ASPEN-FELANPE Clinical Guidelines: Nutrition Support of Adult Patients With Enterocutaneous Fistula

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Abstract

Background: The management of patients with enterocutaneous fistula (ECF) requires an interdisciplinary approach and poses a significant challenge to physicians, wound/stoma care specialists, dietitians, pharmacists, and other nutrition clinicians. Guidelines for optimizing nutrition status in these patients are often vague, based on limited and dated clinical studies, and typically rely on individual institutional or clinician experience. Specific nutrient requirements, appropriate route of feeding, role of immune-enhancing formulas, and use of somatostatin analogues in the management of patients with ECF are not well defined. The purpose of this clinical guideline is to develop recommendations for the nutrition care of adult patients with ECF. Methods: A systematic review of the best available evidence to answer a series of questions regarding clinical management of adults with ECF was undertaken and evaluated using concepts adopted from the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) Working Group. An anonymous consensus process was used to develop the clinical guideline recommendations prior to peer review and approval by the ASPEN Board of Directors and by FELANPE. Questions: In adult patients with enterocutaneous fistula: (1) What factors best describe nutrition status? (2) What is the preferred route of nutrition therapy (oral diet, enteral nutrition, or parenteral nutrition)? (3) What protein and energy intake provide best clinical outcomes? (4) Is fistuloclysis associated with better outcomes than standard care? (5) Are immune-enhancing formulas associated with better outcomes than standard formulas? (6) Does the use of somatostatin or somatostatin analogue provide better outcomes than standard medical therapy? (7) When is home parenteral nutrition support indicated? (JPEN J Parenter Enteral Nutr. XXXX;xx:xx-xx)

Keywords

GI fistula; enterocutaneous fistula; nutrition support

Background

Enterocutaneous fistula (ECF) is defined as an abnormal connection between the gastrointestinal tract and the skin. It may occur spontaneously in patients with underlying malignancy, radiation exposure, or inflammatory conditions such as inflammatory bowel disease but develops more commonly as a complication of gastrointestinal surgery. ECFs can be classified based on anatomy of the fistula tract, including site of origin and volume of output. Small enteric defects (<1 cm) and long fistula tracts (>2 cm) are conditions that favor spontaneous closure. Factors that are associated with failure...
to spontaneously close include intestinal discontinuity, adjacent abscess, strictured or inflamed bowel, radiation therapy, foreign bodies, or distal obstruction.1 Enteroatmospheric fistula, defined as a connection between the gastrointestinal tract and the atmosphere (ie, when bowel is exposed), represents a subset of ECF that will almost never close spontaneously.2 Loss of intestinal fluids that occurs in patients with ECF can result in considerable loss of fluid, electrolytes, minerals, and protein and contribute to complications such as dehydration, electrolyte imbalance, and malnutrition. There is an association between high-output ECF, defined as output exceeding 500 mL/24 hours, and higher patient mortality rates compared with low-output ECF.1,3

Standard medical management focuses on sepsis control, wound care, and optimization of fluid, electrolyte, and nutrition status.3,4 Patients with ECF are often malnourished due to the underlying diagnosis, decreased dietary intake, increased protein requirements associated with systemic inflammation, and increased nutrient loss associated with fistula output. The goals of nutrition management are to provide estimated nutrient requirements, maintain fluid and electrolyte balance, and enhance spontaneous ECF closure whenever feasible. Parenteral nutrition (PN) in conjunction with nil per os (NPO) has been used to provide necessary nutrition while attempting to reduce fistula output, maintain fluid/electrolyte balance, and promote spontaneous closure. Somatostatin analogues have also been used in patients in an attempt to reduce fistula output and enhance spontaneous closure. Depending on the location of the fistula and volume of output, the use of oral diet and/or enteral nutrition (EN) has been proposed as a means to feed the patient and preserve intestinal mucosal integrity. This may involve reinfusion of fistula output along with infusion of enteral formula via the fistula opening, referred to as fistuloclysis.2 The use of fistuloclysis has been attempted in patients with an enteroatmospheric fistula since it is unlikely to spontaneously close without surgical intervention.7 In patients with ECF who fail spontaneous fistula closure with standard medical management, surgical intervention for repair may be indicated. Surgery is generally not recommended until at least 3 months after the initial injury, when the patient is less malnourished and once the acute inflammatory response has resolved.1 Patients with ECF may therefore require long-term medical management and discharge from the hospital with EN or parenteral nutrition (PN), intensive fluid and electrolyte monitoring, and complex wound care while awaiting optimal conditions for surgical intervention.

The management of patients with ECF requires an interdisciplinary approach and poses a significant challenge to physicians, wound/stoma care specialists, dietitians, pharmacists, and other nutrition clinicians. Guidelines for optimizing nutrition status in these patients are often vague, are based on limited and dated clinical studies, and typically rely on individual institutional or clinician experience. Specific nutrient requirements, appropriate route of feeding, role of immune-enhancing formulas, and use of somatostatin analogues in the management of patients with ECF are not well defined. The purpose of this clinical guideline is to develop recommendations for the nutrition care of adult patients with ECF.

**Methodology**

This clinical guideline was developed under the joint guidance of the Boards of Directors of American Society for Parenteral and Enteral Nutrition (ASPEN) and the Federación Latino Americana de Terapia Nutricional, Nutrición Clínica y Metabolismo (FELANPE). Both organizations comprise healthcare professionals representing the disciplines of medicine, nursing, pharmacy, dietetics, and nutrition science. The mission of both societies is to improve patient care by advancing the science and practice of clinical nutrition and metabolism, and they both work vigorously to support quality patient care, education, and research in the fields of nutrition and metabolic support in all healthcare settings.

These clinical guidelines are based on general consensus of health professionals who have balanced potential benefits to be derived from a particular mode of medical therapy against certain inherent risks of the therapy. However, the professional judgment of the attending health professional is the primary component of quality medical care. Since guidelines cannot account for every variation in circumstances, the practitioner must always exercise professional judgment in their application. These clinical guidelines are intended to supplement, but not replace, professional training and judgment.

The ASPEN clinical guidelines process has adopted concepts of the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) Working Group.5–8 A full description of the methodology has been published.9 Specific clinical questions about the management of nutrition therapy in patients with ECF were developed by an international author task force, and key clinical outcomes were identified by this group.

A rigorous search of the PubMed/MEDLINE database was performed, searching articles between January 1995 and June 2016 according to the techniques outlined in McKeever et al.10 Briefly, in the MEDLINE database, the medical subject heading (MeSH) folder “Fistula” was searched for articles cross-referenced in MeSH folders for “Nutritional Support,” “Parenteral Nutrition Solutions,” “Enteral Nutrition,” “Food,” “Dietetics,” “Fat Emulsions, Intravenous,” and “Parenteral Nutrition, Home.” These citations were then restricted to those cross-referenced in the “Humans” MeSH folder. The PubMed (non-MEDLINE) database was then searched using the text terms (Figure 1). To protect against miscalculated terms in MEDLINE, a final search of the MEDLINE database was performed using a text-based search restricted to only citations that contained those search terms in their title or abstract. Analogous search strategies were then constructed and employed to search the non-MEDLINE portions of 3 other databases (EMBASE, CINAHL, and Cochrane Central).
The abstracts were reviewed against the inclusion criteria of adult patients with ECF using articles published in English, Spanish, or Portuguese. Randomized clinical trials (RCTs) and observational studies with a control group were included. Abstracts from studies describing bariatric surgery–related fistulas; gastric, esophageal, or pancreatic fistulas; and hostile abdomen were excluded as the care of these conditions is substantially different from small bowel or colonic ECF. Abstracts reflecting care of children were excluded for this adult guideline. Each published manuscript associated with an included abstract was read independently by 2 authors, who produced a consensus evaluation of the quality of evidence for each study. When the studies reported outcomes in a similar fashion, data from included trials were entered into Review Manager 5.3 (The Cochrane Collaboration, Copenhagen, Denmark) software to create forest plots aggregating the effect size for each intervention and outcome.11 The forest plots supporting the recommendation are included in the text. The quality of the entire body of evidence for a given intervention and outcome was evaluated and graded in a range from very low to high.12

When the evidence quality is very low, any estimate of the effect is very uncertain. When the evidence is moderate, further research is likely to affect confidence in the estimate of effect and change the effect size. When the evidence quality is high, further research is unlikely to change confidence in the effect size. Evidence summary tables are found in the online appendix. A team of authors drafted each recommendation and rationale. These statements were discussed in telephone conferences, and consensus was established using an anonymous modified Delphi scheme, where at least 60% congruence was needed to establish consensus. Dissenting opinions for which consensus was not developed were discussed in the rationale. The recommendation was given a separate grade from the body of evidence.5 Strong recommendations were made when the evidence quality was high and/or net benefits outweighed harms. Weak recommendations were made when evidence quality was low or if important trade-offs to the patient were considered. When no available research directly addressed the questions posed by the guideline authors, the consensus process was used with notation that the recommendation was made based on expert consensus as no evidence is available.

This clinical guideline has undergone peer review by clinical content experts both internal and external to both organizations. The author and reviewer teams for this guideline included members of each of the professional groups who would use such a guideline (dietetics, nursing, medicine, pharmacy, research), the ASPEN Board of Directors, and FELANPE reviewers. All authors participated in the guideline processes as volunteers. The guideline developing organizations (ASPEN and FELANPE) did not receive commercial support for the project. Revision of this guideline is not planned until further research is available.

Results

In total, 872 citations and abstracts were reviewed for inclusion (638 from PubMed/MEDLINE, 34 from EMBASE, 15 from CINAHL, and 185 from Cochrane Central). Of these citations, 6 randomized clinical trials and 20 controlled observational studies met inclusion criteria. Other review articles were used to support the rationale or background issues. Randomized controlled trials were available for only 1 guideline statement (question 6). Four guideline statements were based on controlled observational studies and the remaining 2 by expert consensus. Authors did not have dissenting opinions on any question.

**Question 1:** In adult patients with ECF, what factors best describe nutrition status?

**Recommendation:** We suggest the following:

- Malnutrition be diagnosed by nutrition history, including unintentional weight loss and estimation of energy/nutrient intake, and physical examination.
- Assessment for malnutrition be conducted at the time of diagnosis of an ECF. If malnutrition is not present at baseline, periodic nutrition assessment is warranted as patients with fistulas have a high likelihood of becoming malnourished due to nutrient malabsorption, fluid and electrolyte losses, and sepsis.
- Serum protein concentrations be obtained prior to and during nutrition therapy since they are prognostic outcome indicators, yet are not sensitive nutrition markers.

**Quality of Evidence:** Very low.

**Rationale:** Assessment of nutrition status at the time of ECF diagnosis may be performed using a number of tools, although none has been specifically validated for use in ECF. Subjective Global Assessment (SGA) categorizes patients into
level A (well nourished), level B (moderately or suspected of being moderately malnourished), or level C (severely malnourished) based on food intake, weight loss, functional assessment, and physical examination. The consensus criteria published by the Academy of Nutrition and Dietetics and ASPEN suggest identification of 2 or more of the following 6 characteristics to detect and diagnose malnutrition: insufficient energy intake, weight loss, loss of muscle mass, loss of subcutaneous fat, localized or generalized fluid accumulation that may mask weight loss, and diminished functional status as measured by handgrip strength. While all of these tools include assessment of weight loss, they may fail to diagnose malnutrition in the overweight or obese patient. Critically ill obese patients with malnutrition may have a higher risk of death compared with obese patients without malnutrition. A thorough history of energy/nutrient intake and weight loss are important assessment parameters to obtain in all patients, including those with high body mass index (BMI).

All included studies were observational in design and used BMI, weight loss, and/or serum protein levels to define malnutrition (Supplemental Table S1). There was significant variability among the studies with respect to inclusion of nutrition parameters. Only 1 study assessed malnutrition by SGA. No other studies used a validated nutrition assessment tool.

Four studies examined unintentional weight loss. It is unknown whether weight loss predisposes to ECF development or is a consequence of the clinical course and management of the disease process. Weight loss is not surprising given the underlying diagnoses seen in patients who develop ECF (gastrointestinal cancer, trauma, intestinal obstruction, inflammatory bowel disease, radiation enteritis). However, in at least 1 retrospective study of 53 patients over a 10-year period, the presence of weight loss at the time of presenting symptoms was noted in 21.2% of those who had spontaneous closure and 20% of those who did not. In clinical practice, it is reasonable to document body weight and weight change at the time of presenting symptoms and throughout the course of ECF management.

While serum protein level monitoring was common in the 1980s–1990s, it is now accepted that the measures lack sensitivity and specificity in making a diagnosis of malnutrition. Decreased plasma concentrations of serum albumin, transferrin, retinol binding protein, and prealbumin may be a consequence of ECF-related inflammation. While not an appropriate nutrition assessment parameter, low serum protein concentrations may have prognostic significance. In 1 retrospective study over a 10-year period, increased serum albumin concentration after a course of PN therapy was associated with significantly less fistula drainage and improved rate of spontaneous closure. The odds of spontaneous fistula closure were 18.1-fold greater when serum albumin improved compared with no improvement. In a prospective study of ECF management with EN and PN therapy, serum albumin concentrations decreased during ECF treatment but returned to preoperative levels following fistula closure. By contrast, in a large cohort of 277 patients, serum albumin was not found to be an independent predictive factor for clinical outcomes, a finding confirmed in a retrospective observation of 79 patients with ECF. However, higher serum transferrin concentration did predict spontaneous closure, and low concentration of transferrin, retinol binding protein, and prealbumin were predictive of mortality. Of patients receiving PN with improved serum albumin concentrations and ECF output <500 mL/d, 93.3% had spontaneous closure compared with 70% failure to close among patients with low serum albumin concentrations and ECF output ≥500 mL/d.

**Question 2: In adult patients with ECF, what is the preferred route of nutrition therapy (oral diet, EN, or PN)?**

**Recommendation:** After stabilization of fluid and electrolyte balance, we suggest that oral diet or EN may be feasible and tolerated in patients with low-output (<500 mL/d) ECF (suggesting no distal obstruction). However, patients with high-output ECF (>500 mL/d) may require PN to meet fluid, electrolyte, and nutrient requirements to support spontaneous or surgical closure of the ECF.

**Quality of Evidence:** Very low.

**Rationale:** The ability to give EN in the postoperative period may reduce the development of ECF in patients with open abdomen. However, studies evaluating outcomes associated with use of PN or EN once an ECF has formed are limited (Suppl. Table S2). Two small, retrospective observational studies (one using historical controls) reported conflicting findings in terms of spontaneous fistula closure rates and were underpowered for mortality. A third study reported earlier surgical fistula closure and fewer composite complications when patients received EN within 14 days of hospital admission compared with those who received EN more than 14 days after hospital admission. No RCTs comparing EN to PN following ECF formation were found.

When a fistula occurs, the immediate goal is to accomplish fluid and electrolyte balance, as well as establish fistula location, quantify output, and rule out distal obstruction. Detailed assessment of the fistula characteristics (precise location, length) may not be feasible at that time since the fistula tract is not yet mature. In the absence of distal obstruction, patients with low-output ECF (<500 mL/d) may tolerate oral diet. If oral dietary intake is associated with a significant increase in ECF output or is not tolerated for other reasons, EN may be feasible and tolerated when enteral access can be obtained distal to the fistula (Figure 2). Tolerance to EN and the ability to deliver goal intake should be evaluated regularly. If nutrient goals cannot be achieved solely by EN, combined nutrition therapy (EN and PN) may be indicated. Patients will require PN if ECF output is high (>500 mL/d), there is a bowel obstruction, or the ECF drainage significantly compromises...
energy expenditure in patients with high-output ECF. None of the available review articles comment on application to obese patients with ECF, although this represents a significant percentage of the patient population.

Our recommendation is based on general nutrition support practice paradigms that incorporate the patient’s assessed level of malnutrition with appropriate energy and protein intake levels. Careful management of fluid, electrolyte, and vitamin status is also an important aspect of care. In the obese patient with ECF, we concur with the ASPEN–Society of Critical Care Medicine (SCCM) adult critical care nutrition guidelines for determining calorie and protein requirements. For energy intake, provision of 11–14 kcal/kg/d actual body weight if BMI is 30–50 and 22–25 kcal/kg/d ideal body weight if BMI >50 kg/m² is recommended. For protein intake, provision of 2–g/kg ideal body weight for patients with BMI 30–40 and 2.5 g/kg ideal body weight if BMI >40 kg/m² is recommended.²²

**Question 4: In adult patients with ECF, is fistuloclysis associated with better outcomes than standard care?**

**Recommendation:**

- We suggest the use of fistuloclysis for nutrition therapy for patients with intact intestinal absorptive capability distal to the infusion site and when the infusion ECF site is not expected to close spontaneously.
- We suggest the use of polymeric formulas initially and change to semi-elemental (oligomeric) diet if intolerance occurs.

**Quality of Evidence:** Very low.

**Rationale:** Fistuloclysis is defined as the infusion of EN formula via the distal stoma of an ECF with or without reinfusion of the output from the proximal fistula opening. The technique should only be initiated after confirmation of the integrity and patency of the small intestine beyond the most distal fistula opening and in ECFs that are not expected to close spontaneously. The proximal opening of the fistula can be accessed with a tube or catheter, and EN formula and/or chyme is infused through the opening. The central idea is to use the small intestine to feed both the gut mucosa and the patient and to minimize use of PN. Tolerance is assessed by whether any increase in ECF output is manageable in terms of effluent capture and maintaining hydration and by the ability to deliver adequate nutrition intake. Because semi-elemental (oligomeric) diets are partially digested, greater nutrient delivery may be obtained with their use.
control. In addition to standard medical care that included initiation of PN, a standard polymeric formula was initiated at 30 mL/h and increased by 20 mL/h per day until goal rate was achieved. The formula was changed to semi-elemental if intolerance occurred. PN was stopped when EN at 90 mL/h was achieved. Compared with PN alone, the use of fistuloclysis was associated with lower cost. Fistuloclysis successfully replaced PN in 11 of 12 patients, with only 1 case of failure. In 6 patients, fistuloclysis was associated with an increase in proximal fistula output by 40–330 mL/d, and in 4 patients, the output decreased by 290–1540 mL/d. Nine of the 11 patients proximal fistula output by 40–330 mL/d, and in 4 patients, the 6 patients, fistuloclysis was associated with an increase in recovered bowel function.34 The use of fistuloclysis (n = ECF, with remaining small intestine longer than 100 cm and 155 (range, 19–422) days after initiating fistuloclysis. output decreased by 290–1540 mL/d. Nine of the 11 patients was compared with EN without reinfusion of fistula output (n = 60).34 Fistuloclysis was defined as the reinfusion of the output collected from the proximal fistula into the distal fistula through a feeding tube, while EN formula was infused simultaneously through this tube or another nasojugal tube. All patients received PN during the study. As in the previous study, a balloon retention gastrostomy tube was placed into the distal opening of the fistula. In the fistuloclysis group, the output from the proximal stoma was collected into a sterile bag and reinfused back into the distal limb of the fistula. A polymeric formula was initiated but changed to a semi-elemental formula in cases of intolerance. Biochemical parameters such as hepatic function indexes and C-reactive protein levels significantly improved in fistuloclysis patients. Moreover, hospital costs, hospital stay, and hospital mortality were significantly lower, and 1-year survival was significantly higher in the fistuloclysis group.

**Question 5**: In adult patients with ECF, are immune-enhancing formulas associated with better outcomes than standard formulas?

**Recommendation**: We recommend use of somatostatin analogue in adult patients with high-output (>500 mL/d) ECF as a method to reduce effluent drainage and enhance spontaneous closure.

**Quality of Evidence**: Moderate.

**Rationale**: Somatostatin and somatostatin analogues have been used to treat gastrointestinal (GI) and pancreatic fistulas due to their ability to inhibit the release and secretory effects of a wide variety of GI hormones and enhance water and electrolyte absorption by prolonging intestinal transit time.23 The intended overall effect is to reduce the volume of GI secretions as a method to reduce fistula output and thereby promote spontaneous fistula closure. Six RCTs and 5 observational studies met our inclusion criteria for evaluating the use of somatostatin or somatostatin analogue (octreotide, lanreotide) in adult patients with ECF. The treatment group typically received somatostatin 250 mcg/h continuous infusion or octreotide 100 mcg subcutaneous 3 times daily for 10–20 days or lanreotide 30 mg intramuscular every 10 days. No studies were found testing long-acting depot octreotide or octreotide provided as an additive to the PN admixture. Standard medical management of ECF was provided to all patients (treatment and control groups) that often incorporated PN, but route and details of nutrition intake were not consistently described.

We have relied largely on data from RCTs to address the use of somatostatin or somatostatin analogue for treatment of ECF (Supplemental Table S6).27,36–40 Of these comparable trials that were described as randomized, 3 of 6 used blinding to treat and only 2 used intent-to-treat analysis. The evidence quality was reduced from high to moderate based on risk of
bias. A meta-analysis of 3 RCTs that met our inclusion criteria showed a significant reduction in fistula output with use of somatostatin or somatostatin analogue compared with control (weighted mean difference [WMD], 21.13%; 95% CI, 6.51–35.75; \( P = .005 \)) (Figure 3). A meta-analysis of 6 RCTs that met our inclusion criteria showed a greater likelihood of spontaneous closure when somatostatin or somatostatin analogue was added to standard medical care (OR, 2.82; 95% CI, 1.77–4.51; \( P < .0001 \)) (Figure 4). A meta-analysis of 4 RCTs that met inclusion criteria showed a reduction in time to achieve fistula closure favoring somatostatin analogues with a WMD = −6.45 days (95% CI, −9.67 to −3.23) (Figure 5). Hospital length of stay, cost, and complication rates were not reported consistently in these trials to allow for meta-analysis.

While the use of somatostatin analogue has generally been well tolerated, its physiologic effect on GI hormones may increase risk of biliary stasis, cholelithiasis, liver dysfunction, hypoglycemia, and hyperglycemia. GI disturbances such as diarrhea, nausea, and abdominal discomfort have also been reported.35 Glucose monitoring is recommended and glucose control should be identified and managed. Pain at the injection site has been associated with the subcutaneous route of administration, and the dosing frequency of every 8 hours can be a burden for patients managed in the home setting. Finally, the significant cost and reimbursement challenges for somatostatin analogue pose another barrier to use. It is suggested that a selective approach be used to determine appropriate use of somatostatin analogue in patients with ECF. Patients with high-output ECF (>500 mL/d) are more likely to benefit from the impact of a 20% fistula output reduction than patients with low output. An appropriate duration of trial use to assess efficacy of somatostatin analogues in achieving fistula closure appears to range from 10–20 days, based on available RCTs, although some report fewer days to achieve reduction in ECF effluent volume. Use of somatostatin analogue has been shown to enhance spontaneous fistula closure, but it is also anticipated that a decrease in fistula output would improve the ability to achieve fluid/electrolyte balance, assist with pouching of drainage, and overall make it easier to manage patients with an ECF in the home setting.

**Question 7:** In adult patients with ECF, when is home parenteral nutrition (HPN) therapy indicated?

**Recommendation:** Based on expert consensus, we suggest consideration of HPN when the patient is medically stable and the fistula output is manageable, as well as in patients with high-output ECF (>500 mL/d) when surgical repair is not yet advised.

**Quality of Evidence:** Based on consensus only, as no recent evidence was available.

**Rationale:** Patients with high-output ECF often begin a course of PN during hospitalization as a strategy to stabilize nutrition and fluid balance while permitting healing of the fistula tract. Once patients are medically stable, with manageable fistula output and adequate skin protection, consideration can be made for discharge to the home setting since they will require extended time for healing prior to a definitive surgical procedure. Patients with low-output fistula (<500 mL/d) may...
tolerate oral diet or EN without exacerbating fistula output, as noted in question 2.

Case reports of the use of HPN for patients with ECF appeared in the late 1970s (Supplemental Table S7). A more recent case series described an average duration of 20 days before hospital discharge followed by an average HPN duration of 75 days in 15 patients, 5 of whom had ECF. In this series, patients expressed a preference of HPN to hospital-based PN, with less family stress and greater enjoyment of familiar surroundings. In a large case series in the United Kingdom, HPN was given to 143 patients with ECF for a median of 5 weeks of therapy, the limited reports make it clear that HPN is feasible, outcomes in a similar way or compare HPN with other modes of nutrition care,44 the indication for HPN was ECF in 19% of adult patients enrolled. This rate is similar (10%-36%) to rates reported by other international HPN registries. While these studies do not address clinical outcomes in a similar way or compare HPN with other modalities of therapy, the limited reports make it clear that HPN is feasible, provided HPN services are available.

Area of Future Research

The available body of evidence addressing optimal nutrition management in adult patients with ECF is limited. Only 1 of 7 guideline statements created for this document is based on randomized controlled trials. The multifaceted nature of the condition and heterogeneous population create challenges for study design. Adequately powered studies are difficult to achieve and require multicenter collaboration. Much of our current practice is based on clinical studies performed more than 20 years ago, prior to the obesity epidemic and before conservative assessment of energy requirements, aggressive glucose control, and protocols to minimize central venous access infections and complications. Clearly, further research directed at optimizing nutrition management in patients with ECF is warranted.

Targeted research is needed in the area of establishing protein and energy requirements in patients with ECF, including how best to facilitate controlled weight loss in obese patients. Additional questions to address include the following:

- How does the anatomy/location of the ECF influence nutrient requirements and optimal route of nutrition support?
- What strategies are effective in optimizing use of EN, as well as use of fistuloclysis?
- How does the anatomy/location of the ECF influence nutrient requirements and optimal route of nutrition support?
- What levels of protein and energy provision are most effective in terms of ECF healing? Do these needs vary in patients with malnutrition, in those with obesity?
- Which patients benefit from bowel rest as a method to control fistula output and promote fistula closure?
- Is somatostatin compatible and effective when provided as a component of the PN admixture?
- Is the provision of immune-enhancing nutrients effective in the management of ECF?

Statement of Authorship

V. J. Kumpf, J. E. de Aguilar-Nascimiento, J. I. Diaz-Pizarro Graf, L. McKeever, E. Steiger, M. F. Winkler, and C. W. Compher contributed to the conception/design of the research; V. J. Kumpf, J. E. de Aguilar-Nascimiento, J. I. Diaz-Pizarro Graf, A. M. Hall, L. McKeever, E. Steiger, M. F. Winkler, and C. W. Compher contributed to the acquisition, analysis, or interpretation of the data; V. J. Kumpf, J. E. de Aguilar-Nascimiento, J. I. Diaz-Pizarro Graf, L. McKeever, E. Steiger, M. F. Winkler, and C. W. Compher drafted the manuscript; V. J. Kumpf, J. E. de Aguilar-Nascimiento, J. I. Diaz-Pizarro Graf, L. McKeever, E. Steiger, M. F. Winkler, and C. W. Compher critically revised the manuscript; and V. J. Kumpf, J. E. de Aguilar-Nascimiento, J. I. Diaz-Pizarro Graf, L. McKeever, E. Steiger, M. F. Winkler, and C. W. Compher agree to be fully accountable for ensuring the integrity and accuracy of the work. All authors read and approved the final manuscript.

Supplementary Material

Supplemental Tables S1–S7 are available online at http://jpen.sagepub.com/.

References