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Should Enteral Feeding be Started During Circulatory Shock?

Circulatory shock is one of the most common reasons for intensive care unit (ICU) admission. Clinically, it manifests with low blood pressure and despite resuscitation, vasopressor support is required, and its use may extend beyond the window of current recommendation to start enteral nutrition (EN) within 24-48 hours in critically ill patients. Should a patient in circulatory shock receive EN? To answer this question, we must consider the rationale, safety, and benefits of EN in critically ill patients.

What is the Rationale to Begin Early Enteral Nutrition in Critical Illness?

Circulatory shock reduces systemic blood flow and oxygen delivery. Splanchnic blood flow is reduced, increasing gut oxidative stress and reducing gut pH, which impair gut functions. Enterocytes undergo accelerated apoptosis and mucosal integrity is compromised, weakening gut barrier function. Toxic mediators penetrate across the lumen into systemic circulation through lymphatic channels and promote downstream organ dysfunction. Furthermore, commensal bacteria assume a virulent state and promote inflammation across the breached gut barrier. EN in this early acute phase of critical illness has been shown to preserve gut functions through multiple mechanisms, discussed below.

Is Enteral Nutrition During Circulatory Shock Safe?

Non-occlusive bowel necrosis (NOBN) and non-occlusive mesenteric ischemia (NOMI) are the gravest consequences of introducing luminal nutrients into a hypoperfused gut, with mortality from these conditions exceeding 80%. Fortunately, NOBN and NOMI are rare.

Eight retrospective studies evaluating outcomes of EN in circulatory shock in mixed medical-surgical or strictly medical ICU patients did not identify NOBN (table 1). Three observational studies of medical ICU patients with septic shock identified no cases of NOBN or NOMI. Surgical ICU patients receiving a vasopressor and nasojejunal feeding had the highest incidence of NOBN, though rare at 0.15-3.4% (table 2). More recently, Ohbe et al published the largest observational studies evaluating EN in shock and found NOMI in 0.2-0.3% [1, 2].

NUTRIREA-2 is the largest randomized controlled trial evaluating EN (compared to PN) in shock. Over 2400 patients, majority with septic shock, were enrolled to either early EN or early PN. There was no difference in the primary outcome of 28-day mortality. Two percent in early EN developed NOMI compared to <1% in early PN (p=0.007). Note, patients randomized to early EN received “full dose” EN and the vasopressor norepinephrine (NE) at a mean dose of 0.56 mcg/kg/min, suggesting higher NE dose coupled with large volume EN increased the risk of NOMI [3].

In a review of contemporary nutrition RCTs with at least one arm providing EN and enrolling patients on vasopressor, NOMI and NOBN was rare, ranging 0.5-2% [4].

Finally, splanchnic steal syndrome, where blood is diverted back to the splanchnic circulation, may be a concern with EN provision in circulatory shock. Clinically, splanchnic steal may increase vasopressor requirement (since systemic blood flow may theoretically be reduced). However, two observational studies found no change in vasopressor requirement when introducing EN in circulatory shock [5, 6].

Is Enteral Nutrition During Circulatory Shock Beneficial?

At the luminal level, EN has been shown to promote mucous production, epithelial cell proliferation, and tight junction protein production – all of which preserve gut barrier function. In NUTRIREA-2, plasma citrulline, a marker of enterocyte mass and function, was higher at 3 days in those receiving EN (compared to PN), suggesting EN is associated with preserving enterocyte mass [7].

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At the vascular level, multiple animal models of shock and prospective human studies have demonstrated EN enhanced cardiac index, hepato-splanchnic blood flow, and splanchnic microcirculatory blood flow [8, 9].

What are the clinical benefits of early EN in circulatory shock? In the Ohbe studies, early EN in hemodynamically unstable mechanically ventilated and extracorporeal membrane oxygenation patients was associated with improved 28-day mortality [1, 2]. In another large (propensity-matched) study of 1174 patients in shock, early EN was associated with improved ICU and hospital mortality [10].

A recent pilot RCT comparing early trophic (20 mL/hour) to 'no EN' in mechanically ventilated patients with septic shock found better tolerance and a signal for improved ICU- and ventilator-free days in those receiving early EN [11].

Key take home points:

[1.] Circulatory shock reduces blood flow, which impairs oxygen delivery. To restore oxygen delivery, hemodynamic resuscitation remains a priority.

[2.] In considering EN during circulatory shock, observational and RCT level data show NOMI and NOBN are rare. Full dose EN, higher or escalating vasopressor dose, and nasojejunal feeding may be risk factors for NOMI and NOBM development.

[3.] Low dose early EN in shock has been associated with preserved splanchnic blood flow without concomitant rise in vasopressor requirement.

[4.] Animal models and observational studies show luminal and vascular benefits of early EN in shock.

[5.] Large observational studies and pilot RCT data suggest clinical benefits with early EN in shock.

[6.] The optimal EN dose in shock is unknown but trophic, or 10-30 mL/hour, has been shown to preserve gut barrier function and well-tolerated.

[7.] It is reasonable to start a trophic rate of an isosmotic or semi-elemental after hemodynamic resuscitation in a patient who remains on vasopressor support while monitoring for complications.

Table 1: Retrospective studies of medical and mixed medical-surgical ICU patients evaluating EN in circulatory shock. EN, enteral nutrition; kg, kilogram; mcg, micrograms; MICU, medical intensive care unit; min, minute; NE, norepinephrine; NOBN, non-occlusive bowel necrosis; NOMI, non-occlusive mesenteric ischemia

AUTHORS	STUDY & POPULATION	NOMI and NOBN RATES	OUTCOMES
Patel et al	Retrospective, MICU patients with septic shock	0/78	Trophic EN tolerated and associated with improved outcomes
Flordelis et al	Retrospective, medical-surgical patients	0/37	EN tolerance noted at NE 0.32 mcg/kg/min
Mancl et al	Retrospective, medical-surgical patients	3/359 had NOMI	EN tolerance with NE and dopamine and less with vasopressin
Khalid et al	Retrospective, medical-surgical patients	NR	Early EN associated mortality benefit
Shankar et al	Retrospective, medical-surgical patients	0/308	EN within 6 hours had trend improved outcome
Reignier et al	Retrospective, medical-surgical patients	NR	Early EN associated mortality benefit
Rai et al	Retrospective, MICU patients with septic shock	0/43	Early EN of 40-70% goal calories tolerated over first three days
Merchan et al	Retrospective, MICU patients with septic shock	0/120	Early EN tolerated at NE doses up to 0.14 mcg/kg/min

Patel JJ, Kozeniecki M, Biesboer A, et al. Early Trophic Enteral Nutrition Is Associated With Improved Outcomes in Mechanically Ventilated Patients With Septic Shock: A Retrospective Review. Journal of intensive care medicine. 2014.;Mancl EE, Muzevich KM. Tolerability and safety of enteral nutrition in critically ill patients receiving intravenous vasopressor therapy. JPENJournal of parenteral and enteral nutrition. 2013;37(5):641-651.;Khalid I, Doshi P, DiGiovine B. Early enteral nutrition and outcomes of critically ill patients treated with vasopressors and mechanical ventilation. American Journal of Critical Care : An Official Publication, American Association of Critical-Care Nurses. 2010;19(3):261-268.;Merchan C, Altshuler D, Aberle C, Papadopoulos J, Schwartz D. Tolerability of Enteral Nutrition in Mechanically Ventilated Patients With Septic Shock Who Require Vasopressors. J Intensive Care Med. 2017;32(9):540-546.;Flordelis Lasierra JL, Perez-Vela JL, Umezawa Makikado LD, et al. Early enteral nutrition in patients with hemodynamic failure following cardiac surgery. JPEN J Parenter Enteral Nutr. 2015;39(2):154-162.;Shankar B, Daphnee DK, Ramakrishnan N, Venkataraman R. Feasibility, safety, and outcome of very early enteral nutrition in critically ill patients: Results of an observational study. J Crit Care. 2015;30(3):473-475.

Table 2: Rate of non-occlusive bowel necrosis in observational studies of surgical critical care patients with circulatory shock who received enteral nutrition. NOBN, non-occlusive bowel necrosis, NJ, nasojejunal

AUTHOR	NOBN (n)	COMMENTS
Myers et al	3/1938	NOBN occurred in those with NJ feed
Schunn et al	4/1359	NOBN occurred in those with NJ feed
Smith-Choban et al	5/143	NOBN occurred in those with NJ feed
Lawlor et al	3/386	NOBN occurred in those with NJ feed
Holmes et al	3/222	NOBN occurred in those with NJ feed
Marvin et al	14/4311	4/13 that developed NOBN were on a vasopressor

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