Curr Gastroenterol Rep (2016) 18: 48
DOI 10.1007/s11894-016-0525-x

NUTRITION AND OBESITY (S MCCLAVE, SECTION EDITOR)

Intestinal Failure: New Definition and Clinical Implications

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Published online: 22 July 2016

Abstract Intestinal failure (IF) is a state in which the nutritional demands of the body are not met by the gastrointestinal absorptive surface. It is a long-recognized complication associated with short bowel syndrome, which results in malabsorption after significant resection of the intestine for many reasons or functional dysmotility. Etiologies have included Crohn's disease, vascular complications, and the effects of radiation enteritis, as well as the effects of intestinal obstruction, dysmotility, or congenital defects. While IF has been long-recognized, it has historically not been uniformly defined, which has made both recognition and management challenging. This review examines the previous definitions of IF as well as the newer definition and classification of IF and how it is essential to IF clinical guidelines.

Keywords Acute intestinal failure · Chronic intestinal failure · Intestinal failure · Short gut syndrome · Home parenteral nutrition · Short bowel syndrome

This article is part of the Topical Collection on *Nutrition and Obesity*

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Introduction

Intestinal failure (IF) was first described in 1981 by Fleming and Remington as the "reduction in gut mass resulting in the loss of the ability of digestion and absorption of food molecules [1]." Since then, the definition of IF has changed and been debated but now has been revised to encompass patients with insufficient intestinal capacity to fulfill nutritional demands resulting in the use of parenteral nutrition (PN). IF may be due to acquired or congenital, gastrointestinal or systemic, or benign or malignant diseases and can affect both adults as well as children [2, 3]. IF can have an abrupt onset and be self-limited, or it may develop as a chronic, slowly progressive disorder with long lasting affects (chronic intestinal failure (CIF)). Treatment of CIF is different than treatment of acute-onset IF and relies on intestinal rehabilitation programs that work to restore absorptive capacity of the bowel through nutrition, pharmacological, and/or surgical therapy [4]. If rehabilitation is unsuccessful, patients with CIF will require long-term PN or intestinal transplantation [5•]. The definition of IF has been revised by multiple sources [2–4, 5•, 6]; however, the European Society for Clinical Nutrition and Metabolism (ESPEN) is the first scientific society which has issued a formal definition for intestinal failure [7••]. The purpose of the current review will be to explore these new definitions as well as their potential clinical impact.

Prior Understanding and Challenges in Defining Intestinal Failure

The average small bowel length in a healthy adult human is approximately 600 cm [8]. The average intestinal length in men is felt to be 630 cm and in women 592 cm [7••]. For IF

to occur, a reduction in the number of enterocytes may result in a loss of nutritional autonomy, where normal health and growth and/or development cannot be maintained without PN. The extent of nutritional deficiency and electrolyte imbalances depends on the anatomic segment (duodenum, jejunum, ileum, or colon), length of intestine resected, and the health of the remaining bowel. Therefore, the segment of bowel that is lost will have an impact on whether a patient will progress to IF.

Each segment of the intestine performs distinctly different functions. The proximal small intestine is responsible for absorption of various micronutrients including calcium, magnesium, phosphorous, iron, and folic acid [9]. The resection of the first 150 cm of the small intestine may result in severe metabolic derangements. In addition, the initial 100 to 200 cm of the jejunum is also responsible for the absorption of macronutrients including fats, carbohydrate, protein, micronutrients such as water-soluble vitamins, and water absorption given the large gaps in the intercellular junctions between jejunal epithelial cells [9]. The absorption of carbohydrates determines the osmotic forces and is primarily responsible for regulating fluid flow in the jejunum. In contrast to the jejunum, the ileum has decreased permeability because of tighter intracellular junctions [10] and the ileum relies on active transport of sodium and chloride for significant reabsorption and concentrative ability. The ileum is also the site for vitamin B12 and bile salt absorption, as well as feedback of cholecystokinin, peptide YY, and glucagon-like peptide 1 [11•]. If these regulatory hormones or the ability to reabsorb bile salts is lost with resection of the terminal segment of the small intestine, this results in increased intestinal transit due to hypertonic intestinal contents, increased intestinal secretion of water into the gut lumen, and therefore elevated stool output and risk of dehydration.

The ileocecal (IC) valve plays a crucial role in regulating the delivery of contents into the colon and serves as a mechanical barrier reducing reflux of contents and bacteria from the colon into the small intestine. Whether the ileocecal valve being resected or the length of ileum resected with the IC valve is related to whether a patient loses nutritional autonomy is not completely understood, but clearly resection of the IC valve is an independent predictor for achieving nutritional autonomy [12].

The colon's main function is fluid and electrolyte reabsorption but does also have some role in energy absorption. It typically absorbs approximately 1 to 2 l per day but does have the ability to absorb up to 6 l [13]. In addition to fluid absorption, the colon assists in the conversion of undigested carbohydrates to absorbable short-chain fatty acids, an alternative energy source that can provide as many as 1000 cal per day in process called colonic salvage [14]. The preservation of the colon during surgical resection improves absorptive capacity of water as well as helps attain nutritional autonomy. In addition, placing the colon back in continuity with the small bowel may help wean PN dependent patients.

Depending on the health of the gut, the segment of intestine resected, and the length remaining after surgical resection, nutritional autonomy can be attained. If autonomy is not attained, patients are then diagnosed with IF. One of the difficulties of how IF has been defined previously is that it is often clinically recognized, but defining it has been difficult. Patients who are at risk for developing IF have an inadequate length of small bowel in continuity. This length is less than 35 cm of small bowel with a jejunoileal anastomosis and an intact colon, less than 60 cm of small bowel with a jejunocolic anastomosis, or less than 115 cm of small bowel with an end-jejunostomy [15]. While many providers may recognize features of intestinal failure, the definition of this syndrome has evolved through the years from the original definition by Remington and colleagues [2–4, 5•, 6]. In an effort to develop evidence driven consensus guidelines, ESPEN endorses guidelines to define and classify IF.

Recent Guidelines on Definition and Classification of Intestinal Failure

While IF is often well recognized by clinicians, it is agreed upon that firm definitions are lacking. In an effort to better delineate how it is that IF is diagnosed and categorized, ESPEN has put forth a set of guidelines to better address these issues. The ESPEN definition of IF concludes that IF only occurs when PN is given and uses the term intestinal insufficiency (or deficiency) for when health and growth are maintained with oral/enteral support [7••]. They conclude that the use of PN is an objective observation that helps better define when a patient has IF.

In addition to whether or not PN was in use to define IF, the new guideline wanted to define subtypes of IF based upon the volume and energy given in the PN. The ESPEN IF guideline committee agreed that comparing nutrient requirement and nutrient absorption would be an optimal way to not only identify but also actually quantify the nutrient need in a patient with IF [16]. However, given that very few medical centers have the facilities for the necessary testing to complete these metabolic studies, the use of PN/fluid supplementation would need to be a "surrogate diagnostic criterion" of IF. Micronutrients could not be mentioned in the definition in order to avoid misunderstanding about impaired gut absorption resulting in micronutrient deficiency alone. Micronutrient deficiency in and of itself would as not be considered IF [3, 5•, 6]. The new definition of IF proposes that two criteria must be present for the diagnosis to be made: a decreased absorption of macronutrients and/or water and electrolytes due to a loss of gut function and the need for PN or intravenous fluids. The guideline authors argue that by including both criteria in the

new definition, this reduces ambiguity of true intestinal failure where a patient may have certain macronutrient deficiencies but then be able to be properly supplemented through targeted enteral feeding. The panel proposed that the term "intestinal insufficiency or intestinal deficiency" can be considered in the following conditions (Table 1); where there is reduced food intake but normal gut function, patients with altered gut function but conserved intestinal absorption, patients with inflammatory bowel disease treated with enteral nutrition, patients treated by PN because of refusal of otherwise effective enteral nutrition, patients with a reduction in gut function impairing intestinal absorption but in whom health and growth can be maintained by oral supplementation, enteral nutrition, refeeding enteroclysis, or those who require only vitamins and trace element supplementation.

The 16 subtype descriptors of IF in the new guidelines were determined by the use of previously proposed classification systems [3, 4, 17–21]. These classification systems describe functional and pathophysiological categories, as well as a clinical classification for CIF based on intravenous energy and volume requirements.

Functional Classification

The first section based on functional classification does so on the basis of onset, metabolic, and expected outcome criteria. Type I describes IF that is acute, short-term, and usually due to a self-limiting condition. Type II describes IF due to a prolonged acute condition, often in metabolically unstable patients who require complex multidisciplinary care and intravenous supplementation over periods of weeks or months. Type III describes IF due to a chronic condition, in metabolically stable patients, requiring intravenous supplementation over month or years. This classification may be reversible or irreversible. This set of subtypes, termed as "functional," was also used in the UK project titled "A Strategic Framework for Intestinal Failure and Home Parenteral Nutrition Services for Adults in England" [4]. This system categorizes the medical care, professional expertise, management, and treatment setting as well as the organization and logistic issues required to treat IF.

Table 1 Conditions of intestinal insufficiency

1. Reduced food intake but normal gut function
2. Altered gut function but conserved intestinal absorption
3. Inflammatory bowel disease treated with enteral nutrition
4. Patients treated by PN because of refusal of otherwise effective enteral nutrition
5 Reduced gut function impairing intestinal absorption but in whom health and growth are maintained by oral supplementation, enteral nutrition, re-feeding enteroclysis, or those who require only vitamins and trace element supplementation

Pathophysiological Classification

The subtypes based on pathophysiology were first described in 1991 [17] and revised multiple times to their most current version [21]. This system aims to underline the main mechanisms that alone or in association with one another can determine whether or not a patient will go on to develop IF. These subtypes are short bowel, intestinal fistula, intestinal dysmotility, mechanical obstruction, and extensive small bowel mucosal disease. These pathophysiologic descriptors are meant to allow providers a mechanism by which to communicate about etiologies for IF in a standardized fashion.

Clinical Classification

Lastly, the ESPEN panel agreed on the need for a clinical classification system for IF to facilitate communication and cooperation among healthcare providers. Clinical classification is based on the common experience of the panel of experts, and a consensus was reached on the clinical classification of CIF due to benign disease or active cancer. Clinical classification is based on intravenous energy and volume requirements. As was to be expected, CIF related to benign disease contained a wider range of patient distribution as benign disease has greater variability in the pathophysiological causes of IF and of activity-related energy expenditure. In patients with active cancer, intestinal dysmotility or mechanical obstruction due to cancer are the most frequent causes of IF.

Implication of ESPEN Definition and Classification System

The primary goal of the ESPEN definitions is to formally recognize and classify IF as an organ failure. One of the major benefits of these definitions and classifications is the potential facilitation of communication and cooperation among professionals who treat IF patients in clinical and research practice. Another major benefit of defining IF is the ability of clinicians to apply clinical treatment guidelines. ESPEN released guidelines on the treatment of CIF in 2016 (Table 2). The stated aim of these guidelines was to generate comprehensive recommendations for safe and effective management for CIF patients. Imagine the difficulty of creating and implementing such guidelines in clinical practice without a general working set of IF definitions and classifications. In fact, in these new 2016 treatment guidelines the definitions and classifications are extensively outlined in the introduction highlighting the

Table 2 2016 ESPEN guideline statements for treatment of chronic intestinal failure with STRONG recommendations

Statement of recommendation	Grade of evidence
Management of home parenteral nutrition for benign chronic intestinal failure	
1. An HPN program should include evidence-based therapy, prevent HPN-related complications, and maximize quality of life.	Very low
2. Perform regular audit of therapy and outcomes against standards to ensure safety and efficacy of HPN program.	Very low
3. Patients selected for an HPN program should have confirmed intestinal failure that despite maximal medical therapy would lead to deterioration of nutrition and/or fluid status.	Very low
4. Prior to discharge, patients should be metabolically stable, able to physically and emotionally cope with the HPN therapy, and have an adequate home environment	Very low
5. HPN patients should have access to infusion pumps or devices with specified safety features together with ancillary products, safe compounding and delivery systems.	Very low
6. Patient/caregiver training for HPN management should be patient-centered with a multidisciplinary approach, together with written guidelines. HPN training may take place in hospital or at home	Very low
7. Regular contact by the HPN team with patients should occur, scheduled according to patients' clinical requirements.	Very low
8. Lab testing should be done on a regular basis using appropriate tests and timing relative to PN infusion.	Very low
9. Quality of life for HPN patients should be regularly measured using validated tools as part of standard clinical care. Quality of care should be assessed regularly according to recognized criteria.	Very low
10. A multidisciplinary team with skills and experience in intestinal failure and HPN management should care for CIF patients.	Very low
Parenteral nutrition formulation	
11. Protein and energy requirements for CIF patients should be based on individual patient characteristics and specific needs and the adequacy of the regimen should regularly be evaluated through clinical, anthropometric, and biochemical parameters.	Very low
12. HPN patients should have optimal blood glucose control, based on blood glucose <180 mg/dl (10.0 mmol/L) during HPN infusion and normal HbA1c levels (if diabetic), through regular monitoring.	Very low
13. Insulin should not be added to HPN admixtures due to lack of evidence-based data regarding insulin prescription for HPN patients who have hyperglycemia.	Very low
14. Regular monitoring should be performed for signs and symptoms of dehydration, fluid balance, laboratory tests, and 24-h urine output as well as a timely adjustment of fluid supplementation to prevent chronic renal failure.	Very low
15. The HPN formula should be adjusted to normalize laboratory tests related to fluid, electrolytes, and mineral balance.	Very low
16. Regular monitoring of acid-base status should occur in patients on long-term HPN.	Very low
17. Baseline serum vitamin concentrations should be measured at the onset of HPN and then at least once per year.	Very low
Intestinal rehabilitation strategy-medical: short bowel syndrome	
18. SBS patients should consume regular whole foods and be encouraged to compensate for malabsorption by hyperphagia.	Low
19. SBS patients with a preserved colon should consume a diet high in complex carbohydrates and low in fat; the fat to carbohydrate ratio seems of less importance in patients without a colon.	Low
20. In SBS patients consuming a low fat diet or where the long-chain triglycerides have been replaced by medium-chain triglycerides, attention should be paid to the potential deficiency in essential fatty acids and fat-soluble vitamins.	Low
21. Do not add soluble fiber (e.g., pectin) to the diet to enhance overall intestinal absorption.	Low
22. Do not add glutamine, probiotics, or other supplements to the diet in the aim of promoting intestinal rehabilitation.	Low
23. Use H2-receptor antagonists or PPIs in reducing fecal wet weight and sodium excretion, especially during the first 6 months after surgery, mainly in those SBS patients with a fecal output exceeding 2 l/day.	Moderate
24. Patients treated with octreotide should be carefully monitored to prevent fluid retention and other adverse events.	Strong
25. Oral loperamide should be used to reduce wet weight and sodium fecal excretion in SBS patients with an ostomy.	Moderate
26. Loperamide is preferred to opiate drugs because it is not addictive or sedative.	Moderate
27. In SBS patients with high ostomy output, the use of loperamide should be guided by objective measurements of effect.	Moderate
28. Consider occasional antibiotic treatment in SBS patients with motility disorders and symptoms of bacterial overgrowth.	Very low
29. Do not use routine antibiotics in SBS patients with a preserved colon. Malabsorbed carbohydrates are fermented to short-chain fatty acids by colonic bacteria and may provide additional energy.	Very low
30. Patients with CIF due to SBS should be carefully informed of the potential benefits and risks associated with growth factor treatments; information should deal with the probability of weaning from HPN, the probability of quality of life improvement, the expected duration of treatment, the expected effects after cessation of the treatment, the potential adverse effects and risks of the treatment, the cost-effectiveness of the treatment, and the need for careful monitoring.	Low
31. The efficacy of growth factor treatment should be evaluated according to standardized protocols measuring fluids, electrolytes, and, whenever possible, energy balance.	Low
32. Intestinal growth factors should only prescribed by experts who are experienced in the diagnosis and management of SBS patients and who have the ability and the facilities to objectively evaluate and balance the benefit and clinical meaningfulness of the interventions versus the inconveniences, adverse effects, potential risks, and cost-effectiveness.	Low
33. Drugs should be prescribed on an individual basis to patients with SBS following a careful evaluation of the absorptive capacity of the remnant bowel, knowledge of the physiochemical characteristics of the drug, and an evaluation as to if the drug can be	Very low

Table 2 (continued)

Statement of recommendation	Grade of evidence
titrated according to an objectively measured effect or according to measurements of plasma concentrations. The use of parenteral and transdermal routes and the use of suppositories should also be considered in SBS patients with limited intestinal absorption.	
Chronic intestinal pseudo-obstruction	
34. In patients with CIPO, no specific diet should be prescribed; patients should eat according to individual tolerance.	Very low
35. HPN should not be delayed in malnourished CIPO patients with chronic gastrointestinal motility dysfunctions when oral/enteral nutrition is obviously inadequate.	Very low
36. Attempt a trial with prokinetics in patients with chronic gastrointestinal motility dysfunctions.	Very low
37. Use antibiotic therapy to treat intestinal bacterial overgrowth and to reduce malabsorption in patients with chronic gastrointestinal motility dysfunctions.	Very low
Radiation enteritis	
38. The nutritional regime in chronic radiation enteritis patients follows the same criteria adopted for the HPN of patients with other causes of CIF.	Very low
39. HPN should not be delayed in malnourished radiation enteritis patients if oral nutrition/enteral tube feeding is inadequate.	Very low
Intestinal rehabilitation strategy-non-transplant surgery	
40. Bowel length should be conserved to the fullest extent possible to avoid dependence on HPN.	Low
41. In patients with SBS, restoration of intestinal continuity should be realized when possible to decrease HPN.	Moderate
42. When considering non-transplant surgery, bowel-lengthening procedures can be considered in selected SBS patients.	Very low
43. In patients with SBS, management is performed through a multidisciplinary approach.	Low
Intestinal transplantation	
44. Consider HPN as the primary treatment for patients with CIF and the early referral of patients to intestinal rehabilitation centers with expertise in both medical and surgical treatment for CIF, to maximize the opportunity of weaning off HPN, prevent HPN failure, and ensure timely assessment of candidacy for intestinal transplant.	Very low
45. Assess candidacy for intestinal transplantation, when one of the following indications exists: 1. Failure of HPN: a. Impending or overt liver failure because of intestinal failure-associated liver disease (IFALD) b. Central venous catheter-related thrombosis of two or more central veins c. Frequent central line sepsis i. Two or more episodes per year of systemic sepsis secondary to line infections requiring hospitalization d. Single episode of line-related fungemia e. Septic shock and/or acute respiratory distress syndrome f. Frequent episodes of severe dehydration despite intravenous fluid in addition to HPN 2. High risk of death attributable to the underlying disease a. Invasive intra-abdominal desmoid tumors b. Congenital mucosal disorders (i.e., microvillus inclusion disease, tufting enteropathy) c. Ultra short bowel syndrome (gastrostomy, duodenostomy, residual small bowel <10 cm in infants, < 20 cm in adults 3. Intestinal failure with high morbidity or low acceptance of HPN a. Need for frequent hospitalization, narcotic dependency, or inability to function b. Patient's unwillingness to accept long-term HPN (i.e., young patients)	Very low
46. Patients with impending or overt liver failure due to IFALD and those with an invasive intra-abdominal desmoid tumor should be listed for a life-saving intestinal transplantation (with or without liver transplantation).	Very low
47. We do not recommend listing for a life-saving intestinal transplantation of patients with CIF having any of the indications for assessment of candidacy other than IFALD-related liver failure, intra-abdominal desmoids or CVC-related multiple vein thrombosis.	Very low
48. Whenever possible, patients listed for intestinal transplantation should undergo the procedure while they are in stable clinical condition (i.e., not requiring hospitalization while waiting for transplant). For patients listed for a combined intestinal and liver transplantation, the mechanisms to prioritize patients on the waiting list for liver transplantation should be adopted in order to minimize the risk of mortality while on waiting list and after transplantation.	Very low
Prevention/treatment of CVC-related complications CVC-related infection	
49. The choice of central venous catheter type and location of exit site be made by a multidisciplinary HPN team, along with an experienced specialist and the patient.	Low
50. Access to the upper vena cava is the first choice for CVC placement, via internal jugular vein or subclavian vein.	Moderate
51. The tip of the catheter should be placed at the level of the right atrial-superior vena cava junction.	Moderate
52. The exit site of the catheter should be easily visualized and accessible for patients doing self-care and the preferred site should be marked by clinicians experienced with HPN.	Low
53. Tunneled central venous catheters or totally implanted devices should be used for long-term HPN.	Very low
54. Do not use PICC lines for expected long-term HPN because of the higher risk of thrombosis and issues related to self-administration of HPN.	Low

Table 2 (continued)

Statement of recommendation	Grade of evidence
55. CVC-related infections should be diagnosed according to current guidelines on catheter-related infections.	Very low
56. CVC-related infections should be managed according to current guidelines on long-term intravascular catheters.	Moderate
57. For prevention of central venous catheter-related infections, consider the following: • Education of staff and patients/caregivers • Implementation of an adequate policy of hand washing and disinfection by patients and staff • Hand washing and disinfection by patient and caregivers before touching central venous catheter as well as after catheter care • Disinfection of the hub connector every time it is accessed • Use of tunneled single-lumen catheters whenever possible • Use of chlorhexidine 2 % for antisepsis of hands, catheter exit site, stopcocks, catheter hubs, and other sampling ports • Regular change of i.v. administration sets	HIgh
58. For prevention of CVC-related infections do NOT use: • In-line filters • Routine replacement of catheters • Antibiotic prophylaxis • Use of heparin lock	Low
59. Do not perform catheter locking with 70 % ethanol to prevent CVC-related infections because its use is associated with systemic toxicity, catheter occlusion and catheter damage.	High
60. In patients who repeatedly present with CVC-related infections, consider re-education of the patient and/or caregiver and/or use of an antimicrobial catheter lock.	Low
CVC-related occlusion/thrombosis	
61. Treat HPN patients with CVC-related venous thrombosis with anticoagulation; the duration of this treatment should be chosen on an individual basis and the decision to maintain the catheter be dependent on individual factors.	Low
62. For the primary prevention of CVC-related venous thrombosis, perform insertion of the catheter using ultrasound guidance and placement of the tip at the superior vena cava-right atrium junction.	Low
63. Do not use routine thromboprophylaxis as primary prevention of CVC-related venous thrombosis for all adults	Low
Prevention/treatment of intestinal failure-associated liver disease	
64. For prevention of intestinal failure-associated liver disease: • Prevent or manage sepsis if present • Preserve small intestinal length and retain the colon in continuity with small bowel • Maintain oral/enteral intake • Cycle PN • Avoid overfeeding with PN • Limit the dose of soybean-oil based lipid to less than 1 g/kg/day	Low
Prevention/treatment of gallbladder sludge and stones	
65. For the treatment of gallbladder sludge and stones, perform cholecystectomy and/ or endoscopic procedures in case of biliary complications as for the general population.	Low
Prevention/treatment of intestinal failure-associated renal failure and stones	
66. For the primary prevention of renal failure and of renal stones, perform regular monitoring of renal function and fluid balance as well and adjust fluid supplementation to avoid episodes of dehydration.	Low
67. For the primary prevention of renal failure, acute and chronic infections and dehydration should be addressed.	Low
68. Treat renal failure and renal stones in patients with CIF according to the standards for these conditions.	Very low
Prevention/treatment of intestinal failure-associated metabolic bone disease	
69. For routine purposes, the diagnosis of metabolic bone disease is based on a combination of bone densitometry scanning and biochemistry.	Low
70. The HPN population should be routinely monitored for metabolic bone disease by bone densitometry scanning and biochemistry.	Low
71. General risk factors for developing osteoporosis be promptly addressed in all patients on long-term HPN.	Very low
72. The primary step for treatment of metabolic bone disease is to optimize the program for PN with the required supplements of vitamin D, calcium, and phosphate. Further, medical treatment may be useful to increase bone mineral density and lower fracture risk.	Low

Source: Modified from Pironi, L. et al., ESPEN guidelines on chronic intestinal failure in adults. Clin Nutr, 2016. 35(2): p. 247–307, with permission from Elsevier/European Society for Clinical Nutrition and Metabolism

ESPEN European Society of Parenteral and Enteral Nutrition, *HPN* home parenteral nutrition, *PN* parenteral nutrition, *CIF* chronic intestinal failure, *SBS* short bowel syndrome, *PPIs* proton-pump inhibitors, *CIPO* chronic intestinal pseudo-obstruction, *CVC* central venous catheter

importance of defining the disease state. Other benefits of defining IF as a disease state may include expanded insurance reimbursement to cover cost associated with IF and increased research funding.

Other methods and criteria for defining and classifying IF are certainly possible, but there is currently no better-defined system. A significant critique that the ESPEN guideline authors attempt to address is the requirement of the need for PN in order for the diagnosis of IF to be made. The argument can be made that IF is a disorder encompassing a spectrum of severity as with renal and respiratory failure. Patients are still classified as being in renal failure before they reach an end-stage disease state and require dialysis. Much in the same, many patients are experiencing the spectrum of a failing digestive tract before they reach the need to PN. It may be that adding a definition for recognizing the continuum of the spectrum of IF may be helpful for future direction. While the current ESPEN guidelines are not perfect, they provide a frame work from which we as a clinical community may be able to better determine who needs treatment with PN. Without guidelines defining IF, it is very difficult to apply treatment guidelines to determine those patients who need PN and those who do not need PN.

Conclusions

The next step in the use of the ESPEN definition and classification guidelines is to demonstrate that when applied with the treatment guidelines they are effective in the safe management of IF patients . In addition, if these combined definition and treatment guidelines should be evaluated for effectiveness across different healthcare systems. It would be worth studying the use of this IF classification and treatment in the USA for example to better understand what differences in the healthcare system contribute to the how effective and consistent these guidelines are. There is also opportunity to determine how these guidelines impact management of patients and whether adverse events are reduced. It would be logical to postulate that a more structured approach to defining IF would lead to improved allocation of treatment and avoidance of the negative effects of treatments like PN. Better yet, could it be that a more organized definition for IF combined with treatment guidelines can lead to more appropriate allocation of resources like PN and intestinal transplantation. Both of these treatments are very costly to the healthcare system. This type of impact would not only be important to patients as individuals but to society as a whole.

As a community of clinicians, we are moving forward to better organize and structure the diagnosis of IF. This will help us move past a reliance on the subjective intuition of "knowing it when we see it." A definition will give clinicians a framework by which to communicate with one another. By better defining IF, we can better study indications and impacts of treatment and transplantation on the individual patient as well the impact of resource utilization on society as a whole. As we begin to rely on this new set of guidelines, we will begin to identify in a systematic approach an improved care model for patients with IF.

Compliance with Ethical Standards

Conflicts of Interest The authors declare that they have no conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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