PERFUSION-ORIENTED HEMODYNAMIC RESUSCITATION IN EARLY SEPTIC SHOCK: A STEPWISE ALGORITHM AND ITS IMPLICATIONS FOR EARLY REHABILITATION

Alimov Azam Fayzievich
DSc.,
Saidov Maksud Arifovich,
Sabirov Djakhongir Ruziyevich
DSc., prof.,
National Medical Center, Tashkent, Republic of Uzbekistan
azamalimov1986@gmail.com, saidov_maksud@mtm.uz, gocjahongir@gmail.com
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To present a stepwise perfusion-oriented hemodynamic resuscitation algorithm for early septic shock and to evaluate the prognostic significance of tissue perfusion markers and organ dysfunction dynamics for early rehabilitation outcomes

ABSTRACT

Background: Septic shock remains a leading cause of mortality in intensive care units, and survivors frequently develop Post-Intensive Care Syndrome (PICS), which significantly impairs functional recovery and quality of life. The quality of hemodynamic resuscitation in the acute phase directly influences the severity of organ damage and, consequently, the patient's rehabilitation potential.

Background: Septic shock remains a leading cause of mortality in intensive care units, and survivors frequently develop Post-Intensive Care Syndrome (PICS), which significantly impairs functional recovery and quality of life. The quality of hemodynamic resuscitation in the acute phase directly influences the severity of organ damage and, consequently, the patient's rehabilitation potential.

Objective: To present a stepwise perfusion-oriented hemodynamic resuscitation algorithm for early septic shock and to evaluate the prognostic significance of tissue perfusion markers and organ dysfunction dynamics for early rehabilitation outcomes.

Methods: A clinical algorithm was developed based on current Surviving Sepsis Campaign 2021 guidelines, Sepsis-3 definitions, and evidence from the ANDROMEDA-SHOCK-2 trial. The algorithm incorporates serial assessment of mean arterial pressure, capillary refill time, serum lactate, urine output, fluid responsiveness testing, and Sequential Organ Failure Assessment (SOFA) score dynamics over 72 hours.

Results: The proposed algorithm provides a systematic framework for personalized hemodynamic resuscitation that transitions from initial crystalloid infusion through fluid responsiveness assessment to early vasopressor initiation. The ΔSOFA72 metric serves as an integrative endpoint reflecting both therapeutic efficacy and rehabilitation readiness. Early

normalization of capillary refill time and lactate clearance correlate with reduced organ support requirements and earlier potential for mobilization.

Conclusion: Perfusion-oriented hemodynamic resuscitation in early septic shock, guided by tissue perfusion markers and organ dysfunction monitoring, may reduce the burden of organ damage and facilitate earlier transition to rehabilitation. The ΔSOFA72 parameter may serve as a bridge metric connecting acute intensive care outcomes with rehabilitation planning.

Introduction

Sepsis and septic shock constitute a global health emergency, affecting an estimated 49 million individuals annually and contributing to approximately 11 million deaths worldwide. Despite advances in critical care medicine, including the adoption of evidence-based bundles and early goal-directed therapy, mortality from septic shock remains unacceptably high, ranging from 30% to 50% depending on the population and healthcare setting.

The pathophysiology of septic shock is characterized by profound disturbances in macro- and microcirculation, including systemic vasodilation, endothelial dysfunction, capillary leak, and impaired oxygen extraction at the tissue level. These hemodynamic derangements lead to tissue hypoperfusion and progressive organ dysfunction, which, if inadequately managed in the acute phase, result in irreversible organ damage with long-lasting consequences for the patient's functional recovery.

Traditional approaches to hemodynamic resuscitation in septic shock have focused primarily on achieving target values for systemic arterial pressure. The Surviving Sepsis Campaign (SSC) 2021 guidelines recommend targeting a mean arterial pressure (MAP) of at least 65 mmHg using norepinephrine as the first-line vasopressor, with initial crystalloid resuscitation guided by clinical assessment of fluid responsiveness. However, accumulating evidence indicates that normalization of systemic blood pressure alone does not guarantee adequate tissue perfusion, and excessive fluid administration aimed at achieving pressure targets may cause harm through volume overload, pulmonary edema, and exacerbation of organ dysfunction.

In response to these limitations, a paradigm shift toward perfusion-oriented hemodynamic resuscitation has gained momentum. This approach integrates traditional macrocirculatory targets with markers of tissue perfusion, including capillary refill time (CRT), serum lactate levels and lactate clearance, urine output, and clinical signs of peripheral perfusion. The ANDROMEDA-SHOCK-2 trial provided landmark evidence supporting CRT-guided resuscitation as a clinically meaningful strategy, demonstrating that peripheral perfusion-targeted therapy is associated with favorable outcomes in early septic shock.

Beyond the acute phase, survivors of septic shock face a substantial burden of long-term morbidity. Post-Intensive Care Syndrome encompasses a constellation of physical, cognitive, and psychological impairments that persist for months to years following ICU discharge. Prolonged mechanical ventilation, neuromuscular weakness acquired during critical illness, delirium, and the cumulative effects of organ dysfunction contribute to profound functional disability. Consequently, the quality and timeliness of rehabilitation following septic shock are critical determinants of long-term patient outcomes.

A growing body of evidence supports the concept that the severity of organ dysfunction in the acute phase — as captured by the Sequential Organ Failure Assessment (SOFA) score and its trajectory — serves as a predictor of rehabilitation needs and functional recovery potential. However, no existing framework explicitly links the quality of acute hemodynamic resuscitation with rehabilitation planning and intensity stratification.

The present study addresses this gap by presenting a stepwise perfusion-oriented hemodynamic resuscitation algorithm for early septic shock and analyzing the prognostic significance of tissue perfusion markers and organ dysfunction dynamics as predictors of rehabilitation potential.

Materials and Methods

The clinical algorithm was developed through a structured process incorporating three principal evidence sources: (1) current international guidelines, including the Surviving Sepsis Campaign 2021 recommendations and the Sepsis-3 consensus definitions; (2) results of landmark randomized controlled trials, including the ANDROMEDA-SHOCK-2 trial and the CLASSIC trial on restrictive versus liberal fluid therapy; and (3) a systematic review of the literature on tissue perfusion monitoring, fluid responsiveness assessment, and rehabilitation after critical illness.

The algorithm is structured as a sequential seven-step protocol. Step 1 involves early recognition of sepsis and septic shock with registration of the time point T0, defined as the moment of clinical identification of septic shock. Step 2 comprises standardized baseline assessment of systemic hemodynamics (MAP, heart rate), tissue perfusion markers (CRT, arterial lactate, urine output, mental status, peripheral perfusion), laboratory parameters (arterial blood gas, pH, base excess, creatinine, bilirubin, platelets, PaO2/FiO2), and baseline severity scores (APACHE II, SOFA at T0).

Step 3 encompasses the first-hour bundle: blood culture collection prior to antibiotics (without significant delay), initiation of broad-spectrum antimicrobial therapy, crystalloid fluid resuscitation with preference for balanced crystalloids, and identification and management of the source of infection. Step 4 involves personalized reassessment of fluid responsiveness using passive leg raise testing and, where available, bedside echocardiography. Patients demonstrating fluid responsiveness receive a cautious repeat crystalloid bolus with subsequent reassessment; patients without fluid responsiveness or with signs of fluid overload are transitioned to early vasopressor initiation.

Step 5 involves early vasopressor support with norepinephrine as the first-line agent, targeting MAP of at least 65 mmHg. Vasopressin is considered as a second-line agent, and dobutamine as an inotropic agent in cases of suspected myocardial dysfunction with low cardiac output. Step 6 consists of mandatory perfusion-oriented reassessment at 2–6 hours, evaluating MAP, CRT, lactate dynamics, cumulative urine output, norepinephrine dose, total fluid administered, fluid balance, and signs of fluid overload.

Step 7 addresses organ dysfunction monitoring and transition to supportive care, with assessment of SOFA score dynamics at 24 and 72 hours (ΔSOFA72), development of acute kidney injury according to KDIGO criteria, need for renal replacement therapy, mechanical ventilation requirements, oxygenation index, and cumulative fluid balance. The ΔSOFA72 metric — calculated as the difference between baseline SOFA at T0 and SOFA at 72 hours —

serves as the primary integrative outcome measure reflecting both therapeutic efficacy and rehabilitation readiness.

The prognostic significance of acute-phase parameters for rehabilitation outcomes was evaluated through structured analysis of published evidence linking organ dysfunction trajectories, duration of organ support, and ICU length of stay with functional recovery and rehabilitation needs in septic shock survivors.

Results

The developed algorithm provides a comprehensive, stepwise framework for personalized hemodynamic resuscitation in early septic shock that explicitly integrates tissue perfusion assessment into every decision point. The key distinguishing features of the proposed approach compared to traditional resuscitation protocols are summarized below.

First, the algorithm mandates transition from standardized volume-based resuscitation to individualized fluid therapy guided by dynamic assessment of fluid responsiveness after the initial crystalloid bolus. This approach is supported by evidence demonstrating that continued fluid administration without assessment of preload responsiveness leads to excessive positive fluid balance, which is independently associated with increased mortality, prolonged mechanical ventilation, and delayed recovery.

Second, the algorithm emphasizes that achievement of target MAP alone is insufficient as an endpoint of resuscitation. Patients with normalized systemic blood pressure but persistently abnormal CRT and elevated lactate are classified as having ongoing tissue hypoperfusion requiring further diagnostic and therapeutic intervention. This perfusion-oriented perspective aligns with the ANDROMEDA-SHOCK-2 findings and reflects the pathophysiological reality that macrocirculatory targets do not guarantee microcirculatory adequacy.

Third, the ΔSOFA72 metric emerges as a clinically meaningful integrative parameter that captures the overall trajectory of organ dysfunction during the critical first 72 hours of intensive care. Analysis of the literature reveals that patients with favorable ΔSOFA72 trajectories (declining scores) demonstrate several characteristics relevant to rehabilitation: shorter duration of mechanical ventilation, lower incidence of ICU-acquired weakness, earlier return to spontaneous breathing, earlier recovery of consciousness, reduced need for renal replacement therapy, and shorter ICU and hospital length of stay.

Fourth, the algorithm identifies specific acute-phase parameters with prognostic significance for rehabilitation outcomes. Early normalization of CRT within the first 6 hours is associated with improved peripheral microcirculation, which has implications for early physical mobilization and exercise tolerance during rehabilitation. Lactate clearance exceeding 20% at 6 hours correlates with more effective tissue oxygen delivery and lower risk of persistent organ dysfunction. Excessive cumulative fluid balance at 24 hours (greater than 5% of body weight) is associated with prolonged edema, respiratory impairment, and delayed initiation of physical rehabilitation activities.

Fifth, the review identifies that patients with prolonged vasopressor requirements (exceeding 48–72 hours), persistent lactic acidosis, and worsening SOFA trajectories represent a high-risk subgroup requiring intensive, prolonged, and multidisciplinary rehabilitation, including neuromuscular rehabilitation for ICU-acquired weakness, respiratory

rehabilitation for post-ventilation deconditioning, cognitive rehabilitation for post-delirium cognitive impairment, and psychological support for anxiety, depression, and post-traumatic stress.

Discussion

The present study proposes a conceptual bridge between acute hemodynamic resuscitation in septic shock and subsequent rehabilitation planning — a connection that has been largely absent from the existing literature. While critical care medicine and rehabilitation medicine have traditionally operated as separate domains, the evidence synthesized in this review strongly supports their integration within a continuum-of-care framework.

The perfusion-oriented approach to resuscitation offers several specific advantages from a rehabilitation perspective. By minimizing unnecessary fluid overload, the algorithm reduces the duration of mechanical ventilation and the severity of peripheral and pulmonary edema, both of which are recognized barriers to early mobilization. By targeting tissue perfusion rather than arbitrary pressure thresholds, the approach aims to preserve microcirculatory function, which is essential for skeletal muscle integrity and the capacity to participate in physical rehabilitation activities.

The ΔSOFA72 metric represents a novel bridge parameter that may serve dual purposes: as an outcome measure for acute resuscitation efficacy and as a triage tool for rehabilitation intensity stratification. Patients with rapidly improving SOFA trajectories may be candidates for early, lower-intensity rehabilitation focused on mobilization and secondary prevention, while those with stagnant or worsening trajectories may require delayed, higher-intensity, multidisciplinary rehabilitation programs addressing the full spectrum of PICS.

Several limitations of the present work warrant consideration. The algorithm has been developed on the basis of existing evidence and clinical reasoning but has not yet been validated in a prospective clinical trial. The specific thresholds and decision points within the algorithm, while grounded in current guidelines and trial evidence, require calibration to local clinical contexts. The proposed linkage between acute-phase parameters and rehabilitation outcomes is based on indirect evidence from separate studies rather than integrated prospective data.

Future research directions should include prospective validation of the algorithm in a multicenter cohort, evaluation of ΔSOFA72 as a predictor of specific rehabilitation outcomes using standardized functional assessment tools, development of integrated clinical decision support systems that automatically generate rehabilitation recommendations based on acute-phase data, and randomized controlled trials comparing outcomes of rehabilitation intensity stratified by ΔSOFA72 versus standard rehabilitation protocols.

Conclusion

The proposed perfusion-oriented hemodynamic resuscitation algorithm for early septic shock provides a systematic, evidence-based framework for personalized intensive care that integrates tissue perfusion monitoring into every clinical decision point. By shifting the resuscitation paradigm from pressure-targeted to perfusion-targeted management and by incorporating the ΔSOFA72 metric as an integrative outcome measure, the algorithm establishes a conceptual and practical bridge between acute critical care and rehabilitation

medicine. Early normalization of tissue perfusion markers, avoidance of excessive fluid overload, and favorable organ dysfunction trajectories in the first 72 hours create the pathophysiological conditions necessary for earlier and more effective rehabilitation. The integration of acute resuscitation quality metrics into rehabilitation planning represents a promising and clinically relevant direction that warrants prospective multicenter validation..

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