

DISCLAIMER: These guidelines were prepared by the Department of Surgical Education, Orlando Regional Medical Center. They are intended to serve as a general statement regarding appropriate patient care practices based upon the available medical literature and clinical expertise at the time of development. They should not be considered to be accepted protocol or policy, nor are intended to replace clinical judgment or dictate care of individual patients.

NUTRITIONAL SUPPORT IN SURGICAL PATIENTS

SUMMARY

The importance of the gastrointestinal (GI) tract as an immune organ and the significant benefits of early nutritional support are now widely recognized. Enteral nutrition is preferred to parenteral nutrition in any patient with a functional GI tract. All critically ill patients and any elective surgery patient with an anticipated 7-day delay to resuming goal nutrition are candidates for supplemental nutritional support. Immunonutrition should be considered in the critically ill and in nutritionally compromised elective surgery patients.

RECOMMENDATIONS

Level 1

- Patients with chronic malnutrition benefit from nutritional support.
- Enteral nutrition:
 - Is preferred over parenteral nutrition in patients with a functional GI tract
 - Should be initiated within 18 hours of injury in burn patients.
 - Should be initiated within 24 hours of admission in the critically ill.
- Immunonutrition should be utilized in:
 - Severely injured abdominal / thoracic trauma patients (ISS>18, ATI>20) when given in conjunction with early feeding and adequate protein / calorie support
 - Malnourished elective GI surgical patients (albumin < 3.5 g/dL for upper GI tract and < 2.8 g/dL for lower GI tract)
- Immunonutrition should involve an initial 5-7-day course with subsequent reevaluation.

Level 2

- Patients with severe closed head injury who do not tolerate gastric feedings within 48 hours of injury should receive post-pyloric feedings.
- Nutritional assessments (such as 24-hour UUN and indirect calorimetry studies) should be performed weekly and support titrated to meet the patient's needs.
- Of the visceral protein markers, serial determination of serum pre-albumin is the most sensitive indicator of appropriate nutritional support.

Level 3

- Incompletely resuscitated patients should not receive direct small bowel feedings due to the risk for GI intolerance and possible intestinal necrosis.
- In blunt or penetrating trauma patients undergoing laparotomy, direct small bowel feeding access should be obtained and enteral feeding begun within 12-24 hours of injury.
- Intra-gastric feeding of severe closed head injury patients should be attempted within 12 hours of admission.
- Elective surgery patients with an anticipated NPO status of 7 days or greater should receive supplemental nutritional support.
- In severely injured patients, parenteral nutrition should be started by day 7 if the patient is not tolerating at least 50% of their estimated caloric requirement enterally.

INTRODUCTION

Nutritional support is now recognized as being more than simply a source of protein, fat, or carbohydrate calories. The gastrointestinal tract is the largest immune organ in the body containing 65% of the body's overall immune tissue and up to 80% of its immunoglobulin-producing cells (1,2). The GI tract therefore plays a significant role in modulating a patient's immune response following injury, illness, or surgery.

Intestinal disuse promotes gut dysfunction, progressive ileus, upper gut colonization, gut mucosa atrophy, intestinal permeability, bacterial translocation, priming of neutrophils and macrophages, and ultimately systemic inflammatory response syndrome (SIRS) and multiple organ failure syndrome (MOFS) (3). Nutritional support may perhaps, therefore, more appropriately be considered “nutriceutical therapy” as the timing, method and components of the nutritional regimen administered directly affects a patient’s immune response, resistance to infection, duration of hospitalization, and possibly even mortality. Appropriate, aggressive nutritional support should be considered a major treatment priority in any malnourished or critically ill patient.

A patient’s risk for developing protein-calorie malnutrition in the perioperative or post injury phase can be estimated from their history, physical examination, and presenting illness. Factors such as previous severe weight loss (>10% usual body weight), chronic debilitating disease, chronic drug or alcohol abuse, cachexia, body mass index <15kg/m², and presence of disease states associated with hypermetabolism (such as burns, fever, sepsis, or multiple traumatic injuries) are all associated with a heightened risk for developing protein-calorie malnutrition with its attendant increased morbidity and mortality (4). Other at-risk populations include those previously well-nourished patients who have had either no oral intake for 5-7 days or have an anticipated delay to resuming full oral intake of at least 7 days following surgery (5).

The philosophy of nutritional support in the surgical patient has evolved greatly over the past two to three decades. Whereas dextrose-containing intravenous fluids or waiting until a patient was able to take an oral diet was considered adequate in years past, early aggressive nutritional support within the first 12-24 hours post-injury is now recognized as being essential to improving patient outcome. Whereas parenteral nutrition was previously recognized as “one of the greatest medical advances of the 20th century”, it is now identified as being associated with a significantly increased cost and increased patient morbidity and mortality when used indiscriminately. Whereas patients were routinely overfed with 4000-5000 kcal per day, patients now receive carefully titrated protein, fat, and carbohydrate support to meet their individually measured nutrition needs. The disadvantages of such overfeeding are listed below.

DISADVANTAGES OF OVERFEEDING

Carbohydrate Overfeeding

- Hyperglycemia
- Hypercarbia
- Hypertriglyceridemia
- Hyper- or hypokalemia
- Hypomagnesemia
- Respiratory insufficiency
- Immunosuppression
- Hepatic steatosis or “fatty liver”
- Failure to wean from mechanical ventilation
- Increased susceptibility to infection

Lipid Overfeeding

- Hyperlipidemia
- Hypoxia
- Increased susceptibility to infection
- Increased postoperative mortality

Protein Overfeeding

- Azotemia
- Elevated creatinine
- Acute renal failure

The evolution of nutritional support as a major component of modern surgical care has also led to development of numerous commercial nutrient formulations, each differing in their carbohydrate, fat, protein, fiber, water, and micronutrient content. Selection of formulas with varying component ratios can be utilized to address specific patient needs (4). A list of the general enteral nutrition formula classes with their modifications and rationale is listed below. The current institutional nutrition formulary should always be consulted whenever choosing a formula for clinical use.

Type	Modification	Rationale
Diabetic	High fiber Low simple sugar High fat	Decreased risk of hyperglycemia
Hepatic	Low protein High branch-chain amino acid	Decreased encephalopathy
Pulmonary	High fat High calorie	Decreased CO ₂ production
Renal	High calorie Low electrolyte	Decreased fluid and electrolyte overload
Immune-enhancing	L-arginine Glutamine Omega-3 fatty acids Ribonucleic acid	Improved wound healing Decreased infectious complications Decreased hospital length of stay Decreased mortality

LITERATURE REVIEW

Numerous studies, clinical trials, consensus statements, and evidence-based medicine guidelines have been published. As a result of variations in study design, patient population, and statistical analysis, many of these studies and reviews have conflicting conclusions making the evidence-based recommendation process difficult and, in some cases, impossible (6). The following literature review should not be considered comprehensive, but rather a compilation of recommendations from several previously published guidelines as well as a discussion of several areas of current controversy. The reader is referred to several of the comprehensive reviews of the subject for further detail (2,4,7).

Parenteral Nutrition

The landmark VA Cooperative Study demonstrated that the risks of parenteral nutrition therapy exceeded the benefits when total parenteral nutrition (TPN) was administered to borderline or mildly malnourished patients undergoing elective general surgery procedures (8). Perioperative TPN was shown to increase the risk of major infectious complications without a benefit of improved patient outcome in such patients. Those patients at high-risk for malnutrition-related complications, however, experienced a significant reduction in major non-infectious complications. Similarly, a prospective, randomized trial of early postoperative TPN in patients undergoing pancreatic resection for malignancy demonstrated a significant increase in major complications when compared to those patients receiving intravenous fluids only (9). The risk/benefit ratio of parenteral nutrition thus appears to be high in the less severely ill and lower (and possibly more acceptable) in the critically ill patient who is at risk for malnutrition-related complications (10). Prospective trials comparing TPN with standard care found no difference in morbidity or mortality when TPN was used for less than 14 days (11). Further analysis of the most recent trials suggests that TPN may be associated with an increase in complications and mortality (11). In general, use of parenteral nutrition should be limited to those patients in whom the GI tract is not functional or cannot be accessed and in patients who cannot be adequately nourished by either oral diets or enteral nutrition (4).

Enteral vs. Parenteral Nutrition

Randomized trials of medical, surgical, and trauma patient subpopulations comparing enteral to parenteral nutrition have routinely demonstrated improved wound healing, fewer infectious complications, decreased intestinal mucosal permeability, and decreased patient care costs with the use of enteral feeding (2,11-13). Enteral nutrition is the preferred method of nutritional support as gut-associated lymphoid tissue (GALT) contributes up to 60% of total body immunity and enteral nutrition promotes mucosal viability and immunologic function (1,2,14). Patients with a nonfunctioning gastrointestinal tract, as evidenced by severe peritonitis, intestinal obstruction, short bowel syndrome, or intractable diarrhea, may benefit from parenteral nutrition as opposed to intravenous fluids alone (4). Low rate, trophic enteral nutrition should always be considered in patients receiving parenteral nutrition in order to preserve gut mucosal integrity.

Prospective, randomized trials of enteral vs. parenteral nutrition in severe pancreatitis have found that enteral nutrition is safe, feasible and superior to TPN (15). Patients who receive such enteral feedings

beyond the ligament of Treitz experience fewer total complications, fewer septic complications and a decreased total hospital cost (15-17). In addition, these studies demonstrate that enterally fed patients have a decreased inflammatory response and improvement in disease severity compared to those fed parenterally (15,16).

"Early" vs. "Delayed" Enteral Nutrition

Initiation of enteral nutrition is commonly delayed until several days post-injury / post-operatively in order to ensure complete resuscitation and hemodynamic stability. Anecdotal cases of small bowel necrosis have occurred as a result of vigorous enteral nutrition and shunting of mucosal blood flow prior to adequate resuscitation of the patient. Several prospective, randomized trials, however, have demonstrated a high rate of gastroparesis and enteral nutrition intolerance in patients where initiation of enteral feedings are delayed by more than 12-24 hours post-injury (2). These findings were particularly pronounced in the severely head injured or burned patient population where decreased gastric emptying appears particularly prevalent. Early enteral nutrition within the first 12 hours post-injury has been demonstrated to be safe and highly successful. Evidence suggests that early enteral nutrition, initiated at a low rate within 24 hours of injury and gradually increased to goal rate over a several day period, may reduce the incidence of gastroparesis and ileus that is seen when the start of enteral nutrition is delayed for several days post-injury (2). Early "trophic" feedings, begun as resuscitation is being completed, may also serve to maintain GI tract mucosal integrity and reduce the incidence of bacterial translocation, SIRS, and MOSF (3).

Delivery of Enteral Nutrition

A discussion of the various enteral feeding methods (nasogastric, nasojejunal, gastrostomy, or jejunostomy tube) and their potential risks and benefits is beyond the scope of this evidence-based medicine guideline (18). In general, patients who are anticipated to require enteral feeding access for less than 1 month are best fed through nasoenteric feeding tubes while those who are anticipated to require longer periods of enteral access should have a more definitive access placed such as a percutaneous gastrostomy or jejunostomy tube. Nasoenteric tubes are best placed at the patient's bedside with subsequent radiographic evaluation to confirm appropriate intragastric or transpyloric placement. If placement is unsuccessful, fluoroscopic or endoscopic guidance should be pursued (4). Surgical patients who are likely to require prolonged nutritional support should have an appropriate feeding access placed at the time of laparotomy.

It has been theorized that post-pyloric small bowel feedings should reduce the risk for aspiration, but this has not been borne out in the literature (11). Given its ease, relative safety, and general overall tolerance across patient populations, intragastric feeding should be considered the site of first choice (2,7). Medications that slow gastric emptying should be avoided wherever possible and prokinetic motility agents (such as metoclopramide - 10 mg IV q 6 hrs and intravenous erythromycin - 200 mg IV q 12 hrs) should be instituted where necessary to improve intestinal motility and enteral nutrition tolerance (19). Feedings should be started at full-strength with the patient's head of bed elevated at 30-45 degrees at all times. The current literature addressing the efficacy of bolus versus continuous intragastric feedings is indeterminate. While older studies would suggest that it is feasible, simple, and less costly, this method of feeding has not been found to be superior to continuous feedings (7,20). Feedings should be slowed or held if gastric residuals are greater than 200 mL (4). Patients at risk for pulmonary aspiration due to gastroparesis (i.e., diabetics, closed head injury), gastroesophageal reflux, or those who fail to tolerate intragastric feedings within 24 hours of initiation should have a transpyloric small bowel feeding access placed as soon as possible in order to continue nutritional support (4,7). Enteral nutrition should be initiated cautiously in patients with evidence of marginal systemic perfusion (oliguria or vasoconstriction) due to concern for causing intestinal ischemia. In such patients, small bowel feedings should be initiated and maintained at low rate (10-15 mL/hr) until the patient has been adequately resuscitated.

Nutritional Assessment

Specific literature addressing the optimal method for nutritional assessment is lacking. Multiple formulae have been proposed to estimate a patient's nutritional requirements following injury or illness. No formula has been proven to be superior to the others and all should be considered to provide at best an estimate of the patient's initial protein and caloric needs. Many non-randomized trials have compared indirect

calorimetry to various other methods and mathematical formulas designed to assess caloric energy needs. Indirect calorimetry has been proven to be the most accurate method of assessing energy requirements (2,7). The following table serves as a guide for initiating nutritional support (2,4,5,21). As energy requirements have been demonstrated to change over time, frequent (i.e., weekly) reevaluation of a patient's nutritional support seems prudent (4). The initial caloric requirement for severe burn patients (>20-30%TBSA) is typically overestimated by the Curreri Formula (25 kcal/kg + 40 kcal/TBSA burn) by 25-50%, but underestimated by the Harris-Benedict Formula also by 25-50%. The use of supplemental parenteral nutrition in burn patients to meet the calculated requirements of the Curreri Formula is associated with increased mortality and is not recommended. These patients may benefit from more frequent nutritional assessments as their caloric requirements fluctuate throughout their recovery. Intra-operative feedings should be considered in the burn patient to maintain adequate nutritional support.

Multiple assays are available to assess the adequacy of protein administration. Each of these assays has weaknesses in the critically ill patient population. Twenty-four hour urine urea nitrogen (UUN) studies have been shown to be most accurate in this patient population. No study has addressed the optimal frequency for such assessments. Insufficient data exists to make clear recommendations regarding protein administration in these patient populations.

ESTIMATED CALORIC / PROTEIN REQUIREMENT BY ILLNESS^{2,4,5,21}

Patient Population	Caloric Requirement	Protein Requirement
Trauma (ISS 25-30)	25-30 kcal/kg/day	1.25-1.5 gm protein/kg/day
Severe head-injury (GCS<8) <ul style="list-style-type: none"> • Non-pharmacologically paralyzed • Pharmacologically paralyzed 	30 kcal/kg/day 25 kcal/kg/day	1.5-2.0 gm protein /kg/day 1.5 gm protein/kg/day
Spinal cord injury <ul style="list-style-type: none"> • Quadriplegics • Paraplegics 	20-22 kcal/kg/day 22-24 kcal/kg/day	1.25-1.5 gm protein/kg/day 1.25-1.5 gm protein/kg/day
Burns <ul style="list-style-type: none"> • < 20% TBSA • >20-30% TBSA 	25-30 kcal/kg/day See text	1.25-1.5 gm protein/kg/day Up to 2 gm protein/kg/day

If the patient is greater than 20% above ideal body weight (IBW), the adjusted body weight should be used in such calculations. IBW (using the Devine formula) and adjusted body weight (ABW) are derived as follows:

$$\begin{aligned}
 \text{IBW (male)} &= 50 + (2.3 * (\text{height [in inches]} - 60)) \\
 \text{IBW (female)} &= 45.5 + (2.3 * (\text{height [in inches]} - 60)) \\
 \text{ABW} &= 0.25 * (\text{actual body weight} - \text{IBW}) + \text{IBW}
 \end{aligned}$$

Conclusive evidence regarding the use of various acute-phase visceral protein measurements (such as serum albumin, prealbumin, retinol binding protein, and transferrin) is lacking (2,4). Of these measurements, serum pre-albumin appears to be the most sensitive indicator of appropriate nutritional support (2).

Upon initiating nutritional support, serum electrolytes (sodium, potassium, chloride, bicarbonate, phosphorus, and magnesium) should be measured and monitored routinely until stable. Blood glucose should be closely monitored with institution of sliding slide insulin or other equivalent therapy to prevent iatrogenic hyperglycemia with its attendant increase in infection risk and decrease in wound healing. Serum glucose levels should be aggressively maintained below 150 mg/dL (4,22). Patients receiving intravenous fat emulsion should have serum triglyceride levels monitored until stable. Liver function test should be monitored periodically in patients receiving parenteral nutrition (4).

Standard Enteral Nutrition vs. Immunonutrition

Over the past decade, the importance of enteral nutrition in regulating immune function, reducing intestinal permeability and bacterial translocation, and improving patient survival from sepsis and critical illness has been increasingly recognized. An explosion of preclinical (animal) studies and numerous clinical trials have been performed to determine which nutrients are essential to survival. Unfortunately, many of the significant findings identified in preclinical trials have not been replicated in the counterpart human trials. Further, significant differences in study design and nutrient administration have made

comparisons between human studies difficult. Many studies have failed to feed patients early or have not aggressively pursued adequate protein / calorie support resulting in significant confusion between studies as to which nutrients should be administered and in what combination. Consequently, the majority of prospective, randomized trials evaluating the immune-enhancing diets (IED) have not found a consistent benefit across all patient groups nor a reduction in overall mortality (2,23-27). Given the significant cost of these nutritional formulas (10 times the cost of standard formulations), many have questioned the benefit of this therapy. Studies that have focused upon specific patient populations, however (i.e., severe trauma, malnourished GI surgery), have routinely identified reductions in infectious complications, length of hospital stay, antibiotic days, ventilator days, and incidence of MOSF with a trend towards improved survival that would make this therapy cost-effective (2,7). Based upon these studies, the following recommendations have been made:

- Patients who SHOULD receive early enteral nutrition with an IED
 - Severely injured abdominal / thoracic trauma patients (ISS>18-20, ATI>20-25) when given in conjunction with early feeding and adequate protein / calorie support
 - Malnourished elective GI surgical patients (albumin < 3.5 g/dl for upper GI tract and < 2.8 g/dl for lower GI tract)
- Patients who MAY benefit from early enteral nutrition with an IED
 - Aortic reconstruction with known chronic obstructive pulmonary disease (COPD) and an anticipated prolonged need for mechanical ventilation
 - Major head and neck surgery with preexisting malnutrition
 - Severe head injury (Glasgow Coma Score < 8) with an abnormal head CT scan
 - Burns ≥ 30% (third degree)
 - Ventilator dependent, nonseptic medical and surgical patients at risk of subsequent infectious morbidity
- Patients who SHOULD NOT receive early enteral nutrition with an IED
 - Those expected to resume an oral diet within 5 days
 - Those admitted to the ICU for monitoring reasons only
 - Those with a bowel obstruction distal to the site of access
 - Those with incomplete resuscitation or splanchnic hypoperfusion
 - Those with major upper GI hemorrhage

Limited data exists on the use of IED in septic patients. There is some concern that IED may increase mortality in sepsis, however, the data is conflicting (7). At this time, no recommendations can be made on the use of IED in the septic patient population. There is also no evidence to support the use of immune-enhancing parenteral formulations.

Under the above guidelines, an IED should be started before the insult wherever possible. In patients undergoing elective major surgical procedures, preoperative administration of an IED for 5-7 days before elective surgery appears to improve clinical outcome (7). Once started, an IED should be aggressively administered with the goal of providing at least 50-60% of the patient's calculated daily nutrient goal and continued for at least five days with subsequent reevaluation (7,11).

Complicating analysis of IED therapy is the myriad of formulations available containing the following major ingredients: glutamine, L-arginine, nucleotides, and omega-3 fatty acids. Few human studies have investigated individual enteral components and outcome. A review of each of these components, its purported risks and benefits, and the available clinical experience follows:

- **Glutamine**

Glutamine is a conditionally essential amino acid and the preferred fuel for rapidly replicating cells such as gastrointestinal mucosal cells (enterocytes and colonocytes) and immune cells (lymphocytes and macrophages) (26,28). It is a precursor for nucleotide synthesis, a substrate for hepatic gluconeogenesis, a precursor of the antioxidant glutathione, and essential to the renal handling of ammonia (28). Patients under catabolic stress are at risk for glutamine deficiency as

a result of their increased metabolic demand for this amino acid, inadequate nutritional intake, and the relative instability of this amino acid in standard protein solutions (29). Preclinical (animal) studies of glutamine supplementation have consistently demonstrated decreased mucosal atrophy, decreased intestinal permeability, and increased resistance to the effects of gut ischemia and reperfusion (29). A recent meta-analysis of 14 randomized trials evaluating human enteral glutamine therapy demonstrated fewer infectious complications and a shorter hospital stay of almost 3 days (30). An association between high-dose glutamine and decreased mortality has been identified (31). Further prospective, randomized trials are necessary to recommend widespread utilization of glutamine in nutritional support.

- Arginine

L-arginine, a dibasic amino acid, has numerous important roles in the transport, storage, and excretion of nitrogen; formation of nitric oxide; mediation of macrophage function after injury; and regulation of wound healing (26). Although historically considered a nonessential amino acid, recent studies have suggested that, like glutamine, arginine is a conditionally essential amino acid in the presence of catabolic stress and critical illness where endogenous synthesis becomes insufficient to meet body demands (28). Preclinical studies have demonstrated decreased intestinal permeability and bacterial translocation in animals receiving arginine supplementation (29). Meta-analyses of arginine-containing enteral nutrition formulas have demonstrated a decreased incidence of infectious complications, a shorter hospital length of stay, and fewer ventilator days (6,25,29). Such differences were most marked in the surgical patient subpopulation and less so in the critically ill. Of potential concern, the relative risk of death was higher (although not significantly) (RR 1.19; 95% CI 0.99-1.43) in patients receiving the arginine-containing formulas at the same time that infectious complications were significantly reduced (6). Further prospective, randomized trials are necessary to recommend widespread utilization of arginine in nutritional support.

- Nucleotides

Nucleotides serve as the building blocks of deoxyribonucleic acid (DNA) and ribonucleic acid (RNA). Nucleotides are required for catalysis, energy transfer, and coordination of hormonal signals (28). *De novo* synthesis of nucleotides is an energy-demanding process and nucleotide recycling (from dead cells) or exogenous nucleotides are preferred to endogenous synthesis. In the absence of an adequate nucleotide supply, replication of rapidly growing cells (such as gastrointestinal mucosa and lymphocytes or macrophages) is down regulated. Prospective, randomized trials evaluating the impact of isolated nucleotide preparations on patient outcome do not currently exist.

- Omega-3 fatty acids

Of the long chain fatty acids, the omega-3 polyunsaturated fatty acids appear to have the greatest potential for clinical benefit in modulating immune response and improving patient outcome. These fatty acids are precursors of the prostacyclins, thromboxanes, prostaglandins, lipoxins, and leukotrienes. Unlike glutamine, L-arginine, and nucleotides, the omega-3 fatty acids do not directly stimulate the immune system, but compete with arachidonic acid (an omega-6 fatty acid) for cyclo-oxygenase metabolism (28). The ratio of omega-3 to omega-6 fatty acids appears to be important to optimizing immune function. The omega-3 family of fatty acids has been shown to reduce the development of atherosclerosis and incidence of myocardial infarction, reduce hypertension, and improve outcome from various proinflammatory states (26).

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