

Perioperative nutrition: what do we know?

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Abstract

Surgery patients are at risk for iatrogenic malnutrition and subsequent deleterious effects. The benefits of nutrition support on patient outcomes have been demonstrated and the possible benefit of perioperative nutrition support thus implied.

Enhanced recovery after surgery (ERAS) protocols, including perioperative nutrition support as a component thereof, is indicated in the management of patients. In contrast to this, it seems the current trend is to follow the traditional perioperative management even when existing data demonstrate no merit in continuing with these practices. Data suggests that all surgical patients should receive early postoperative nutrition support.

Immunonutrition, as part of ERAS has also been reported to derive beneficial effects in surgery patient outcomes but current clinical practice guidelines are inconsistent with regards to the administration of specific immunonutrients. Arginine is an immunonutrient that is of specific interest in surgical patients due to an assumed deficiency thereof. Insufficient arginine levels can lead to immunosuppression with an increased risk for complications. Available evidence indicates that all patients undergoing elective surgery with substantial risk of infectious complications should be prescribed arginine-supplemented diets along with omega-3 fatty acids, preferably pre- and postoperatively. No recommendations can be made on the practice of combined glutamine and arginine supplementation.

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Introduction

Disease-related malnutrition is often prevalent in hospitalized patients and results in increased morbidity, mortality and healthcare costs.^{1,2} Historically there has been some confusion on the classification of disease-related malnutrition due to the variety of definitions that existed but recently an International Guideline Committee developed a consensus approach to defining adult malnutrition in clinical settings.³ Due to the past lack in clear classification of malnutrition, the actual prevalence of malnutrition, using defined criteria, is unknown. The prevalence varies depending on the type of disease ranging for instance from 25% in chronic obstructive pulmonary disease to 85% in pancreatic cancer and 88% in head and neck cancer patients.¹ Furthermore, patients with preoperative malnutrition have a significantly higher risk of postoperative complications and death along with increased hospital length of stay (LOS) and overall costs.^{2,4} Postoperative malnutrition or delayed / insufficient nutrition support has also been associated with higher risk for complication rates and mortality.⁴ This suggests that perioperative nutrition support may positively affect outcomes.⁴ This review will focus on postoperative nutritional support and arginine supplementation in surgical patients.

Effect of nutrition on patient outcomes

Several studies and reviews have demonstrated the benefits of nutrition therapy, specifically enteral nutrition (EN) in critically ill patients including surgical patients.⁴ A meta-analysis by Stratton et al identified functional benefits of enteral nutrition support administered to hospitalized patients in varied clinical settings as well as in postoperative surgical patients. These benefits included reduced prevalence of complications, reduced mortality rates, and/or shorter length of stay.¹ The limited available data on the direct assessment of cost-savings arising from improved outcomes associated with EN therapy indicate that it is a cost effective treatment.¹ Similarly, there are also limited data in this regard which compare EN to parenteral nutrition (PN) as well as preoperative to postoperative nutrition with regards to treatment effect and the cost to benefit ratio.¹

Traditional management of surgical patients

Traditional perioperative management of patients entailed keeping a patient nil per os (NPO) from the previous evening (six to 12 hours preoperatively) and postoperatively for several days. Only IV fluids were administered until bowel function returned, this being perceived

as the passing of flatus, a bowel movement or the presence of bowel sounds. Once bowel function returned, enteral nutrition or diet per mouth was initiated. The reasons for this approach was related to the fear for anastomotic breakdown and prolonged feeding intolerance due to postoperative ileus (POI) which was seen as an inevitable consequence of surgery. Traditionally also, a more conservative dietary progression was followed which consisted of a clear liquid diet, followed by a full liquid diet advancing to a soft or normal diet.⁵ This slow commencement of dietary intake has limited nutritional value and along with the delayed commencement of nutritional support is known to contribute to the development of nutritional deficits and accentuated postoperative weight loss.²

Current perioperative patient management recommendations

Currently an important focus of perioperative patient management is the enhanced recovery of patients after surgery (ERAS) or the so-called “fast track” protocols.⁴ The key aspects of ERAS from a metabolic and nutritional point of view are avoidance of long periods of preoperative fasting, re-establishment of oral feeding as soon as possible after surgery, integration of nutrition support, including administration of specialized nutrients into the overall management of the patient, metabolic control, early mobilization and reduction of factors known to exacerbate stress-related catabolism or impair gastrointestinal function (Table I).⁵⁻⁷

Table I: Components of enhanced recovery after surgery (ERAS) protocols.^{4,5,7}

Preoperative period
Preoperative counselling
Prebiotics/probiotics administration
Oral carbohydrate load
Fasting limited to three hours
No bowel preparation
Omission of nasogastric tube
Perioperative period
Nasogastric tube removal
Transverse incision
Administration of specialized nutrients
Postoperative period
Nasogastric tube removed
Avoidance of postoperative drains
Immediate postoperative fluid and diet initiation
Epidural analgesia
Diet initiation on postoperative day 1
Aggressive mobilisation program

Findings from various studies on ERAS indicate possible benefits from these programs for both patient and institution, thus contradicting traditional management. Some of these benefits include shorter length of stay (LOS) in hospital, earlier return of bowel function, decreased length of time to mobilization, fewer postoperative complications, ability to tolerate solid food sooner and

lower readmission rate 30 days postoperatively. In addition, there was no difference in reported pain or fatigue in patients treated with the ERAS protocols when compared with traditional management. It should, however be borne in mind that the ERAS protocols incorporate a number of components and as such it is difficult to associate the claimed benefits with one specific component such as nutritional support.⁵

Regarding perioperative nutrition support, the ESPEN guidelines on EN in surgery and organ transplantation recommend that patients with severe nutritional risk should receive nutritional support 10–14 days prior to major surgery even if it means delaying surgery (Grade A evidence). The enteral route is preferred except in patients with intestinal obstruction, ileus, severe shock or intestinal ischaemia (Grade C evidence).⁶ Preoperative fasting from midnight is unnecessary in most patients (Grade A evidence) with solids allowed up to six hours in patients with no specific risk for aspiration and clear fluids up to two hours preoperatively.^{6,8} Patients who do not meet their requirements from a normal diet should be encouraged to take oral supplements (Grade C evidence) or enteral nutrition should be administered prior to hospital admission.⁶ In severely undernourished patients who cannot be fed adequately enterally, parenteral nutrition is recommended but this route is costly and mostly administered in hospital.⁸ Early postoperative feeding, whether it is via normal food intake or enteral feeding is recommended and, in the case of colon resection, even within hours after surgery. Care should be taken to adapt oral intake according to individual tolerance as well as to the type of surgery. In cases where enteral nutrition is not feasible in undernourished patients, parenteral nutrition should be administered.⁸

With regards to the early enteral nutrition component of ERAS, the first study on this aspect was conducted in 1979. Currently there are about 30 randomised control trials on early enteral nutrition, most of them on surgical oncology patients. These studies do not support the traditional nutritional management of postoperative patients and clearly indicates the positive effects on outcomes in patients receiving early EN. A recent meta-analysis confirmed the statistically significant reduction in total postoperative complications following surgery with the introduction of nutritionally significant nutrition, early, postoperatively within 24 hours.⁹

What is currently happening postoperatively?

A study comparing critically ill surgical and medical patients in relation to the nutritional support they received during the course of their illness reported that surgical patients had received less nutrition support and were more at risk for iatrogenic malnutrition than internal medicine patients.⁴

More specifically, surgical patients were less likely to receive EN, more likely to receive parenteral nutrition (PN), and when started on EN it was found that they received EN, on average, 21 hours later than medical patients. As a result, surgical patients received

a lower proportion of their initial prescription from EN alone or even from a combination of EN, propofol and appropriate PN.⁴ Surgical subgroup comparisons indicated that those patients undergoing cardiovascular and gastrointestinal surgery were more likely to receive PN, less likely to receive EN as well as delayed EN, and lower total nutrition adequacy when compared with other surgical groups.⁴

Among the reasons identified for the delay in initiating nutrition support were anticipated return of the patient to surgery and possible extubation with subsequent oral intake. Another reason for the delay was hemodynamic instability, especially in the cardiovascular surgical subgroup. This is in contrast to consistent data indicating that early EN is associated with improved outcomes in hemodynamically compromised critically ill patients. In the case of distal gastrointestinal anastomoses, the delay centered on the belief that EN might compromise the integrity of the anastomosis,⁴ indicating that traditional beliefs still persist among surgeons, despite the established ERAS protocols.

Proposed strategies to overcome these perceived barriers are trophic feeding, administration of EN at reduced doses for the first day with subsequent reassessment the following day, the implementation of feeding protocols along with protocols for blood glucose control, the utilization of motility agents and small bowel feeding tubes.⁴

Immunonutrition: an integral element of ERAS

Immunonutrition therapy has also been demonstrated to result in fewer infectious complications and reduced length of stay in hospital in selected populations of surgical patients. However, the clinical benefit of immunonutrition remains controversial with some studies indicating potential harm, especially in patients with underlying sepsis. In addition, the limited experience of immunonutrition in patients with gastrointestinal intolerance has also been documented.¹⁰ In order to address these limitations, the approach to pharmacotherapy has evolved to administering immunonutrients on their own, separate from other forms of nutrition.¹¹ In summary, current clinical practice recommendations of the Canadian Clinical Practice Guidelines (CCPG), European Society for Parenteral and Enteral Nutrition (ESPEN) on both enteral and parenteral nutrition in surgery, and the Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (ASPEN) guidelines on immunonutrients for elective surgery, specifically relating to arginine, are inconsistent or absent.^{6,8,11} There is also a paucity of practice guidelines regarding the use of glutamine, omega-3-fatty acids and antioxidant nutrients in such patients.

With regard to role of arginine in major surgery, a deficiency state is thought to develop which results in an immunosuppression and an increased risk for infectious complications. Patients with sepsis and surgical trauma appear to regulate arginine metabolism differently, with lower arginine circulating levels and increased arginase activity having been observed in surgical trauma when compared with that of sepsis.¹² An arginine deficiency appears most likely in the earlier

stages of sepsis and deteriorates progressively with the severity of sepsis.¹⁰ It would therefore appear that the effect of arginine supplementation may differ in different patient populations.

A recent meta-analysis on the evidence for specifically supplementing arginine in surgical patients, which included thirty five studies, reported that arginine supplementation resulted in a considerable reduction in infectious complications and shorter length of hospital stay without having an overall significant effect on mortality when compared with standard care. Limitations of the meta-analysis include the time span over which the studies included were conducted (two decades) and the small nature of the studies. The heterogeneity of the populations studied and included in the meta-analysis was also addressed. In subgroup analysis, arginine supplementation seemed to have a consistent beneficial effect across all types of patients with gastrointestinal (GI) and non-GI surgery in term of duration of hospitalisation, with an average reduction in LOS of 2 days in GI surgery and 3.7 days in non-GI surgery. However, no substantial reduction in LOS was observed in lower GI surgical patients as a subset.¹³

A similar meta-analysis on the use of arginine in combination with other immunonutrients, reported that immunonutrition formulas containing both arginine and fish oil reduced the risk for acquired infections, reduced wound complications, and shortened hospital LOS in patients at high risk of postoperative complications.¹² The patient populations included in this meta-analysis included patients with GI malignancies, general abdominal surgery, head and neck malignancy and cardiac surgery. The treatment benefit was noted in all such groups of patients and did not depend on the timing of initiation, thus suggesting that both peri- and postoperative supplementation may be beneficial.

Another study² concluded that the largest treatment effect of arginine supplementation was seen with perioperative administration of arginine-supplemented diets and hypothesized that the use of arginine-supplemented diets both pre- and postoperatively may be beneficial. The authors proposed that arginine-supplemented diets can overcome the arginine deficiency observed in surgical patients by increasing systemic arginine availability through supraphysiological supplementation doses (Figure 1). Furthermore, it was proposed that the addition of omega 3 fatty acids along with arginine probably blunted the upregulation of arginase 1, the enzyme responsible for arginine degradation and for which elevated levels have been reported in surgical patients, whereas the inclusion of vitamin A supplementation could downregulate arginase 1 expression, thus resulting in lower levels of the enzyme. It is currently not clear though how elective surgery patients who develop systemic infections should be treated and further studies are necessary before an optimal nutrition support therapy regimen with regard to immunonutrients in this specific population is established.¹²

There are currently no recommendations regarding glutamine supplementation in conjunction with arginine in surgical patients.

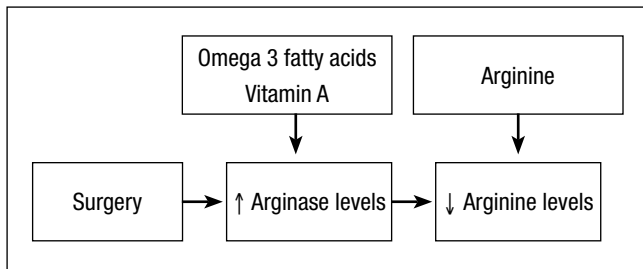


Figure 1: Proposed mechanism by which immunonutrients could possibly increase circulating arginine levels in surgical patients

Glutamine is considered a conditionally essential amino acid in catabolic states due to the muscle stores being rapidly depleted. Glutamine supplementation, especially high dose parenteral supplementation, in elective surgical patients is documented to reduce infectious complications and LOS.¹⁴ In addition to glutamine supplementation itself, a recent study conducted found that that an arginine-supplemented immune-enhancing diet increased plasma glutamine levels.¹⁵ The speculative effects (Table II) of the potentially beneficial effects of combined glutamine and arginine supplementation remain to be substantiated.

Table II: Speculative effects of combined arginine and glutamine¹⁴

	Glutamine	Arginine	Glutamine + arginine
Immune response	↑↑	↑↑	↑↑↑
Oxidative stress	↓↓	↓ or →	↓↓
Inflammatory response	↓↓	↓ or →	↓↓
Nitric oxide production	↓ or →	↑↑	→
Gut barrier	↑↑	↑	↑↑
Insulin resistance	↓	↓	↓↓
Wound healing	→	↑↑	↑↑

Conclusion

Early postoperative nutrition is recommended in all surgery patients. All patients undergoing elective surgery with substantial risk of infectious complications should be prescribed arginine-supplemented diets along with omega-3 fatty acids preferably pre- and postoperatively. No recommendation can be made on the combined supplementation of glutamine and arginine.

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