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Early Lactate-Guided Resuscitation in Septic Shock Patients in the ICU

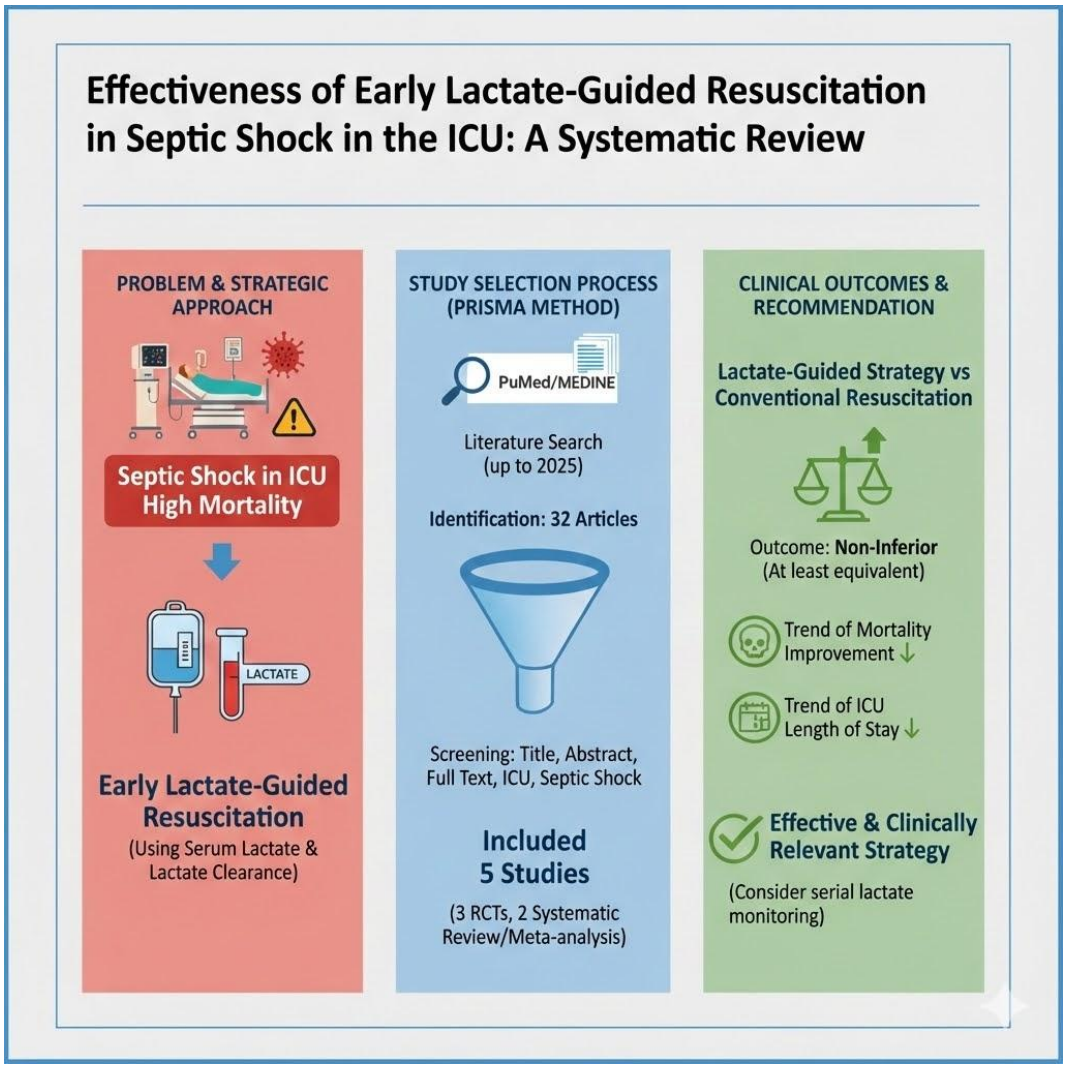
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Graphical Abstract



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ABSTRACT

Background*: Septic shock is a critical condition in the intensive care unit (ICU) with persistently high mortality. Early resuscitation plays a key role in improving tissue perfusion, and serum lactate and lactate clearance have been used as markers of hypoperfusion and response to resuscitation. However, the effectiveness of early lactate-guided resuscitation on clinical outcomes remains to be systematically evaluated.* ***Objective****: To assess the effectiveness of early lactate-guided resuscitation on clinical outcomes in patients with septic shock treated in the ICU.* ***Methods****: This study was conducted as a systematic review in accordance with the PRISMA guidelines. A literature search was performed in the PubMed database through 2025. Studies involving adult patients with septic shock in the ICU that used serum lactate or lactate clearance as a target for early resuscitation were included. Study selection was conducted through title and abstract screening, followed by full-text review based on predefined inclusion and exclusion criteria. Data were synthesized narratively.* ***Results****: Of the 32 articles identified, five studies met the inclusion criteria, comprising three randomized controlled trials and two systematic reviews/meta-analyses. Overall, early lactate-guided resuscitation demonstrated clinical outcomes that were at least non-inferior to conventional resuscitation strategies, with a trend toward improved mortality, shorter ICU length of stay, and better clinical parameters in several studies.* ***Conclusion****: Early lactate-guided resuscitation is an effective and clinically relevant strategy in the management of septic shock in the ICU. Serial monitoring of serum lactate and lactate clearance may be considered as targets for early resuscitation to support improved patient outcomes.Keywords: septic shock; lactate; lactate clearance; early resuscitation; ICU*

INTRODUCTION

Background

Septic shock is the most severe form of sepsis and is associated with significant mortality in the intensive care unit (ICU). According to the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3), septic shock is defined as a sepsis-related condition with circulatory and metabolic abnormalities, characterized by the need for vasopressors to maintain a mean arterial pressure ≥65 mmHg and a serum lactate level >2 mmol/L despite adequate fluid resuscitation.1 Organ dysfunction in sepsis is assessed using the Sequential Organ Failure Assessment (SOFA) score, which plays a key role in stratifying disease severity and predicting mortality.[1]

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Serum lactate reflects the imbalance between tissue oxygen supply and demand and the cellular metabolic disturbances common in septic shock. Elevated lactate levels and failure to decrease them after initial resuscitation have been associated with increased mortality, making lactate an important prognostic marker in patients with severe sepsis and septic shock.[2]

The latest Surviving Sepsis Campaign (SSC) recommends measuring initial lactate levels and repeating measurements if the initial level is elevated as part of the early resuscitation package for sepsis and septic shock[3]. This approach emphasizes target-based resuscitation to improve tissue perfusion. As routine central venous oxygen saturation ($ScvO_2$) use wanes, lactate and lactate clearance monitoring are gaining prominence as more practical and easily implemented alternative resuscitation targets in the ICU.[3]Several randomized controlled clinical trials have shown that lactate clearance-based early resuscitation strategies provide comparable clinical outcomes to $ScvO_2$-based approaches, particularly in reducing mortality in patients with septic shock.[4]

Research Gap

Although lactate is included in the Sepsis-3 definition and recommended in SSC guidelines, implementation of early lactate-based resuscitation remains variable, including the target lactate reduction, the timing of evaluation, and the interpretation of absolute lactate values versus lactate clearance. Furthermore, differences in study designs and patient population characteristics lead to heterogeneity in results, making it difficult to consistently implement lactate-based resuscitation strategies in ICU clinical practice.[1,2,3]

Therefore, a systematic review is needed to comprehensively evaluate the role of early lactate-based resuscitation in septic shock patients in the ICU based on current scientific evidence.

Objective

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systematic review aims to evaluate the role of early lactate-based resuscitation in septic shock patients in the ICU and assess its association with key clinical outcomes, particularly mortality.

RESEARCH METHODS

Research Design

This study is a systematic review conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The review aimed to evaluate the effectiveness of lactate-based early resuscitation on clinical outcomes among patients with septic shock admitted to the intensive care unit (ICU).

Subjects and Samples

The subjects of this systematic review were adult patients (≥18 years) diagnosed with severe sepsis or septic shock who were treated in the ICU. The study sample consisted of scientific articles that met the following inclusion and exclusion criteria:

Inclusion Criteria

- Adult patients (≥18 years)
- Diagnosis of septic shock or severe sepsis
- Admission to the ICU or initial resuscitation phase progressing to the ICU
- Using serum lactate and/or lactate clearance as the TARGET for early resuscitation (protocol-based / guided therapy)
- Have a comparator (conventional or non-lactate resuscitation)
- Reporting clinical outcomes (e.g., mortality, ICU length of stay, duration of mechanical ventilation)
- RCT or systematic review/meta-analysis study design
- English language articles and *full-text available*

Exclusion Criteria

- Purely observational or prognostic studies without lactate-based resuscitation interventions
- Lactate is only recorded as a biomarker, not a therapeutic target.

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- Non-ICU, pediatric, or sepsis-free population
- Design narrative reviews, editorials, case reports/series, or conference abstracts
- Methodology unclear or does not report clinical outcomes
- Non-English or *full-text publications* are not available.

Procedure

A systematic literature search was conducted using the PubMed database. PubMed was chosen because it is the primary database covering clinical medicine literature, including randomized controlled trials and meta-analyses in the field of intensive care and septic shock.

The search was conducted through 2025 using a combination of Medical Subject Headings (MeSH) and free-text terms related to septic shock, lactate, early resuscitation, and intensive care.

The keyword combinations used include:

- *Septic shock*
- *Lactic acid*
- *Lactate clearance*
- *Early resuscitation*
- *Early goal-directed therapy*
- *Intensive care unit*

All articles obtained from the search results were collected and screened based on **title and abstract** . Articles deemed relevant were then assessed through **full-text review** to determine eligibility for inclusion. The selection process was conducted based on predetermined inclusion and exclusion criteria. The study selection flow is reported using a PRISMA diagram.

Variables

Main Variables

- Lactate-based early resuscitation strategy, defined as the use of serum lactate and/or lactate clearance as therapeutic targets in resuscitation protocols for patients with septic shock.

Output Variable

- **Primary output** :
  - Mortality (ICU mortality, in-hospital mortality, or 28-day mortality)
- **Secondary output** :
  - Length of ICU stay

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- Duration of mechanical ventilation
- Resolution of shock or improvement of perfusion parameters
- Development of organ dysfunction

Statistical Analysis

Data analysis was conducted descriptively and narratively. The research results are presented in the following format:

- summary of study characteristics,
- comparison of clinical outcomes between the lactate-based resuscitation group and the control group,
- and interpretation of trends in results between studies.

Quantitative meta-analysis was not performed due to heterogeneity of study designs, variations in interventions, and differences in outcome definitions among the included studies.

Ethical Approval

This study did not require ethical clearance *because* it used secondary data derived from published scientific articles and did not involve direct intervention or individual patient identification. All data were analyzed and reported in accordance with the principles of research ethics and scientific integrity.

RESULTS

Study Selection Results

A literature search through the PubMed database yielded 32 articles. After screening titles and abstracts and reviewing the full text based on inclusion and exclusion criteria, five studies met the criteria and were included in this systematic review. The included studies consisted of three randomized controlled trials (RCTs) and two systematic reviews/meta-analyses evaluating early lactate-guided resuscitation strategies in patients with septic shock in the ICU.

Characteristics of Included Studies

The studies analyzed involved adult patients diagnosed with septic shock or severe sepsis undergoing early resuscitation in the ICU. The primary intervention in all studies was the use of serum lactate or lactate clearance as the resuscitation target, with a comparison

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group consisting of conventional resuscitation or a non-lactate strategy.

Table 1. Main Characteristics of Included Studies

Author (Year)	Study Design	Population	Intervention (Group A)	Comparator (Group B)	Main Output
Jones et al., 2010	RCT	Severe sepsis / septic shock	Lactate clearance–guided resuscitation	Conventional EGDT	Mortality
Castro et al., 2020	RCT	Septic shock ICU	Lactate-guided resuscitation	Capillary refill–guided	Mortality, ICU LOS
Chen et al., 2021	RCT	Septic shock ICU	Lactate clearance–guided therapy	Standard care	Mortality
Pan et al., 2019	Meta-analysis	Septic shock	Lactate-guided resuscitation	Non-lactate strategies	Mortality
Graziani et al., 2025	Meta-analysis	Septic shock ICU	Lactate-based resuscitation	Usual care	Mortality, ICU outcomes

Note: RCT = randomized controlled trial; ICU = intensive care unit; LOS = length of stay; EGDT = early goal-directed therapy.

Clinical Outcomes

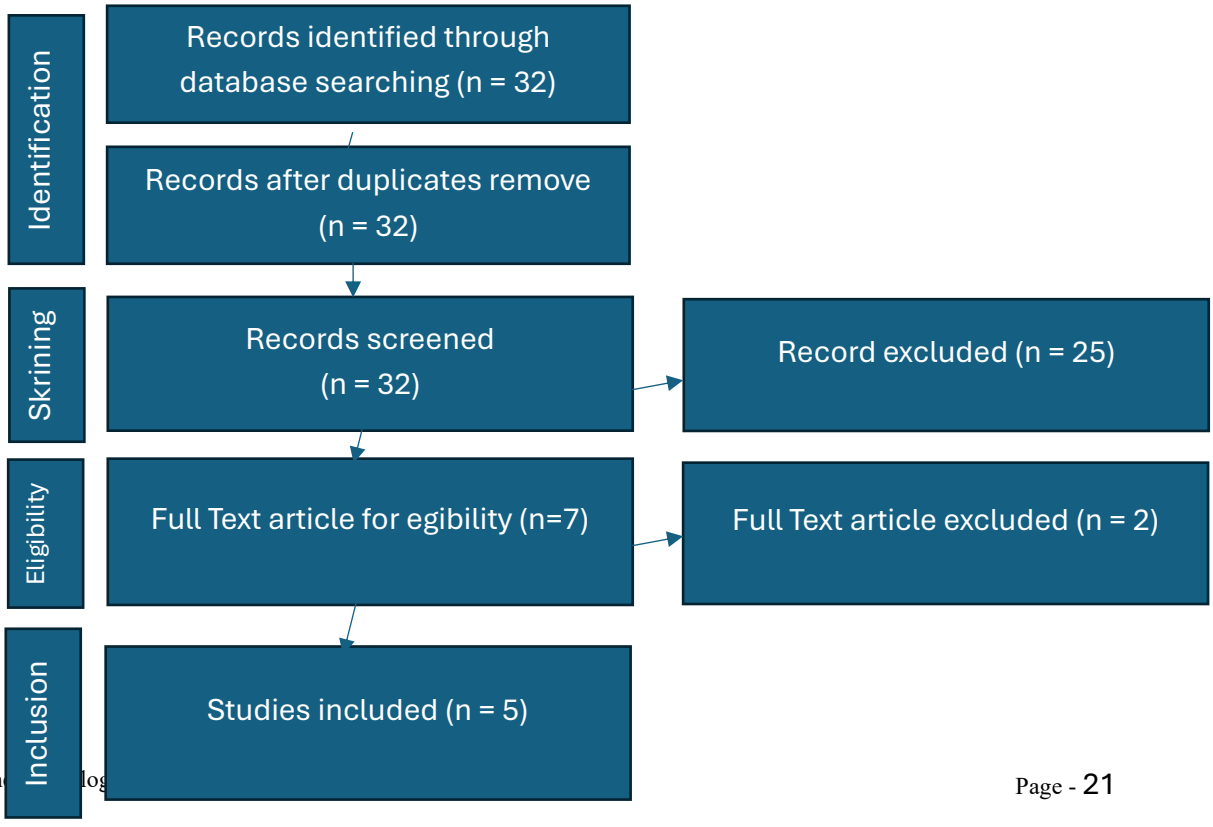
Overall, early lactate-guided resuscitation strategies demonstrate clinical outcomes that are at least non-inferior to conventional resuscitation strategies. Several studies have reported a trend toward reduced mortality, shorter ICU stays, and improved perfusion parameters in the lactate-guided resuscitation group. The included meta-analyses also demonstrated that the use of lactate as a target for early resuscitation is associated with improved clinical outcomes in patients with septic shock.[5]

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Table 2. Summary of Clinical Outcomes of Resuscitation Strategies

Variables	Lactate-Guided Resuscitation (Group A)	Conventional / Non-Lactate Resuscitation (Group B)
Mortality	Non-inferior / tends to be lower	Comparator
Length of ICU stay	Tends to be shorter	Longer
Duration of mechanical ventilation	Shorter in some studies	Comparator
Shock resolution	Faster in subgroups	Comparator

Note: Results are presented narratively due to heterogeneity of design and outcomes across studies; quantitative meta-analysis was not performed.



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Figure 1. Study Selection Flowchart Based on PRISMA

DISCUSSION

Interpretation of Main Results

This systematic review shows that early lactate-guided resuscitation strategies in patients with septic shock in the ICU provide clinical outcomes that are at least non-inferior to conventional resuscitation strategies.[4–9] Several studies analyzed showed a trend toward reduced mortality, shortened ICU length of stay, and improved tissue perfusion parameters in the lactate-based resuscitation group.[5–9] These findings support the role of serum lactate and lactate clearance not only as markers of hypoperfusion but also as clinically relevant therapeutic targets in the early phase of septic shock.

Comparison with Previous Studies

The results of this review are consistent with earlier randomized controlled trials comparing lactate clearance–guided therapy with conventional resuscitation strategies, which showed that using lactate as an early resuscitation target resulted in comparable or better outcomes than traditional hemodynamic parameter-based approaches.[5] Furthermore, the meta-analyses included in this review reinforce the finding that lactate-based resuscitation does not increase the risk of adverse outcomes and may potentially provide some clinical benefit in patients with septic shock.[10,11]

Comparison with studies evaluating alternative resuscitation strategies, such as capillary refill time-based approaches, suggests that lactate remains an important resuscitation target, particularly in the context of monitoring systemic perfusion and therapeutic response in the early phase of ICU care. [10,11]

Clinical Implications

The findings of this systematic review have relevant clinical implications. The use of serum lactate and lactate clearance as early resuscitation targets is a practical, accessible, and widely applicable approach, including in healthcare facilities with limited resources.[3,4] This approach can be used as an alternative

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or complementary resuscitation target to conventional hemodynamic parameters in the management of septic shock in the ICU.[12]

In addition, serial lactate monitoring allows clinicians to dynamically assess the resuscitation response and adjust therapy more targetedly, potentially preventing both inadequate and excessive resuscitation.[10,13].

Research Strengths

A key strength of this systematic review is the use of stringent inclusion criteria, which focused the analysis on randomized controlled trials and meta-analyses with lactate-based resuscitation interventions as the therapeutic target.[9] All core studies were from reputable journals and indexed by PubMed, enhancing the internal validity of the findings. Furthermore, the use of PRISMA guidelines ensured transparency and reproducibility of the study selection process.[14]

Research Limitations

Several limitations should be considered when interpreting the results. First, the literature search was conducted in only one database, potentially limiting the scope of the studies. Second, heterogeneity in study designs, outcome definitions, and variations in resuscitation protocols across studies limit the possibility of conducting a quantitative meta-analysis. Third, the number of included studies is relatively limited, so the results of this review should be interpreted with caution.[8,9]

Further Research Directions

Future studies are expected to evaluate lactate-based resuscitation strategies in a more standardized clinical trial design, including determining optimal lactate clearance targets and the most effective monitoring duration.[3,9] Comparative studies between lactate and alternative perfusion parameters, as well as studies in specific patient subgroups, such as those with severe comorbidities or refractory septic shock, are also needed to clarify the role of lactate in the management of septic shock in the ICU.[6,9,15]

CONCLUSION

This systematic review demonstrates that early lactate-guided resuscitation is an effective and safe strategy in the management of patients with septic shock in the ICU. The

use of serum lactate and *lactate clearance* as early resuscitation targets provides clinical outcomes that are at least non-inferior to conventional resuscitation strategies, with the potential for improvements in mortality and other clinical parameters. Serial lactate monitoring can be considered a clinically relevant resuscitation target in intensive care practice.

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CONFLICT OF INTEREST

The author declares that there is no conflict of interest in the preparation and publication of this research.

FUNDING

This research did not receive any specific funding from any public, commercial, or not-for-profit organization.

ETHICAL APPROVAL

This study is a systematic review using secondary data from published scientific articles, and therefore does not require ethical approval from a research ethics committee. The systematic review protocol has been registered with PROSPERO under registration number 1302947.

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