DOI: 10.1002/jpen.2364

CONSENSUS STATEMENT

When is enteral nutrition indicated?

Matthew L. Bechtold MD[1] | Patricia M. Brown RD[2] | Arlene Escuro MS, RD[3] | Brandee Grenda MBA, RD[4] | Theresa Johnston MSN, RN[5] | Michelle Kozeniecki MS, RD[6] | Berkeley N. Limketkai MD, PhD[7] | Krystie K. Nelson RDN, AP[8] | Jan Powers PhD, RN[9] | Andrea Ronan MS, RD[10] | Nathan Schober MS, RD[11] | Brian J. Strang PharmD[12] | Cristina Swartz MS, RD[13] | Justine Turner MD, PhD[14] | Lauren Tweel MSc, RD[15] | Renee Walker MS, RD[16] | Lisa Epp RD[17] | Ainsley Malone MS, RD[18] | the ASPEN Enteral Nutrition Committee

[1]University of Missouri – Columbia, Columbia, Missouri, USA

[2]The Johns Hopkins Hospital, Baltimore, Maryland, USA

[3]Cleveland Clinic, Cleveland, Ohio, USA

[4]Morrison Healthcare at Atrium Health Navicant, Charlotte, North Carolina, USA

[5]Nutrition Support Team, Christiana Care Health System, Newark, Delaware, USA

[6]Froedtert Hospital, Milwaukee, Wisconsin, USA

[7]David Geffen School of Medicine at UCLA, Los Angeles, California, USA

[8]Sodexo/Billings Clinic, Billings, Montana, USA

[9]Nursing Research and Professional Practice, Parkview Health System, Fort Wayne, Indiana, USA

[10]Fanconi Anemia Research Fund, Eugene, Oregon, USA

[11]Cancer Treatment Centers of America – Atlanta, Newnan, Georgia, USA

[12]Tucson Medical Center, Tucson, Arizona, USA

[13]Northwestern Medicine Delnor Cancer Center, Chicago, Illinois, USA

[14]Department of Pediatrics, Division of Gastroenterology and Nutrition, University of Alberta, Edmonton, Canada

[15]Chinook Regional Hospital, Alberta, Canada

[16]Michael E. DeBakey Veteran Affairs Medical Center, Houston, Texas, USA

[17]Mayo Clinic, Rochester, Minnesota, USA

[18]American Society for Parenteral and Enteral Nutrition, Silver Spring, Maryland, USA

Correspondence
Ainsley Malone, MS, RD, American Society for Parenteral and Enteral Nutrition, 8401 Colesville Rd, Suite 510, Silver Spring, MD 20910, USA.
Email: ainsleym@nutritioncare.org

Abstract

Enteral nutrition (EN) is a vital component of nutrition around the world. EN allows for delivery of nutrients to those who cannot maintain adequate nutrition by oral intake alone. Common questions regarding EN are when to initiate and in what scenarios it is safe. The answers to these questions are often complex and require an evidence-based approach. The Board of Directors of the American Society for Parenteral and Enteral Nutrition (ASPEN) established an Enteral Nutrition Committtee to address the important questions surrounding the indications for EN. Consensus recommendations were established based on eight extremely

clinically relevant questions regarding EN indications as deemed by the Enteral Nutrition Committee. These consensus recommendations may act as a guide for clinicians and stakeholders on difficult questions pertaining to indications for EN. This paper was approved by the ASPEN Board of Directors.

KEYWORDS
enteral nutrition, indications, recommendations

SUMMARY OF RECOMMENDATIONS

1. **What is the optimal time frame to initiate enteral nutrition (EN) in the high-risk nutrition patient, the malnourished patient, and the stable well-nourished patient?**
   A. Initiate EN within 24–48 h of admission to the hospital, including the intensive care unit (ICU), in the patient who is at high risk for malnutrition or who is malnourished.
   B. A delay in initiation of EN can be considered in hospitalized patients who are low risk, well nourished, and expected to resume volitional oral intake within 5–7 days of admission.
   C. Advance EN cautiously in patients at risk for refeeding and in patients with symptoms of gastrointestinal (GI) intolerance.
2. **What are the indications for EN in the oncology patient?**
   A. As soon as feasible, use EN in adult oncology patients who have solid tumors, are unable to receive oral intake or >60%–75% of goal nutrient intake, and present with moderate/severe malnutrition.
   B. Use EN in patients unable to or expected to be unable to tolerate >60% of energy and protein needs by mouth despite education and pharmacologic and oral supplementation for >7–14 days if previously well nourished.
   C. Consider a postpyloric short-term access or jejunal tube in those with refractory nausea and vomiting (N/V) or intolerance of adequate gastric intake.
   D. Consider early aggressive EN therapy for patients in pre-cachexia/cachexia if intake is inadequate.
   E. Consider symptom management and maximization of oral intake for patients with refractory cachexia, life expectancy <3 months, or Karnofsky performance status (KPS) score <50 or who do not wish to continue anticancer treatment.
   F. As soon as feasible after transplant, use EN in adult patients receiving hematopoietic stem cell transplant (HSCT) who are unable to receive oral intake or meet >60%–75% of goal intake and who present with moderate/severe malnutrition.
      i. Use EN in patients unable to or expected to be unable to tolerate >60% of energy and protein needs by mouth despite education and pharmacologic and oral supplementation for >7–14 days if previously well nourished.
      ii. Consider EN vs parenteral nutrition (PN) for nutrition support in the absence of graft vs host disease (GVHD) of the gut mucosa or GI symptoms refractory to pharmacological interventions following transplant.
3. **What are the indications for enteral feedings in patients with GI diseases?**
   A. EN is indicated in patients with GI diseases—including but not limited to inflammatory bowel diseases, chronic liver disease, and acute pancreatitis—when the patient is at risk or has emerging malnutrition due to inadequate oral intake.
      i. Patients most likely to require EN will be those with underlying malnutrition at the time of diagnosis or who are developmentally undergoing periods of rapid growth (notably, infants and adolescents).
      ii. Refractory inflammation and severe malabsorption (notably, in patients with liver disease) will increase the likelihood of requiring EN.
   B. EN is indicated as a therapeutic option for the induction of remission in Crohn's disease (CD).
      i. Exclusive EN (EEN) should be considered as a first-line therapy for the induction of remission in children with CD.
      ii. EEN may be an alternative to corticosteroid therapy for the induction of remission in adults with CD and a high likelihood of treatment adherence.
   C. EN is indicated in preference to PN in patients predicted to have severe acute pancreatitis (SAP).
      i. It is safe to commence EN within 48 h of admission in stable patients predicted to have SAP.
      ii. EN by the nasogastric route can be considered first line; the nasojejunal route is indicated when nasogastric feeding is not tolerated.
      iii. Polymeric formula is the first choice for EN in severe acute pancreatitis.
4. **What are the indications for enteral feedings in patients with specific non-GI diseases?**
   A. Evaluate all patients who have had a stroke for dysphagia as early as possible to establish route of nutrition support.
      i. Initiate EN using a nasogastric tube (NGT) in a patient who has had a stroke, for whom oral intake is deemed unsafe, and who is not likely to recover within 7 days. Evaluate the patient for a nasal tube retaining system to reduce the risk of tube displacement.

ii. Consider placement of a percutaneous endoscopic gastrostomy (PEG) tube in patients with persistent inability to swallow safely for >2–4 weeks.

B. Initiate EN in adult patients with CF and malnutrition who are unable to meet their nutrition needs with diet and oral supplements alone.

C. Initiate EN in malnourished patients with chronic kidney disease (CKD) who are unable to meet nutrition needs with diet and oral supplements alone. This includes patients who are not on dialysis and patients on either intermittent hemodialysis or peritoneal dialysis.

D. Initiate EN in malnourished or at-risk patients with chronic obstructive pulmonary disease (COPD) if energy and protein requirements cannot be achieved through oral diet combined with oral nutrition supplements.

5. **When should early EN be initiated in hemodynamically unstable patients?**

A. Vasopressor administration is not a contradiction to providing early EN with careful monitoring.

i. Consider the following factors when administering EN concomitantly with vasopressor administration: type of vasopressor agent, vasopressor equivalent dosage, timing of EN, and feeding location.

ii. Consider trophic only or holding EN if vasopressor dose equivalent (VDE) score is >12.

iii. Initiate EN within 48 h of vasopressor initiation depending on dosage (see recommendation ii).

iv. Gastric feeding is preferred during vasopressor administration.

v. Insufficient data exist to use lactate levels as a monitoring parameter for EN tolerance.

vi. Routine monitoring of gastric residual volumes (GRVs) is not recommended in critical illness. If GRVs are measured, it would be reasonable to hold EN in adults if GRVs > 300 ml based on limited, low-quality evidence.

vii. EN may be administered in adults if the mean arterial pressure (MAP) is ≥60 mm Hg but should be held when the MAP < 50 mm Hg.

B. When feeding with vasopressors, use a 1.0–1.2 kcal/ml, higher-protein, low-fiber formula. Both semi-elemental and polymeric formulas are tolerated.

C. Initiate EN within the first 24 h of extracorporeal membrane oxygenation (ECMO) support.

i. Initiate EN as continuous intragastric feeding at trophic rate of 10–20 ml/h and increase rate every 4 h over 24–36 h to target rate.

ii. Continue to provide EN infusion if patients on venous arterial (VA) or veno-venous (VV) ECMO are placed in prone position.

iii. Develop and implement clear and comprehensive guidelines for initiation and maintenance of EN support for patients on VA or VV ECMO.

6. **Can patients be fed when undergoing paralytic therapy?**

A. Do not hold or delay EN in patients undergoing paralytic therapy.

7. **Can patients be fed on while on bilevel positive airway pressure (BiPAP) and/or other noninvasive ventilation (NIV) treatments?**

A. The decision to start EN in adults requiring NIV should be multidisciplinary and made on a case-by-case basis, with careful consideration of the patient's overall medical and nutrition status.

B. Placement of an EN tube with a standard NIV mask will cause an additional air leak. If the additional leak is unable to be compensated for, it is recommended to look into a mask with an adaptor or sealing pad.

C. If choosing to enterally feed a patient who is on noninvasive ventilation, postpyloric placement would be preferred because of the likely increased aspiration risk.

8. **What are the indications and strategies to use for "catch-up" feedings?**

A. Consider use of a volume-based feeding protocol to improve the likelihood that the full amount of prescribed EN is received.

B. Consider patient condition factors in formulating the feeding regimen to promote tolerance and meet energy, protein, and fluid needs safely.

INTRODUCTION

Malnutrition is a common issue in the United States. Malnutrition affects all age groups, from children to older adults, and all aspects of healthcare, from outpatient clinics to ICUs. Malnutrition has been shown to be associated with poor patient outcomes for a variety of medical conditions. When malnutrition is present and oral intake is not adequate or not possible, EN may be a therapeutic option.

EN is the administration of supplemental or sole-source nutrition to a functioning GI tract, bypassing the mouth, and is a vital component of nutrition therapy for those patients with malnutrition.[1] Over many decades, EN has been used for those patients with or at risk of malnutrition without obvious contraindications[2] (Table 1). EN has been shown to be beneficial in numerous medical conditions, including SAP,[3,4] inflammatory bowel disease (IBD),[5,6] and critical illness.[7] Given through multiple avenues NGT/nasojejunal tube [NJT], gastrostomies, or jejunostomies), EN may be used to combat malnutrition in those patients who have cancer and are expecting surgery in the preoperative period. With all the potential indications for EN, a few indications are less studied but do constitute a surprising part of daily clinical practice. It is these indications that deserve attention and are the focus of this paper.

In 2018, the American Society for Parenteral and Enteral Nutrition (ASPEN) formed a multidisciplinary EN task force to examine the use of EN. Members of this task force were physicians, dietitians, nurses, and pharmacists. The goals of this task force were to educate healthcare providers and patients on EN and examine the evidence surrounding EN. In 2020, the task force become the Enteral Nutrition Committee under ASPEN. Of the many projects of the committee, a need was identified to examine indications for EN,

TABLE 1 Relative and absolute contraindications for enteral nutrition

Relative contraindications	Absolute contraindications
Severe hemodynamic instability	Bowel obstruction
Ileus	Major gastrointestinal ischemia
Vomiting/diarrhea	High-output fistula
Upper gastrointestinal bleeding	

especially in areas of medicine that are controversial or difficult clinical scenarios. The EN committee was asked to identify areas in EN indications that are clinically relevant, requiring a need for further investigation and recommendations to assist the practicing clinician. Based on these discussions, eight questions were identified. Once identified, each question was researched by literature review to establish a recommendation.

This paper uses consensus recommendations and should not be confused with guidelines. Based on the lack of evidence from many of these tough clinical questions, Grading of Recommendations Assessment, Development, and Evaluation (GRADE) level recommendations are not supported. Therefore, recommendations in this paper rely mostly on weaker literature and expert opinion, which are used to formulate a consensus recommendation. These consensus recommendations are intended to provide healthcare providers help in difficult clinical everyday decisions to improve patient outcomes and patient safety. Furthermore, these recommendations are mostly focused on the adult population, with some pediatric information. Therefore, a comprehensive review of the pediatric literature was not performed, and recommendations from adult studies should not be generalized to the pediatric population. Any recommendations in this paper do not constitute medical or other professional advice and should not be taken as such. To the extent that the information published herein may be used to assist in the care of patients, this is the result of the sole professional judgment of the attending healthcare professional whose judgment is the primary component of quality medical care. The information presented here is not a substitute for the exercise of such judgment by the healthcare professional. Circumstances in clinical settings and patient indications may require actions different from those recommended in this document, and in those cases, the judgment of the treating professional should prevail. This paper was approved by the ASPEN Board of Directors.

METHODS

Members of the EN Committee identified many core questions regarding indications for EN. Upon review of these questions by the entire group, eight questions were identified as the most impactful for the healthcare provider. An extensive literature search was performed for each of the questions in this paper in multiple databases, including but not limited to PubMed, MEDLINE, Cochrane Database of Systematic Reviews, EMBASE, and Google Scholar through December 2020. Furthermore, a manual search of article citations was performed on full-text articles in the English language. Evidence was prioritized in each recommendation based on study quality. Randomized controlled trials (RCTs) were preferred but not always available for a given question. Therefore, prospective and retrospective observational studies, case series, and nonrandomized cohort studies were utilized as well.

A question-answer format has been used in this paper to address common clinical questions surrounding EN indications that were identified by the committee. These consensus recommendations are expert opinions based on the review of the available evidence in the literature for each question. No industry sponsorship and no industry representatives were part of the task force or committee.

REFERENCES

1. Bankhead R, Boullata J, Brantley S, et al. A.S.P.E.N. Board of Directors. Enteral nutrition practice recommendations. *JPEN J Parenter Enteral Nutr*. 2009;33(2):122-167.
2. McClave SA, Martindale RG, Vanek VW, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). *JPEN J Parenter Enteral Nutr*. 2009;33(3):277-316.
3. Song J, Zhong Y, Lu X, et al. Enteral nutrition provided within 48 hours after admission in severe acute pancreatitis: a systematic review and meta-analysis. *Medicine (Baltimore)*. 2018;97(34):e11871.
4. Quan H, Wang X, Guo C. A meta-analysis of enteral nutrition and total parenteral nutrition in patients with acute pancreatitis. *Gastroenterol Res Pract*. 2011;2011:698248.
5. Brennan GT, Ha I, Hogan C, et al. Does preoperative enteral or parenteral nutrition reduce postoperative complications in Crohn's disease patients: a meta-analysis. *Eur J Gastroenterol Hepatol*. 2018;30(9):997-1002.
6. Nguyen DL, Palmer LB, Nguyen ET, et al. Specialized enteral nutrition therapy in Crohn's disease patients on maintenance infliximab therapy: a meta-analysis. *Therap Adv Gastroenterol*. 2015;8(4):168-175.
7. Taylor BE, McClave SA, Martindale RG, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). *Crit Care Med*. 2016;44(2):390-438.

1. What is the optimal time frame to initiate EN in the high-risk nutrition patient, the malnourished patient, and the stable well-nourished patient?

Recommendations

A. Initiate EN within 24–48 h of admission to hospital, including the ICU, in the patient who is at high risk for malnutrition or is malnourished.
B. A delay in initiation of EN can be considered in hospitalized patients who are low risk, well nourished, and expected to resume volitional oral intake within 5–7 days of admission.

C. Advance EN cautiously in patients at risk for refeeding syndrome and in patients with symptoms of GI intolerance.

Rationale

Early EN has an impact on mucosal integrity, immune modulation, and downregulation of the inflammatory response.[1] Nutrition status and disease severity both contribute to a patient's nutrition risk. Early EN reduces mortality compared with delayed enteral intake, based on systematic review of 16 RCTs; however, the specific timing of early EN varies in the literature and in practice.[1] Nutrition interventions show a significant reduction in nonelective admissions, based on 22 RCTs.[2] Short-term underfeeding for the first 4–7 days may be as effective as full feeding in the first week, based on multiple large random controlled trials showing no statistical differences in mortality, infection, GI intolerance, pneumonia, intensive care or hospital length of stay (LOS), and mechanical ventilation (MV) days between underfeeding and standard feeding.[3] Observational data from a few prospective trials report an increase in organ failure, hospital LOS, infection, and complications, with an increasing energy deficit strongly suggesting that EN should be advanced to goal after the acute phase of ICU admission.[4]

As compared with delayed enteral intake, early EN reduced mortality.[1] EN should be initiated promptly within the first 24–48 h of admission in hospitalized patients at high nutrition risk who are unable to maintain adequate nutrition status through volitional oral intake.[4] Advance EN as tolerated over 24–48 h with the goal of providing ≥80% of goal energy unless the patient is at risk for refeeding syndrome[12] or if symptoms of GI intolerance are present.[5]

In patients at high risk, defined as a serious medical condition that may lead to significant morbidity due to malnutrition, a significant reduction in mortality is associated with an increase in EN from 0% to 100% of goal energy.[5] A study of 55 critically ill malnourished patients with high nutrition risk in the critically ill or NUTRIC scores, a measure of adverse risk development, showed that after 7 days of gastric EN, diverting to postpyloric EN and achieving 65% of energy requirements reduced mortality.[6]

Specialized nutrition therapy, EN or PN, is not recommended for hospitalized patients who are at low nutrition risk, well nourished, and expected to resume volitional intake within 5–7 days after admission.[4] Heyland et al showed low-risk patients had no difference in mortality over a range of energy delivery from 0% to 100% of goal energy.[5] The PeRMIT (permissive underfeeding vs target enteral feeding) multicenter RCT compared reduced (40%–60%) nonprotein energy goal vs full (70%–100%) nonprotein energy goal, with full protein in both groups showing no difference in 90-day all-cause mortality between patients with high nutrition risk or low nutrition risk.[3] In well-nourished patients with acute sepsis, early EN with protein (1 g/kg/day) and moderate nonprotein energy (15 kcal/day) is beneficial.[7]

Energy restriction for 2–3 days is a therapeutic option for critically ill adults who develop refeeding syndrome.[8] Aggressive advancement of EN toward goal in patients at risk for refeeding syndrome suggests increased infection risk and lower survival.[3,9] Advance EN cautiously toward goal over 3–4 days if the patient is at risk for refeeding.[4]

Eight RCTs found no statistical differences in mortality, infection, GI intolerance, pneumonia, ICU LOS, hospital LOS, and MV days between the low-energy and high-energy groups.[10] Several recent large RCTs suggest that early full nutrition does not benefit critically ill patients and may induce harm.[11] However, an increase in energy and protein after acute phase of sepsis following ICU admission is warranted.[7] A retrospective cohort study of 88 adult patients with abdominal trauma compared early EN (within 72 h) and delayed EN (after 72 h) and found no difference in mortality or GI intolerance but found a decrease in infectious complications and short ICU LOS and hospital LOS in the early EN group.[12] Seven reviews—by Arabi[13,14] Rice,[15] Rugeles,[16,17] Charles,[18] and Petros[19] showed that hypocaloric feeding (20%–60% of energy requirements) has no significant effect on morbidity and mortality in critically ill patients, in comparison with full EN.

Full feeding may impose potential harm secondary to GI complications, particularly ischemia, as shown in the NUTRIREA-2 study.[20] Most patients were receiving vasopressors and at high nutrition risk.[5] Consider permissive underfeeding in patients with acute lung injury/acute respiratory distress syndrome for the first week.[4,5] The early delivery of early nutrition (EDEN) Trial compared trophic (15%–25% of energy requirement) with full EN for the first 6 days of acute lung injury and found no difference in MV days, infection, or mortality.[3]

REFERENCES

1. Tian F, Heighes PT, Allingstrup MJ, Doig G. Early enteral nutrition provided within 24 hours of ICU admission: a meta-analysis of randomized controlled trials. *Crit Care Medicine*. 2018;46(7):1049-1056.
2. Bally M, Yildirim PZ, Bounoure L, et al. Nutritional support and outcomes in malnourished medical inpatients: a systematic review and meta-analysis. *JAMA Intern Med*. 2016;176(1):43-53.
3. Arabi, YM, Al-Dorzi HM. Trophic or full nutritional support? *Curr Opin Crit Care*. 2018;24(4):262-268.
4. McClave S, DiBaise JK, Mullin GE, Martindale RG. ACG Clinical Guideline: nutrition therapy in the adult hospitalized patient. *Am J Gastroenterol*. 2016;111(3):315-334.
5. Heyland DK, Dhaliwal R, Jiang X, Day AG. Identifying critically ill patients who benefit the most from nutrition therapy: the development and initial validation of a novel risk assessment tool. *Crit Care*. 2011;15(6):R628.
6. Wang WN, Yan MF, Wang CY, Hsu CY, Lee BJ, Fu PK. Optimal time and target for evaluating energy delivery after adjuvant feeding with small bowel enteral nutrition in critically ill patients at high nutrition risk. *Nutrients*. 2019;11(3):645.
7. Wischmeyer P. Nutrition therapy in sepsis. *Crit Care Clin*. 2018:34(1):107-125.
8. Doig GS, Simpson F, Heighes PT, et al. Restricted versus continued standard caloric intake during the management of refeeding syndrome in critically ill adults: a randomized, parallel-group, multicentre, single-blind controlled trial. *Lancet Respir Med*. 2015;3(12):943-952.

9. Patel J, Martindale R, McClave S. Controversies surrounding critical care nutrition: an appraisal of permissive underfeeding, protein, and outcomes. *JPEN J Parenter Enteral Nutr*. 2018;42(3):508-515.
10. Tian F, Wang X, Gao X, et al. Effect of initial calorie intake via enteral nutrition in critical illness: a meta-analysis of randomized controlled trials. *Crit Care*. 2015;19(1):180.
11. Dyck L, Casaer M, Gunst, J. Autophagy and its implications against early full nutrition support in critical illness. *Nutr Clin Pract*. 2018;33(3):339-347.
12. Yin J, Wang J, Zhang S, et al. Early versus delayed enteral feeding in patients with abdominal trauma: a retrospective cohort study. *Eur J Trauma Emerg Surg*. 2015;41(1):99-105.
13. Arabi YM, Tamim HM, Dhar GS, et al. Permissive underfeeding and intensive insulin therapy in critically ill patients: a randomized controlled trial. *Am J Clin Nutr*. 2011;93(3):569-577.
14. Arabi YM, Haddad SH, Tamim HM, et al. Near-target caloric intake in critically ill medical-surgical patients is associated with adverse outcomes. *JPEN J Parenter Enteral Nutr*. 2010;34(3):280-288.
15. Rice TW, Mogan S, Hays MA, Bernard GR, Jensen GL, Wheeler AP. Randomized trial of initial trophic versus full-energy enteral nutrition in mechanically ventilated patients with acute respiratory failure. *Crit Care Med*. 2011;39:967-974.
16. Rugeles SJ, Rueda JD, Dıaz CE, Rosselli D. Hyperproteic hypocaloric enteral nutrition in the critically ill patient: a randomized controlled clinical trial. *Indian J Crit Care Med*. 2013;17(6):343-349.16.
17. Rugeles S, Villarraga-Angulo LG. Ariza-Gutíerrez A, Chaverra-Kornerup S, Lasalvia P, Rosseli D. High-protein hypocaloric vs normocaloric enteral nutrition in critically ill patients: a randomized clinical trial. *J Crit Care*. 2016;35:110-114.
18. Charles EJ, Petroze RT, Metzger R, et al. Hypocaloric compared with eucaloric nutritional support and its effect on infection rates in a surgical intensive care unit: a randomized controlled trial. *Am J Clin Nutr*. 2014;100(5):1337-1343.
19. Petros S, Horbach M, Seidel F, Weidhase L. Hypocaloric vs nor-mo caloric nutrition in critically ill patients: a prospective randomized pilot trial. *JPEN J Parenter EnteralNutr*. 2016;40(2):242-249.
20. Reignier J, Boisrame-Helms J, Brisard L, et al. Enteral versus parenteral early nutrition in ventilated adults with shock: a randomised, controlled, multicentre, open-label, parallel-group study (NUTRIREA-2). *Lancet*. 2018;391(10116):133-143.

2. What are the indications for enteral tube feedings in the oncology patient?

Recommendations

A. As soon as feasible, use EN in adult oncology patients who have solid tumors, are unable to receive oral intake or >60%–75% of goal nutrient intake, and who present with moderate/severe malnutrition.
B. Use EN in patients unable to or expected to be unable to tolerate >60% of energy and protein needs by mouth despite education and pharmacologic and oral supplementation for >7–14 days, if previously well nourished.
C. Consider a postpyloric short-term access or jejunal tube in those with refractory N/V or intolerance of adequate gastric intake.
D. Consider early aggressive EN therapy for patients with pre-cachexia/cachexia if intake is inadequate.
E. Consider symptom management and maximization of oral intake for patients with refractory cachexia, life expectancy <3 months, or KPS score <50 or those who do not wish to continue anticancer treatment.
F. As soon as feasible after transplant, use EN in adult patients undergoing HSCT who are unable to receive oral intake or meet >60%–75% of goal intake and who present with moderate/severe malnutrition.
   i. Use EN in patients unable to or expected to be unable to tolerate >60% of energy and protein needs by mouth despite education and pharmacologic and oral supplementation for >7–14 days, if previously well nourished.
   ii. Consider EN vs PN for nutrition support in the absence of GVHD of the gut mucosa or GI symptoms refractory to pharmacological interventions following transplant.

Oncological diseases

Rationale

Patients with head and neck, lung, hepatic, gastric, and colorectal cancers are at greatest risk for malnutrition.[1] The ASPEN and Academy of Nutrition and Dietetics (AND) criteria for diagnosing malnutrition include parameters for clinically significant weight loss, reduced oral intake over a set time frame, and muscle and adipose wasting observed through a nutrition-focused physical exam.[2] There is evidence from multiple studies that those with a malnutrition diagnosis at the start of treatment have further decline in nutrition status throughout the duration of chemotherapy.[3] Compromised nutrition status is also thoroughly documented to be associated with increased hospitalizations and readmissions, longer hospital stay, reduced quality-of-life scores, higher mortality, and reduced tolerance of chemotherapy and radiation therapy.[4] Unfortunately, there is a significant disparity between those who are malnourished and would benefit from nutrition intervention and whether those patients actually receive nutrition intervention. A cross-sectional analysis of malnutrition and prevalence of nutrition support was conducted in 1903 patients with cancer and found the highest incidence of malnutrition in patients with head and neck cancer (48.9%), followed by those with lung cancer (45.3%) and leukemia or lymphoma (34%).[5] Nutrition support in the form of EN was received by 19.7% of those who were identified as malnourished and 10% of those who were nonmalnourished.[5]

Aggressive nutrition support is justified at the start of treatment for patients who have moderate to severe malnutrition. AND guidelines promote early nutrition intervention for precachexia or cancer cachexia to minimize the effects of altered metabolism that lead to weight loss and muscle and adipose wasting.[4] ASPEN guidelines reflect these recommendations, suggesting the use of EN for patients undergoing anticancer treatment who are unable to meet nutrient needs for 7–14 days.[6] If the patient is not tolerating oral intake adequately to meet nutrition needs, EN is indicated.

There is no confirmed effect of EN on stimulating tumor growth. A systematic review of three studies inclusive of 28 oncology patients failed to demonstrate EN having an impact on tumor growth. A third study on six patients with head and neck cancer, performed 33 years ago, found tumor growth after 6 days of EN therapy.[7] The detrimental consequences of withholding nutrition support to treat malnutrition far outweigh theoretical risks of tumor promotion.[8-10]

If the gut is functional and no other contraindications exist, EN should be the first line of nutrition intervention. There is a widespread belief among clinicians that EN is superior to PN because of the benefits of reducing bacterial translocation and limiting infectious complications [4,11,12] Seres et al examined published data on the advantages of EN over PN and concluded that for patients requiring nutrition support, EN is preferred; however, there is a lack of well-designed, high-powered studies looking at artificial nutrition support therapies.[13] Benefits of EN include reduced infection rates in some literature, ease of administration, and savings on associated costs.[9,10,14,15]

Routine use of EN during chemotherapy is not recommended.[4,6,11,12] Dietary counseling from a registered dietitian is an appropriate first approach to improve nutrition intake. There seems to be no role for prophylactic EN in general oncology, and initiating EN is a response to failed nutrition counseling and oral nutrition support attempts.[7,16] For patients with precachexia, cancer cachexia, and/or severe malnutrition refractory to oral nutrition intervention, nutrition support may be proposed. Indications, route, and schedule for EN in oncology patients depends on the patient's diagnosis, treatment modality, nutrition status, energy and protein requirements, and estimated duration of nutrition intervention.[6,11] Nutrition support algorithms may be useful for deciding which patients would benefit from nutrition support intervention and timing (see Figure 1).

Malnourished patients with GI cancer are at high risk for morbidity, mortality, and decreased efficacy of treatment. These patients are at risk of malnutrition before diagnosis or as a consequence of treatment-induced nutrient malabsorption, dietary intolerances, vitamin and mineral deficiencies, bacterial overgrowth, dumping syndrome, poor oral intake, and consequential weight loss.[17] Surgical cancer treatments often predispose a patient to malnutrition, especially when the GI tract is manipulated.[18] ASPEN and the European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines do encourage the use of nutrition support via the enteral route for moderately or severely malnourished patients in the 7–14 days leading up to surgery.[6,19] The enteral route is preferred when the gut is functional and there are no contraindications (see Table 1). In these cases, it is worth considering whether attempts to improve nutrition status outweigh the possible risk of delaying surgery.[6,9,11,19] In both undernourished and well-nourished patients, nutrition support therapy should be initiated if anticipated oral intake will be insufficient for >7 days following surgery.[19-21] Patients with severe malnutrition and GI cancers have been studied regarding the use of preoperative and postoperative nutrition support. Reducing the risk of malnutrition, managing symptom severity, and minimizing nutrient deficiencies are key in this population. The use of perioperative EN in GI cancer patients undergoing surgery reduces infection risk and shortens hospital LOS.[15,22-24]

Gastroparesis is often an overlooked disorder, characterized by delayed gastric emptying contributing to symptoms including nausea, vomiting, early satiety, bloating, and GI discomfort. Etiology commonly stems from diabetes mellitus; however, malignant gastroparesis is less well known and therefore often undiagnosed.[25] Higher incidence is found in upper-GI and pancreatic cancers, adding to the disposition for GI motility disruptions as a result of the disease itself (eg, dysphagia, intestinal pseudo-obstruction).[26-28] Untreated

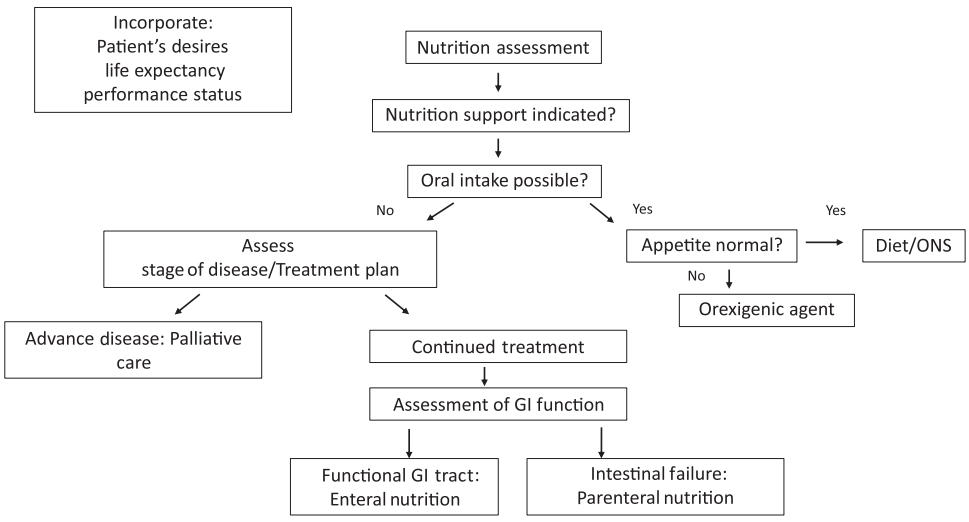

FIGURE 1 Decision tree in improving nutrition status in the cancer patient with nutrition and pharmacological therapies. GI, gastrointestinal; ONS, oral nutrition supplement. Adapted from Mattox TW. Cancer cachexia: cause, diagnosis, and treatment. *Nutr Clin Pract*. 2017;32(5):599-606

gastroparesis increases susceptibility to intractable N/V with dehydration and associated electrolyte deficiencies, anorexia, consequential cachexia, interruptions to anticancer treatment, and quality of life.[25,29] Proper and early management of mild gastroparesis through diet modifications can effectively divert these risks.[25] When diet changes are inadequate to manage symptoms and malnutrition is observed, a more aggressive approach is warranted. Rehydration and electrolyte replacement are priorities, followed by intravenous (IV) antiemetics and prokinetics. Patients who are unable to maintain hydration, electrolytes within range, and adequate perfusion are candidates for feeding through NJT or jejunostomy tube, with consideration of gastric tubes for decompression or newer combination (gastrostomy with jejunal extension) tubes.[30] Separate tubes for feeding and decompression, although more cumbersome for patients and caregivers, may be beneficial because of the risk of tube migration with compromised peristalsis when using a gastrostomy-jejunostomy tube.[30]

The etiology of cancer-associated cachexia syndrome differs from malnutrition alone and is in part due to metabolic alterations caused by the presence of a tumor. Chronic inflammation, catabolism, futile energy-cycling pathways, and anabolic resistance are metabolic features in these cases.[31] Coupled with metabolic derangements are a decreased ability to consume adequate nutrition due to treatment-related symptoms and side effects such as nausea, vomiting, dysgeusia, dysphagia, mucositis, anorexia, pain, and depression.[18,31,32] Also, the disease itself plays a role such as GI-obstructing tumors, or altered organ function such as exocrine pancreatic insufficiency may limit adequate nutrient comsumption.[18,31,32] Clinical observations in cancer cachexia syndrome include significant, unintentional weight loss; muscle and adipose wasting; and fluid accumulation presenting as edema or ascites.

An international Delphi panel agreed that cancer cachexia is defined by chronic muscle wasting (with or without adipose loss) that is irreversible with standard nutrition intervention.[33,34] Interventions should be aimed at anorexia and compromised nutrition intake, catabolism, muscle preservation, and functionality improvement.[33] The *International Classification of Diseases, Tenth Revision* code for cachexia is simply defined by involuntary weight loss >10% and muscle atrophy resulting from inadequate dietary intake, malabsorption, or hypermetabolism.[35]

Sarcopenia is another nutrition-related risk factor for frailty, weakness, and decreased performance status. Similar to cancer cachexia, sarcopenia involves inflammation-driven metabolic changes from chronic disease. It is different in that muscle fibers are replaced with fibrotic tissue, causing functional deterioration.[36]

Patients with precachexia/cachexia with compromised nutrient intake qualify for early aggressive EN to prevent further decline in nutrition status and associated risks. EN has repeatedly demonstrated an improvement in the quality of life, nutrition status, and survival in oncology research. However, aggressive nutrition therapy should be used conservatively and with ethical considerations for patients with severe cachexia, anorexia, limited aspiration, and limited life expectancy.[37] First, it is important to weigh the possible burdens of nutrition support compared with the perceived benefits. Obtaining access for EN involves possibly painful or uncomfortable endoscopic or surgical procedures. If nutrition support therapy is initiated, consider whether the patient, caregiver, and medical team are willing to take on known side effects and potential complications such as infections, edema, ascites, and GI symptoms.

As clinical guidelines recommend to limit the use of nutrition support in the context of limited life expectancy, many questions arise.[6,11,16,38] It has been recommended that nutrition support be withheld or withdrawn under the circumstances of reduced life expectancy, KPS score <50 or Eastern Cooperative Oncology Group (ECOG) performance status of 3 or 4, severe organ dysfunction, uncontrolled nutrition-impacting symptoms, or patient-directed wishes for care or under the circumstance in which the patient may not benefit from aggressive nutrition interventions.[3,39,40]

The National Comprehensive Cancer Network (NCCN) guidelines encourage the use of nutrition support in the form of EN or PN if the life expectancy exceeds a year to months.[41] For patients with advanced cancer who are expected to pass in months to weeks or days, nutrition support is not indicated for the purpose of reversing weight loss.[41] Clinicians are guided to educate the patient and caregiver on conservative end-of-life nutrition comfort measures and ethical considerations surrounding withdrawing or withholding nutrition support care.[41]

REFERENCES

1. World Health Organization. Cancer Fact sheet [online]. eq 2017. Accessed February 16, 2022. https://www.who.int/news-room/fact-sheets/detail/cancer
2. White JV, Guenter P, Jensen GL, et al. Consensus statement: Academy of Nutrition and Dietetics and American Society for Parenteral and Enteral Nutrition: characteristics recommended for the identification and documentation of adult malnutrition (undernutrition). *JPEN J Parent Ent Nutr*. 2012;36(3):275-283.
3. Cotogni P. Enteral versus parenteral nutrition in cancer patients: evidences and controversies. *Ann Palliat Med*. 2016;5(1):42-49.
4. Thompson K, Elliott L, Fuchs-Tarlovsky V, Levin RM, Voss AC, Piemonte T. Oncology evidence-based nutrition practice guideline for adults. *J Acad Nutr Diet*. 2017;117(2):297-310.
5. Heburerne X, Lemarie E, Michallet M, Beauvillain de Montreuil C, Schneider SM, Goldwasser F. Prevalence of malnutrition and current use of nutrition support in patients with cancer. *JPEN J Parent Ent Nutr*. 2014;38(2):169-204.
6. August DA, Huhmann MB; American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) Board of Directors. A.S.P.E.N. clinical guidelines: nutrition support therapy during adult anticancer treatment in hematopoietic cell transplantation. *JPEN J Parent Ent Nutr*. 2009;33(5):472-500.
7. Bossola M. Nutritional intervention in head and neck cancer patients undergoing chemoradiotherapy: a narrative review. *Nutrients*. 2015;7(1):265-276.
8. Akbulut G. New perspective for nutritional support of cancer patients: enteral/parenteral nutrition. *Exp Ther Med*. 2011;2(4):675-684.
9. Huhmann MB, August DA. Perioperative nutrition support in cancer patients. *Nutr Clin Pract*. 2012;27(5):586-592.

10. Ryan A. Nutrition support in the oncology setting. In: Lesser M, Ledesma N, Bergeson S, et al, eds. *Oncology Nutrition for Clinical Practice*. Oncology Nutrition Dietetic Practice Group; 2018: 123-134.
11. Arends J, Bachmann P, Baracos V, et al. ESPEN guidelines on nutrition in cancer patients. *Clin Nutr*. 2017;36(1):11-48.
12. De Las Penas R, Majem M, Perez-Altozano J, et al. SEOM clinical guidelines on nutrition in cancer patients. *Clin Transl Oncol*. 2019; 21(1):87-93.
13. Seres D, Valcarcel M, Guillaume A. Advanced of enteral nutrition over parenteral nutrition. *Therap Adv Gastroenterol*. 2013;6(2): 157-167.
14. Chow R, Bruera E, Chiu L, et al. Enteral and parenteral nutrition in cancer patients: a systematic review and meta analysis. *Ann Palliat Med*. 2016;5(1):30-41.
15. Braunschweig CL, Levy P, Sheean PM, Wang X. Enteral compared with parenteral nutrition; a meta-analysis. *Am J Clin Nutr*. 2001; 74(4):534-542.
16. Bozzetti F. Nutritional support of the oncology patient. *Crit Rev Oncol Hematol*. 2013;87(2):172-200.
17. Radigan AE. Post-gastrectomy: managing the nutrition fall-out. *Pract Gastroenterol*. 2004;28(6):63-75.
18. Santarpia L, Contaldo F, Passanisi F. Nutritional screening and early treatment of malnutrition in cancer patients. *J Cachexia Sarcopenia Muscle*. 2011;2(1):27-35.
19. Weimann A, Braga M, Harsanyi L, et al. ESPEN guidelines on enteral nutrition: surgery including organ transplantation. *Clin Nutr*. 2006; 25(2):224-244.
20. Benoist S, Broquet A. Nutritional assessment and screening for malnutrition. *J Vasc Surg*. 2015;152(S1):S3-S7.
21. Raspe C, Flother L, Schneider R, Baucher M, Piso P. Best practice for perioperative management of patients with cytoreductive surgery and HIPEC. *Eur J Surg Oncol*. 2017;43(6):1013-1027.
22. Elia M, Van Bokhorst-de van der Schueren MA, Garvey J, et al. Enteral (oral or tube administration) nutritional support and eicosapentaenoic acid in patients with cancer: a systematic review. *Int J Oncol*. 2006;28(1):5-23.
23. Wu GH, Liu ZH, Wu ZH, Wu ZG. Perioperative artificial nutrition in malnourished gastrointestinal patients. *World J Gastroenterol*. 2006; 12(15):2441-2444.
24. Senesse P, Assenat E, Schneider S, et al. Nutritional support during oncologic treatment of patients with gastrointestinal cancer: who could benefit? *Cancer Treat Rev*. 2008;34(6):568-575.
25. Donthireddy K, Ailawadi S, Nasser E, et al. Malignant gastroparesis: pathogenesis and management of an underrecognized disorder. *J Support Oncol*. 2007;5(8):355-363.
26. Schraml F, Krueger W. Presentation of gastric carcinoma on a radionuclide gastric-emptying study. *Clin Nucl Med*. 2005;30: 574-576.
27. Leung V, Kan P, Lai M. Cholangiocarcinoma presenting as pseudoachalasia and gastroparesis. *Hong Kong Med J*. 2003;9(4): 296-298.
28. Leung J, Silverman W. Diagnostic and therapeutic approach to pancreatic cancer-associated gastroparesis: literature review and our experience. *Dig Dis Sci*. 2009;54(2):401-405.
29. Hewitt A, Levine M, Rubesin S, Laufer I. Gastric bezoars: reassessment of clinical and radiographic findings in 19 patients. *Br J Radiol*. 2009;82(983):901-907.
30. Camilleri M, Parkman H, Schafi M, et al. Clinical guideline: management of gastroparesis. *Am J Gastroenterol*. 2013;108(1): 18-37.
31. Baracos V. Cancer-associated malnutrition. *Eur J Clin Nutr*. 2018; 72(9):1255-1259.
32. Ravasco P. Nutrition in cancer patients. *J Clin Med*. 2019;8(8): 1211-1224.
33. Fearon K, Strasser F, Anker SD, et al. Definition and classification of cancer cachexia: an international consensus. *Lancet Oncol*. 2011; 12(5):489-495.
34. Martin L, de van der Schuren MAE, Blauwhoff-Buskermolen S, Baracos V, Gramlich L. Identifying the barriers and enablers to nutrition care in head and neck esophageal cancers: an international qualitative study. *JPEN J Parent Ent Nutr*. 2016;40(3):355-366.
35. ICD-10-CM Diagnosis Code R64 Cachexia. ICD10Data.com. 2022. Accessed January 15, 2020. https://www.icd10data.com/ICD10CM/Codes/R00-R99/R50-R69/R64-/R64
36. Ongaro E, Buoro V, Cinausero M, et al. Sarcopenia in gastric cancer: when the loss costs too much. *Gastric Cancer*. 2017;20(4):563-572.
37. Niv Y, Abuksis G. Indications for percutaneous endoscopic gastrostomy insertion: ethical aspects. *Dig Dis*. 2002;20(3-4):253-256.
38. Kempf E, Tournigand C, Rochigeneux P, Aubry R, Morin L. Discrepancies in the use of chemotherapy and artificial nutrition near the end of life for hospitalised patients with metastatic gastric or oesophageal cancer. A countrywide, register-based study. *Eur J Cancer*. 2017;79:31-40.
39. Karnofsky DA, Abelmann WH, Craver LF, et al. The use of nitrogen mustards in the palliative treatment of carcinoma: with particular reference to bronchogenic carcinoma. *Cancer*. 1948;1(4):634-656.
40. Oken MM, Creech RH, Tormey DC, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. *Am J Clin Oncol*. 1982;5(6):649-655.
41. Dans M, Smith T, Back A, et al. NCCN Guidelines Insights: palliative care, version 2.2017. *J Natl Compr Canc Netw*. 2017;15(8):989-997.

Hematopoietic stem cell transplant

Rationale

There is an important need to establish and maintain adequate nutrition before, during, and after HSCT to prevent malnutrition, which is a well-known predictor of transplant-related morbidity, mortality, and disease relapse.[1,2] A malnutrition diagnosis has been repeatedly documented to increase complications and independently predict mortality in patients who underwent HSCT.[3]

Existing guidelines state that patients who have preexisting malnutrition and are not expected to maintain adequate oral nutrition for 7–14 days are appropriate candidates for nutrition support. EN is the preferred route of nutrient delivery, rather than PN, which increases risks for complications such as infections and metabolic derangements.[4-7] However, clinical practice and guidelines may differ.[8,9] Severe malnutrition diagnosis was an independent risk factor for GVHD, nonrelapse mortality, and worse progression-free and overall survival compared with those who were well nourished or moderately malnourished.[10] For patients who are malnourished and unable to meet nutrient needs on assessment prior to undergoing HSCT, EN can be used to prevent short-term and long-term complications, circumvent decline in nutrition status, and promote improved survival.[8-10]

In both allogenic HSCT (allo-HSCT) and autologous HSCT (auto-HSCT), conditioning regimens can induce nutrition consequences for the well-nourished patient owing to compromised immunity and decreased GI functional integrity.[11] Compared with patients who receive allogeneic HSCT, patients who receive peripheral stem cells

and growth factors through auto-HSCT experience mucositis, reduced time to engraftment, and reduced length of neutropenia. Patients who underwent allo-HSCT are at risk for GVHD, which significantly impacts gut function, and complications that result in rapid decline in nutrition status.[11]

The incidence of preexisting enteral feeding tubes in patients prior to undergoing HSCT is difficult to quantify. The trend in published data is toward tube insertion following transplant for acute nutrition support needs. Clinical trials have used <80% of estimated needs as a benchmark for indication to start nutrition support therapy via NGT.[12,13] Use of EN as a first-line intervention for gut and immune benefits and to reduce risk for weight loss is indicated. Well-nourished patients who are unable to meet <80% of nutrient needs despite interventions should be considered for EN to prevent weight loss during any part of the peritransplant phase.

Nonrelapse mortality has been identified as a greater risk for underweight patients than for well-nourished controls.[13] In results from one study on energy intake during HSCT, the majority of patients were meeting <60% of their energy needs from transplant to engraftment, with the deficit secondary to GI symptoms, including diarrhea and anorexia.[14] Barriers to initiating nutrition support to prevent weight loss in 50 well-nourished patients enrolled in a RCT included patient resistance and physician preference. The study aimed to compare early nutrition support (oral intake <80% of estimated needs) vs standard care (oral intake < 50%). At discharge, patients in the early nutrition support group better maintained weight (−0.4%) compared with the later group, who lost −3.4% of their body weight ($P = 0.001$), but the difference was not significant at 6-month follow-up. No other outcomes were significant between groups.[13]

Relapse rates continue to be affected by weight changes even after hospital discharge following completion of HSCT. In a retrospective study, patients who experienced weight loss of 10% in 3 months following stem cell transplant ($n = 45$) had a 27.3% 2-year nonrelapse mortality rate, compared with the group with <5% loss ($n = 53$), who had a 3.8% nonrelapse mortality rate.[1]

GVHD is a common barrier to initiating and maintaining EN as the primary route of nutrition support during HSCT engraftment. GVHD is a common outcome of allo-HSCT, impairing immune and organ function and reducing overall survival.[15] Symptoms of GVHD create nutrition and survival disadvantages for the HSCT recipient. In 210 patients, those with GVHD who were malnourished had 69% survival at 3-year follow-up, compared with 82% in those identified as well nourished.[16] Multivariate regression analysis on 105 patients who underwent allo-HSCT indicated that GVHD was a significant factor influencing deterioration in nutrition status evidenced by weight loss, decrease in body mass index (BMI), and loss of muscle and adipose tissue.[17]

EN may be an effective tool for improving clinical outcomes and reducing risk for nutrition issues provoked by GVHD. In a nonrandomized study of 44 patients who underwent allo-HSCT, a 17% lower incidence of GVHD was observed in those who received EN vs those who did not (EN: $n = 22$, 18% GVHD; PN: $n = 22$ or standard oral feeding $n = 1$, 35% GVHD) ($P = 0.011$).[18] The EN group also experienced lower infection-related mortality at day +100 following transplant.[18] These results have been replicated in a larger group of 121 patients who underwent allo-HSCT, in whom EN was isolated as a protective factor against acute grade III/IV GVHD by 23% (36% with EN compared with 59% non-EN; $P = 0.009$).[19] In another cohort of 484 patients who underwent allo-HSCT, there was an increase in GI GVHD of any stage and all GVHD grade >2 in patients receiving PN compared with those receiving EN.[20] EN was protective against grades 3 and 4 acute GVHD in 94 patients receiving EN and 27 patients not receiving EN following allo-HSCT and myeloablative conditioning in another study.[19] However, one study comparing early outcomes in 28 patients who underwent allo-HSCT and received EN vs 28 patients who received PN could not confirm a significant difference in GVHD incidence.[6]

PN is often perceived as a more easily delivered route of nutrition support because patients in this population often already have central lines. This causes patient and physician resistance to placing enteral access devices, which may be considered as more invasive procedures, especially for pediatric patients and families.[13] Per ASPEN guidelines, EN is an appropriate first line of nutrition support during HSCT, followed by PN under the conditions of severe mucositis grade >3, clinically significant weight loss, ileus, malabsorptive disorders, intractable vomiting, or GI failure.[4]

Risks of obtaining enteral access following HSCT include compromised coagulation, aspiration and pneumonia, sinusitis, diarrhea, ileus, abdominal pain, gastroparesis, and emesis.[4] It is important to note that there may be an increased risk of local bleeding in this population, related to low platelet count, and this risk must be considered with tube placement.[21] NJTs were placed at the start of induction conditioning for 14 patients undergoing allo-HSCT. One patient experienced epistaxis in the nare where the tube was placed, and one had epistaxis in the opposite nare.[22] The main issues identified with NJ feedings were tube forceful vomiting and tube displacement. It was recommended that scheduled antiemetics be provided to minimize risk. Otherwise, place NJTs and initiate feeds on day +1 following induction treatment, prior to onset of possible pancytopenia and mucositis.

Evidence exists for increased morbidity, higher rates of diarrhea, hyperglycemia, and delayed engraftment but reduced weight loss and loss of adipose when using PN.[4] No significant difference was found in development or grade of GVHD.[4] More recent studies have replicated results and reinforced recommendations. Posttransplant patients have continued to demonstrate tolerance to EN with improved survival, decreased disease recurrence, and confirmed benefits for reducing GVHD.

Andersen and colleagues randomized patients to EN or PN following HSCT. All who were randomized to EN ($n = 5$) tolerated feeds for 10 days, until they experienced GI toxicity and were switched to PN.[23] Despite the short duration of therapy, the authors proposed that 10 days of EN therapy may predispose the patient to improved outcomes and reduced risk for complications documented in PN groups, such as infections and rates of GVHD.

Greater survival and relapse-free survival was reported when comparing EN vs PN in multiple HSCT groups. Cohort studies have provided evidence that nonrelapse mortality is higher in those who were undernourished and that EN is superior to PN for reducing nonrelapse mortality, improving survival, time to engraftment, and GVHD-free relapse and survival for up to 5 years.[6,19]

There is evidence that short-term EN through an NGT during HSCT should be considered as standard of care for benefits to survival, quicker engraftment, and reduced GVHD. Proposed mechanisms include EN maintaining mucosal integrity, modulating immunity, and contributing to gut microflora diversity.[20]

REFERENCES

1. Fuji S, Mori T, Khattry N, et al. Nutritional Support Working Group of the Asian Pacific Bone Marrow Transplantation. Severe weight loss in 3 months after allogeneic hematopoietic SCT was associated with an increased risk of subsequent non-relapse mortality. *Bone Marrow Transplant*. 2014;50(1):100-105.
2. Fuji S, Einsele H, Savani BN, Kapp M. Systematic nutritional support in allogeneic hematopoietic stem cell transplant recipients. *Biol Blood Marrow Transplant*. 2015;21(10):1707-1713.
3. Bumgartner A, Bargetzi M, Bargetzi A, et al. Nutritional support practices in hematopoietic stem cell transplantation centers: a nationwide comparison. *Nutrition*. 2017;35:43-50.
4. August DA, Huhmann MB. American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) Board of Directors. A.S.P.E.N. clinical guidelines: nutrition support therapy during adult anticancer treatment in hematopoietic cell transplantation. *JPEN J Parenter Enteral Nutr*. 2009;33(5):472-500.
5. Bozzetti F, Arends J, Lundholm K, Micklewright A, Zurcher G, Muscaritoli M. ESPEN guidelines on parenteral nutrition: non-surgical oncology. *Clin Nutr*. 2009;28(4):445-454.
6. Guieze R, Lamal R, Cabrespine A, Hermet E. Enteral versus parenteral nutritional support in allogeneic haematopoietic stem-cell transplantation. *Clin Nutr*. 2014;33(3):533-538.
7. Arends J, Bodoky G, Bozzetti F, et al. ESPEN guidelines on enteral nutrition: non-surgical oncology. *Clin Nutr*. 2006;25(2):245.
8. Lowder Y, Mayers M, Seckar J et al. Nutrition practices in hematopoietic stem cell transplantation (HSCT): a comparison between guidelines and clinical practice. *Biol Blood Marrow Transplant*. 2018;25(3): S304-S305.
9. Habschmidt MG, Bacon CA, Gregoire MB, Rasmussen HE. Medical nutrition therapy provided to adult hematopoietic stem cell transplantation patients. *Nutr Clin Pract*. 2012;27(5):655-660.
10. Hirose EY, de Molla VC, Goncalves MV, et al. The impact of pretransplant malnutrition on allogeneic hematopoietic stem cell transplantation outcomes. *Clin Nutr*. 2019;33:213-219.
11. Muscaritoli M, Grieco G, Capri S, Paola Lori A, Rossi Fanelli F. Nutritional and metabolic support in patients undergoing bone marrow transplantation. *Am J Clin Nutr*. 2002;75(2):183-190.
12. Andersen S, Kennedy G, Banks M. A randomised controlled comparison of enteral versus parenteral nutritional support post allogeneic haematopoietic cell transplantation. *Clin Nutr*. 2015;10(3): e102-e106.
13. Kiss N, Seymour JF, Prince HM, Dutu G. Challenges and outcomes of a randomized study of early nutrition support during autologous stem-cell transplantation. *Curr Oncol*. 2014;21(2):334-339.
14. Walrath M, Bacon C, Foley S, Fung H. Gastrointestinal side effects and adequacy of enteral intake in hematopoietic stem cell transplant patients. *Nutr Clin Pract*. 2015;30(2):305-310.
15. Syrjala KL, Martin PJ, Lee SJ. Delivering care to long-term adult survivors of hematopoietic cell transplantation. *J Clin Oncol*. 2012; 30(30):3746-3751.
16. Bassim CW, Fassil H, Dobbin M, et al. Malnutrition in patients with chronic GVHD. *Bone Marrow Transplant*. 2014;49(10):1300-1306.
17. Urbain P, Birlinger J, Lambert C, Finke J, Bertz H, Biesalski HK. Longitudinal follow-up of nutritional status and its influencing factors in adults undergoing allogeneic hematopoietic cell transplantation. *Bone Marrow Transplant*. 2013;48(3):446-451.
18. Seguy D, Berthon C, Micol JB, et al. Enteral feeding and early outcomes of patients undergoing allogeneic stem cell transplantation following myeloablative conditioning. *Transplantation*. 2006; 82(6):835-839.
19. Seguy D, Duhamel A, Rejeb MB, et al. Better outcome of patients undergoing enteral tube feeding after myeloablative conditioning for allogeneic stem cell transplantation. *Transplantation*. 2012;94(3): 287-294.
20. Beckerson J, Szyldo RM, Hickson M, et al. Impact of route and adequacy of nutritional intake on outcomes of allogeneic haematopoietic cell transplantation for haematologic malignancies. *Clin Nutr*. 2019;38(2):738-744.
21. Arends J, Bachmann P, Baracos V, et al. ESPEN guidelines on nutrition in cancer patients. *Clin Nutr*. 2017;36(1):11-48.
22. Sefcick A, Anderton D, Byrne JK, Teahon K, Russell NH. Naso-jejunal feeding in allogenic bone marrow transplant recipients: results of a pilot study. *Bone Marrow Transplant*. 2002;28(12):1135-1139.
23. Andersen S, Weber N, Kennedy G, Brown T, Banks M, Bauer J. Tolerability of proactive enteral nutrition post allogeneic haematopoietic progenitor cell transplant: a randomised comparison to standard care. *Clin Nutr*. 2020;39(5):1364-1370.

3. What are the indications for enteral feedings in patients with GI diseases?

Recommendations

A. EN is indicated in patients with GI diseases—including but not limited to IBDs, chronic liver disease, and acute pancreatitis—when the patient is at risk or has emerging malnutrition due to inadequate oral intake.
   i. Patients most likely to require EN will be those with underlying malnutrition at the time of diagnosis or who are developmentally undergoing periods of rapid growth (notably, infants and adolescents).
   ii. Refractory inflammation and severe malabsorption (notably, in patients with liver disease) will increase the likelihood of requiring EN.

B. EN is indicated as a therapeutic option for the induction of remission in CD.
   i. EEN should be considered as a first-line therapy for the induction of remission in children with CD.
   ii. EEN may be an alternative to corticosteroid therapy for the induction of remission in adults with CD and a high likelihood of treatment adherence.

C. EN is indicated in preference to PN in patients predicted to have SAP.

i. It is safe to commence EN within 48 h of admission in stable patients predicted to have SAP.
ii. EN by the NGT route can be considered first line; the NJ route is indicated when NG feeding is not tolerated.
iii. Polymeric formula is the first choice for EN in SAP.

Inflammatory bowel disease

Rationale

The potential roles of EN in the management of IBD include its use as (1) an anti-inflammatory therapy and (2) a source of nutrition. The premise behind the use of EEN for the treatment of IBD is the reduced consumption and intestinal exposure to proinflammatory food constituents. EN additionally has putative effects on cytokine production and intestinal permeability.[1,2] In clinical trials, EEN has been found to be effective for inducing, but not maintaining, remission in CD.[3,4]

For the induction of remission in CD, most studies that evaluated the efficacy of EEN compared its use with corticosteroids, finding both to have comparable remission rates. Practice guidelines from medical and nutrition societies, such as the North American Society for Pediatric Gastroenterology, Hepatology & Nutrition (NASPGHAN) and ESPEN, therefore recommend the use of EN as a first-line corticosteroid-sparing therapy in children.[5,6] Nonetheless, subgroup analysis from a recent meta-analysis by the Cochrane Collaboration found corticosteroids to be superior to EEN among adults but not children.[3] When considering per-protocol subgroup analyses, corticosteroids were still superior to EEN among adult patients who supposedly adhered to the protocol. Analyses that compared EN formulations found no difference in remission rates based on type (elemental, semi-elemental, polymeric) or fat content. One very small randomized trial that compared glutamine-enriched and standard polymeric formulas found no difference in remission rates.[7]

Other than for the induction of remission in CD, there is no clear role for EN as an anti-inflammatory therapy. For the maintenance of remission in CD, there are currently too few studies to conclude whether EN would be helpful. Earlier trials with 12-month and 24-month follow-up did not show the benefit of EN for maintenance of remission.[8-10] Nonetheless, a recent trial found partial EN coupled with a CD Exclusion Diet (CDED) to be superior at maintaining remission compared with partial EN with a standard diet.[11] This finding highlights a potential limitation of prior studies in which the type of solid food diet may have negated the benefit of EN. Future studies may need to explore whether partial EN with CDED is superior to the CDED alone. If not, then there may be no significant benefit of EN for the maintenance of remission in CD. For ulcerative colitis, the utility of EN for the induction or maintenance of remission is even less clear because of a lack of available data.

As patients with active IBD possess a high risk of developing protein-energy malnutrition, EN serves an important role in nutrition support. Patients with IBD often reduce their oral intake to reduce or avoid symptoms, experience malabsorption, and exhibit a catabolic state from active inflammation. In patients who cannot maintain an adequate nutrition status despite solid food intake, oral nutrition supplementation or EN is a viable option for nutrition. In the perioperative setting, the importance of nutrition optimization and its benefits on postoperative outcomes are well established.[12] This relationship also holds true for IBD, for which preoperative nutrition optimization with EN has also been found to improve postoperative outcomes.[13,14] However, the optimal algorithm to determine when to consider oral nutrition supplements, EN, or PN is under-studied and thus unclear. ESPEN guidelines provide grade B recommendations that EN be considered for surgical patients who are unable to maintain adequate nutrition intake with solid food and oral nutrition supplements.[6]

REFERENCES

1. Sanderson IR, Boulton P, Menzies I, Walker-Smith JA. Improvement of abnormal lactulose/rhamnose permeability in active Crohn's disease of the small bowel by an elemental diet. *Gut*. 1987;28(9):1073-1076.
2. Sanderson IR, Croft NM. The anti-inflammatory effects of enteral nutrition. *JPEN J Parenter Enteral Nutr*. 2005;29(4 suppl):S134-S138.
3. Narula N, Dhillon A, Zhang D, Sherlock ME, Tondeur M, Zachos M. Enteral nutritional therapy for induction of remission in Crohn's disease. *Cochrane Database Syst Rev*. 2018;4(4):CD000542.
4. Akobeng AK, Zhang D, Gordon M, MacDonald JK. Enteral nutrition for maintenance of remission in Crohn's disease. *Cochrane Database Syst Rev*. 2018;8(8):CD005984.
5. Critch J, Day AS, Otley A, et al. Use of enteral nutrition for the control of intestinal inflammation in pediatric Crohn disease. *J Pediatr Gastroenterol Nutr*. 2012;54(2):298-305.
6. Forbes A, Escher J, Hebuterne X, et al. ESPEN guideline: clinical nutrition in inflammatory bowel disease. *Clin Nutr*. 2017;36(2):321-347.
7. Akobeng AK, Miller V, Stanton J, Elbadri AM, Thomas AG. Double-blind randomized controlled trial of glutamine-enriched polymeric diet in the treatment of active Crohn's disease. *J Pediatr Gastroenterol Nutr*. 2000;30(1):78-84.
8. Verma S, Holdsworth CD, Giaffer MH. Does adjuvant nutritional support diminish steroid dependency in Crohn disease? *Scand J Gastroenterol*. 2001;36(4):383-388.
9. Hanai H, Iida T, Takeuchi K, et al. Nutritional therapy versus 6-mercaptopurine as maintenance therapy in patients with Crohn's disease. *Dig Liver Dis*. 2012;44(8):649-654.
10. Takagi S, Utsunomiya K, Kuriyama S, et al. Effectiveness of an "half elemental diet" as maintenance therapy for Crohn's disease: a randomized-controlled trial. *Aliment Pharmacol Ther*. 2006;24(9):1333-1340.
11. Levine A, Wine E, Assa A, et al. Crohn's disease exclusion diet plus partial enteral nutrition induces sustained remission in a randomized controlled trial. *Gastroenterol*. 2019;157(2):440-450.e8.
12. Schwegler I, von Holzen A, Gutzwiller J-P, Schlumpf R, Mühlebach S, Stanga Z. Nutritional risk is a clinical predictor of postoperative mortality and morbidity in surgery for colorectal cancer. *Br J Surg*. 2010;97(1):92-97.
13. Ge X, Tang S, Yang X, et al. The role of exclusive enteral nutrition in the preoperative optimization of laparoscopic surgery for patients with Crohn's disease: a cohort study. *Int J Surg*. 2019;65:39-44.

14. Heerasing N, Thompson B, Hendy P, et al. Exclusive enteral nutrition provides an effective bridge to safer interval elective surgery for adults with Crohn's disease. *Aliment Pharmacol Ther*. 2017;45(5):660-669.

Chronic liver disease

Rationale

Patients with chronic liver disease, particularly those with hepatic cirrhosis or end-stage liver disease, possess a high risk of malnutrition, estimated to affect more than half of patients with cirrhosis.[1] Several hypothesized mechanisms for malnutrition may include hypermetabolism, protein catabolism, fat malabsorption, and impaired glycogen storage. The latter leads more readily to states of starvation and prompts gluconeogenesis to mobilize glucose from other macronutrients. Patients with cirrhosis may additionally experience altered taste and altered mental status from hepatic encephalopathy, which compromise oral nutrient intake. In these settings, EN can serve as an important source of nutrition for patients who cannot consume adequate energy and protein by mouth.

Different types of EN formulations have been explored for chronic liver disease. In particular, ESPEN guidelines have forwarded that formulas enriched with branched-chain amino acids (BCAA) are superior to those with standard whole protein for patients with hepatic encephalopathy.[2] An underlying rationale for the use of BCAA relates to the cirrhotic liver's impaired metabolism of aromatic amino acids (AAA), whose accumulation could lead to neurocognitive effects. By contrast, BCAAs do not rely on hepatic metabolism and compete with AAA for the same blood-brain transporters.[3] The ESPEN recommendations were primarily based on two randomized trials that found oral supplementation with BCAA improved health-related outcomes among patients with cirrhosis.[4,5] However, updated guidelines from ASPEN noted no advantage of BCAA-enriched formulas among patients with hepatic encephalopathy to whom first-line therapy of antibiotics or lactulose was administered. A more recent systematic review by the Cochrane Collaboration found that BCAA had beneficial effects on hepatic encephalopathy in 16 trials with 827 participants (graded as high quality of evidence).[6] Use of BCAA did not appear to affect mortality, quality of life, or nutrition status. Nonetheless, the optimal type of EN formula for chronic liver disease remains controversial.

REFERENCES

1. Cheung K, Lee SS, Raman M. Prevalence and mechanisms of malnutrition in patients with advanced liver disease, and nutrition management strategies. *Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc*. 2012;10(2):117-125.
2. Plauth M, Cabre E, Riggio O, et al. ESPEN guidelines on enteral nutrition: liver disease. *Clin Nutr*. 2006;25(2):285-294.
3. James JH, Ziparo V, Jeppsson B, Fischer JE. Hyperammonaemia, plasma aminoacid imbalance, and blood-brain aminoacid transport: a unified theory of portal-systemic encephalopathy. *Lancet*. 1979;2(8146):772-775.
4. Marchesini G, Bianchi G, Merli M, et al. Nutritional supplementation with branched-chain amino acids in advanced cirrhosis: a double-blind, randomized trial. *Gastroenterology*. 2003;124(7):1792-1801.
5. Muto Y, Sato S, Watanabe A, et al. Effects of oral branched-chain amino acid granules on event-free survival in patients with liver cirrhosis. *Clin Gastroenterol Hepatol Off Clin Pract J Am Gastroenterol Assoc*. 2005;3(7):705-713.
6. Gluud LL, Dam G, Les I, et al. Branched-chain amino acids for people with hepatic encephalopathy. *Cochrane Database Syst Rev*. 2017;5(2):CD001939.

Acute pancreatitis

Rationale

Acute pancreatitis represents the third most common GI diagnosis at hospital discharge.[1] By far the majority of cases (approximately 80%–90%) are mild/moderate, and overall, the risk of mortality is <5%. However, mortality rises steeply to 25% in adults who develop severe necrotizing pancreatitis.[1] Given the significance of SAP, research has focused most often on patients predicted to develop SAP at the time of hospital admission. In this population, there are consistent and longstanding global recommendations for the use of EN.[2] This systematic review of 11 international society guidelines published prior to 2009 (including by ASPEN and ESPEN) endorsed the use of nutrition support only for SAP and the use of EN over PN.[2] Recommendations were based on high levels of evidence in predicted SAP and have not changed with subsequent trial data or meta-analyses.[3] Although it had been traditional dogma "to rest the pancreas," evidence indicated increased risks when using PN in SAP, particularly for hyperglycemia and sepsis.[4] By contrast, early EN (vs delayed EN) has now been associated with decreased risk of infection, multiorgan failure, pancreatic necrosis, and infected necrosis.[3] This may relate to the direct benefit of luminal nutrients on intestinal barrier and immune function, rather than simply to the absence of PN.

Recent research has focused on addressing the specifics of EN support where consensus has not been universally achieved and guidelines were unclear. In contrast to the early guidelines,[2] early EN (within 48 h) compared with delayed oral nutrition or EN appears to be beneficial.[5-8] Furthermore, newer data support safe oral feeding within 24 h of admission.[9] In short, in SAP there is no longer a role for prescribing nil per os. Current evidence suggests NG feeds can be tolerated in SAP and does not support the superiority of the NJ route in terms of nutrition or disease outcomes.[10,11] The use of jejunal feeding is primarily indicated when NG feeding is not tolerated. Finally, at this time, there is no evidence that semi-elemental formula should be used instead of a more cost-effective polymeric formula.[12] Immunonutrition cannot be endorsed without more supportive evidence from higher-quality trials.[12,13]

The guideline review by Mirtallo et al reported a strong global consensus that nutrition support was not necessary for mild/moderate acute pancreatitis.[2] They reported moderate global consensus, despite low-quality evidence, for initial use of nil per os orders in that population. Yet at the time, trials rarely included mild or moderate acute pancreatitis, and only recently has this gap been addressed. Mild or moderate acute pancreatitis is anticipated to have a good outcome. Early nutrition by oral or enteral routes can reduce the length of hospital stay in this population.[9,14-16] The appropriate oral diet requires further study, but limited available evidence does not support clear fluids over a solid food diet.[17]

Despite a high degree of consensus for some time for using EN and avoiding routine nil per os orders in SAP, adherence to guidelines has been an ongoing concern.[18,19] It is plausible that difficulty in managing enteral tolerance is one of the factors leading to poor knowledge translation of nutrition guidelines. Optimizing understanding of predictors of enteral tolerance and development of strategies to address this common problem are key future research directions.[20] Future guidelines should also include specific nutrition recommendations in acute pancreatitis for common high-risk groups, both those who are undernourished, such as alcoholics, and those with obesity. The role of supplemental PN when EN fails because of poor tolerance, particularly in these high-risk adult populations and in children, will need to be clarified.

REFERENCES

1. Lowenfels AB, Maisonneuve P, Sullivan T. The changing character of acute pancreatitis: epidemiology, etiology, and prognosis. *Curr Gastroenterol Rep*. 2009;11(2):97-103.
2. Mirtallo JM, Forbes A, McClave SA, Jensen GL, Waitzberg DL, Davies AR; International Consensus Guideline Committee Pancreatitis Task Force. International consensus guidelines for nutrition therapy in pancreatitis. *JPEN J Parenter Enteral Nutr*. 2012;36(3):284-291.
3. Crockett SD, Wani S, Gardner TB, Falck-Ytter Y, Barkun AN. American Gastroenterological Association Institute Clinical Guidelines Committee. American Gastroenterological Association Institute guideline on initial management of acute pancreatitis. *Gastroenterology*. 2018;154(4):1096-1101.
4. Petrov MS, Whelan K. Comparison of complications attributable to enteral and parenteral nutrition in predicted severe acute pancreatitis: a systematic review and meta-analysis. *Br J Nutr*. 2010;103(9):1287-1295.
5. Bakker OJ, Besselink MG, Gooszen HG. Early versus on-demand tube feeding in pancreatitis. *N Engl J Med*. 2015;372(7):684-685.
6. Stimac D, Poropat G, Hauser G, et al. Early nasojejunal tube feeding versus nil-by-mouth in acute pancreatitis: a randomized clinical trial. *Pancreatology*. 2016;16(4):523-528.
7. Vaughn VM, Shuster D, Rogers MAM, et al. Early versus delayed feeding in patients with acute pancreatitis: a systematic review. *Ann Intern Med*. 2017;166(12):883-892.
8. Song J, Zhong Y, Lu X, et al. Enteral nutrition provided within 48 hours after admission in severe acute pancreatitis: a systematic review and meta-analysis. *Medicine (Baltimore)*. 2018;97(34):e11871.
9. Márta K, Farkas N, Szabó I, et al. Meta-analysis of early nutrition: the benefits of enteral feeding compared to a nil per os diet not only in severe, but also in mild and moderate acute pancreatitis. *Int J Mol Sci*. 2016;17(10):1691.
10. Nally DM, Kelly EG, Clarke M, Ridgway P. Nasogastric nutrition is efficacious in severe acute pancreatitis: a systematic review and meta-analysis. *Br J Nutr*. 2014;112(11):1769-1778.
11. Chang YS, Fu HQ, Xiao YM, Liu JC. Nasogastric or nasojejunal feeding in predicted severe acute pancreatitis: a meta-analysis. *Crit Care*. 2013;17(3):R118.
12. Petrov MS, Loveday BP, Pylypchuk RD, McIlroy K, Phillips AR, Windsor JA. Systematic review and meta-analysis of enteral nutrition formulations in acute pancreatitis. *Br J Surg*. 2009;96(11):1243-1252.
13. Poropat G, Giljaca V, Hauser G, Štimac D. Enteral nutrition formulations for acute pancreatitis. *Cochrane Database Syst Rev*. 2015;25(3):CD010605.
14. Li J, Xue GJ, Liu YL, et al. Early oral refeeding wisdom in patients with mild acute pancreatitis. *Pancreas*. 2013;42(1):88-91.
15. Petrov MS, McIlroy K, Grayson L, Phillips AR, Windsor JA. Early nasogastric tube feeding versus nil per os in mild to moderate acute pancreatitis: a randomized controlled trial. *Clin Nutr*. 2013;32(5):697-703.
16. Vaughn VM, Shuster D, Rogers MAM, et al. Early versus delayed feeding in patients with acute pancreatitis: a systematic review. *Ann Intern Med*. 2017;166(12):883-892.
17. Rajkumar N, Karthikeyan VS, Ali SM, Sistla SC, Kate V. Clear liquid diet vs soft diet as the initial meal in patients with mild acute pancreatitis: a randomized interventional trial. *Nutr Clin Pract*. 2013;28(3):365-370.
18. Dua MM, Worhunsky DJ, Tran TB, et al. Severe acute pancreatitis in the community: confusion reigns. *J Surg Res*. 2015;199(1):44-50.
19. Greenberg JA, Hsu J, Bawazeer M, et al. Compliance with evidence-based guidelines in acute pancreatitis: an audit of practices in University of Toronto hospitals. *Gastrointest Surg*. 2016;20(2):392-400.
20. Bevan MG, Asrani VM, Bharmal S, Wu LM, Windsor JA, Petrov MS. Incidence and predictors of oral feeding intolerance in acute pancreatitis: a systematic review, meta-analysis, and meta-regression. *Clin Nutr*. 2017;36(3):722-729.

4. What are the indications for enteral feedings in patients with specific non-GI diseases?

Recommendations

A. Evaluate all patients who have had a stroke for dysphagia as early as possible to establish route of nutrition support.
   i. Initiate EN using an NGT in a patient who has had a stroke, for whom oral intake has been deemed unsafe, and who is not likely to recover within 7 days. Evaluate the patient for a nasal tube retaining system to reduce the risk of tube displacement.
   ii. Consider placement of a PEG tube in patients with persistent inability to swallow safely for >2–4 weeks.

B. Initiate EN support in adult patients with CF and malnutrition who are unable to meet their nutrition needs with diet and oral supplements alone.

C. Initiate EN in malnourished patients with CKD who are unable to meet nutrition needs with diet and oral supplements alone. This includes patients who are not on dialysis and patients on either intermittent hemodialysis (HD) or peritoneal dialysis (PD).

D. Initiate EN in malnourished or at-risk patients with COPD if energy and protein requirements cannot be achieved through oral diet combined with oral nutrition supplements.

Stroke

Rationale

Swallowing requires multiple neurologic inputs to perform adequately. Strokes may damage these circuits.[1] Feeding of a patient who has had a stroke should be performed around the time of hospital admission, depending on the patient's condition and medical/surgical history. If the gut is functional and there are no other contraindications, EN is preferred.[2] Dysphagia is common after a stroke, occurring in about 25%–50% of all patients who have had a stroke, and can impair safe oral intake, leading to poorer outcomes (malnutrition, aspiration pneumonia, dehydration).[3-5] Katzan et al found that pneumonia was not uncommon in hospitalized patients who have had an acute stroke (5.6%), increasing hospital cost per patient by $15,000.[6] Dysphagia after a stroke increases the odds of being malnourished.[7] However, it was suggested that the relationship may not be causal. Although the greatest determinants of swallowing function are stroke size and location, the dysphagia is also an indicator of greater stroke severity. For prognostic purposes, early detection of stroke-related dysphagia and implementation of appropriate nutrition interventions (eg, modified diet, oral nutrition supplements, tube feeding) are cornerstones in the treatment of stroke.

EN may represent the sole or supplemental source of nutrition following a stroke. EN as the sole source of nutrient intake is reserved for patients for whom oral feeding is considered unsafe. However, patients without dysphagia may also be candidates for EN in the presence of malnutrition and inadequate oral intake. About 10%–30% of all patients are tube fed in the early phase of stroke.[8] Guidelines recommend EN using an NGT if oral intake is not likely to be recovered within 7 days.[8-11] It is often difficult to estimate how long patients who have had a stroke will require enteral access. Predicting the duration of post-stroke dysphagia remains imprecise, mainly relying on clinicians' experience and risk assessment.[12] Various risk factors for prolonged swallowing problems have been identified in the literature, including age, bilateral infarcts, signs of aspiration, and the National Institutes of Health Stroke Scale (NIHSS). A large percentage of patients receiving EN in the acute period of stroke will likely return to oral feeding within 3 months.[13] Galovic and colleagues recently developed and validated a prognostic model (predictive swallowing score [PRESS]) to predict swallowing recovery and guide the EN decision in patients with ischemic stroke dysphagia.[12] This study postulated a five-area scoring system (age, stroke severity on admission, stroke location, initial risk of aspiration, and initial impairment of oral intake) was effective in predicting the return of swallow function.[12]

NGT feeding is not without risk and can be associated with tube misplacement, local ulcerations, discomfort, and the need to restrain.[2,10] Patients should be considered for a nasal tube retaining system or nasal bridle when they are at risk of inadvertent NGT removal or require frequent tube replacement.[11] Aspiration is one of the risks associated with nasal feeding tube dislodgment, especially if the tube becomes only partially displaced, in which feeding would be introduced into the pharynx or upper esophagus, for an undetected over a period of time.[14] Nasal bridles have been shown to be safe, well tolerated, and effective at delivering full EN.[15,16]

Stroke guidelines recommend time-limited trials of NGT feeding, typically 2–4 weeks, prior to PEG tube placement.[8,9,11] Limited data are available on the specific timing of PEG tube placement and factors that impact the timing of tube placement. Most studies do not incorporate how often a discussion of PEG tube placement occurs for stroke admissions or insight into the patient/family discussions, which often lead to the shared decision of PEG tube placement. A retrospective observational study of 34,623 patients with acute ischemia and stroke showed that more than half (53%) received their PEG tubes within 7 days of admission and that age was the greatest determinant of early PEG tube placement (≥85 vs 18–54 years), suggesting a mismatch between practice reality and stroke guidelines.[17] In another study, later placement of PEG tubes (median 17 days from admission to tube placement) was associated with a lower 30-day mortality but higher severe disability at discharge.[18] A Cochrane review analyzing 33 RCTs ($n = 6779$) was performed to assess dysphagia treatment, feeding strategies and timing, fluid supplementation, and the effects of nutrition supplementation on patients with acute or subacute stroke. Results suggested that PEG and NGT feedings do not differ in terms of case fatality, death, or dependency, but PEG is associated with fewer treatment failures, less GI bleeding, and greater nutrition delivery.[4]

REFERENCES

1. Martino R, Foley N, Bhogal S, Diamant N, Speechley M, Teasell R. Dysphagia after stroke: incidence, diagnosis, and pulmonary complications. *Stroke*. 2005;36(12):2756-2763.
2. Kirby DF, DeLegge MH, Fleming CR. American gastroenterological association technical review on tube feeding for enteral nutrition. *Gastroenterology*. 1995;108(4):1282-1301.
3. Mann G, Hankey GJ, Cameron D. Swallowing function after stroke: prognosis and prognostic factors at 6 months. *Stroke*. 1999;30(4):744-748.
4. Geeganage C, Beavan J, Ellender S, Bath PM. Interventions for dysphagia and nutritional support in acute and subacute stroke. *Cochrane Database Syst Rev*. 2012;10:CD000323.
5. Davalos A, Ricart W, Gonzalez-Huix F, et al. Effect of malnutrition after acute stroke on clinical outcome. *Stroke*. 1996;27(6):1028-1032.
6. Katzan IL, Dawson NV, Thomas CL, Vortruba ME, Cebul RD. The cost of pneumonia after stroke. *Neurology*. 2007;68(22):1938-1943.
7. Foley NC, Martin RE, Salter KL, Teasell RW. A review of the relationship between dysphagia and malnutrition following stroke. *J Rehabil Med*. 2009;41(9):707-713.
8. Wirth R,Smoliner C, Jäger M, Warnecke T, Leischker AH, Dziewas R; DGEM Steering Committee. Guideline clinical nutrition in patients with stroke. *Exp Transl Stroke Med*. 2013;5(1):14.
9. Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke. *Stroke*. 2019;50(12):e344-e418.

10. Dennis M, Lewis S, Cranswick G, Forbes J; FOOD Trial Collaboration. FOOD: a multicentre randomized trial evaluating feeding policies in patients admitted to hospital with a recent stroke. *Health Technol Assess*. 2006;10(2):iii-iv, ix-x, 1-120.
11. Burgos R, Breton I, Cereda E, et al. ESPEN guideline clinical nutrition in neurology. *Clin Nutr*. 2018;37(1):354-396.
12. Galovic M, Stauber AJ, Leisi N, et al. Development and validation of a prognostic model of swallowing recovery and enteral tube feeding after ischemic stroke. *JAMA Neurol*. 2019;76(5):561-570.
13. Ickenstein GW, Stein J, Ambrosi D, Goldstein R, Horn M, Bogdahn U. Predictors of survival after severe dysphagic stroke. *J Neurol*. 2005; 252(12):1510-1516.
14. Boullata J, Carrera AL, Harvey L, et al. ASPEN safe practices for enteral nutrition therapy. *JPEN J Parenter Enteral Nutr*. 2017;41(1): 15-103.
15. Anderson MR, O'Connor M, Mayer P, O'Mahony D, Woodward J, Kane K. The nasal loop provides an alternative to percutaneous endoscopic gastrostomy in high-risk dysphagic stroke patients. *Clin Nutr*. 2004;23(4):501-506.
16. Beavan J, Conroy SP, Harwood R, et al. Does looped nasogastric tube feeding improve nutritional delivery for patients with dysphagia after acute stroke? A randomized controlled trial. *Age Ageing*. 2010; 39(5):624-630.
17. George BP, Kelly AG, Albert GP, Hwang DY, Holloway RG. Timing of percutaneous endoscopic gastrostomy for acute ischemic stroke: an observational study from the US nationwide inpatient sample. *Stroke*. 2017;48(2):420-427.
18. Joundi RA, Saposnik G, Martion R, Fang J, Kapral MK. Timing of direct enteral tube placement and outcomes after acute stroke. *J Stroke Cerebrovasc Dis*. 2019;28(12):104401.

Cystic fibrosis

Rationale

Individuals with CF are at risk for malnutrition owing to decreased appetite and oral intake related to abdominal pain, reflux, gastroparesis, constipation, and declining respiratory status, as well as malabsorption.[1,2] The incidence of adult CF patients with malnutrition, defined as BMI <19 kg/m^2, has been found to range from 9.5% to 22%.[2,3] Multiple studies in patients with CF have shown that a higher severity of lung disease results in a lower BMI, poor nutrition status, and higher rates of mortality.[1-4] Several studies indicate that CF patients who maintained at a higher BMI and stable nutrition status are found to have improved pulmonary function.[3-6]

The use of EN in malnourished adult CF patients has been associated with improved nutrition status through increased energy intake, increased lean mass, and weight and BMI stabilization.[1,5,7,8] EN support is recommended in adult CF patients with moderate to severe malnutrition who are unable to meet their nutrition needs through diet and oral nutrition supplements alone.[1,2,4,5] The use of nocturnal EN to promote oral intake during the day should be a first-line approach.[3,4,7,9] Whereas the use of a nasoenteric tube is acceptable for short-term use, patients expected to use EN >3 months should have a percutaneous endoscopic or radiologically placed feeding tube placed to minimize complications associated with a surgically placed feeding tube.[7] Gastric feeds should be considered first line unless patient-specific factors indicate the need for jejunal feeds, such as gastroparesis, severe reflux, or pancreatitis.[6,7] Consistent information has been published indicating that starting EN prior to the development of severe lung disease has resulted in more successful outcomes than when EN is initiated in patients with advanced or end-stage pulmonary disease.[3,5]

REFERENCES

1. Schindler T, Michel S, Wilson AWM. Nutrition management of cystic fibrosis in the 21st century. *Nutr Clin Pract*. 2015;30(4):488-500.
2. Hollander FM, de Roos NM, van Meerkerk GB, van Berkhout FT, Heijerman HGM, van de Graaf EA. Body weight and body mass index in patients with end-stage cystic fibrosis stabilize after the start of enteral tube feeding. *J Acad Nutr Diet*. 2017;117(11): 1808-1815.
3. Erskine JM, Lingard C, Sontag M. Update on enteral nutrition support for cystic fibrosis. *Nutr Clin Pract*. 2007;22(2):223-232.
4. Turck D, Braegger CP, Colombo C, et al. ESPEN-ESPGHAN-ECFS guidelines on nutrition care for infants, children, and adults with cystic fibrosis. *Clin Nutr*. 2016;35(3):557-577.
5. Shimmin D, Lowdon J, Remmington T. Enteral tube feeding for cystic fibrosis (review). *Cochrane DB Syst Rev*. 2019;7(7):CD001198.
6. Sullivan JS, Mascarenhas MR. Nutrition: prevention and management of nutritional failure in cystic fibrosis. *J Cyst Fibros*. 2017; 16(suppl 2):S87-S93.
7. Schwarzenberg SJ, Hempstead SE, McDonald CM, et al. Enteral tube feeding for individuals with cystic fibrosis: cystic fibrosis foundation evidence-informed guidelines. *J Cyst Fibros*. 2016;15(6):724-735.
8. White H, Morton AM, Conway SP, Peckham DG. Enteral tube feeding in adults with cystic fibrosis; patient choice and impact on long term outcomes. *J Cyst Fibros*. 2013;12(6):616-622.
9. Nguyen DL. Guidance for supplemental enteral nutrition across patient populations. *Am J Manag Care*. 2017;23(12 suppl): S210-S219.

Chronic obstructive pulmonary disease

Rationale

Chronic obstructive pulmonary disease (COPD) is a common disease characterized by ongoing respiratory symptoms due to airway abnormalities.[1] In 2015, global prevalence was estimated to be approximately 13.1%, and an estimated 3.2 million individuals died of the disease.[2]

Malnutrition is common in COPD, with prevalence rates ranging based on how malnutrition is defined. A recent 2021 cohort evaluation of hospitalized patients with COPD identified a prevalence of moderate and severe malnutrition of 50% by using subjective global assessment and 54.4% by using the Academy/ASPEN consensus diagnostic tools.[3] Common attributes include weight loss and muscle wasting, which has been associated with an accelerated decline of functional status, leading to unfavorable outcomes such as higher mortality.[4] Multiple etiologies contribute to malnutrition in COPD and are often a function of the individual patient's disease severity. Increased energy expenditure is frequent in COPD and is related to increased work of breathing.[5] In addition, COPD is

recognized as an inflammatory disorder with increased circulating cytokines, known to impact weight and appetite.[6] Other contributors to malnutrition include early satiety, age-related factors (loss of taste, poor dentition), and medication use, specifically steroids.[4,7]

Few studies exist evaluating the use of EN in COPD. A 2021 evaluation demonstrated the benefit of a 2-week course of EN compared with oral diet alone in hospitalized patients with COPD requiring noninvasive ventilatory therapy. Outcome parameters evaluated were immunologic and cardiopulmonary variables. Inflammatory measures, including levels of high-sensitivity C-reactive protein and procalcitonin, were significantly lower in the group receiving EN compared with the control ($P < 0.001$ for both). Arterial oxygen and carbon dioxide levels were significantly improved in the intervention group compared with those of the controls ($P < 0.0001$ for both).[8] A very early small study ($n = 10$) in malnourished patients with COPD demonstrated that 16 days of EN compared with minimal oral intake (approximately 100 kcal/day) resulted in greater weight gain and improved maximal expiratory pressure compared with that in controls.[9]

The majority of existing evidence supports the use of oral nutrition supplements in stable and malnourished COPD patients. A 2012 Cochrane review[10] included 17 studies evaluating nutrition supplementation in stable patients with COPD, compared with a usual diet. All but one study included oral supplementation, whereas one evaluated EN via tube feeding.[9] The authors concluded that moderate-quality evidence demonstrated nutrition supplementation promotes significant weight gain among patients with COPD, especially if malnourished (95% CI, 0.14–3.16).[10] Those well-nourished patients may not respond to the same degree to supplemental nutrients. The authors also identified a significant change from baseline of fat mass/fat mass index (95% CI, 0.04–1.09) and midarm muscle circumference (as a measure of lean body mass) (95% CI, 0.02–0.57).[10] In addition, there were significant improvements in respiratory muscle strength in those who received supplementation (95% CI, 4.91–20.55).[10] In a recent (2021) single RCT, Deutz et al demonstrated a mortality reduction for stable malnourished older adults with COPD who consumed a high-protein oral supplement containing beta-hydroxy-beta-methylbutyrate for up to 90 days after hospital discharge. Mortality was 71% lower compared with that of the control group, who did not consume the oral supplement ($P = 0.0395$).[11]

It is clear that nutrition supplementation of an oral diet in patients with COPD is beneficial. The use of EN, however, has not been well studied and therefore cannot be routinely recommended as a first-line treatment approach. Patients with COPD often experience eating difficulties that can impact their overall nutrient intake. Appetite is frequently decreased related to both the disease's inflammatory process and increased work of breathing.[12] A recent evaluation in patients with COPD and long-term oxygen therapy in Poland demonstrated from a 3-day food record that in 51.8% of participants, energy consumption was less than the recommended standards.[13] A stepwise approach to nutrition management in COPD as is outlined by the British Association of Parenteral and Enteral Nutrition (BAPEN) includes a step for EN initiation if nutrition goals are not met with a combination of an oral diet and oral nutrition supplements.[14]

REFERENCES

1. Global Initiative for Chronic Obstructive Lung Disease. 2021. Accessed December 6, 2021. www.goldcopd.org
2. GBD 2015 Chronic Respiratory Disease Collaborators. Global, regionals and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990-2015; a systematic analysis for the global burden of disease study 2015. *Lancet Respir Med*. 2017;5(9);691-706.
3. Araújo BE, Kowalski V, Leites GM, da Silva Fink J, Silva FM. AND-ASPEN and ESPEN consensus, and GLIM criteria for malnutrition identification in AECOPD patients: a longitudinal study comparing concurrent and predictive validity. *Eur J Clin Nutr*. Accepted manuscript. Published online October 26, 2021. doi:10.1038/s41430-021-01025-x
4. Rawal G, Yadav S. Nutrition in chronic obstructive pulmonary disease: a review. *J Transl Int Med*. 2015;3(4):151-154.
5. Wilson DO, Donahoe M, Rogers, RM, Pennock BE. Metabolic rate and weight loss in chronic obstructive lung disease. *JPEN J Parenter Enter Nutr*. 1990;14(1):7-11.
6. Koehler F, Doehner W, Hoernig S, Witt C, Anker SD, John M. Anorexia in chronic obstructive pulmonary disease-association to cachexia and hormonal derangement. *Int J Cardiol*. 2007;119(1):83-89.
7. Collins PF, Yang IA, Chang YC, Vaughan A. Nutritional support in chronic obstructive pulmonary disease (COPD): an evidence update. *J Thorac Dis*. 2019;11(suppl 17):S2230-S2237.
8. Zhang C, Ren D, Ouyang C, et al. Effect of standardized enteral nutrition on AECOPD patients with respiratory failure. *Am J Transl Res*. 2021;13(9):10793-10800.
9. Whittaker JS, Ryan CF, Buckley PA, Road JD. The effects of refeeding on peripheral and respiratory muscle function in malnourished chronic obstructive pulmonary disease patients. *Am Rev Respir Dis*. 1990;142(2):283-288.
10. Ferreira IM, Brooks D, White J, Goldstein R. Nutritional supplementation for stable chronic obstructive pulmonary disease (Review). *Cochrane Database Syst Rev*. 2012,12:CD000998.
11. Deutz NE, Ziegler TR, Matheson EM, et al. Reduced mortality risk in malnourished hospitalized older adult patients with COPD treated with a specialized oral nutritional supplement: Sub-group analysis of the NOURISH study. *Clin Nutr*. 2021;40(3):1388-1395.
12. Itoh M, Tsuji T, Nemoto K, et al. Undernutrition in patients with COPD and its treatment. *Nutrients*. 2013;5(4):1316-1335.
13. Mekal D, Czerw A, Deptala A. Dietary behaviour and nutrition in patients with copd treated with long-term oxygen therapy. *Int J Environ Res Public Health*. 2021;18(23):12793.
14. Managing malnutrition in COPD. 2nd ed. 2020. Accessed December 15, 2021. https://www.malnutritionpathway.co.uk/library/mm_copd.pdf

Chronic renal disease

Rationale

Literature on the use of EN in adult patients with chronic renal disease is sparse, with very few studies, recent or in the past, evaluating the use of EN in adult patients with renal disease. When evaluating the need for EN in patients with chronic renal disease, one

must consider not only a patient's need for dialysis but also the type of dialysis the patient is receiving.

Patients with stage 5 CKD have been found to have higher levels of inflammatory cytokines, which may lead to decreased appetite, increased weight loss, and decreased serum albumin levels.[1-3] Decreased nutrient intake in CKD has been linked to uremia, taste abnormalities, and decreased appetite, among other factors.[3] Protein-energy wasting or malnutrition in CKD may be indicated by a decreased serum albumin level and weight loss.[2] There has been documentation that a decreased serum albumin level in patients with CKD can lead to increased mortality.[1-3] Patients with stage 5 CKD should be identified as nutritionally at risk by increasing trends of serum albumin and C-reactive protein levels.[1] This will allow for identification of individuals for whom nutrition support should be considered.

If initial interventions with dietary counseling and oral nutrition supplements do not improve nutrition status and outcomes, or worsening of nutrition status occurs, then EN via feeding tube is recommended.[2,4] Patients who have severe malnutrition, have an energy intake of <20 kcal/kg/day, experience an increased stress response, or have swallowing issues should have EN support initiated.[3]

ESPEN recommends EN in patients who are not able to meet their needs orally or in those who are diagnosed as malnourished.[3,4] EN may be provided as supplemental nocturnal feeds in patients who are not meeting their full needs by mouth, or as a complete daily provision of required nutrients in patients who are unable to tolerate oral nutrition or experiencing catabolic acute conditions.[3,4] Although a lack of studies exists regarding the nutrient requirements and need for nutrition support in elderly patients with CKD, the prevalence of uremia in patients over 75 years of age is increasing.[4] Therefore, any elderly patients experiencing decreased nutrition intake or signs of malnutrition should be considered a candidate for initiation of EN.

Chronic HD can lead to decreased protein and energy intake, resulting in malnutrition.[5] Malnutrition has been found in up to 50%–75% of patients with CKD who are on HD.[6,7] This may be related to inflammation, decreased protein and/or energy intake, or uremia.[6] Although there is limited data indicating the benefits of EN in adult patients with renal disease, recommendations exist for early identification of malnutrition and initiation of EN to aid in improving nutrition status.[2,8,9] The recommendations from the results of these studies were for use of EN via NGT or PEG tube.[2] In patients with gastroparesis for whom prokinetic therapy has failed, administration of EN via an NJT or percutaneous endoscopic jejunostomy (PEJ) should be considered.[4] Studies have shown that nutrition support with supplemental EN in patients on HD can lead to improvements in serum albumin level and prevent or correct malnutrition.[2,7,8] One trial of EN use in malnourished patients on HD who did not improve with oral supplements or intradialytic PN showed significant improvements in weight, midarm circumference, triceps skinfold thickness, and serum albumin level at 3 months.[9] A second study of patients with CKD on HD received partial or full nutrition needs with EN via NGT or PEG tube, with results showing significant improvement in serum albumin levels and suggesting an improvement in the nutrition status of the patients.[7]

ESPEN recommends that malnourished patients with CKD requiring maintenance HD be started on supplemental EN based on low BMI, weight loss, and low serum albumin or prealbumin levels.[4] In addition, patients with CKD on HD who are hypercatabolic or are unable to maintain adequate nutrition with dietitian counseling and oral nutrition supplements should be considered candidates for EN.[4]

Patients on chronic PD have increased protein losses, which increase the need for dietary protein.[10] In addition, patients on PD were found to have impaired gastric emptying,[11] which can lead to decreased oral intake and declining nutrition status. Whereas studies of EN in patients on PD have been completed in pediatric patients, most of the information on adult patients on PD has been from case studies or abstracts.[4] Nutrition support should be initiated in malnourished patients on PD, based on the same nutrition indices as in patients on HD.[4] EN is indicated when adequate oral nutrition and supplements are insufficient to meet a patient's nutrition needs.[4] Because of an increased incidence of peritonitis, PEG/PEJ is contraindicated in adult patients on PD,[4] so the use of an NGT or NJT feed tube should be considered based on the patient's clinical status and associated conditions (eg, gastroparesis).

REFERENCES

1. Brown RO, Compher C. American Society for Parenteral and Enteral Nutrition Board of Directors. A.S.P.E.N. clinical guidelines: nutrition support in adult acute and chronic renal failure. *JPEN J Parenter Enteral Nutr*. 2010;34(4):366-377.
2. Kalantar-Zadeh K, Cano NJ, Budde K, et al. Diets and enteral supplements for improving outcomes in chronic kidney disease. *Nat Rev Nephrol*. 2011;7(7):369-384.
3. Sabatino A, Regolisti G, Gandolfini I, et al. Diet and enteral nutrition in patients with chronic kidney disease not on dialysis: a review focusing on fat, fiber and protein intake. *J Nephrol*. 2017;30(6):743-754.
4. Cano N, Fiaccadori E, Tesinsky P, et al. ESPEN guidelines on enteral nutrition: adult renal failure. *Clin Nutr*. 2006;25(2):295-310.
5. Caglar K, Fedje L, Dimmitt R, Hakim RM, Shyr Y, Ikizler TA. Therapeutic effects of oral nutritional supplementation during hemodialysis. *Kidney Int*. 2002;62(3):1054-1059.
6. Fouque D, Kalantar-Zadeh K, Kopple J, et al. A proposed nomenclature and diagnosis criteria for protein-energy wasting in acute and chronic kidney disease. *Kidney Int*. 2008;73(4):391-398.
7. Holley JL, Kirk J. Enteral tube feeding in a cohort of chronic hemodialysis patients. *J Ren Nutr*. 2002;12(3):177-182.
8. Kopple JD. Therapeutic approaches to malnutrition in chronic dialysis patients: the different modalities of nutritional support. *Am J Kidney Dis*. 1999;33(1):180-185.
9. Sayce HA, Rowe PA, McGonigle RJS. Percutaneous endoscopic gastrostomy feeding in haemodialysis out-patients. *J Hum Nutr Diet*. 2000;13(5):333-341.
10. Westra WM, Kopple JD, Krediet RT, Appell M, Mehrotra R. Dietary protein requirements and dialysate protein losses in chronic peritoneal dialysis patients. *Perit Dial Int*. 2007;27(2):192-195.
11. Van Vlem, BA, Schoonjans RS, Struijk DG, Verbanck JJ, Vanholder RC, Van Biesen WV, et al. Influence of dialysate on gastric emptying time in peritoneal dialysis patients. *Perit Dial Int*. 2002;22(1):32-38.

5. When to initiate early EN in hemodynamically unstable patients?

A. Vasopressor administration is not a contradiction to providing early EN with careful monitoring.
   i. Consider the following factors when administering EN concomitantly with vasopressor administration: type of vasopressor agent, vasopressor equivalent dosage, timing of EN, and feeding location.
   ii. Consider trophic only or holding EN if VDE score is >12.
   iii. Initiate EN within 48 h of vasopressor initiation depending on dosage (see recommendation ii).
   iv. Gastric feeding is preferred during vasopressor administration.
   v. Insufficient data exist to use lactate levels as a monitoring parameter for EN tolerance.
   vi. Routine monitoring of GRVs is not recommended in critical illness. If GRVs are measured, it would be reasonable to hold EN in adults if GRVs >300 ml based on limited, low-quality evidence.
   vii. EN may be administered in adults if the MAP is ≥60 mm Hg but should be held when the MAP < 50 mm Hg.

B. When feeding patients receiving vasopressors, use a 1.0–1.2 kcal/ml, higher-protein, low-fiber formula. Both semi-elemental and polymeric formulas are tolerated.

C. Initiate EN within the first 24 h of ECMO support.
   i. Initiate EN as continuous intragastric feeding at trophic rate of 10–20 ml/h and increase rate every 4 h over 24–36 h to target rate.
   ii. Continue to provide EN infusion if patients on VA or VV ECMO are placed in prone position.
   iii. Develop and implement clear and comprehensive guidelines for the initiation and maintenance of EN support for patients on VA or VV ECMO.

Clinical monitoring parameters on vasopressors

Rationale

Controversy exists on whether to provide EN while a patient is receiving vasopressor support. This confusion most likely exists as a result of positive and negative perfusion that occurs following the administration of vasopressor support.[1] Vasopressors are often used in critically ill patients when the blood pressure is dropping dangerously low, as well as in patients with sepsis to help maintain adequate hemodynamic parameters, such as MAP.[2] Vasopressors, such as norepinephrine and epinephrine, function by shunting blood to the heart away from other organs. This raises blood pressure but also leaves the nonvital organs, such as the GI tract, with reduced blood flow and may result in necrosis, although unlikely.[3] This small risk of decreased GI blood flow with vasopressor therapy is why EN is often not recommended by practitioners for patients who are currently receiving vasopressor support.[3]

Vasopressors used concomitantly with EN are associated with nonocclusive bowel necrosis in hemodynamically unstable patients with critical illness. The incident of bowel ischemia, however, is very low at ~1%,[4-7] suggesting administration of EN while receiving IV vasopressors appears to be relatively safe.[1] Signs of small-bowel necrosis may include sudden massive abdominal distention, pain, bloating, cramps, high NGT output, signs of ileus, intramural bowel gas, hypotension, and tachycardia.[3,5,6] Bowel sounds and bowel movements are also important to monitor, as a decrease in either one may be an early predictor of bowel ischemia.[1]

Consider the type of vasopressor when administering EN. Not all vasopressors have the same mechanism of action. Studies report varied enteral tolerance depending on the type of vasopressor used (Table 2). Dopamine, epinephrine, phenylephrine, and vasopressin typically decrease GI blood flow.[8] Epinephrine, norepinephrine, and phenylephrine have all been shown to increase MAP.[8] Epinephrine and norepinephrine increase cardiac output but reduce intestinal blood flow. In one evaluation, epinephrine lowered splanchnic blood flow; however, concomitant use of dobutamine and norepinephrine appeared to have no effect on blood flow.[1,2]

The inotropes dobutamine and milrinone, when used by themselves, increase cardiac index and GI blood flow.[3] As a result, enteral intolerance is less likely if inotropes are used independently of vasopressors; thus, their use should not preclude the start of EN.[2] Dopamine is also an inotrope but has varied responses dependent on the dose administered and therefore should be considered similarly to vasopressors when determining whether EN should be initiated.[2]

A retrospective chart review evaluating enteral tolerability—defined as a GRV <300 ml without emesis, abnormal imaging findings, or evidence of bowel ischemia—in adult ICU patients receiving EN

TABLE 2 Vasopressors and inotropic agents and their action on the GI tract[3,8,9]

	GI blood flow	Mean arterial pressure	Cardiac output
Vasopressors			
Dopamine (inotropic agent considered as vasopressor for EN initiation)	↓		
Epinephrine	↓	↑	↑
Norepinephrine	↓	↑	↑
Phenylephrine	↓	↑	
Vasopressin	↓		
Inotropic agents			
Dobutamine	↑		↑
Milrinone	↑		↑

Abbreviations: EN, enteral nutrition; GI, gastrointestinal.

while concomitantly receiving IV vasopressors found enteral tolerability differed according to type of vasopressor administered (dopamine tolerated in 44 of 69 [63.8%], epinephrine tolerated in 35 of 53 [66.4%], norepinephrine tolerated in 203 of 273 [74.4%], phenylephrine tolerated in 24 of 24 [100%], and vasopressin tolerated in 33 of 56 [58.9%].[1] The study showed that there was no dose-dependent relationship between phenylephrine administration and EN tolerability; those who received phenylephrine were more likely to tolerate EN than those that did not (100% vs 73%, $P = 0.0023$).[1] A higher percentage of patients tolerated EN if they had never received dopamine (77.6% vs 63.8%, $P = 0.018$).

Mancl et al suggest monitoring for administration of phenylephrine as well as absence of dopamine and vasopressin administration because tolerability was higher if the patient never received them (dopamine tolerated in 215 of 277 [77.6%], vasopressin tolerated in 226 of 290 [77.9%].[1] Moreover, administration of dobutamine has been noted to confound the norepinephrine data regarding gastric perfusion.[2] Norepinephrine appears to be the most widely used vasopressor in the surgical and medical ICU (MICU), with vasopressin being the second most used vasopressor.[7]

Confusion may occur with vasopressors because of their complex function. For example, when epinephrine is administered during septic shock, its effects on splanchnic blood flow vary. However, most studies indicate it decreases blood flow to the gut, whereas data evaluating norepinephrine's impact on gut perfusion may be confounded if dobutamine is also administered.[2] Most authors advise to interpret results with caution because they are meant to be hypothesis generating for future studies that would provide support and guidance for clinicians.[1,8]

The vasopressor dosage administered may also impact tolerance. Studies have found a relationship between the norepinephrine dosage and EN tolerance. Studies have been conducted evaluating the impact of norepinephrine, epinephrine, phenylephrine, dopamine, and dobutamine on the GI system.[9] Mancl and Muzevich conducted a retrospective chart review evaluating enteral tolerance in adult ICU patients who received concomitant EN and IV vasopressor (dopamine, epinephrine, norepinephrine, phenylephrine, and/or vasopressin; $N = 346$).[1] An inverse relationship existed between maximum norepinephrine equivalent (NE) dose and EN tolerability. Those who tolerated EN received a lesser NE dose than those who did not tolerate EN (12.5 vs 19.4 mcg/min).[1] More recently, in 2017, another study utilized NE to evaluate EN tolerance in those with septic shock ($N = 120$).[8] Authors found EN was poorly tolerated when NE doses were >0.14 mcg/kg/min. There was a 70% likelihood of tolerating EN when NE doses were <0.14 mcg/kg/min. When EN was not tolerated, NE dose median was 0.14 mcg/kg/min, with 26% of the intolerant patients receiving two vasopressors (12 of 46 [26%]).[8]

VDE score[10] = the sum of

- norepinephrine dose (mcg/kg/min) × 100,
- epinephrine dose (mcg/kg/min) × 100,
- phenylephrine dose (mcg/kg/min) × 10,
- dopamine dose (mcg/kg/min) × 1,
- vasopressin dose (U/min) × 250,
- angiotensin II dose (mcg/kg/min) × 1000, and
- metarominol dose (mcg/kg/min) × 12.5.

Dopamine has been found to have different effects dependent on dosage; lower doses of 3–5 mcg/kg/min are associated with improved renal and mesenteric blood flow, moderate doses of 5–10 mcg/kg/min have inotropic and chronotropic effects, and high doses of 10–20 mcg/kg/min impact arterial circulation.[9] Low doses of dopamine appear relatively safe and are not thought to contribute to EN complications.[2]

An ICU study ($N = 70$) that evaluated enteral tolerability in cardiac surgery found an inverse relationship between EN and the dopamine and norepinephrine dosage.[11]

Timing of EN

Rationale

Many practitioners still hold EN when administering vasopressor support to minimize the risk of bowel ischemia.[9] However, there are benefits to early EN in those receiving vasopressor support. A reduction in mortality was noted in MICU ventilated patients who received EN within 48 h of intubation when compared with those who received EN later; the sickest patients (the ones receiving vasopressors) were more likely to benefit.[12]

Earlier studies with burn patients also found that early EN (defined as within 48–72 h) had similar benefits with decreased mortality in addition to little impact on splanchnic perfusion.[13,14] The timing of EN initiation mattered; when EN initiation was delayed, establishing EN tolerance was more difficult.[13] Unfortunately, earlier studies did not capture the impact vasopressors may have had on EN tolerability. A more recent study by Merchan et al did evaluate the timing of EN initiation in those receiving vasopressors and found it to be an important consideration.[8] ICU patients with sepsis who were receiving vasopressors and started EN early (within 48 h of vasopressor initiation) demonstrated better tolerance than those who started later (58 of 74 [78%] vs 22 of 46 [48%]; $P = 0.015$).[8] Although early EN may be beneficial, high-dose early EN is not recommended in unstable patients with shock.[15]

The EN location may impact EN tolerability. According to Mancl and Muzevich, EN tolerability was higher in those who were gastrically fed (328 of 346 [94.8%]) when compared with those receiving postpyloric feeding (18 of 346 [5.2%]).[1] A later study evaluating EN tolerability in patients with sepsis receiving vasopressors also found gastric feeding to be better tolerated; 62% of those receiving EN gastrically tolerated it (72 of 116).[8] To further support feeding gastrically, it is important to note that the majority of mesenteric ischemia cases associated with EN in surgery, trauma, and burn patients included feeding in the jejunum via surgically placed tubes; the incidence of nonocclusive bowel necrosis as a result of enteral jejunal feeding is reported to be 0.29%–1.15%.[4-6] This may be

due to the decreased mesenteric blood flow that may occur during postoperative hemodynamic instability, which increases risk for bowel ischemia when feeding in the small bowel. Gastric EN feeding is preferred, but if small-bowel EN is provided, monitor for GI intolerance, increasing NGT output, and abdominal distention/pain and constipation.[2,16]

Some suggest rising lactate levels may be useful in determining EN tolerability, as rising levels may help identify hypoperfusion and uncontrolled shock.[8] EN intolerability (as defined by vomiting, elevated GRVs >250–300 ml, abnormal findings on imaging, or bowel perforation) was present in 30%–46% of patients with a rising lactate level; 57%–60% of the patients had a lactate level >2 mg/dl.[1,8] The rising lactate levels were significantly associated with intolerance (odds ratio, 0.26; 95% CI, 0.09–0.74; $P = 0.012$).[8] However, once adjusted for confounders, statistical significance between lactate and EN tolerance was not maintained.[1] Recent case studies by Sabino et al also demonstrate that serum lactate levels are inconsistent before the onset of bowel ischemia and point out that elevations may be a delayed response to an existing ischemic bowel.[7] At this time, there are insufficient data to support utilizing lactate as a monitoring parameter.

A retrospective study ($N = 120$) of enteral tolerability in MICU patients with septic shock receiving vasopressor support found that a GRV >250 ml was the most common reason for enteral intolerance; 74% of those with enteral intolerance had a GRV >250 ml (34 of 46).[8] In a 2020 study by Sabino et al, GRVs >300 ml were almost three times more likely in those receiving EN and vasopressors ($N = 178$) when compared with those only receiving EN ($N = 141$) (20% vs 7%; $P < 0.01$).[7] Professional societies differ in opinion regarding GRVs. ASPEN/SCCM do not recommend routine measuring of GRV to monitor enteral tolerance but rather suggest monitoring for signs and symptoms (ie, abdominal distention/pain, increasing NGT output, and decreased bowel movements).[16] By contrast, Canadian guidelines do not appear to discourage the use of GRVs but are unable to define an amount at which to hold EN because of elevated GRVs.[17]

MAP may be used to determine whether to administer or hold enteral feeding. ASPEN/SCCM recommend administering EN when the patient is hemodynamically stable. One of the parameters to monitor the patient's stability is MAP. According to the guidelines, EN may be administered if the MAP is ≥60 mm Hg but should be held when the MAP <50 mm Hg.[16]

REFERENCES

1. Mancl EE, Muzevich KM. Tolerability and safety of enteral nutrition in critically ill patients receiving intravenous vasopressor therapy. *JPEN J Parenter Enteral Nutr*. 2013;37(5):641-651.
2. Wells DL. Provision of enteral nutrition during vasopressor therapy for hemodynamic instability: an evidence-based review. *Nutr Clin Pract*. 2012;27(4):521-526.
3. Yang S, Wu X, Yu W, Li J. Early enteral nutrition in critically ill patients with hemodynamic instability: an evidence-based review and practical advice. *Nutr Clin Pract*. 2014;29(1):90-96.
4. Schunn CD, Daly JM. Small bowel necrosis associated with postoperative jejunal tube feeding. *J Am Coll Surg*. 1995;180(4):410-416.
5. Spalding DRC, Behrannwala KA, Straker P, et al. Non-occlusive small bowel necrosis in association with feeding jejunostomy after elective upper gastrointestinal surgery. *Ann R Coll Surg Engl*. 2009;91(6):477-482.
6. Lawlor DK, Malthaner R II. Small bowel necrosis associated with jejunal tube feeding. *Can J Surg*. 1998;41(6):459-472.
7. Sabino KM, Fuller J, May S, et al. Safety and tolerance of enteral nutrition in the medical and surgical intensive care unit patient receiving vasopressors. *Nutr Clin Pract*. 2021;36(1):192-200.
8. Merchan C, Alshuler D, Aberle C, et al. Tolerability of enteral nutrition in mechanically ventilated patients with septic shock who require vasopressors. *J Intensive Care Med*. 2017;32(9):540-546.
9. Allen JM. Vasoactive substances and their effects on nutrition in the critically ill patient. *Nutr Clin Pract*. 2012;27(3):335-339.
10. Goradia S, Sardaneh AA, Narayan SW, Penm J, Patanwala AE. Vasopressor dose equivalence: a scoping review and suggested formula. *J Crit Care*. 2021;61:233-240.
11. Berger MM, Revelly JP, Cayeux MC, et al. Enteral nutrition in critically ill patients with severe hemodynamic failure after cardiopulmonary bypass. *Clin Nutr*. 2005;24(1):124-132.
12. Khalid I, Doshi P, digiovine B. Early enteral nutrition and outcomes of critically ill patients treated with vasopressors and mechancal ventilation. *Am J Crit Care*. 2010;19(3):261-268.
13. Raff T, Hartmann B, Germann G. Early intragastric feeding of seriously burned and long-term ventilated patients: a review of 55 patients. *Burns*. 1997;23(1)19-25.
14. Andel H, Rab M, Andel D, et al. Impact of early high caloric duodenal feeding on the oxygen balance of the splanchnic region after severe burn injury. *Burns*. 2001;27(4):389-393.
15. Van Zanten RH. Changing paradigms in metabolic support and nutrition therapy during critical illness. *Curr Opin Crit Care*. 2018;24(4):223-227.
16. Mcclave SA, Taylor BE, Martindale RG, et al. Society of Critical Care Medicine; American Society for Parenteral and Enteral Nutrition. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N). *JPEN J Parenter Enteral Nutr*. 2016;40(2):159-211.
17. Dhaliwal R, Cahil N, Lemieux M, et al. The Canadian critical care nutrition guidelines in 2013: an update on current recommendations and implementation stratefies. *Nutr Clin Pract*. 2014;29(1):29-43.

Feeding and vasopressors

Rationale

When feeding patients who are receiving vasopressors, the question arises as to which enteral formula will be best tolerated. Factors to consider include (1) the concentration of the formula (from 1.0 up to 2.0 kcal/ml), (2) the protein and fiber content, and (3) the composition (polymeric vs semi-elemental vs completely elemental). In evaluating the literature examining EN while patients are receiving vasopressors, a 1.0–1.2 kcal/ml, higher-protein, low-fiber formula appears to be well tolerated. In these studies, both semi-elemental and polymeric formulas were used.[1-4]

Revelly et al in 2001 provided a polymeric 1.0-kcal/ml formula containing 22% protein (no data on fiber content) and found that EN increased mesenteric GI blood flow with no evidence of gastric ischemia.[1] In 2005, Berger et al evaluated a polymeric 1–1.2 kcal/ml,

20% protein, fiber-free formula in patients receiving vasopressors and demonstrated no significant GI complications.[2] More recently, Patel et al in 2016 evaluated trophic feedings (<600 kcal/day) in patients with sepsis using a 1.2-kcal/ml, low-fiber formula (no data on composition or protein content) and found no significant GI complications.[3] By contrast, Mancl et al in 2013 evaluated formulas with a median energy density of 1.5 kcal/ml, with patients receiving an average of 58% of goal energy and demonstrating three ischemic bowel events (0.9%).[4] Similarly, in 2018, the TARGET investigators conducted a multicenter, double-blind, randomized trial to evaluate energy-dense (1.5 kcal/ml) vs energy-neutral (1.0 kcal/m) EN at a dose of 1 ml/kg of ideal body weight per hour in critically ill patients, 60% of whom received vasopressors.[5] Their results indicated meeting full energy provision with an increased feeding goal and energy-dense formulas (1.5 kcal/ml) does not improve patient outcome but rather increases GI symptoms (gastric residuals, vomiting, and need for promotility drugs) and hyperglycemia, compared with standard feedings (1.0 kcal/ml).[5] In 2020, Ong et al studied EN in patients requiring vasopressors using a semi-elemental, 1.2-kcal/ml, 25% protein, low-fiber formula and found no increased incidence of ischemic bowel.[6]

Providing a higher-protein formula when initiating EN in patients requiring vasopressors may be associated with improved outcomes, although the question of whether high-protein intakes are beneficial overall remains unanswered. In 2014, Yang et al reported that high-protein formulas generate a notable hyperemia effect to increase oxygen delivery to the gut; however, the impact of this effect is unclear.[7] This occurs by shunting systemic blood instead of increasing cardiac output.[7] Association of improved outcome with early higher protein intakes has been demonstrated by Koekkoek et al.[8] In their retrospective evaluation, a low protein intake (<0.8 g/kg) before day 3 and high protein after day 3 were associated with lower 6-month mortality.[8]

7. Yang S, Wu X, Yu W, Li J. Early enteral nutrition in critically ill patients with hemodynamic instability: an evidence-based review and practical advice. *Nutr Clin Pract*. 2014;29(1):90-96.
8. Koekkoek WA, van Setten CH, Olthof LE, Hans Kars JC, van Zanten AR. Timing of PROTein INtake and clinical outcomes of adult critically ill patients on prolonged mechanical VENTilation: The PROTINVENT retrospective study. *Clin Nutr*. 2019;38(2):883-890.

ECMO: VA or VV

Rationale

EN initiated with the first 24 h of VA or VV ECMO support appears to be safe and well tolerated without adverse events in adult patients compared with PN and helps to decrease gut barrier dysfunction and prevent bacterial translocation.[1,2] Patients who receive adequate EN with delivery of about 80% of nutrition goals of 25 kcal/kg and 1.2–1.5 g/kg/day protein within the first 7 days of VA and VV ECMO have significantly better outcomes and fewer complications compared with patients who received PN.[2-5] The use of medication paralysis and sedation during VA or VV ECMO does not appear to affect feeding tolerance significantly in terms of time to reach goal EN rate.[3,4] EN is not associated with harm but rather with lower mortality in patients with cardiogenic or obstructive shock requiring ECMO.[6] The key is to develop and implement clear and comprehensive guidelines for EN support in patients on VA or VV ECMO to maximize delivery and identify barriers to reaching nutrition goals.[1,4,5,7,8] The review of literature related to EN for patients on VA or VV ECMO shows that most studies were retrospective case reviews or prospective observational reviews, with most recommendations based on expert opinion with very low quality of evidence. The Extracorporeal Life Support Organization states that energy and protein support is essential to improve patient outcomes.

REFERENCES

1. Revelly JP, Tappy L, Berger MM, Gersbach P, Cayeux C, Chioléro R. Early metabolic and splanchnic responses to enteral nutrition in postoperative cardiac surgery patients with circulatory compromise. *Intensive Care Med*. 2001;27(3):540-547.
2. Berger M, Revelly JP, Cayeux MC, Chiolero RL. Enteral nutrition in critically ill patients with severe hemodynamic failure after cardiopulmonary bypass. *Clin Nutr*. 2005;24(1):124-132.
3. 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. *J Intensive Care Med*. 2016;31(7):471-477.
4. Mancl EE, Muzevich KM. Tolerability and safety of enteral nutrition in critically ill patients receiving intravenous vasopressor therapy. *JPEN J Parenter Enteral Nutr*. 2013;37(5):641-651.
5. TARGET Investigators, for the ANZICS Clinical Trials Group; Chapman M, Peake SL, Bellomo R, et al. Energy-dense versus routine enteral nutrition in the critically ill. *N Engl J Med*. 2018;379(19):1823-1834.
6. Ong C, Brown PM, Yesantharao P, et al. Vasoactive and inotropic support, tube feeding and ischemic gut complications after cardiac surgery. *JPEN J Parenter Enteral Nutr*. 2020;44(8):1461-1467.

REFERENCES

1. Blaser, AR, Starkopf J, Alhazzani W, et al. ESICM Working Group on Gastrointestinal Function. Early enteral nutrition in critically ill patients: ESICM clinical practice guidelines. *Intensive Care Med*. 2017;43(3):380-398.
2. Lu MC, Yang MD, Li PC, et al. Effects of nutritional intrvention on the survival of patients with cardiopulmonary failure undergoing extracorporeal membrane oxygenation therapy. *In Vivo*. 2018;32(4):829-834.
3. Ferrie S, Herkes R, Forrest P. Nutrition support during extracorporeal membrane oxygenation (ECMO) in adults: a retrospective audit of 86 patients. *Intensive Care Med*. 2013;39(11):1989-1994.
4. MacGowan L, Smith E, Elliott-Hammond C, et al. Adequacy of nutrition support during extracorporeal membrane oxygenation. *Clin Nutr*. 2019;38(1):324-331.
5. Scott L, Boudreaux K, Thaljeh F, Grier LR, Conrad SA. Early enteral feedings in adults receiving venovenous extracorporeal membrane oxygenation. *JPEN J Parenter Enteral Nutr*. 2004;28(5):295-300.
6. Ohbe H, Jo T, Yamana H, et al. Enteral nutrition for cardiogenic or obstructive shock requiring venoarterial extracorporeal membrane oxygenation: a nationwide inpatient database study. *Intensive Care Med*. 2018;44(8):1258-1265.

7. Lukas, G. Davies, A, Hilton AK, et al. Nutritional support in adult patients receiving extracorporeal membrane oxygenation. *Cri Care Resusc*. 2010;12(4):230-234.
8. Ridley EJ, Davies, AR, Robins EJ, et al. Nutrition therapy in adult patients receiving extracorporeal membrane oxygenation: a prospective, multicenter, observational study. *Crit Care Resusc*. 2015; 17(3):183-189.

6. Can patients receive EN when undergoing paralytic therapy?

A. Do not hold or delay EN in patients undergoing paralytic therapy.

Rationale

Feeding patients enterally who require the use of paralytics or neuromuscular blocking agents (NMBs) has been a subject of controversy in nutrition and critical care for decades. Hesitation to feed patients enterally revolved around the concerns for delayed gastric emptying and/or GI paralysis.[1] An earlier study by Tamion et al[2] using plasma paracetamol concentrations did not find any difference in gut absorptive capacity in mechanically vented, sedated patients requiring NMBs vs patients in the same population not requiring NMBs. A retrospective study by Ohbe et al[1] reviewed patients who started EN with 2 days of sustained neuromuscular blockade treatment to assess in-hospital mortality. Their results showed a significant decrease in mortality and length of hospital stay, with no differences noted in time on MV or hospital-acquired pneumonia.[1] Recent guidelines from the European Society of Intensive Care Medicine (ESICM) recommend that EN not be held or delayed simply because of the use of NMBs but that the critical condition requiring their use is taken into account.[3] The "Guidelines for the Management of Severe Traumatic Brain Injury, Fourth Edition" recommend initiating early EN (within 72 h of injury) and meeting estimated requirements by days 5–7 to decrease mortality.[4,5] Whereas NMBs should not have a paralytic effect on the smooth muscle of the GI tract, prokinetics can be considered to help counter slowed GI motility and optimize EN tolerance.[6]

REFERENCES

1. Ohbe H, Jo T, Matsui H, Fushimi K, Yasunaga H. Early enteral nutrition in patients undergoing sustained neuromuscular blockade: a propensity-matched analysis using a nationwide inpatient database. *Crit Care Med*. 2019;47(8):1072-1080.
2. Tamion F, Hamelin K, Duflo A, Girault C, Richard J-C, Bonmarchand G. Gastric emptying in mechanically ventilated critically ill patients: effect of neuromuscular blocking agent. *Intensive Care Med*. 2003;29(10):1717-1722.
3. Reintam Blaser A, Starkopf J, Alhazzani W, et al. ESICM Working Group on Gastrointestinal Function. Early enteral nutrition in critically ill patients: ESICM clinical practice guidelines. *Intensive Care Med*. 2017;43(3):380-398.
4. Kochanek PM, Tasker RC, Carney N, et al. Guidelines for the Management of Pediatric Severe Traumatic Brain Injury, Third Edition: update of the brain trauma foundation guidelines, executive summary. *Neurosurgery*. 2019;84(6):1169-1178.
5. Carney N, Totten AM, O'Reilly C, et al. Guidelines for the Management of Severe Traumatic Brain Injury, Fourth Edition. *Neurosurgery*. 2017;80(1):6-15.
6. Warr J, Thiboutot Z, Rose L, Mehta S, Burry LD. Current therapeutic uses, pharmacology, and clinical considerations of neuromuscular blocking agents for critically ill adults. *Ann Pharmacother*. 2011;45(9): 1116-1126.

7. Can patients be fed while on BiPAP and/or other noninvasive ventilation (NIV) treatments?

Recommendations

A. The decision to start EN in adults requiring NIV should be multidisciplinary and made on a case-by-case basis with careful consideration of the patient's overall medical and nutrition status.
B. Placement of an enteral feeding tube with a standard NIV mask will cause additional air leak. If the additional leak is unable to be compensated for, it is recommended to look into a mask with adaptor or sealing pad.
C. If choosing to enterally feed a patient who is on NIV, postpyloric tube placement would be preferred because of the likely increased aspiration risk.

Rationale

Achieving adequate oral nutrition intake in patients on NIV is a common problem in the ICU. Reeves et al found that 78% of patients requiring NIV met <80% of estimated needs via oral intake.[1] When oral intake is inadequate or not feasible, early initiation of EN in the critically ill population has been shown to provide benefits such as reduction in mortality and infectious morbidity.[2,3] Patients who require high-flow volumes via NIV can have increased risk of aspiration, which makes practitioners less likely to start EN in this population. However, in a qualitative review of randomized trials, it was found that the incidence of aspiration pneumonia was <5%, and vomiting was an infrequent complication.[4] The study by Reeves et al also found that patients who were unable to maintain oral intake and consequently started enteral feeding while on NIV had increased airway complications.[1] The increased air volumes provided via NIV can cause gastric distention that may in turn worsen patients' respiratory status because of its effects on diaphragm function.[5] A retrospective cohort study by Terzi et al compared patients on NIV with various diet orders in the first 2 days of treatment: nil per os, PN, EN, and oral nutrition. They found increased incidence of nosocomial infection and ventilator-associated pneumonia in the EN group vs

in the nil per os group. The EN group also had increased mortality and fewer ventilator-free days.[6] Kogo et al studied airway complications associated with EN in patients on NIV. Airway complications were defined as episodes of vomiting followed by desaturation, mucus plug, and aspiration pneumonia. All three complications were higher in the EN group vs in the nil per os group, with the EN group also requiring a longer duration of NIV and increased LOS.[7] Despite the overarching theme of these study outcomes being in favor of holding EN during NIV, limitations such as small sample sizes and study design also cloud the picture. The investigators agree that further research is necessary to confirm these results. In an editorial discussing these issues, an interesting solution is proposed in which the recommendation of when to start EN while on NIV would be determined by the patient's nutrition status on admission. If a patient is well nourished on admission, feeding can be held for the first few days. In the malnourished patient, feeding should be started early, and preferably, the patient could be transitioned to high-flow nasal oxygen (HFNO).[5] A prospective cohort study in adult ICU patients who were determined to be appropriate by an intensivist, nurse, or speech therapist found that 100% of patients were able to resume oral intake while receiving HFNO.[8] If the patient cannot tolerate HFNO, a mask with an adaptor would be the next best option; however, these types of mask adaptors can be expensive or difficult to obtain.[5]

This leads into the second concern that arises with EN and NIV: the EN tubing can affect the seal of the NIV mask. Increased air leaks contribute to patient-ventilator asynchrony and patient discomfort.[9] In a meta-analysis of complications of NIV, it was found that patient discomfort occurred in 30%–50% of patients. Tightening the mask to decrease air leaks can lead to skin breakdown, which can happen in up to 50% of patients on NIV, with the incidence increasing up to 100% if the patient remains on NIV for >48 h.[4] Leak-compensation algorithms built into more recent ventilators are another line of defense, although increasing the flow could further worsen mask seal or cause aerophagia and gastric distension.[10] Increased gastric distention can decrease lung compliance, requiring even more increased ventilation pressure.[4] As discussed earlier, in the editorial by Singer and Rattanachaiwong, specialty masks made for EN tubing or adaptors would be the best option if a patient requires EN while on NIV.[5] Quintero et al investigated the efficacy of a novel tube adaptor in reducing leaks and patient comfort in a quasi-experimental study. They found that the mean air leak percentage decreased from 32.5% with conventional therapy (14–20 French nasoenteric tube for gastric drainage and medication and 12 French tube for EN via standard oronasal mask) to 9.2% with the adaptor. Patients also reported significantly improved comfort with the adaptor.[11]

If a practitioner decides to start EN in a patient requiring NIV, the next issue is whether postpyloric tube placement is necessary or whether gastric placement is considered safe. Because of limited research on outcomes of EN and NIV, the following addresses enteral feeding tube placement in patients who are at increased risk of aspiration. The 2016 ASPEN guidelines for critical care recommend initiation of gastric feeding for most ICU patients, although patients with increased aspiration risk should have postpyloric placement.[2] The 2018 ESPEN guidelines agree and go a step further to specify that jejunal feeding would be preferred in high-risk patients.[12] A meta-analysis of randomized controlled studies showed a decreased rate of pneumonia with postpyloric placement, as well as increased nutrient delivery.[13] One issue with postpyloric placement is that it can cause feeding to be delayed because of the increased difficulty of placement.[13] If postpyloric placement is not feasible and the patient is fed via gastric placement, it is imperative to monitor closely for signs and symptoms of aspiration and intolerance.

REFERENCES

1. Reeves A, White H, Sosnowski K, Tran K, Jones M, Palmer M. Energy and protein intakes of hospitalised patients with acute respiratory failure receiving non-invasive ventilation. *Clin Nutr*. 2014;33(6):1068-1073.
2. McClave SA, Taylor BE, Martindale RG, et al. Society of Critical Care Medicine; American Society for Parenteral and Enteral Nutrition. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). *JPEN J Parenter Enteral Nutr*. 2016;40(2):159-211.
3. McClave SA, Martindale RG, Rice TW, Heyland DK. Feeding the critically ill patient. *Crit Care Med*. 2014;42(12):2600-2610.
4. Carron M, Freo U, BaHammam AS, Dellweg D, et al. Complications of non-invasive ventilation techniques: a comprehensive qualitative review of randomized trials. *Br J Anaesth*. 2013;110(6):896-914.
5. Singer P, Rattanachaiwong S. To eat or to breathe? The answer is both! Nutritional management during noninvasive ventilation. *Crit Care*. 2018;22(1):27.
6. Terzi N, Darmon M, Reignier J, et al. OUTCOMEREA Study Group. Initial nutritional management during noninvasive ventilation and outcomes: a retrospective cohort study. *Crit Care*. 2017;21(1):293.
7. Kogo M, Nagata K, Morimoto T, et al. Enteral nutrition is a risk factor for airway complications in subjects undergoing noninvasive ventilation for acute respiratory failure. *Respir Care*. 2017;62(4):459-467.
8. Leder SB, Siner JM, Bizzarro MJ, McGinley BM, Lefton-Greif MA. Oral alimentation in neonatal and adult populations requiring high-flow oxygen via nasal cannula. *Dysphagia*. 2016;31(2):154-159.
9. Vignaux L, Vargas F, Roeseler J, et al. Patient-ventilator asynchrony during non-invasive ventilation for acute respiratory failure: a multicenter study. *Intensive Care Med*. 2009;35(5):840-846.
10. De Luca A, Sall FS, Khoury A. Leak compensation algorithms: the key remedy to noninvasive ventilation failure? *Respir Care*. 2017;62(1):135-136.
11. Quintero OI, Sanchez AI, Chavarro PA, Casas IC, Tascón GAO. Impact of using a novel gastric feeding tube adaptor on patient's comfort and air leaks during non-invasive mechanical ventilation. Arch Bronconeumol (Engl Ed). 2019;56(6):353-359.
12. Singer P, Blaser AR, Berger MM, et al. ESPEN guideline on clinical nutrition in the intensive care unit. *Clin Nutr*. 2019;38(1):48-79.
13. Alkhawaja S, Martin C, Butler RJ, Gwadry-Sridhar F. Post-pyloric versus gastric tube feeding for preventing pneumonia and improving nutritional outcomes in critically ill adults. *Cochrane Database Syst Rev*. 2015;2015(8):CD008875.

8. What are the indications and strategies to use for "catch-up" feedings?

Recommendations

A. Consider use of a volume-based feeding (VBF) protocol to improve the likelihood that the full amount of prescribed EN is received.
B. Consider patient condition factors in formulating the feeding regimen to promote tolerance and meet energy, protein, and fluid needs safely.

Rationale

Rate-based feeding (RBF) is the traditional method of providing EN in the ICU setting, characterized by initiation at a low rate and slow up-titration toward a fixed 24-h goal rate. Studies using RBF indicate that EN is interrupted or withheld up to 7 h/day, on average, resulting in EN intakes as low as 33% of the prescribed EN volume.[1] Incomplete EN delivery has been attributed to a variety of factors, including process-related factors, ICU-related interruptions, real or perceived intolerance, and provider attitudes and behavior.[2] Although the optimal energy and protein intake required to improve outcomes remain unknown, implementation of a feeding strategy that ensures the delivery of prescribed EN volumes for ICU patients may at least eliminate much of the guesswork involved with traditional EN prescribing practices. Several strategies have been suggested as a way to "catch up" (ie, compensate) for the volume of EN lost because of interruptions. One example of compensatory feeding entails establishing a higher fixed hourly infusion rate from the start by dividing the 24-h volume goal by 20 h, in anticipation of at least 4 h of EN interruptions daily. Although well tolerated and effective in increasing EN delivery overall, this strategy has demonstrated a high rate of overfeeding.[3] Societal guidelines, based on expert consensus, suggest that a VBF protocol be considered in the adult ICU setting as a way to increase delivery of EN.[4] VBF is a catch-up feeding strategy, in which a 24-h EN volume goal is established and the hourly infusion rate is increased only after an EN interruption. Results from 14 studies conducted in a mix of medical, surgical, trauma, and neurosurgical ICUs consistently demonstrate an increase in mean percentage of prescribed energy and protein delivered by using VBF when compared with traditional RBF.[5-18]

Compared with RBF, VBF is reportedly well tolerated, with no increase in feeding-related complications such as diarrhea, tube dislodgement, GRVs exceeding institutional thresholds, or vomiting. As demonstrated by the differences in VBF protocols reported in the literature, institutions may individualize the protocol to maximize the likelihood of tolerance in their populations by anticipating and preventing complications. This may include the use of a specific nutrition risk assessment tool, enteral formula, initial infusion rate, and maximum infusion rate. Protocols have also included a trophic feeding option, early protein supplementation, and motility agents. Despite versatility in protocol design, VBF may not be appropriate for patients receiving multiple or high-dose vasopressor support, patients at high risk of refeeding or feeding intolerance, or those who have previously experienced feeding intolerance.

Glucose control and glycemic variability have also been evaluated to better understand the safety of VBF. Brierley-Hobson and colleagues[15] reported no difference in the amount of insulin prescribed between patients receiving VBF and RBF but did note higher morning blood glucose levels in the VBF group. Similarly, Holyk et al[16] reported no difference in average blood glucose levels between VBF and RBF but noted an increased incidence of moderate hyperglycemia during catch-up periods compared with non–catch-up periods in the same patients. One study reported a decreased occurrence of hyperglycemia and hypoglycemia in the VBF cohort,[17] and another found no difference in hyperglycemia and glycemic variance between groups.[18]

ORCID

Matthew L. Bechtold http://orcid.org/0000-0002-0205-3400
Arlene Escuro http://orcid.org/0000-0002-3615-1084
Michelle Kozeniecki http://orcid.org/0000-0002-2048-2532
Berkeley N. Limketkai http://orcid.org/0000-0003-2714-6934
Ainsley Malone http://orcid.org/0000-0001-8345-0303

REFERENCES

1. Cahill NE, Murch L, Cook D, Heyland DK, Canadian Critical Care Trials Group. Improving the provision of enteral nutrition in the intensive care unit: a description of a multifaceted intervention tailored to overcome local barriers. *Nutr Clin Pract*. 2014;29(1):110-117.
2. Kozeniecki M, Pitts H, Patel JJ. Barriers and solutions to delivery of intensive care unit nutrition therapy. *Nutr Clin Pract*. 2018;33(1):8-15.
3. Lichtenberg K, Guay-Berry P, Pipitone A, Bondy A, Rotello L. Compensatory increased enteral feeding goal rates: a way to achieve optimal nutrition. *Nutr Clin Pract*. 2010;25(6):653-657.
4. McClave SA, Taylor BE, Martindale RG, et al. Society of Critical Care Medicine; American Society for Parenteral and Enteral Nutrition. Guidelines for the provision and assessment of nutrition support therapy for the adult critically ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). *JEPN J Parenter Enteral Nutr*. 2016;40(2):159-211.
5. Yeh D, Cropano C, Quraishi S, et al. Implementation of an aggressive enteral nutrition protocol and the effect on clinical outcomes. *Nutr Clin Pract*. 2017;32(2):175-181.
6. Taylor B, Brody R, Denmark R, et al. Improving enteral delivery through the adoption of the "Feed Early Enteral Diet Adequately for Maximum Effect (FEED ME)" protocol in surgical trauma ICU: a quality improvement review. *Nutr Clin Pract*. 2014;29(5); 639-648.
7. Wang C, Huang C, Chen C, et al. Optimal energy delivery, rather than the implementation of a feeding protocol, may benefit clinical outcomes in critically ill patients. *Nutrients*. 2017;9(5):527.
8. Heyland DK, Cahill NE, Dhaliwal R, et al. Enhanced protein-energy provision via the enteral route in critically ill patients: a single center feasibility trial of the PEP uP protocol. *Crit Care Med*. 2010;14(2):R78.
9. Heyland D, Murch L, Cahill N, et al. Enhanced protein-energy provision via the enteral route feeding protocol in critically ill patients: results of a cluster randomized trial. *Crit Care Med*. 2013; 41(12):2743-2753.

10. Kinikin J, Phillipp R, Altamirano C. Using volume-based tube feeding to increase nutrient delivery in patients on a rehabilitation unit. *Rehabil Nurs*. 2020;45(4):186-194.
11. Haskins IN, Baginsky M, Gamsky N, et al. Volume-based enteral nutrition support regimen improves caloric delivery but may not affect clinical outcomes in critically ill patients. *JPEN J Parenter Enteral Nutr*. 2017;41(4):607-611.
12. Krebs ED, O'Donnel K, Berry A, et al. Volume-based feeding improves nutritional adequacy in surgical patients. *Am J Surg*. 2018; 216(6):1155-1159.
13. McClave SA, Saad MA, Esterle M, et al. Volume-based feeding in the critically ill patient. *JPEN J Parenter Enteral Nutr*. 2015;39(6): 707-712.
14. Roberts S, Brody R, Rawal S, et al. Volume-based vs rate-based enteral nutrition in the intensive care unit: Impact on nutrition delivery and glycemic control. *JPEN J Parenter Enteral Nutr*. 2019; 43(3):365-375.
15. Brierley-Hobson S, Clarke G, O'Keeffe V. Safety and efficacy of volume-based feeding in critically ill, mechanically ventilated adults using the "Protein & Energy Requirements Fed for Every Critically ill patient every Time" (PERFECT) protocol: a before-and-after study. *Crit Care*. 2019;23(1):105.
16. Holyk A, Belden V, Sirimaturos M, Chiles K, et al. Volume-based feeding enhances enteral delivery by maximizing the optimal rate of enteral feeding (FEED MORE). *JPEN J Parenter Enteral Nutr*. 2020; 44(6):1038-1046.
17. Prest PJ, Justice J, Bell N, et al. A volume-based feeding protocol improves nutrient delivery and glycemic control in a surgical trauma intensive care unit. *JPEN J Parenter Enteral Nutr*. 2020;44(5): 880-888.
18. Sachdev G, Backes K, Thomas BW, Sing RF, Huynh T. Volume-based protocol improves delivery of enteral nutrition in critically ill trauma patients. *JPEN J Parenter Enteral Nutr*. 2020;44(5): 874-879.

AREAS FOR FUTURE RESEARCH

Science in the field of nutrition is changing every year. Although many great studies have been performed or are in active trials, more new studies are needed to answer some of the more difficult clinical scenarios providers are faced with each and every day.

In patients with oncological issues, a large gap is apparent in the literature regarding the use of EN compared with routine nutrition care for neoadjuvant or adjuvant treatment (with the exception of upper-GI malignancies). There is a great deal of opportunity for examining the use of various forms of EN compared with control cases in randomized trials. Furthermore, the oncology community would benefit from RCTs in patients without head and neck cancer to create stronger evidence-based guidelines on nutrition support indications. Areas for research may include well-designed studies investigating the use of nasoenteric or gastrostomy/jejunostomy feeding tubes compared with standard of care, with end points including weight changes, markers of malnutrition, hospital admission days, treatment toxicities, GI symptoms, tolerance to treatment/completion, disease-free survival, infections, and/or tube malfunction/complications. The current body of literature on the use of nutrition support in HSCT is also lacking in depth but provides promising opportunities for future research. Implementing a nutrition support protocol can be useful for improved adherence to the guidelines and promoting optimal outcomes for patients who undergo HSCT. Research investigating the potential benefits of implementing institution-wide nutrition support pathways would be useful for increasing the efficacy of nutrition intervention throughout peritransplant phases. Research can focus on the timing of nutrition support interventions, establishment of interventions to circumvent common GI complications after transplant to maintain the use of an enteral route of feeding, and strategies to maximize the use of EN to promote improved treatment outcomes. Research on reducing the risk of malnutrition or decreasing the progression would benefit patients with oncological diseases.

Patients with non-GI disease may also benefit from future research. In patients who have had a stroke, future studies may focus on the effects of early vs late PEG tube placement on patient outcomes and predictors of PEG tube removal (swallow function recovery) during stroke rehabilitation. In patients with chronic renal disease, more studies examining outcomes such as weight maintenance, renal disease progression, and malnutrition prevention would be beneficial for future research.

Finally, further research is needed to determine whether the use of VBF is safe and effective in all subtypes of patients and whether more precise delivery of EN by using VBF impacts clinical outcomes.

AUTHOR CONTRIBUTIONS

Matthew L. Bechtold, Patricia M. Brown, Arlene Escuro, Brandee Grenda, Theresa Johnston, Michelle Kozeniecki, Berkeley N. Limketkai, Krystie K. Nelson, Jan Powers, Andrea Ronan, Nathan Schober, Brian J. Strang, Cristina Swartz, Justine Turner, Lauren Tweel, Renee Walker, and Ainsley Malone equally contributed to the conception and design of the research; Matthew L. Bechtold, Patricia M. Brown, Arlene Escuro, Brandee Grenda, Theresa Johnston, Michelle Kozeniecki, Berkeley N. Limketkai, Krystie K. Nelson, Jan Powers, Andrea Ronan, Nathan Schober, Brian J. Strang, Cristina Swartz, Justine Turner, Lauren Tweel, Renee Walker, and Ainsley Malone equally contributed to the design of the research; Matthew L. Bechtold, Patricia M. Brown, Arlene Escuro, Brandee Grenda, Theresa Johnston, Michelle Kozeniecki, Berkeley N. Limketkai, Krystie K. Nelson, Jan Powers, Andrea Ronan, Nathan Schober, Brian J. Strang, Cristina Swartz, Justine Turner, Lauren Tweel, Renee Walker, and Ainsley Malone equally contributed to the acquisition and analysis of the data; Matthew L. Bechtold, Patricia M. Brown, Arlene Escuro, Brandee Grenda, Theresa Johnston, Michelle Kozeniecki, Berkeley N. Limketkai, Krystie K. Nelson, Jan Powers, Andrea Ronan, Nathan Schober, Brian J. Strang, Cristina Swartz, Justine Turner, Lauren Tweel, Renee Walker, and Ainsley Malone equally contributed to the acquisition, analysis, and interpretation of the data. All authors drafted the manuscript, critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

CONFLICT OF INTERESTS

Matthew L. Bechtold receives speaker honorarium from Exact Sciences. Michelle Kozeniecki receives speaker honorarium from Baxter and a consultant fee from Nestlé. Justine Turner receives research funding from Baxter Cooperation. Jan Powers is on the speakers bureau of Abbott Nutrition and Stryker (not nutrition related). Lisa Epp receives speaker honoraria from Nestlé and a consultant fee from Avanos. Patricia M. Brown, Arlene Escuro, Brandee Grenda, Theresa Johnston, Berkeley N. Limketkai, Ainsley Malone, Krystie K. Nelson, Andrea Ronan, Nathan Schober, Cristina Swartz, Lauren Tweel, and Renee Walker declare no conflict of interests.

How to cite this article: Bechtold ML, Brown PM, Escuro A, et al. When is enteral nutrition indicated? *J Parenter Enteral Nutr*. 2022;46:1470-1496. doi:10.1002/jpen.2364