

Shock Patients and Enteral Nutrition?

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Abstract: Shock is a life-threatening condition characterized by microcirculatory disturbances and inadequate tissue perfusion. In hemodynamically unstable individuals, arterial pressure is maintained with vasoactive agents. Enteral nutrition (EN) is crucial for the intensive treatment of critically ill patients, facilitating intestinal recovery and improving clinical outcomes such as reducing infections, shortening hospital stays, and lowering costs. The impact of vasoactive agents on gastrointestinal blood flow varies, depending on the drug, dose, body size, and individual sensitivity. EN is categorized into early and delayed, and multiple guidelines recommend delayed EN due to the risks in the early stage, which may lead to EFI, non-obstructive mesenteric ischemia and necrosis. Guidelines for early EN in shock patients are still evolving, exploring the optimal timing and safety thresholds. Studies have shown that early EN can be safely implemented in hemodynamically stable patients maintaining a mean arterial pressure of 70 mmHg with stable doses of antihypertensives. This review summarizes the optimal and safe timing of initiating EN in shock patients to guide clinical practice. The pathophysiology of shock, EN selection, considerations, nutritional regimens, effects of antihypertensive agents, and feeding regimens are further discussed.

Keywords: Enteral Nutrition; Feeding Intolerance; Risk Factor.

1. Foreword

Shock is a life-threatening condition characterized by microcirculatory disturbances and inadequate tissue perfusion. In hemodynamically unstable patients, vasoactive drugs are used to maintain target arterial pressure. Enteral nutrition (EN) plays a crucial role in the intensive therapy of critically ill patients, offering benefits for intestinal recovery. Studies show that EN improves clinical outcomes, including fewer infectious complications, shorter hospital stays, and lower costs [1-3]. Vasoactive drugs affect gastrointestinal blood flow differently based on the drug type, dosage rate, body type, and individual sensitivity. EN can be categorized into early EN and delayed EN; most guidelines recommend delayed EN due to risks associated with early support. Early EN may lead to severe complications such as enteral nutrition intolerance (EFI), non-occlusive mesenteric ischemia, and non-occlusive intestinal necrosis [5]. Guidelines for the clinical use of early enteral nutrition (EN) in shock patients are still evolving, with ongoing exploration of optimal timing and safety thresholds. Studies suggest that haemodynamically stable patients maintaining a mean arterial pressure of 70 mmHg can safely continue early EN while on stable doses of antihypertensive agents [53]. This review aims to summarize evidence on the optimal and safe timing for initiating early EN in shock patients receiving vasoactive medications to enhance clinical practice.

2. Early or Delayed

Shock is a common critical illness in the intensive care unit (ICU), leading to circulatory disturbances and inadequate cellular oxygen utilization, which triggers significant pathophysiological changes. In the intestinal tract, shock can cause increased necrosis of intestinal cells and impaired barrier function. Reperfusion injury and vasoactive drug administration may worsen these conditions [1-3]. Gastrointestinal dysmotility frequently occurs in patients

experiencing shock [4]. Critically ill patients often endure continuous stress and hypermetabolic states, resulting in energy deficiencies. High doses of vasopressors further elevate their metabolic demands while contributing to gastrointestinal dysmotility [4-7]. Some studies recommend initiating enteral nutrition (EN) within 24-48 hours post-admission. Early EN not only replenishes energy but also enhances visceral blood flow, maintains intestinal cell barrier integrity, and stimulates immune responses [2]. However, caution is necessary when administering EN to shocked patients. The hemodynamic changes induced by early EN—especially with vasoactive agents—can reduce blood flow and create an imbalance between gastrointestinal oxygen delivery and consumption, increasing risks of mesenteric ischemia (MI) and necrosis [7]. Consequently, guidelines recommend postponing enteral nutrition (EN) in patients experiencing shock until full resuscitation and hemodynamic targets are achieved [8-10]. However, there is growing evidence supporting the safe use of EN in shock patients requiring pressor agents [11-16]. The benefits of early EN for those on multiple pressor medications are becoming increasingly clear [17].

3. Early Enteral Nutrition

Multiple factors must be considered in patients seeking early enteral nutrition (EN). The use of catecholamines during EN is a known risk factor for feeding intolerance [43]. Other contributing factors include sedatives, analgesics, hyperglycemia, elevated intra-abdominal pressure, and increased serum lactate levels [43-47]. Non-occlusive mesenteric ischemia (NOMI) and non-occlusive bowel necrosis (NOBN) are rare but life-threatening complications with a mortality rate of 50% to 85% in shocked patients on vasopressors when EN is initiated [48]. Early recognition and diagnosis of NOMI are essential. High suspicion for NOMI/NOBN should arise with sudden abdominal pain, distension, peritonitis, muscle guarding, gastrointestinal

bleeding, multi-organ dysfunction or failure, along with imaging findings like enlarged thickened bowel loops with thumbprint signs, air within the bowel wall, portal venous gas, or free air in the abdominal cavity [52,37]. In the NUTRIVAD study, patients on vasoactive medications reached target feeds within three days after starting EN; results showed that limited early EN was safe and not linked to serious complications [50]. The NUTRIREA-2 and NUTRIREA3 studies showed that in shock-ventilated patients receiving high doses of norepinephrine (up to 0.5 mg/kg/min), early complete enteral nutrition (EN) increased the risk of adverse gastrointestinal outcomes [35,38]. It is recommended to maintain norepinephrine or equivalent doses below 0.3 mg/kg/min. Merchan et al. [11] found that 62% of 120 septic shock patients tolerated early EN with a norepinephrine dose under 0.14 mg/kg/min. Ortiz-Reyes et al., in a multicenter trial, reported that early EN improved prognosis for mechanically ventilated patients with circulatory shock at norepinephrine doses up to 0.3 mg/kg/min [19]. Additionally, it is crucial to consider the effects of vasopressor dose variability on intestinal injury. The NUTRIVAD study indicated that even when shocked patients received high vasopressin doses (>0.5 mg/kg/min) within the first 48 hours post-admission to ICU, EN remained feasible and safe if dosages were reduced in subsequent days [40]. These findings suggest further investigation is needed regarding the use of early EN in shocked patients on high-dose vasoactive agents while evaluating its feasibility with low-dose drugs.

4. Selection of Nutrition Programmes

A pronounced metabolic and immune response is often seen in critically ill patients. Delayed nutritional support can lead to negative energy balance, impairing the body's ability to meet increased metabolic demands. Clinical studies link enteral fasting and delayed enteral nutrition to gastrointestinal barrier dysfunction [20-22]. Within the first 48 hours, patients needing higher norepinephrine doses and showing elevated blood lactate levels typically experience poorer microcirculation. These individuals struggle with enteral feeding, resulting in reduced energy and protein intake while increasing reliance on parenteral nutrition. This exacerbates intestinal barrier integrity issues and functional complications, alongside more severe clinical symptoms reflected by higher SOFA scores. Blood lactate levels, norepinephrine dosage, and SOFA scores are significant predictors of energy and protein delivery via enteral nutrition (EN) in critically ill patients. The study found that administering EN to those receiving high catecholamine doses was safe; however, the amount of EN used remained limited. Additionally, nutritional enteral feeding was safe for reducing the risk of acute mesenteric ischemia [23, 24]. On the other hand, selecting the appropriate enteral nutrition preparation involves several considerations. 1. Sequential Enteral Nutrition Program: In critically ill patients during early stages, gastrointestinal function may be compromised. Starting with warm boiled water or hypotonic non-nutritional solutions like sugar saline can aid intestinal resuscitation and digestion, reducing feeding intolerance [54]. Research shows that a sequential administration regimen for enteral nutrition significantly improves feeding tolerance and helps achieve nutritional goals more quickly than a continuous regimen [49]. 2. Microecological Immune Nutrition: This method enhances standard enteral nutrition formulas by adding ingredients such

as oligomannose and oligogalactose to regulate intestinal disturbances and boost immune function. These components promote beneficial gut bacteria growth, strengthen intestinal barriers, activate the intestinal immune system, and modulate systemic responses. Studies indicate that integrating specialized immunonutritional preparations into conventional regimens can enhance overall immune function while improving feeding tolerance in sepsis patients. Thus, microecological immunonutritional preparations provide safe and effective support for the nutritional needs of these patients [5]. 3. Studies show that modified enteral nutrition (EN) regimens, especially those with fat formulations supplemented by carnitine and taurine, improve feeding tolerance in critically ill patients and help them reach nutritional goals earlier. Therefore, when implementing EN, it is crucial to consider not only blood lactate levels, norepinephrine dosage, and SOFA scores but also the specific nutritional regimen for individualized care.

5. Effects of Antihypertensive Drugs

The effects of vasoactive drugs on the gastrointestinal tract are complex, with varying impacts on blood flow based on the drug and dosage. Norepinephrine has a modest effect on gastrointestinal perfusion [25]. Animal studies show that norepinephrine infusion significantly reduces blood flow in the superior mesenteric artery and microcirculation in the jejunal mucosa and pancreas. However, at low doses, it may enhance gastric mucosal perfusion [26]. In contrast, epinephrine's impact is more intricate. Some research indicates it compromises gastrointestinal perfusion during septic shock, while other studies suggest it may improve mucosal perfusion due to increased cardiac output. Notably, its negative effect appears dose-dependent; higher doses can reduce microcirculation perfusion [28,29,31]. Dopamine also shows a dose-response relationship regarding its influence on gastrointestinal perfusion [32,33]. Low doses of dopamine enhance gastrointestinal microcirculatory perfusion, while high doses reduce it. Dobutamine improves gastrointestinal mucosal perfusion in septic shock patients [33-34]. In contrast, norepinephrine—alone or with dobutamine—worsens mesenteric ischemia (MI) [28,34,36]. Early enteral nutrition (EN) can enhance gastrointestinal microcirculatory perfusion [41], but starting EN during complete mesenteric artery occlusion may worsen MI and hypoxia [42]. Therefore, clinicians must consider the complex effects of vasopressors—used alone or in combination—when initiating EN in shock patients.

6. Choice of Feeding Programme

When starting enteral nutrition therapy, a thorough assessment of the patient's health and disease characteristics is essential, including whether they are on vasoactive medications. Enteral nutrition is indicated for patients at risk of malnutrition with normal gastrointestinal function, such as those who are unconscious or have dysphagia, in a hypermetabolic state, or whose gastrointestinal condition is stable. However, it is crucial to ensure that the patient's pathophysiological condition has stabilized before initiating enteral nutrition. If symptoms like hypoxaemia, severe acidosis, or active gastrointestinal bleeding are present, initiation should be delayed. Enteral nutrition is contraindicated in cases of severe gastrointestinal bleeding, intestinal obstruction, or ischemia. In clinical practice, both

the dosage and formula of enteral nutrition should be adjusted gradually based on individual patient needs. Initially low energy density fluid formulas may be used before transitioning to total nutritional products. Close monitoring of patient tolerance is imperative to prevent adverse effects like diarrhea. In critically ill patients, enteral nutrition should begin as soon as hemodynamics stabilize. However, this should occur in small doses with strict monitoring of patient tolerance. Research shows that low-calorie enteral nutrition (EN) can reduce insulin requirements and the risk of enteral intolerance while lowering diarrhea incidence and gastric retention. Several studies and guidelines recommend early initiation of EN in patients with septic shock once hemodynamic stability is achieved. For example, the ESPEN Guidelines for Nutrition in the Critically Ill Patient (2023 edition) suggest that infected patients should start EN progressively after stabilizing hemodynamics, noting its role in reducing morbidity and mortality while extending non-mechanical ventilation duration. Additionally, both the American Society of Critical Care Medicine (SCCM) and the European Society of Intensive Care Medicine (ESICM) stress that EN should be prescribed as soon as possible post-hemodynamic stabilization or successful resuscitation. In summary, for patients experiencing septic shock, initiating EN promptly after hemodynamic stabilization is crucial. The initial dosage should be carefully controlled at a lower level (e.g., 20%-50% of full nutritional needs) and gradually increased based on tolerance. Clinicians must also closely monitor gastrointestinal responses and hemodynamic status to minimize potential complications from EN administration.

There is some disagreement in current research and guidelines regarding enteral nutrition (EN) support in patients with septic shock, but in general it is considered safer and beneficial to initiate EN as early as possible after haemodynamic stabilisation.

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