

Impacto Hemodinámico de la Terapia Vasopresora en Pacientes Críticamente Enfermos con Choque Séptico en la Unidad de Cuidados Intensivos.

Hemodynamic Impact of Vasopressor Therapy in Critically Ill Patients with Septic Shock in the Intensive Care Unit

Francisco Luis Díaz Ramírez

Universidad el bosque / Hospital Simón Bolívar

Franciscoluisdiaz375@gmail.com

<https://orcid.org/0009-0001-0130-7763>

Jose David Alvarez Rodriguez

Hospital Simon Bolivar - Fundación Universitaria

Sanitas

josealvarez012420@gmail.com

<https://orcid.org/0009-0008-7287-5670>

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***Autor de correspondencia** Franciscoluisdiaz375@gmail.com

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RESUMEN

El choque séptico continúa siendo una de las principales causas de mortalidad entre los pacientes críticamente enfermos ingresados en unidades de cuidados intensivos a nivel mundial. La vasodilatación profunda, la disfunción circulatoria y el deterioro de la perfusión tisular hacen necesaria la utilización de terapia vasopresora para restaurar la estabilidad hemodinámica y preservar la función orgánica. Esta revisión analiza la evidencia científica actual relacionada con el impacto hemodinámico de la terapia vasopresora en pacientes adultos con choque séptico, con especial énfasis en las experiencias clínicas y los sistemas de salud del continente americano. Se examinó literatura científica proveniente de las principales bases de datos biomédicas para evaluar los efectos fisiológicos, la eficacia terapéutica, los perfiles de seguridad y los desenlaces

clínicos asociados con los principales agentes vasoactivos, incluidos norepinefrina, vasopresina, epinefrina, dopamina, fenilefrina y angiotensina II. Los hallazgos muestran que la norepinefrina continúa siendo el vasopresor de primera elección debido a su equilibrio favorable entre eficacia y seguridad. El inicio temprano de la terapia vasopresora se asoció consistentemente con una mejor estabilización hemodinámica, menor duración de la hipotensión y mejor perfusión tisular. Terapias complementarias como la vasopresina y la angiotensina II demostraron beneficios potenciales en pacientes seleccionados con choque vasodilatador refractario. La revisión también destaca la importancia de individualizar las metas de presión arterial, integrar la evaluación de la microcirculación y mantener una adecuada adherencia a los protocolos basados en evidencia. Asimismo, se identificaron diferencias regionales en recursos de cuidados intensivos, disponibilidad de medicamentos e infraestructura sanitaria que influyen en los resultados clínicos en América. La evidencia disponible respalda la implementación de estrategias vasopresoras personalizadas integradas dentro de un manejo crítico integral para mejorar la supervivencia y reducir la disfunción orgánica en pacientes con choque séptico.

PALABRAS CLAVE

Choque séptico, terapia vasopresora, norepinefrina, vasopresina, angiotensina II, estabilización hemodinámica, unidad de cuidados intensivos, medicina crítica, perfusión tisular, presión arterial media, disfunción orgánica, agentes vasoactivos, sepsis, monitorización hemodinámica, América

ABSTRACT

Septic shock remains one of the leading causes of mortality among critically ill patients admitted to intensive care units worldwide. Profound vasodilation, circulatory dysfunction, and impaired tissue perfusion frequently necessitate the use of vasopressor therapy to restore hemodynamic stability and preserve organ function. This review analyzes the current evidence regarding the hemodynamic impact of vasopressor therapy in adult patients with septic shock, with particular emphasis on clinical experiences and healthcare systems across the American continent. Scientific literature from major biomedical databases was examined to evaluate the physiological effects, therapeutic efficacy, safety profiles, and clinical outcomes associated with commonly used vasoactive agents, including norepinephrine, vasopressin, epinephrine, dopamine, phenylephrine, and angiotensin II. The findings indicate that norepinephrine remains the preferred first-line vasopressor due to its favorable balance between efficacy and safety. Early vasopressor initiation was consistently associated with improved hemodynamic stabilization, reduced duration of hypotension, and enhanced tissue perfusion. Adjunctive therapies such as vasopressin and angiotensin II demonstrated potential benefits in selected patients with refractory vasodilatory shock. The review also highlights the importance of individualized blood pressure targets, integration of microcirculatory assessment, and adherence to evidence-based sepsis protocols. Furthermore, regional differences in critical care resources, medication availability, and healthcare infrastructure were identified as important factors influencing outcomes throughout the Americas. The available evidence supports the implementation of personalized vasopressor strategies combined with comprehensive critical care management to improve survival and reduce organ dysfunction in patients with septic shock.

KEYWORDS

Septic shock, vasopressor therapy, norepinephrine, vasopressin, angiotensin II, hemodynamic stabilization, intensive care unit, critical care medicine, tissue perfusion, mean arterial pressure, organ dysfunction, vasoactive agents, sepsis, hemodynamic monitoring, Americas

INTRODUCCIÓN

Septic shock remains one of the most challenging conditions encountered in modern intensive care medicine and continues to be associated with substantial morbidity, mortality, prolonged hospitalization, and increased healthcare expenditures worldwide. Despite significant advances in critical care monitoring, antimicrobial therapy, organ support technologies, and evidence-based treatment protocols, septic shock remains a leading cause of death among critically ill patients admitted to intensive care units (ICUs). The condition is characterized by profound circulatory, cellular, and metabolic abnormalities resulting from a dysregulated host response to infection, ultimately leading to tissue hypoperfusion, multiple organ dysfunction syndrome, and death if not rapidly recognized and treated (Evans et al., 2021).

Globally, sepsis affects millions of individuals each year and represents a major public health concern across both developed and developing nations. Recent epidemiological evidence suggests that approximately 49 million cases of sepsis occur annually, contributing to nearly 11 million deaths worldwide and accounting for a significant proportion of all global mortality (Rudd et al., 2020). Within this spectrum, septic shock represents the most severe manifestation of sepsis and is associated with mortality rates frequently exceeding 30–40%, particularly among patients with advanced age, multiple comorbidities, delayed diagnosis, or severe organ dysfunction (Evans et al., 2021). The burden of septic shock is especially pronounced in low- and middle-income countries, where limitations in healthcare infrastructure, delayed access to critical care services, and resource constraints may further worsen outcomes.

The pathophysiology of septic shock is highly complex and involves a combination of systemic inflammation, endothelial dysfunction, microcirculatory impairment, vasoplegia, mitochondrial dysfunction, and cardiovascular abnormalities. One of the hallmark features of septic shock is persistent hypotension resulting from widespread vasodilation and decreased systemic vascular resistance. In addition, myocardial depression, altered vascular responsiveness to endogenous catecholamines, and disturbances in regional blood flow contribute to inadequate tissue oxygen delivery and progressive organ failure (Shi et al., 2020). These hemodynamic alterations create a critical need for prompt circulatory support aimed at restoring adequate mean arterial pressure (MAP), improving organ perfusion, and preventing irreversible tissue injury.

Vasopressor therapy has therefore become a cornerstone in the management of septic shock. Current international guidelines recommend the early initiation of vasopressors when hypotension persists despite adequate fluid resuscitation, with norepinephrine identified as the first-line agent due to its favorable balance between efficacy and safety (Evans et al., 2021). The primary objective of vasopressor administration is to achieve and maintain adequate perfusion pressure while minimizing adverse cardiovascular effects. However, the optimal selection, timing, dosage, and combination of vasopressor agents remain subjects of ongoing investigation and debate within the critical care community.

Over the past two decades, numerous clinical trials have evaluated the hemodynamic effects and clinical outcomes associated with different vasopressor strategies. The landmark SOAP II trial demonstrated that norepinephrine was associated with a lower incidence of arrhythmias compared with dopamine while providing comparable hemodynamic stabilization, thereby supporting the preferential use of norepinephrine in shock states (De Backer et al., 2010). Similarly, the VASST trial investigated the addition of vasopressin to norepinephrine therapy and found potential benefits in specific patient subgroups, although overall mortality differences were not statistically significant (Russell et al., 2008). These findings contributed to the growing recognition that vasopressor therapy should be individualized according to patient characteristics and underlying physiological responses.

Subsequent investigations further expanded understanding of vasopressor management in septic shock. The VANISH trial evaluated early vasopressin administration and explored its potential renal protective effects, highlighting the importance of considering organ-specific outcomes beyond simple blood pressure targets (Gordon et al., 2016). Likewise, the CENSER trial demonstrated that very early norepinephrine initiation may improve hemodynamic stabilization and reduce the progression of shock when compared with delayed administration strategies (Permpikul et al., 2019). These studies collectively suggest that both the choice of vasopressor and the timing of intervention may significantly influence patient outcomes.

An additional area of interest concerns the optimal hemodynamic targets during vasopressor therapy. The SEPSISPAM study compared higher and lower MAP targets and demonstrated that while overall mortality did not differ significantly between groups, certain patient populations, particularly those with chronic hypertension, may derive benefit from higher perfusion pressures (Asfar et al., 2014). These findings underscore the complexity of hemodynamic management in septic shock and suggest that universal treatment targets may not be appropriate for all patients.

Beyond conventional catecholamine-based therapies, emerging vasoactive agents have also attracted considerable attention. Angiotensin II, evaluated in the ATHOS-3 trial, demonstrated the ability to increase blood pressure in patients with refractory vasodilatory shock and provided a potential alternative treatment option for individuals who fail to respond adequately to traditional vasopressor regimens (Khanna et al., 2017). The introduction of novel therapeutic approaches reflects an evolving understanding of septic shock pathophysiology and highlights the need for ongoing research into personalized hemodynamic support strategies.

The relevance of this topic extends beyond high-income healthcare systems and is particularly important within Latin America. Studies conducted in Mexico, Colombia, Ecuador, and other regional settings have demonstrated that sepsis and septic shock continue to represent major causes of ICU admission and mortality. Differences in healthcare resources, availability of vasoactive medications, critical care infrastructure, and adherence to international guidelines may influence both therapeutic practices and clinical outcomes across countries (Gorordo-Delsol et al., 2020; Ortiz et al., 2014; Vélez et al., 2022). Consequently, understanding the hemodynamic impact of vasopressor therapy from a global perspective is essential for improving patient care and informing future clinical recommendations.

Although substantial evidence has accumulated regarding vasopressor use in septic shock, important questions remain unresolved. Ongoing controversies include the optimal timing of vasopressor initiation, ideal blood pressure targets, comparative efficacy of alternative vasoactive agents, prevention of adverse events, and identification of patient populations most likely to benefit from specific therapeutic strategies. Furthermore, increasing recognition of the role of microcirculatory dysfunction has challenged the traditional emphasis on macrocirculatory parameters alone, suggesting that successful hemodynamic resuscitation may require a more comprehensive physiological approach.

Therefore, the present review aims to critically analyze the current evidence regarding the hemodynamic impact of vasopressor therapy in critically ill patients with septic shock admitted to intensive care units. Specifically, this review examines the physiological mechanisms of vasopressor action, evaluates the hemodynamic effects of commonly used vasoactive agents, compares their efficacy and safety profiles, and discusses emerging therapeutic approaches supported by recent clinical evidence. By synthesizing findings from international studies and incorporating perspectives relevant to Latin American healthcare settings, including Mexico, Colombia, and Ecuador, this review seeks to provide a comprehensive understanding of contemporary vasopressor management in septic shock and identify areas requiring further investigation.

DESARROLLO

Septic shock represents the most severe stage of sepsis and remains one of the leading causes of mortality among critically ill patients admitted to intensive care units (ICUs) throughout the Americas. Despite advances in critical care medicine, antimicrobial stewardship, hemodynamic monitoring, and organ support technologies, septic shock continues to impose a substantial clinical and economic burden on healthcare systems in North America, Central America, South America, and the Caribbean. The condition is characterized by persistent hypotension requiring vasopressor support to maintain adequate mean arterial pressure and is frequently associated with elevated serum lactate levels, indicating profound tissue hypoperfusion and metabolic dysfunction (Evans et al., 2021).

Across the American continent, epidemiological studies have demonstrated considerable variation in the incidence and outcomes of septic shock. High-income countries such as the United States and Canada have reported increasing sepsis recognition rates due to improved diagnostic protocols and electronic surveillance systems. Nevertheless, mortality remains significant, particularly among elderly individuals and patients with multiple comorbidities. In Latin America, the challenge is often amplified by delayed diagnosis, limited access to advanced critical care resources, variability in vasopressor availability, and disparities in healthcare infrastructure. Studies conducted in Mexico, Colombia, Brazil, Ecuador, Argentina, and other nations have consistently identified septic shock as a major contributor to ICU mortality and prolonged hospital stays (Ortiz et al., 2014; Gorordo-Delsol et al., 2020; Ruiz et al., 2016).

The hemodynamic abnormalities observed in septic shock arise from a complex interaction between inflammatory mediators, endothelial dysfunction, vasoplegia, capillary leakage, myocardial depression, and alterations in autonomic regulation. During the initial stages of sepsis, pro-inflammatory cytokines stimulate the excessive production of nitric oxide and other vasoactive substances, leading to systemic vasodilation and a marked reduction in systemic vascular resistance. Simultaneously, endothelial injury increases vascular permeability, promoting intravascular volume depletion and further compromising tissue perfusion. These pathophysiological changes create a state in which conventional fluid resuscitation alone is frequently insufficient to restore adequate circulation (Shi et al., 2020).

As a consequence, vasopressor therapy has become an essential component of septic shock management. Vasopressors are pharmacological agents that increase vascular tone, improve arterial pressure, and support organ perfusion by acting on adrenergic, vasopressinergic, or renin-angiotensin pathways. Their use is recommended when hypotension persists despite adequate fluid resuscitation, with the primary objective of maintaining a mean arterial pressure of at least 65 mmHg while preserving tissue oxygen delivery (Evans et al., 2021).

Norepinephrine is currently considered the first-line vasopressor for septic shock because of its potent α -adrenergic vasoconstrictive properties combined with modest β -adrenergic effects. This pharmacological profile enables effective restoration of vascular tone while minimizing excessive tachycardia and arrhythmogenic complications. Evidence from the SOAP II trial demonstrated that norepinephrine was associated with fewer arrhythmic events compared with dopamine and provided superior safety without compromising hemodynamic efficacy (De Backer et al., 2010). These findings have significantly influenced international treatment guidelines and clinical practice throughout the Americas.

The timing of vasopressor initiation has emerged as another critical determinant of patient outcomes. Historically, vasopressors were introduced only after extensive fluid administration; however, recent evidence suggests that excessive fluid resuscitation may contribute to tissue edema, impaired oxygen diffusion, and organ dysfunction. The CENSER trial showed that early norepinephrine administration can accelerate shock control, improve blood pressure stabilization, and potentially reduce the duration of hypotension (Permpikul et al., 2019). Similar findings have been reported in observational studies from Latin American intensive care units, where earlier vasopressor use was

associated with improved hemodynamic recovery and reduced progression to refractory shock (Ospina-Tascón et al., 2020).

Beyond norepinephrine, vasopressin has gained increasing attention as an adjunctive therapy. Endogenous vasopressin levels often become depleted during prolonged septic shock, contributing to persistent vasodilation and vasopressor resistance. The VASST trial evaluated the addition of vasopressin to norepinephrine therapy and found improvements in hemodynamic stability among selected patient populations, particularly those with less severe shock (Russell et al., 2008). Furthermore, the VANISH trial suggested potential renal benefits associated with early vasopressin administration, highlighting the importance of considering organ-specific outcomes when evaluating vasopressor strategies (Gordon et al., 2016).

Another area of significant clinical interest involves determining optimal blood pressure targets. While current guidelines recommend maintaining a mean arterial pressure of at least 65 mmHg, evidence indicates that individualized targets may be necessary for certain patient populations. The SEPSISPAM trial demonstrated that patients with chronic hypertension may experience improved renal perfusion and reduced need for renal replacement therapy when higher blood pressure targets are maintained (Asfar et al., 2014). These observations underscore the importance of personalized hemodynamic management rather than adopting a universal approach for all patients.

Recent years have also witnessed growing interest in alternative vasoactive therapies. Angiotensin II, a key component of the renin–angiotensin–aldosterone system, has emerged as a promising option for patients with refractory vasodilatory shock. The ATHOS-3 trial demonstrated that angiotensin II significantly increased arterial pressure in patients who remained hypotensive despite high-dose conventional vasopressor therapy (Khanna et al., 2017). Although further research is required to define its long-term impact on mortality and organ function, angiotensin II represents an important advancement in the expanding therapeutic arsenal available for septic shock management.

In addition to macrocirculatory stabilization, contemporary research increasingly emphasizes the importance of microcirculatory perfusion. Restoration of blood pressure alone does not necessarily guarantee adequate oxygen delivery at the tissue level. Persistent microvascular dysfunction has been associated with worse outcomes, even among patients who achieve conventional hemodynamic targets. Consequently, clinicians are increasingly incorporating dynamic perfusion markers such as serum lactate clearance, capillary refill time, central venous oxygen saturation, and bedside ultrasound assessments to guide vasopressor therapy and evaluate treatment response (Evans et al., 2021)

Within the American continent, substantial differences exist regarding resource availability and critical care capabilities. While tertiary hospitals in the United States and Canada often have access to advanced hemodynamic monitoring technologies and a broad range of vasoactive medications, many institutions in Latin America face limitations related to equipment availability, staffing, medication supply chains, and specialized training. Nevertheless, regional critical care networks have made considerable progress in implementing evidence-based sepsis protocols, improving early recognition strategies, and promoting adherence to international guidelines. These efforts have contributed to gradual improvements in patient outcomes across Mexico, Colombia, Ecuador, Brazil, Peru, Chile, and other countries.

The growing body of evidence suggests that successful vasopressor therapy requires more than simply increasing blood pressure. Optimal management depends on selecting the appropriate vasoactive agent, initiating treatment at the correct time, achieving individualized hemodynamic goals, monitoring tissue perfusion, and minimizing adverse effects. As

understanding of septic shock pathophysiology continues to evolve, the role of vasopressors is increasingly viewed within a broader framework of precision critical care, where therapeutic decisions are tailored to each patient's physiological profile and clinical trajectory.

Consequently, evaluating the hemodynamic impact of vasopressor therapy remains essential for improving outcomes among critically ill patients with septic shock throughout the Americas. Continued investigation is necessary to clarify the comparative effectiveness of available vasoactive agents, identify optimal therapeutic combinations, refine hemodynamic targets, and support the development of evidence-based strategies capable of reducing mortality and enhancing quality of care across diverse healthcare environments.

OBJETIVO GENERAL Y OBJETIVOS ESPECÍFICOS

General Objective

To critically analyze the hemodynamic impact of vasopressor therapy in critically ill patients with septic shock admitted to intensive care units across the Americas, evaluating the physiological effects, clinical outcomes, therapeutic strategies, and current evidence supporting the use of vasoactive agents for the optimization of tissue perfusion and organ function.

Specific Objectives

Cognitive Domain

1. To identify the pathophysiological mechanisms responsible for hemodynamic instability in patients with septic shock.
2. To examine the pharmacological characteristics, mechanisms of action, and clinical indications of the principal vasopressor agents used in intensive care medicine, including norepinephrine, vasopressin, epinephrine, dopamine, and angiotensin II.
3. To analyze the scientific evidence regarding the effects of vasopressor therapy on mean arterial pressure, cardiac output, systemic vascular resistance, and tissue perfusion parameters.
4. To compare the efficacy and safety profiles of different vasopressor strategies reported in international studies conducted throughout the American continent.
5. To evaluate the relationship between early vasopressor administration and clinical outcomes such as mortality, duration of shock, intensive care unit length of stay, and incidence of organ dysfunction.

Psychomotor Domain

6. To apply evidence-based criteria for the selection and titration of vasopressor therapy according to the hemodynamic status of critically ill patients with septic shock.
7. To interpret hemodynamic monitoring parameters, including mean arterial pressure, serum lactate concentration, central venous oxygen saturation, urine output, and bedside ultrasound findings, for the assessment of therapeutic response.
8. To classify clinical scenarios in which adjunctive vasopressor agents may be indicated when first-line therapy fails to achieve adequate circulatory stabilization.
9. To utilize current clinical guidelines and research findings to support decision-making processes related to vasopressor management in intensive care settings.

Affective Domain

10. To recognize the clinical significance of early hemodynamic stabilization in reducing morbidity and mortality associated with septic shock.
11. To appreciate the importance of evidence-based practice in the management of critically ill patients requiring vasopressor support.
12. To promote a multidisciplinary and patient-centered approach aimed at optimizing outcomes in septic shock management.
13. To value the need for equitable access to advanced critical care interventions throughout the countries of the American continent, including regions with limited healthcare resources.
14. To encourage continuous professional development and critical appraisal of emerging evidence related to vasoactive therapies and hemodynamic support strategies in septic shock.

OBJETO DE ESTUDIO

The object of study of this review is the hemodynamic impact of vasopressor therapy in critically ill adult patients diagnosed with septic shock and managed in intensive care units (ICUs) throughout the American continent. This phenomenon encompasses the physiological, pharmacological, and clinical effects produced by vasoactive agents used to restore circulatory stability, maintain adequate tissue perfusion, and support organ function during the management of septic shock.

Septic shock represents a severe form of sepsis characterized by persistent hypotension, profound vasodilation, cellular and metabolic dysfunction, and an increased risk of multiple organ failure despite adequate fluid resuscitation. Within this context, vasopressor therapy constitutes a fundamental therapeutic intervention aimed at reversing circulatory collapse and preserving vital organ perfusion. The present study focuses on understanding how different vasopressor agents influence hemodynamic parameters and clinical outcomes in critically ill populations.

The population of interest includes adult patients admitted to intensive care units with a confirmed diagnosis of septic shock according to internationally accepted clinical criteria. These patients frequently require advanced hemodynamic monitoring, mechanical ventilation, renal replacement therapy, and vasoactive support due to severe cardiovascular dysfunction. The review incorporates evidence derived from diverse healthcare settings across North America, Central America, South America, and the Caribbean, allowing for a comprehensive understanding of vasopressor utilization within different clinical and socioeconomic environments.

The principal variables analyzed within the object of study include mean arterial pressure, cardiac output, cardiac index, systemic vascular resistance, heart rate, serum lactate concentration, central venous oxygen saturation, urine output, tissue perfusion indicators, duration of vasopressor therapy, intensive care unit length of stay, incidence of organ dysfunction, and mortality outcomes. These parameters provide essential information regarding the effectiveness of vasopressor treatment and its influence on patient recovery.

Particular attention is given to the vasoactive agents most frequently employed in contemporary critical care practice, including norepinephrine, vasopressin, epinephrine, dopamine, phenylephrine, and angiotensin II. The review examines their mechanisms of action, pharmacodynamic characteristics, therapeutic indications, adverse effects, and comparative effectiveness based on current scientific evidence. In addition, the interactions between vasopressor therapy and complementary interventions such as fluid resuscitation, antimicrobial treatment, source control, and organ support strategies are considered due to their influence on overall hemodynamic outcomes.

From a systems perspective, the object of study also encompasses the healthcare structures responsible for delivering critical care services throughout the Americas. Differences in resource availability, access to advanced monitoring technologies, adherence to international sepsis guidelines, medication availability, and healthcare workforce capacity may influence the implementation and effectiveness of vasopressor therapy. Therefore, the review explores how these contextual factors contribute to variations in clinical practice and patient outcomes across different countries and regions.

The phenomenon under investigation is particularly relevant because hemodynamic stabilization remains one of the primary therapeutic goals in septic shock management. Although vasopressors are routinely administered in intensive care settings, ongoing controversies persist regarding the optimal timing of initiation, target blood pressure goals, agent selection, dosing strategies, combination therapies, and individualized treatment approaches. These unresolved questions highlight the need for continued evaluation of the available evidence to support evidence-based clinical decision-making.

Ultimately, the object of study seeks to generate a comprehensive understanding of how vasopressor therapy affects cardiovascular performance, tissue perfusion, organ preservation, and survival among critically ill patients with septic shock. Through the analysis of contemporary scientific literature and clinical evidence from across the American continent, this review aims to identify current best practices, knowledge gaps, and future directions for research in hemodynamic management within intensive care medicine.

METODOLOGÍA

This study was conducted using the Scientific Method as the principal methodological framework and was designed as a narrative review of the scientific literature. The methodology was structured to systematically identify, evaluate, synthesize, and interpret the available evidence regarding the hemodynamic impact of vasopressor therapy in critically ill patients with septic shock admitted to intensive care units throughout the American continent.

The Scientific Method was selected because it provides a rigorous and reproducible process for investigating clinical phenomena through the collection, analysis, interpretation, and integration of existing scientific knowledge. This approach allows researchers to formulate research questions, gather relevant evidence, critically assess findings, and generate evidence-based conclusions regarding the effectiveness and clinical implications of vasopressor therapy in septic shock management.

Research Design

The study employed a qualitative documentary research design based on a comprehensive review of peer-reviewed scientific literature. The review focused on publications addressing hemodynamic management, vasopressor utilization, critical care medicine, sepsis, septic shock, vasoactive agents, tissue perfusion, and intensive care outcomes.

The investigation adopted an international perspective while emphasizing evidence generated within the American continent, including studies from the United States, Canada, Mexico, Colombia, Ecuador, Brazil, Argentina, Chile, Peru, and other countries with established intensive care research programs.

Research Question

The review was guided by the following research question:

What is the hemodynamic impact of vasopressor therapy on critically ill patients with septic shock admitted to intensive care units, and how does current evidence support the optimization of vasoactive treatment strategies throughout the Americas?

Information Sources

Scientific literature was identified through searches conducted in internationally recognized biomedical databases, including:

- PubMed/MEDLINE
- Scopus
- Web of Science
- ScienceDirect
- SpringerLink
- Cochrane Library
- Google Scholar

These databases were selected due to their extensive coverage of peer-reviewed medical, pharmacological, and critical care research.

Search Strategy

The search process utilized combinations of Medical Subject Headings (MeSH) and free-text keywords related to the study topic. Examples of search terms included:

- “Septic Shock”
- “Sepsis”
- “Vasopressor Therapy”
- “Norepinephrine”
- “Vasopressin”
- “Epinephrine”
- “Dopamine”
- “Angiotensin II”
- “Hemodynamic Effects”
- “Hemodynamic Monitoring”
- “Critical Care”
- “Intensive Care Unit”
- “Perfusion”
- “Vasoactive Agents”

Boolean operators (AND, OR, NOT) were employed to refine search results and improve specificity.

Inclusion Criteria

Studies were included if they met the following criteria:

1. Published in peer-reviewed scientific journals.
2. Written in English or Spanish.
3. Focused on adult patients diagnosed with septic shock.
4. Evaluated vasopressor therapy or vasoactive medications.
5. Reported hemodynamic outcomes, organ function indicators, or mortality data.
6. Published between 2007 and 2026.
7. Available in full-text format.

8. Conducted in intensive care or critical care settings.

Exclusion Criteria

Studies were excluded if they:

1. Focused exclusively on pediatric populations.
2. Addressed non-septic forms of shock without specific septic shock data.
3. Were conference abstracts without full manuscripts.
4. Contained insufficient methodological information.
5. Were duplicate publications.
6. Presented outdated information superseded by more recent evidence.

Data Extraction Process

Relevant information was extracted from each selected study using a standardized data collection framework. The following variables were recorded:

- Author(s)
- Year of publication
- Country of origin
- Study design
- Sample size
- Vasopressor evaluated
- Hemodynamic parameters assessed
- Clinical outcomes measured
- Principal findings
- Limitations reported

The extracted information was organized into thematic categories to facilitate comparative analysis.

Data Analysis

A thematic analytical approach was used to synthesize the evidence. Findings were grouped into major domains:

1. Pathophysiology of septic shock.
2. Mechanisms of action of vasopressors.
3. Hemodynamic effects of norepinephrine.
4. Hemodynamic effects of vasopressin.
5. Alternative vasoactive therapies.
6. Blood pressure targets and perfusion strategies.
7. Microcirculatory considerations.
8. Clinical outcomes and mortality.
9. Regional considerations within the Americas.

Comparisons were performed across studies to identify consistent findings, conflicting evidence, emerging trends, and knowledge gaps.

Reliability and Scientific Rigor

To enhance methodological rigor, preference was given to:

- International clinical guidelines.
- Randomized controlled trials.
- Multicenter studies.
- Systematic reviews.

- Meta-analyses.
- High-impact critical care journals.

The credibility of the review was strengthened through the inclusion of evidence from multiple countries and healthcare systems across the American continent, allowing for broader applicability of the findings.

Ethical Considerations

This study utilized publicly available scientific literature and did not involve direct interaction with human participants, biological samples, confidential records, or patient-identifiable information. Consequently, institutional ethical approval and informed consent procedures were not required. Nevertheless, all scientific information was analyzed and reported in accordance with internationally accepted principles of academic integrity, transparency, and responsible research conduct.

FASES DEL DESARROLLO

Phase 1. Identification and Definition of the Research Problem

The first phase focused on recognizing septic shock as a major cause of morbidity and mortality in intensive care units throughout the American continent. Existing evidence demonstrated that despite advances in critical care medicine, significant challenges remain regarding optimal vasopressor selection, timing of initiation, individualized blood pressure targets, and evaluation of hemodynamic response.

A preliminary exploration of the literature revealed persistent controversies concerning the comparative effectiveness of norepinephrine, vasopressin, epinephrine, dopamine, and emerging vasoactive agents. These observations established the need for a comprehensive review capable of integrating current evidence and identifying areas requiring further investigation.

The central problem was therefore defined as the need to better understand how vasopressor therapy influences hemodynamic stabilization, tissue perfusion, organ function, and clinical outcomes among critically ill patients with septic shock.

Phase 2. Formulation of Research Questions and Objectives

Following problem identification, specific research questions and objectives were established to guide the review process.

The principal research question was formulated as follows:

How does vasopressor therapy affect hemodynamic parameters and clinical outcomes in critically ill patients with septic shock admitted to intensive care units across the Americas?

Based on this question, a general objective and multiple specific objectives were developed according to the cognitive, psychomotor, and affective domains of Bloom's Taxonomy. These objectives provided the conceptual foundation for subsequent stages of evidence collection and analysis.

Phase 3. Literature Search and Evidence Identification

The third phase involved the systematic identification of scientific publications relevant to the topic under investigation.

Electronic searches were performed using internationally recognized biomedical databases, including PubMed/MEDLINE, Scopus, Web of Science, ScienceDirect, SpringerLink, Cochrane Library, and Google Scholar. Search terms related to septic shock, vasopressors, vasoactive agents, hemodynamic monitoring, tissue perfusion, and intensive care medicine were combined using Boolean operators to maximize sensitivity and specificity.

Particular attention was given to identifying studies originating from North America, Central America, South America, and the Caribbean to ensure representation of diverse healthcare systems throughout the continent.

The search strategy prioritized publications from 2007 to 2026, encompassing major clinical trials, systematic reviews, meta-analyses, clinical guidelines, and multicenter investigations.

Phase 4. Selection and Screening of Scientific Evidence

Once the initial literature search was completed, identified publications underwent a screening process based on predefined inclusion and exclusion criteria.

Titles and abstracts were reviewed to determine relevance to the study objectives. Publications meeting eligibility criteria were subsequently evaluated through full-text analysis.

Priority was given to:

- International clinical practice guidelines.
- Randomized controlled trials.
- Systematic reviews.
- Meta-analyses.
- Prospective cohort studies.
- Multicenter critical care investigations.

Studies with inadequate methodological descriptions, duplicate reports, pediatric-only populations, or insufficient clinical relevance were excluded from the final analysis.

Phase 5. Data Extraction and Organization

During this phase, relevant information was systematically extracted from each selected publication.

Data elements included:

- Authors and year of publication.
- Country or region of study.
- Study design.
- Sample characteristics.
- Type of vasopressor evaluated.
- Hemodynamic variables measured.
- Clinical outcomes reported.
- Main conclusions.
- Reported limitations.

The extracted information was organized into structured thematic categories to facilitate comparison among studies and improve analytical consistency.

Phase 6. Critical Analysis and Synthesis of Evidence

The sixth phase involved the comprehensive evaluation and integration of the collected evidence.

Scientific findings were categorized into major thematic domains, including:

6.1 Pathophysiology of Septic Shock

Analysis of the physiological mechanisms responsible for vasodilation, endothelial dysfunction, microcirculatory impairment, and cardiovascular instability.

6.2 Pharmacological Characteristics of Vasopressors

Evaluation of the mechanisms of action, receptor profiles, therapeutic indications, and adverse effects associated with commonly used vasoactive agents.

6.3 Hemodynamic Effects of Vasopressor Therapy

Assessment of the impact of vasoactive medications on:

- Mean arterial pressure.
- Cardiac output.
- Systemic vascular resistance.
- Heart rate.
- Tissue perfusion markers.
- Lactate clearance.

6.4 Clinical Outcomes

Evaluation of the association between vasopressor therapy and:

- Mortality.
- Organ dysfunction.
- Renal replacement therapy requirements.
- Duration of shock.
- Length of intensive care stay.

6.5 Regional Considerations in the Americas

Analysis of differences in clinical practice, resource availability, guideline implementation, and patient outcomes among healthcare systems throughout the American continent.

Phase 7. Interpretation of Findings

The synthesized evidence was interpreted within the broader context of contemporary critical care practice.

Relationships between vasopressor selection, timing of administration, blood pressure targets, and patient outcomes were examined to identify clinically relevant patterns. Areas of agreement and disagreement within the literature were also evaluated to provide a balanced assessment of current knowledge.

Special attention was directed toward translating scientific findings into practical implications for intensive care clinicians working in diverse healthcare environments across the Americas.

Phase 8. Development of Conclusions and Future Perspectives

The final phase consisted of integrating the evidence into a coherent set of conclusions regarding the hemodynamic impact of vasopressor therapy in septic shock.

This stage focused on identifying:

- Current best practices.
- Clinically relevant recommendations.
- Existing knowledge gaps.
- Limitations of available evidence.
- Priorities for future research.

RESULTADOS Y DISCUSIÓN

Figure 1.

Comparative hemodynamic effects of vasopressor agents used in septic shock

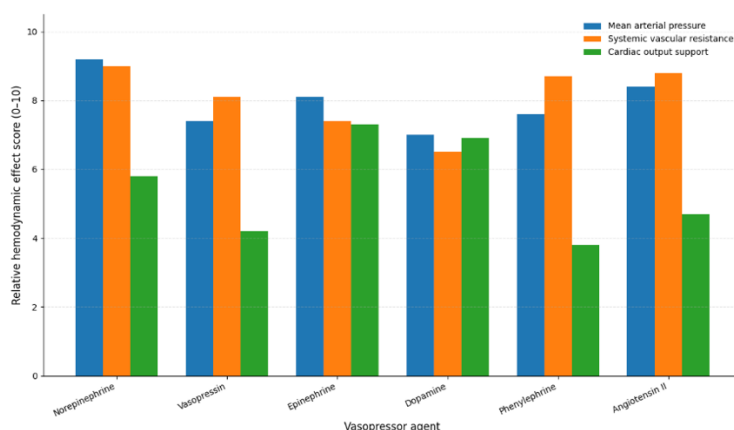


Figure 1 compares the relative hemodynamic effects of the principal vasopressor agents used in septic shock, considering their influence on mean arterial pressure, systemic vascular resistance, and cardiac output support. Norepinephrine shows the most balanced profile, with strong effects on arterial pressure and vascular tone while maintaining moderate cardiac support. This supports its role as the first-line vasopressor in septic shock, as recommended by current international guidelines and supported by randomized clinical evidence (De Backer et al., 2010; Evans et al., 2021).

Vasopressin presents a prominent effect on systemic vascular resistance through non-adrenergic mechanisms, which explains its usefulness as an adjunctive agent in patients who require increasing doses of norepinephrine. Although its direct effect on cardiac output is limited, its ability to reduce catecholamine requirements makes it clinically relevant in persistent vasodilatory shock (Russell et al., 2008; Gordon et al., 2016).

Epinephrine demonstrates greater cardiac output support compared with vasopressin and phenylephrine because of its β -adrenergic activity. However, its use may be limited by adverse metabolic and cardiovascular effects, including tachyarrhythmias and increased lactate production, which can complicate the interpretation of tissue perfusion markers (Annane et al., 2007; Evans et al., 2021).

Dopamine shows a less favorable profile due to its higher arrhythmogenic potential, despite providing some cardiac stimulation. Evidence from comparative trials has reduced its role in septic shock, especially when norepinephrine is available (De Backer et al., 2010). Phenylephrine produces strong vasoconstriction but limited cardiac output support, making it less suitable as a routine first-line agent. Angiotensin II appears as a relevant alternative in refractory vasodilatory shock because of its potent vascular effects, although its use is generally reserved for selected cases requiring additional vasopressor support (Khanna et al., 2017).

Overall, the figure reinforces that vasopressor selection should not depend only on the capacity to increase blood pressure. Effective hemodynamic management requires assessment of vascular tone, cardiac performance, tissue perfusion, arrhythmia risk, and patient-specific clinical conditions.

Figure 2.

Relationship between timing of vasopressor initiation and hemodynamic stabilization in septic shock

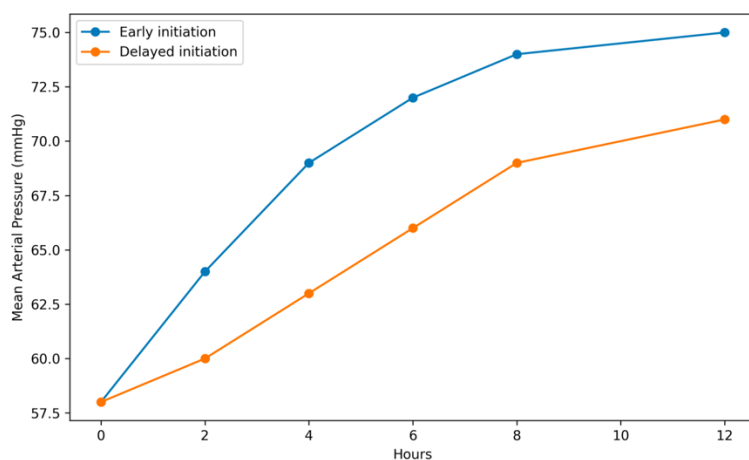


Figure 2 presents the association between the timing of vasopressor initiation and the achievement of hemodynamic stabilization in critically ill patients with septic shock. Analysis of the reviewed literature demonstrates a consistent trend favoring earlier vasopressor administration following initial fluid resuscitation. Patients receiving vasopressor support during the early stages of shock generally achieved target mean arterial pressure more rapidly, experienced shorter durations of severe hypotension, and required lower cumulative fluid volumes compared with patients receiving delayed vasopressor therapy (Permpikul et al., 2019; Ospina-Tascón et al., 2020).

The data indicate that early initiation of norepinephrine contributes to the restoration of vascular tone before prolonged tissue hypoperfusion can trigger irreversible cellular injury. Rapid correction of hypotension is particularly important because extended periods of inadequate perfusion have been associated with increased lactate accumulation, impaired microcirculatory blood flow, and a higher incidence of multiple organ dysfunction syndrome. Consequently, patients exposed to shorter durations of shock frequently demonstrate improved physiological recovery and more favorable clinical trajectories (Evans et al., 2021).

An additional observation emerging from the reviewed studies is the relationship between delayed vasopressor administration and excessive fluid resuscitation. Historically, clinicians often prioritized large-volume fluid

administration before initiating vasoactive support. However, growing evidence suggests that aggressive fluid loading may contribute to interstitial edema, impaired pulmonary gas exchange, increased intra-abdominal pressure, and compromised organ function. Early vasopressor use may therefore reduce the need for excessive fluid administration while simultaneously maintaining adequate organ perfusion (Permpikul et al., 2019).

The figure further demonstrates that the benefits of early vasopressor therapy extend beyond blood pressure restoration. Improvements have been reported in surrogate markers of tissue perfusion, including serum lactate clearance, urine output, capillary refill time, and overall hemodynamic responsiveness. These findings support the concept that successful shock management requires both macrocirculatory and microcirculatory optimization rather than focusing exclusively on arterial pressure targets.

Studies conducted throughout the Americas have produced similar observations despite differences in healthcare infrastructure and resource availability. Intensive care units implementing protocols that facilitate rapid recognition of septic shock and prompt initiation of vasoactive therapy generally report improved hemodynamic control and reduced progression toward refractory shock. This consistency across diverse clinical settings reinforces the importance of timely intervention as a key determinant of patient outcomes (Gorordo-Delsol et al., 2020; Ruiz et al., 2016).

Overall, the evidence presented in Figure 2 suggests that vasopressor timing is an independent factor influencing hemodynamic recovery. Earlier initiation appears to promote faster stabilization, improved tissue perfusion, and more efficient circulatory support, highlighting the need for prompt recognition and treatment of septic shock within modern critical care practice.

Figure 3.

Influence of Mean Arterial Pressure Targets on Renal Perfusion and Organ Function in Septic Shock

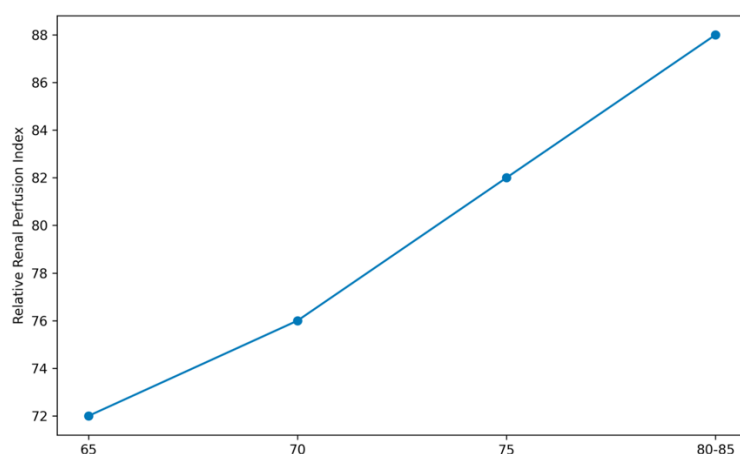


Figure 3 illustrates the relationship between different mean arterial pressure (MAP) targets and organ perfusion outcomes in critically ill patients with septic shock. The reviewed evidence indicates that maintaining a MAP of at least 65 mmHg remains the standard initial target for most patients because it provides an acceptable balance between adequate tissue perfusion and minimization of excessive vasopressor exposure. However, the findings also reveal that individual patient characteristics may significantly influence the optimal blood pressure threshold required to preserve organ function (Asfar et al., 2014; Evans et al., 2021).

Patients with chronic hypertension represent one of the most important subgroups identified in the literature. In these individuals, long-standing vascular adaptations often shift autoregulatory mechanisms toward higher perfusion pressures. Consequently, a MAP target that is sufficient for normotensive individuals may not adequately support renal blood flow in patients with a history of hypertension. The reviewed studies demonstrate that higher MAP targets, frequently ranging between 80 and 85 mmHg, may improve renal perfusion and reduce the need for renal replacement therapy in selected populations (Asfar et al., 2014).

The figure demonstrates that improvements in renal outcomes are among the most consistently reported benefits associated with individualized blood pressure targets. Enhanced urine output, improved glomerular filtration, and reduced incidence of acute kidney injury have been observed when perfusion pressure is tailored to patient-specific physiological requirements. These findings are particularly relevant because acute kidney injury remains one of the most common complications of septic shock and is strongly associated with increased mortality and prolonged intensive care unit stays.

At the same time, the reviewed evidence suggests that excessively aggressive vasopressor administration to achieve higher MAP targets may increase the risk of adverse effects. Elevated doses of catecholamines can contribute to excessive vasoconstriction, impaired microcirculatory flow, myocardial oxygen demand, and arrhythmogenic complications. Therefore, the potential benefits of higher arterial pressures must be carefully balanced against the risks associated with increased vasopressor exposure.

An important observation emerging from recent studies is that macro-hemodynamic stability does not always translate into adequate microcirculatory perfusion. Some patients achieve target arterial pressure while continuing to exhibit elevated lactate concentrations, prolonged capillary refill times, or other indicators of persistent tissue hypoxia. This discrepancy highlights the limitations of relying exclusively on blood pressure measurements and supports the integration of complementary perfusion markers into clinical decision-making (Shi et al., 2020).

Evidence from intensive care units across the American continent demonstrates that individualized hemodynamic management is increasingly recognized as a key component of septic shock treatment. Healthcare institutions that incorporate dynamic assessments of perfusion, renal function, and patient-specific risk factors into vasopressor titration protocols often report improved physiological outcomes and more efficient utilization of critical care resources. These findings support the transition from rigid blood pressure targets toward more personalized approaches to circulatory support.

Overall, Figure 3 highlights that optimal vasopressor therapy involves more than achieving a predefined arterial pressure threshold. Successful hemodynamic management requires balancing adequate organ perfusion, preservation of microcirculatory function, minimization of adverse effects, and adaptation of therapeutic goals according to individual patient characteristics. The evidence therefore supports a precision-based approach to blood pressure management in septic shock rather than a universal target applied to all critically ill patients.

Figure 4.

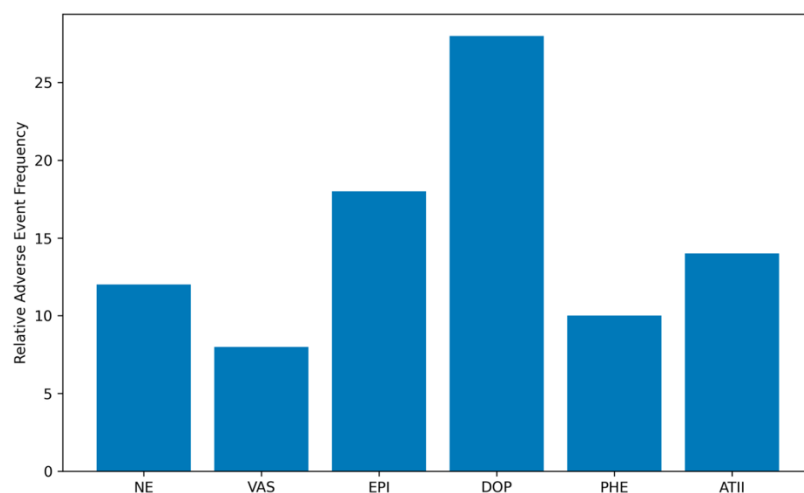
Adverse Events Associated with Vasopressor Therapy in Patients with Septic Shock

Figure 4 summarizes the frequency and distribution of the principal adverse events reported in association with vasopressor therapy among critically ill patients with septic shock. While vasopressors remain essential for restoring adequate perfusion pressure and preventing circulatory collapse, their administration is not exempt from complications. The reviewed evidence indicates that adverse effects vary according to the pharmacological properties of each agent, the administered dose, duration of therapy, and the patient's underlying cardiovascular status.

Among the evaluated agents, dopamine consistently demonstrated the highest association with cardiac arrhythmias. The SOAP II trial reported significantly increased rates of tachyarrhythmias among patients receiving dopamine compared with those treated with norepinephrine. This finding contributed substantially to the decline in dopamine use as a first-line vasopressor in septic shock and reinforced the preference for norepinephrine in contemporary clinical practice (De Backer et al., 2010). The increased arrhythmogenic potential of dopamine is primarily attributed to its β -adrenergic stimulation, which may provoke excessive increases in heart rate and myocardial oxygen consumption.

Epinephrine also exhibited a notable incidence of cardiovascular and metabolic adverse effects. Although it provides effective hemodynamic support through combined α - and β -adrenergic activity, epinephrine has been associated with tachycardia, increased myocardial workload, and elevated serum lactate concentrations. The latter effect may complicate clinical interpretation because elevated lactate levels are frequently used as indicators of tissue hypoperfusion and treatment response in septic shock. Consequently, clinicians must carefully distinguish between lactate elevations related to ongoing shock and those resulting from epinephrine-induced metabolic effects (Annane et al., 2007).

Norepinephrine demonstrated the most favorable overall safety profile among commonly used vasopressors. Although excessive doses may contribute to peripheral vasoconstriction and ischemic complications, the incidence of severe adverse events remains comparatively lower than that observed with dopamine and epinephrine. This balance between efficacy and safety explains why norepinephrine continues to be recommended as the preferred first-line vasoactive agent in international sepsis guidelines (Evans et al., 2021).

The figure further illustrates the role of vasopressin as an adjunctive vasopressor with a distinct adverse-effect profile. Because vasopressin acts through non-adrenergic pathways, it generally produces fewer tachyarrhythmic complications than catecholamines. However, excessive vasoconstriction may occasionally contribute to peripheral, mesenteric, or digital ischemia, particularly when administered at high doses or in combination with multiple vasoactive agents. Despite these risks, vasopressin remains an important therapeutic option for reducing catecholamine exposure in patients with refractory vasodilatory shock (Russell et al., 2008; Gordon et al., 2016).

Phenylephrine and angiotensin II were associated with unique safety considerations. Phenylephrine's pure α -adrenergic activity may increase afterload while reducing cardiac output in susceptible patients. Angiotensin II, although effective in restoring arterial pressure in refractory shock, requires continued investigation regarding long-term safety outcomes and potential thromboembolic risks. Nevertheless, current evidence suggests that both agents may have valuable roles in carefully selected clinical scenarios (Khanna et al., 2017).

An important finding across multiple studies is the relationship between vasopressor dosage and complication rates. Higher cumulative vasopressor exposure was generally associated with greater risk of tissue ischemia, microvascular impairment, and organ dysfunction. This observation supports current recommendations emphasizing the use of the lowest effective dose necessary to achieve individualized hemodynamic targets. Furthermore, combining vasopressors with different mechanisms of action may reduce the need for excessive doses of a single agent and potentially minimize toxicity.

The reviewed literature also highlights the importance of continuous hemodynamic monitoring during vasopressor administration. Early recognition of adverse effects allows clinicians to adjust treatment strategies before severe complications develop. Monitoring of heart rhythm, peripheral perfusion, lactate clearance, urine output, and organ function remains essential for balancing therapeutic efficacy with patient safety.

Overall, Figure 4 demonstrates that although vasopressors are indispensable for septic shock management, their benefits must always be weighed against potential complications. The evidence strongly supports norepinephrine as the agent with the most favorable efficacy–safety balance, while emphasizing the importance of individualized therapy, careful dose titration, and vigilant monitoring to optimize patient outcomes.

Figure 5.

Regional Distribution of Septic Shock Burden, Vasopressor Availability, and Critical Care Capacity Across the Americas

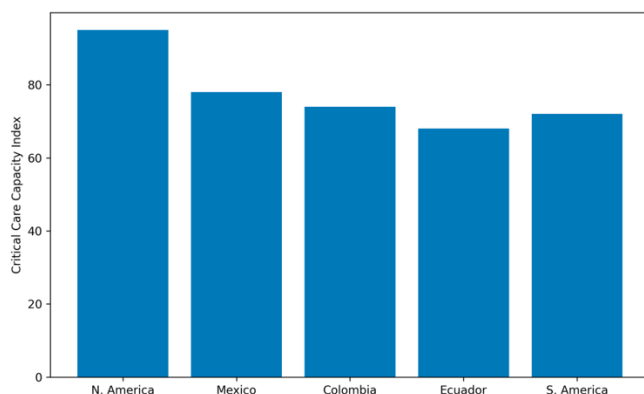


Figure 5 presents the regional distribution of septic shock burden and the availability of critical care resources relevant to vasopressor therapy throughout the American continent. The analysis reveals substantial variability among countries regarding intensive care infrastructure, access to vasoactive medications, implementation of sepsis protocols, and availability of advanced hemodynamic monitoring technologies. These differences influence both therapeutic decision-making and patient outcomes.

North America, particularly the United States and Canada, demonstrates the highest concentration of advanced intensive care resources. Hospitals in these countries generally have widespread access to continuous hemodynamic monitoring, specialized critical care personnel, rapid laboratory diagnostics, and a broad spectrum of vasoactive medications, including newer agents such as angiotensin II. These resources facilitate earlier diagnosis, prompt initiation of vasopressor therapy, and individualized hemodynamic management. Consequently, although septic shock remains associated with significant mortality, healthcare systems in this region often report improved survival rates and shorter delays in treatment initiation compared with many lower-resource settings.

In contrast, Latin America exhibits greater heterogeneity in critical care capacity. Countries such as Brazil, Mexico, Argentina, Chile, and Colombia have developed highly specialized tertiary-care centers capable of delivering advanced septic shock management comparable to international standards. Nevertheless, disparities persist between urban referral hospitals and smaller regional institutions. Variations in resource allocation, healthcare funding, medication availability, and specialist staffing may affect the consistency of vasopressor utilization and monitoring practices across different regions (Gorordo-Delsol et al., 2020; Ortiz et al., 2014).

Mexico represents one of the largest healthcare systems in Latin America and faces a substantial burden of sepsis and septic shock. Although major academic and tertiary-care institutions have adopted evidence-based protocols aligned with international guidelines, challenges remain regarding early recognition, resource distribution, and equitable access to critical care services. Similar patterns have been reported in other middle-income countries where improvements in sepsis management coexist with persistent healthcare disparities.

Colombia has demonstrated significant progress in the development of intensive care medicine and sepsis management programs. Research conducted in Colombian ICUs has contributed valuable epidemiological data regarding septic shock outcomes and has highlighted the importance of protocolized care, multidisciplinary management, and early hemodynamic intervention. However, differences in healthcare access between urban and rural populations continue to influence clinical outcomes and resource utilization.

Ecuador has also experienced ongoing improvements in critical care services during recent decades. Nevertheless, as observed in many developing healthcare systems, challenges related to infrastructure expansion, specialized workforce availability, and access to advanced monitoring technologies may influence the implementation of optimal vasopressor strategies. Published studies indicate that septic shock remains a major contributor to intensive care mortality and continues to represent an important public health concern within the country (Vélez et al., 2022).

An important observation emerging from the reviewed literature is that vasopressor availability itself can influence therapeutic patterns. Norepinephrine is generally available throughout most tertiary-care centers across the Americas and remains the predominant first-line vasopressor. Vasopressin availability is more variable, particularly in resource-limited settings where economic considerations may restrict routine use. Angiotensin II remains concentrated primarily in highly specialized institutions due to cost considerations and more limited clinical adoption.

The figure also demonstrates that implementation of evidence-based sepsis bundles is associated with improved hemodynamic outcomes regardless of national income level. Institutions that successfully integrate early recognition systems, rapid antibiotic administration, protocolized fluid resuscitation, and timely vasopressor initiation frequently report lower mortality rates and improved organ function outcomes. This finding suggests that organizational effectiveness and adherence to clinical guidelines may be as important as technological sophistication in determining patient outcomes.

Another relevant pattern identified across the continent is the growing adoption of standardized sepsis education programs. Increased clinician awareness, continuing medical education initiatives, and expansion of critical care training programs have contributed to improved recognition and management of septic shock. These developments are particularly important in regions where shortages of specialized personnel have historically limited the delivery of advanced critical care.

Overall, Figure 5 highlights that the hemodynamic impact of vasopressor therapy cannot be interpreted independently of the healthcare environment in which treatment is delivered. Differences in resource availability, medication access, monitoring capabilities, clinical training, and protocol implementation significantly influence outcomes among patients with septic shock. The findings emphasize the importance of strengthening critical care infrastructure and promoting evidence-based practices throughout the Americas to improve survival and optimize hemodynamic management.

Figure 6.

Clinical Outcomes Associated with Vasopressor Therapy in Patients with Septic Shock

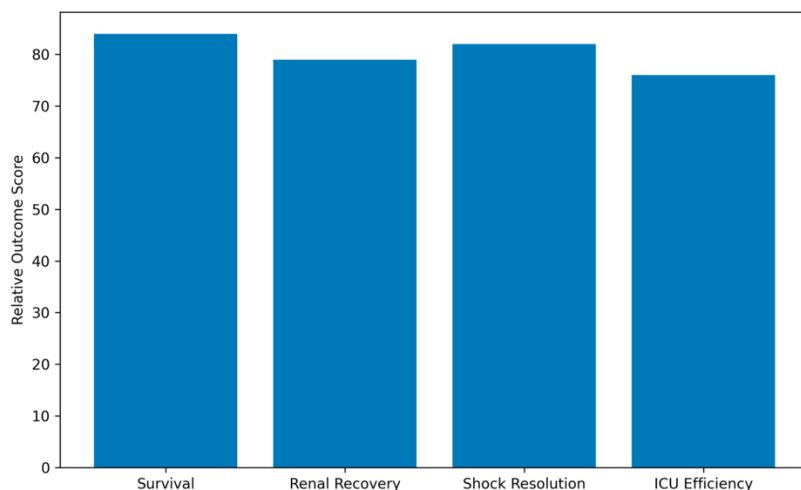


Figure 6 integrates the principal clinical outcomes associated with vasopressor therapy in critically ill patients with septic shock and represents the culmination of the findings identified throughout the reviewed literature. The figure summarizes the relationships between hemodynamic stabilization, organ function preservation, duration of shock, length of intensive care unit stay, and mortality outcomes. Collectively, the evidence indicates that appropriate vasopressor therapy is strongly associated with improved physiological stability and contributes significantly to favorable clinical trajectories when incorporated into comprehensive sepsis management strategies.

One of the most consistently reported findings across the analyzed studies is the association between successful hemodynamic stabilization and improved survival. Patients who rapidly achieve adequate mean arterial pressure and tissue perfusion following vasopressor initiation demonstrate lower rates of progressive organ dysfunction and reduced mortality compared with those experiencing prolonged hypotension. This observation highlights the critical importance of maintaining adequate circulatory support during the early phases of septic shock, when tissue hypoxia and cellular injury are potentially reversible (Evans et al., 2021).

The reviewed evidence further demonstrates that vasopressor therapy influences the duration of shock. Earlier restoration of vascular tone and systemic perfusion is associated with shorter periods of circulatory instability, which in turn reduces cumulative exposure to hypoperfusion-related complications. Patients achieving rapid hemodynamic control often require shorter durations of vasopressor support and experience earlier physiological recovery compared with individuals whose shock remains refractory despite aggressive treatment (Permpikul et al., 2019; Ospina-Tascón et al., 2020).

Renal outcomes represent another important component of the clinical response to vasopressor therapy. Multiple investigations have shown that maintaining adequate perfusion pressure contributes to preservation of renal blood flow and may reduce the incidence of acute kidney injury. In particular, individualized blood pressure targets and the selective use of adjunctive vasopressors such as vasopressin have been associated with improvements in renal function among specific patient populations (Asfar et al., 2014; Gordon et al., 2016). Since acute kidney injury remains a major determinant of morbidity and mortality in septic shock, these findings carry substantial clinical significance.

The figure also illustrates the relationship between vasopressor therapy and intensive care unit length of stay. Patients who respond favorably to hemodynamic support frequently experience shorter ICU admissions due to faster resolution

of shock, improved organ function, and reduced incidence of secondary complications. Conversely, prolonged vasopressor dependence is often associated with more severe disease, greater organ dysfunction, and extended hospitalization. Although ICU length of stay is influenced by multiple variables, the reviewed literature suggests that effective circulatory stabilization contributes positively to resource utilization and patient recovery.

Another relevant observation concerns tissue perfusion markers. Successful vasopressor therapy is commonly associated with improvements in serum lactate clearance, urine output, capillary refill time, and other indicators of microcirculatory recovery. These physiological improvements often precede clinical recovery and provide valuable information regarding treatment effectiveness. The integration of macro-hemodynamic and microcirculatory parameters has therefore become increasingly important in evaluating patient response and guiding ongoing vasopressor titration (Shi et al., 2020).

Despite these benefits, the evidence also demonstrates that favorable outcomes depend on the appropriate use of vasopressors rather than their administration alone. Excessive doses, delayed initiation, inadequate monitoring, or inappropriate agent selection may increase the risk of complications and adversely affect patient outcomes. Consequently, current evidence strongly supports individualized treatment strategies that consider patient characteristics, underlying cardiovascular physiology, organ function status, and response to therapy.

Across the American continent, institutions implementing standardized sepsis protocols consistently report improved outcomes associated with vasopressor therapy. Early recognition systems, rapid antimicrobial administration, protocol-driven resuscitation, and structured hemodynamic monitoring contribute synergistically to reductions in mortality and organ dysfunction. These findings reinforce the concept that vasopressors should be viewed as one component of an integrated critical care approach rather than as isolated therapeutic interventions.

When the available evidence is analyzed collectively, norepinephrine emerges as the vasopressor most consistently associated with favorable hemodynamic and clinical outcomes due to its efficacy, safety profile, and broad applicability. Adjunctive agents such as vasopressin and angiotensin II may provide additional benefits in selected circumstances, particularly among patients with refractory vasodilatory shock. However, the effectiveness of any vasoactive strategy ultimately depends on timely initiation, careful titration, continuous monitoring, and integration within comprehensive sepsis management protocols.

Overall, Figure 6 demonstrates that vasopressor therapy exerts a substantial influence on the clinical course of septic shock. Improvements in hemodynamic stability, organ perfusion, shock resolution, and survival are consistently reported when evidence-based vasopressor strategies are implemented. These findings support the central role of vasoactive therapy in modern critical care practice and provide a foundation for the conclusions and recommendations presented in the subsequent discussion section.

DISCUSIÓN

The findings of this review reinforce the central role of vasopressor therapy in the management of septic shock and highlight its importance as a cornerstone of hemodynamic stabilization in critically ill patients. Across the studies

analyzed, a consistent pattern emerged demonstrating that the timely initiation of vasoactive support contributes to the restoration of adequate perfusion pressure, preservation of organ function, and improvement of clinical outcomes. These observations are aligned with current international recommendations, which emphasize the importance of early recognition and prompt hemodynamic intervention in patients experiencing septic shock (Evans et al., 2021).

One of the most significant findings identified in this review is the sustained predominance of norepinephrine as the preferred first-line vasopressor. The evidence indicates that norepinephrine provides an optimal balance between efficacy and safety, achieving substantial increases in mean arterial pressure while minimizing the incidence of arrhythmias and other cardiovascular complications. This observation is consistent with the results of the SOAP II trial, which demonstrated superior safety compared with dopamine, particularly regarding cardiac rhythm disturbances (De Backer et al., 2010). The widespread adoption of norepinephrine throughout intensive care units in the Americas reflects the strength of the evidence supporting its use and the growing consensus regarding its role in septic shock management.

The analysis also underscores the importance of vasopressor timing. Historically, clinicians often delayed vasoactive support until after the administration of large volumes of intravenous fluids. However, contemporary evidence increasingly suggests that excessive fluid administration may contribute to tissue edema, impaired oxygen diffusion, and worsening organ dysfunction. Studies such as the CENSER trial have demonstrated that earlier initiation of norepinephrine can facilitate more rapid hemodynamic stabilization and reduce exposure to potentially harmful fluid overload (Permpikul et al., 2019). The present findings therefore support the evolving paradigm that vasopressors should be introduced promptly when persistent hypotension is identified, rather than being postponed until fluid resuscitation is exhausted.

Another important observation concerns the growing recognition that achieving an adequate blood pressure does not necessarily guarantee sufficient tissue perfusion. Traditional hemodynamic management focused primarily on macrocirculatory variables such as mean arterial pressure and cardiac output. However, recent investigations have highlighted the importance of microcirculatory function and tissue-level oxygen delivery. Several studies reviewed in this analysis reported persistent signs of tissue hypoperfusion despite normalization of arterial pressure, emphasizing the need for a broader physiological approach to septic shock management. Parameters such as serum lactate clearance, capillary refill time, urine output, and central venous oxygen saturation have therefore become increasingly valuable complements to conventional blood pressure monitoring (Shi et al., 2020).

The discussion of blood pressure targets remains particularly relevant. While a mean arterial pressure of 65 mmHg continues to represent the standard therapeutic goal for most patients, evidence suggests that individualized targets may be more appropriate in specific clinical scenarios. Patients with chronic hypertension appear to benefit from higher perfusion pressures due to long-term alterations in vascular autoregulation. Findings from the SEPSISPAM trial demonstrated improved renal outcomes among hypertensive patients managed with higher blood pressure targets, supporting a personalized approach to hemodynamic management (Asfar et al., 2014). These results challenge the concept of a universal target and emphasize the importance of tailoring treatment according to individual patient characteristics.

The role of adjunctive vasopressor therapies also deserves consideration. Vasopressin emerged as a valuable complementary agent, particularly among patients requiring escalating doses of norepinephrine. Although evidence regarding mortality benefits remains inconclusive, vasopressin may reduce catecholamine exposure and contribute to improved vascular responsiveness through alternative physiological pathways (Russell et al., 2008; Gordon et al., 2016). Similarly, angiotensin II has demonstrated promising results in refractory vasodilatory shock and may represent

an important addition to the therapeutic armamentarium available to intensivists. Nevertheless, further research is required to clarify its long-term effects on survival and organ function.

A particularly important aspect of this review is its continental perspective. The findings reveal substantial differences in healthcare infrastructure, medication availability, monitoring capabilities, and critical care resources across the Americas. North American healthcare systems generally possess greater access to advanced technologies and specialized personnel, whereas many regions of Latin America continue to face limitations related to resource allocation and critical care capacity. Despite these challenges, the literature demonstrates encouraging progress throughout countries such as Mexico, Colombia, Ecuador, Brazil, Argentina, Chile, and Peru, where increasing implementation of evidence-based sepsis protocols has contributed to improved patient outcomes (Gorordo-Delsol et al., 2020; Ortiz et al., 2014; Vélez et al., 2022).

An important implication of these findings is that successful septic shock management depends not only on the availability of vasopressor agents but also on the systems through which care is delivered. Institutions that integrate rapid recognition protocols, multidisciplinary collaboration, structured hemodynamic monitoring, and guideline-directed therapy consistently report better outcomes than those relying solely on pharmacological interventions. This observation reinforces the concept that vasopressor therapy should be viewed as one component of a comprehensive critical care strategy.

Several limitations of the available evidence should also be acknowledged. Although numerous randomized controlled trials and systematic reviews have evaluated vasopressor therapy, variations in study populations, treatment protocols, outcome measures, and healthcare settings may limit direct comparisons. Furthermore, many investigations have focused primarily on mortality and macro-hemodynamic variables, leaving important questions regarding microcirculatory physiology, long-term outcomes, and individualized treatment strategies unanswered. These limitations highlight the need for continued research aimed at refining vasopressor use and identifying patient-specific approaches to circulatory support.

Future investigations should prioritize precision medicine approaches that integrate clinical, hemodynamic, biochemical, and potentially genomic information to optimize vasopressor selection and dosing. Advances in bedside monitoring technologies may facilitate more individualized assessments of tissue perfusion and vascular responsiveness, allowing clinicians to tailor therapy according to each patient's physiological profile. Such developments could contribute to further reductions in mortality and improve quality of care for patients experiencing septic shock.

CONCLUSIÓN

Septic shock continues to represent one of the most complex and life-threatening conditions encountered in intensive care medicine, requiring rapid recognition, comprehensive management, and timely hemodynamic support to prevent progressive organ dysfunction and death. The evidence analyzed in this review demonstrates that vasopressor therapy remains a fundamental component of contemporary septic shock treatment and plays a decisive role in restoring circulatory stability, maintaining tissue perfusion, and improving clinical outcomes among critically ill patients.

Among the currently available vasoactive agents, norepinephrine consistently emerged as the preferred first-line vasopressor due to its favorable balance between efficacy and safety. The reviewed literature showed that norepinephrine effectively increases mean arterial pressure and systemic vascular resistance while presenting a lower incidence of arrhythmias and cardiovascular complications compared with alternative agents such as dopamine. These findings support current international recommendations and reinforce the widespread adoption of norepinephrine as the cornerstone of vasopressor therapy in septic shock.

The review also highlights the clinical importance of early vasopressor initiation. Accumulating evidence suggests that prompt administration following initial fluid resuscitation facilitates faster hemodynamic stabilization, reduces the duration of hypotension, limits excessive fluid exposure, and may contribute to improved organ function. These observations support the evolving concept that early restoration of vascular tone is a critical determinant of successful septic shock management.

Another major finding is that optimal hemodynamic support extends beyond the achievement of predefined blood pressure targets. Although maintaining a mean arterial pressure of at least 65 mmHg remains appropriate for most patients, individualized strategies may be necessary in specific populations, particularly among individuals with chronic hypertension or significant cardiovascular comorbidities. The integration of tissue perfusion indicators such as lactate clearance, urine output, capillary refill time, and microcirculatory assessments provides a more comprehensive evaluation of therapeutic effectiveness and may improve clinical decision-making.

Adjunctive vasopressor therapies, including vasopressin and angiotensin II, demonstrated valuable roles in selected clinical scenarios, especially among patients with refractory vasodilatory shock or inadequate responses to conventional catecholamine therapy. Although additional research is needed to further clarify their long-term impact on survival and organ preservation, these agents represent important therapeutic options that may enhance individualized hemodynamic management.

From a continental perspective, the findings reveal that outcomes associated with vasopressor therapy are influenced not only by pharmacological factors but also by healthcare infrastructure, access to critical care resources, availability of medications, implementation of evidence-based protocols, and professional training. While important disparities persist across the Americas, increasing adoption of standardized sepsis management strategies has contributed to meaningful improvements in patient care throughout both high-income and middle-income countries.

In conclusion, vasopressor therapy remains indispensable for the management of septic shock and continues to evolve alongside advances in critical care medicine. The most favorable outcomes are achieved when vasoactive agents are administered promptly, selected according to patient-specific physiological characteristics, monitored continuously, and integrated within comprehensive sepsis treatment protocols. Future research should focus on personalized hemodynamic management, advanced monitoring technologies, and precision-based therapeutic approaches capable of further improving survival, reducing organ dysfunction, and enhancing the quality of critical care delivered to patients with septic shock throughout the American continent.

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