

Nutritional support in sepsis and septic shock: current evidence and future directions

Prama Bose

Therapeutic Nutrition, KPC Medical College and Hospital, West Bengal, India

Abstract

Nutritional support plays a critical role in the management of sepsis and septic shock, significantly influencing patient outcomes through modulation of immune function, organ recovery, and metabolic balance. Sepsis induces a hypermetabolic and catabolic state, increasing energy and protein requirements, which necessitates timely and appropriate nutritional intervention to preserve lean body mass and optimize immune response. Early enteral nutrition (EEN), ideally initiated within 24–48 hours of diagnosis, is recommended when feasible, as it maintains gut integrity, reduces bacterial translocation, and may lower infection rates and ICU length of stay. In patients with hemodynamic instability or on high-dose vasopressors, cautious initiation of EEN—such as trophic feeding or delayed feeding—is advised due to the risk of intestinal ischemia. Parenteral nutrition (PN) is indicated when EN is contraindicated or insufficient, although early PN may increase infection risk and metabolic complications, requiring strict aseptic technique and close monitoring. Permissive underfeeding is recommended during the acute phase to prevent overfeeding-related complications, with gradual escalation to full caloric requirements as patients stabilize. Protein intake should be individualized, targeting 1.2–2.0 g/kg/day for patients with significant catabolism, while micronutrient supplementation, such as magnesium and vitamin C, may offer adjunctive benefits. Advances in personalized nutrition, including predictive modeling and artificial intelligence, hold promise for tailoring energy and nutrient delivery to dynamic patient-specific needs, optimizing outcomes while minimizing complications. Overall, enteral nutrition remains the preferred route in sepsis and septic shock, with parenteral nutrition reserved for select scenarios, and individualized, evidence-based nutritional strategies are essential to improve clinical outcomes in this critically ill population.

Keywords: Therapeutic nutrition, diet, health, foods, sepsis

Introduction

Nutritional support in sepsis and septic shock is a critical component of intensive care, influencing patient outcomes through its effects on immune function, organ recovery, and metabolic balance (De Waele & Wischmeyer, 2020^[1]; Singer *et al.*, 2019)^[4]. Sepsis induces a hypermetabolic state characterized by increased energy expenditure and protein catabolism, necessitating timely and appropriate nutritional intervention to mitigate muscle wasting and support immune response (Reignier & Azoulay, 2025)^[3]. Early enteral nutrition (EEN), initiated within 24–48 hours of diagnosis, is recommended when feasible, as it preserves gut integrity, reduces bacterial translocation, and may decrease infection rates and ICU length of stay (Grillo-Ardila *et al.*, 2024^[2]; Xu *et al.*, 2024)^[8]. However, in patients with hemodynamic instability or requiring high-dose vasopressors, the initiation of EEN should be cautious, considering the risk of intestinal ischemia (Wang *et al.*, 2024)^[6]. In such cases, starting with trophic feeding or delaying EN until stabilization may be prudent (De Waele & Wischmeyer, 2020)^[1].

Parenteral nutrition (PN) is generally reserved for situations where EN is contraindicated or insufficient to meet nutritional needs, as early PN has been associated with increased infection rates and adverse outcomes (Wasyluk & Kwiatkowska, 2019)^[7]. When PN is necessary, it should be administered with strict aseptic techniques and close monitoring to minimize complications (Singer *et al.*, 2019)^[4]. Regarding energy delivery, permissive underfeeding is advised in the early acute phase to avoid overfeeding, which can exacerbate hyperglycemia and respiratory failure (Grillo-Ardila *et al.*, 2024)^[2]. In the later stages, as the patient stabilizes, gradual escalation to meet full caloric requirements is appropriate, aiming to achieve energy

balance and support recovery (Reignier & Azoulay, 2025)^[3]. Protein intake should be tailored to the patient's condition, with higher targets (1.2–2.0 g/kg/day) for those with significant catabolism or muscle wasting (De Waele & Wischmeyer, 2020)^[1]. Micronutrient supplementation, including magnesium and vitamin C, may offer benefits in sepsis patients, but high-dose supplementation is not recommended due to potential adverse effects (Xu *et al.*, 2024)^[8].

Future research should focus on large-scale, multicenter randomized controlled trials to refine nutritional strategies, determine optimal timing and routes of feeding, and explore the role of personalized nutrition approaches in sepsis management (Tan *et al.*, 2025)^[5]. Additionally, the development of predictive models using artificial intelligence could aid in individualizing nutritional support based on patient-specific factors and dynamic clinical conditions (Wang *et al.*, 2024)^[6]. In summary, while enteral nutrition remains the preferred approach in sepsis and septic shock, careful consideration of patient status, hemodynamic stability, and individualized nutritional needs is essential to optimize outcomes and minimize complications (Singer *et al.*, 2019;^[4] De Waele & Wischmeyer, 2020)^[1].

Enteral Nutrition in Sepsis

Enteral nutrition is preferred over parenteral nutrition in most critically ill patients due to its benefits in maintaining gut integrity and function (Grillo-Ardila *et al.*, 2024)^[2]. Early enteral nutrition (within 24–48 hours) has been associated with reduced infection rates and shorter intensive care unit (ICU) stays (Xu *et al.*, 2024)^[8]. However, its initiation in patients with septic shock, particularly those on high-dose vasopressors, remains controversial (Wang *et al.*,

2024) [6]. Some studies suggest that early enteral nutrition may be safe and feasible in patients with shock receiving vasopressors, while others advise caution due to the risk of intestinal ischemia and feeding intolerance (De Waele & Wischmeyer, 2020) [1].

Parenteral Nutrition in Sepsis

Parenteral nutrition is indicated when enteral feeding is not feasible or sufficient to meet nutritional requirements (Wasyluk & Kwiatkowska, 2019) [7]. It provides complete nutrient delivery intravenously, bypassing the gastrointestinal tract. However, PN is associated with complications such as catheter-related bloodstream infections, metabolic derangements, and liver dysfunction (Singer *et al.*, 2019) [4]. Therefore, its use should be reserved

for situations where enteral nutrition is not possible or inadequate, and it should be administered with careful monitoring and infection control measures (Reignier & Azoulay, 2025) [3].

Personalized Nutrition Strategies

Advancements in technology have paved the way for personalized nutrition approaches in sepsis management (Tan *et al.*, 2025). Predictive models and artificial intelligence are being explored to tailor nutritional support based on individual patient characteristics and dynamic physiological changes. These personalized strategies aim to optimize energy delivery, prevent overfeeding or underfeeding, and improve clinical outcomes (Wang *et al.*, 2024) [6].

Table 1: Nutritional Support in Sepsis and Septic Shock: Current Evidence, Recommendations, and Considerations

Aspect	Recommendations / Evidence	Key Considerations	References
Early Enteral Nutrition (EEN)	Initiate within 24–48 hours if hemodynamically stable; preserves gut integrity, reduces bacterial translocation, may decrease infection rates and ICU stay.	Caution in patients on high-dose vasopressors; consider trophic feeding or delayed initiation to prevent intestinal ischemia.	De Waele & Wischmeyer, 2020 [1]; Grillo-Ardila <i>et al.</i> , 2024 [2]; Xu <i>et al.</i> , 2024 [8]; Wang <i>et al.</i> , 2024 [6]
Parenteral Nutrition (PN)	Reserved for patients where EN is contraindicated or insufficient; provides complete nutrient delivery intravenously.	Associated with catheter-related infections, metabolic derangements, liver dysfunction; requires strict aseptic technique and close monitoring.	Singer <i>et al.</i> , 2019 [4]; Wasyluk & Kwiatkowska, 2019 [7]; Reignier & Azoulay, 2025
Energy Provision	Permissive underfeeding in acute phase to avoid overfeeding; gradual escalation to full caloric requirements as patient stabilizes.	Overfeeding can worsen hyperglycemia and respiratory failure.	Grillo-Ardila <i>et al.</i> , 2024 [2]; Reignier & Azoulay, 2025
Protein Targets	1.2–2.0 g/kg/day for patients with high catabolism or muscle wasting.	Adjust based on individual metabolic needs and severity of illness.	De Waele & Wischmeyer, 2020
Micronutrients	Supplement magnesium, vitamin C, and other essential nutrients.	High-dose supplementation not recommended due to potential adverse effects.	Xu <i>et al.</i> , 2024 [8]
Hemodynamic Considerations	Monitor vasopressor support and intestinal perfusion before initiating EN.	High-dose vasopressors increase risk of feeding intolerance and gut ischemia.	Wang <i>et al.</i> , 2024 [1, 6]; De Waele & Wischmeyer, 2020
Personalized Nutrition	Use predictive models and AI to individualize energy/protein delivery.	Aims to optimize nutrition, prevent underfeeding or overfeeding, and improve outcomes.	Tan <i>et al.</i> , 2025 [5]; Wang <i>et al.</i> , 2024 [6]

Conclusion

Nutritional support is a cornerstone in the management of sepsis and septic shock. While enteral nutrition is generally preferred due to its benefits in maintaining gut function and reducing infection rates, parenteral nutrition remains a vital option when enteral feeding is not feasible. Future research should focus on personalized nutrition strategies, utilizing advanced technologies to tailor interventions to individual patient needs, thereby improving outcomes in sepsis management.

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