



Tissue hypoperfusion markers and their prognostic value in the mortality of critical patients in a polyvalent unit.

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* Autor de correspondencia

Email: Stenio Eduardo Cevallos Espinar

<steniocevallos@hotmail.com>

Dirección: Unidad de Cuidados Intensivos, Hospital Alcívar. Calle Coronel 2301 y Azuay. CP 090109. Teléfono [593] 04-3720-100.

Stenio Eduardo Cevallos Espinar ¹ *, Diana Vera González ¹ , Mayra Narcisca Layana Castro¹ .

1. Critical Care Service, Alcívar Hospital, Guayaquil, Ecuador.

Abstract

Introduction: Early detection of tissue hypoperfusion is crucial for the prognosis of critically ill patients. Traditional hemodynamic markers, such as lactate, the venoarterial carbon dioxide gradient (Delta PCO₂), and central venous oxygen saturation (SvCO₂), allow the assessment of different domains of cellular perfusion and cardiac output. The objective of this study was to correlate serum lactate, Delta PCO₂, and SvO₂ levels with mortality in critically ill patients treated in a polyvalent unit.

Methodology: An observational and analytical study was conducted at Alcívar Hospital in 2024, with a sample of 193 patients. Demographic, clinical (surgical vs. clinical pathology), and physiological variables (lactate, Delta PCO₂, SvCO₂, and APACHE II scale) were collected. The statistical analysis included measures of central tendency, Pearson correlation, bilateral significance, and diagnostic performance, as measured by the area under the ROC curve (AUC), to assess sensitivity and specificity with respect to mortality.

Results: The sample showed a predominance of males (67.4%) and surgical patients (81.4%), with an overall mortality of 16.5%. Delta PCO₂ was the most frequently altered marker (>6 mmHg in 58.5% of cases) and was significantly associated with the APACHE II scale ($\rho = 0.039$). However, lactate demonstrated the best diagnostic performance for mortality (AUC = 0.625), with an optimal cutoff of 1.25 mmol/l, yielding a sensitivity of 78% and a specificity of 61%. Mortality was significantly higher in medical patients (41.7%) than in surgical patients (10.8%; $P < 0.0001$), whereas SvCO₂ did not show significant discriminative capacity in this sample.

Conclusions: Serum lactate is confirmed as the most sensitive predictor of mortality, even at borderline levels (1.25 mmol/l). Although Delta PCO₂ is a frequent indicator of hemodynamic alteration in critically ill patients, its use should be complementary. Close multiparametric monitoring is recommended, especially in patients with a clinical profile, to guide timely resuscitation and reduce mortality rates in the intensive care unit.

Keywords: Lactate, Delta CO₂, Venous Oxygen Saturation, Mortality, Intensive Care, Tissue Perfusion.



Introduction

Serum lactate and venous oxygen saturations—both mixed (SvO₂) and central (SvcO₂)—are the most valuable biomarkers for detecting tissue hypoxia. Since measuring SvO₂ requires pulmonary artery catheterization (an invasive, costly procedure associated with potential complications), central venous catheterization has become the standard alternative. This allows the measurement of SvcO₂, which serves as an effective clinical surrogate for assessing tissue oxygenation in various critical scenarios [1, 2]. In pathologies such as septic shock, cardiogenic shock, and cardiovascular surgery, the decline of these values—specifically below the critical threshold of approximately 40%—is directly associated with an unfavorable prognosis [3]. Complementing this assessment, the veno-arterial carbon dioxide gradient (Delta PCO₂ or Delta CO₂) has emerged as a key tool to evaluate the adequacy of cardiac output relative to cellular metabolic demand [4, 5]. An elevated Delta PCO₂ serves as an early warning sign of hypoperfusion, indicating that blood flow is insufficient to eliminate CO₂ produced by tissues. Although the international Surviving Sepsis Campaign guideline has not yet formally included it as a resuscitation target [6], recent research (2021–2023) emphasizes that the persistence of this elevated gradient during the first 24 hours in the Intensive Care Unit (ICU) is positively associated with increased mortality, surpassing conventional markers in sensitivity for cases of occult hypoperfusion [5]. On the other hand, serum lactate is the classic marker of anaerobic metabolism, derived from glycolysis, in states of acute circulatory dysfunction [7, 8]. While its elevation is often attributed to hypoxia, hyperlactatemia can originate from multiple acute etiologies, ranging from sepsis and shock to non-hypoxic causes, such as hepatic insufficiency or ketoacidosis [9]. In this context, the ANDROMEDA-SHOCK study demonstrated that although lactate-guided resuscitation is the standard, a strategy based on peripheral perfusion (capillary refill time) allows more conservative fluid resuscitation and reduces organ dysfunction at 72 hours, with no significant difference in 28-day mortality [10]. Specifically, in the postoperative period after cardiac surgery, hyperlactatemia is classified by its timing. The early form, developed in the operating room or upon immediate admission to the ICU, often responds to both hypoxic (microcirculatory shock) and non-hypoxic mechanisms [11]. In contrast, late hyperlactatemia (6 to 12 hours post-admission) is generally considered a benign, self-limiting condition that resolves within 24 hours, with no evidence of regional hypoxia [11]. Under this theoretical framework, the present study aims to correlate serum lactate levels, Delta PCO₂, and SvcO₂ with mortality in critically ill patients treated in the polyvalent unit of Alcívar Hospital during the period from January 1 to December 31, 2024.

Materials and Methods

Study Design

This study is observational, the source is retrospective.

Setting

The present study was conducted in the intensive care unit of Alcívar Hospital in Guayaquil, Ecuador. The observation period was from January 1 to December 31, 2024.



Participants

Adults over 20 years of age were included, with first admission to the ICU, surgical and non-surgical pathologies, and mortality within 7 days in the ICU. Patients with incomplete medical records or who underwent surgical reintervention were excluded.

Variables

Demographic variables collected included sex, age, discharge status, type of pathology, discharge diagnosis, serum lactate measurements, delta CO₂, and venous oxygen saturation. Apache II severity indices

Data sources/measurements

The source was indirect. Age was recorded in completed years and grouped into the ranges of 18-30, 31-60, 61-90, and over 90 years. Regarding clinical and length-of-stay variables, the clinical discharge condition was recorded as a dichotomous variable (alive or dead), the type of pathology classified as clinical or surgical, and their respective diagnostic subcategories, covering neurological, pneumological, and cardiological areas for clinical cases, as well as cardiological and neurosurgical areas for surgical cases. Likewise, the number of ICU days and the specific discharge diagnosis, such as septic shock, cardiogenic shock, or asystole, were recorded. For physiological variables and perfusion markers, serum lactate was measured in mmol/l (with cutoff points of >2 mmol/l and >1.25 mmol/l), delta CO₂ (Δ PCO₂) in mmHg (analyzing thresholds of >6 mmHg and >7.5 mmHg), and venous oxygen saturation (SvO₂ or SvcO₂) in percentage (evaluating thresholds of <70% and <62.5%). Lastly, prognostic and statistical indices were combined using the APACHE II scale to assess severity upon admission, and diagnostic performance variables were calculated through ROC curve analysis, including the area under the curve (AUC), sensitivity, and specificity of each marker regarding mortality.

Biases

Observation and selection bias were prevented by applying participant selection criteria. The principal investigator consistently used a guide and records approved in the research protocol to avoid potential interviewer, information, and recall biases. Data collectors were trained on the forms. Two researchers independently analyzed each record twice, and variables were entered into the database after verifying their consistency.

Study Size

The sample was probabilistic. In 2024, 722 patients were admitted, representing the total population. With an expected frequency of 21.4%, a 5% confidence limit, and a 95% confidence level, the sample size was 190 cases. Epi Info Version 7.2.7 (CDC, Atlanta, USA, released on March 9, 2025) was used.

Quantitative Variables

The results are presented as frequencies and percentages. The variables collected on a scale were not converted into categorical variables.

Statistical analysis

For the statistical analysis of this study, descriptive statistics were initially used to analyze demographic and clinical variables, using frequencies and percentages for qualitative data, and measures of central tendency (mean, median, and mode) along with dispersion (standard

deviation) for quantitative variables. To assess the relationship between tissue perfusion markers, Pearson's correlation coefficient and the coefficient of determination R^2 were applied, enabling evaluation of the strength of association and the explained variability between lactate, ΔPCO_2 , and SvO_2 . The clinical severity's statistical significance was evaluated using the APACHE II scale, with a bilateral significance test (ρ) for each marker. Lastly, a diagnostic performance analysis was performed using ROC curves to determine the area under the curve (AUC), sensitivity, and specificity, successfully identifying the optimal cutoff points of biomarkers in relation to mortality in critically ill patients. The statistical software used was SPSS Statistics for Windows, version 26.0. Armonk, NY: IBM Corp.

Results

Participants

A total of 193 cases were included in the study.

Sample Description

There were 130 men and 63 women admitted to the intensive care unit, resulting in a sociodemographic profile with a male predominance of 45.79% ($n=92$) and a mean age of 62.4 SD: 15.79 years ([Table 1](#)).

Table 1. Age and sex by ranges.

Age (years)	Male n (%)	Female n (%)
18 - 30	11 (8.5)	1 (1.6)
31 - 60	32 (24.6)	21 (33.3)
61 - 90	86 (66.2)	40 (63.5)
>90	1 (0.7)	1 (1.6)
Total	130 (67.4)	63 (32.6)

In the study patients, measurements of tissue hypoperfusion markers such as lactate, delta CO_2 , and SvO_2 were performed, of which 1 showed a proportion outside their normal range, such as delta $\text{CO}_2 > 6$ mmHg (58.5%); however, SvO_2 did not show greater relevance ($< 70\%$; 39.4%), and lactate > 2 mmol/L in 32.1% of cases ([Table 2](#)). Regarding the measures of central tendency, lactate shows the greatest asymmetry, with a large difference among the mean, median, and mode. However, Delta CO_2 has values that are closer to each other, making this variable more symmetric. The same occurs with SvO_2 . Despite this, its standard deviation of 11.99 is the highest among the three markers, indicating greater dispersion ([Table 3](#)).

According to the clinical condition, it was observed that from 1 to 43 days ($\bar{x} = 5.69$; $\sigma = 8.52$), the mortality rate in the ICU was 16.5% ($n = 32$), with males predominating (19/32, 59.4%). Among the presented pathologies, surgical pathologies predominated at 81.4% ($n=157$), with a mortality rate of 10.8% ($n=17$); by contrast, clinical pathologies accounted for 18.6% ($n=15$) and had a mortality rate of 41.7% ($n=6$). Among clinical pathologies, neurological pathologies predominated at 4.7% ($n=9$), followed by pulmonary and cardiological pathologies at 3.6% each. Regarding surgical pathologies, cardiological pathologies were more frequent at 60.1% ($n=116$), followed by neurosurgical pathologies at 9.8% ($n=19$) ([Table 4](#)).



Table 2. Distribution of tissue perfusion markers.

Tissue perfusion marker	Frequency (n)	Percentage (%)
Lactate		
< 2mmol/l	131	67.9
> 2mmol/l	62	32.1
Delta CO2		
< 6 mmHg	80	41.5
> 6 mmHg	113	58.5
SvO2		
< 70%	76	39.4
>70%	117	60.6

Table 3. Central tendency measures.

Marker	Mean	Median	Mode	Standard deviation
Lactate	2.3	1.5	1.3	2.49
Delta CO2	8.0	7.0	6.0	4.68
SvO2	72.2	73.0	72	11.99

Table 4. Measures of central tendency.

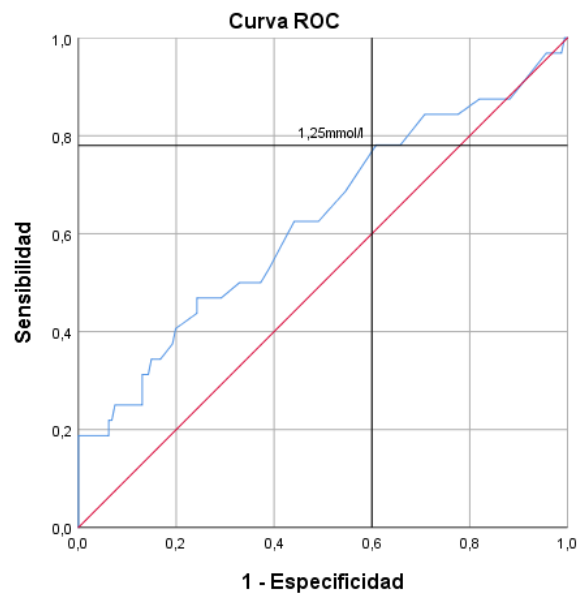
Gender	Clinical condition		P
	Deceased n=32	Vivos =161	
Men	19 (59.4%)	111 (68.9)	0.2930
Clinical vs. surgical pathology	15 (46.9%)	21 (13.0%)	<0.0001

Mortality study and regression analysis

The APACHE II prognostic scale was used ($\bar{x} = 20.53$; $\sigma = 8.42$), which showed a bilateral association with Delta CO2 ($P = 0.039$) but a 5% risk probability for lactate ($P = 0.050$), and was not significant for SvO2 ($P = 0.826$). The Pearson correlation between Lactate and SvO2 was $R = 0.023$. Between Lactate and Delta CO2, $R = 0.024$. Between SvO2 and Delta CO2, it was 0.181.

Diagnostic tests

Mortality vs lactate. It has an AUC=0.625. With Sensitivity 78%, Specificity 61% for a cutoff point of 1.25 mmol/l, with an overall mortality of 16.5% (n=32). Values above this point were 78.12% (n=25) (Figure 1). Other diagnostic test studies were not significant: Mortality vs Delta CO2. It has an AUC of 0.461, indicating no discriminatory capacity. With Sensitivity 53%, Specificity 48% for a cutoff point of 7.5 mmHg, with an overall mortality of 16.5% (n=32). Values above this point were 53.11% (n=17). Mortality vs SvO2. It has an AUC of 0.502, indicating poor performance. With Sensitivity 87%, Specificity 80% for a cutoff point of 62.5%, with an overall mortality of 16.5% (n=32). Values below this point were 18.75% (n=6).

Figure 1. Roc Curve

Discussion

Main Findings

The main findings of this study reveal that, in a predominantly male and elderly sample treated in the polyvalent unit of Hospital Alcívar, the overall mortality rate was 16.5%, with a statistically significant difference ($p < 0.0001$) between medical patients (41.7% mortality) and surgical patients (10.8%). Regarding perfusion markers, the veno-arterial carbon dioxide gradient (Delta PCO_2) had the highest frequency of initial alteration (58.5% of cases with values above 6 mmHg) and showed a significant association with severity, as measured by the APACHE II scale ($\rho = 0.039$). However, serum lactate proved to be the biomarker with the best diagnostic performance for predicting mortality, achieving an area under the curve (AUC) of 0.625 with a cutoff point of 1.25 mmol/l, which implied a sensitivity of 78% and a specificity of 61%, surpassing the discriminatory capacity of SvO_2 and Delta PCO_2 itself.

Interpretations

The interpretation of these results suggests that, although Delta PCO_2 is a highly sensitive indicator for detecting states of low cardiac output, which explains its frequent alteration in a population with 60.1% of cardiac surgical patients, its ability to, in isolation, discriminate who will die is limited (AUC = 0.461). This could be because the CO_2 gradient is a flow marker, whereas lactate, which has a stronger correlation with mortality, more directly reflects metabolic damage and accumulated oxygen debt. The low Pearson correlation observed between the three markers ($R < 0.2$ in all cases) reinforces the interpretation that these parameters evaluate different domains of hemodynamics: systemic flow, tissue oxygenation, and cellular metabolism, which operate independently and not necessarily in a linear manner during critical illness.



Practical Implications

The practical implications of this research underscore the need for multiparameter monitoring that does not rely on a single threshold value. The fact that a lactate cutoff as low as 1.25 mmol/l has shown 78% sensitivity in predicting death suggests that even mild elevations in lactate, below the traditional 2 mmol/l threshold, should be interpreted with caution in critically ill patients. Similarly, given the strong association between clinical pathologies and higher mortality rates than surgical ones, the care team must intensify hemodynamic monitoring in non-surgical patients, using Delta PCO₂ as an early warning sign of occult hypoperfusion, while always validating metabolic status through serial lactate monitoring to guide resuscitation goals.

Contrast with scientific literature

Several studies indicate that elevated lactate is an indicator of poor cellular metabolism and is strongly associated with an increased risk of death. This relationship was observed in different types of patients, including those with sepsis, shock, and after cardiac surgeries [12]. One study even mentions that higher lactate levels upon admission are directly linked to higher mortality. The predictive capacity of lactate is considered good to moderate [13]. It differs from the study because a low mortality incidence, 32 (16.5%), was observed in the ICU, with a mean of 5.69 days, and, in turn, it was not correlated with tissue markers.

Research shows that a high CO₂ gap indicates inadequate perfusion and is associated with higher mortality in patients with shock [4]. A particular study highlights that this gap remains a predictor of mortality even after accounting for other factors [14] and correlates with markers such as a low cardiac index, high lactate levels, and low blood oxygen saturation [4]. However, one study found that its predictive utility for adverse outcomes after cardiac surgery was null, suggesting that its value may depend on the clinical context [15]. There is agreement with previous studies, as the CO₂ gap is significant when correlated with the APACHE II severity scale and can be used as a predictor in clinical and surgical pathologies.

The findings on SvO₂ are inconsistent. While one study found that an elevated CO₂ gap correlates with low SvO₂ [4], another concluded that SvO₂ was not a predictor of adverse outcomes in patients after cardiac surgery [15]. Additionally, one investigation found that lactate and SvO₂ have a weak correlation, indicating that they do not always move in the same direction [16]. This may be because SvO₂ reflects the balance between oxygen consumption and supply, while lactate reflects cellular metabolism. It is agreed that tissue markers do not always move in the same direction, as they were not correlated with each other, since they are independent variables.

Limitations

Despite the significant findings, this study has limitations that must be considered when interpreting the results. First, the retrospective and single-center nature of the research at Alcívar Hospital limits the generalizability of the data to other populations with distinct epidemiological profiles or different technological resources. Second, the marked disproportion between the sample of surgical patients (81.4%) and clinical patients (18.6%) may have biased the survival averages and perfusion profiles, given that post-cardiac surgery patients typically exhibit lactate and CO₂ kinetics that differ markedly from those of septic or neurological patients. Finally, the analysis was based on single admission or discharge measurements, which precluded evaluation of lactate clearance or the dynamics of ΔPCO₂



over time, factors that the current literature recognizes as more robust predictors of mortality than a single static measurement.

Future research

Based on the critical points identified, it is suggested that future research in the local context adopt a prospective, multicenter design that enables longitudinal monitoring of biomarkers during the first 24 to 48 hours of ICU stay. It would be of great academic value to conduct subgroup analysis, particularly by comparing the sensitivity of ΔPCO_2 between patients with cardiogenic shock and septic shock, to determine whether intervention thresholds should be differentiated. Additionally, it is recommended to investigate integrating the APACHE II scale with artificial intelligence algorithms that combine lactate and CO_2 gradient in real time to develop a proprietary predictive model that optimizes clinical decision-making and resource allocation in critical care units in the region.

Conclusion

In conclusion, the current study at the polyvalent unit of Hospital Alcívar demonstrates that monitoring tissue hypoperfusion markers remains a critical part of managing critically ill patients. It highlights serum lactate as the most reliable predictor of mortality, with a cutoff point of 1.25 mmol/l, indicating the need for intervention even with mild elevations below traditional thresholds. Although Delta PCO_2 showed many abnormalities and a significant link to clinical severity according to the APACHE II scale, its ability alone to predict death was less effective than lactate. Lastly, the notable difference in mortality rates between medical and surgical patients, along with the weak linear correlation among the three biomarkers studied, confirms that hemodynamic assessment must be multiparametric and tailored to each patient, combining flow, oxygenation, and metabolism to improve outcomes in intensive care.

Abbreviations

APACHE II: Acute Physiology and Chronic Health Evaluation II (Acute Physiology and Chronic Health Evaluation II Scale).

AUC: Area Under the Curve (Area under the curve).

CO_2 : Carbon dioxide.

ΔPCO_2 : Venoarterial carbon dioxide gradient or delta.

SD: Standard deviation.

mmol/l: Millimoles per liter.

mmHg: Millimeters of mercury.

ROC: Receiver Operating Characteristic (Receiver Operating Characteristic).

SvO_2 : Mixed venous oxygen saturation.

SvcO_2 : Central venous oxygen saturation.

ICU: Intensive Care Unit.

\bar{x} : Arithmetic mean.

σ : Standard deviation (symbolic representation).

ρ : Statistical significance value (p-value).

Supplementary information

Supplementary materials have not been declared.

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Not declared.

Author contributions

Stenio Eduardo Cevallos Espinar: Conceptualization, data curation, investigation, methodology, visualization, writing-original draft.



Diana Vera González: Conceptualization, data curation, investigation, project administration, and writing the original draft.

Mayra Narcisca Layana Castro: Conceptualization, data curation, investigation, project administration, and original draft writing.

All authors read and approved the final version of the manuscript.

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Data or materials availability

Not applicable.

Declarations

Ethics Committee Approval and Consent to Participate

The study was approved by the Ethics Committee of the Faculty of Medicine at the University of Guayaquil, Ecuador.

Consent for Publication

Not applicable when specific patient images, X-rays, or photographs are not published.

Conflicts of Interest

The authors declare no conflicts of interest.

Use of generative AI

The authors declare that they used generative AI responsibly in the "Discussion" section, without substituting for the authors' critical thinking, expertise, and judgment. The AI was used under supervision and control to develop the discussion section. The use of the AI tool maintains the privacy and confidentiality of data and contributions, including published and unpublished manuscripts, as well as any personally identifiable information. The journal's policies allowing the use of generative AI only in the introduction and discussion sections have been complied with. Only limited rights are granted to the AI to provide a service. The accuracy, completeness, and impartiality of all AI-generated results were carefully reviewed and verified to ensure that the manuscript reflects an authentic and original contribution.

Author Information

Stenio Eduardo Cevallos Espinar, Doctor of Medicine and Surgery from the Catholic University of Santiago de Guayaquil (Guayaquil, 2006). Specialist in Intensive Care from the Catholic University of Santiago de Guayaquil (Guayaquil, 2007). Physician of the Critical Medicine Service, Intensive Care Unit, Alcívar Hospital, Guayaquil, Ecuador.

Email: steniocevallos@hotmail.com

ORCID <https://orcid.org/0009-0003-7645-894X>

Diana Vera González, Physician from the University of Guayaquil (Guayaquil, 2011). Specialist in Intensive Care at the Hospital Nacional Profesor Alejandro Posadas (El Palomar, Argentina). Specialist in Pneumology from the University of Buenos Aires (Argentina 2024). Attending Physician in Critical Care and Pneumology, Alcívar Hospital, Guayaquil, Ecuador.

Email: mddinav31@gmail.com

ORCID <https://orcid.org/0009-0003-1853-0886>

Mayra Narcisca Layana Castro, R3 Critical Medicine Resident Physician.

Email: smpla5@hotmail.com

ORCID <https://orcid.org/0000-0002-1179-725X>

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