ACG Clinical Guideline: Nutrition Therapy in the Adult Hospitalized Patient

Stephen A. McClave, MD[1], John K. DiBaise, MD, FACG[2], Gerard E. Mullin, MD, FACG[3] and Robert G. Martindale, MD, PhD[4]

The value of nutrition therapy for the adult hospitalized patient is derived from the outcome benefits achieved by the delivery of early enteral feeding. Nutritional assessment should identify those patients at high nutritional risk, determined by both disease severity and nutritional status. For such patients if they are unable to maintain volitional intake, enteral access should be attained and enteral nutrition (EN) initiated within 24–48 h of admission. Orogastric or nasogastric feeding is most appropriate when starting EN, switching to post-pyloric or deep jejunal feeding only in those patients who are intolerant of gastric feeds or at high risk for aspiration. Percutaneous access should be used for those patients anticipated to require EN for >4 weeks. Patients receiving EN should be monitored for risk of aspiration, tolerance, and adequacy of feeding (determined by percent of goal calories and protein delivered). Intentional permissive underfeeding (and even trophic feeding) is appropriate temporarily for certain subsets of hospitalized patients. Although a standard polymeric formula should be used routinely in most patients, an immune-modulating formula (with arginine and fish oil) should be reserved for patients who have had major surgery in a surgical ICU setting. Adequacy of nutrition therapy is enhanced by establishing nurse-driven enteral feeding protocols, increasing delivery by volume-based or top-down feeding strategies, minimizing interruptions, and eliminating the practice of gastric residual volumes. Parenteral nutrition should be used in patients at high nutritional risk when EN is not feasible or after the first week of hospitalization if EN is not sufficient. Because of their knowledge base and skill set, the gastroenterologist endoscopist is an asset to the Nutrition Support Team and should participate in providing optimal nutrition therapy to the hospitalized adult patient.

Am J Gastroenterol advance online publication, 8 March 2016; doi:10.1038/ajg.2016.28

INTRODUCTION

The modern era of clinical nutrition began with the development of total parenteral nutrition (PN) by Dudrick (1) in 1966, suggesting for the first time that clinicians could compensate for intestinal failure with the potential to supply nutrients to any hospitalized patient. Further support for the unique contribution of PN came from a paper entitled "The Skeleton in the Hospital Closet" by Butterworth (2), which indicated that nearly 50% of patients in an urban hospital setting (in the United States) were malnourished. The response to these innovative concepts spurred the growth of nutrition support teams and PN-based therapy over the next two decades with the primary objective being to maintain lean body mass, achieve nitrogen balance, and prevent malnutrition (3). Over this time period, however, randomized controlled trials (RCTs) showed little outcome effect from the use of PN compared with standard therapy (where patients are managed with intravenous (IV) fluids, no enteral or parenteral therapy, and advancement to oral diet as tolerated) (4,5). Meta-analyses showed that, outside the setting of intestinal failure, in the absence of severe malnutrition, PN had little effect on clinical outcomes and actually had the potential to cause net harm (6). In the 1990s, a paradigm shift ensued toward enteral nutrition (EN)-based therapy, with the goal changing as well to maintaining gut integrity, providing immune modulation, and downregulating inflammatory responses (3). Early meta-analyses showed that EN was both superior to PN-based therapy and more effective in improving outcome than standard therapy (4,7,8). Lately, challenges to the practice of clinical nutrition have occurred in response to the introduction of immune- and metabolic-modulating nutrition therapy, the evolving epidemic of obesity in the United States, and recent clinical trials suggesting that short-term (4–7 days) low-dose "trophic" feeding (aka, permissive underfeeding or hypocaloric feeding) might be equally as effective as full feeding for the first week of hospitalization (9–11). Furthermore, in an era of

[1]Department of Medicine, Division of Gastroenterology, Hepatology, and Nutrition, University of Louisville School of Medicine, Louisville, Kentucky, USA; [2]Department of Medicine, Mayo Clinic, Scottsdale, Arizona, USA; [3]Department of Medicine, Johns Hopkins University, Baltimore, Maryland, USA; [4]Department of Surgery, Oregon Health Sciences University, Portland, Oregon, USA. **Correspondence:** Stephen A. McClave, MD, Department of Medicine, Division of Gastroenterology, Hepatology, and Nutrition, University of Louisville School of Medicine, 550S, Jackson St, Louisville, Kentucky 40202, USA. E-mail: samcclave@louisville.edu

moderate glucose control, better care of central lines, protocolized management of risk, and avoidance of overfeeding, the outcome benefits of PN may be approaching that of EN (12).

Support for the benefit of EN-based therapy on clinically important outcomes is derived from five distinct bodies of research in the literature. Multiple RCTs comparing early vs. delayed EN suggest that feedings started within the first 24 to 36 h of admission to the intensive care unit (ICU) are associated with significantly reduced infection, hospital length of stay, and mortality compared with feedings started after that time point (13–15). RCTs comparing early EN vs. standard therapy (in elective surgery, surgical critical care, and patients being operated on for complications of pancreatitis) showed a significant correlation between enteral feeding initiated the day after the operation and reductions in infection, hospital length of stay, and mortality (8,16,17). Observational data from five prospective trials suggest that an increasing caloric deficit (created by daily patient energy expenditure and delays in delivery of nutrition therapy) is associated with significant increases in organ failure, hospital length of stay, infectious morbidity, and total complications (18,19). Nutrition therapy designed to reduce the caloric deficit has been associated with improved outcomes, as shown by significant reductions in infection and mortality (20). The positive impact of nurse-driven protocols, which serve to increase delivery of EN, has been demonstrated in RCTs and prospective trials (before and after implementation of the protocol), where the use of such strategy has been associated with subsequent reductions in infection, hospital length of stay, and mortality compared with non-protocolized therapy (21,22). Finally, three decades of mechanistic data in animal models and clinical studies show that early EN helps maintain gut integrity, supports the role of commensal bacteria, reduces the gut/lung axis of inflammation, sustains the mass of gut-associated and mucosal-associated lymphoid tissue, and attenuates systemic inflammatory responses (23).

Although the intended target patient population of these guidelines is the hospitalized patient, most of the information on providing nutrition therapy is derived from the management of patients in the ICU. Every hospitalized patient has a unique metabolic/immune response to surgery, illness, or injury, which may be modulated or attenuated by appropriate nutrition therapy (24). As a result, nutrition therapy has emerged as a primary therapeutic intervention. The degree to which a patient benefits from nutrition therapy depends on disease severity, baseline nutritional status, and design of the nutrition regimen itself (24). The timing, route, content, delivery, and patient tolerance are all variables that influence the potential for those benefits. Successful nutrition therapy depends on the appropriate assessment of gut function, achievement of enteral access, the creation of protocols to standardize delivery, and an ongoing process to monitor tolerance.

METHODOLOGY

A list of questions and recommendations were compiled by the group of experts on the guideline committee. A literature search was performed using Embase, Pubmed, MEDLine, Cochrane Database, Google search for scholarly articles, and personal files of committee members. Search terms included tube feeding, EN, PN, enteral access, percutaneous endoscopic gastrostomy and jejunostomy, nasojejunal, and nutritional risk.

Quality of evidence was determined using GRADE methods, based on study design, study quality, consistency, and directness (**Table 1**) (25). Four levels of evidence were assigned based on study limitations, inconsistency of results, and uncertainty about the directness of evidence (**Table 2**) (25). Strength of recommendation was assigned as "Strong" if supported by moderate-to-high quality of evidence (RCTs and high-quality observational studies) or "Conditional" if supported by low quality of evidence (low-quality RCTs, observational studies, or expert opinion; **Table 3**) (25,26).

The target population for these guidelines was the adult hospitalized patient, unable to sustain volitional intake, expected to remain in the hospital for >3 days. Unless otherwise stated, these guidelines are focused on all hospitalized patients, whether they are in an ICU or in a general ward. Specialized Nutrition Therapy was defined as providing either EN via an enteral access device or

Table 2. Significance of the four levels of evidence (25)

High	We are very confident that the true effect lies close to that of the estimate of effect
Moderate	We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of effect, but there is a possibility that it is substantially different
Low	Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of effect
Very low	We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

Table 1. Derivation of rating for quality of evidence (25)

Study design	Initial quality of evidence	Quality adjustors	Final quality of evidence
Randomized trials	High (++++)	Decrease quality: risk of bias, inconsistency, indirectness, imprecision, publication bias	High ++++ Moderate +++
Observational studies	Low (++)	Increase quality: large effect, dose response, adjustment for all plausible residual confounders	Low ++ Very low +
Expert consensus			

Table 3. Strength of recommendation (25)

Strong	The desirable effects of the intervention clearly outweigh the undesirable effects or clearly do not
Conditional	The tradeoffs are less certain between the desirable and undesirable effects of an intervention

PN via a central line catheter. Standard therapy was defined as the provision of IV fluids, no EN or PN, and advancement to oral diet as tolerated.

A. Indications for nutritional therapy

Question: Which hospitalized patients should be considered for specialized nutrition therapy and by which route (enteral or parenteral) should it be provided?

Recommendations:

1. Specialized nutrition therapy in the form of EN should be initiated promptly in the hospitalized patient who is at high nutritional risk and is unable to maintain volitional oral intake (conditional recommendation, low level of evidence).
2. EN should be used preferentially over PN in hospitalized patients who require non-volitional specialized nutrition therapy and do not have a contraindication to the delivery of luminal nutrients (conditional recommendation, low level of evidence).
3. Specialized nutrition therapy (EN or PN) is not required for hospitalized patients who are at low nutritional risk, appear well nourished, and are expected to resume volitional intake within 5 to 7 days following admission (conditional recommendation, very low level of evidence).
4. PN should be reserved for the hospitalized patient under specific circumstances, when EN is not feasible or sufficient enough to provide energy and protein goals (conditional recommendation, very low level of evidence).

Summary of evidence. Evidence for a negative impact from malnutrition on clinical outcome in the hospitalized patient dates back over eight decades (27). Nevertheless, malnutrition remains difficult to define and, therefore, poorly understood. A multidisciplinary international committee recently divided malnutrition into three categories, recognizing the important contribution of inflammation to the deterioration of nutritional status (28). (i) Starvation-related malnutrition occurs in the absence of calories and protein, has minimal to no inflammation, and is exemplified by the syndrome of anorexia nervosa. (ii) Chronic disease-related malnutrition has a low-grade degree of inflammation and is characterized by disorders such as chronic obstructive pulmonary disease, cancer, and obesity. (iii) Acute disease-related malnutrition has a high degree of inflammation and is characterized by disorders such as burns, trauma, and sepsis (28). Recognizing poor nutritional status or overt evidence of "malnutrition" has important implications with regard to health-care economics and quality measures of care. For the clinician, however, these categories of malnutrition may have more theoretical than practical value.

In contrast, "nutritional risk" is an important relatively new concept that is more easily defined and is determined by both disease severity and poor nutritional status (29,30). Patients who are at high nutritional risk are those patients in a hospital setting who are in greatest need of nutrition therapy and are most likely to see an improvement in clinical outcome in response to aggressive enteral feeding (29,30).

The benefit of nutrition therapy in the hospitalized patient, particularly the critically ill patient, is mainly related to the provision of early EN. Achievement of enteral access and provision of early enteral tube feeding have both non-nutritional and nutritional benefits (see **Table 4**) (24). Non-nutritional benefits, which are probably seen in all patients in the hospital setting and may be achieved at lower doses, involve the gastrointestinal (GI), immune, and metabolic responses to the provision of luminal nutrients (23,24). Nutritional benefits are seen in those patients at high nutritional risk, who require higher doses closer to goal caloric/protein requirements, and are needed for protein synthesis and maintenance or restoration of lean body mass (23,24).

Potential benefits of EN over PN have been suggested in the past by multiple meta-analyses over a wide range of patient populations including trauma, burn, head injury, major elective surgery, and pancreatitis (4,7,31,32). These meta-analyses have shown an association between reduced infection, decreased total complications, and shorter hospital length of stay with EN compared with PN (with no difference seen in mortality). More recent trials suggest that the differences in outcome between EN and PN may be diminishing as clinicians increasingly utilize moderate glucose control, better IV lipid formulations, avoidance of overfeeding, and protocolized management of risk (to prevent blood-stream infections, ventilator-associated pneumonia, thrombogenesis, and so on). In a recent large RCT involving 2,400 critically ill patients in multiple ICUs across England, there was no difference in outcomes (infection, organ failure, hospital length of stay, and mortality) between the two routes of nutrition therapy (12). Nonetheless, the risk/benefit ratio of PN is much narrower than that of EN. Thus, the use of PN should be reserved for high-risk patients when EN is not feasible or sufficient enough to meet energy or protein goals (see the section "Parenteral nutrition").

In a patient at low nutritional risk, provision of EN or PN is unlikely to change clinical outcome. Such patients need to be frequently re-assessed, however, to monitor for any complications that would lead to deterioration of nutritional status or an increase in disease severity that would necessitate specialized nutrition therapy.

Absolute contraindications to enteral feeding include mechanical obstruction of the GI tract, uncontrolled peritonitis, and ischemic bowel (33). Many conditions that were previously considered to be contraindications to enteral feeding may be situations where it is appropriate to provide EN with caution in order to improve outcome. Such conditions include ileus, open abdomen, recent gut anastomoses, GI bleeding, bowel-wall edema, and a stable patient on vasopressor therapy to maintain adequate mean arterial blood pressure (34).

Table 4. Benefits of early enteral nutrition (24)

Non-nutrition benefits
Gastrointestinal responses
Maintain gut integrity
Reduced gut/lung axis of inflammation
Enhance motility/contractility
Absorptive capacity
Maintain mass of GALT tissue
Support and maintain commensal bacteria
Production of secretory IgA
Trophic effect on epithelial cells
Reduced virulence of endogenous pathogenic organisms
Immune responses
Modulate key regulatory cells to enhance systemic immune function
Promote dominance of anti-inflammatory Th-2 over proinflammatory Th-1 responses
Stimulate oral tolerance
Influence anti-inflammatory nutrient receptors in the GI tract (duodenal vagal, colonic butyrate)
Maintain MALT tissue at all epithelial surfaces (lung, liver, lacrimal, genitourinary, and pulmonary)
Modulate adhesion molecules to attenuate trans-endothelial migration of macrophages and neutrophils
Metabolic responses
Promote insulin sensitivity through the stimulation of incretins
Reduce hyperglycemia (AGEs), muscle, and tissue glycosylation
Attenuating stress metabolism to enhance more physiologic fuel utilization
Nutrition benefits
Sufficient protein and calories
Provide micronutrient and anti-oxidants
Maintain lean body mass by providing substrate for optimal protein synthesis
Support cellular and subcellular (mitochondria) function
Stimulate protein synthesis to meet metabolic demand of the host

AGEs, advanced glycolytic end products; GALT, gut-associated lymphoid tissue; GI, gastrointestinal; MALT, mucosal-associated lymphoid tissue.

B. Nutritional assessment

Question: How should the hospitalized patient be assessed prior to initiation of specialized nutrition therapy, and how are energy and protein requirements determined?

Recommendations:

5. Prior to initiation of specialized nutrition therapy (either EN or PN), a determination of nutritional risk should be performed using a validated scoring system such as the Nutritional Risk Score 2002 (NRS-2002) or the NUTRIC Score on all patients admitted to the hospital for whom volitional intake is anticipated to be insufficient (conditional recommendation, very low level of evidence).

6a. An additional assessment should be performed prior to initiation of nutrition therapy of factors that may impact the design and delivery of the nutrition regimen (conditional recommendation, very low level of evidence).

6b. Use of "traditional" nutrition indicators (albumin, prealbumin, transferrin, and anthropometry) should be avoided (conditional recommendation, very low level of evidence).

6c. Surrogate markers of infection or inflammation should not be used for nutritional assessment (conditional recommendation, very low level of evidence).

7a. Caloric requirements should be determined and then be used to set the goal for delivery of nutrition therapy (conditional recommendation, very low level of evidence).

7b. One of the three strategies should be used to determine caloric requirements:

(i) Indirect calorimetry (conditional recommendation, very low level of evidence).

(ii) Simple weight-based equations (conditional recommendation, very low level of evidence).

(iii) Published predictive equations (conditional recommendation, very low level of evidence).

8. Protein requirements should be determined independently of caloric needs, and an ongoing assessment of protein provision should be performed (conditional recommendation, very low level of evidence).

Summary of evidence. Although dietitians and health-care policy makers emphasize a difference between an initial "nutritional screen" of all hospitalized patients, followed by a more comprehensive "nutritional assessment" of select patients, physicians rarely make this distinction as they evaluate patients prior to initiating nutrition therapy. Previous nutritional assessment tools have tended to focus only on evaluation of nutritional status. Such tools include the Mini-Nutritional Assessment, the Simplified Nutritional Assessment Questionnaire, the Subjective Global Assessment, the Malnutrition Universal Screening Tool, and the Nutritional Risk Index (35). These assessment tools, although appropriate for a non-ICU patient, have not been validated for use in critical care and the ICU setting. They also fail to recognize the importance of disease severity and the contribution of inflammation and oxidative stress in causing deterioration of nutritional status and alteration in utilization of feeding substrates (36).

The concept of nutritional risk, however, incorporates both nutritional status and disease severity, as both contribute to poor outcome and the need for nutrition therapy. Two assessment tools that determine nutritional risk are the NRS-2002 and the NUTRIC Score (29,30,37). Nutritional risk is more easily defined than malnutrition, as objective parameters are used to determine both components of risk. Nutritional status is determined by body mass index (BMI), percent weight loss, and reduced oral intake (38) or the duration of hospitalization prior to being admitted to the ICU (29,37). Disease severity is determined by a table of clinical examples (30) or by the Acute Physiologic and Chronic Health Evaluation (APACHE) II and Simplified Organ Failure Assessment scores (29,37) (see **Table 5**). In a prospective study from China conducted

Table 5. Nutrition assessment scoring systems used to determine nutrition risk

NRS-2002: factors used to determine score (30)

Impaired nutritional status		Severity of disease	
Absent score 0	Normal nutritional status	Absent score 0	Normal nutritional requirements
Mild score 1	Weight loss >5% in 3 months OR Food intake <50–75% of normal requirement in preceding week	Mild score 1	Hip fracture Chronic patients in particular with acute complications: cirrhosis, COPD Chronic hemodialysis, diabetes, oncology
Moderate score 2	Weight loss >5% in 2 months OR BMI 18.5–20.5+impaired general condition OR Food intake 25–50% of normal requirement in preceding week	Moderate score 2	Major abdominal surgery, stroke Severe pneumonia, hematologic malignancy
Severe score 3	Weight loss >5% in 1 month (15% in 3 months) OR BMI <18.5+impaired general condition OR Food intake <25% of normal requirement in preceding week	Severe score 3	Head injury Bone marrow transplantation Intensive care patients (APACHE II>10)

NUTRIC Score: factors used to determine score (29)

Factors	NUTRIC points			
	0	1	2	3
Age (years)	<50	50–74	≥75	—
APACHE II Score	<15	15–19	20–27	≥28
Baseline SOFA Score	<6	6–9	≥10	—
No. of comorbidities	0–1	≥2	—	—
Days in hospital to ICU admit	0	≥1	—	—
Interleukin-6 (μ/ml)	0–399	≥400	—	—

APACHE, Acute Physiologic and Chronic Health Evaluation; BMI, body mass index; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; NRS-2002, Nutritional Risk Score 2002; SOFA=Simplified Organ Failure Assessment.
If age≥70 years, add 1 point (for NRS-2002).
Total score=(Points for nutritional status)+(Points for disease severity)+(Points for age) (for NRS-2002).
Total score is from six separate factors (for NUTRIC Score).

in over 1,000 patients awaiting major elective surgery, NRS-2002 scores were calculated, and patients were evaluated to see whether they had received sufficient nutrition therapy (defined as >10 kcal/kg per day for 7 days prior to surgery) (39). In those patients at high nutritional risk with NRS-2002 scores≥5, receipt of sufficient nutrition therapy was associated with a significant 50% reduction in nosocomial infection and total complications. In those patients determined to be at low nutritional risk (NRS-2002 score≤3), nutrition therapy was not associated with any change in outcome regardless of whether patients received sufficient or insufficient nutrition therapy (39). The NUTRIC score was used in a large international observational study in an ICU setting to differentiate low from high nutritional risk (29). Patients with high nutritional risk (NUTRIC scores 6–10) showed a significant decrease in mortality the closer the receipt volume of nutrition therapy was to goal feeding. In those patients at low nutritional risk (NUTRIC scores 0–5), there was no association between the amount of nutrition therapy received and mortality. In an RCT of 132 patients at higher nutritional risk (NRS-2002 scores>3), intervention with more aggressive nutrition therapy resulted in 30% greater receipt of calories and protein, which was associated with significant reductions in total complications and the need for re-hospitalization compared with standard hospital care (40). These three studies emphasize the point that patients at high nutritional risk who receive adequate nutrition therapy will experience improved outcomes, whereas patients at low nutritional risk are unlikely to alter their clinical course in response to nutrition therapy regardless of the amount delivered over the short term (29,39,40).

Additional assessment prior to initiation of nutrition therapy should include an evaluation of comorbid conditions, function of the GI tract, and risk of aspiration. Serum albumin, pre-albumin, and transferrin should not be used as markers of nutritional status but instead should be considered surrogate markers of risk and level of inflammation (41). Serum albumin levels alone at the time of admission may provide valuable prognostic information prior to a surgical procedure (42). Because albumin, pre-albumin, and transferrin are negative acute-phase proteins, their levels will fall precipitously in any significant acute inflammation and critical illness due to increased vascular permeability, change in priority of hepatic protein synthesis (from homeostatic protein synthesis to production of acute-phase proteins such as fibrinogen and α-glycoprotein), and selective catabolism of albumin to make available cysteine for the glutathione antioxidant defense system (43,44). Neither albumin nor pre-albumin should be used as a marker for adequacy of nutrition therapy, as their levels will only rise once the inflammation and degree of oxidative stress abates. C-reactive protein alone or in combination with pre-albumin may provide some useful information to the clinician with regard to changes in the level of inflammation and resolution of the systemic inflammatory response syndrome. Aside from basic measures of height, weight, and BMI, anthropometric measures such as mid-arm muscle circumference, creatinine-height index, and skin fold thickness are inaccurate, poorly reproducible, and provide little accurate information with regard to overall nutritional status for the hospitalized patient (45). Additional markers such as procalcitonin, interleukin-1, tumor necrosis factor, interleukin-6, and citrulline are surrogate markers of critical illness and possible bowel compromise, are considered investigational, and should not be used routinely in patient care at this time (46–48). In the future, the use of cross-sectional imaging such as computerized tomography scan, nuclear magnetic resonance imaging standardized at the level of the third lumbar vertebrae, and mid-thigh ultrasound may serve as important measures of lean body mass and appropriate tools to rule out sarcopenia (49,50).

Indirect calorimetry (IC) is the most accurate method to determine caloric needs and should be considered where available (51–55). For clinicians, IC is the gold standard, as results correlate well with direct whole-chamber calorimetry (56). IC requires specialized equipment and support staff for accurate, consistent, and reliable results (51,52). In high-risk individuals, energy expenditure should be measured once or twice per week and strategies should be in place to promote delivery of nutrition therapy to match energy expenditure (51,52).

If IC is not available or easily accessible, a weight-based equation (e.g., 25 to 30 kcal/kg per day) can be used (53–55). Furthermore, a number of predictive equations (e.g., Harris–Benedict, Penn State, Mifflin-St Jeor, Ireton–Jones, and so on) are also available (57–62). With over 200 published equations in the literature, none has been shown to be consistently superior to the others in accuracy (63,64). Equations derived from measurements on hospitalized patients (Ireton–Jones, American College of Chest Physicians, Penn State, Swinamer) are no more accurate than equations derived in research labs by measuring ambulatory healthy volunteers (Harris–Benedict, Mifflin-St Jeor) (63). Accuracy rates of published predictive equations range from 40 to 70% of that value measured by IC (65,66). These predictive equations should be used with caution, with an understanding of the potential errors in estimates for specific groups such as patients with extreme obesity (51).

Recent evidence suggests that protein may be the most important macronutrient when compared with fat and carbohydrate, as the provision of adequate protein is more likely to improve outcome than adequate caloric delivery (67,68). In the past, providing 1.2–1.5 g protein/kg per day was thought to be sufficient; however, recent studies suggest that the amount needed to optimize therapy may need to be higher in a range of 1.5–2.0 g/kg per day (69). Protein needs may be even higher in patients with trauma or large wounds (70). Besides the weight-based equation above, protein requirements may be determined by calculating the nitrogen balance using a 24-h urine collection to measure urine urea nitrogen (UUN) with the following calculation: protein g/day=[(UUN+4)×6.25].

C. Enteral access

Question: How should enteral access be achieved, and at what level of the GI tract should EN be infused?

Recommendations:

9a. A nasogastric or orogastric feeding tube should be used as the initial access device for starting EN in a hospitalized patient (conditional recommendation, very low level of evidence).

Table 6. Summary of recommendations

Indications for nutritional therapy
Question: Which hospitalized patients should be considered for specialized nutrition therapy and by which route (enteral or parenteral) should it be provided?
Recommendations:
1. Specialized nutrition therapy in the form of EN should be initiated promptly in the hospitalized patient who is at high nutritional risk and is unable to maintain volitional oral intake (conditional recommendation, low level of evidence).
2. EN should be used preferentially over PN in hospitalized patients who require non-volitional specialized nutrition therapy, and do not have a contraindication to the delivery of luminal nutrients (conditional recommendation, low level of evidence).
3. Specialized nutrition therapy (EN or PN) is not required for hospitalized patients who are at low nutritional risk, appear well nourished, and are expected to resume volitional intake within 5 to 7 days following admission (conditional recommendation, very low level of evidence).
4. PN should be reserved for the hospitalized patient under specific circumstances, when EN is not feasible or sufficient enough to provide energy and protein goals (conditional recommendation, very low level of evidence).
Nutritional assessment
Question: How should the hospitalized patient be assessed prior to initiation of specialized nutrition therapy, and how are energy and protein requirements determined?
Recommendations:
5. Prior to initiation of specialized nutrition therapy (either EN or PN), a determination of nutritional risk should be performed using a validated scoring system such as the NRS-2002 or the NUTRIC Score on all patients admitted to the hospital for whom volitional intake is anticipated to be insufficient (conditional recommendation, very low level of evidence).
6a. An additional assessment should be performed prior to initiation of nutrition therapy of factors, which may impact the design and delivery of the nutrition regimen (conditional recommendation, very low level of evidence).
6b. Use of "traditional" nutrition indicators (albumin, pre-albumin, transferrin, and anthropometry) should be avoided (conditional recommendation, very low level of evidence).
6c. Surrogate markers of infection or inflammation should not be used for nutritional assessment (conditional recommendation, very low level of evidence).
7a. Caloric requirements should be determined and then be used to set the goal for delivery of nutrition therapy (conditional recommendation, very low level of evidence).
7b. One of the three strategies should be used to determine caloric requirements:
Indirect calorimetry (conditional recommendation, very low level of evidence).
Simple weight-based equations (conditional recommendation, very low level of evidence).
Published predictive equations (conditional recommendation, very low level of evidence).
8. Protein requirements should be determined independently of caloric needs, and an ongoing assessment of protein provision should be performed (conditional recommendation, very low level of evidence).
Enteral access
Question: How should enteral access be achieved, and at what level of the GI tract should enteral nutrition be infused?
Recommendations:
9a. A nasogastric or orogastric feeding tube should be used as the initial access device for starting EN in a hospitalized patient (conditional recommendation, very low level of evidence).
9b. Radiologic confirmation of placement in the stomach should be carried out prior to feeding (except with use of electromagnetic transmitter-guided feeding tubes). Repeated periodic radiologic confirmation of correct tube position in the GI tract is not required unless there is concern for tube displacement because of nausea/vomiting, regurgitation, coughing, retching, or overt displacement (conditional recommendation, very low level of evidence).
10a. Conversion to a post-pyloric feeding tube should be carried out only when gastric feeding has been shown to be poorly tolerated or the patient is at high risk for aspiration (strong recommendation, moderate-to-high level of evidence).
10b. Simultaneous aspiration/decompression of the stomach with jejunal feeding may be accomplished by using a dual lumen aspirate/feed nasoenteric tube, a combined percutaneous GJ tube, or the use of both gastrostomy and jejunostomy tubes (conditional recommendation, very low level of evidence).
11. When long-term enteral access is needed in a patient with gastroparesis or chronic pancreatitis, a jejunostomy tube should be placed (conditional recommendation, very low level of evidence).
12. A percutaneous enteral access device should be placed, either via the gastric or jejunal route, if enteral feeding is anticipated to be required for greater than 4 weeks duration (conditional recommendation, very low level of evidence).
13. A percutaneous gastrostomy should be placed preferentially in the gastric antrum in order to facilitate conversion to a GJ tube in the event that the patient is intolerant to gastric feeding (conditional recommendation, very low level of evidence).
14. For the patient at high risk for tube displacement, steps should be taken proactively to secure the access device at the time of placement (conditional recommendation, very low level of evidence).

Table 6 continued on following page

Table 6. Continued

Initiating enteral nutrition
Question: How soon, at what dose, and with which formula should enteral nutrition be initiated in the hospitalized patient?
Recommendations:
15. In the patient at high nutritional risk unable to maintain volitional intake, EN should be initiated within 24–48 h of admission to the hospital (conditional recommendation, low level of evidence).
16a. Although early EN should be initiated within 24–48 h of admission, the timing by which to advance to goal is unclear. When tolerated, feeding should be advanced to goal within 48–72 h (conditional recommendation, very low level of evidence).
16b. With reduced tolerance, feeding should be advanced with caution to goal by 5 to 7 days (conditional recommendation, very low level of evidence).
17. Permissive underfeeding (i.e., hypocaloric feeding) is an acceptable alternative to full feeding and may be considered in three separate patient scenarios:
Acute lung injury/acute respiratory distress syndrome (strong recommendation, high level of evidence).
Obesity with BMI>30 (conditional recommendation, very low level of evidence).
Placement on PN over the first week of nutrition therapy (conditional recommendation, low level of evidence).
18a. A standard polymeric formula or a high-protein standard formula should be used routinely in the hospitalized patient requiring EN (conditional recommendation, very low level of evidence).
18b. An immune-modulating formula containing arginine and omega-3 fish oil should be used for patients who have had major surgery and are in a surgical ICU setting (conditional recommendation, very low level of evidence).
18c. An immune-modulating formula containing arginine and omega-3 fish oil should not be used routinely in patients in a medical ICU (conditional recommendation, very low level of evidence).
Monitoring tolerance and adequacy of enteral nutrition
Question: How should adequacy and tolerance of enteral nutrition be assessed in the hospitalized patient?
Recommendations:
19a. Hospitalized patients on EN should be monitored daily by physical exam (conditional recommendation, very low level of evidence).
19b. Patients on EN should be monitored for adequacy of provision of EN as a percent of target goal calories, cumulative caloric deficit, and inappropriate cessation of EN (conditional recommendation, very low level of evidence).
20. In the patient at high risk for refeeding syndrome, feeding should be ramped up slowly to goal over 3 to 4 days, while carefully monitoring electrolytes and volume status (conditional recommendation, very low level of evidence).
21a. Enteral feeding protocols should be used in hospitalized patients in need of nutrition therapy (strong recommendation, moderate-to-high level of evidence).
21b. A validated protocol should be used, such as a volume-based feeding protocol or a multi-strategy (bundled) top-down protocol (conditional recommendation, very low level of evidence).
22. Gastric residual volume should not be used routinely as a monitor in hospitalized patients on EN (conditional recommendation, very low level of evidence).
23a. Patients on EN should be assessed for risk of aspiration (conditional recommendation, very low level of evidence).
23b. For patients determined to be at high risk, the following steps should be taken to proactively reduce that risk:
Use a prokinetic agent (conditional recommendation, low level of evidence).
Divert the level of feeding lower in the GI tract (strong recommendation, moderate-to-high level of evidence).
Switch to continuous infusion (conditional recommendation, very low level of evidence).
Use chlorhexidine mouthwash twice daily (conditional recommendation, very low level of evidence).
24a. For the patient receiving EN who develops diarrhea, an evaluation should be initiated to identify an etiology and direct management (conditional recommendation, very low level of evidence).
24b. The patient receiving EN who develops diarrhea should be managed by one of the three strategies:
Use of fermentable soluble fiber as an adjunctive supplement to a standard EN formula (conditional recommendation, very low level of evidence).
Switching to a commercial mixed fiber (soluble and insoluble) formula (conditional recommendation, low level of evidence).
Initiating a small peptide/MCT oil formula (conditional recommendation, very low level of evidence).
Complications of enteral access
Question: How should complications of enteral feeding in the hospitalized patient be assessed and treated?
Recommendations:
25. The percutaneous enteral access site should be monitored by cleaning daily with mild soap and water and maintaining correct positioning of the external bolster (conditional recommendation, very low level of evidence).

Table 6 continued on following page

Table 6. Continued

26a. Prevention of tube clogging is important to successful EN and may be achieved by frequent water flushes delivered every shift and each time medications are given (conditional recommendation, very low level of evidence).
26b. When a clogged tube is encountered and the use of water flushes is unsuccessful at clearing, a de-clogging solution comprising a nonenteric-coated pancreatic enzyme tablet dissolved in a sodium bicarbonate solution should be used (conditional recommendation, very low level of evidence).
26c. If still unsuccessful, a mechanical de-clogging device should be considered prior to exchanging the tube for a new one (conditional recommendation, very low level of evidence).
27a. A patient who inadvertently dislodges a recently placed percutaneous gastrostomy tube (<7–10-day old) should be brought back immediately to the endoscopy or radiology suite and a new tube placed endoscopically or radiologically through the same site on the abdominal wall (conditional recommendation, very low level of evidence).
27b. If a percutaneous gastrostomy tube becomes dislodged that has been in place long enough for a partially formed tract to develop (>7–10 days), a tube of similar diameter should be placed blindly as expeditiously as possible to maintain patency and prevent closure of the tube tract. In this latter circumstance, radiologic confirmation should be carried out prior to feeding if there is any question of inappropriate location of the tube (conditional recommendation, very low level of evidence).
28a. For a patient with deterioration, breakdown, increased drainage/leakage, or enlarging stoma around the percutaneous tube site, an evaluation should be performed to determine etiology and appropriate management (conditional recommendation, very low level of evidence).
28b. Placement of a larger tube should not be used to manage leakage caused by an enlarging stoma around the percutaneous access device (conditional recommendation, very low level of evidence).
29. A percutaneous enteral access device that shows signs of fungal colonization with material deterioration and compromised structural integrity should be replaced in a non-urgent but timely manner (conditional recommendation, very low level of evidence).
Parenteral nutrition
Question: When and how should parenteral nutrition be utilized in the hospitalized patient?
Recommendations:
30a. If early EN is not feasible and the patient is at low nutritional risk upon admission, no specialized nutrition therapy should be provided and PN should be withheld for the first week of hospitalization (conditional recommendation, very low level of evidence).
30b. If a patient is at high nutritional risk on admission to the hospital and EN is not feasible, PN should be initiated as soon as possible (strong recommendation, moderate level of evidence).
31. Supplemental PN should be considered for the patient already on enteral tube feeding only after 7 to 10 days, when unable to meet greater than 60% of energy and/or protein requirements by the enteral route alone. Initiating supplemental PN prior to this 7–10-day period in those patients already receiving EN does not improve outcomes and may be detrimental to the patient (strong recommendation, moderate level of evidence).
32. In hospitalized patients receiving PN, mild permissive underfeeding (delivery 80% of energy requirements with full protein provision) should be considered initially for the first 7 to 10 days. Following this first week (if long-term PN is required), energy provision should be increased to meet energy goals (conditional recommendation, low level of evidence).
33. Peripheral PN should not be used, as it leads to inappropriate use of PN, has a high risk of phlebitis and loss of venous access sites, and generally provides inadequate nutrition therapy (conditional recommendation, very low level of evidence).
34a. Careful transition feeding should be used in the patient on PN, for whom EN is now being initiated. As tolerance to EN improves and volume of delivery increases, PN should be tapered to avoid overfeeding (conditional recommendation, very low level of evidence).
34b. PN should be stopped when the EN provides >60% of energy and protein goals (conditional recommendation, very low level of evidence).
Nutritional therapy at end-of-life
Question: Should specialized nutrition therapy be provided to a hospitalized patient at end-of-life?
Recommendations:
35a. The decision to place a gastrostomy tube in an end-of-life situation should be determined by patient autonomy and the wishes of that patient and their family, even though the nutrition therapy may do little to change traditional clinical outcomes (conditional recommendation, very low level of evidence).
36b. Regardless of prognosis, placement of a gastrostomy device should be based on whether achieving enteral access and initiating EN successfully meet the goals of the patient and/or their family. Percutaneous gastrostomy placement should be considered even if the only benefit is to provide improvement in the quality of life for the family, increased ease of providing nutrition, hydration, and medications, or to facilitate transfer out of the hospital setting to a facility closer to home (conditional recommendation, very low level of evidence).
36. The clinician is not obligated to provide hydration and nutrition therapy in end-of-life situations. The decision to initiate nutrition therapy is no different than the decision to stop therapy once it has started (thus, clinicians are not obligated to provide therapy that is unwarranted) (conditional recommendation, very low level of evidence).
37a. If requested, nutrition therapy in end-stage malignancy should be provided by the enteral route (conditional recommendation, very low level of evidence).
37b. Use of PN in this setting may cause net harm and should be highly or aggressively discouraged (conditional recommendation, very low level of evidence).
38. The clinician who has ethical concerns of his own in a difficult end-of-life situation should excuse himself from the case, as long as he can transfer care to an equally qualified and willing health-care provider (conditional recommendation, very low level of evidence).

BMI, body mass index; EN, enteral nutrition; GI, gastrointestinal; ICU, intensive care unit; NRS-2002, Nutritional Risk Score 2002; PN, parenteral nutrition.

9b. Radiologic confirmation of placement in the stomach should be carried out prior to feeding (except with the use of electromagnetic transmitter-guided feeding tubes). Repeated periodic radiologic confirmation of correct tube position in the GI tract is not required unless there is concern for tube displacement because of nausea/vomiting, regurgitation, coughing, retching, or overt displacement (conditional recommendation, very low level of evidence).

10a. Conversion to a post-pyloric feeding tube should be carried out only when gastric feeding has been shown to be poorly tolerated or the patient is at high risk for aspiration (strong recommendation, moderate-to-high level of evidence).

10b. Simultaneous aspiration/decompression of the stomach with jejunal feeding may be accomplished by using a dual lumen aspirate/feed nasoenteric tube, a combined percutaneous gastrojejunostomy (GJ) tube, or the use of both gastrostomy and jejunostomy tubes (conditional recommendation, very low level of evidence).

11. When long-term enteral access is needed in a patient with gastroparesis or chronic pancreatitis, a jejunostomy tube should be placed (conditional recommendation, very low level of evidence).

12. A percutaneous enteral access device should be placed, either via the gastric or the jejunal route, if enteral feeding is anticipated to be required for >4-week duration (conditional recommendation, very low level of evidence).

13. A percutaneous gastrostomy should be placed preferentially in the gastric antrum in order to facilitate conversion to a GJ tube in the event that the patient is intolerant to gastric feeding (conditional recommendation, very low level of evidence).

14. For the patient at high risk for tube displacement, steps should be taken proactively to secure the access device at the time of placement (conditional recommendation, very low level of evidence).

Summary of evidence. Gastric feeding is successful in the vast majority of patients requiring nasoenteric feeding in the hospital (71). Although GI dysfunction occurs in 30–70% of ICU patients, most will tolerate gastric feeding (72,73). Importantly, the presence of bowel sounds is not a sensitive marker of GI function and is not required to initiate EN (74,75). Greater disease severity, however, is associated with a worsening degree of ileus and GI dysmotility, and, in those circumstances, there may be more of a need for small bowel feeding (73). In a recent RCT involving patients with APACHE II Scores>20, the use of small bowel feeding significantly reduced hospital length of stay, decreased total complications, and increased EN delivery compared with gastric feedings (76). In contrast, there was no difference in the outcome between gastric and small bowel feeds in patients with APACHE II Scores<20 (76).

The use of nasogastric feeding is more physiologic, expedites delivery of nutrition therapy, requires a low level of expertise for placement, and results in minimal delay in initiation of feeding (76,77). Radiologic confirmation of placement of a nasoenteric or an oroenteric tube in the stomach or small bowel is required (78). Alternative methods to confirm the location of the tube tip in the GI tract below the diaphragm, such as auscultation, detection of CO_2, and measurement of pH are not accurate enough to confirm placement (78). Tubes that are designed to allow determination of their location using electromagnetic tracking obviate the need for radiologic confirmation, as the accuracy of this system in confirming placement of the tube in the stomach or small bowel has been validated by multiple studies (79,80). New optical guidance feeding tubes have recently been approved by the Federal Drug Administration but will require further validation studies before radiologic confirmation can be avoided (81).

The incidence of reflux, regurgitation, and aspiration all decrease significantly as the level of infusion of formula is diverted lower in the GI tract, from the stomach to the proximal jejunum (82). A meta-analysis of 12 RCTs showed a reduction in ventilator-associated pneumonia with small bowel compared with gastric feeding; yet, duration of mechanical ventilation, hospital length of stay, and mortality did not change (83). These findings suggest that the appearance of an infiltrate on chest X-ray in a patient on enteral tube feeding may have minimal consequences. Placement of a feeding tube in the small bowel requires greater expertise, which may lead to delays in initiation of feeding (77). For these reasons, it is best to start with gastric feeds, take additional steps to promote tolerance, and to monitor closely while awaiting expertise for small bowel placement if subsequently required.

Increasing use of oroenteric access in the mechanically ventilated patient is related to the documented incidence of sinusitis of ~11.4–13.0% in those patients with nasoenteric access (84).

Long-term jejunal access is best achieved by the use of a jejunostomy tube placed endoscopically, radiologically, or surgically, depending upon available expertise. Because of frequent displacement of the jejunal extension tube back into the stomach with a GJ device, this is generally not a good long-term option. Recent changes in the design of tubes (such as the use of a stiffer double pigtail catheter with a spring in the jejunal portion of the tube), however, seem to result in less displacement. Given the greater ease of placement compared with a direct jejunostomy, reconsideration of the use of such GJ tubes may be warranted.

If the duration of provision of EN is anticipated to exceed 4 weeks, then a percutaneous enteral access device is generally indicated. The 4-week cutoff, although arbitrary, is based on the potential morbidity of a nasoenteric tube, which includes erosion of the nares, an increase in aspiration pneumonia, sinusitis, and esophageal ulceration or stricture (85). Certain institutional practices may dictate early placement of a tracheostomy and percutaneous gastrostomy tube in trauma patients. Early gastrostomy tube placement in stroke patients may be needed to facilitate transfer to a rehabilitation center. More than any other patient population, those with a cerebral vascular accident benefit from percutaneous gastrostomy placement as a bridge to oral feeding, as the incidence of dysphagia may drop to less than half the initial rate at 4 months (29–45 to 20%) following an acute stroke (86,87). In patients with amyotrophic lateral sclerosis, timing of gastrostomy placement is important, before the forced vital capacity drops below 50% (88).

Placement prior to this time point has been shown to extend survival of the amyotrophic lateral sclerosis patient (88).

Initial positioning of the gastrostomy tube in the gastric antrum (on the patient's right side close to the level of the umbilicus) may provide important benefits (89). In this position, there is apposition of the stomach to the anterior abdominal wall over a greater surface area, and the pathway into the stomach is shorter and more perpendicular than the more traditional position above and to the patient's left of midline. Most importantly, if the patient demonstrates intolerance and evidence of gastroparesis in the days following gastrostomy tube placement, the access device is better positioned to be converted to a GJ tube (89). Reluctance to positioning percutaneous gastrostomy tubes in the gastric antrum in the past related, in part, to concern for interference with the antral grinding mechanism, bleeding from passage through the falciform ligament, and potential obstruction of the pylorus. Extensive clinical experience does not support any of these concerns. When feasible, we suggest that all percutaneous gastrostomy tubes be placed to the right of the midline, close to the level of the umbilicus.

A variety of measures can help secure the enteral access device at the time of placement (89). A nasal bridle fashioned from a 5-French neonatal feeding tube or a commercial device with magnetic-tipped flexible rods and surgical ribbon may be used to secure a nasoenteric tube placed through the nose. A recent meta-analysis showed that the use of a nasal bridle nearly eliminates displacement (90). With placement of a percutaneous gastrostomy, the use of T-fastener or "T-Tacks" keep the stomach adherent to the anterior wall, facilitating replacement should inadvertent dislodgement occur (85). With a skin-level "button" gastrostomy, patients are more likely to dislodge the connector tubing leaving the access device in place. A commercial clamping device is available that impedes a patient's ability to inadvertently displace the gastrostomy tube. Although an abdominal binder is helpful in protecting the percutaneous gastrostomy tube, it should be loose enough to avoid crushing the access device and positioned with support at the level of the skin to prevent excess side torsion to the gastrostomy tract (85). Ultimately, whenever possible, the reason(s) for inadvertent removal of the tube (e.g., delirium, dementia, pain, and so on) needs to be determined and corrected.

D. Initiating Enteral Nutrition

Question: How soon, at what dose, and with which formula should enteral nutrition be initiated in the hospitalized patient?

Recommendations:

15. In the patient at high nutritional risk unable to maintain volitional intake, EN should be initiated within 24–48 h of admission to the hospital (conditional recommendation, low level of evidence).

16a. Although early EN should be initiated within 24–48 h of admission, the timing by which to advance to goal is unclear. When tolerated, feeding should be advanced to goal within 48–72 h (conditional recommendation, very low level of evidence).

16b. With reduced tolerance, feeding should be advanced with caution to goal by 5 to 7 days (conditional recommendation, very low level of evidence).

17. Permissive underfeeding (i.e., hypocaloric feeding) is an acceptable alternative to full feeding and may be considered in three separate patient scenarios:
    (i) Acute Lung Injury/Acute Respiratory Distress Syndrome (ALI/ARDS) (strong recommendation, high level of evidence).
    (ii) Obesity with BMI>30 (conditional recommendation, very low level of evidence).
    (iii) Placement on PN over the first week of nutrition therapy (conditional recommendation, low level of evidence).

18a. A standard polymeric formula or a high-protein standard formula should be used routinely in the hospitalized patient requiring EN (conditional recommendation, very low level of evidence).

18b. An immune-modulating formula containing arginine and omega-3 fish oil should be used for patients who have had major surgery and are in a surgical ICU setting (conditional recommendation, very low level of evidence).

18c. An immune-modulating formula containing arginine and omega-3 fish oil should not be used routinely in patients in a medical ICU (conditional recommendation, very low level of evidence).

Summary of Evidence. The timing of initiation of EN in the hospitalized patient (especially critically ill patients in an ICU setting) is based on two categories of studies in the literature, early vs. delayed EN and early EN vs. standard therapy. In meta-analyses by Marik and Doig comparing early vs. delayed EN, early feeds started within the first 24–48 h (average 36 h) of admission were associated with significantly reduced infection, hospital LOS, and mortality compared with feeds started after that time point (15,91). Additional meta-analyses comparing early EN to standard therapy after elective surgery, in the surgical ICU, and in patients undergoing surgery for complications of pancreatitis, showed that early EN was associated with significant reductions in infection, hospital LOS, and mortality (16,17). More recent meta-analyses combining these categories of patients continue to show a correlation between use of early EN and significant reductions in infection (with a trend toward reduced mortality) (14,15).

In patients at high-nutritional risk, delivery of ≥ 80% of goal calories was associated with the lowest mortality in a large observational study in mixed ICU patients (92). Tolerance determines how quickly and how aggressively to increase EN delivery.

In a large multi-center randomized trial, patients with ARDS/ALI were shown to have equivalent outcomes whether they were randomized to trophic feeding at 20 ml/h (providing 25% of requirements) for the first 6 days then advanced to goal, or to full feeds from the time of admission (providing 80% of caloric requirements at end of study) (10). Patients in this study were moderately critically ill with an average age of 52 years, BMI of 30, short stay in the ICU of 5 days, and a mortality rate of 10%. Trophic feeding may not be appropriate in patients who are at extremes of age, BMI, or disease severity (24). It is appropriate to place obese critically ill patients with a BMI>30 on a high protein, hypocaloric regimen providing 2.0–2.5 g protein/kg ideal body weight per day,

and 60–65% of estimated or measured energy expenditure for total caloric delivery (93). Such a regimen should maintain lean body mass while depleting the fat mass, with no increase in adverse outcomes (94). In ICU patients who are appropriate candidates for PN over the first week of therapy, hypocaloric feeding providing 80% of caloric requirements while providing full protein delivery at 1.5–2.0 g/kg per day promotes mild weight loss and improves insulin sensitivity (95,96). Such a regimen was shown to be associated with significant reductions in infection and hospital LOS compared with full caloric feeding (95).

Indications for use of specialized formulae are limited, and their use should be reserved for certain subsets of hospitalized patient populations. The vast majority of hospitalized patients requiring EN will tolerate a standard polymeric formula with or without fiber. Critically ill patients in the medical ICU will also generally tolerate a standard polymeric formula (or high-protein standard formula) and routine use of formulas designed to be immune-modulatory, elemental/semi-elemental, disease-specific (diabetes), and organ-specific (hepatic, renal, pulmonary) are discouraged (88,97–100). Pre-operative patients awaiting major elective surgery and critically ill patients admitted to a surgical ICU may benefit from an arginine-containing immune-modulating formula (also containing fish oil, glutamine, and antioxidants). Use of such formulas in this patient population has been shown to be associated with significant reductions in infection and hospital LOS, but not mortality (88,101,102). No recommendation can be made at this time for non-arginine anti-inflammatory lipid formulas in ARDS/ALI due to conflicting results in the seven RCTs (five continuous infusions, two bolus infusions) that have compared their use with standard enteral formulations (24,103).

E. Monitoring tolerance and adequacy of EN

Question: How should adequacy and tolerance of EN be assessed in the hospitalized patient?

Recommendations:

19a. Hospitalized patients on EN should be monitored daily by physical exam (conditional recommendation, very low level of evidence).

19b. Patients on EN should be monitored for adequacy of provision of EN as a percent of target goal calories, cumulative caloric deficit, and inappropriate cessation of EN (conditional recommendation, very low level of evidence).

20. In the patient at high risk for refeeding syndrome, feeding should be ramped up slowly to goal over 3 to 4 days, while carefully monitoring electrolytes and volume status (conditional recommendation, very low level of evidence).

21a. Enteral feeding protocols should be used in hospitalized patients in need of nutrition therapy (strong recommendation, moderate-to-high level of evidence).

21b. A validated protocol should be used, such as a volume-based feeding protocol or a multi-strategy (bundled) top-down protocol (conditional recommendation, very low level of evidence).

22. Gastric residual volume (GRV) should not be used routinely as a monitor in hospitalized patients on EN (conditional recommendation, very low level of evidence).

23a. Patients on EN should be assessed for risk of aspiration (conditional recommendation, very low level of evidence).

23b. For patients determined to be at high risk, the following steps should be taken to proactively reduce that risk:
- (i) Use a prokinetic agent (conditional recommendation, low level of evidence).
- (ii) Divert the level of feeding lower in the GI tract (strong recommendation, moderate-to-high level of evidence).
- (iii) Switch to continuous infusion (conditional recommendation, very low level of evidence).
- (iv) Use chlorhexidine mouthwash twice daily (conditional recommendation, very low level of evidence).

24a. For the patient receiving EN who develops diarrhea, an evaluation should be initiated to identify an etiology and direct management (conditional recommendation, very low level of evidence).

24b. The patient receiving EN who develops diarrhea should be managed by one of the three strategies:
- (i) Use of fermentable soluble fiber as an adjunctive supplement to a standard EN formula (conditional recommendation, very low level of evidence).
- (ii) Switching to a commercial mixed fiber (soluble and insoluble) formula (conditional recommendation, low level of evidence).
- (iii) Initiating a small peptide/MCT oil formula (conditional recommendation, very low level of evidence).

Summary of evidence. Patients on EN should be monitored daily by physical exam to detect the presence of bowel sounds, passage of stool and gas, abdominal distention, and volume status (104). Caloric and protein target goals should be clearly identified and intake and output should be followed to determine the percent of goal calories delivered. Cumulative caloric deficit should be followed and documented in the chart, as increasing caloric deficit has been shown in five observational studies to be associated with increased adverse outcomes (18,105,106). Increased delivery of calories to reduce the deficit is associated with improved outcome.

Patients at high risk for refeeding syndrome are those with low BMI<20 kg/m^2, recent weight loss prior to admission, or prolonged period nil per os (107). Such patients should be monitored closely for up to 5 days for electrolyte abnormalities (hypokalemia, hypophosphatemia, and hypomagnesemia), and volume status after feeding is initiated (107). It is not clear whether risk of refeeding syndrome is more common with EN or PN (108).

The use of feeding protocols with nursing directives is an important strategy for improving the timeliness, adequacy, and safety of delivering EN (109). Multiple RCTs and trials before and after implementation of such protocols have shown that their use increases delivery to a greater percentage of patients over the first week of hospitalization in the ICU (22,110–114). Important elements of nurse-driven protocols include the use of universal EN connectors, monitoring by focused physical exam, consideration of fluid volumes, management of GRVs, rates for advancement of EN based on tolerance, and measures to reduce risk of aspiration. A volume-based feeding strategy identifies the volume to be

delivered over a 24 h period and empowers the nurse to increase the rate to make up for interruptions in delivery (115). A multistrategy top-down protocol has been described for use in critically ill patients based on the presumption that these patients are at increased risk of feeding intolerance and that multiple strategies can be used with the initiation of EN to promote better tolerance including the use of volume-based feeding, elevation of the head of the bed, chlorhexidine mouth washes, small bowel feeding, and the use of prokinetic medications (114). Multiple strategies are utilized together with the initiation of EN and then individually removed as tolerance is achieved.

GRV has been shown to be a poor marker of true gastric volume, gastric emptying, risk of aspiration, pneumonia, and poor outcomes (116–118). Furthermore, the practice of checking GRV is not well standardized, the values are difficult to interpret, and expense involved with allocation of health-care resources (nursing time) is substantial (119). The use of GRVs as a monitor increases the likelihood of tube clogging tenfold (120). The sensitivity of GRV to detect aspiration is poor (shown to be<2–8%) (118). Lowering the cutoff value does not protect the patient from aspiration but instead simply turns off the delivery of EN. Ironically, by reducing EN delivery, the use of GRV may increase risk for pneumonia (121). A prospective trial before and after implementation of a protocol mandating no use GRV, and a multicenter RCT comparing the use of GRV with non-use, showed no difference in clinical outcome (122,123).

A number of risk factors identify those patients who are at increased risk for aspiration such as age >70 years, altered mental status, presence of an endotracheal or nasoenteric tube, prolonged supine position, and bolus infusion of formula (82). Steps to reduce risk for aspiration include elevation of the head of the bed, switching to continuous infusion of formula, diverting the level of infusion lower in the GI tract, initiating prokinetic agents, using chlorhexidine mouthwash, and considering simultaneous aspiration/decompression of stomach contents with small bowel feeding (124). Bundling individual strategies may be more effective in changing outcome (82).

Diarrhea in the patient receiving EN is common, with an incidence ranging from 2 to 95% (125). Differences in definition mostly account for the wide range of incidence. Much of what is referred to as diarrhea in hospitalized patients on EN actually represents low-volume fecal incontinence. Although most cases are mild and self-limited, diarrhea in the hospitalized patient on EN may result in electrolyte imbalance, dehydration, perianal skin breakdown, and wound contamination (125). Although factors associated with the formula (e.g., fiber, osmolarity), delivery mode, and enteral feeding contamination are often blamed, the most common etiology of diarrhea in a patient receiving EN is the receipt of sorbitol-containing medications (which accounts for 55% of such cases) (126). Presence of *Clostridium difficile* infection is also important, accounting for 17–20% of diarrhea in patients on tube feeding (127). There is abundant data to recommend stopping prokinetics in individuals who develop non-*C. difficile* diarrhea while on EN (128–130). When an underlying cause cannot be identified and diarrhea persists, the addition of a fermentable soluble fiber supplement (e.g., inulin, fructo-oligosaccharides, guar gum, achasia gum, and so on) to a standard enteral formula has been shown to more consistently reduce diarrhea (131–134) than the use of a commercial mixed soluble/insoluble fiber-containing formula (135,136). The prebiotic effect of the soluble fiber helps foster a more balanced and biodiverse gut microbiome (137). Although the use of small peptide/MCT oil formulas (designed physiologically to increase the efficiency of absorption in a situation of compromised bowel) would seem to be an appropriate alternative strategy, prospective RCTs have failed to show significant outcome benefits with their use compared with standard formulations (83).

F. Complications of enteral access

Question: How should complications of enteral feeding in the hospitalized patient be assessed and treated?

Recommendations:

25. The percutaneous enteral access site should be monitored by cleaning daily with mild soap and water and maintaining correct positioning of the external bolster (conditional recommendation, very low level of evidence).

26a. Prevention of tube clogging is important to successful EN and may be achieved by frequent water flushes delivered every shift and each time medications are given (conditional recommendation, very low level of evidence).

26b. When a clogged tube is encountered and the use of water flushes is unsuccessful at clearing, a de-clogging solution comprising a nonenteric-coated pancreatic enzyme tablet dissolved in a sodium bicarbonate solution should be used (conditional recommendation, very low level of evidence).

26c. If still unsuccessful, a mechanical de-clogging device should be considered prior to exchanging the tube for a new one (conditional recommendation, very low level of evidence).

27a. A patient who inadvertently dislodges a recently placed percutaneous gastrostomy tube (<7–10-day old) should be brought back immediately to the endoscopy or radiology suite and a new tube placed endoscopically or radiologically through the same site on the abdominal wall (conditional recommendation, very low level of evidence).

27b. If a percutaneous gastrostomy tube becomes dislodged that has been in place long enough for a partially formed tract to develop (>7–10 days), a tube of similar diameter should be placed blindly as expeditiously as possible to maintain patency and prevent closure of the tube tract. In this latter circumstance, radiologic confirmation should be carried out prior to feeding if there is any question of inappropriate location of the tube (conditional recommendation, very low level of evidence).

28a. For a patient with deterioration, breakdown, increased drainage/leakage, or enlarging stoma around the percutaneous tube site, an evaluation should be performed to determine etiology and appropriate management (conditional recommendation, very low level of evidence).

28b. Placement of a larger tube should not be used to manage leakage caused by an enlarging stoma around the percutaneous access device (conditional recommendation, very low level of evidence).

29. A percutaneous enteral access device that shows signs of fungal colonization with material deterioration and compromised structural integrity should be replaced in a non-urgent but timely manner (conditional recommendation, very low level of evidence).

Summary of evidence. Daily cleaning with mild soap and water is important to avoid the drying desiccating effects on the skin from hydrogen peroxide or scented alcohol-based soaps (138). For the first 4 days following tube placement, the external bolster, if present, should be positioned up against the anterior wall with a single layer of gauze underneath against the skin. Thereafter, the bolster should be repositioned/loosened to avoid excessive tightening of the bolster against the skin, which can lead to an increased risk of stomal-site infection and "buried bumper syndrome" (138). In addition, we suggest minimizing side torsion or excessive traction on the tube tract wall, as this can lead to an enlarging stoma and excessive drainage/leakage (138). This side-traction can usually be prevented by using a commercial clamping device or a bolster system to keep the percutaneous gastrostomy exiting the anterior abdominal wall at 90° (85).

The initial step when attempting to declog a tube is to instill warm water in an agitated "back-and-forth" motion using a syringe (139). If unsuccessful, a nonenteric-coated pancreatic enzyme tablet (e.g., Viokase) and a 650 mg sodium bicarbonate tablet are crushed together in warm water and then instilled in a similar manner in an agitated motion with a syringe (140). Use of a carbonated soft drink is an acceptable alternative, but the use of papain (meat tenderizer) should be avoided (139). If still not corrected, a small-bore tube (such as an ERCP catheter) may be placed down through the feeding tube to the level of the clot and flushing attempts repeated. If still unsuccessful, before replacing the tube, mechanical de-clogging with a commercial corkscrew de-clogging device, a cytology brush, or a wire stylet should be considered (albeit used with caution to prevent penetration of the sidewall of the tube and puncture of the intestinal wall) (139).

Deterioration, breakdown, and increased drainage at the percutaneous access site should be evaluated carefully to rule out buried bumper syndrome, side torsion on the tract, absence of an external bolster, granulation tissue, or a tube site infection (141). Hypergranulation tissue at the stomal-site should be treated with a topical high potency steroid ointment (e.g., 0.5% triamcinolone) or chemical cauterization with silver nitrate sticks (141). We suggest treating tube site infections empirically using a broad-spectrum antibiotic administered either orally or through the tube (rarely is a parenteral antibiotic needed) (85). Because of the high risk of contamination with skin organisms, culture of the tract or tissue is not recommended in routine situations. Although most stomal-site infections are minor, severe infections including necrotizing fasciitis can occur and require rapid recognition to optimize management. Rarely does the tube need to be removed. For the patient with increased leakage to the point of severe skin injury, we suggest high-dose acid suppression, diverting the level of infusion of formula lower in the GI tract, simultaneous jejunal feeding with gastric aspiration, and involvement of a wound-care expert (141). Occasionally, the tube will need to be removed and the tract allowed to close prior to placing a new tube in the same or different location.

G. Parenteral nutrition

Question: When and how should PN be utilized in the hospitalized patient?

Recommendations:

30a. If early EN is not feasible and the patient is at low nutritional risk upon admission, no specialized nutrition therapy should be provided and PN should be withheld for the first week of hospitalization (conditional recommendation, very low level of evidence).

30b. If a patient is at high nutritional risk on admission to the hospital and EN is not feasible, PN should be initiated as soon as possible (strong recommendation, moderate level of evidence).

31. Supplemental PN should be considered for the patient already on enteral tube feeding only after 7 to 10 days, when unable to meet >60% of energy and/or protein requirements by the enteral route alone. Initiating supplemental PN prior to this 7–10-day period in those patients already receiving EN does not improve outcomes and may be detrimental to the patient (strong recommendation, moderate level of evidence).

32. In hospitalized patients receiving PN, mild permissive underfeeding (delivery 80% of energy requirements with full protein provision) should be considered initially for the first 7 to 10 days. Following this first week (if long-term PN is required), energy provision should be increased to meet energy goals (conditional recommendation, low level of evidence).

33. Peripheral PN (PPN) should not be used, as it leads to inappropriate use of PN, has a high risk of phlebitis and loss of venous access sites, and generally provides inadequate nutrition therapy (conditional recommendation, very low level of evidence).

34a. Careful transition feeding should be used in the patient on PN, for whom EN is now being initiated. As tolerance to EN improves and volume of delivery increases, PN should be tapered to avoid overfeeding (conditional recommendation, very low level of evidence).

34b. PN should be stopped when the EN provides >60% of energy and protein goals (conditional recommendation, very low level of evidence).

Summary of evidence. The clinical benefit of PN in hospitalized patients (other than those with PN-dependent intestinal failure, such as short bowel syndrome, chronic intestinal pseudo-obstruction, high-output enterocutaneous fistula) has been difficult to demonstrate. Three recent trials looked at the use of exclusive PN in the hospitalized patient. The Early Parenteral Nutrition in Insufficient Enteral Feeding (EPaNIC) trial showed that early provision of PN on the third day of hospitalization in a subset of patients in which there was a contraindication to enteral feeding (because bowel was in discontinuity) led to an increase in infectious morbidity and a reduced likelihood of being discharged alive from the ICU compared with controls in which PN was started on

the eighth day (142). Doig *et al.* (143) studied hospitalized patients in whom there was thought to be a relative contraindication to EN for at least 3 days. The patients randomized to early PN showed only a 0.46-day reduction in duration of mechanical ventilation compared with controls on standard therapy. All other outcome parameters ranging from infection and organ failure to hospital length of stay and mortality were no different between the two groups. In a multi-centered ICU trial of nearly 2,400 patients comparing EN with exclusive PN, there was no difference between the groups in clinical outcome (12). Although the latter reports demonstrate that, under well-controlled protocolized conditions, PN can be administered safely and may even approach the outcomes seen with receipt of EN, PN offers no clear advantage over EN with regard to mortality or infections (12,143).

In a well-nourished patient, particularly in the first week of hospitalization, the use of PN appears to provide no benefit over standard therapy and may actually cause net harm (4). At some point in the patient at low nutritional risk, failure to provide nutrition therapy will lead to deterioration of nutritional status and adverse outcome. In an older study, Sandstrom showed increased mortality and hospital length of stay if standard therapy was continued beyond the first 2 weeks of hospitalization compared with receipt of PN (144). Most societal recommendations indicate a reluctance to extend standard therapy beyond the first week of hospitalization, suggesting instead initiating PN in the patient at low nutritional risk beginning the second week of hospitalization (145).

In the patient at high nutritional risk with increased disease severity and evidence for deterioration of nutritional status, priorities of therapy change. If EN is not feasible, PN is more likely to benefit these patients than standard therapy. In two early meta-analyses, the use of PN in patients with evidence of malnutrition was associated with reduced overall complications and mortality compared with standard therapy (4,5). Thus, in patients with high nutritional risk for whom EN is not feasible, PN should be initiated as soon as possible following admission.

In patients with a diagnosis indicating PN dependence (short bowel syndrome, chronic intestinal pseudo-obstruction), PN should be initiated immediately after admission unless there is evidence for ongoing bacteremia.

The addition of supplemental PN during the first week of therapy to patients already receiving EN, where the enteral feeding is not meeting caloric goals, appears to provide little benefit and may cause net harm (92). The original design of the EPaNIC study addressed the timing of supplemental PN added to hypocaloric tube feeding (142). Results showed that for study patients, PN added on the third day of hospitalization was associated with worse outcome with respect to virtually every clinical parameter (except mortality) compared with controls where PN was added beginning on the eighth day (142). Specifically, significant increases in infection, organ failure, hospital and ICU length of stay, cost, and likelihood of being discharged alive were all worse with receipt of early supplemental PN (142). In another study evaluating the need for supplemental PN, Heidegger *et al.* (106) evaluated patients on EN who were determined by the third day to be receiving <60% of goal calories and protein, randomizing them to supplemental PN vs. placebo. Receipt of supplemental PN from the fourth day through the ninth day succeeded only in reducing "other infections" (relatively minor infections of the skin, bone, nose, and so on) compared with controls receiving placebo, with no difference between groups with regard to mortality or major infection (pneumonia, sepsis, or bacteremia) (106). The optimal timing for adding supplemental PN is not clear but should be considered after the first week of hospitalization in patients receiving <60% of goal calories by the EN route alone (106).

In the patient who is determined to be an appropriate candidate for PN, the risk/benefit ratio of this nutrition therapy over the first week of hospitalization may be improved by providing hypocaloric nutrition therapy (80% of goal calories) (95). Such strategy may result in some weight loss, but leads to better insulin sensitivity, avoids the effects of overfeeding, and may improve outcome. In a meta-analysis of five RCTs involving patients with trauma, pancreatitis, and major abdominal surgery, the use of hypocaloric PN was associated with reduced infection and hospital length of stay compared with PN provided at goal feeds (20 vs. 25 kcal/kg per day) (95). Once the patient is more stabilized in the second week of hospitalization, PN delivery should be increased to meet 100% of goal calories and protein requirements.

The use of PPN is severely limited by intolerance of peripheral veins to the osmolarity of any solution >800–900 mosm/l (central venous access allows tolerance of solutions up to 2,000 mosm/l) (146). As a result, the use of PPN is associated with increased use of IV lipid emulsions to decrease the osmolarity, decreased delivery of overall calories and protein, and increased likelihood for venous sclerosis (146). Routine use of PPN is associated with increasing loss of venous access sites and abuses derived from inappropriate short-term PN.

In a patient receiving both EN and PN, careful transition feeding is necessary to avoid overfeeding as EN tolerance improves and the need for PN is decreased. By convention, PN may be stopped when EN provides >60% of goal energy and protein.

H. Nutritional Therapy at End-of-Life

Question: Should specialized nutrition therapy be provided to a hospitalized patient at end-of-life?

Recommendations:

35a. The decision to place a gastrostomy tube in an end-of-life situation should be determined by patient autonomy and the wishes of that patient and their family, even though the nutrition therapy may do little to change traditional clinical outcomes (conditional recommendation, very low level of evidence).

35b. Regardless of prognosis, placement of a gastrostomy device should be based on whether achieving enteral access and initiating EN successfully meet the goals of the patient and/or their family. Percutaneous gastrostomy placement should be considered even if the only benefit is to provide improvement in the quality of life for the family, increased ease of providing nutrition, hydration, and medications, or to facilitate transfer out of the hospital setting to a facility closer to home (conditional recommendation, very low level of evidence).

36. The clinician is not obligated to provide hydration and nutrition therapy in end-of-life situations. The decision to initiate nutrition therapy is no different than the decision to stop therapy once it has started (thus, clinicians are not obligated to provide therapy that is unwarranted) (conditional recommendation, very low level of evidence).

37a. If requested, nutrition therapy in end-stage malignancy should be provided by the enteral route (conditional recommendation, very low level of evidence).

37b. Use of PN in this setting may cause net harm and should be highly or aggressively discouraged (conditional recommendation, very low level of evidence).

38. The clinician who has ethical concerns of his own in a difficult end-of-life situation should excuse himself from the case, as long as he can transfer care to an equally qualified and willing health-care provider (conditional recommendation, very low level of evidence).

Summary of evidence. Traditional outcome parameters (infection, organ failure, hospital length of stay, and mortality) are not likely to change in response to nutrition therapy in dementia, metastatic malignancy, or end-of-life situations (147,148). In end-stage dementia, placement of a percutaneous gastrostomy and provision of EN are not likely to improve the patient's quality of life, heal pressure sores, reduce risk of aspiration pneumonia, or reduce mortality (147,149,150). However, nutrition therapy is likely to improve a cancer patient managed surgically who is cured from the malignancy but has altered GI anatomy or function postoperatively. The use of PN in the non-operative management of malignancy should be avoided, as it may lead to worse outcomes compared with standard therapy with no nutrition support (4).

Provision of hydration and nutrition therapy is no different than provision of any other medical therapy, including mechanical ventilation, dialysis, and supplemental oxygen (151). There is no difference between non-invasive and invasive therapy, and the distinction between ordinary and extraordinary therapy is meaningless. Clinicians are never obligated to provide nutrition therapy to a patient at end-of-life and they certainly are not "stuck" providing nutrition therapy once initiated, as the courts have clarified that there is no difference between stopping therapy on any day and the original decision to initiate therapy in the first place (151). Evidence suggests that, even though nutrition therapy may not be provided, the subsequent development of dehydration and starvation does not add to suffering (as only a third of patients will sense any degree of hunger or thirst) (152). In those situations, minimal therapy with oral mouth care, rinses, candies, or throat lozenges will ameliorate symptoms.

Subtle goals and outcome benefits may be achieved by gastrostomy placement in certain end-of-life situations (153). Quality of life for the family of the patient may improve with placement of a percutaneous gastrostomy, as the ease of providing medications, hydration, and nutrition is facilitated and frustration with anorexia and poor oral intake is reduced. Percutaneous gastrostomy placement may allow transfer out of the hospital setting to a nursing home or skilled nursing facility closer to home (153). Converting a nasogastric tube to a percutaneous gastrostomy, or a gastrostomy to a GJ tube, does reduce aspiration and regurgitation (118,154) but may or may not reduce actual pneumonia (as aspiration pneumonia may be more closely linked to aspiration of oropharyngeal secretions). In amyotrophic lateral sclerosis, benefit from gastrostomy placement may be seen by reduced coughing and choking with eating, less prolongation of mealtimes, and greater ease with taking medications (155,156). If performed in a timely manner, gastrostomy placement may even extend survival (157,158). A patient with malignant obstruction of the GI tract may benefit from gastrostomy placement through palliative decompression to reduce nausea and vomiting (159).

Gastroenterologists are trained to recognize indications and contraindications for a procedure. Placing a percutaneous gastrostomy in a patient with poor prognosis at high risk for mortality seems like an exercise in futility to the clinician, especially when allocation of health-care resources is limited (160). Ethicists would argue that refusal to place a percutaneous endoscopic gastrostomy in this situation violates the ethical principles of futility and justice. With regard to futility, refusal to place a percutaneous endoscopic gastrostomy generates a clash of values between the family and the caregiver. With regard to justice, patients should never become aware that their low socio-economic status, lack of insurance, or low points on a survival scoring system has ultimately led to the denial of the procedure by health-care providers (160).

The most important ethical principle that drives management is patient autonomy, as the patient is the final arbiter of their own destiny (153). Patients or their surrogate decision maker/family member decides whether to accept or refuse medical therapy. What ultimately should determine tube placement is the clarification of goals of therapy by the patient and/or their family and whether the placement of the access device helps meet those goals. Decisions on gastrostomy placement and provision of nutrition therapy at end-of-life often have little to do with scientific data or medical evidence derived from RCTs (161). Decision making in end-of-life situations is often influenced by both the health-care literacy and the spiritual literacy of the patient and their families (160).

If at any time in this process, the clinician becomes uncomfortable or conflicted with the management decisions, he or she may excuse themselves from the care of a particular patient. This can only be done if they are able to transfer the care to an equally qualified and willing practitioner. At no time should a patient or their families feel abandoned by the health-care process.

ACKNOWLEDGMENTS

This guideline was produced in collaboration with the Practice Parameters Committee of the American College of Gastroenterology. The Committee gives special thanks to Brian P. Bosworth, who served as guideline monitor for this document.

CONFLICT OF INTEREST

Guarantor of the article: Stephen A. McClave, MD.

Specific author contributions: All authors contributed to the manuscript.

Financial support: None.

Potential competing interests: Stephen A. McClave is a speaker and an advisor for Nestle, Abbott, Covidien, and Kimberly Clark, a speaker for Nutricia, and has received research support from Nestle. Robert G. Martindale is a advisor for Nestle, Covidien, and Fresenius Kabi. John K. DiBaise has received research support from GI Dynamics. Gerald E. Mullin has no potential competing interests.

REFERENCES

1. Dudrick SJ. History of parenteral nutrition. J Am Coll Nutr 2009;28: 243–51.
2. Butterworth CE. The skeleton in the hospital closet. Nutr Today 1974;9:4.
3. Bistrian BR. Brief history of enteral and parenteral nutrition in the hospital in the USA. In Elia M, Bistrian B (eds). The Economic, Medical/ Scientific and Regulatory Aspects of Clinical Nutrition Practice: What Impacts What? Vol 12: pp 127–36. Nestec Ltd., Vevey/S. Karger AG: Basel, Switzerland, 2009.
4. Braunschweig CL, Levy P, Sheean PM *et al.* Enteral compared with parenteral nutrition: a meta-analysis. Am J Clin Nutr 2001;74:534–42.
5. Heyland DK, MacDonald S, Keefe L *et al.* Total parenteral nutrition in the critically ill patient: a meta-analysis. JAMA 1998;280:2013–9.
6. Perioperative total parenteral nutrition in surgical patients. The Veterans Affairs Total Parenteral Nutrition Cooperative Study Group. N Engl J Med 1991;325:525–32.
7. Moore FA, Feliciano DV, Andrassy RJ *et al.* Early enteral feeding, compared with parenteral, reduces postoperative septic complications. The results of a meta-analysis. Ann Surg 1992;216:172–83.
8. Lewis SJ, Egger M, Sylvester PA *et al.* Early enteral feeding versus "nil by mouth" after gastrointestinal surgery: systematic review and meta-analysis of controlled trials. BMJ 2001;323:773–6.
9. Choi EY, Park DA, Park J. Calorie Intake of enteral nutrition and clinical outcomes in acutely critically ill patients: a meta-analysis of randomized controlled trials. J Parenter Enteral Nutr 2014;39:291–300.
10. Rice TW, Wheeler AP, Thompson BT *et al.* National Heart, Lung, and Blood Institute, Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network. Initial trophic vs full enteral feeding in patients with acute lung injury: the EDEN randomized trial. JAMA 2012;307: 795–803
11. 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;100:1337–44.
12. Harvey SE, Parrott F, Harrison DA *et al.* Trial of the route of early nutritional support in critically ill adults. NEJM 2014;371:1673–84.
13. Heyland DK, Dhaliwal R, Drover JW *et al.* Canadian Critical Care Clinical Practice Guidelines Committee: Canadian clinical practice guidelines for nutrition support in mechanically ventilated, critically ill adult patients. J Parenter Enteral Nutr 2003;27:355–73.
14. Koretz RL, Lipman TO. The presence and effect of bias in trials of early enteral nutrition in critical care. Clin Nutr 2014;33:240–5.
15. Doig GS, Heighes PT, Simpson F *et al.* Early enteral nutrition, provided within 24 h of injury or intensive care unit admission, significantly reduces mortality in critically ill patients: a meta-analysis of randomised controlled trials. Intensive Care Med 2009;35:2018–27.
16. Lewis SJ, Andersen HK, Thomas S. Early enteral nutrition within 24 h of intestinal surgery versus later commencement of feeding: a systematic review and meta-analysis. J Gastrointest Surg 2009;13:569–75.
17. McClave SA, Chang WK, Dhaliwal R *et al.* Nutrition support in acute pancreatitis: a systematic review of the literature. J Parenter Enteral Nutr 2006;30:143–56.
18. Villet S, Chiolero RL, Bollmann MD *et al.* Negative impact of hypocaloric feeding and energy balance on clinical outcome in ICU patients. Clin Nutr 2005;24:502–9.
19. Dvir D, Cohen J, Singer P. Computerized energy balance and complications in critically ill patients: an observational study. Clin Nutr 2006;25:37–44.
20. Alberda C, Gramlich L, Jones N *et al.* The relationship between nutritional intake and clinical outcomes in critically ill patients: results of an international multicenter observational study. Intensive Care Med 2009;35:1728–37.
21. Martin CM, Doig GS, Heyland DK *et al.* Southwestern Ontario Critical Care Research Network. Multicentre, cluster-randomized clinical trial of algorithms for critical-care enteral and parenteral therapy (ACCEPT). CMAJ 2004;170:197–204.
22. Taylor SJ, Fettes SB, Jewkes C *et al.* Prospective, randomized, controlled trial to determine the effect of early enhanced enteral nutrition on clinical outcome in mechanically ventilated patients suffering head injury. Crit Care Med 1999;27:2525–31.
23. McClave SA, Heyland DK. The physiologic response and associated clinical benefits from provision of early enteral nutrition. Nutr Clin Pract 2009;24:305–15.
24. McClave SA, Martindale RG, Rice TW *et al.* Feeding the critically ill patient. Crit Care Med 2014;42:2600–10.
25. Balshem H, Helfand M, Schunemann HJ *et al.* GRADE guidelines: 3. Rating the quality of evidence. J Clin Epidem 2011;64:401–6.
26. Oxman AD, GRADE Working Group. Grading quality of evidence and strength of recommendations. BMJ 2004;328:1490–7.
27. Studley HO. Percentage of weight loss, a basic indicator of surgical risk in patients. JAMA 1936;106:458–60.
28. Jensen GL, Compher C, Sullivan DH *et al.* Recognizing malnutrition in adults: definitions and characteristics, screening, assessment, and team approach. J Parenter Enteral Nutr 2013;37:802–7.
29. Heyland DK, Dhaliwal R, Jiang X *et al.* 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:R268.
30. Kondrup J, Johansen N, Plum LM *et al.* Incidence of nutritional risk and causes of inadequate nutritional care in hospitals. Clin Nutr 2002;21:461–8.
31. Gramlich L, Kichian K, Pinilla J *et al.* Does enteral nutrition compared to parenteral nutrition result in better outcomes in critically ill adult patients? A systematic review of the literature. Nutrition 2004;20:843–8.
32. Peter JV, Moran JL, Phillips-Hughes J. A metaanalysis of treatment outcomes of early enteral versus early parenteral nutrition in hospitalized patients. Crit Care Med 2005;33:213–20.
33. Phillips MS, Ponsky JL. Overview of enteral and parenteral feeding access techniques: principles and practice. Surg Clin North Am 2011;91:897–911
34. Khalid I, Doshi P, DiGiovine B. Early enteral nutrition and outcomes of critically ill patients treated with vasopressors and mechanical ventilation. Am J Crit Care 2010;19:261–8.
35. Anthony PS. Nutrition screening tools for hospitalized patients. Nutr Clin Pract 2008;23:373–82.
36. Kondrup J. Nutritional-risk scoring systems in the intensive care unit. Curr Opin Clin Nutr Metab Care 2014;17:177–82.
37. Rahman A, Asan RM, Agarwala R *et al.* Identifying critically ill patients who will benefit most from nutritional therapy: further validation of the "modified NUTRIC" nutritional risk assessment tool. Clin Nutr 2016;35:158–62.
38. White JV, Guenter P, Jensen G *et al.* Consensus statement of the academy of nutrition and dietetics/American Society for Parenteral and Enteral Nutrition: characteristics recommended for the identification and documentation of adult malnutrition (undernutrition). J Acad Nutr Diet 2012;112:730–8.
39. Jie B, Jiang ZM, Nolan MT *et al.* Impact of preoperative nutritional support on clinical outcome in abdominal surgical patients at nutritional risk. Nutrition 2012;28:1022–7.
40. Starke J, Schneider H, Alteheld B *et al.* Short-term individual nutritional care as part of routine clinical setting improves outcome and quality of life in malnourished medical patients. Clin Nutr 2011;30:194–201.
41. Davis CJ, Sowa D, Keim KS *et al.* The use of prealbumin and C-reactive protein for monitoring nutrition support in adult patients receiving enteral nutrition in an urban medical center. J Parenter Enteral Nutr 2012;36:197–204.
42. Daley J, Khuri SF, Henderson W *et al.* Risk adjustment of the postoperative morbidity rate for the comparative assessment of the quality of surgical care: results of National Veterans Affairs Surgical Risk Study. J Am Coll Surg 1997;185:328–40.
43. Fleck A, Path FR. Acute phase response: implications for nutrition and recovery. Nutrition 1988;4:109–17.
44. Bernstein LH, Leukhardt-Fairfield CJ, PlebanW *et al.* Usefulness of data on albumin and prealbumin concentrations in determining effectiveness of nutritional support. Clin Chem 1989;35:271–4.
45. Di Sebastiano KM, Mourtzakis M. A critical evaluation of body composition modalities used to assess adipose and skeletal muscle tissue in cancer. Appl Physiol Nutr Metab 2012;37:811–21.

46. Thurnham DI. Interactions between nutrition and immune function: using inflammation biomarkers to interpret micronutrient status. Proc Nutr Soc 2014;73:1–8.
47. Gruys E, Toussaint MJ, Niewold TA *et al.* Monitoring health by values of acute phase proteins. Acta Histochem 2006;108:229–32.
48. Heper Y, Akalin EH, Mistik R *et al.* Evaluation of serum C-reactive protein, procacitonin, tumor necrosis factor alpha, and interleukin-10 levels as diagnostic and prognostic parameters in patients with community-acquired sepsis, sepsis syndrome and septic shock. Eur J Clin Microbiol Infect Dis 2006;25:481–91.
49. Baracos V, Kazemi-Bajestani SM. Clinical outcomes related to muscle mass in humans with cancer and catabolic illnesses. Int J Biochem Cell Biol 2013;45:2302–8.
50. Puthucheary ZA, Rawal J, McPhail M *et al.* Acute skeletal muscle wasting in critical illness. JAMA 2013;310:1591–600.
51. McClave SA, Martindale RG, Kiraly L. The use of indirect calorimetry in the intensive care unit. Curr Opin Clin Nutr Metab Care 2013;16: 202–8.
52. Schlein KM, Coulter SP. Best practices for determining resting energy expenditure in the critically ill adults. Nutr Clin Practice 2014;29:44–55.
53. Stapleton RD, Jones N, Heyland DK. Feeding critically ill patients: what is the optimal amount of energy? Crit Care Med 2007;35:S535–40.
54. Walker RN, Heuberger RA. Predictive equations for energy needs for the critically ill. Repiratory Care 2009;54:509–21.
55. Frankenfield D, Hise M, Malone A *et al.* Prediction of resting metabolic rate in critically ill adult patients: results of a systematic review of the evidence. J Am Diet Assoc 2007;107:1552–61.
56. Daly J, Heymsfield SB, Head CA *et al.* Human energy requirements: overestimation by widely used predictive equation. Am J Clin Nutr 1985;42:1170–4.
57. Neelemaat F, van Bokhorst-de van der Schueren MA, Thijs A *et al.* Resting energy expenditure in malnourished older patients at hospital admission and three months after discharge: predictive equations versus measurements. Clin Nutr 2012;31:958–66.
58. Frankenfield DC, Ashcraft CM, Galvan DA. Longitudinal prediction of metabolic rate in critically ill patients. J Parenter Enteral Nutr 2012;36:700–12.
59. Kee AL, Isenring E, Hickman I *et al.* Resting energy expenditure of morbidly obese patients using indirect calorimetry: a systematic review. Obes Rev 2012;13:753–65.
60. Frankenfield DC, Coleman A, Alam S *et al.* Analysis of estimation methods for resting metabolic rate in critically ill adults. J Parenter Enteral Nutr 2009;33:27–36.
61. Ireton-Jones C, Jones JD. Improved equations for predicting energy expenditure in patients: the Ireton-Jones equations. Nutr Clin Pract 2002;17:29–31.
62. Mifflin MDSt, Jeor ST, Hill LA *et al.* A new predictive equation for resting energy expenditure in healthy individuals. Am J Clin Nutr 1990; 51:241–7.
63. Boullata J, Williams J, Cottrell F *et al.* Accurate determination of energy needs in hospitalized patients. J Am Diet Assoc 2007;107:393–401.
64. Foster GD, Knox LS, Dempsey DT *et al.* Caloric requirements in total parenteral nutrition. J Am Coll Nutr 1987;6:231–53.
65. De Waele E, Opsomer T, Honore PM *et al.* Measured versus calculated resting energy expenditure in critically ill adult patients. Do mathematics match the gold standard? Minerva Anestesiol 2014;81:272–82.
66. Neelemaat F, Bosmans JE, Thijs A *et al.* Oral nutritional support in malnourished elderly decreases functional limitations with no extra costs. Clin Nutr 2012;31:183–90.
67. Allingstrup MJ, Esmailzadeh N, Wilkens Knudsen A *et al.* Provision of protein and energy in relation to measured requirements in intensive care patients. Clin Nutr 2012;31:462–8.
68. Weijs PJ, Sauerwein HP, Kondrup J. Protein recommendations in the ICU: G protein/kg body weight - which body weight for underweight and obese patients? Clin Nutr 2012;31:774–5.
69. Dickerson RN, Pitts SL, Maish GO3rd *et al.* A reappraisal of nitrogen requirements for patients with critical illness and trauma. J Trauma Acute Care Surg 2012;73:549–57.
70. Magne H, Savary-Auzeloux I, Temond D *et al.* Nutritional strategies to counteract muscle atrophy caused by disuse and to improve recovery. Nutrit Res Rev 2013;26:149–65.
71. Singh N, Sharma B, Sharma M *et al.* Evaluation of early enteral feeding through nasogastric and nasojejunal tube in severe acute pancreatitis: a noninferiority randomized controlled trial. Pancreas 2012;41:153–9.
72. Stupak DP, Adelsayed GG, Soloway GN. Motility disorders of the upper gastrointestinal tract in the intensive care unit: pathophysiology and contemporary management. J Clin Gastroent 2012;46:449–56.
73. Rohm KD, Boldt J, Piper SN. Motility disorders in the ICU: recent therapeutic options and clinical practice. Curr Opin Clin Nutr Metab Care 2009;12:161–777.
74. Reintam A, Parm P, Kitus R *et al.* Gastrointestinal symptoms in intensive care patients. Acta Anaesthesiol Scand 2009;53:318–24.
75. Nguyen T, Frenette AJ, Johanson C *et al.* Impaired gastrointestinal transit and its associated morbidity in the intensive care unit. J Crit Care 2013;28:537.
76. Hsiu-Hua H, Sue-Joan C, Chien-Wei H *et al.* Severity of illness influences the efficacy of enteral feeding route on clinical outcomes in patients with critical illness. J Acad Nutr Diet 2012;112:1138–46.
77. Davies AR, Morrison SS, Bailey MJ *et al.* A multicenter, randomized controlled trial comparing early nasojejunal with nasogastric nutrition in critical illness. Crit Care Med 2012;40:2342–8.
78. Bankhead R, Boullata J, Brantley S *et al.* A.S.P.E.N. Board of Directors. Enteral nutrition practice recommendations. J Parenter Enteral Nutr 2009;33:122–67.
79. Kaffarnik MMF, Lock JF, Wassilew G *et al.* The use of bedside electromagnetically guided nasointestinal tube for jejunal feeding of critically ill surgical patients. Technol Health Care 2013;21:1–8.
80. Boyer N, McCarthy MS, Mount CA. Analysis of an electromagnetic tube placement device vs a self-advancing nasal jejunal device for postpyloric feeding tube placement. J Hosp Med 2014;9:23–8.
81. Fang J. The University of Utah www.biodesign.utah.edu/Documents/VeritractTCOConnect.docx.
82. McClave SA, DeMeo MT, DeLegge MH *et al.* North American summit on aspiration in the critically ill patient: consensus statement. J Parenter Enteral Nutr 2002;26(6 Suppl):S80–5.
83. Dhaliwal R, Cahill N, Lemieux M *et al.* The Canadian critical care nutrition guidelines in 2013: an update on current recommendations and implementation strategies. Nutr Clin Pract 2014;29:29–43.
84. George DL, Falk PS, Umberto Meduri G *et al.* Nosocomial sinusitis in patients in the medical intensive care unit: a prospective epidemiological study. Clin Infect Dis 1998;27:463–70.
85. McClave SA, Chang WK. Complications of enteral access. Gastro Endosc 2003;58:739–51.
86. Geeganage C, Beavan J, Ellender S *et al.* Interventions for dysphagia and nutritional support in acute and subacute stroke. Cochrane Database Syst Rev 2012;10:CD000323.
87. Borum ML, Lynn J, Zhong Z *et al.* The effect of nutritional supplementation on survival in seriously ill hospitalized adults: an evaluation of the SUPPORT data. J Am Geriatr Soc 2000;48(5 Suppl):533–8.
88. Miller RG, Jackson CE, Kasarskis EJ *et al.* Quality Standards Subcommittee of the American Academy of Neurology. Practice parameter update: the care of the patient with amyotrophic lateral sclerosis: drug, nutritional, and respiratory therapies (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2009;73:1218–26.
89. McClave SA, Chang WK. Techniques in enteral access. In: Clinical Gastrointestinal Endoscopy, Ginsberg G, Kocheman ML, Norton I, Gostout CJ (eds) 2nd edn Elsevier: Saunders, Co. Philadelphia, PA, 2012, pp 279–96.
90. Bechtold ML, Nguyen DL, Palmer LB *et al.* Nasal Bridles for securing nasoenteric tubes: a meta-analysis. Nutr Clin Pract 2014;29:667–71.
91. Marik PE, Zaloga GP. Early enteral nutrition in acutely ill patients: a systematic review. Crit Care Med 2001;29:2264–70.
92. Heyland DK. Early supplemental parenteral nutrition in critically ill adults increased infections, ICU length of stay and cost. Evid Based Med 2012;17:86–7.
93. Port AM, Apovian C. Metabolic support of the obese intensive care unit patients: a current perspective. Current Opinion Clin Nutr Metab Care 2010;13:184–91.
94. Frankenfield DC. Obesity. World Rev Nutr Diet 2013;105:144–53.
95. Jiang H, Sun MW, Hefright B *et al.* Efficacy of hypocaloric parenteral nutrition for surgical patients: a systematic review and meta-analysis. Clin Nutr 2011;30:730–7.
96. Zhu XH, Wu YF, Qiu YD *et al.* Effect of early enteral combined with parenteral nutrition in patients undergoing pancreaticoduodenectomy. World J Gastroenterol 2013;19:5889–96.
97. Kudsk KA, Moore FA. Consensus recommendations from the US summit on immune-enhancing enteral therapy. J Parenter Enteral Nutr 2001; 25(Supplement):S61–2.

98. Beale RJ, Sherry T, Lei K *et al.* Early enteral supplementation with key pharmaconutrients improves sequential organ failure assessment score in critically ill patients with sepsis: outcome of a randomized, controlled, double-blind trial. Crit Care Med 2008;36:131–44.
99. Heys SD, Walker LG, Smith I *et al.* Enteral nutritional supplementation with key nutrients in patients with critical illness and cancer: a meta-analysis of randomized controlled clinical trials. Ann Surg 1999;229: 467–77.
100. Heyland DK, Novak F, Drover JW *et al.* Should immunonutrition become routine in critically ill patients? A systematic review of the evidence. JAMA 2001;286:944–53.
101. Martindale RG, McClave SA, Taylor B *et al.* Perioperative nutrition: what is the current landscape? J Parenter Enteral Nutr 2013;37(5 Suppl): 5S–20S.
102. Evans DC, Martindale RG, Kiraly LN *et al.* Nutrition optimization prior to surgery. Nutr Clin Pract 2014;29:10–21.
103. Turner KL, Moore FA, Martindale RG. Nutrition support for the acute lung injury/adult respiratory distress patient: a review. Nutr Clin Pract 2011;26:14–25.
104. Kolacek S. Enteral nutrition. World Rev Nutr Diet 2013;108:86–90
105. Faisy C, Candela Llerena M, Savalle M *et al.* Early ICU energy deficit is a risk factor for Staphylococcus aureus ventilator-associated pneumonia. Chest 2011;140:1254–60.
106. Heidegger CP, Berger MM, Graf S *et al.* Optimisation of energy provision with supplemental parenteral nutrition in critically ill patients: a randomized controlled clinical trial. Lancet 2013;381:385–93.
107. Crook MA. Refeeding syndrome: problems with definition and management. Nutrition 2014;30:1448–55.
108. Walmsley RS. Refeeding syndrome: screening, incidence, and treatment during parenteral nutrition. J Gastroenterol Hepatol 2013;28(Suppl 4):113–7.
109. Lottes SM. Nutrition support protocols and their influence on the delivery of enteral nutrition: a systematic review. Worldviews Evid Based Nurs 2014;11:194–9.
110. Kozar RA, McQuiggan MM, Moore EE *et al.* Postinjury enteral tolerance is reliably achieved by a standardized protocol. J Surg Res 2002;104:70–5.
111. Doig GS, Simpson F, Finfer S *et al.* Effect of evidence-based feeding guidelines on mortality of critically ill adults: a cluster randomized controlled trial. JAMA 2008;300:2731–41.
112. Barr J, Hecht M, Flavin KE *et al.* Outcomes in critically ill patients before and after the implementation of an evidence-based nutritional management protocol. Chest 2004;125:1446–57.
113. Spain DA, McClave SA, Sexton LK *et al.* Infusion protocol improves delivery of enteral tube feeding in the critical care unit. J Parenter Enteral Nutr 1999;23:288–92.
114. Heyland DK, 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;41:2743–53.
115. McClave SA, Saad MA, Esterle M *et al.* Volume-based feeding in the critically ill patient. J Parenter Enteral Nutr 2014;39:707–12.
116. Deane A, Chapman MJ, Fraser RJ *et al.* Mechanisms underlying feed intolerance in the critically ill: Implications for treatment. World J Gastroenterol 2007;13:3909–17.
117. Moreira TV, McQuiggan M. Methods for the assessment of gastric emptying in critically ill, enterally fed adults. Nutr Clin Pract 2009;24: 261–73.
118. McClave SA, Lukan JK, Stefater JA *et al.* Poor validity of residual volumes as a marker for risk of aspiration in critically ill patients. Crit Care Med 2005;33:324–30.
119. Hurt RT, McClave SA. Gastric residual volumes in critical illness: what do they really mean? Crit Care Clin 2010;26:481–90.
120. Powell KS, Marcuard SP, Farrior ES *et al.* Aspirating gastric residuals causes occlusion of small-bore feeding tubes. J Parenter Enteral Nutr 1993;17:243–6.
121. Nseir S, Zerimech F, Jaillette E *et al.* Microaspiration in intubated critically ill patients: diagnosis and prevention. Infect Disord Drug Targets 2011;11:413–23.
122. Reignier J, Mercier E, Le Gouge A *et al.* Effect of not monitoring residual gastric volume on risk of ventilator-associated pneumonia in adults receiving mechanical ventilation and early enteral feeding: a randomized controlled trial. JAMA 2013;309:249–56.
123. Poulard F, Dimet J, Martin-Lefevre L *et al.* Impact of not measuring residual gastric volume in mechanically ventilated patients receiving early enteral feeding: a prospective before-after study. J Parenter Enteral Nutr 2010;34:125–30.
124. Efrati S, Deutsch I, Antonelli M *et al.* Ventilator-associated pneumonia: current status and future recommendations. J Clin Monit Comput 2010;24:161–8.
125. Chang SJ, Huang HH. Diarrhea in enterally fed patients: blame the diet? Curr Opin Clin Nutr Metab Care 2013;16:588–94.
126. Thorson MA, Bliss DZ, Savik K. Re-examination of risk factors for non-*Clostridium difficile*-associated diarrhoea in hospitalized patients. J Adv Nurs 2008;62:354–64.
127. Bartel B, Gau E. Nosocomial diarrhea: a review of pathophysiology, etiology, and treatment strategies. Hosp Pract 2012;40:130–8.
128. Nguyen NQ, Ching K, Fraser RJ *et al.* Risk of *Clostridium difficile* diarrhoea in critically ill patients treated with erythromycin-based prokinetic therapy for feed intolerance. Intensive Care Med 2008;34:169–73.
129. Nguyen NQ, Yi Mei SL. Current issues on safety of prokinetics in critically ill patients with feed intolerance. Ther Adv Drug Saf 2011;2:197–204
130. Nguyen NQ. Pharmacological therapy of feed intolerance in the critically ill. World J Gastrointest Pharmacol Ther 2014;5:148–55.
131. Rushdi TA, Pichard C, Khater YH. Control of diarrhea by fiber-enriched diet in ICU patients on enteral nutrition: a prospective randomized controlled trial. Clin Nutr 2004;23:1344–52.
132. Hart GK, Dobb GJ. Effect of a fecal bulking agent on diarrhea during enteral feeding in the critically ill. J Parenter Enteral Nutr 1988;12: 465–8.
133. Spapen H, Diltoer M, Van Malderen C *et al.* Soluble fiber reduces the incidence of diarrhea in septic patients receiving total enteral nutrition: a prospective, double-blind, randomized, and controlled trial. Clin Nutr 2001;20:301–5.
134. Heather DJ, Howell L, Montana M *et al.* Effect of a bulk-forming cathartic on diarrhea in tube-fed patients. Heart Lung 1991;20:409–13.
135. Chittawatanarat K, Pokawinpudisnun P, Polbhakdee Y. Mixed fibers diet in surgical ICU septic patients. Asia Pac J Clin Nutr 2010;19:458–64.
136. Dobb GJ, Towler SC. Diarrhoea during enteral feeding in the critically ill: a comparison of feeds with and without fibre. Intensive Care Med 1990;16:252–5.
137. Holscher HD, Caporaso JG, Hooda S *et al.* Fiber supplementation influences phytogenic structure and functional capacity of the human intestinal microbiome: follow-up of a randomized controlled trial. Am J Clin Nutr 2015;101:55–64
138. Itkin M, DeLegge MH, Fang JC *et al.* Society of Interventional Radiology; American Gastroenterological Association Institute; Canadian Interventional Radiological Association; Cardiovascular and Interventional Radiological Society of Europe. Multidisciplinary practical guidelines for gastrointestinal access for enteral nutrition and decompression from the Society of Interventional Radiology and American Gastroenterological Association (AGA) Institute, with endorsement by Canadian Interventional Radiological Association (CIRA) and Cardiovascular and Interventional Radiological Society of Europe (CIRSE). Gastroenterology 2011;141:742–65.
139. Marcuard SP, Stegall KL, Trogdan S. Clearing obstructed feeding tubes. J Parenter Enteral Nutr 1989;13:81–3.
140. Sriram K, Jayanthi V, Lakshmi RG *et al.* Prophylactic locking of enteral feeding tubes with pancreatic enzymes. J Parenter Enteral Nutr 1997; 21:353–6.
141. McClave SA, Neff RL. Care and long-term maintenance of percutaneous endoscopic gastrostomy tubes. JPEN 2005;30:S27–38.
142. Casaer MP, Mesotten D, Hermans G *et al.* Early versus late parenteral nutrition in critically ill adults. N Engl J Med 2011;365:506–17.
143. Doig GS, Simpson F, Sweetman EA *et al.* Early parenteral nutrition in critically ill patients with short-term relative contraindications to early enteral nutrition: a randomized controlled trial. JAMA 2013;309: 2130–8.
144. Sandstrom R, Drott C, Hyltander A *et al.* The effect of postoperative intravenous feeding (TPN) on outcome following major surgery evaluated in a randomized study. Ann Surg 1993;217:185–95.
145. Martindale RG, McClave SA, 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 the American Society for Parenteral and Enteral Nutrition (ASPEN): executive summary. Crit Care Med 2009;37:1757–61.
146. Mirtallo JM, Patel M. Overview of parenteral nutrition. In the A.S.P.E.N. Adult Nutrition Support Core Curriculum. CM Mueller (ed) A.S.P.E.N. Press: Silver Spring, MD, 2012, pp 234–44.
147. Albrecht JS, Gruber-Baldini AL, Fromme EK *et al.* Quality of hospice care for individuals with dementia. J Am Geriatr Soc 2013;61:1060–5.

148. McCann RM, Hall WJ, Groth-Junker A. Comfort care for terminally ill patients: the appropriate use of nutrition and hydration. JAMA 1994;272:1263–6.
149. Finucane TE, Christmas C, Travis K. Tube feeding in patients with advanced dementia: a review of the evidence. JAMA 1999;282:1365–70.
150. Sampson EL, Candy B, Jones L. Enteral tube feeding for older people with advanced dementia. Cochrane Database Syst Rev 2009, CD007209.
151. Mayo TW. Forgoing artificial nutrition and hydration: legal and ethical considerations. Nutr Clin Pract 1996;11:254–64.
152. McCann RM, Hall WJ, Groth-Junker J. Comfort care for terminally ill patients: the appropriate use of nutrition and hydration. JAMA 1994;272:1263–6.
153. Delegge MH, McClave SA, DiSario JA *et al.* Ethical and medicolegal aspects of percutaneous endoscopic gastrostomy tube placement and provision of artificial nutritional therapy. ASGE task force on enteral nutrition. Gastroint Endosc 2005;62:952–62.
154. Lien HC, Chang CS, Chen GH. Can percutaneous endoscopic jejunostomy prevent gastroesophageal reflux in patients with pre-existing reflux? Am J Gastroent 2000;95:3439–43.
155. Sarfaty M, Nefussy B, Gross D *et al.* Outcome of percutaneous endoscopic gastrostomy insertion in patients with amyotrophic lateral sclerosis in relation to respiratory dysfunction. Amyotroph Lateral Scler Frontotemporal Degener 2013;14:528–32.
156. Andersen PM, Abrahams S, Borasio GD *et al.* EFNS guidelines on the clinical management of amyotrophic lateral sclerosis (ALS): revised report of an EFNS task force. Eur J Neurol 2012;19:360–75.
157. Eisen A. Amyotrophic lateral sclerosis: a 40-year personal perspective. J Clin Neurosci 2009;16:505–12.
158. Shimizu T. Nutritional management in amyotrophic lateral sclerosis: palliative and end-of-life care. Rinsho Shinkeigaku 2013;53:1292–4.
159. Issaka RB, Shapiro DM, Parikh ND *et al.* Palliative venting percutaneous endoscopic gastrostomy tube is safe and effective in patients with malignant obstruction. Surg Endosc 2014;28:1668–73.
160. Wilcox CM, McClave SA. To PEG or not to PEG. Clin Gastroenterol Hepatol 2013;11:1451–2.
161. Ganzini L. Artificial nutrition and hydration at the end of life: ethics and evidence. Palliat Support Care 2006;4:135–43.