Perioperative Nutrition in Elective Gastrointestinal Surgery – Potential for Improvement?

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Key Words

Perioperative nutrition · Gastrointestinal surgery · Immunonutrition · Early feeding · Enteral nutrition · Enteral feeding

Abstract

Nutritional concern is one of the most important issues to be addressed in the perioperative care given to gastrointestinal patients. Not at least, malnutrition may be detrimental and relate to postoperative morbidity. Perioperative nutritional management, integrated with other modern perioperative care policies, allows the establishment of multimodal strategies with an attempt to optimize the patients' course of disease. The present review evaluates available data regarding pre- and postoperative nutrition, nutritional supplements, including immunonutrition, and their clinical role. It is to be concluded that pre- and postoperative prolonged fasting has no routine role in management. Instead, for example, early postoperative feeding administered perorally or enterally may reduce postoperative complications and length of hospital stay. There are also indications that perioperative immunonutrition may reduce postoperative infectious complications and length of hospital stay, though further studies in this field are needed.

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Introduction

Despite important advances in surgical care and minimized surgical trauma, postoperative complications are still of great concern. Not at least, malnutrition is a well-known cause of increased morbidity and mortality in surgical patients, and severe malnutrition may cause ongoing energy deficits in the postoperative period, resulting in an increased risk of infectious complications [1–4]. Gastrointestinal patients, especially with underlying malignancy, are at high risk of developing malnutrition, and surgical stress can also accentuate this catabolic problem.

In recent years, several traditionally accepted rules and 'truths' regarding perioperative nutritional cares have been challenged. The ultimate goals have not at least been to prevent malnutrition and its detrimental effects in favor of the patient and the healthcare system.

Reducing the length of pre- and postoperative fasting are among the issues that have drawn attention in more recent studies. Nutritional supplementation in the form of dietary supplementation and immunonutrition are other topics. The latter is a novel mode of intervention with the aim of decreasing infectious complications [5]. Data gathered from the above studies, beside other non-nutritional perioperative care policies, may form multimodal strategies resulting in improved clinical outcome [6].

The present review aims at investigating reported data on different aspects of perioperative nutritional care and their role in patients undergoing elective gastrointestinal surgery, with a more detailed focus on immunonutrition.

Early Postoperative Nutrition

Postoperative management of patients after gastrointestinal surgery traditionally involved a period of 'nil by mouth' and nasogastric decompression in order to prevent postoperative nausea and vomiting and to protect an intestinal anastomosis. The fasting period continued until resolution of postoperative ileus, indicated by the passage of flatus and return of bowel sounds.

However, this type of management is not supported by scientific evidence [6–9]. On the contrary, experimental and clinical studies have demonstrated that early postoperative feeding increases strength and healing of an intestinal anastomosis [9–14]. Neither did a meta-analysis of 26 trials, including approximately 4,000 patients, support the routine use of nasogastric decompression in the postoperative period [15]. There are data reporting that early nutrition after surgery prevents an increase in gut mucosal permeability, produces a positive nitrogen balance, improves total calorie intake, and reduces infectious complications [16, 17].

When reviewing early versus late inserted postoperative enteral nutrition following colorectal surgery, no statistically significant difference in postsurgical complications was found, though early enteral feeding (within 24 h) tended to be favorable [18, 19]. Despite heterogeneity of the clinical studies evaluated, both reviews state the safety, feasibility and potential benefits (on postsurgical complications and the length of hospital stay) by early postoperative nutrition.

Early Oral Feeding

Early oral feeding after lower gastrointestinal surgery has been shown to be safe. It reduces the risk of any type of infection and the mean length of hospital stay [20–31].

Based on the rationale that laparoscopic colorectal surgery is minimally invasive with decreased bowel manipulation, some authors believe that early feeding can be better tolerated following this type of surgery. A limited number of studies have been performed concerning early enteral nutrition following open versus laparoscopic colorectal surgery. Overall, there seems to be no differ-

ence when it comes to the tolerance of early enteral feeding when comparing open and laparoscopic surgery, and early enteral feeding is tolerated following both types of intervention [32–36].

In contrast to the quite numerous studies following colorectal procedures, less is known about the outcome of early oral nutrition following major upper gastrointestinal surgery [37]. Early oral feeding (within 48 h) following gastrectomy did not seem to increase morbidity and shortened the length of hospital stay [38–40]. When reviewing five prospective, randomized controlled clinical trials, totally including 333 patients, on early enteral nutrition following liver resection, this management was shown to be both safe and associated with a lower incidence of postoperative complications [37].

Early Tube Feeding

Initiation of early enteral feeding via a tube has proven to be beneficial, practicable and cost-effective in upper gastrointestinal surgery, as demonstrated in several studies [41–50]. Among beneficial effects, early enteral nutrition after upper gastrointestinal surgery prevents the otherwise occurring increase in gut permeability, the exaggerated inflammatory response following surgery, lipid oxidation, whole-body protein catabolism and pronounced perioperative weight loss [16, 50, 51]. It should, however, also be mentioned that some studies have not shown any beneficial effect by routine early enteral nutrition in patients subjected to gastrointestinal surgery [52–54]. In 195 patients undergoing upper gastrointestinal cancer surgery, the importance of patient selection was stressed in order to identify those actually in gain of early enteral nutrition [52]. Immediate postoperative jejunal feeding was also reported to be associated with impaired respiratory mechanics and postoperative mobility and no influence of early enteral feeding was found concerning loss of muscle strength or fatigue [54].

Early enteral nutrition can cause complications that are categorized as tube- and feeding-related adverse effects. Tube dislodgement, clogging, infection at the entry site, intestinal obstruction, small bowel necrosis, massive intestinal pneumatosis and intra-abdominal leakage of enteral feeding that can lead to death are all complications reported related to the use of jejunostomy tubes. Gastrointestinal adverse effects related to early nutrition are abdominal cramps, bloating, diarrhea, vomiting, delayed gastric emptying and aspiration [7, 41, 50, 55–57].

Braga et al. compared complications of jejunostomy and nasojejunal tubes in 650 patients who underwent major digestive surgery for cancer. They found similar

rates of gastrointestinal adverse effects, but a higher rate of displacement and clogging following the use of naso-jejunal tubes. The same authors reviewed 13 studies with nearly 5,000 cases and concluded that the overall jejunostomy-related complication rate was 2.9%, ranging from 0.8 to 16%, while the incidence of major complications (bowel necrosis, pneumatosis or obstruction) was less than 1.5% [7].

The recommendation is to start enteral tube feeding with a low flow rate (e.g. 10 to max. 20 ml/h), after which the target intake can be reached within 5–7 days [58]. Feeding jejunostomy tubes can also be used for the administration of medications and can also ascertain longer nutritional support required at home or during chemoradiotherapy [7, 41].

Preoperative Oral Carbohydrate Loading

Nutritional preoperative management has been challenged regarding the use of prolonged fasting prior to surgery. Among potential factors, the general rationale of preoperative fasting has been to prevent the risk of aspiration of gastric contents during the induction of anesthesia. However, convincing evidence has emerged and for example the administration of fluids perorally has not increased the risk of aspiration and therefore the traditional routine long preoperative fasting period previously practiced can no longer be recommended [59, 60].

A significant mechanism to be considered is the insulin resistance occurring during the postoperative period [61]. Carbohydrate-rich beverages have been found to be as safe as clear fluids even when administered shortly before elective surgery, and oral carbohydrates given prior to elective surgery reduce the otherwise occurring postoperative insulin resistance [62–65]. Several studies on preoperative oral carbohydrate loading in gastrointestinal surgery patients have shown beneficial effects also by reducing preoperative patient discomfort, preservation of skeletal muscle mass and strength and most likely also on postoperative nausea and vomiting [66–69]. However, in a randomized clinical study on 94 patients undergoing laparoscopic cholecystectomy, no difference was found when evaluating clinical improvements after surgery by oral carbohydrate administration, a lack of effect by the authors explained may be due to the less invasiveness of the type of surgery performed [70].

Dietary Supplements

Oral dietary supplements (Fortisip®), providing 1.5 kcal, 0.05 g protein and 0.18 g carbohydrate per milliliter, have been studied in patients subjected to gastrointesti-

nal surgery [71–73]. Smedly et al. [71] studied 152 patients undergoing lower gastrointestinal tract surgery, and randomized them into four groups with no nutritional supplements, perioperative supplements, only postoperative supplements, and only preoperative supplements, respectively. The authors concluded that perioperative oral nutritional supplementation significantly decreased weight loss and postoperative morbidity regardless of body mass index. Interestingly, the beneficial effects were not restricted to malnourished patients alone. Beneficial effects by postoperative oral dietary supplementation have also been noted during the inpatient phase with the prevention of infectious complications [72], weight loss and postoperative complications [73]. The routine use of perioperative oral dietary supplementation in well-nourished patients was, however, not found to be of any additional value [74].

Immunonutrition

The use of different nutrients in order to modulate the function of the immune system has become an important issue not at least in the management of patients undergoing gastrointestinal surgery. The different specific nutrients used in the various studies have included amino acids (arginine and glutamine), ω -3 fatty acids and RNA nucleotides.

Glutamine. Glutamine is essential for protein and nucleotide synthesis. Increased metabolic demands of inflammation or injury lead to glutamine consumption, which is associated with progressive changes in intestinal morphology. Glutamine supplementation administered enterally can reverse the intestinal atrophy and prevent bacterial translocation [75]. Furthermore, glutamine seems to have effects on immune function and may decrease the inflammatory response and infectious complications [76, 77].

Arginine. Arginine is considered as a semi-essential amino acid, acting as an immunomodulator and with favorable effects in catabolic conditions such as severe sepsis and postoperative stress [78, 79]. The role of postoperative arginine supplementation on immune, metabolic and endocrine parameters was studied in a randomized clinical trial in patients undergoing gastrointestinal cancer surgery. Faster recovery of immunologic parameters was seen during the postoperative period in the arginine group as compared to glycine-treated patients [80]. Arginine supplementation has also been reported to improve wound healing and improve phagocytic ability and respiratory burst of polymorphonuclear monocytes, most likely due to increased levels of nitric oxide [81].

ω-3 Fatty Acids. ω-3 fatty acids replace arachidonic acid in cell membranes and modulate immune function [81]. They alter the formation of prostaglandin E₂ to prostaglandin E₃, which has a less immunosuppressive effect [82]. The use of these fatty acids has been reported to decrease the total number of gastrointestinal and infectious complications and improve postoperative liver and kidney function through modulation of tissue prostaglandin levels [83, 84].

Nucleotides. The value of supplemental nucleotides has been studied to a less degree but they seem essential for cell-mediated immunity and helper/inducer T-lymphocyte function [75].

Clinical Outcome of Immunonutrition

The most common reported beneficial effects of immunonutrition are reductions in the rate of postoperative infectious complications and the length of hospital stay [43, 46, 85–98]. Moreover, a reduction in stoma fistula and improved surgical wound healing are other favorable outcomes reported [92, 99]. Some studies have also shown a cost-effectiveness of immunonutritional administration, related to the reduction in postoperative infectious complications and length of hospital stay [87, 90, 100].

In 32 patients undergoing liver transplantation, pre- and postoperative immunonutrition reduced the incidence of postoperative infectious complications, though this study was not a randomized clinical trial [101]. Not all studies, though, have been able to demonstrate any significant advantage of immunonutrition [52, 102–105]. A summary of data from randomized clinical trials on immunonutrition in elective gastrointestinal surgery is presented in table 1.

Laboratory Outcomes

Immunomodulatory effects have been observed following immunonutrition regarding both cellular and humoral immunity, phagocytic ability, levels of plasma proteins and inflammatory mediators. Among the effects observed are increase in the mean total lymphocyte count [103], cell-mediated immune response, activated T lymphocytes, CD4 expression [92, 104], IL-2 expression [106, 107], plasma levels of IL-2 and CD4/CD8 ratio [98, 106, 108], B-lymphocyte indices, interferon-γ, and immunoglobulins G and M [92, 104].

In patients undergoing elective surgery for colorectal cancer, preoperative immune-enhanced nutritional supplementation corrected the Th1/Th2 balance [109]. Other effects are the prevention of early postoperative decrease of both phagocytic ability and respiratory burst of

polymorphonuclear cells [81, 93, 98, 108] and improvement in delayed hypersensitivity responses [93, 106].

Immunonutrition also reduces levels of inflammatory markers measured like C-reactive protein (CRP), tumor necrosis factor-α (TNF-α) and endotoxin [81, 105], and acute phase mediators (TNF-α, CRP and IL-6) [81, 92, 98, 106–108] postoperatively.

Preoperative administration of immunonutrition (Impact®) in patients undergoing upper gastrointestinal cancer surgery resulted in a significant increase in levels of eicosapentaenoic acid, docosahexaenoic acid, and total ω-3 fatty acids, while levels of linoleic acid, arachidonic acid, and thromboxane B₂ decreased significantly [110]. Other studies have shown an increase in plasma and peripheral white blood cell ω-3/ω-6 ratio, but decreased PGE₂ production [85, 111]. Furthermore, immunonutrition has been reported to result in an increase in nitric oxide plasma concentrations [98, 108], local hydroxyproline production [99], and serum concentrations of prealbumin and retinol-binding protein [93, 111]. Moreover, immunonutrition causes improved intestinal microperfusion and improved postoperative gut mucosal oxygen metabolism [98, 108].

Immunonutrition Administered in Upper or Lower Gastrointestinal Tract Surgery

In the majority of randomized clinical trials performed, the impact of immunonutrition has been studied in upper gastrointestinal tract cancer patients, a category of patients with more malnourishment and difficulties with nutrition. However, it has been implied that the impact of immunonutrition could be similar in the whole gastrointestinal tract, thus including also patients with lower gastrointestinal tract cancer surgery [86, 88, 89, 91, 98].

Pre-, Post- or Perioperative Administration of Immunonutrition?

Historically, the first RCTs were designed to study the effects of postoperative supplemental diet. Later on, due to the rationale that the effects of surgical stress occur immediately as a response to the surgical trauma, studies were planned to record the impact of preoperative administration of immunonutrients [112]. In three studies, pre- and perioperative administration of immunonutrition was compared and no significant differences were found regarding the clinical outcome [86, 88, 89]. A reduction in postoperative infection and the occurrence of stoma fistula have been reported in a study comparing preoperative immunonutrition with controls without

Table 1. Randomized clinical trials of immunonutrition in elective gastrointestinal surgery

Group [Ref.]	Pa-tients	Upper/ lower/ whole GI	Pre-/post-/ peri-operative	Groups and diets	Optimal dose	Number of days	Clinical outcome	Comments
Daly [95]	85	Upper GI	Post-operative	2 groups Impact Standard	75–100 ml/h	First POD, discharge	Reduced postoperative infection, wound complications and length of hospital stay	Low-protein control diet; more esophagectomy and pancreatotomy in control group
Daly [85]	60	Upper GI	Post-operative	4 groups Impact (inpatient) Impact (in- and outpatient) Standard (inpatient) Standard (in- and outpatient)	75–100 ml/h	Inpatient: first POD, discharge Outpatient: first POD 12–16 weeks after discharge	Reduced postoperative infection, wound complications and length of hospital stay	
Senkal [87]	154	Upper GI	Post-operative	2 groups Impact Standard	80 ml/h	12 h after surgery, discharge	Reduced late postoperative infection (after POD 5) Reduced overall costs for complication treatment	Not intention-to-treat study
Helsin [52]	195	Upper GI	Post-operative	2 groups Impact IV crystalloid	1 l/day	Within 24 h after surgery, discharge	Early enteral feeding was not beneficial	
Schilling [103]	48	Whole GI	Post-operative	3 groups Impact Standard (Fresubin) IV solution	1 l/day	Within 24 h after surgery, discharge	Early enteral feeding was not beneficial	
Braga [43, 46, 93, 94, 96, 97]	*	Upper GI	Post-operative	3 groups Impact Standard TPN	25 kcal/kg/day	Within 12 h after surgery, discharge	Reduced severity of infection and length of hospital stay compared to TPN group	
Braga [91, 98]	*	Whole GI	Peri-operative	2 groups Impact Standard	1 l/day	7 days before surgery POD 7	Reduced postoperative infections and length of hospital stay	
Braga [88]	200	Lower GI	Peri-operative	4 groups Impact (preoperative) Impact (perioperative) Standard (preoperative) No supplementation	1 l/day	Pre: 5 days before surgery Peri: 5 days before surgery, discharge	Reduced postoperative infections and length of hospital stay, but no significant difference between pre- and perioperative groups	
Braga [89]	150	Whole GI	Peri-operative	3 groups Impact (preoperative) Impact (perioperative) Standard (postoperative)	1 l/day	Pre: 7 days before surgery Peri: 7 days before surgery, POD 7	Reduced postoperative complications and length of hospital stay comparing perioperative and control groups	Malnourished (weight loss $\geq 10\%$)
Gianotti [86]	305	Whole GI	Peri-operative	3 groups Impact (preoperative) Impact (perioperative) Standard (perioperative)	1 l/day	Pre: 5 days before surgery Peri: 5 days before surgery, oral food initiation	Reduced postoperative infections in normal, overweight and obese patients Preoperative supplementation is as effective as perioperative approach	Weight loss $\leq 10\%$
Kemen [104]	42	Upper GI	Post-operative	2 groups Impact Standard	80 ml/h	POD 1–POD 10	No significant clinical outcome	
Senkal [90]	154	Upper GI	Peri-operative	2 groups Impact Standard	80 ml/h	Peri: 5 days before surgery, POD 10	Reduced postoperative infectious complications Reduced overall costs for complication treatment	Not intention-to-treat study

Table 1 (continued)

Group [Ref.]	Pa-tients	Upper/lower/whole GI	Pre-/post-/peri-operative	Groups and diets	Optimal dose	Number of days	Clinical outcome	Comments
Giger [105]	46	Upper GI	Peri-operative	3 groups Impact (preoperative) Impact plus (preoperative) Control (no supplements) All → postoperative impact	80 ml/h	Pre: impact: 5 days, impact plus: 2 days Post: 7 days	No significant clinical outcome	
Dileep [102]	108	Upper GI	Post-operative	2 groups Stresson Nutrison high protein	75 ml/h	4 h after surgery, discharge	No significant clinical outcome	
Farreras [99]	60	Upper GI (gastric cancer)	Post-operative	2 groups Impact Isosource protein	According to the caloric requirements	12–18 h after surgery, POD 7	Improved surgical wound healing	
Xu [92]	60	Whole GI	Pre-operative	2 groups Impact Standard	25 kcal/kg/day	7 days before surgery	Reduced postoperative infection and stoma fistula	

GI = Gastrointestinal; POD = postoperative day. * There are some patients included in more than one article.

immunonutrition [92]. Preoperative immunonutrition is now recommended (ESPEN Guidelines) in patients with elective gastrointestinal cancer surgery [58].

Oral Impact® has been the most commonly used formula studied. The optimal goal set was 1 liter/day or 75–80 ml/h. The energy goal was 25 kcal/kg/day. In general, this goal can be achieved after a few days postoperatively, mostly 3–5 days.

Available data suggests that immunonutrition may be of benefit when administered preoperatively in elective gastrointestinal cancer patients and in trauma patients [113]. Some authors have emphasized patient selection in order to identify those who would gain more advantage from supplemental immunonutrition like malnourished patients [52], though Braga et al. [86] stressed the fact that regardless of the baseline nutritional status, perioperative immunonutrition was efficacious and well-nourished patients may also have some beneficial effects from immunomodulating diets.

Discussion

Traditional perioperative nutritional management in patients undergoing elective gastrointestinal surgery has merely been based on tradition – rather than on strict evidence-based fundamentals. Thus, available data do not support the routine use of nasogastric decompression in

the postoperative period, and neither is there any clinical benefit from keeping patients starved after surgery [114]. Instead, early institution of postoperative oral or enteral nutrition is both safe and beneficial, though additional studies especially regarding early oral nutrition following upper gastrointestinal surgery are needed. Furthermore, a prolonged period of fasting prior to surgery is not accepted anymore. The administration of preoperative oral carbohydrates is safe and can be done without fear of increasing risk of aspiration and among other effects prevents postoperative insulin resistance.

Different immunonutrients have been used in order to modulate immune function and shown beneficial both when used in trauma and elective surgical patients. However, the use of immunonutrition in critically ill patients should be selective in order to avoid potential harmful effects as has been described in this category of patients [115–119].

In nearly all studies performed, an immunonutritional diet was compared with isocaloric and isonitrogenous standard enteral diets. Perioperative administration of immunoenhancing diets reduced postoperative infections both in well-nourished and malnourished patients.

Administration of a preoperative diet may be optimal both clinically and economically for well-nourished patients, though perioperative use of nutritional supplementation seemed to be more clinically beneficial than

the preoperative intervention in malnourished patients [100]. Nutritional support has a better impact in reducing infectious than non-infectious complications. Immune modulators can positively influence on the association between immune suppression and postoperative infections. These findings also point towards the surgical trauma and the related 'stress' is a risk factor for immune suppression leading to postoperative infections regardless of the basal nutritional status [120].

Overall, old traditions have been challenged and new, more evidence-based recommendations and guidelines have appeared. As important is, however, the compliance with newly set guidelines. So, for example, non-compliance with evidence-based practice regarding perioperative nutrition and routines among colorectal surgeons in different centers in five northern European countries and heterogeneous policies in postoperative nutritional support and oral intake could be found [121, 122].

Fast-track surgery has been developed and gained increasing popularity and used with benefits for both patients and healthcare providers. Multimodal strategies including minimal invasive surgery, nutritional care, anesthesia, enforced mobilization and other measures have resulted in reduction in morbidity and length of hospital

stay [123–126]. Therefore, nutritional management plays a great role in the fast-track surgery concept.

There still are issues to clarify regarding perioperative nutrition in elective gastrointestinal surgery. The effects of early oral feeding in upper gastrointestinal surgery, the role of nucleotides in supplemental diets, and the effects of immunonutrition in lower gastrointestinal surgery are among these issues. There are also some concerns in designing the clinical studies. Immunomodulators are beneficial when patients receive the critical minimum amount of them. This is a crucial issue, since many of the studies failed to identify and reach this minimal but 'beneficial' amount. The patient groups should also be stratified according to the severity of their underlying disease and type of surgery they are going to be subjected to.

In conclusion, preoperative carbohydrate administration, the use of postoperative early feeding, and also perioperative immunonutrition are beneficial policies to be used in association with elective gastrointestinal surgery. The inclusion of novel evidence-based information in recommendations and guidelines, and not at least the compliance with these, are of outmost importance, all in favor of our patients. There is a potential for improvement!

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