INTRODUCTION

Perioperative nutrition is a vital yet often overlooked aspect of surgical care. The association between poor nutritional status and surgical outcomes has been clearly, eloquently, and repeatedly demonstrated for decades. That being said, a review of the literature on surgical nutrition reveals a disparity between the recommendations of well-designed studies and the nutritional practices commonly applied to surgical patients. Diversity of surgical specialties, entrenchment of surgical dogma, and a closely monitored outcome-based climate all play substantial roles in the maintenance of this divergence. Surgeons are frequently comfortable with tradition and skeptical of change. Convincing a successful surgeon to alter his or her perioperative management, particularly in ways that run in opposition to time-honored teachings, is not the easiest of tasks. Fortunately, a robust collection of rigorous clinical studies offers high-quality evidence supporting the current recommendations on perioperative nutrition.

Surgical nutrition has been a dynamic and evolving discipline from the start. The initial description of the complex metabolic response to surgical stress paved the way for an understanding of the hypermetabolic postoperative state, which led to research into perioperative replacement of stress-induced nutritional deficits.
Parenteral nutrition was thus invented and subsequently improved. The benefits of enteral nutrition then became apparent, and early initiation of gastrointestinal feeding postoperatively was recommended. The idea of attenuating the surgical stress response through optimization of the preoperative state was investigated. Prehabilitation, preoperative carbohydrate loading, and immunonutrition currently pervade any discussion on perioperative care. The risks of inadequate perioperative nutrition are well known and potentially disastrous. The purpose of this article is to provide a concise review of perioperative nutrition while emphasizing the attainable clinical benefits demonstrated in current research.

NUTRITION ASSESSMENT

Nutritional assessment is an important component of the preoperative evaluation of surgical patients. Patients at nutritional risk before surgery have an elevated risk of postoperative complications. The Joint Commission recognizes this and requires a nutrition screening within 24 hours of admission on all inpatients followed by a complete assessment for those considered high risk. The goal of effective preoperative screening is to identify high-risk patients allowing for targeted intervention that ultimately decreases surgical morbidity. To that point, evidence suggests that providing preoperative enteral nutrition to those at high risk reduces major postoperative morbidity by 50%. Unlike cardiac risk assessment, there is no standard algorithm for preoperative nutrition. Thus, the surgeon is often responsible for assessing nutritional risk, frequently relying on individual preferences rather than using a validated stratification strategy.

The goal of the preoperative nutritional assessment is not to correct years of nutritional deficits but to identify and optimize or prehabilitate patients at nutritional risk for the stress of surgery. Importantly, malnutrition and nutritional risk are not synonymous. Malnutrition is defined as an inability to match metabolic and nutrient requirements. The American Society for Parenteral and Enteral Nutrition (ASPEN) categorizes malnutrition as starvation related, chronic disease related, or acute disease related. Nutritional requirements vary based on the category of malnutrition and the presence of a disease state. Potential causes of preoperative malnutrition include neoplasm, an inability to swallow, a lack of access to nutrition, or gastrointestinal tract dysfunction. It behooves the clinician to elucidate the cause and tailor preoperative intervention to individual patients.

Preoperative risk assessment should consider the patients’ nutritional state, the risk of the proposed surgery, and potential postoperative anatomic alterations. Understandably, accurately assessing risk in the preoperative period can be difficult. Patients undertaking esophageal, pancreatic, abdominal wall reconstruction, or hepatobiliary operations are reported to be at an elevated risk. It has been suggested that the American Heart Association’s preoperative cardiac risk stratification be used to estimate nutritional risk, acknowledging intraperitoneal and intrathoracic cases lasting more than 2 hours are inherently higher risk.

The need for an available and facile nutrition assessment tool led to the creation of multiple risk calculators of various design. The Malnutrition Universal Screening Tool, the Nutritional Risk Index, the Nutritional Risk Screening (NRS-2002), the Mini Nutritional Assessment, and the Subjective Global Assessment are all examples of suggested risk stratifiers. Unfortunately, only the Nutritional Risk Screening (NRS-2002) has been validated and supported by level I evidence.

Traditional teaching in many surgical textbooks and training programs emphasized the use of albumin as an important marker of nutritional status. Albumin is important in
body fluid distribution, acid-base balance, and substrate transport.\textsuperscript{6} Additionally, albumin is an excellent prognostic indicator, with values of less than 3 associated with poor surgical outcomes.\textsuperscript{7} However, albumin has been found lacking in terms of its utility as a nutritional marker.\textsuperscript{2} Although albumin composes more than half of the total human serum protein, its concentration is regulated by multiple factors outside of synthesis and degradation. Inflammation, immobility, and capillary permeability all affect plasma albumin levels.\textsuperscript{6} Albumin is also generally understood to be a negative acute phase protein. Hepatic protein production during stress is thought to shift toward the production of acute-phase reactants and immune cells and away from albumin synthesis.\textsuperscript{8} These factors make albumin an unreliable nutritional indicator in surgical patients, although it bears mentioning that a recent literature review noted increased albumin synthesis in the postoperative period particularly following nutritional supplementation.\textsuperscript{6} Finally, normal albumin levels have been observed in patients dying of starvation, further underscoring that albumin is a suboptimal nutritional parameter.\textsuperscript{9}

The serum prealbumin level has also been touted as a marker of nutritional status. Prealbumin has a half-life of 2 days, substantially shorter than the 20-day half-life of albumin. This shortened half-life has led to the suggestion that prealbumin levels reflect a more acute and, therefore, accurate assessment of nutritional status. Unfortunately, prealbumin is also a negative acute-phase protein and, therefore, subject to the same unreliability as albumin.\textsuperscript{2,9}

Rather than relying solely on a highly variable serum marker, the North American Surgical Nutrition Summit recommends a multifactorial, broad-based assessment. The clinician should gather details regarding the recent oral intake, body weight, and weight loss. Declining recent oral intake, an actual body weight of less than 90\% of the ideal body weight, body mass index (BMI) less than 18.5 or greater than 40, and weight loss greater than 5.0\% in 1 month, 7.5\% in 3 months, and 10\% in 6 months indicate nutritional risk. Biomarkers are not excluded from the recommendations but should be used as a part of a comprehensive preoperative assessment. Serum C-reactive protein, albumin, and glycated hemoglobin (HgbA1C) levels all broaden the assessment.\textsuperscript{5} Postponement of major elective surgery is recommended in order to achieve a HgbA1C less than 7.5, attempt weight loss in those with a BMI greater than 35, attempt smoking cessation, and address poor nutrition.\textsuperscript{5}

**SURGICAL RESPONSE TO STRESS**

The response to surgical stress is complex and diverse. An understanding of the physiologic response to stress is integral to providing excellent perioperative care and achieving optimal surgical outcomes. Unsurprisingly, much attention has, therefore, been devoted to understanding the stress response. Sir David Cuthbertson\textsuperscript{10} described the metabolic ebb and flow occurring after major trauma in 1942. Less than a decade later, Moore and Ball\textsuperscript{11} described the altered metabolism experienced by surgical patients in *The Metabolic Response to Surgery*. In 1959, Moore\textsuperscript{12} described the impact of perioperative nutrition in *Metabolic Care of the Surgical Patient*. These foundational works clarified the stress response and launched interest in perioperative nutrition.

The surgical stress response is now understood to involve endocrine and inflammatory arms. Additionally, the stress response correlates with the degree of insult.\textsuperscript{13} Injury stimulates the hypothalamic-pituitary-adrenal (HPA) axis that ultimately results in increased secretion of cortisol, epinephrine, glucagon, growth hormone, aldosterone, and antidiuretic hormone.\textsuperscript{9} On the other hand, the inflammatory response is
mediated via numerous cytokines including tumor necrosis factor-alpha, interleukin-1 (IL-1), and IL-6. Cytokines are largely responsible for the subsequent activation of the immune system and have also been shown to stimulate the HPA axis, thus creating interplay between the inflammatory and endocrine responses.

The above-mentioned mediators ultimately create a catabolic state designed to meet the increased energy demands of stressed patients. Glucose, fatty acids, and protein are all readily available substrates; however, glycogen stores are rapidly depleted and skeletal muscle is then subsequently used for hepatic gluconeogenesis. The role of perioperative nutrition is, therefore, to attenuate the stress response and provide appropriate supplementation to mitigate the effects of postoperative catabolism.

ROUTE OF DELIVERY

The enteral and parenteral routes of delivery are available for perioperative supplementation. Total parenteral nutrition was invented by Dr Stanley Dudrick and revolutionized perioperative care. Parenteral nutrition is undoubtedly capable of providing excellent nutrition; however, there are significant risks with this form of supplementation. First, patients require central venous access creating the potential for line complications. Next, hyperglycemia is frequently encountered and close attention to glycemic control is necessary. Further, standard parenteral formulations in the United States often lack important substrates, such as glutamine. Additionally, lipid formulations frequently include proinflammatory omega-6 rather than antiinflammatory omega-3 fatty acids. Finally, infectious complications overall occur more frequently in comparison to enteral nutrition.

The importance of the gastrointestinal tract to immunity is well recognized and cannot be overstated. The gut is home to the largest source of immune tissue in the body. Gut-associated lymphoid tissue (GALT), a form of mucosa-associated lymphoid tissue, is responsible for 60% to 70% of total immunity. GALT plays an important role in both innate and adaptive immunity. Paneth cells secrete nonspecific antimicrobial substrates, whereas microvilli cells present intraluminal antigens to lymphocytes in Peyer patches. These lymphocytes are subsequently sensitized and circulate systemically via rich mesenteric lymphatics. The ultimate result of this process is the production of targeted antibodies. Immunoglobulin A antibodies are of particular importance as they provide intraluminal immunity and prevent bacterial translocation. Finally, the gut provides a physical barrier to infection through the production of mucin and the presence of tight junctions.

Importantly, gut starvation and/or critical illness induce changes to the immune function of the gastrointestinal tract. Lack of enteral feeding causes villous blunting and increased mucosal permeability potentially allowing bacterial translocation and bacteremia. Additionally, gut starvation decreases hepatic and peritoneal immune function. Enteral nutrition attenuates these deleterious effects, and multiple studies have demonstrated improved outcomes with early initiation of enteral feeding.

Enteral nutrition is currently recommended over parenteral nutrition by all major nutrition and critical care organizations. According to the North American Surgical Nutrition Summit, contraindications to enteral nutrition include obstruction, ischemia, acute peritonitis, and lack of bowel continuity. Additional relative contraindications may include high-output fistulas and severe malabsorption. Enteral feeding has been shown to be safe in patients with open abdomens and those requiring vasopressors. Additionally, animal studies suggest that early enteral feeding proximal to a gastrointestinal anastomosis actually strengthens the newly joined bowel.
absence of a definite contraindication, enteral nutrition should be initiated in all patients, preferably within 24 hours of surgery. Parenteral nutrition should be considered as an adjunct for patients unable to meet their full nutrition requirements with enteral nutrition or as a primary modality in patients with a contraindication to enteral feeding.

**IMMUNONUTRITION**

Immunonutrition is a relatively new aspect of perioperative care and refers to the supplementation of specific nutrients, including arginine, omega-3 fatty acids, nucleotides, and/or glutamine. These nutrients are hypothesized to influence the immune and inflammatory response to surgical stress as well as encourage protein synthesis. Two studies published in the early 2000s demonstrated improved outcomes in patients with cancer receiving perioperative immunonutrition and subsequently ignited interest in this area. In the interim, investigation has focused on describing the mechanism of action of these supplements and understanding their overall clinical impact. The following serves as a brief overview of the key components of immunonutrition.

**ARGININE**

Arginine is considered a conditional amino acid as it is used and depleted during stress. Its biological functions include stimulating immune cells (particularly lymphocytes), promoting wound healing, and acting as a precursor of nitric oxide (NO). NO is of particular relevance because of its ability to improve microvascular perfusion through vasodilation. Arginine supplementation was viewed with skepticism in critically ill patients as increased vasodilation was thought to contribute to cardiovascular compromise. However, a meta-analysis of previously published randomized controlled trials found decreased postoperative infectious complications, a shorter length of stay, and no increase in morbidity or mortality with arginine supplementation. Further, the clinical implications of the arginine-to-asymmetric dimethylarginine (ADMA) ratio have recently been described. ADMA acts in opposition to arginine inhibiting NO and, therefore, impairing microvascular perfusion. In critical illness, arginine is depleted creating a relative abundance of ADMA. A reduced arginine-to-ADMA ratio has been shown to correlate with increased mortality in the critically ill. The potential clinical benefit of arginine supplementation to correct the arginine/ADMA ratio is under investigation. Overall, the available evidence on arginine supplementation in the perioperative period seems to be favorable.

**OMEGA-3 FATTY ACIDS**

Omega-3 fatty acids are polyunsaturated fatty acids that play a role in the maintenance of cell membranes and modulation of the inflammatory response. Important, they are relatively less abundant in the Western diet compared with omega-6 fatty acids that are linked to a host of negative health effects. Docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) are 2 biologically active omega-3 fatty acids. Recent research indicates that DHA and EPA are converted to resolvins, substances that have potent antiinflammatory and analgesic properties. To date, the clinical potential of this discovery remains unknown.

The results regarding perioperative supplementation of omega-3 fatty acids have been divergent. A meta-analysis of randomized controlled trials in critically ill patients demonstrated a significant reduction in mortality in patients receiving enteral
supplementation. However, recent randomized controlled trials comparing omega-3 fatty acid supplementation with conventional perioperative nutrition in patients with colorectal and esophageal cancer failed to demonstrate improved outcomes. At least one meta-analysis has demonstrated improved outcomes in those receiving both omega-3 fatty acid and arginine supplementation suggesting the potential for therapeutic interplay. Omega-3 fatty acid supplementation seems safe, but more data are necessary to define the clinical impact.

GLUTAMINE

Like arginine, glutamine is a conditional amino acid and composes 70% of the amino acids mobilized during the stress response. Its biological functions include acting as an antioxidant via its role as a precursor to glutathione, providing energy for enterocytes and, thus, maintaining gut integrity, participating in wound healing, and promoting protein synthesis. A recent meta-analysis of 16 randomized controlled trials found that parenteral perioperative supplementation decreased postoperative infections, shortened length of stay, and improved nitrogen balance. Another study demonstrated that perioperative parenteral administration to moderately and severely malnourished patients improved glucose homeostasis, decreased infections, and reduced intensive-care-unit stay. Importantly, this study found a benefit in multivariate analysis in the cohort receiving perioperative glutamine over those supplemented only in the postoperative period. Regarding enteral supplementation, a recent prospective randomized trial of head and neck oncology patients demonstrated improved fat-free body mass and quality of life in those receiving glutamine. Again, more research is necessary before reaching a definitive conclusion on glutamine supplementation, although the balance of evidence seems favorable, particularly in those at nutritional risk.

To summarize, immunonutrition is clearly a promising area of perioperative nutrition. Four recent meta-analyses attest to improved clinical outcomes. Continued research is necessary to define the precise biochemical mechanisms and ultimately describe the optimal perioperative formula. At present, perioperative immunonutrition should be recommended for all patients undergoing major elective gastrointestinal surgery at risk for infectious complications, particularly in the malnourished. It should be initiated 5 to 7 days preoperatively and continued postoperatively.

PREOPERATIVE NUTRITION

As early as 1936, Studley demonstrated that preoperative weight loss was associated with increased operative mortality. Unfortunately, as mentioned previously, preoperative nutritional optimization is often time consuming and difficult to quantify. Surgeons and patients alike frequently do not have the luxury of optimizing nutritional status over an extended period of time. Even in purely elective surgery, the time required for correction of nutritional deficits is individualized and highly variable. The concept of prehabilitation, or a short-course optimization in preparation for surgery, was created to address these concerns. Prehabilitation represents a preoperative bundle designed to prepare the body for the metabolic insult of the perioperative period. Exercise tolerance and weight, nutrition, and glucose control are all addressed. The benefit of such a regimen has been demonstrated in clinical trials.

The impact of preoperative nutritional supplementation on various surgical subgroups has been investigated. A recent multicenter prospective cohort study of more than 1000 patients investigated preoperative supplementation with either enteral or parenteral nutrition. All patients receiving preoperative nutrition were supplemented
for at least 7 days before surgery. Nutritional assessment was performed on all study participants using the NRS-2002 survey. According to the authors of the NRS-2002, a score greater than 3 indicates nutritional risk. In the cohort study, patients with an NRS-2002 score of at least 5 that received preoperative supplementation had a significantly shortened length of stay and a postoperative complication rate of half of the nonsupplemented group. No benefit in the subgroup with an NRS-2002 score of 3 to 4 was noted, although the number of patients was small. This study demonstrates that high-risk patients significantly benefit from preoperative nutrition.

Although the prior study used both enteral and parenteral nutrition, the optimal route of delivery has previously been investigated. In 1991, The Veterans Affairs Total Parenteral Nutrition Cooperative Study Group published a landmark trial on preoperative parenteral nutrition. Patients were again stratified according to nutritional risk. Increased rates of infection without significant benefit were observed in the borderline and mildly malnourished groups receiving parenteral nutrition. There was a benefit to parenteral supplementation in severely malnourished patients, although this subgroup represented less than 5% of the study. The investigators commented that the benefit noted in severely malnourished patients should be viewed with caution because of the small sample size. Nevertheless, the results from this study represented a paradigm shift in clinical practice. As of 2009, ASPEN and the Society of Critical Care Medicine continue to recommend parenteral nutrition for 7 days preoperatively in severely malnourished patients unable to tolerate enteral feeding.

As mentioned earlier, enteral nutrition has a myriad of benefits and is the preferred source of feeding whenever possible. This is no different in the preoperative period. Recently, the idea of preoperative carbohydrate loading has been investigated. Traditionally, patients are made nil per os after midnight the evening before their operation. This practice stems from concerns over aspiration risk in patients receiving monitored or general anesthesia. It is now, however, increasingly recognized that fasting for this length of time depletes glycogen stores before the start of surgery. This depletion creates a situation whereby lean body mass is sacrificed during the actual operation to meet energy demands. In order to attenuate the loss of skeletal muscle, carbohydrate supplements are given before surgery. Preoperative carbohydrate loading often includes taking 800 mL of a 12.6% carbohydrate drink the night before surgery and 400 mL of a similar preparation 2 to 3 hours before induction of anesthesia. Contrary to conventional teaching regarding the need for lengthy fasts before surgery, there are now abundant data demonstrating the safety and efficacy of preoperative carbohydrate loading. Since 2010, 3 meta-analyses of randomized controlled trials have found improved insulin resistance, shortened hospital stay, and no increase in pulmonary complications with preoperative carbohydrate loading. Additionally, a randomized trial demonstrates preservation of muscle mass with carbohydrate loading, whereas animal data find improved maintenance of the intestinal mucosal barrier and earlier return of oral intake. Should concerns over aspiration persist, a Cochrane database review from 2003 established that there was no evidence suggesting oral intake of fluids closer to the induction of anesthesia increases pulmonary complications. From these data, the American Society of Anesthesiologists' guidelines are currently accepting of clear liquids up to 2 hours before the induction of anesthesia.

Preoperative carbohydrate loading is an important component of the Enhanced Recovery After Surgery (ERAS) protocols for perioperative care. ERAS protocols represent another bundle approach to perioperative management that has demonstrated a clinical benefit. Multiple studies confirm improved patient outcomes and satisfaction as well as decreased lengths of stay after implementation of ERAS.
ERAS protocols have been intensely investigated in colorectal surgery and are being increasingly applied to wider patient populations. These protocols provide evidenced-based recommendations for preoperative, intraoperative, and postoperative care.

Preoperative supplementation provides a significant benefit in the severely malnourished. The gastrointestinal tract is the preferred route of supplementation, but severely malnourished patients unable to tolerate enteral feeds have drastically improved outcomes with parenteral nutrition. Prehabilitation and ERAS bundles are beneficial and will likely become increasingly incorporated into clinical management. Preoperative carbohydrate loading is safe and effective and should be considered in all patients.

**POSTOPERATIVE NUTRITION**

Providing adequate postoperative nutrition improves outcomes. Substantial evidence indicates that early enteral nutrition is associated with significant reductions in morbidity and mortality. Multiple meta-analyses have demonstrated the positive clinical impact of beginning enteral nutrition within 24 hours of surgery. Early stimulation of the gastrointestinal tract maintains the mucosal barrier and prevents the bacterial translocation described in gut starvation. The significant role of the gut in immune function is again emphasized by a recent study in which infectious complications following liver transplantation decreased drastically in those receiving early enteral nutrition.

Most patients are able to tolerate enteral nutrition without untoward effects. As mentioned earlier, studies have demonstrated that early enteral feeding is advisable in critically ill patients requiring mechanical ventilation or vasopressor support and in trauma patients with open abdomens. trauma patients with open abdomens receiving early enteral nutrition had higher fascial closure rates and decreased mortality. Failure to achieve fascial closure is significant as it can result in long-term debilitating rehabilitation with increased risk of entero-atmospheric fistula formation.

Concern over anastomotic dehiscence has led many surgeons to avoid feeding a fresh anastomosis. Enteral feeding distal to an anastomosis is acceptable and commonly practiced in proximal gastrointestinal surgery. Randomized data indicate that early enteral feeding via a jejunostomy tube is associated with improved outcomes in proximal gastrointestinal cancer resections. Additionally, there is evidence in animal studies that early enteral feeding proximal to a fresh gastrointestinal anastomosis promotes healing without increasing the rates of disruption. This finding has yet to be evaluated in a human trial.

Concerns over aspiration with early feeding seem to be overstated. Similar to evidence suggesting routine postoperative reliance on nasogastric decompression is unnecessary, a clinically significant increase in aspiration has not been demonstrated in early enteral feeding. To that end, the North American Surgical Nutrition Summit recommends judicious use of enteral nutrition even in the presence of postoperative ileus. Routine gastric residual monitoring may be unnecessary as prospective randomized data in critically ill ventilated patients fail to demonstrate a decrease in pneumonia with this practice. To summarize, early enteral nutrition improves outcomes and is indicated in most postoperative patients.

Despite the overwhelming support in favor of aggressive nutrition, many patients’ nutritional needs are not met postoperatively for a variety of reasons. Adhering to a few principles can facilitate postoperative enteral nutrition. The ERAS group’s recommendations for colorectal surgery emphasize judicious fluid management and multimodal pain management. Preventing fluid overload decreases bowel wall edema,
and adequate analgesia facilitates early ambulation. Additionally, oral intake should be resumed early, and there is no reason to await the return of bowel function. Finally, the regimented process of initiating a clear liquid diet and sequentially advancing may be unnecessary and delay resumption of adequate nutrition.

Although most patients are candidates for enteral nutrition, some must rely on parenteral supplementation. The current recommendations for postoperative parenteral nutrition are based on its necessity preoperatively. Patients receiving parenteral nutrition preoperatively should have it restarted on postoperative day 1. In the absence of preoperative parenteral nutrition, patients expected to have a nonfunctional gastrointestinal tract for 7 days postoperatively should be started on parenteral therapy, although it should be noted that there is little benefit unless supplementation is continued for greater than 7 days. Unlike enteral nutrition, early initiation of parenteral nutrition is not recommended. A recent randomized controlled trial of critically ill patients with contraindications to enteral nutrition did not find any benefit to the early initiation of parenteral nutrition.

SUMMARY

The importance of perioperative nutrition cannot be overstated. An abundance of high-quality research provides guidelines regarding safe and efficacious management. Unfortunately, old habits seem to die hard, and antiquated practices continue to permeate surgical culture. Frankly speaking, poor nutrition is associated with poor surgical outcomes. Preoperative nutrition assessment, though often tedious, identifies high-risk patients that benefit dramatically from nutritional supplementation. Preoperative assessment should proceed with an eye toward prehabilitation or the preparation of patients for the metabolic onslaught of the perioperative period. Attenuation of the stress response through carbohydrate loading improves outcomes and shortens the length of stay. Fears over increased aspiration with carbohydrate loading have been discredited. Early initiation of enteral feeding within 24 hours of surgery improves outcomes, particularly in the critically ill in whom feeding was previously considered dangerous. There are relatively few contraindications to enteral nutrition, but those who truly cannot receive gastrointestinal feeding benefit from parenteral supplementation. Immunonutrition seems efficacious, although more research into its precise mechanisms is necessary. ERAS protocols have demonstrated clinical utility and will likely continue to expand to broader surgical populations.

Patient care and outcomes are important to every practicing surgeon. In this time of cost control and monitored outcomes, surgeons must remain keenly up to date and open-minded on areas of potential improvement. Surgical nutrition often lags behind the voluminous well-designed studies emphasizing the benefits of aggressive perioperative care. There is room for improvement. Ultimately, it is incumbent on the surgeon to practice the evidence-based recommendations demonstrated to improve outcomes.

REFERENCES


34. Azman M, MohdYunus MR, Sulaiman S, et al. Enteral glutamine 0.3-0.4mg/kg/day supplementation in surgical patients with head and neck malignancy: a randomized controlled trial. Head Neck 2014. [Epub ahead of print].


