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When is parenteral nutrition indicated in the hospitalized, acutely ill patient?

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When is parenteral nutrition indicated in the hospitalized, acutely ill patient?

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ABSTRACT

Purpose of review: This review discusses current practices regarding appropriate indications for parenteral nutrition (PN) in acutely ill hospitalized patients. We address specific indications for PN in the peri-operative period, and in inflammatory bowel disease, oncology, hepatobiliary, critical care and end-stage renal disease patients.

Recent findings: Acutely ill hospitalized patients can develop intestinal failure requiring PN. Recent studies have provided insight into the main indications. The most common indications for inpatient PN include post-surgical complications, including prolonged ileus sepsis, fistula and leaks, and bowel obstruction, predominantly malignant. Severe or complicated inflammatory bowel disease and cancer treatment-related mucosal enteropathies (mucositis, enterocolitis, gut graft-versus-host disease) are the next commonest indications. Less frequent indications are primary motility disorders and inability to secure enteral access for enteral nutrition. Gastrointestinal failure of the intensive care patient is a separate entity resulting from multiple mechanisms, including an enteropathy and dysmotility.

Summary: Despite the wider availability of nutrition support teams, use of PN is not without risk. The risks and benefits of PN in the acute setting need to be carefully considered even when it is indicated.

Keywords: parenteral nutrition, hospitalized patient, intestinal failure

INTRODUCTION

The use of parenteral nutrition (PN) in acutely ill patients has risen in recent years, as reported in multicenter studies [1,2**]. These studies have also demonstrated inappropriate initiation of PN in certain occasions [3–6*]. Multidisciplinary nutrition support teams within hospitals can help guide PN prescribing for appropriate indications [3,6*–9*], and ensure these patients are safely and effectively managed [7*,10], improving patient outcomes, decreasing length of hospitalization, and improving cost effectiveness [7*,11–15].

Considering an appropriate feeding route is often the prompt for referral for PN. PN should be considered in patients who are malnourished or at risk for malnutrition when a contraindication to enteral nutrition exists, and the patient cannot tolerate adequate enteral nutrition or lacks sufficient bowel function to maintain or restore nutrition status [6*,8] (see Table 1 for definitions of nutritionally at risk). PN is indicated in patients that have developed intestinal failure or intestinal insufficiency [2**,11,16,17], which is not predicted to resolve within three days [5]. PN requirement is not based solely on medical diagnosis or disease state [17–19]. The duration of being at nutritional risk before starting PN can vary between centers. For example, the joint American Society for Parenteral and Enteral Nutrition (ASPEN) and Society for Critical Care Medicine 2016 guidelines advise that PN is not initiated for the first 7 days in low nutrition risk patients due to concerns about increased infectious morbidity and mortality, compared to delayed (day 8) introduction [20,21].

Intestinal failure is the reduction of gut function below the minimum necessary for the absorption of macronutrients and/or water and electrolytes such that intravenous supplementation is required to maintain health and/or growth [2**,16,19,22**]. There are three types of intestinal failure which necessitate PN through five pathophysiological mechanisms: short bowel, intestinal fistula, dysmotility, mechanical obstruction, and extensive small bowel mucosal injury [16]. Type I is a common, acute, short-term, and self-limiting condition, which occurs following abdominal surgery or in association with critical illness, typically lasting less than 14 days. Type II is a prolonged, acute condition; often in septic, metabolically unstable patients, requiring complex multidisciplinary care. It often occurs in association with an intra-abdominal catastrophe. Type III is a chronic condition in metabolically stable

patients; the condition may be reversible or irreversible. Most acutely ill hospitalized patients requiring PN have Type I intestinal failure, with Type II and III occurring less frequently [16,17,22**].

In the present review we discuss the main conditions where PN is indicated in acutely ill hospitalized patients. This is based on a literature review but also our experience from working within a tertiary intestinal failure service. Indications for PN can be divided as total replacement therapy in intestinal failure, supplemental PN due to insufficient gut tolerance of adequate enteral nutrition (EN) and lastly elective PN for bowel rest. The indications discussed in this manuscript are shown in Table 2.

---Table 1, Table 2 here---

INDICATIONS FOR PN

Acute bowel obstruction and surgical pathologies

Acute bowel obstruction is caused by intrinsic luminal obstruction or extrinsic compression. The dominant etiologies are adhesions, hernias and neoplasms in the small bowel [23,24], and neoplasms, volvulus and diverticular disease in the large bowel [25,26]. This pathological mechanism necessarily requires bowel rest and decompression by various means [27*]. The contraindication of oral intake or EN in the initial management increases the risk of malnutrition. In those patients who undergo surgery, malnutrition risk predicts poor clinical outcomes [28,29].

The timeframe to initiate PN in these patients is guided by the stratification of their nutritional status and associated risk of malnutrition. The ASPEN 2017 consensus recommends PN delay and initiation after 7 days for well-nourished, stable adult patients, after 3-5 days for those nutritionally at-risk and as soon as possible for those with existing moderate or severe malnutrition, and also where the duration of PN is likely to be prolonged (>7 days) [17]. The UK National Institute for Health & Care Excellence guidelines recommend PN in patients without oral intake for 5 days or more [21,30].

The indications for PN in other acute surgical pathologies such as mesenteric ischemia and acute abdominal trauma are again defined by pre-operative malnutrition risk and, critically, the nature of resulting surgery with regards to remnant bowel length and state of continuity.

Malignant bowel obstruction

Malignant bowel obstruction is a common manifestation of advanced cancer caused by mechanical, vascular or neurological dysfunction in the small or large bowel and involves incurable primary intra-abdominal cancer or non-intra-abdominal primary cancer with peritoneal disease [31]. In the acute presentation, symptom relief is achieved though bowel rest and gastric aspiration. However, without nutritional support, the mean survival has been reported as 52 days in hospitalized patients and ranged from 15-27 days in discharged patients [32]. In those discharged with home PN, median survival varies between 15-155 days [33,34]. The European Society for Clinical Nutrition and Metabolism (ESPEN) and ASPEN guidelines support PN being offered to an appropriate subset of patients whose prognosis is greater than 3 months and for whom there are no oral or EN options [35,36].

Pre-operative nutritional support

Pre-operative PN is recommended in ESPEN [21] and ASPEN [20] guidelines only in patients with severe malnutrition. A well-established timeframe of seven to fourteen days of PN is recommended to reduce post-operative complications and a trend to reduced mortality [37–39]. More generally, peri-operative nutritional support to correct undernutrition is advised if the patient is expected to be unable to eat for more than 5 days peri-operatively, with EN preferred to PN unless contra-indicated (bowel obstruction, severe shock, intestinal ischemia, high output fistula, severe intestinal hemorrhage) [21].

Post-operative nutritional support

In ileus and acute colonic pseudo-obstruction, acute intestinal failure is driven by a lack of enteric propulsion as opposed to total obliteration of the bowel lumen seen with mechanical obstruction [40]. Disordered motility, including prolonged paralytic ileus, accounts for 51.5% of acute intestinal failure [2**]. It has multiple triggers including excess fluid administration, opiates and intraoperative gut handling resulting in pan-enteric inflammation and a clinical syndrome of nausea, vomiting, distension and absolute constipation [41]. Early EN is a key component of enhanced post-operative recovery and

improves outcomes versus delayed EN [42,43] and versus PN [44]. PN is indicated according to nutritional risk or once the patient has been nil by mouth for more than 5 days [21].

Other indications for post-operative PN include direct surgical complications such as leaks or anastomotic breakdown, high output fistulae (>500mL/day) and chyle leaks [21].

Inflammatory Bowel Disease

Malnutrition is highly prevalent in inflammatory bowel disease, especially Crohn's disease, as a result of reduced oral intake, increased nutrient requirements and increased gastrointestinal nutrient loss. Malnutrition in Crohn's disease is common in remission and active disease, is linked to malabsorption and is more likely in hospitalized patients [45,46]. Furthermore sarcopenia, a loss in lean muscle mass and strength, has been shown in subgroup analyses to be a predictor of surgical complications [47,48]. It is estimated that up to 85% of Crohn's disease patients awaiting surgery are malnourished [49]. ESPEN recommends that PN is indicated for patients with symptomatic proximal or high output fistulae and symptomatic obstructing fibrostenotic disease where EN supplementation is inadequate [50,51]. EN is recommended over PN for use in pre-operative optimization [49,52,53*].

In ulcerative colitis, trials show no benefit of PN in the management of acute severe colitis, both in terms of inflammatory disease and pre-colectomy optimization [54,55]. Usual PN indications remain for example if EN is not possible and bowel rest is required for >5-7 days.

Graft-versus-host disease

Graft-versus-host disease of the gastrointestinal tract occurs in 10-60% of patients who undergo an allogenic stem cell transplantation [56,57]. The pathological process of mucosal epithelial cell apoptosis with or without inflammation results in a clinical syndrome that includes diarrhea, malabsorption, protein-losing enteropathy and a risk of malnutrition [58]. Oral and enteral nutrition is limited to patients with diarrheal volumes <500mL/day, with PN and bowel rest recommended in patients with larger volumes [59]. PN is recommended to be continued until stool volumes reduce to <500mL/day for 2 days [60]. There is limited data assessing PN outcomes specifically in severe gut graft-versus-host disease but more broadly, small studies point to better survival outcomes [61*] and reduced likelihood

of gut graft-versus-host disease in patients receiving EN over PN in the initial post-transplant period [62–64**].

Mucositis and neutropenic colitis

Mucositis refers to inflammatory or ulcerative lesions of the oral or gastrointestinal tract with causes being microorganisms, chemotherapy, targeted treatment agents and ionizing radiation [64]. Insertion of nasogastric tubes is not routinely advised during this acute setting due to bacterial translocation or gastrointestinal bleeding due to associated pancytopenia [65]. Preventive strategies are not always effective in maintaining oral feeding/EN and if the symptoms render patients nutritionally at risk, PN is administered as the preferred feeding route. For example, in pediatric cancer patients, mucositis was the indication in 40% of patients who received PN [66*].

Neutropenic enterocolitis is linked to several chemotherapeutic agents [67] and its pathogenesis is similar to mucositis with symptoms including abdominal pain, fever, diarrhea, nausea, melaena, and an increased risk of bowel perforation. Bowel rest is commonly used in cases of neutropenic enterocolitis [68]. PN can be used to maintain a nutritional source in patients who are at nutritional risk, despite various sources advocating maintaining oral or EN depending on the risks and benefits [69].

Radiation-induced bowel injury

Pelvic radiation disease is characterized by gastrointestinal symptoms in over 50% of patients [70,71]. It is a result of ionizing radiation to the pelvic area for gynecological, urological, gastrointestinal or abdominal tumors [72–74]. PN is indicated in patients with pelvic radiation disease that develop intestinal failure due to extensive mucosal enteropathy or subacute bowel obstruction secondary to fibrotic strictures. If these episodes are transient and resolve, they will usually not need PN beyond their hospital admission; otherwise home PN becomes a suitable option for discharge. Malnutrition is prevalent in this group of patients [75] due to small intestinal bacterial overgrowth, vitamin D and B12 deficiency, bile acid malabsorption, trace element deficiency, iron deficiency anemia and pancreatic insufficiency [73]. Conservative treatment of subacute bowel obstruction episodes is preferred to

surgical management in patients with pelvic radiation disease as the latter is the associated mortality up to 15%, morbidity up to 50% and re-operation rates up to 60% [75,76].

Chronic intestinal pseudo-obstruction and functional gastrointestinal disorders

Functional gastrointestinal and motility disorders are the most common gastrointestinal disorders in the general population [77]. Chronic intestinal pseudo-obstruction is a rare intestinal motility disorder caused by abnormal intestinal contractions which simulates mechanical obstruction of either the small or large bowel when no anatomical explanation can be found [78,79]. Primary motility disorders account for about 1% of inpatient PN cases [2**].

Inpatient PN is needed in this group, if patients are nutritionally at-risk and oral or EN cannot be established, usually due to severe constipation, diarrhea and/or vomiting [78,79]. With severe constipation, the primary aim is to stimulate colonic motility and treat small intestinal bacterial overgrowth, before deciding that oral or EN has failed [78–80]. With diarrhea, identifying and treating the cause or symptomatic management with nutritional monitoring usually prevent the use of PN or minimizes its duration if started. Usually post pyloric EN may prevent the need for PN in patients with chronic intractable vomiting [81].

Acute pancreatitis

Acute pancreatitis is characterized by inflammation of the pancreatic parenchyma, typically running a mild clinical course but rarely becoming a necrotizing pancreatitis with high mortality (around 15%) [82]. Acute pancreatitis presents frequently with vomiting, nausea, abdominal pain or even bowel obstruction and ileus [83,84]. PN offers the option to feed patients with moderate to severe pancreatitis with associated mechanical and motility derangements caused by the pancreatic inflammation, to allow a period of ‘pancreatic rest’. It also avoids the need for placement of a nasal enteral feeding tubes, which are associated with discomfort, dislodgement and occlusion [84,85]. Overall though, evidence suggests that EN should be considered in all patients with severe pancreatitis because it is better than PN in terms of outcome and safety profile [85]. However, practices are still not universal.

Gastrointestinal failure in intensive care

Gastrointestinal function in intensive care patients is complex to evaluate, and various factors (digestive, endocrinologic, immunologic and intestinal barrier) can lead to a separate entity known as gastrointestinal failure as part of multiple organ dysfunction syndrome [86]. This condition is caused by splanchnic hypoperfusion due to an initial insult (e.g. sepsis, surgical complications) followed by hormonal-mediated delayed gastric emptying [87]. This leads to altered mucosal barrier function, dysmotility [86] and an inflammatory enteropathy [88]. EN (post-pyloric if possible) with concomitant prokinetic medicines is the preferred primary feeding route due to its trophic effects and reduction of bacterial translocation [89]. Intolerance of oral/enteral feeding may necessitate PN in some patients.

End-stage renal disease

Patients with end stage renal disease are frequently admitted to hospital for dialysis and medical treatment. In patients with concomitant short bowel syndrome, the latter might have led to renal failure [16]. Protein-energy malnutrition is prevalent in this group of patients due to inadequate nutrient intake, hypercatabolism/hypermetabolism, dialysis, decreased physical activity, and comorbidities affecting nutritional status (e.g. heart or liver disease) [90]. Patients with end stage renal failure and established malnutrition despite oral or EN require PN. In hemodialysis patients this is often administered as intradialytic PN [91].

Lack of enteral access and bridging till establishing oral/enteral access

This occurs for a multitude of reasons. Patients might need general anesthetics or complex procedures that need planning and take time to organize. For example, therapeutic upper gastrointestinal endoscopy under general anesthetic may be required to undertake esophageal or gastric stenting or gastro-jejunostomy insertion in complex neurology patients. As such PN is used as a bridge until enteral access is established. In the recent point-of-prevalence study, this indication was noted in 8.0% of cases needing inpatient PN [2**].

Type III intestinal failure

Patients who are established on home PN are frequently admitted with complications of their underlying conditions or of home PN. During their admissions, they receive PN if clinically permitted. In the recent point-of-prevalence study, this was noted in 14.5% of cases needing inpatient PN [2**].

CONCLUSION

PN is a specialist but increasingly accessible therapeutic intervention that can help to optimize a patient's nutritional state in the acute setting. In hospitalized patients identified as at nutritional risk, PN is an important adjunctive therapy to improve outcomes of other therapeutic interventions such as surgery or chemotherapy. However, inappropriately initiated PN is associated with unnecessary risks to the patient and costs to health systems. As such EN is preferred in most circumstances to PN. Therefore, discretion is required with best outcomes achieved when a dedicated multidisciplinary NST is involved in the initiation and management of PN. is. Key areas for future research and guidance include patient selection in malignant bowel obstruction and accurate scheduling of PN in bowel rest that balances resource allocation with prevention of malnutrition.

KEY POINTS

- Parenteral nutrition is indicated in patients who are malnourished and have intestinal failure.
- In the hospitalized, acutely ill patient, risk stratification of malnutrition should always be carried out.
- Parenteral nutrition is indicated in patients at moderate to high risk of malnutrition, when nil by mouth for 5 days or more or when in a hypercatabolic state.
- A nutrition support team is key to timely and safe management of parenteral nutrition.

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CONFLICTS OF INTEREST

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TABLE LEGENDS

Table 1. Malnutrition risk stratification.

Table 2. List of indications for acute intestinal failure.

TABLES

Table 1. Malnutrition risk stratification

European Society of Clinical Nutrition and Metabolism 2015 Consensus Statement on malnutrition [92]	***Nutritionally at-risk adults*** [17]
BMI less than or equal to 18.5 kg/m^2	Involuntary weight loss of 10% of usual body weight within 6 months or 5% within 1 month
Combined findings of weight loss greater than 10% of habitual weight, greater than 5% over 3 months, and 1 of the following: (1) reduced BMI less than 20 kg/m^2, or less than 22 kg/m^2 in adults older than 70 years; or (2) reduced fat-free mass index, of less than 15 kg/m^2 in females or less than <17 kg/m^2in men	Involuntary loss of 10 lb. within 6 months BMI less than 18.5 kg/m^2 Increased metabolic requirements Altered diets or diet schedules Inadequate nutrition intake, including not receiving food or nutrition products for more than 7 days

Table 2. List of indications for acute intestinal failure.

Mechanism	***Conditions***
Short bowel syndrome, intestinal fistula, need to restrict oral or enteral intake: bowel rest	short bowel syndrome, complications of surgery (colorectal or bariatric), ischemic bowel, severe pancreatitis, chylous fistula, preoperative status, mesenteric thrombosis
Extensive mucosal enteropathy	radiation or chemotherapy related enteritis, mucositis, neutropenic colitis, gut graft-versus-host disease, inflammatory bowel disease, coeliac disease, gastrointestinal failure in intensive care
Mechanical bowel obstruction	acute pancreatitis, gastrointestinal failure in intensive care, malignant bowel obstruction, intestinal adhesions, intrinsic or extrinsic blockage of intestinal lumen (stenosis or strictures, inflammatory disease)
Motility disorders	acute pancreatitis, gastrointestinal failure in intensive care, intestinal adhesions, gut graft-versus-host disease, chronic intestinal pseudo-obstruction, functional gastrointestinal disorders, ileus, scleroderma, hollow visceral myopathy
Other	inability to secure oral or enteral access

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