Management of perioperative nutrition support

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Purpose of review

Perioperative nutrition has been extensively studied, but numerous questions remain unanswered. This review focuses on new developments in nutrient delivery in the immediate perioperative period. Issues specifically addressed include which patients are most likely to benefit from perioperative nutritional supplementation, and the optimal route, timing, and quantity of nutrient delivery.

Recent findings

Visceral proteins, particularly albumin, play an important role in nutritional and perioperative risk assessment. Although the recommendation to use the enteral route for delivery of nutrition whenever possible is clear, the cautious introduction of enteral feeds in the labile group of patients with circulatory failure is essential. Preoperative use of immune-modulating enteral formulas, preoperative carbohydrate loading, and the concept of early enteral feeding are important developments. Supplementary arginine, glutamine, and ω-3 fats play a potential role in nutritional management, as does 'permissive' hypocaloric feeding.

Summary

The particulars of nutritional support for perioperative and critically ill patients remain controversial. Recent studies addressing specific issues in this diverse discipline perhaps raise more questions than are answered. However, each new contribution to the literature brings us closer to an understanding of optimal nutritional management in the metabolically stressed patient.

Keywords

arginine, glutamine, hypocaloric feeding, ω-3 fats

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Abbreviation

ICU intensive care unit

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Introduction

Nutrient delivery in the immediate perioperative period has been the subject of numerous randomized trials, metaanalyses, review articles and editorial opinions. Yet several questions remain. Which patients will benefit? What is the optimal route of nutrition support? When should nutrients be delivered for optimal results? What and how much nutrient should be given?

In terms of nutritional support, it is generally accepted that earlier is better than later, that enteral is superior to parenteral, that the quality of nutrient appears more important than the quantity, and that select populations will show additional benefit from specific nutrient supplementation. Goals of nutritional support have changed in the past few years from attempts to preserve lean body mass following a surgical or traumatic stress to efforts to attenuate the hypermetabolic response, reverse loss of lean body mass, prevent oxidant stress, favorably modulate the immune response with early enteral feeding, attain meticulous glycemic control and administer appropriate macro and micronutrients, including glutamine, arginine, ω-3 fatty acids, and other novel substrates.

Which patients need perioperative nutritional support?

In an effort to identify which patients will benefit from preoperative nutritional preparation, Kudsk *et al.* [1] used albumin levels to stratify nutritional risk. In this retrospective cohort study, the authors reported that albumin levels are an accurate and inexpensive indicator of potential morbidity. They also noted that the significance of preexisting hypoalbuminemia is under-recognized and therefore under-treated. They recommended that in esophageal, gastric and pancreatic surgery, when albumin is below 3.25 g/dl, the operation should be postponed whenever possible for additional nutritional and metabolic support [1]. Another large, prospective, preoperative risk assessment involving more than 87 000 patients confirmed the conclusions of Kudsk *et al.* [1]. This study demonstrated that serum albumin is the best single indicator of postoperative complications [2]. Nutritional assessment following surgical or traumatic stress has continued to be evaluated at best by educated guesswork. Despite the availability of numerous global assessment tools, visceral proteins (albumin, transferrin, prealbumin, and retinol-binding protein) and various combinations of the two, no single assessment tool or laboratory value consistently yields information that would change nutritional practice in the acute setting. Recent data using the ratio of prealbumin (half-life, 48 h) and C-reactive protein may be of some value. C-reactive protein is an acute-phase reactant that correlates well with the severity of the inflammatory response [3]. It has a half-life of 8 h and is altered minimally by perioperative interventions. The ratio of prealbumin and C-reactive protein may indicate when the patient starts to produce visceral proteins as the inflammatory response wanes [4].

What is the optimal route of nutrient delivery?

The optimal route of preoperative nutrition is clearly the enteral route whenever feasible. The use of total parenteral nutrition in the preoperative period has limited utility except in the severely malnourished [5,6]. The comparison of enteral with parenteral nutrition is beyond the scope of this brief review and has been reviewed recently by others [5,6]. The use of enteral nutrition in critically ill patients with hemodynamic failure has recently been addressed by Villet *et al.* [7]. In a prospective descriptive study evaluating patients with circulatory failure, 83% requiring norepinephrine and 25% requiring intraaortic balloon pump, they reported that enteral nutrition is possible in the majority of patients with hemodynamic compromise [7]. Caution is the key in this labile population, as there have been reports of jejunal feeding inducing small-bowel necrosis in critically ill and immediately postoperative patients [8]. However, in general, the data overwhelmingly support the use of the gastrointestinal tract as the route of nutrient delivery whenever feasible.

What is the optimal time for nutrient delivery?

The optimal timing of nutritional intervention also remains a controversial topic. Preoperative preparation of the patient gained support following several landmark studies by Gianotti, Braga and colleagues [9,10] demonstrating that major morbidity could be reduced by approximately 50% in patients undergoing resection for malignancy of the esophagus, stomach or pancreas. This benefit was noted in both the well nourished and malnourished patient populations [9,10]. They provided an immune-modulating formula (Impact; Novartis Nutrition, Minneapolis, Minnesota, USA) given 5 days preoperatively. The patients consumed 1 l a day of the immune-modulating formula in addition to their regular diet. The formula contained additional arginine, ω-3 fatty acids and nucleic acids, and resulted in significant decreases in infectious morbidity, length of hospital stay, and hospital-related expenses [9–11].

Another area of recent interest in the preoperative setting, popularized by Svanfeldt *et al.* [12•], is carbohydrate loading. This strategy utilizes an isotonic carbohydrate solution given at midnight on the night before surgery, then 3 h preoperatively, to maximally load the tissues with glycogen prior to the surgical stress. In most Western medical centers the routine is to have the patient fast from midnight prior to surgery; hence, glycogen stores are nearly depleted prior to the surgical insult. Soop *et al.* [13] and Fearon *et al.* [14] have demonstrated this concept of so-called carbo-loading in several animal and clinical studies. They recently reported that a group receiving multimodality treatment, including avoidance of drains, controlled perioperative sodium and fluid administration, epidural anesthesia, early mobilization and carbohydrate loading, displayed less hepatic insulin resistance, decreased postoperative nitrogen loss, and better retention of muscle function [13,14].

The optimal time to start postoperative nutritional intervention is significantly influenced by a host of factors such as age, premorbid conditions, route of delivery, metabolic state, organ involvement, etc. The reported benefits of early enteral feeding are, among others, prevention of adverse structural and functional alterations in the mucosal barrier, augmentation of visceral blood flow, and enhancement of local and systemic immune response [15]. The clinical benefits of early enteral feeding have recently been the focus of two meta-analyses, which report a benefit of reducing infections and length of hospital stay with minimal risk and virtually no increase in major morbidity [16,17]. Numerous recent reports continue to support the concept that bowel sounds and evidence of bowel function – passing flatus or stool – is not required for resumption of oral intake. In a randomized trial, Suehiro *et al.* [18] initiated oral feeding within 48 h of gastrectomy. They reported no increase in morbidity and successfully reduced hospital stays. A similar study in colorectal surgery by Feo *et al.* [19] randomized patients to either nasogastric tube and feeding with signs of bowel-function return or no nasogastric tube and feeding on postoperative day 1. They concluded that early postoperative feeding was safe and did not increase morbidity.

Although the benefits of early enteral feeding have been uniformly reported, feeding in the immediate postoperative period in critically ill patients yields an entirely different set of problems. Gastrointestinal dysfunction in the setting of the intensive care unit (ICU) ranges from 30 to 70%, depending on the diagnosis, premorbid condition, mode of ventilation, medications, and metabolic state [20]. Proposed mechanisms of ICU and postoperative gastrointestinal dysfunction can be separated into three general categories: mucosal barrier disruption, altered motility and atrophy of the mucosa, and gut-associated lymphoid tissue.

Barrier disruption appears most commonly to be associated with splanchnic hypoperfusion, which is precipitated by numerous factors in the critical care setting and immediate postoperative period, including hypovolemia, increased catecholamines, increased proinflammatory cytokines and decreased cardiac output. All ultimately lead to reduced mucosal blood flow, barrier disruption, altered gastrointestinal motility, and changes in the bacterial flora and virulence of the organisms [21,22].

An excellent explanation of the mechanism inducing ileus was given recently by Kalff *et al.* [23]. In an elaborate series of human and animal studies, these investigators described the sequence of events following bowel manipulation. Following visceral manipulation, activation of transcription factors is noted, with upregulation of intracellular adhesion molecule-1 on the endothelium of the muscularis vessels. Leukocyte extravasation into the muscularis occurs, with resultant upregulation of inducible nitric oxide synthase, cyclooxygenase-2, interleukin-6, and signal transducer and activator of transcription-3 protein phosphorylation. This inflammatory focus then decreases the contractile response and alters electrical activity, resulting in ileus.

Recent approaches to maximize gut function in the postoperative and critical care settings include maintenance of visceral perfusion, strict glycemic control, electrolyte correction, early enteral feeding, and minimization of medications that alter gastrointestinal function, such as anticholinergic agents, narcotics, and high-dose pressors [24]. Numerous papers have demonstrated that successful early enteral feeding can be accomplished in the ICU and postoperative setting using standardized protocols. When these protocols are followed then rates of gastrointestinal tolerance in the 70–85% range can be achieved [25]. A recent study by Barr *et al.* [26], in which a standardized, evidence-based enteral feeding protocol was implemented, reported shortened duration of mechanical ventilation and a reduced mortality.

What is the optimal nutrient to deliver?

Regarding specific macronutrients, the requirement for carbohydrates is estimated at 3 to 6 mg/kg per min (roughly 200–300 g/day), for protein is 1.25–2.0 g/kg per day, and for lipids is 10–25% of total calories, depending on the route and lipid composition [27]. These figures vary depending on the specific patient condition. Ideally, one would like to provide sufficient nutrients to minimize the catabolic loss associated with stress, injury, and surgery while avoiding the problems associated with overfeeding, such as hyperglycemia, azotemia, excess CO_2 production, etc.

What to feed in the ICU and immediate postoperative period remains a controversial topic. Well over 200 enteral formulas are currently available for use, and several are considered appropriate for the ICU and postoperative setting. The most recent trials suggest additional benefit with immune-modulating compared to the standard formulas when the appropriate population is chosen [28–30]. More than 27 prospective randomized trials using immune-modulating formulas have resulted in very similar conclusions, demonstrating a decrease in infectious complications and shortened hospital stays with no change in overall mortality [28–30]. Yet some editorials continue to advocate immune formulas as a panacea [31••], while others report them as poison [32].

The greatest debate revolves around the pros and cons of additional arginine in the ICU setting. One school of thought holds that arginine is potentially toxic [32], whereas another argument is that arginine is deficient in critical illness and should be supplemented. A complete explanation and support for each of these arguments is beyond the scope of this article and can be found in recent peer-reviewed articles (see [31••] and Kalil and Danner, pp. 303–308 in this issue). Suffice to say, no prospective clinical data are currently available proving that arginine is harmful, whereas numerous prospective articles have demonstrated arginine to be beneficial, especially in the surgical and trauma population.

Glutamine is the other conditionally essential amino acid that has recently gained even greater support in the critical care setting. Over the past 20 years, glutamine has been reported to offer a myriad of benefits, including maintenance of acid/base balance, provision of primary fuel for rapidly proliferating cells (i.e. enterocytes and lymphocytes), synthesis of glutathione and arginine, lowering of insulin resistance, and function as a key substrate for gluconeogeneis [33]. Recent evidence that glutamine can induce heat-shock protein is yet another beneficial molecular effect of this amino acid [34•]. The heat-shock proteins are a class of cellular chaperone proteins that support appropriate protein folding [35]. With glutamine enhancing heat-shock protein, the cell protects itself from subsequent stress.

Understanding lipid modulation of the metabolic response in the surgical and critical care setting is hampered because lipids are traditionally given as one of many active components of an immune-enhancing formula. Determining the exact contribution of the lipid is virtually impossible. This is made even more confusing by recent data demonstrating that eicosapentaenoic acid modulates arginine metabolism [36]. The ω-3 fats in fish oil have multiple beneficial effects in the perioperative period, including modulation of leukcocyte function and regulation of cytokine release through nuclear signaling and gene expression [37]. Leukotrienes, thromboxane, and prostaglandins derived from ω-6 lipids have demonstrated a much higher inflammatory response than that associated with the ω-3 class [38]. The ω-3 lipids have recently been reported to enhance the production of a new group of prostaglandin derivatives called resolvins and neuroprotectins, which play a role in accelerating the resolution of the proinflammatory state [39••]. Abundant data report the influence of ω-3 fats on nuclear signaling and gene expression [37]. For example, polyunsaturated fatty acids interact with various nuclear receptor proteins, such as peroxisome proliferator-activated receptor, which then influence nuclear factor κB and gene expression. In effect, by decreasing nuclear factor κB migration into the nucleus, ω-3 fats downregulate the proinflammatory response to stressful stimuli [40]. Heller *et al.* [41••] recently reported that ω-3 fatty acids given intravenously at a dose of 0.11 g/kg per day for a mean of 8.7 days demonstrated a decrease in mortality in 661 surgical and ICU patients. The route of delivery of ω-3 fats may be of importance. Utilizing the enteral route, it takes approximately 3 days to achieve adequate ω-3 fat levels in the cellular membrane. However, when given parenterally, a clinically relevant response can be achieved in 3 h [37].

How much to feed?

The caloric requirement for the perioperative and ICU patient is evolving as the concept of hypocaloric feeding, or so-called permissive underfeeding, in the early ICU and postoperative period gains support. A teleologic argument states that a relative 'anorexia of illness' develops with significant injury and that supply of nutrients during this period induces a proinflammatory state which then exacerbates the condition. This concept has led several investigators to advocate hypocaloric feeding in the early phases of critical illness. Several retrospective studies and a few prospective studies have evaluated caloric delivery and outcome. Krishnan *et al.* [42] reported that underfeeding the septic medical ICU patient resulted in a small improvement in survival. In a study evaluating total parenteral nutrition and caloric delivery, McCowan *et al.* [43] demonstrated an interesting but not statistically significant trend in decreasing infectious complications. Several studies in critically ill obese patients use a hypocaloric high-protein regimen with excellent metabolic results [44,45]. While the optimal caloric load for the hypermetabolic (nonobese) patient remains in transition, the caloric delivery currently considered safe for the perioperative period is in the range of 20–30 kcal/kg per day (excluding the morbidly obese).

Conclusion

Nutritional support for the perioperative and critically ill patient, despite the volumes of literature available, remains somewhat controversial. Current data continue to support the use of albumin as a risk indicator for significant perioperative morbidity. In the postoperative setting, no current laboratory studies offer significant benefit over good clinical judgement. Little, if any, question remains that enteral delivery is superior to parenteral delivery when the gastrointestinal tract is functional. It does appear that earlier nutritional intervention is superior to later, but large, prospective, randomized studies are needed. The clinical information available on specific supplemental nutrients in the perioperative period has consistently reported benefits. In patients undergoing major surgery gastrointestinal surgery or suffering from major trauma, specific formulas may offer a significant benefit in lowering infectious morbidity. The molecular biological influences of these specific nutrients are being delineated, and ongoing research will uncover additional mechanisms in the future. The quantity of nutrient being administered is evolving toward lower initial caloric levels (permissive hypocaloric feeding), followed by liberalizing the calories toward estimated or calculated goals after the patient has resolved the hyperdynamic response at 3–5 days.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:
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- •• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 370).

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