

Challenges and strategies for anesthetic management in patients with septic shock

Guangling Feng¹, Peng Ji², Song Yao², Jinyu Wang², Jie Gao³, Xianling Guo³, Zhui Ke^{3*}

¹First People's Hospital of Guiyang, Guiyang City, Guizhou Province, 550000, China

²Xiangshui County People's Hospital, Jiangsu, 224600, China

³Tenth People's Hospital Affiliated to Tongji University, Shanghai, 200092, China

Abstract

Septic shock is a serious surgical complication with a high mortality rate and presents challenges for anesthetic management. This review examines the pathophysiological mechanisms, perioperative risks, and impact of septic shock on the function of multiple organs, as well as the latest advances and strategies in anesthetic management for surgical patients with septic shock. Remimazolam and ketamine are preferred for anesthetic management of these patients in view of their minimal impact on hemodynamics. Regional anesthesia and nerve block techniques may improve the prognosis in high-risk patients. Rational use of vasopressors, advanced hemodynamic monitoring, and restrictive transfusion strategies are also key elements in management. Agents such as fentanyl, which may exacerbate circulatory suppression, should be avoided, and the risks of general anesthesia in specific populations should be carefully considered. This review provides a systematic and practical clinical reference for young anesthesiologists, emphasizing individualized and multidisciplinary management to improve perioperative outcomes in patients with septic shock.

Keywords: septic shock, anesthetic management, sepsis, hemodynamic monitoring, perioperative management

Introduction

Septic shock is a syndrome of circulatory failure and disorders of cell metabolism triggered by entry of pathogenic microorganisms into the bloodstream and is classified as a critical clinical condition. In recent years, the incidence of septic shock in China has been on the rise, with a mortality rate of 30%–50%. Survivors often have a poor prognosis, making this condition a major healthcare challenge [1, 2].

Definition and treatment of septic shock

Definition

Septic shock is the most severe stage of sepsis and is characterized by the onset of severe circulatory, cellular, and metabolic abnormalities in response to infection. The diagnosis requires the following conditions to be met: persistent hypotension despite adequate volume resuscitation; vasopressors are needed to maintain a mean

***Correspondence:**

Ke Zhui; Email: kezhu1314@163.com

arterial pressure ≥ 65 mmHg, and the blood lactate level is >2 mmol/L [3, 4].

Septic shock can lead to multiple organ dysfunction and is associated with a significantly increased risk of mortality. Several studies have reported a 28-day mortality rate as high as 30%–50%, particularly in patients with fungal infections, those who are elderly, those with immunodeficiency, and those who do not receive timely and appropriate antibiotic treatment [3, 5]. Furthermore, septic shock is often accompanied by severe complications, including acute kidney injury, myocardial dysfunction, and liver damage, which significantly prolong the stay in the intensive care unit (ICU) and increase the medical burden [6, 7]. In terms of pathophysiology, septic shock is closely associated with a systemic inflammatory response, damage to endothelial cells, microcirculatory dysfunction, and immune suppression [8, 9]. Zou et al also indicates that septic shock has a poor long-term prognosis, with survivors often having physical, cognitive, and psychological impairments, known as “post-intensive care syndrome” [9].

In summary, septic shock has not only a high mortality rate but also a severe negative impact on organ function and long-term quality of life for patients. Therefore, early identification, active intervention, and multidisciplinary management are essential.

Treatment

The standard treatment for septic shock is essentially supportive and antimicrobial. Early aggressive management, including broad-spectrum antibiotics, source control, fluid resuscitation, vasopressors, and organ support (e.g., ventilation and renal replacement), is the mainstay of care [10, 11]. Although these measures are essential, they do not directly modulate the pathological response in the host, and despite best efforts, the mortality rate remains high [12]. Furthermore, empirical use of broad-spectrum

antibiotics, while often life-saving, contributes to the rise of global antimicrobial resistance [13, 14]. In 2019, antimicrobial resistance was directly responsible for 4.95 million deaths and indirectly caused even more fatalities [14, 15]. Multidrug-resistant pathogens complicate the treatment of sepsis, in that infections caused by resistant microorganisms often require second-line or toxic antibiotics, are harder to eradicate, and are associated with higher mortality rates [14, 16]. In brief, the limitations of current treatments, namely, insufficient control of dysregulated inflammation and the threat of antimicrobial resistance, highlight an urgent need for new approaches to improve the outcomes of sepsis.

Surgical procedures and septic shock

Although septic shock can occur after various types of surgery, the risk is particularly high in certain contexts. Surgical procedures for intra-abdominal infection are a major source of postoperative septic shock and include emergency abdominal surgeries for perforated diverticulitis, perforated appendicitis, and intestinal ischemia. If the source of infection is not controlled in a timely manner, it can easily progress to severe sepsis and septic shock [17]. For complex intra-abdominal infections, the staged approach of damage control surgery has been shown to effectively stabilize the patient’s physiological status, create conditions for subsequent definitive surgery, and improve the prognosis [17, 18]. Patients undergoing cardiac surgery, particularly those with infective endocarditis and those requiring cardiopulmonary bypass, are another group at high risk of septic shock. A systematic review and meta-analysis found that the in-hospital mortality rate in patients with infective endocarditis complicated by shock was 62.3% and that the mortality risk was nearly six times higher than that in patients without septic shock (odds ratio, 5.83) [19]. Extracorporeal circulation itself can trigger systemic inflammatory response syndrome, exacerbating vasodilation and organ

damage ^[19]. Orthopedic and trauma surgeries, especially after open fractures, may occasionally lead to fulminant infections, such as necrotizing fasciitis, which can rapidly result in septic shock. There has been a case report of a patient with a Gustilo–Anderson type I open fracture of the distal radius who developed *Aeromonas hydrophila* infection after application of a cast, which subsequently caused necrotizing fasciitis, arterial embolism, and septic shock, ultimately requiring life-saving amputation ^[20]. Furthermore, postoperative surgical site infections after major surgeries are also important factors in inducing septic shock, such as cystectomy and other major urological surgeries ^[21] and various types of gynecological surgery ^[22].

The impact of septic shock in surgical patients is multifaceted and often has catastrophic consequences. Its mortality rate is extremely high. In addition to infective endocarditis, which was mentioned earlier, there have been reports of pediatric deaths as a result of ingestion of magnets, causing intestinal perforation and septic shock ^[23]. The fundamental cause lies in the refractory nature of shock and the subsequent multi-organ failure. Septic shock is also a common cause of postoperative multiple organ dysfunction. For example, in preterm infants with necrotizing enterocolitis, postoperative septic shock-like states are the leading cause of acute kidney injury, and severe acute renal injury is a strong predictor of a poor prognosis ^[24]. Moreover, shock can trigger acute respiratory distress syndrome (ARDS), liver dysfunction, myocardial suppression, and neurological complications, creating an irreversible vicious cycle ^[19].

Patients with septic shock have a significantly increased risk of postoperative complications, including anastomotic leak, wound infection, and deep (e.g., mediastinal) abscess ^[25], as well as pleural empyema ^[26], as a consequence of inadequate tissue perfusion and immune system dysregulation. These patients often require further surgical intervention, which adds to their trauma burden.

From a healthcare resource perspective, patients with septic shock typically require prolonged intensive care and longer hospitalization overall, which increases the burden on the medical system.

Anesthetic management in patients with septic shock

Septic shock is one of the leading causes of mortality in the ICU, and its management is a complex challenge involving early recognition, antibiotic therapy, source control, and organ function support. When patients with septic shock require surgical intervention (such as source control) or invasive procedures, the role of the anesthesiologist becomes critical. Anesthetic management not only involves stabilizing vital signs during surgery but also directly influences the pathophysiology of septic shock and long-term prognosis for the patient.

Core role and challenges

The core goal of anesthetic management in patients with septic shock is to provide suitable conditions for surgery while maintaining tissue perfusion and oxygenation and avoiding exacerbation of pre-existing organ dysfunction. These patients often present with pathological features that include reduced systemic vascular resistance, vasodilation, capillary leakage, and myocardial suppression, which together lead to highly unstable hemodynamics.

In this context, the depressive effects of anesthetic agents on the cardiovascular system may further reduce systemic vascular resistance and myocardial contractility, thereby increasing the severity of shock. Therefore, effective management of hemodynamics during induction and maintenance of anesthesia becomes the primary challenge in clinical practice. By contrast, maintaining organ perfusion is the fundamental task in management of septic shock. Considering that the nature of the dis-

ease involves insufficient tissue perfusion, anesthetic management must focus on avoiding hypotension and maintaining adequate mean arterial pressure to ensure an adequate blood supply to vital organs, including the heart, brain, and kidneys.

Anesthetic management strategies proven or suggested to have a positive impact in patients with septic shock

Prudent Selection of Anesthetic Agents

Remimazolam is a novel benzodiazepine derivative with advantages for induction and maintenance of general anesthesia in patients with septic shock. Its characteristics include rapid onset and recovery, mild suppressive effects on the respiratory system, and relatively stable hemodynamic effects. One study found that remimazolam maintained relatively stable hemodynamics regardless of whether it was administered in a low, medium, or high dose, with less requirement for rescue anesthesia in the medium-dose and high-dose groups than in the low-dose group [27]. Furthermore, postoperative recovery of liver and kidney function was better in the medium-dose and high-dose groups than in the low-dose group, with a trend of dose-dependent improvement. There has also been a case report in which use of remimazolam helped to maintain intraoperative hemodynamic stability in a patient with septic shock attributable to necrotizing fasciitis who was receiving high vasopressor doses [28].

Notably, the hemodynamic properties of ketamine are more favorable than those of fentanyl in patients with septic shock. A randomized controlled trial found that patients who received a bolus of ketamine 1 mg/kg had significant increases in cardiac output, stroke volume, heart rate, and mean arterial pressure whereas those who received a bolus of fentanyl 1 µg/kg showed decreases in these parameters [29]. This finding suggests that ketamine can be a good choice for maintaining cardiac output and

blood pressure during sedation or induction of anesthesia in patients with septic shock

Regional Anesthesia and Nerve Block Techniques

Regional anesthesia has advantages in certain types of surgery. A large retrospective study found that in patients with congestive heart failure undergoing lower limb amputation, 30-day mortality, pneumonia, septic shock, postoperative transfusion, and readmission rates were significantly lower in those who received regional anesthesia than in those who received general anesthesia [30]. These results suggest that avoiding general anesthesia may help to improve clinical outcomes in high-risk populations.

In terms of nerve block techniques, stellate ganglion blockade has multiple positive effects in elderly patients with septic shock. One study in such patients showed that preoperative stellate ganglion blockade could alleviate the systemic inflammatory response (evidenced by reduced procalcitonin and C-reactive protein levels), improve perioperative mechanical ventilation parameters and postoperative recovery of respiratory function, and stabilize mean arterial pressure [31]. These findings suggest that nerve blockade may have beneficial effects on the pathophysiology of septic shock by modulating neuroimmune pathways.

The erector spinae plane block has also demonstrated value in clinical practice. In a case of pediatric empyema that required surgery, combined use of ultrasound-guided erector spinae plane block and general anesthesia reduced intraoperative opioid use, improved postoperative respiration, and avoided use of agents that might lower the seizure threshold, achieving multimodal analgesia and promoting more rapid recovery [32].

Rational Use and Exploration of Vasopressor Agents

Existing expert consensus provides important guidance for the rational use of vasopressors in clinical practice.

The consensus document from the Italian Society of Anesthesia, Analgesia, Resuscitation, and Intensive Care states that after exclusion of hypovolemia, vasopressor agents should be considered for treatment of persistent tachycardia, with a preference for intravenous administration, in patients with septic shock [33]. Another expert consensus on the use of vasopressors and positive inotropic agents provides evidence-based guidance for clinicians when selecting medications for septic shock and cardiogenic shock [34].

In terms of exploration of new agents, glibenclamide (a KATP channel blocker) has shown promise in the treatment of refractory vasodilation. Glibenclamide was observed to have potent pressor effects in a porcine model of vasoplegia after cardiopulmonary bypass [35]. It increased systemic vascular resistance and blood pressure, thereby reducing the need for norepinephrine and successfully reversing the vasoplegia syndrome. These observations provide a potential new direction for treating refractory vasodilation in patients with septic shock. Furthermore, in a rodent model of septic shock associated with acute kidney injury, angiotensin II was superior to norepinephrine in terms of improving renal function parameters, renal blood flow, inflammation, and oxidative stress markers. This protective mechanism may be related to activation of the AMPK/PGC-1 α /NRF-2 pathway, which results in better functioning of the renal mitochondria [36].

Circulatory Monitoring and Fluid Management

When monitoring circulatory function, advanced techniques such as pulmonary thermal dilution can assess and quantify extravascular lung water and the pulmonary vascular permeability index, providing an objective basis for diagnosing the severity of ARDS, which is a common complication of septic shock. Research has shown that the pulmonary vascular permeability index is an effective indicator of the severity of infection-related ARDS, with a critical value of 3.9 having high sensitivity and speci-

ficity for prediction of severe ARDS [37].

In circulatory support management, refined fluid management serves as the cornerstone of septic shock treatment. Although current guidelines emphasize initial adequate resuscitation to correct tissue hypoperfusion, strategies for subsequent fluid management remain controversial. The CLOVERS trial, led by the National Heart, Lung, and Blood Institute, provided an in-depth investigation into this issue by comparing restrictive fluid strategies (prioritizing vasopressor use) versus liberal fluid strategies in septic patients with hypotension during the early resuscitation phase. The results demonstrated that, compared to liberal fluid management, the restrictive strategy significantly reduced the 24-hour fluid infusion volume (difference of medians, -2134 ml) and led to earlier and more frequent use of vasopressors. However, no significant difference was observed in 90-day mortality between the two groups [38]. These findings suggest that, in the pursuit of resuscitation goals, the key lies in individualizing the balance between positive and negative fluid balance based on the patient's specific condition, rather than simply adopting extreme restrictive or liberal strategies. Additionally, as an important component of fluid management, restrictive red blood cell transfusion strategies have been widely implemented in the perioperative period, particularly in pediatric patients. A survey involving pediatric patients in Nordic countries revealed that anesthesiologists generally adhere to restrictive transfusion principles, aligning with the recommendations of the international TAXI consensus. The survey further indicated that transfusion thresholds are only appropriately elevated in specific high-risk scenarios, such as severe sepsis or septic shock [39]. The implementation of this strategy aims to ensure tissue oxygen supply while effectively reducing the risk of transfusion-related complications.

Other Supportive Measures

Low-dose corticosteroids have been demonstrated to have supportive effects on hemodynamics [40]. A retrospective study in patients undergoing surgery for abdominal sepsis showed that intraoperative use of low-dose corticosteroids achieved transient hemodynamic improvement in patients with septic shock, including increased urine output on the first postoperative day and less need for vasopressors, but did not improve overall hospital mortality or shorten the ICU stay [41]. Therefore, the role of these agents in the management of septic shock may be adjunctive only.

Midodrine, an α_1 receptor agonist, is often used to prevent hypotension after spinal anesthesia and has also been used in the treatment of hypotension during the recovery phase of septic shock [42], suggesting its potential value in specific clinical scenarios.

Optimizing use of antibiotics and therapeutic drug monitoring are essential. Research has shown that excessive serum β -lactam levels are independently associated with neurological deterioration, a prolonged hospital stay, and delayed extubation, highlighting the importance of therapeutic drug monitoring in critically ill patients to ensure efficacy while avoiding drug-related toxicity [43].

Warnings and precautions in anesthetic management

Hemodynamic Suppression by Certain Opioids

In patients with septic shock and hemodynamic instability, opioids such as fentanyl should be used with caution in view of their significant depressant effects on the cardiovascular system. The available evidence indicates that a bolus injection of fentanyl can reduce cardiac output, stroke volume, and mean arterial pressure to a significantly greater extent than ketamine [30]. Therefore, in clinical practice, consideration should be given to using lower single doses of such agents or combining them

with medications that have less impact on the circulation to reduce the risk of worsening the shock state.

Potential Risks of General Anesthesia and Regional Anesthesia

The choice of anesthesia method is particularly important in high-risk patients. Research has demonstrated that the risk of complications, including the incidence of septic shock, is greater with general anesthesia than with regional anesthesia in certain high-risk patients (such as those with congestive heart failure) [31]. This means that the choice of anesthesia itself is an important decision point. In the absence of contraindications and when technically feasible, prioritizing regional anesthesia may afford a more favorable prognosis for patients with septic shock.

Depth of anesthesia and monitoring of neurological function

Evaluation of depth of anesthesia and neurological function presents unique challenges in patients with septic shock. There has been a report of postoperative delirium in an elderly patient with septic shock who was found to have an abnormally low preoperative bispectral index value of 30 and an electroencephalogram showing persistent slow waves [44]. This case suggests that severe infection itself can lead to sepsis-associated encephalopathy, and anesthetic agents may further exacerbate or mask the true state of brain function. Therefore, relying solely on monitoring of the bispectral index may not accurately reflect the neurological status of such patients. Continuous electroencephalographic monitoring may help with earlier identification of sepsis-associated encephalopathy, but depth of anesthesia must still be carefully managed to avoid worsening suppression of brain function.

Patient Factors and Increased Anesthetic Risk

Patient-specific factors influence the anesthetic risk in pa-

tients with septic shock. Several studies have confirmed that advanced age, a high American Society of Anesthesiologists (ASA) classification, and emergency surgery are significant risk factors for postoperative complications and mortality, which are particularly prominent in patients with septic shock. For example, the risk of death following ambulatory surgery is much higher in patients with an ASA IV classification than in their healthy counterparts ^[45]. Another study found that emergency surgery and poor ASA status were associated with a higher risk of perioperative cardiac arrest, with septic shock and hemorrhagic shock being significant causes of cardiac arrest ^[46]. Therefore, anesthesiologists must have a full understanding of these high-risk factors and manage them carefully during the perioperative period.

Overall, anesthetic management plays a key role in the treatment of septic shock. Effective management includes the following: selection of anesthetic agents with minimal hemodynamic impact, such as remimazolam and ketamine; application of regional anesthesia or nerve block techniques when appropriate to reduce surgical stress and systemic effects; use of vasopressors based on consensus and evidence with exploration of new therapies, such as glibenclamide and angiotensin II; use of advanced hemodynamic monitoring to guide fluid and vasopressor management; and implementation of restrictive transfusion strategies and therapeutic drug monitoring for antibiotics. Lack of consideration of the patient's specific status, blind use of opioids such as fentanyl, which have depressive effects on the circulation, preference for general anesthesia over regional anesthesia when feasible, and overlooking older age, a high ASA classification, and emergency surgery as risk factors can worsen the patient's condition and increase the risk of complications and mortality.

In conclusion, anesthetic management in patients with septic shock is a highly individualized and dynamic

process that requires anesthesiologists to have a detailed understanding of the pathophysiological mechanisms of shock, to be proficient in the use of various anesthetic techniques and medications, and to work closely with surgical and intensive care teams to improve the clinical outcomes for patients.

Summary and outlook

Anesthetic management plays a multidimensional role in the treatment of septic shock. It starts with rapid preoperative assessment and resuscitation, continues through precise intraoperative hemodynamic management and rational use of medication guided by point-of-care ultrasound, and extends to continuous monitoring postoperatively and coordination of treatment. The anesthesiologist is not only the navigator of surgery but also the coordinator and decision-maker regarding perioperative life support for patients with septic shock.

Treatment of septic shock prioritizes early recognition, timely source control, precise anti-infection therapy, and individualized hemodynamic support. In terms of vasopressors, non-adrenergic vasopressors (e.g., vasopressin and angiotensin II) and adjunctive medications (e.g., methylene blue) in addition to traditional catecholamines (such as norepinephrine) have shown potential in treating refractory shock, not only helping to improve hemodynamic status but also offering new hope for reduction of patient mortality ^[47-49].

Nevertheless, clinical practice still faces many challenges, with the most prominent being the lack of a unified biomarker system and no clear definition of vasoplegia. These challenges have resulted in significant inconsistencies between studies and hindered comparative analysis and establishment of standardized treatment protocols ^[50]. Future research should focus on advancing the standardization process for relevant definitions, strength-

ening clinical validation of biomarkers, and conducting in-depth explorations of individualized treatment strategies according to phenotype, thereby improving clinical outcomes for surgical patients with septic shock.

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Author Contributions

Feng Guangling was responsible for writing the manuscript; Ji Peng, Yao Song, Wang Jinyu, and Gao Jie were responsible for collection of data and analysis of literature; Guo Xianling was responsible for the design and guidance of the manuscript; Ke Zhui was responsible for revising and proofreading the manuscript.

Conflicts of Interest

All authors declare no conflicts of interest.

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