BMC Infectious Diseases

RESEARCH

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The role of serum lactate and hypotension in mortality risk stratification for critically ill COVID-19 patients: insights from a large retrospective ICU cohort

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Abstract

Purpose To determine the association of serum lactate levels with ICU outcomes in COVID-19 patients, particularly concerning hypotension, shock, and mortality.

Methods Retrospective single center cohort study conducted in the intensive care unit. Adult patients (≥ 18 years) pneumonia admitted to the ICU with confirmed COVID-19 between March 2020 and December 2021. Patients were categorized into four lactate level categories: *Very Low* (< 1.7 mmol/L), *Low* (1.7–2.1 mmol/L), *Intermediate* (2.1–2.7 mmol/L), and *High* (> 2.7 mmol/L). Univariate and multivariate stepwise logistic regression analyses were conducted to identify independent predictors of all-cause mortality. The primary outcome was in-hospital mortality.

Results Among the 1,371 patients studied, in-hospital mortality rates increased progressively across lactate categories, with 23% in the *Very Low* category, 31% in the *Low* category, 38% in the *Intermediate* category, and 51% in the *High* category ($p < 0.001$). Relative risk of in-hospital mortality was 1.37 (95% CI 0.99–1.89; $p = 0.14$) for the *Low* category, 1.66 (95% CI 1.23–2.23; $p = 0.018$) for the *Intermediate* category, and 2.24 (95% CI 1.69–2.97; $p < 0.001$) for the *High* category, compared to *Very Low* category. After regrouping the "Very Low" and "Low" categories as "Lower" ($n = 446$) and the "Intermediate" and "High" categories as "Higher" ($n = 925$), the mortality rate was 22.8% in the "Lower" category and 77.2% in the "Higher" category (RR 1.63 CI 95% 1.38–1.92) (Pearson Chi-Square, $p < 0.001$). The presence of hypotension significantly increased the risk of death across all categories, with relative risks ranging from 4.38 to 5.81.

Conclusion Elevated lactate levels are associated with increased mortality, and hypotension significantly exacerbates this risk across all lactate categories, highlighting its strong predictive power for adverse outcomes in this patient population.

Keywords Lactate, COVID-19, Sepsis, Septic shock, Hypotension, Intensive care unit

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Introduction

Sepsis, caused by bacterial or viral infections, is a prevalent reason for Intensive Care Unit (ICU) admission and a leading cause of mortality within critical care settings [1]. In recent years, viral pneumonia, most notably those associated with SARS-CoV-2, has exacerbated the strain on healthcare systems worldwide and has become a significant cause of ICU admissions due to respiratory failure or hemodynamic instability [2]. For patients with COVID-19 who are presenting with shock, the Surviving Sepsis Campaign guidelines emphasize using serum lactate as a resuscitation guide, targeting a mean arterial pressure of 65 mmHg to mitigate hypotension and support perfusion [3].

Elevated serum lactate, often linked with tissue hypoxia, indicates worse prognoses across critically ill populations [3–7]. Beyond indicating hypoperfusion, serum lactate elevation in septic shock may reflect broader pathophysiological disturbances, including adrenergic-driven aerobic glycolysis, reduced hepatic lactate clearance, mitochondrial dysfunction affecting pyruvate metabolism, and inflammation-driven metabolic responses [8, 9].

Septic shock is characterized by progressive circulatory failure, leading to hypoperfusion and bioenergetic depletion, often accompanied by hypotension [3]. Additionally, sepsis-induced hypotension without hyperlactatemia, often referred to as vasoplegic shock, is commonly observed in ICU patients. The absence of hyperlactatemia in these cases suggests a distinct pathophysiological mechanism, potentially linked to impaired vascular tone rather than tissue hypoxia [10]. While the prognosis for patients with vasoplegic shock varies, they generally have a lower mortality rate than those with tissue dysoxic shock, though it remains significant [11].

A few studies have noted an association between elevated lactate levels and worse outcomes in COVID-19 patients, yet limited data exists on the interplay between serum lactate levels and hypotension. A study involving very old ICU patients with COVID-19 found that a baseline lactate concentration ≥ 2.0 mmol/L was associated with higher ICU and 3-month mortality [12]. Other researchers have highlighted that elevated lactate levels and reduced lactate clearance are significant predictors of mortality [13]. Given the ongoing burden of viral pneumonia on healthcare systems, clarifying the relationship between serum lactate, hypotension, and clinical outcomes remains critical. Therefore, this study aims to evaluate lactate levels in COVID-19 ICU patients with and without hypotension and assess the impact on their outcomes.

Methods

Ethics

The study was approved by the local Institutional Review Board (CAAE: 31725720.2.0000.5415) and followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [14], in accordance with the Declaration of Helsinki.

Study design and setting

This retrospective cohort study evaluated patients admitted to the COVID-19 dedicated ICU at Hospital Base de São José do Rio Preto between March 2020 and December 2021.

Inclusion and exclusion criteria

Inclusion criteria required clinical signs of pneumonia in patients admitted with suspected COVID-19 and at least one of the following severity criteria: respiratory rate > 30 breaths/min, hypoxic acute respiratory failure, or oxygen saturation (SpO_2) < 90% on room air. Exclusion criteria were a negative polymerase chain reaction (PCR) test for COVID-19 from a nasopharyngeal sample, age under 18 years, absence of lactate measurements or death within the first 48 h after admission.

Study outcomes

In this study, the primary outcome was in-hospital mortality according to serum lactate categories. This measured the survival status of patients from ICU admission until discharge or death during their hospital stay, making it the primary endpoint of interest.

The secondary outcomes included:

- *Incidence of Hypotension and Shock Types*: The occurrence and characteristics of hypotension and the development of septic or vasoplegic shock during ICU admission.
- *ICU Length of Stay*: Duration of time each patient spent in the ICU.
- *Organ Support Needs*: This included the use of vasoactive medications (e.g., noradrenaline, vasopressin), mechanical ventilation and renal replacement therapy (RRT).

These secondary outcomes aimed to provide a comprehensive view of the clinical course and resource requirements associated with severe COVID-19 in ICU settings.

Data collection

Physicians trained in data extraction reviewed patients' electronic medical records, gathering comprehensive information on demographics, comorbidities, clinical presentation, vital signs, laboratory tests, and the use and duration of organ support, including mechanical

ventilation, dialysis, and vasoactive drugs [15]. Radiologic assessments included chest radiography and, when available, either computed tomography (CT) or chest angiotomography. The Simplified Acute Physiology Score 3 (SAPS 3) and the Charlson Comorbidity Index were calculated upon ICU admission [16]. The probability of death is calculated using a formula based on the SAPS 3 score [17].

We grouped the patients into categories based on the highest lactate levels measured on the first and second days of hospitalization. Category "very low" included patients with lactate levels less than 1.7 mmol/L, "Low" with levels between 1.7 and lower than 2.1 mmol/L, "Ïntermediate" with levels between 2.1 and 2.7 mmol/L, and "High" with levels greater than 2.7 mmol/L. The lactate cutoffs used were based on predefined ranges chosen for clinical interpretability and to approximate quartile boundaries from our preliminary dataset, rather than statistical quartiles calculated to yield equal-sized groups. For further analysis, we regrouped the lactate categories by combining the "Very Low" and "Low" categories into a single "Lower Lactate" category, and the "Intermediate" and "High" categories into a "Higher Lactate" category.

Hypotension was defined by the need for vasopressor support at any dose to keep mean arterial pressure > 65 mm Hg, while septic shock was defined as the need for vasopressors along with serum lactate levels above 2.0 mmol/L [3]. Vasoplegic shock was defined as persistent sepsis-induced hypotension requiring vasopressor support with serum lactate ≤ 2.0 mmol/L. This cutoff was arbitrarily selected to align with the most frequently reported threshold for hyperlactatemia in sepsis studies, allowing us to distinguish patients with likely predominant vasoplegia from those with hyperlactatemia suggestive of tissue hypoperfusion.

Statistical analysis

We presented categorical variables as frequencies and percentages. Continuous variables were expressed as means with standard deviations (SD) when normally distributed, and as medians with interquartile ranges (IQR) when non-normally distributed. Normality was assessed using the Shapiro–Wilk test, supplemented by inspection of histograms and quantile–quantile plots. Comparisons between groups were performed using the Chi-square test for categorical variables and the Kruskal–Wallis test (adjusted for ties) for continuous non-Gaussian variables. Relative risks (RR) with 95% confidence intervals (CIs) and absolute risk reductions were calculated. For unadjusted pairwise comparisons of in-hospital mortality across lactate categories, p-values were corrected for multiple testing using the Holm–Bonferroni method.

Univariate and multivariate (stepwise backward) logistic regression analyses were conducted to identify independent predictors of in-hospital mortality. The logistic regression analysis included variables with a p-value < 0.05 when comparing survivors and non-survivors. The independent variables tested included age, SAPS 3, Charlson comorbidity index, hypotension, and "Higher" lactate level category. Variance inflation factor (VIF) analysis was performed to assess multicollinearity, and no significant multicollinearity was observed (VIF < 1.5 for all covariates). Adjusted odds ratios (OR) with 95% confidence intervals (95% CIs) were calculated for each predictor. A significance level of 5% ($p < 0.05$) was applied to all statistical tests.

Cumulative survival curves (Kaplan-Meier) were generated to illustrate differences in early event-free survival (in-hospital mortality) based on lactate level categories. Statistical analyses were performed using IBM SPSS Statistics (version 25.0), R (version 3.4.1), and Minitab 17 Statistical Software.

Results

Patient characteristics

We evaluated a total of 1447 patients, with 530 admitted in 2020 and 917 in 2021, ultimately including 1371 patients in the study (Fig. 1). The most common comorbidities among these patients were arterial hypertension (48%), obesity (26%), and diabetes (28%) (Table 1). Patients categorized in the "Intermediate" and "High" categories tended to be older, had more severe disease presentations, required increased ventilatory support and vasopressors, and experienced higher in-hospital mortality rates. Among all patients, 461 (34%) experienced septic shock, and 217 (16%) developed vasoplegic shock.

Mortality

The overall in-hospital mortality rate was 39.3% (539 patients). Mortality rates varied by categories, with 23% in the "Very Low", 31% in the "Low", 38% in the "Intermediate", and 51% in the "High" (Table 1). Compared with the "Very Low" category, the risk of death increased progressively across other categories, being not significant in the 'Low' (RR 1.37; 95% CI 0.99–1.89, $p = 0.14$), but significant in the "Intermediate" (RR 1.66; 95% CI 1.23–2.23, $p = 0.018$) and highly significant in the "High" (RR 2.24; 95% CI 1.69–2.97, $p < 0.001$) after Bonferroni adjustment. After regrouping the "Very Low" and "Low" categories as "Lower" ($n = 446$) and the "Intermediate" and "High" categories as "Higher" ($n = 925$), the mortality rate was 22.8% in the "Lower" category and 77.2% in the "Higher" category (RR 1.63 CI 95% 1.38–1.92) (Pearson Chi-Square, $p < 0.001$).

The number of patients in categories according to serum lactate levels in survivors and non-survivors are shown in Table 2. Non-survivors were older, had higher

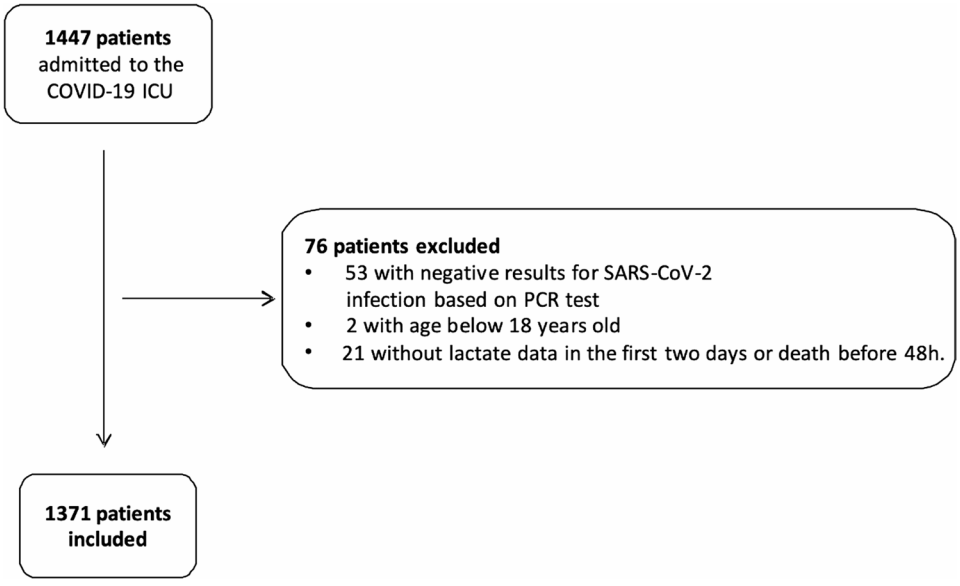

Fig. 1 Flowchart of patients through the study

Table 1 Clinical and demographic characteristics, according to serum lactate categories

	All (*n* = 1371)	"Very low" (*n* = 181)	"Low" (*n* = 265)	"Intermediate" (*n* = 402)	"High" (*n* = 523)	*P* Value
Age, Years	54.7 ± 15.9	51.9 ± 16.7	52.3 ± 16.4	54.5 ± 15.8	57.1 ± 15.4	**< 0.001**
Lactate (mEq/L)*	2.4 [1.2–1.5]	1.4 [1.2–1.5]	1.9 [1.8-2.0]	2.3 [2.2–2.5]	3.2 [2.9–3.9]	**< 0.001**
Male sex	799 (58.3)	95 (52.5)	145 (57.7)	237 (59)	322 (61.6)	0.099
SAPS 3	53 [45–68]	47.5 [41–59]	50 [44–59]	53 [45–66]	59 [49–77]	**< 0.001**
Mortality risk**	22 [11-52.5]	14 [7–33]	18 [10–35]	22 [11–48]	35 [16–69]	**< 0.001**
Comorbidities						
CCI	0.0 [0.0–1.0]	0.0 [0.0–2.0]	0.0 [0.0–2.0]	0.0 [0.0–1.0]	1.0 [0.0–2.0]	**< 0.001**
SAH	657 (47.9)	94 (52)	126 (47.6)	182 (45.3)	255 (49)	**< 0.001**
Obesity	356 (26.0)	68 (37.6)	92 (34.7)	87 (22)	109 (21)	**< 0.001**
DM	389 (28.4)	49 (27)	68 (25.6)	108 (27)	164 (31.4)	**< 0.001**
COPD	75 (5.5)	8 (4.4)	13 (4.9)	25 (6.2)	29 (5.6)	**< 0.001**
Use of Vasopressors (%)						
Noradrenaline	819 (59.8)	75 (41.4)	142 (53.6)	237 (59)	365(69.8)	**< 0.001**
Vasopressine	288 (21.7)	23 (12.7)	45 (17)	77 (19.15)	143 (27.3)	**< 0.001**
Mechanical Ventilation	902 (65.8)	86 (47.5)	150 (56.6)	270 (67)	396 (75.7)	**< 0.001**
RRT	232 (17.2)	28 (15.5)	45 (17.2)	65 (16.5)	94 (18.3)	0.8279
ICU LOS, days	11[6–20]	10[5–17]	10 [5–19]	12 [6–20]	11[6–20]	**0.020**
Hospital LOS, days	15[9–26]	15[9–23]	15[9–25]	16 [10–26]	15[8–27]	0.179
Mortality	539 (39.3)	41 (22.7)	82 (31)	151 (37.6)	265 (50.7)	**0.001#**

CCI Charlson Comorbidity Index, *SAH* Systemic Arterial Hypertension, *SAPS 3* Simplified Acute Physiology Score 3, *DM* Diabetes Mellitus, *COPD* Chronic Obstructive Pulmonary Disease, *RRT* Renal replacement therapy, *LOS* Length of Stay, Numbers are presented as mean ± standard deviation, median with interquartile ranges [IQR] or n (%). * Median [IQR] levels of serum lactate (higher value in the first 48 h). ** Calculated using the SAPS 3 score model. #: for adjusted analysis: (Low vs. Very Low: $p = 0.14$; Int vs. Very Low: $p = 0.036$; High vs. Very Low: $p = 0.003$)

SAPS 3 score and mortality risk, higher incidence of hypotension and more comorbidities ($p < 0.001$ for all).

Figure 2 shows mortality rates in patients with and without hypotension. Among patients without hypotension, in-hospital mortality did not differ significantly across lactate categories when using the "Very Low" category as reference. The relative risk (RR) of death in the "Low" category was 1.37 (95% CI 0.99–1.89), while mortality was significantly higher in the "Intermediate" category (RR 1.66; 95% CI 1.23–2.23) and the "High" category (RR 2.24; 95% CI 1.69–2.97). In contrast, the presence of hypotension markedly increased in-hospital mortality across all lactate categories compared with patients without hypotension. The RR of death was 4.38 (95% CI 2.29–8.38) in the "Very Low" category, 5.59 (95% CI 3.10–10.06) in the "Low" category, 5.81 (95% CI

Table 2 Clinical and demographic characteristics in survivors and nonsurvivors

	Survivors (*n* = 832)	Non survivors (*n* = 539)	*P* Value
Age, years	50.1 ± 14.4	61.8 ± 15.8	**< 0.001**
Lactate (mEq/L)*	2.3 [1.8–2.8]	2.6 [2.1–3.3]	**< 0.001**
SAPS 3	49 [42–57.5]	64 [53–81]	**< 0.001**
Mortality risk**	15.9 [8.0 –30.5]	44.0 [22.1–75.0]	**< 0.001**
Comorbidities			
CCI	0 [0–1]	1 [0–2]	**< 0.001**
Hypotension	342 (41.2)	477 (88.7)	**< 0.001**
Categories, number of patients	140 (16.8)	41 (7.6)	**< 0.001**
Very Low			
Low	183 (22.0)	82 (15.2)	**< 0.001**
Intermediate	251 (30.2)	151 (28.0)	**< 0.001**
High	258 (31.0)	265 (49.2)	**< 0.001**
Lower	323 (38.8)	123 (22.8)	**< 0.001**
Higher	509 (61.2)	416 (77.2)	**< 0.001**

CCI Charlson Comorbidity Index, *SAH* Systemic Arterial Hypertension, *SAPS 3* Simplified Acute Physiology Score 3, *DM* Diabetes Mellitus, *COPD* Chronic Obstructive Pulmonary Disease, *LOS* Hospital Length of Stay. Numbers are presented as mean ± standard deviation, median with interquartile ranges [IQR] or n (%). * Median [IQR] levels of serum lactate (higher value in the first 48 h).** Calculated using the SAPS 3 score model

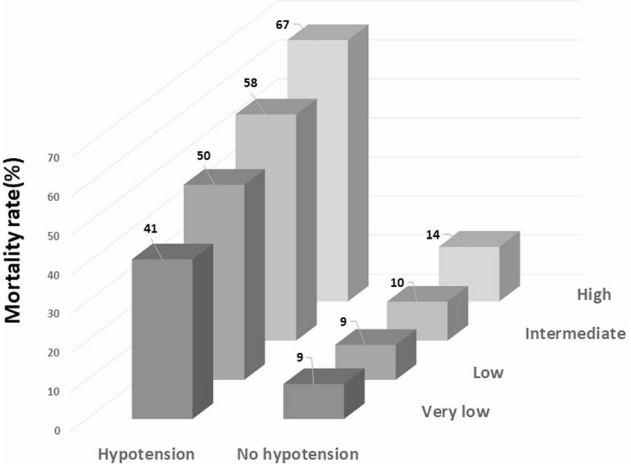

Fig. 2 Mortality rates across lactate level categories ("Very Low," "Low," "Intermediate," and "High") in patients with and without hypotension

3.60–9.38) in the "Intermediate" category, and 4.74 (95% CI 3.19–7.02) in the "High" category. The absolute risk increase (ARI) attributable to hypotension was 31.9% in the "Very Low" category, 41.1% in the "Low" category, 47.0% in the "Intermediate" category, and 52.4% in the "High" category.

Figure 3 present the Kaplan-Meier survival curves for all patients with and without hypotension, A and B, respectively.

Predictors of Mortality

The binary logistic regression analysis identified age, gender, Charlson comorbidity index, SAPS 3 score, "Higher" category, and hypotension as independent predictors of in-hospital mortality. The corresponding odds ratios, 95% confidence intervals, and p-values are presented in Table 3. In the univariate analysis, higher age, SAPS 3 score, Charlson Comorbidity Index, "Higher" category, and vasopressor use were significantly associated with the outcome. In the multivariate analysis, higher age (OR 1.034; 95% CI 1.023–1.045), SAPS 3 (OR 1.026; 95% CI 1.015–1.037), Charlson Comorbidity Index (OR 1.260; 95% CI 1.127–1.409), serum lactate levels in the "Higher" category (OR 1.411; 95% CI 1.011–1.970), and hypotension (OR 7.553; 95% CI 5.209–10.95) remained independently associated with the outcome.

Discussion

The main findings of our study on COVID-19 cases admitted to the ICU were: (1) higher lactate levels were strongly associated with in-hospital mortality; (2) elevated lactate combined with hypotension markedly increased the risk of death across all lactate categories, underscoring its predictive value for adverse outcomes; and (3) age, disease severity and comorbidities increased mortality risk.

Hyperlactatemia, a hallmark of shock and poor prognosis in critical illness, was also linked to in-hospital mortality in COVID-19. Mortality rose progressively with higher lactate categories, being significantly higher in the intermediate category and more than doubled in the high category compared with the very low category.

Elevated lactate levels were independently associated with increased in-hospital mortality, and this risk was significantly amplified in the presence of hypotension. Non-survivors were more likely to experience hypotension, and its presence increased in-hospital mortality across all lactate groups, indicating a synergistic effect. Relative risks ranged from 4.38 to 5.81, confirming that hypotension compounded the prognostic impact of lactate levels. In the multivariable logistic regression, higher lactate levels (Intermediate and High categories combined) predicted mortality (OR 1.41; 95% CI 1.01–1.97). Hypotension, using the need for vasopressor support as a proxy to maintain a mean arterial pressure > 65 mmHg, showed a much stronger association (OR 7.55; 95% CI 5.21–10.95). The Kaplan-Meier curves also showed that higher lactate levels at ICU admission are associated with lower early survival rates in COVID-19 patients, further highlighting lactate as a potential early indicator of poor prognosis.

Other authors reported similar findings. Ramkumar et al. [18] demonstrated that elevated lactate levels were associated with worse outcomes in ICU COVID-19

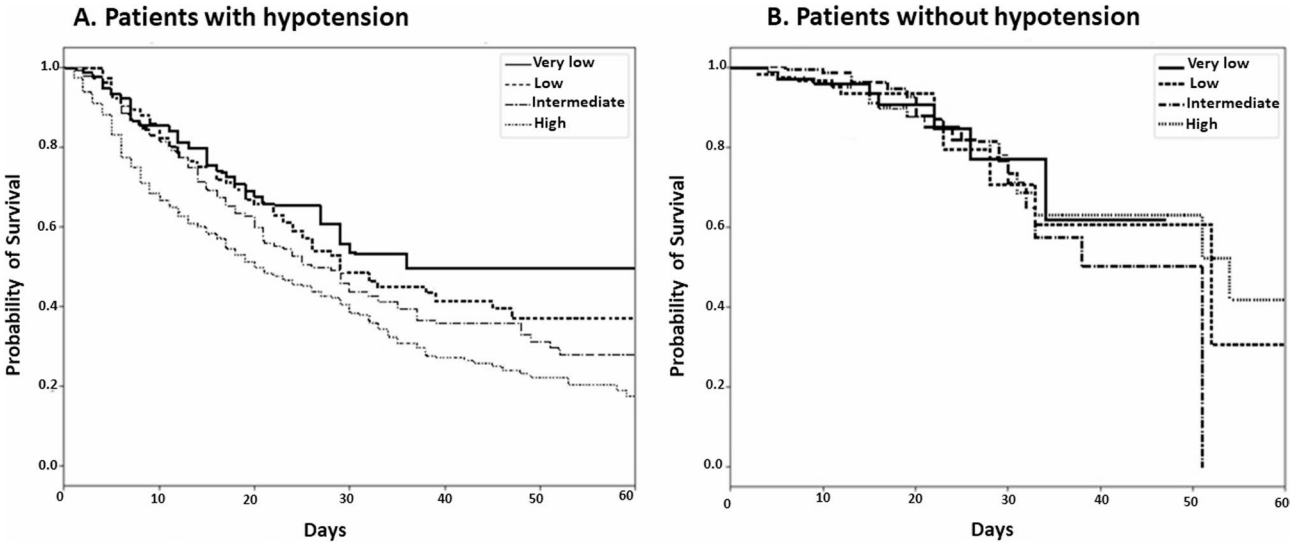

Fig. 3 Kaplan-Meier Survival Curves for patients with hypotension (**A**) and without hypotension (**B**). Log-rank "very low" category vs. "low" category: p-value = 0.31; Log-rank "very low" category vs. "intermediate" category: p-value = 0.055; Log-rank "very low" category vs. "high" category: p-value = 0,000

Table 3 Logistic regression analysis with hospital mortality as the dependent variable

	Univariate			**Multivariate**		
Variables	OR	CI 95	*p* value	OR	CI 95	*p* value
Model 1						
Age	1.035	1.023;1.045	**< 0.001**	1.034	1.023; 1.045	**< 0.001**
SAPS 3	1.026	1.015;1.037	**< 0.001**	1.026	1.015–1.037	**< 0.001**
CCI	1.260	1.127;1.409	**< 0.001**	1.260	1.127; 1.409	**< 0.001**
"Higher"category	1.411	1.011;1.970	**0.043**	1.411	1.011–1.970	**0.043**
Hypotension	7.553	5.209;10.95	**< 0.001**	7.553	5.209; 10.95	**< 0.001**

Legend: *SAPS 3* Simplified Acute Physiology Score 3, *CCI* Charlson Comorbidity Index, *OR* Odds Ratio, CI 95%: 95% Confidence Interval

patients. Similarly, Howell et al. [4] found that lactate levels between 2.5 and 4.0 mmol/L increased the odds of death by 2.2 times, and levels ≥ 4.0 mmol/L raised in-hospital mortality odds by 7.1 times in septic shock patients. Additionally, Vassiliou et al. [19] highlighted that lactate kinetics are a strong indicator of organ dysfunction and adverse outcomes in COVID-19 patients, while Cidade et al. identified serum lactate levels and vasopressor dosage as the main predictors of mortality in this category [20].

These results indicate that serum lactate levels may provide valuable insights into a patient's physiological status and may reflect multiple underlying issues. Elevated lactate in critical illness reflects diverse mechanisms, including tissue hypoxia, adrenergic-driven aerobic glycolysis, impaired hepatic clearance, mitochondrial dysfunction, and systemic inflammation. The study also identified vasoplegic shock, characterized by sepsis-induced hypotension without hyperlactatemia, suggesting a pathophysiology linked to vascular tone rather than tissue hypoxia. In this cohort, septic shock occurred in 34% of patients, while vasoplegic shock, meaning hypotension with serum lactate lower than 2 mEq/L, accounted for 16%. Specifically, the findings support using lactate as a risk stratification tool to help clinicians identify patients at higher risk of death, guiding timely and targeted interventions.

A key distinction in our study is between septic and vasoplegic shock, differentiated by lactate levels and vasopressor requirements. Among severe and critical COVID-19 patients, 34% developed septic shock as defined by the 2021 Consensus [3], with a mortality rate of 58.4%, while 16% experienced vasoplegic shock, showing a mortality rate of only 10.7%. This 47.8% absolute difference in mortality highlights distinct mechanisms underlying these shock types. Similar to our findings, Hernandez et al. [21] analyzed a COVID-19 cohort categorized by hyperlactatemia status, revealing substantial mortality differences: 42.9% in patients with hyperlactatemia versus 7.7% in those without. Sterling et al. [22] compared outcomes between patients with vasoplegic septic shock and those with tissue dysoxic septic shock (impaired oxygen utilization despite adequate circulation) and found that patients with tissue dysoxic shock had significantly worse outcomes, including higher mortality rates, compared to those with vasoplegic shock. All these studies underscore the importance of blood

pressure monitoring alongside lactate in managing severe COVID-19 patients and distinguishing between the types of septic shock for better prognosis and tailored treatment strategies.

However, our study also revealed high in-hospital mortality rates among patients with "normal" lactate levels. In patients with hypotension, mortality reached 51% within these groups, which is notably higher than in bacterial sepsis populations(1, 3, 6). Wacharasint et al. [23], in their retrospective analysis of the Vasopressin in Septic Shock Trial (VASST), found that patients in the second lactate quartile (1.4 < lactate < 2.3 mmol/L) had significantly higher mortality and organ dysfunction compared to those in the lowest quartile (≤ 1.4 mmol/L). Interestingly, outcomes in this quartile were comparable to those in the third quartile (2.3 ≤ lactate < 4.4 mmol/L), suggesting that even "normal" lactate levels could hold prognostic value in COVID-19 patients with septic shock.

Our study's findings reflect differences in COVID-19 pathophysiology compared to bacterial sepsis. Hutchings et al. [24] reported that critically ill COVID-19 patients demonstrate unique microcirculatory, endothelial, and inflammatory responses compared to those with traditional septic shock, showing less endothelial activation and lower levels of specific inflammatory markers. These findings imply that COVID-19-induced hyperlactatemia might be more indicative of mitochondrial dysfunction and adrenergic stimulation rather than tissue hypoxia [23]. As such, COVID-19 patients may benefit from tailored treatment approaches that account for these distinctive pathophysiological changes.

Besides lactate levels and hypotension, our study also determined age, SAPS 3 score, and comorbidities independently associated with mortality. Each additional year of age was associated with a 3.4% increase in the odds of death. Greater clinical severity and the presence of comorbidities were also linked to higher mortality. Literature consistently highlights these as strong independent predictors of mortality in severe COVID-19 [12, 25]. Older patients face higher risks due to decreased physiological reserves, increased comorbidities, and diminished immune response. Researchers also supports the value of SAPS 3 and the Charlson Comorbidity Index in assessing ICU mortality risk for diverse critical illness populations, including COVID-19 [26–28]. Highlighting these independent predictors aids resource prioritization, allowing ICU teams to allocate intensive monitoring and therapeutic resources more effectively to patients at greatest risk, ultimately supporting improved survival outcomes.

This study has several strengths. With a large cohort of 1,371 patients, the study offers enhanced statistical power, allowing its findings to be more broadly applicable to ICU populations facing similar challenges. By focusing on data from a low-to-middle-income country, the study also provides valuable insights into how disease outcomes may vary in settings with different healthcare resources compared to high-income countries. Additionally, the focus on hypotension and distinguishing between types of shock (septic vs. vasoplegic) facilitates a thorough analysis of different forms of circulatory failure and their unique impacts on mortality risk.

This study has several limitations. Its retrospective, single-center design may introduce biases related to data quality and limit generalizability to other ICUs with different patient populations, protocols, or resources. Hypotension was defined indirectly by vasopressor use rather than direct arterial pressure, and vasoplegic shock was pragmatically defined as vasopressor use with lactate ≤ 2.0 mmol/L, a cutoff lacking universal consensus and rather than using direct measures of arterial pressure, the study used the need for vasopressors as a surrogate marker of hypotension. Furthermore, the study focused exclusively on critically ill patients with COVID-19, the results may not apply to other viral sepsis.

In conclusion, this study supports lactate as a valuable prognostic marker in critically ill COVID-19 patients, particularly when assessed alongside hemodynamic status. Monitoring lactate and identifying hypotension provide complementary insights into disease severity, enabling early recognition of high-risk patients and informing tailored management strategies beyond standard sepsis protocols. Future research should establish explore dynamic measures such as lactate clearance to optimize prognostic accuracy and strengthen clinical decision-making.

Acknowledgements
The authors thank the Institutional Scientific Initiation Scholarship Program (PIBIC) of the National Council for Scientific and Technological Development (CNPq) of the Brazilian Federal Government.

Authors' contributions
•Authors' contributionsConceptualization: MMJ, JVG, SMLData curation: MMJ, TH, JVG, JBE, SMLFormal analysis: TH, SMLInvestigation: MMJ, TH, JVG, JBE, SML Methodology: JVG, SMLProject administration: JVG, SMLSupervision: SMLValidation: MMJ, TH, JVG, JBE, SMLVisualization: MMJ, TH, JVG, JBE, SML Writing - original draft: MMJ, TH, JVG, JBE, SMLWriting - review & editing: MMJ, TH, JVG, JBE, SML.

Funding
None.
• Acknowledgements.
The authors thank the Institutional Scientific Initiation Scholarship Program (PIBIC) of the National Council for Scientific and Technological Development (CNPq) of the Brazilian Federal Government.

Data availability
The data can be obtained in the access to our drive – link: [https://docs.google.com/spreadsheets/d/1ZVsK1RSBKiisZIli-tzFc4SoQRoEvXTrvLvD9qLDm2o/edit? usp=sharing](https:/docs.google.com/spreadsheets/d/1ZVsK1RSBKiisZIli-tzFc4SoQRoEvXTrvLvD9qLDm2o/edit? usp=sharing)[https://docs.google.com/document/d/17HvFZ-O3otoCft4NmUXohfMyAbbyRHAz/edit? usp=sharing&ouid=116306902732588374518&rtpof=true&sd=true](https:/docs.google.com/document/d/17HvFZ-O3otoCft4NmUXohfMyAbbyRHAz/edit?usp=sharing&ouid=116306902732588374518&rtpof=true&sd=true).

Declarations

Ethics approval and consent to participate
The study was approved by the local Institutional Review Board (CAAE: 31725720.2.0000.5415). The need for consent to participate was waived by an Institutional Review Board - The Research Ethics Committee – CEP of the Faculty of Medicine of São José do Rio Preto (FAMERP), in accordance with the attributions defined in CNS Resolution No. 466, of 2012, and in Operational Standard No. 001, of 2013, of the CNS, expresses its approval of the research protocol.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 20 February 2025 / Accepted: 29 August 2025
Published online: 21 November 2025

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