Review Article

Tissue Perfusion–Guided Vasoactive Therapies in the Critically Ill: Role of Minimally Invasive and Invasive Hemodynamic Monitoring

Angélica Dayanna Rodriguez Luna[1*], Ciara María Murillo González[2], María Orozco Arguedas[3], José Agustín Matamoros Bustamante[4], Cristian Ismael Gomez Saborío[5]

[1, 2]Medical Doctor, Independent Researcher, San José, Costa Rica.
[3]Medical Doctor, Independent Researcher, Heredia, Costa Rica
[4]Medical Doctor, San Juan de Dios Hospital, San José, Costa Rica
[5]Medical Doctor, San Rafael de Alajuela Hospital, Alajuela, Costa Rica
[*]Corresponding author email: **angrodriguezluna@gmail.com**

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Abstract

Critical illness is characterized by profound alterations in tissue perfusion resulting from complex interactions between macrocirculation, microcirculation, and cellular oxygen utilization. Although macrocirculatory parameters such as mean arterial pressure and cardiac output are traditionally used to guide resuscitation, they frequently fail to reflect the adequacy of tissue oxygen delivery. Disruption of hemodynamic coherence, driven by endothelial dysfunction, microvascular thrombosis, and altered vasoregulatory balance, may lead to persistent microcirculatory impairment and cellular hypoxia despite apparent systemic stabilization. These pathophysiological mechanisms underscore the need for perfusion-oriented approaches in the management of shock. Vasoactive therapies remain central to hemodynamic support in critically ill patients, yet their effectiveness depends on appropriate selection and titration. Vasopressors primarily restore arterial pressure, while inotropes

improve cardiac output and vasodilators may optimize forward flow in selected contexts. However, excessive reliance on pressure-based targets can result in overtreatment, increasing the risk of ischemia, arrhythmias, and adverse outcomes. Consequently, contemporary strategies emphasize the integration of direct tissue perfusion markers, including lactate kinetics, capillary refill time, and venous oxygen-derived variables, to individualize hemodynamic goals. Advanced hemodynamic monitoring plays a key role in this paradigm. Minimally invasive techniques allow continuous trend assessment with lower procedural risk, whereas invasive modalities provide detailed physiological data essential in complex scenarios such as cardiogenic shock or advanced heart failure. Optimal management relies on combining static and dynamic variables with bedside clinical evaluation to guide fluid and vasoactive therapy. Emerging personalized frameworks and data-driven approaches further support individualized decision-making.

Key words

Tissue perfusion; Hemodynamic monitoring; Vasoactive therapy; Microcirculation; Critical illness; Personalized resuscitation.

Introduction

The rationale for perfusion-guided resuscitation arises from the recognition that traditional pressure-based targets do not consistently reflect adequate tissue oxygen delivery. Mean arterial pressure thresholds, such as the commonly applied target of 65 mmHg in septic shock, may fail to ensure sufficient tissue perfusion and can result in excessive vasopressor exposure. This approach has been associated with clinically relevant adverse effects, including arrhythmias and renal impairment, underscoring the limitations of relying on arterial pressure alone as a surrogate for perfusion [1].

In this context, microcirculatory considerations play a central role. Tissue perfusion is determined not only by global hemodynamic parameters but also by microvascular flow distribution, which is not captured by mean arterial pressure measurements. Clinical markers such as capillary refill time and serum lactate levels provide more direct insight into the adequacy of tissue oxygenation and cellular metabolism, allowing clinicians to identify persistent hypoperfusion despite apparently acceptable systemic pressures [2, 3].

Building on this framework, personalized perfusion monitoring has emerged to better align resuscitation efforts with individual patient physiology. By integrating multiple hemodynamic markers that encompass both macro- and microcirculatory domains, clinicians can adopt a more tailored approach to resuscitation. This multimodal strategy acknowledges interpatient variability and has the potential to improve outcomes by avoiding unnecessary escalation of vasoactive therapy while ensuring adequate tissue perfusion [4].

The clinical relevance of this approach becomes particularly evident in heterogeneous shock states. In septic shock, evidence suggests that targeting peripheral perfusion parameters, such as capillary refill time, may guide resuscitation more effectively than mean arterial pressure alone. Importantly, continued resuscitation in patients who already demonstrate normal peripheral perfusion has not been associated with improved outcomes, highlighting the risk of overtreatment when perfusion markers are not incorporated into decision-making [5].

Similarly, in cardiogenic shock, the frequent uncoupling between macrohemodynamic variables and microcirculatory perfusion further emphasizes the limitations of pressure-based targets. Peripheral perfusion markers, including capillary refill time, have demonstrated value in risk stratification and may offer more clinically

meaningful guidance for therapy than systemic hemodynamic parameters alone [3].

Within this paradigm, the use of vasopressors and inotropes must be guided by both arterial pressure and tissue perfusion. Norepinephrine remains the first-line vasopressor in many shock states due to its efficacy in restoring arterial pressure; however, persistent signs of hypoperfusion despite adequate pressure may indicate the need for adjunctive inotropic support. In such cases, agents like dobutamine can be introduced to augment cardiac output and improve tissue perfusion, illustrating the importance of integrating perfusion endpoints into the selection and titration of vasoactive therapies [6].

The objective of this article is to analyze the role of tissue perfusion–guided vasoactive therapy in critically ill patients, focusing on the integration of minimally invasive and invasive hemodynamic monitoring to support individualized resuscitation beyond pressure-based targets.

Methodology

This work was conceived as a narrative review focused on the role of tissue perfusion–guided vasoactive therapy in the management of critically ill patients, with particular emphasis on the clinical integration of minimally invasive and invasive hemodynamic monitoring. Rather than adhering to a rigid methodological framework, the manuscript was structured around physiological interpretation and clinical decision-making, highlighting the interaction between macrocirculatory parameters, microcirculatory perfusion, and the use of vasoactive agents in heterogeneous shock states. The discussion was oriented toward clarifying how perfusion-oriented monitoring informs therapeutic reasoning beyond pressure-based targets.

The conceptual framework of the review was informed by contemporary scientific literature addressing hemodynamic monitoring, tissue perfusion assessment, and vasoactive drug use in critical care. Peer-reviewed publications published between 2021 and 2026 in English or Spanish were selectively consulted from PubMed, Scopus, and Web of Science, prioritizing studies that contributed to understanding perfusion physiology, minimally invasive and invasive monitoring techniques, microcirculatory assessment tools, and perfusion-guided resuscitation strategies. Sources lacking peer review, presenting redundant data, or not directly relevant to perfusion-oriented hemodynamic management were not included. Search concepts were applied flexibly to capture clinically relevant themes rather than to achieve exhaustive coverage.

The information incorporated into the manuscript was analyzed through an integrative and qualitative perspective, allowing hemodynamic and perfusion variables to be organized according to clinical relevance and applicability. Particular attention was given to areas of concordance and dissociation between systemic hemodynamics and tissue perfusion, as well as to the practical limitations of available monitoring modalities. Artificial intelligence–based resources were used exclusively to support thematic organization and conceptual coherence during manuscript preparation. This narrative approach facilitated a logically connected and clinically oriented synthesis, underscoring the value of perfusion-guided strategies for individualized vasoactive therapy in critically ill patients.

Pathophysiology of Tissue Perfusion in Critical Illness

The relationship between macrocirculation, microcirculation, and cellular oxygenation is fundamental to understanding tissue perfusion in critical illness. Macrocirculation refers to large-scale blood flow through major vessels, whereas microcirculation encompasses flow through small vessels and capillaries, which is essential for tissue-level oxygen delivery. Effective cellular oxygenation depends on the successful

transfer of oxygen from the macrocirculation to the microcirculation and its subsequent utilization within cells. In this process, mitochondrial function plays a central role, as it governs cellular oxygen utilization and energy production; mitochondrial dysfunction can therefore impair energy metabolism and contribute to tissue hypoxia [7]. In critically ill patients, this coordinated relationship may become disrupted, leading to inadequate tissue oxygenation despite apparently normal macrocirculatory parameters, highlighting the potential dissociation between systemic hemodynamics and tissue-level perfusion [8].

This dissociation is closely related to the loss of hemodynamic coherence, which describes the alignment between macrocirculatory and microcirculatory responses. Loss of coherence is characterized by persistent microcirculatory dysfunction despite normalization of macrocirculatory metrics, reflecting a failure of systemic stabilization to translate into effective tissue perfusion [8, 9]. Several mechanisms contribute to this phenomenon, including endothelial dysfunction, microvascular thrombosis, and imbalances between vasodilatory and vasoconstrictive mediators, all of which disrupt microvascular flow regulation [3]. Observations using sublingual videomicroscopy have further demonstrated that microcirculatory dysfunction may persist in conditions such as sepsis even after apparent macrocirculatory stabilization, reinforcing the clinical relevance of this loss of coherence [9].

Within this pathophysiological framework, hypoperfusion and maldistribution of flow emerge as key contributors to tissue hypoxia in critical illness. Hypoperfusion may result from reduced cardiac output, systemic vasodilation, or primary microvascular dysfunction, each leading to insufficient tissue perfusion [10, 11]. In parallel, maldistribution of flow occurs when blood is unevenly distributed within the microcirculation, often due to heterogeneous capillary perfusion and increased intercapillary distances, which limit effective oxygen diffusion. In sepsis, these alterations are exemplified by decreased capillary density and an increased proportion of stopped-flow capillaries, both of which contribute to tissue hypoxia [12]. Similarly, cardiogenic shock illustrates how microcirculatory dysfunction can persist despite therapeutic interventions aimed at improving macrocirculatory parameters, underscoring the need for strategies that specifically target microvascular perfusion in addition to systemic hemodynamics [10, 11].

Principles of Vasoactive Therapy

Vasoactive agents exert distinct physiological effects that are central to hemodynamic management in critically ill patients. Vasopressors, such as norepinephrine, primarily act by increasing systemic vascular resistance, thereby elevating arterial pressure and supporting organ perfusion. Norepinephrine is frequently preferred because it provides consistent vasoconstrictive effects while exerting minimal influence on heart rate, which contributes to a more predictable hemodynamic response [6, 13]. In contrast, inotropes such as dobutamine primarily enhance myocardial contractility, leading to an increase in cardiac output and, consequently, improved tissue perfusion. These agents are particularly valuable in situations where vasopressor therapy alone fails to restore adequate perfusion due to impaired cardiac performance. Vasodilators, although less commonly employed in shock management, reduce systemic vascular resistance and afterload and may improve cardiac output in selected clinical scenarios, especially when excessive vasoconstriction compromises forward flow [6, 14].

Beyond these pharmacological effects, contemporary hemodynamic management increasingly recognizes the limitations of mean arterial pressure as the sole therapeutic target. Although mean arterial pressure remains a commonly used parameter, it does not consistently correlate with adequate tissue

perfusion. Direct assessment of tissue perfusion, using markers such as capillary refill time or serum lactate levels, provides a more physiologically meaningful evaluation of hemodynamic adequacy and cellular oxygen delivery [4, 15]. This perspective has led to the adoption of personalized hemodynamic targets that account for individual patient physiology and the dynamic evolution of critical illness, an approach that appears to offer advantages over fixed, population-based thresholds [16].

Within this framework, the risks associated with inappropriate vasoactive dosing warrant careful consideration. Excessive vasoconstriction resulting from high-dose vasopressor therapy can impair blood flow to vital organs, increasing the risk of ischemic injury despite apparent normalization of arterial pressure [17]. Similarly, elevated doses of certain inotropes and vasopressors, including epinephrine and dopamine, have been associated with a higher incidence of arrhythmias and other adverse cardiovascular events [6]. Importantly, accumulating evidence suggests that greater vasopressor exposure does not necessarily translate into improved survival and may, in some populations such as older patients, increase morbidity and adverse outcomes, reinforcing the need for judicious, perfusion-guided titration of vasoactive therapies [1, 17].

Hemodynamic Monitoring: Conceptual Framework

Advanced hemodynamic monitoring is indicated in critically ill patients who fail to respond to initial therapeutic measures and require a more precise characterization of their cardiovascular status. This is particularly relevant in individuals with acute circulatory failure or established shock, in whom basic monitoring modalities are insufficient to capture the complexity of underlying hemodynamic disturbances [18]. In severe cases, techniques such as transpulmonary thermodilution and pulmonary artery catheterization are recommended, as they provide comprehensive information on cardiac function, preload, and fluid status, thereby supporting more informed therapeutic decisions [19]. Within this context, personalized monitoring approaches, including the HM-TARGET framework, have been proposed to use real-time hemodynamic data to individualize therapeutic targets, a strategy that may contribute to reductions in intensive care unit mortality [16].

A central component of advanced hemodynamic assessment involves distinguishing between static and dynamic variables. Static parameters, such as central venous pressure, offer baseline information regarding hemodynamic status but have limited ability to predict fluid responsiveness or reflect tissue perfusion accurately [5]. In contrast, dynamic variables, including cardiac output and stroke volume variation, provide insight into the cardiovascular response to fluid challenges and have demonstrated greater utility in guiding fluid resuscitation and vasoactive therapy. Consequently, the incorporation of dynamic measures is emphasized in personalized resuscitation strategies aimed at optimizing fluid administration while minimizing the risk of fluid overload [19, 20].

Effective hemodynamic management ultimately depends on the integration of monitored data with bedside clinical assessment. Clinical signs such as skin mottling and capillary refill time remain essential for evaluating tissue perfusion and contextualizing numerical hemodynamic values. Advanced monitoring techniques, including echocardiography and transpulmonary thermodilution, should therefore be interpreted alongside clinical findings to provide a more comprehensive assessment of volume status and to guide fluid and vasoactive therapy [5]. In parallel, emerging machine learning approaches are being explored to synthesize complex hemodynamic data, predict cardiovascular insufficiency, and support personalized treatment strategies, with the potential to further improve outcomes in critically ill patients [20].

Minimally Invasive Hemodynamic Monitoring

Pulse contour analysis represents a minimally invasive approach to hemodynamic monitoring that estimates cardiac output continuously and in real time from the arterial pressure waveform. Systems such as FloTrac offer the advantage of providing ongoing hemodynamic data with minimal invasiveness, making them particularly useful in perioperative settings and in patients who require frequent reassessment without the risks associated with more invasive techniques, such as pulmonary artery catheterization [21, 22].

Despite these advantages, pulse contour analysis has important limitations that must be considered in clinical practice. Studies have demonstrated limited agreement between pulse contour–derived cardiac output measurements and the thermodilution method, which remains the reference standard. Percentage errors exceeding acceptable thresholds have been reported across various clinical scenarios, indicating that pulse contour analysis cannot be considered interchangeable with invasive methods, particularly in patients with marked hemodynamic instability or rapidly changing vascular tone [21].

In clinical practice, pulse contour analysis is most frequently applied in cardiac surgery and critical care environments where continuous monitoring is desirable, but the potential complications of invasive techniques are a concern. Its primary utility lies in tracking trends in cardiac output over time rather than providing precise absolute measurements, which limits its role in certain high-risk scenarios but preserves its value as a monitoring tool for dynamic assessment [21, 23].

Esophageal Doppler monitoring offers an alternative noninvasive method for estimating cardiac output by measuring blood flow velocity in the descending aorta. This technique is particularly advantageous in the operating room, where it is commonly used to guide goal-directed fluid therapy and allows rapid adjustments to intravascular volume based on real-time flow measurements [24, 25].

However, the clinical applicability of esophageal Doppler is influenced by several limitations. Measurement accuracy may be affected by patient positioning and anatomical variability, and the technique requires specific operator training to ensure reliable data acquisition. In addition, the lack of continuous monitoring can be a drawback in highly dynamic clinical environments, where rapid hemodynamic changes may occur [22, 24].

Within these constraints, esophageal Doppler is most employed in surgical contexts for intraoperative fluid management and in selected critically ill patients for whom noninvasive monitoring is preferred. It is particularly useful in individuals with contraindications to invasive hemodynamic monitoring, where it provides valuable information to support fluid and perfusion management while avoiding the risks associated with invasive catheterization [25].

Invasive Hemodynamic Monitoring

Arterial waveform analysis and central venous measurements constitute fundamental components of invasive hemodynamic monitoring in critically ill patients. Arterial waveform analysis provides continuous, real-time information on blood pressure and derived cardiac output variables, enabling detailed assessment of vascular tone and cardiac performance. This continuous feedback is particularly valuable for the early detection of hemodynamic changes and supports timely therapeutic interventions in dynamic clinical settings [18]. Complementing this approach, central venous pressure measurements are commonly used to estimate right ventricular preload. Low central venous pressure values may suggest hypovolemia, whereas elevated values can indicate fluid overload, thereby contributing

to fluid management decisions when interpreted within the broader clinical context [6].

Pulmonary artery catheterization has historically played a central role in advanced hemodynamic assessment. Introduced in the 1970s, the pulmonary artery catheter provided unprecedented access to detailed cardiovascular data, including cardiac output and pulmonary artery pressures, and significantly influenced the management of complex conditions such as cardiogenic shock and advanced heart failure [26]. Despite this physiological value, the routine use of pulmonary artery catheters has declined over time, largely due to studies such as the ESCAPE trial, which questioned their impact on survival in patients with heart failure. Nevertheless, more recent evidence suggests that pulmonary artery catheterization may retain clinical utility in selected scenarios, including cardiac surgery and severe or refractory heart failure, where detailed hemodynamic information can guide advanced therapeutic strategies [27].

The ongoing controversy surrounding pulmonary artery catheter use reflects the heterogeneity of available evidence regarding its efficacy and safety. While some studies emphasize its potential role in reducing mortality and optimizing complex therapeutic decisions, others highlight the absence of a consistent survival benefit and raise concerns about procedure-related complications [28].

In this setting, risk–benefit considerations are central to the use of invasive hemodynamic monitoring in critical care practice. The decision to implement invasive techniques should be individualized, considering the patient's clinical condition, the likelihood that the information obtained will meaningfully influence management, and the potential risks associated with invasive procedures, such as infection or vascular injury [27]. Contemporary approaches to personalized hemodynamic management, including frameworks such as HM-TARGET, further emphasize tailoring interventions to patient-specific physiology and dynamic clinical responses, an approach that has demonstrated potential in reducing intensive care unit mortality [16]. When applied judiciously, monitoring modalities such as pulmonary artery catheterization and transpulmonary thermodilution can provide comprehensive data to guide fluid and vasoactive therapy, helping to prevent fluid overload and its associated complications [5].

Tissue Perfusion–Oriented Monitoring Tools

Serum lactate and lactate kinetics are widely used markers of tissue perfusion and metabolic stress in critical care. Elevated lactate concentrations are frequently interpreted as indicators of inadequate tissue oxygenation and have strong prognostic value across a range of critical illnesses. However, lactate levels may also be influenced by factors unrelated to tissue hypoxia, including altered metabolism and impaired clearance, which necessitates their interpretation in conjunction with other clinical and hemodynamic measurements [29]. Within this context, the dynamic assessment of lactate clearance has gained importance as a marker of resuscitation effectiveness. Monitoring changes in lactate over time provides insight into the response to therapy, and evidence from pediatric shock populations has shown that lactate clearance is a reliable predictor of survival, with clearance rates exceeding 10% being associated with improved outcomes [30]. In parallel, advances in non-invasive lactate monitoring technologies, including the development of continuous sensors, are being explored to reduce invasiveness and enhance the timeliness of lactate assessment, potentially improving real-time clinical decision-making [31].

Central and mixed venous oxygen saturation measurements offer additional insight into the balance between oxygen delivery and consumption at the systemic level. Central venous oxygen saturation and mixed venous oxygen saturation are commonly used to infer

global oxygen utilization; however, their interpretation is complex, particularly in conditions such as sepsis, where values may appear normal or even elevated despite the presence of impaired tissue perfusion and ongoing cellular hypoxia. To address these limitations, complementary variables such as the venous-to-arterial carbon dioxide difference and the ratio of venous-to-arterial carbon dioxide difference to arteriovenous oxygen content difference have emerged as promising markers. An increased venous-to-arterial carbon dioxide difference reflects impaired perfusion, while an elevated ratio suggests the presence of tissue dysoxia, thereby providing additional physiological context beyond oxygen saturation alone [29].

Peripheral perfusion markers and emerging microcirculatory assessment techniques further contribute to a more comprehensive evaluation of tissue perfusion. Clinical parameters such as capillary refill time and skin perfusion are simple, bedside tools that offer valuable information regarding peripheral circulation. The ANDROMEDA-SHOCK trial underscored the potential role of capillary refill time as a resuscitation target in septic shock, demonstrating that rapid normalization of this parameter is associated with improved outcomes [32]. Beyond these clinical markers, techniques aimed at directly assessing the microcirculation, including sublingual microcirculatory imaging, are gaining increasing attention. These methods seek to provide a more detailed understanding of tissue perfusion that extends beyond conventional macrohemodynamic variables. Despite their promise, the integration of microcirculatory assessments into routine clinical practice remains challenging due to technical complexity and the current lack of clearly defined, targeted therapeutic interventions. Ongoing advances in non-invasive and real-time monitoring technologies may help overcome these limitations and enhance the clinical utility of microcirculatory monitoring in the future [33, 34].

Perfusion-Guided Vasoactive Strategies in Clinical Practice

The application of perfusion-guided vasoactive strategies varies according to the underlying shock etiology, with septic, cardiogenic, and postoperative shock representing distinct but overlapping clinical contexts. In septic shock, the primary therapeutic objective is the restoration of adequate tissue perfusion and oxygen delivery. Current clinical guidelines traditionally recommend targeting a mean arterial pressure of 65 mm Hg; however, emerging evidence suggests that higher vasopressor exposure may not confer additional benefit and may instead increase the risk of adverse effects, including arrhythmias. Studies indicate that limiting vasopressor use when tissue perfusion is adequate may reduce mortality and treatment-related complications, supporting a more conservative and physiologically guided approach to resuscitation. Within this framework, individualized strategies that incorporate peripheral perfusion parameters allow clinicians to identify patients who may benefit from restrained resuscitation efforts rather than continued escalation of vasoactive support [1, 5].

In cardiogenic shock, the preservation and optimization of cardiac output are central to effective management. Norepinephrine is commonly employed as a first-line vasopressor to maintain arterial pressure, while inotropic support with agents such as dobutamine is frequently added when tissue perfusion remains inadequate due to impaired myocardial contractility. The use of inotropes in this setting should be guided by continuous hemodynamic and perfusion monitoring, enabling clinicians to balance improvements in cardiac output against the potential risks associated with excessive inotropic stimulation [6, 35].

Postoperative shock represents another clinical scenario in which perfusion-guided management is particularly relevant. In the perioperative period, careful monitoring of hemodynamic parameters is essential to ensure adequate tissue

perfusion and to promptly identify evolving circulatory instability. The incorporation of tissue perfusion monitoring into postoperative care facilitates individualized therapeutic adjustments, allowing vasoactive and fluid therapies to be tailored to the patient's physiological response and potentially improving clinical outcomes [4].

Across these shock states, tailoring vasoactive therapy based on perfusion endpoints has become a cornerstone of personalized hemodynamic management. This strategy involves defining individualized targets for mean arterial pressure and complementary perfusion markers according to patient-specific characteristics and the temporal phase of shock. Such personalization helps reconcile the need to maintain adequate tissue perfusion with the goal of minimizing vasopressor-related adverse effects [1, 18]. Dynamic monitoring of perfusion indicators, including lactate levels, capillary refill time, and central venous oxygen saturation, supports the ongoing titration of vasoactive agents and allows real-time therapeutic adjustments that reflect the patient's evolving clinical status [18, 29].

The implementation of multimodal monitoring–driven therapeutic algorithms further strengthen this individualized approach. By integrating advanced technologies such as echocardiography and transpulmonary thermodilution, clinicians can obtain a comprehensive view of both macro- and microcirculatory function. This integration enables the development of structured algorithms that align hemodynamic interventions with tissue perfusion goals, enhancing the precision of therapeutic decisions [4, 29]. Through this multimodal strategy, interventions can be more accurately tailored to individual patient physiology, a principle consistent with precision medicine and associated with the potential for improved outcomes in critically ill populations [36].

Clinical Evidence, Limitations, and Future Perspectives

The impact of advanced hemodynamic monitoring on clinical outcomes has been most extensively studied in patients with heart failure and cardiogenic shock, particularly with the use of pulmonary artery catheters. These devices provide detailed physiological data that can inform complex therapeutic decisions; however, their routine use remains controversial because evidence regarding mortality benefit has been mixed [38]. Despite this debate, approaches that move beyond fixed targets appear promising. Personalized hemodynamic strategies, exemplified by the HM-TARGET model, have been associated with lower intensive care unit mortality when compared with static, population-based targets, suggesting that individualized goal setting may better align therapy with patient-specific physiology [18].

Comparative evidence between minimally invasive and invasive monitoring modalities further illustrates the trade-offs inherent in hemodynamic assessment. Minimally invasive approaches, including non-invasive cardiac output monitoring, are increasingly explored due to their favorable safety profile; however, they do not yet provide the depth and granularity of data obtainable through invasive techniques such as right heart catheterization. As a result, invasive monitoring remains indispensable in selected clinical contexts, particularly in advanced heart failure management and cardiogenic shock, where comprehensive hemodynamic profiling is critical to guide therapeutic interventions and advanced support strategies [38, 39].

Despite ongoing advances, several limitations continue to constrain the optimal application of hemodynamic monitoring. A lack of standardized protocols and significant variability in hemodynamic assessment contribute to inconsistent implementation and underscore the need for truly individualized treatment plans [38, 39]. Future research should therefore prioritize

innovative trial designs capable of capturing patient heterogeneity and evaluating personalized management strategies more effectively. In parallel, the integration of machine learning techniques offers a potential pathway to identify patient-specific therapeutic trajectories and refine decision-making, supporting a more precise and adaptive approach to hemodynamic management in critical care [40].

Conclusions

Tissue perfusion in critical illness cannot be reliably inferred from macrocirculatory parameters alone, as frequent dissociation between macro- and microcirculation leads to persistent cellular hypoxia despite normalized systemic hemodynamics. Loss of hemodynamic coherence, driven by microvascular and endothelial dysfunction, underscores the need to directly assess tissue perfusion and microcirculatory flow when guiding resuscitation and vasoactive therapy.

Perfusion-guided, individualized vasoactive management offers a physiologically superior alternative to fixed pressure-based strategies, as mean arterial pressure targets do not consistently reflect adequate tissue oxygen delivery. Integrating dynamic perfusion markers with advanced hemodynamic monitoring allows more precise titration of vasopressors and inotropes, reducing unnecessary drug exposure and associated adverse effects while optimizing cardiac output and tissue perfusion.

A multimodal hemodynamic monitoring approach, combining clinical assessment, minimally invasive and invasive techniques, and perfusion-oriented markers, represents the most coherent strategy for managing shock, particularly in complex scenarios such as septic and cardiogenic shock. While invasive monitoring remains essential in selected high-risk patients, future progress depends on personalized frameworks, standardized integration of perfusion endpoints, and emerging data-driven tools to refine decision-making and improve outcomes in critically ill populations.

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