Among the total patients), 75/14(among surgical patients),40/20(among non-surgical patients) respectively. Cumulative infection#: encompassing both infections present at the time of admission and those acquired after ICU admission

The primary reasons for hospitalization were cerebrovascular accidents (35.8%), fractures (18.5%), infectious diseases (11.9%), and malignant tumors (13.9%). Of the 28 patients with fractures, 9 had multiple fractures, including 6 in the control group and 3 in the rhabdomyolysis group. The incidence of malignant tumors was significantly lower in the RML group compared to the control group (0% vs. 17.9%, $p=0.017$). Among the 21 tumor patients, 18 underwent tumor surgery, 1 experienced gastrointestinal hemorrhage, 1 developed a pulmonary infection following tumor surgery and chemotherapy, and 1 was diagnosed with acute promyelocytic leukemia complicated by cerebral hemorrhage.Regarding patient history, there were no significant differences between the two groups in the incidence of hypertension, diabetes, coronary heart disease, trauma, and fall.

As shown in Table 1, the median APACHE II scores were 14 (IQR: 10–20) in the control group and 14.5 (IQR: 10–24) in the RML group, with no significant difference between the two ($p=0.536$). Similarly, the proportion of patients with APACHE II scores ≥ 15 showed no significant difference between the RML group (50.0%) and the control group (46.1%) ($p=0.688$). Further analysis by surgical and non-surgical subgroups also revealed no significant differences in APACHE II scores between the two groups.

Among comorbidities and complications, the incidence of cumulative infection was significantly higher in the RML group (88.2% vs. 68.4%, $p=0.022$). Although the incidences of sepsis (32.4% vs. 17.1%, $p=0.053$) and AKI (58.8% vs. 42.7%, $p=0.098$) were higher in the RML group, these differences were not statistically significant. Regarding clinical manifestations of rhabdomyolysis, the incidence of muscle weakness was notably higher in the RML group (41.2% vs. 13.7%, $p<0.001$).

In terms of treatment, the surgical intervention rate was significantly lower in the RML group (41.2% vs. 65.0%, $p=0.013$). While the rate of mechanical ventilation was higher in the RML group (55.9% vs. 44.4%, $p=0.075$), this difference did not reach statistical significance.

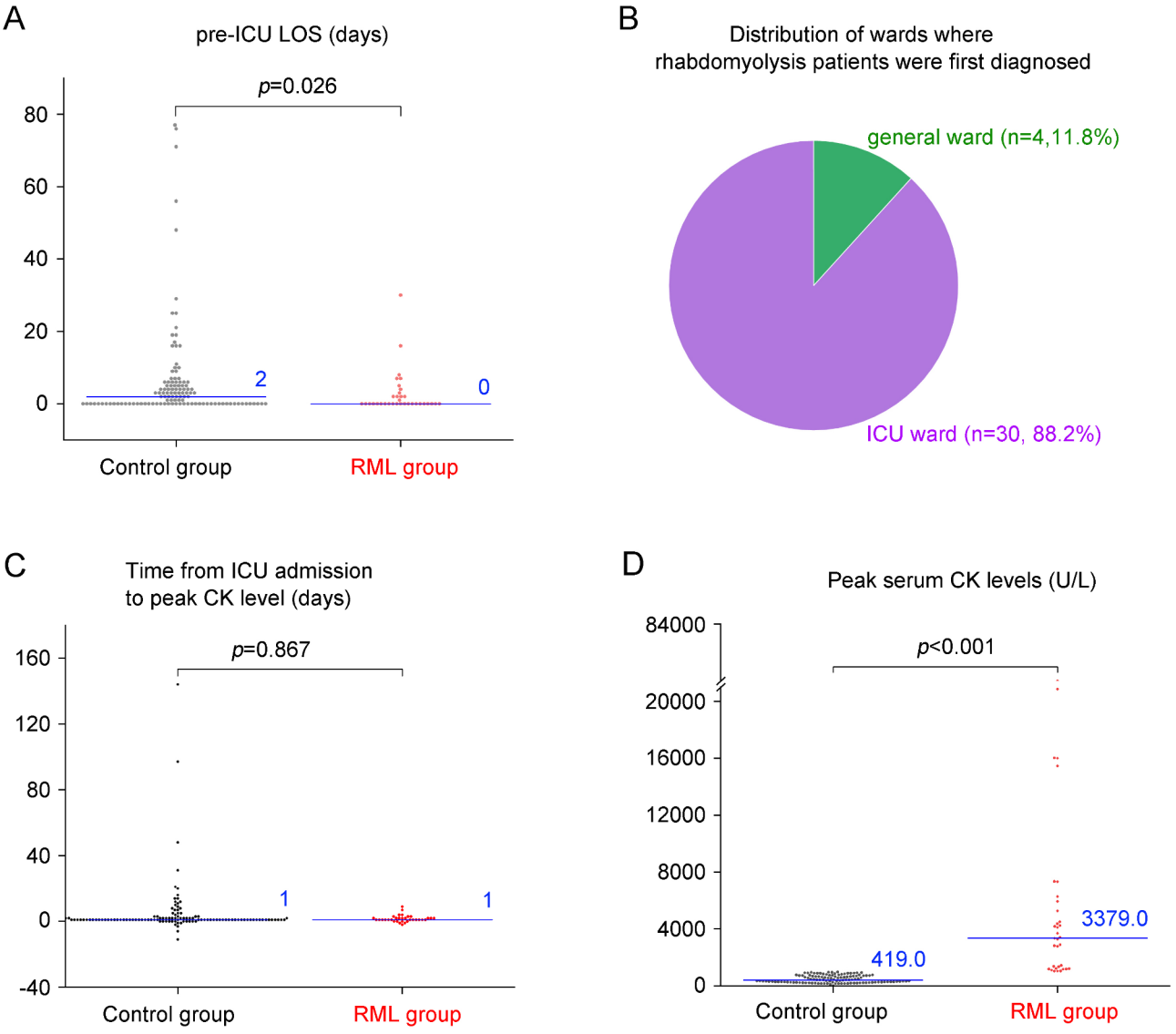

Fig. 2 Temporal characteristics and diagnostic distribution of rhabdomyolysis patients. **A**: Comparison of the length of hospital stay before ICU admission(pre-ICU LOS) (days) using swarm plots with medians. **B**: Comparison of the time from ICU admission to peak CK level (days) using swarm plots with medians. **C**: Comparison of peak serum CK levels (U/L) using swarm plots with medians. D: Distribution of wards where rhabdomyolysis patients were first diagnosed. The blue line represents the median, and the blue number indicates its value

Laboratory characteristics of ICU patients with and without rhabdomyolysis

As shown in Table 2, the initial laboratory examinations conducted post-admission revealed that 39.7% of patients had anemia (hemoglobin < 11 g/dL), 53.0% had elevated white blood cell counts (WBC > 9.5×10^9/L), 76.2% had elevated C-reactive protein (CRP > 10 mg/L), 39.7% had an elevated serum creatinine(SCr > 111μmol/L in males; or > 81μmol/L in females), and 47.0% had low albumin levels (< 35 g/L). No statistically significant differences were observed between the RML and control groups for these parameters, or for uric acid (> 420 μmol/L), alanine aminotransferase (ALT > 40 U/L), total bilirubin (> 21 μmol/L), abnormal potassium levels (< 3.4 or > 5.3 mmol/L), or proteinuria.

As presented in Table 2; Fig. 2C, the time interval between peak CK levels and ICU admission was 1.0 (1.0–2.0) days in both the control and RML groups, with no significant difference observed ($p = 0.867$). As shown in Table 2; Fig. 2D, peak CK levels were significantly higher in the rhabdomyolysis group compared to the control group (3,379.0 [1,217.0–6,019.5] U/L vs. 419.0 [251.0–717.0] U/L; $p < 0.001$). At peak CK levels, the incidence of myoglobin in rhabdomyolysis patients (> 1000 U/L) was significantly higher compared to controls (55.9% vs. 14.5%, $p < 0.001$). Among ICU patients, 56.3% exhibited elevated troponin I levels (> 0.03 U/L); however, no

Table 2 Laboratory characteristics of ICU patients without and with Rhabdomyolysis

	Total (*n* = 151)	Control group (*n* = 117)	RML group (*n* = 34)	*p* value
Initial post-admission laboratory results				
Hb(< 11 g/L)	60(39.7)	50(42.7)	10(29.4)	0.162
WBC(> 9.5 × 10^9/L)	80(53.0)	60(51.3)	20(58.8)	0.438
CRP(> 10 mg/L)	115(76.2)	92(79.3)	23(67.6)	0.157
Elevated creatinine	60(39.7)	43(36.7)	17(50.0)	0.165
Alb(< 35 g/L)	71(47.0)	52(44.8)	19(55.9)	0.256
UA(> 420umol/L)	36(28.8)	27(27.6)	9(33.3)	0.557
ALT (> 40U/L)	22(14.7)	15(12.9)	7(20.6)	0.404
TBL(>21umol/L)	31(20.7)	21(18.1)	10(29.4)	0.152
K^+ (< 3.4 or > 5.3mmol/L)	42(27.8)	33(28.2)	9(26.5)	0.843
proteinuria	87(66.4)	63(63.0)	24(77.4)	0.137
Laboratory test results at the time of peak CK levels				
Peak CK-ICU (days)	1.0(1.0–2.0))	1.0(1.0–2.0)	1.0(1.0–2.0)	0.867
Peak CK(U/L)	602.0(290.0-955.0)	419.0(251.0-717.0)	3379.0(1217.0-6019.5)	< 0.001
CK(>1000U/L)	34(22.5)	0(0)	34(100.0)	< 0.001
Myoglobin(> 1000U/L)	36(23.8)	17(14.5)	19(55.9)	< 0.001
Troponin I (> 0.03ng/ml)	85(56.3)	64(54.7)	21(61.8)	0.465

Categorical data are presented as frequencies and percentages [n (%)]. Non-normal distributions are summarized using the median and interquartile range (IQR)

Because some patients did not undergo certain tests, the actual number of tests for the control group and RML group is 116/34 (CRP), 116/34(Alb), 98/27(UA), 116/34(ALT), 116/34(TBL), and 100/31(proteinuria)

Elevated creatinine: SCr > 111μmol/L in males; or > 81μmol/L in females. Creatine kinase (CK), troponin I, and myoglobin concentrations represent measurements taken at the peak level of creatine kinase activity, whereas all other parameters correspond to the initial test results obtained upon admission

statistically significant difference was observed between the two groups (61.8% vs. 54.7%, $p = 0.465$).

Outcome of ICU patients without and with rhabdomyolysis

As demonstrated in Table 3, compared to the control group, there was no statistically significant difference in total hospitalization stay, ICU stay, or hospitalization costs for patients with rhabdomyolysis. While the mortality and cessation of treatment in the RML group were higher than those in the control group, these differences were not statistically significant. As shown in Fig. 3, the poor outcome rate (POR, the combined rate of death and cessation of treatment), was significantly higher in the RML group compared to the control group (52.9% vs. 33.3%, $p = 0.038$). The POR in the AKI group was significantly higher than in the non-AKI group (51.56% vs. 27.59%, $p = 0.003$). We compared four subgroups of ICU patients, with POR as follows: non-AKI/non-RML (19.40%), AKI/non-RML (52.00%), non-AKI/RML (55.00%), and AKI/RML (50.00%). Statistical analysis revealed significant differences between the non-AKI/non-RML group and the other three groups ($p < 0.001$, $p = 0.002$, and $p = 0.016$, respectively). However, no significant differences were observed between the AKI/RML group and the AKI/non-RML or non-AKI/RML groups ($p = 0.895$ and $p = 0.774$). In the control group of 50 AKI patients, 7 (14%) received blood purification therapy (BPT). Among 14 AKI patients in the RML group, 5 (35.71%) underwent BPT. There was no significant difference in the proportion of AKI patients who received BPT between the two groups (14% vs.35.71%, $p = 0.146$). Further analysis of AKI patients receiving BPT revealed high POR in both groups; however, the difference was not statistically significant (71.43% vs. 100%, $p = 0.318$).

Table 3 Outcome of ICU patients without and with Rhabdomyolysis

	Total (*n* = 151)	Control group (*n* = 117)	RML group (*n* = 34)	*p* value
Total Hospital Stay	21.0(14.0–34.0)	20.0(14.0-34.5)	21.0(8.8–30.3)	0.454
ICU stay	7.0(3.0–18.0)	5.0(3.0–16.0)	7.0(2.8–21.0)	0.558
Cost (×1000 RMB) *	110.6(68.0-180.5)	100.6(69.88–181.8)	116.9(52.3-177.6)	0.572
Mortality#	41.0(27.2)	29.0(24.8)	12.0(35.3)	0.225
COT †	16.0(10.6)	10.0(8.5)	6.0(17.6)	0.230
POR ‡	57(37.7)	39(33.3)	18(52.9)	0.038

Categorical data are presented as frequencies and percentages [n (%)].Non-normal distributions are summarized using the median and interquartile range (IQR)

Cost*: hospitalization costs

Mortality#: all-cause in-hospital mortality rate

COT †:cessation of treatment, due to the patient's critical condition and failure to recover, the family decided to terminate treatment, resulting in an automatic discharge. The chances of survival for such patients are extremely low. POR ‡: poor outcome rate, defined as the combined rate of death and cessation of treatment

Logistic regression analysis of risk factors associated with poor outcome in ICU patients

As indicated in Fig. 4, multivariate logistic regression analysis revealed that male gender [OR = 2.829; 95% CI, 1.120–7.147; $p = 0.028$], sepsis [OR = 3.675; 95% CI, 1.234–10.949; $p = 0.019$], and mechanical ventilation [OR = 3.553; 95% CI, 1.489–8.478; $p = 0.004$] were independent risk factors for poor outcome in ICU patients. Notably, rhabdomyolysis [OR = 0.966; 95% CI, 0.334–2.793; $p = 0.949$] was not identified as a statistically significant risk factor for poor outcomes within this patient population.

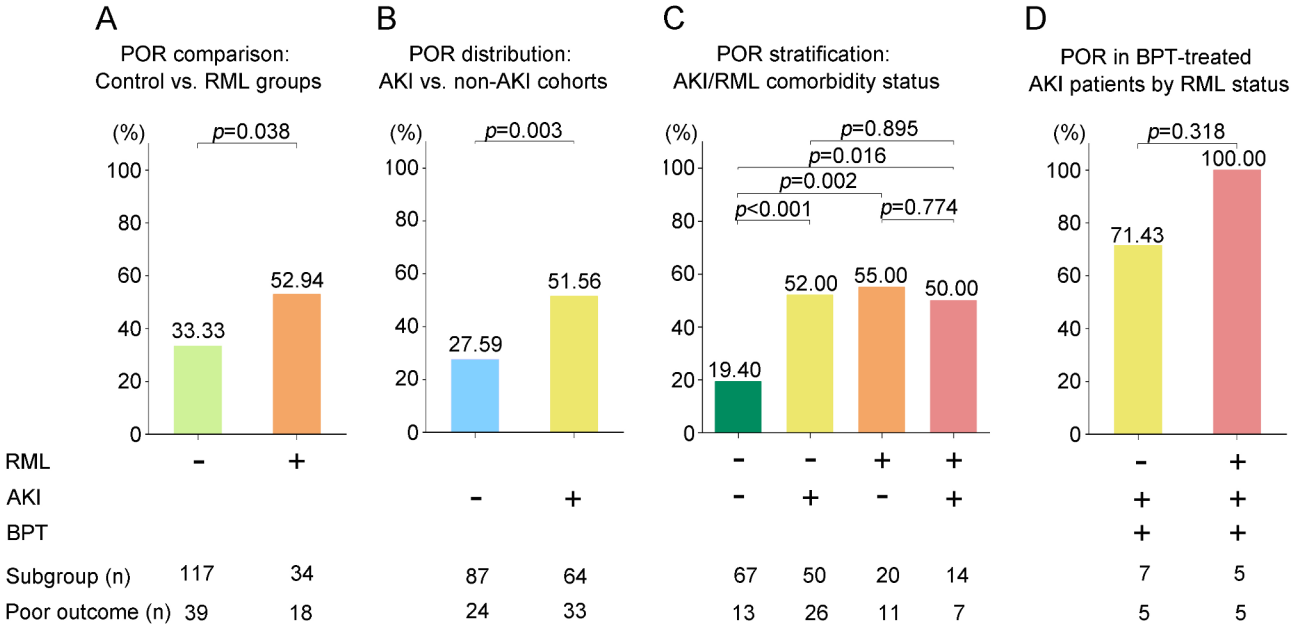

Fig. 3 Comparison of Poor Outcome Rates (POR) Among Different Subgroups: (**A**) Control Group vs. Rhabdomyolysis (RML) Group; (**B**) Acute Kidney Injury (AKI) Group vs. Non-AKI Group; (**C**) POR by Presence of AKI and/or Rhabdomyolysis; (**D**) POR in AKI Patients Treated with Blood Purification Therapy (BPT), Stratified by RML Status

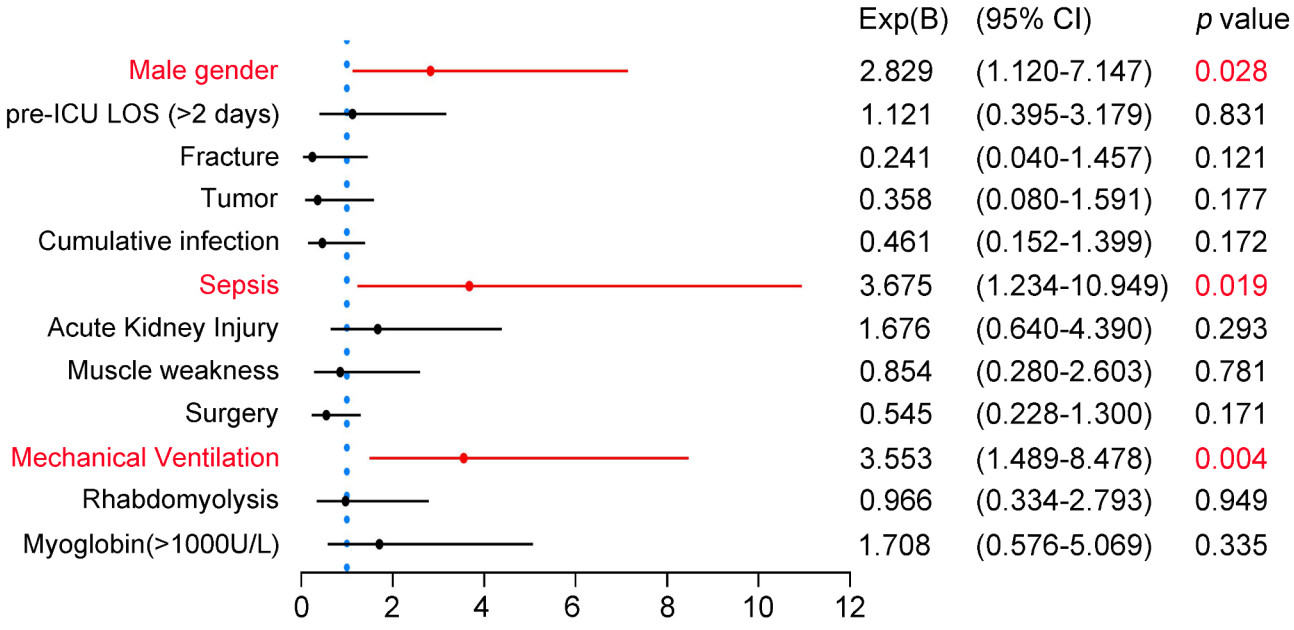

Fig. 4 The forest plot provides a comprehensive overview of the risk factors associated with poor outcomes in ICU patients. pre-ICU LOS: the length of hospital stay before ICU admission

Discussion

Our study underscores statistically significant variations in gender distribution, infection rates, muscle weakness incidence, and surgical intervention frequency between ICU patients with and without rhabdomyolysis. Notably, the RML group exhibited a significantly higher proportion of male patients, corroborating previous findings that suggest male gender is a critical predisposing factor for rhabdomyolysis [13].

Regarding the relationship between in-hospital mortality rates and pre-ICU LOS, patients with a longer pre-ICU LOS have been reported to exhibit higher mortality rates [14]. However, other studies suggest no significant correlation between pre-ICU LOS and ICU mortality or ICU length of stay (LOS) [15].In our study,

the significantly shorter pre-ICU LOS and lower proportion of extended pre-ICU stays in the RML group reflect the acute nature of rhabdomyolysis requiring urgent critical care. These findings emphasize the importance of early recognition and intervention in at-risk patients. Future studies should focus on developing predictive models to optimize ICU admission timing and improve outcomes for patients with rhabdomyolysis.

Although infections were not the predominant reason for hospitalization, ICU patients experienced a high incidence of cumulative infection (72.8%). Previous study indicate that the incidence of infection among ICU patients with a hospital stay exceeding 24 h is 32.3%(95%CI 31.3–33.3%) [16]. However, this incidence varies significantly across different ICUs, ranging from 1.5–66.5% [16]. Infection rates are notably higher among internal medicine patients and emergency surgery patients compared to trauma patients and those undergoing planned surgery. Notably, the cumulative incidence of infection in our ICU is 72.8%. The RML group had a significantly higher infection rate (88.2%) compared to the control group.Several factors in this study likely contribute collectively to the elevated infection rates observed. Firstly, the median age of the study population was 73 years, with many patients suffering from comorbidities such as hypertension, diabetes, and cerebrovascular accidents. Older age and the presence of comorbidities are well-established risk factors for infections, particularly in ICU settings [17]. Secondly, the study population not only has a high prevalence of infections but also a significant incidence of diseases such as cerebrovascular accidents, which inherently raises the risk of secondary infections during an ICU stay [18].Thirdly, trauma patients have a higher infection rate compared to those undergoing elective surgery [19]. In addition, the study reported a higher rate of mechanical ventilation (48.3%), indicating the severity of illness in this population. Mechanical ventilation is a well-documented risk factor for hospital-acquired infections, particularly ventilator-associated pneumonia [20]. Proposed mechanisms for infection-induced rhabdomyolysis include bacterial invasion of muscle tissue, reduced energy-related enzymatic activity, tissue hypoxia due to factors like sepsis and acidosis, and the impact of endotoxins [21].

Interestingly, although rhabdomyolysis has been reported in tumor patients following targeted therapy, chemotherapy, and surgery [22–24], our study found a lower incidence of malignant tumors in the RML group. This suggests that while rhabdomyolysis is a potential complication, it is relatively uncommon among ICU patients with malignancies. Muscle weakness, a notable symptom of rhabdomyolysis, was significantly more common in the RML group, highlighting its diagnostic importance. Additionally, the RML group had a markedly lower surgical intervention rate, suggesting that other factors contribute prominently to rhabdomyolysis occurrence.

For diagnosing rhabdomyolysis, while medical history and physical examinations offer valuable insights, laboratory studies confirm the diagnosis. CK levels are the most sensitive indicators of myocyte injury in rhabdomyolysis [25]. Our analysis revealed significantly elevated CK levels in the RML group, alongside increased serum myoglobin and troponin I levels. Elevated myoglobin can lead to AKI through myoglobin precipitation with Tamm-Horsfall protein in acidic urine, causing tubular occlusion, and through hydroxyl radical oxidation [26]. Troponin levels, although typically associated with cardiac conditions, can also be elevated due to non-cardiac causes such as rhabdomyolysis [27]. Our findings confirmed abnormally elevated levels of troponin in the RML group.

The mortality rate for patients with rhabdomyolysis closely relates to the underlying cause and concurrent comorbidities [28]. Rhabdomyolysis with AKI is a common occurrence, and the impact of rhabdomyolysis on mortality may be mediated through AKI development [29, 30]. ICU patients diagnosed with both rhabdomyolysis and AKI have a reported mortality rate of 59% [31]. Our research found an all-cause in-hospital mortality rate of 27.2% for ICU patients, increasing to 35.3% for those with rhabdomyolysis. Additionally, 10.6% of ICU patients opted to discontinue treatment due to poor prognoses, rising to 17.6% among those with rhabdomyolysis. The significantly higher rate of poor outcomes (POR) in the RML group (52.9%) compared to the control group (33.3%) underscores the association between the adverse prognostic and rhabdomyolysis in ICU settings. Our study investigating rhabdomyolysis and/or AKI revealed that both conditions were independently associated with higher rates of POR. Regarding the finding that the combination of rhabdomyolysis and AKI does not result in a significantly elevated POR compared to having either condition alone, several potential explanations can be considered. First, there may be a pathophysiological overlap between rhabdomyolysis and AKI, as both conditions share related mechanisms, such as myoglobin-induced tubular injury, oxidative stress, and systemic inflammation, which may result in non-additive effects on POR [32]. Second, statistical limitations, including the small sample size of patients with both conditions, may have reduced the study's power to detect significant differences in POR. Third, confounding variables, such as male gender, sepsis, and mechanical ventilation, identified as independent risk factors for poor outcomes, may overshadow the combined impact of rhabdomyolysis and AKI. Fourth, effective ICU management strategies, including early recognition and treatment of rhabdomyolysis and AKI, may mitigate their combined impact on

outcomes [33]. Further research with larger sample sizes and more detailed analyses of disease severity and treatment effects is needed to better understand these findings.Our findings indicate that AKI patients treated with blood purification therapy (BPT) in the ICU experience high rates of poor outcomes, irrespective of rhabdomyolysis. This likely reflects that BPT is reserved for severe or refractory conditions, meaning it targets critically ill patients already at high risk of adverse events and mortality [34, 35].

Logistic regression analysis identified male gender, sepsis, and mechanical ventilation as independent risk factors for poor outcomes in ICU patients. Sepsis is notably linked to increased morbidity and mortality, with rhabdomyolysis in septic patients associated with a high mortality rate [36, 37]. The mechanisms contributing to rhabdomyolysis in sepsis may include bacterial muscle invasion, elevated levels of interleukin-1, enzyme activation, fever, hypotension, and microthrombi [38]. Mechanical ventilation, while pivotal in critical care, often reflects the underlying severity of illness and can be complicated by rhabdomyolysis, influencing patient outcomes [39]. In our study, MV emerged as an independent risk factor for poor outcome, reflecting both the illness severity and the systemic impact of rhabdomyolysis. In pediatric ICU patients, rhabdomyolysis was associated with increased utilization of intensive care resources but not higher mortality rates [40]. Our findings suggest that rhabdomyolysis itself is not an independent risk factor for poor outcome. Rather, rhabdomyolysis appears to indicate a more severe clinical state, as it is associated with other prognostic factors that significantly impact patient outcomes, such as male gender, sepsis, and the need for mechanical ventilation. These findings underscore the complex role of rhabdomyolysis in the ICU setting and highlight the importance of considering a range of factors when assessing the prognosis of patients with rhabdomyolysis.

However, the study's retrospective design imposes certain limitations, including potential selection bias and the reliance on recorded clinical and laboratory data. For example, the median age of ICU patients varies significantly across different studies and patient populations, ranging from 46 years in trauma patients to 92 years in critically ill elderly patients [41, 42]. In our study, the median age was 73 years, which may account for the high prevalence of patients with cerebrovascular accidents, infections, and tumors. At the same time, we recognize that our study is retrospective and includes a relatively small sample size in the rhabdomyolysis group. Implementing pairwise matching strategies under these conditions could further reduce the sample size, potentially compromising statistical power. A prospective study design or a larger retrospective study with adequate patient numbers would better facilitate matching on key variables (e.g., APACHE ≥ 15, mechanical ventilation, and sepsis). In such designs, patient pairing would more effectively control for confounding factors. In addition, our study lacks data on acute compartment syndrome (ACS) and its potential impact on outcomes among ICU patients. We recommend that future studies prospectively collect detailed clinical information, including the presence or absence of ACS, to enable a more comprehensive analysis. Future prospective studies are necessary to validate these findings and explore the underlying mechanisms. Expanding the research to include a more diverse patient population across multiple ICUs could enhance the generalizability of these results.

Conclusions

In conclusion, rhabdomyolysis in ICU patients is associated with distinct clinical characteristics and a higher rate of adverse outcomes. Male gender, sepsis, and mechanical ventilation are key risk factors for poor outcomes, highlighting the need for vigilant monitoring. The presence of rhabdomyolysis alone does not constitute an independent predictor of adverse outcomes in our patient cohort. While these findings offer valuable insights, the study's retrospective nature calls for prospective research to confirm results and improve clinical approaches for managing rhabdomyolysis in diverse ICU populations.

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Author contributions

Dr. Wang Zhen and Dr. Wang Qing were responsible for the collection of clinical and laboratory data. Dr. Wang Qing and Dr. Chen Jinghan conducted the verification and analysis of the clinical data and compiled Table 1. For the laboratory data, Dr. Chen Jinghan and Dr. Cai Leiming undertook the verification and analysis, culminating in the creation of Table 2. Dr. Wang Zhen further analyzed the data and developed Table 3, and Figs. 1, 2, 3 and 4. Following a comprehensive summary of the findings, he authored the manuscript. The paper was subsequently proofread and revised by Dr. Wang Qing. All authors have reviewed and approved the final version of the manuscript.

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Data availability

The data supporting the conclusions of this study are not publicly available due to sensitivity considerations.

Declarations

Consent for publication

Not applicable.

Competing interests
The authors declare no competing interests.

Ethics Statement
This study adhered to the principles of the Declaration of Helsinki and received approval from the Ethics Committee of Shanghai Baoshan District Wusong Central Hospital (Project Number: 2024-P-01), which also granted a waiver of informed consent.

Conflict of interest
All authors have no conflicts of interest directly relevant to this article.

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