Nutritional care in patients undergoing laparoscopic/minimally invasive surgeries for gastrointestinal tumours

Zhou Xuefen, Bian Yuanyuan, Li Qin, Wu Xiaoyang

Department of Gastrointestinal Surgery, Affiliated Kunshan Hospital to Jiangsu University, Suzhou Jiangsu, China

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Abstract

The introduction of minimally invasive surgeries for gastrointestinal tumours has been associated with many favourable postoperative outcomes and a reduced impact on nutritional status. The literature review begins by discussing the impact of minimally invasive procedures on the nutritional status of patients with gastrointestinal tumours, followed by indications for enteral nutrition (EN) in this population, including preoperative nutritional support and postoperative nutritional support. The review then examines the evidence that favours the use of EN in this population, including studies demonstrating improved outcomes with preoperative EN and reduced postoperative complications with postoperative EN. It also discusses potential strategies for improving outcomes with EN, such as early initiation of feeding and individualized nutrition plans. Overall, current evidence shows that EN improves outcomes, reduces complications, and enhances the quality of life. However, the optimal timing, composition of EN, and long-term outcomes are still unclear, indicating the need for future investigations.

Key words: *enteral nutrition, nutrition, gastrointestinal, perioperative care, cancer, tumour, surgery, complications.*

Introduction

Gastrointestinal tumours are among the commonest aetiologies of morbidity and mortality globally [1, 2]. These tumours might be correlated with various life-threatening complications that require urgent interventions to enhance the patient's prognosis. In many cases, surgical treatment is necessary to manage gastrointestinal tumours [3, 4]. Surgery can be used to remove tumours or reduce their size and relieve symptoms such as pain or obstruction. However, surgery can be associated with some adverse events that might worsen patient outcomes. For instance, malnutrition might result from decreased nutrient intake or absorption following the procedure [5–7], in addition to potentially developing as a complication of gastrointestinal tumours [8, 9]. It can further boost the potential of developing adverse events such as infection or wound healing problems [9]. Therefore, patients undergoing gastrointestinal surgery must receive adequate nutrition to reduce these risks and improve outcomes.

Several strategies have been established to enhance perioperative feeding in patients with gastrointestinal conditions. These include oral nutritional supplements (ONS) such as protein shakes or fortified foods; parenteral nutrition (PN), which involves delivering nutrients directly into the bloodstream; and enteral nutrition (EN), which involves delivering nutrients directly into the digestive tract via a tube placed in either the small intestine or stomach. EN is more effective than PN at providing essential nutrients while reducing complications associated with malnutrition, such as infection and delayed recovery time [10, 11]. Moreover, introducing minimally invasive

Address for correspondence
Wu Xiaoyang MD, Department of Gastrointestinal Surgery, Affiliated Kunshan Hospital to Jiangsu University, Suzhou Jiangsu 215300, China, e-mail: wxy640707@126.com

surgical approaches has been associated with favourable outcomes in this context. For instance, there are several risks associated with total gastrectomy, most notably to one's haematological and nutritional state, both of which may lead to significant decreases in body weight and levels of physical activity. To reduce the danger of postoperative malnutrition and body weight loss while still being oncologically acceptable, efforts have been made to prevent total gastrectomy, particularly in elderly or high-risk patients.

Aim

This literature review provides an overview of using EN for patients with gastrointestinal tumours undergoing minimally invasive surgery. It also highlights the screening tools used for nutrition assessment, and immunonutrition. It also discusses current studies to compare EN with PN to determine which route is preferred and most effective in clinical practice.

Methods

The design of this article is a comprehensive review aiming to discuss the different parameters of using EN for patients with gastrointestinal tumours undergoing surgeries. Therefore, we conducted a comprehensive search within PubMed, Google Scholar, Embase, Web of Science, and Scopus with relevant keywords such as the following: (Nutrition OR "Enteral nutrition" OR "tubal nutrition" OR "jejunostomy nutrition" OR feeding OR "parenteral nutrition" OR Immunonutrition OR "oral nutrition) AND ("Gastrointestinal tumor" OR "gastrointestinal cancer" OR "Digestive cancer") AND (Surgery OR surgical OR Laparoscopy OR laparoscopic OR endoscopy OR endoscopic OR "Minimally-invasive"). The search was conducted in January 2023 with no restrictions regarding the country and language of publication. However, we aimed to obtain our evidence from the most recent investigations without neglecting essential information from the older ones. Finally, we mainly obtained data from original investigations. However, secondary studies were also used in the qualitative synthesis of this article because these studies provide high-quality evidence.

The impact of minimally invasive surgery on nutrition

Because of reduced postoperative anxiety and better nutritional status, minimally-invasive surgery is preferred [12]. Some studies have investigated whether performing a minimally invasive surgery for gastrointestinal tumours is associated with the patient's postoperative nutritional status. However, it has been suggested that such an impact might be limited to the organ where the surgery was performed. For instance, Shim *et al.* [6] demonstrated that the nutritional status following minimally invasive surgeries was remarkably affected in patients with gastric but not colon cancer. However, the authors concluded that performing these surgeries positively impacts the postoperative nutritional status of the affected patients. Therefore, minimally invasive procedures have been advocated for use on patients who are at high risk of postoperative malnutrition.

Subtotal or proximal gastrectomy with a small stomach residual has become more common. Reflux oesophagitis and stenosis are major drawbacks of proximal gastrectomy; for instance, heartburn and vomiting caused by reflux disrupt oral intake. However, in recent years, proximal gastrectomy has been done without reluctance, even for elderly patients, because the rebuilding methods have been consistent, although with minor changes to avoid reflux [13]. Furthermore, Furukawa *et al.* [14] found that short-term results and nutritional status were better after laparoscopic subtotal gastrectomy with a very tiny stomach remnant than after laparoscopic whole and proximal gastrectomy. They reasoned that although the residual stomach is little, it still plays a role in maintaining ghrelin production and lowering reflux thanks to the preserved cardia.

Stomach emptying, mechanical digestion, and reservoir capacity are all negatively impacted by gastrectomy. Post-gastrectomy symptoms manifest because of the stomach's changed structure and performance. Taking age and the potential for cure into consideration, a new trend towards preserving gastric function has been reported. The functional preservation diet has been shown to offer postoperative nutritional advantages. The postoperative nutrition and long-term survival of patients with clinically diagnosed early gastric cancer were found to be optimal with laparoscopic pylorus-preserving gastrectomy by Tsujiura *et al.* [15]. The nutritional advantages of laparoscopic surgery are anticipated to include faster healing with less pain and fewer analgesics, earlier mobilization, faster intestinal peristalsis recovery, and a shorter length of hospital stay. However, there seems to be no difference in the short-term postoperative nutritional status, including body weight loss, even though disparities in surgical techniques may be nutritionally connected to a worse prognosis. When comparing patients who did not have morbidities after either laparoscopic or open distal gastrectomy, Aoyama *et al.* [16] found no significant differences in the amount of surgical stress (interleukin-6 level and white blood cell count).

Evaluating the nutritional status and current tools

Evaluating the patients' nutritional profile when undergoing surgeries for gastrointestinal tumours is important for the appropriate application of nutritional therapy for these patients. Six main categories have been proposed for the tools used for nutritional assessment in this context, including instrumental examinations, functional tests, biochemical assessments, validated questionnaires, conventional anthropometric parameters, and particular tests. Body mass index (BMI) is the most conventional anthropometric factor used in clinical settings and is known as an efficacious tool for initial screening. However, this parameter is limited by its ability to determine body composition, being unable to differentiate between lean mass and fat mass [17]. Moreover, a high BMI is usually observed among obese patients with gastric cancer and those suffering from malnutrition, indicating the need to consider the potential of malnutrition in these patients [18]. Another category is the validated questionnaires, which determine the timing of weight loss, pre-existing diseases, physical activity, and dietary habits. Various validated questionnaires are used in clinical settings, including the Short Nutritional Assessment Questionnaire, the Mini Nutritional Assessment Short Form, and the nutrition Risk Screening tool [19, 20]. Furthermore, many biochemical evaluation tools are also used for nutritional assessment, including the Geriatric Nutritional Risk Index, the Control Nutritional Score, the neutrophil-to-lymphocyte ratio, the Glasgow Prognostic Score, and the Prognostic Nutritional Index [21].

Estimates show that sarcopaenia can be prevalent in up to 83% of cancer patients and patients receiving chemotherapy [22]. It has been reported that the risk and numbers of severe postoperative events are more common among sarcopaenic patients. Therefore, early screening for these patients is vital for preventing these complications and enhancing postoperative outcomes. Moreover, a complex geriatric assessment, including assessment for nutritional and functionality statuses, should be considered for the elderly population [23, 24]. The ESPEN nutritional risk score (NRS) can be effectively used for surgical patients [25]. Data from observational studies indicate that NRS can significantly predict postoperative complications, duration of hospital stay, and patient compliance [26]. Various other parameters, like the assessment of body composition for the GLIM criteria, dual X-ray absorptiometry, routine CT, and bioelectrical impedance evaluation, have been reported as valid and essential parameters for assessing nutritional status [11, 27]. Several clinical investigations have implied the advantageous use of these modalities for assessing muscular masses and other factors that can significantly predict sarcopaenia and nutritional status in general [28–31].

Enteral nutrition

Overview

After an adequate and comprehensive evaluation of the patient's nutritional status, healthcare providers should be able to determine the most appropriate regimen that meets the nutritional needs of these patients. In this context, it has been demonstrated that patients have inadequate food intake when the estimated energy input is < 60% of their nutritional demand for 1–2 weeks, indicating the need for artificial nutrition [32]. Evidence also shows that EN should be considered for perioperative nutrition during major abdominal surgeries because it is more consistent with the body's physiological pattern. Early EN reported various favourable outcomes, including functional recovery promotion of the gastrointestinal tract, decreased risk of postoperative events, reduced hospital stay, and more favourable levels of immune and nutritional indicators and body weight [33, 34]. It has been demonstrated that performing minimally invasive surgeries might be favourable in many cases. For instance, patients having minimally invasive oesophagectomy had a postoperative direct oral nutrition with no impact on functional recovery, pneumonia rate, anastomotic leakage, or the incidence of postoperative surgical complications [35].

ESPEN and ERAS recommend early oral feeding and EN for patients undergoing surgeries for gastrointestinal cancers. However, it has been demonstrated that the main barrier to early EN administration is poor compliance and early feeding intolerance [25, 36]. Estimates from previous investigations indicate that feeding intolerance is common among patients who have undergone a radical gastrectomy (49.3%) [37, 38]. Moreover, it has been shown that postoperative complications following colorectal cancer surgeries can be significantly predicted by feeding intolerance. On the other hand, it has been shown that the risk of feeding intolerance can be reduced by adequately positioning the feeding tube, maintaining good oral hygiene, and determining the best feeding route [39].

There are many efforts to improve these patients' early postoperative feeding intolerance. For instance, many clinical investigations demonstrated that early oral feeding and ONS could significantly shorten the hospital stay and the associated costs and improve patients' clinical outcomes with no negative impact on postoperative healing anastomosis for patients undergoing colorectal cancer surgeries [25, 40–42]. It has been further shown that early oral feeding is feasible, safe, and can be associated with many favourable outcomes and reduced incidence of complications, even after total or partial gastrectomy [43–47]. On the other hand, He *et al.* [48] attempted to improve early postoperative feeding intolerance among patients with gastric cancer by using ONS for 7 days. However, they did not observe any favourable outcome. Another clinical trial showed that early oral feeding was correlated with an elevated risk of postoperative severe events and did not impact the hospital stay duration following distal gastrectomy procedures [49]. Another study demonstrated that post-discharge EN could enhance postoperative caloric intake. However, it did not impact healthcare-associated economics, quality of life, and tiredness [50]. This indicates the need for future investigations to understand the mechanism of feeding intolerance for these patients, and to develop new strategies to reduce its risk.

Nutrition before surgery

The nutritional plan should be decided based on the assessment of patients, as previously discussed. In surgery settings for gastrointestinal patients, nutritional support should be mainly directed to patients with a nutritional risk and others with malnutrition. In these patients, nutritional therapy is recommended for 7–10 days when indicated to have surgery. It is also recommended that a perioperative nutritional plan be initiated for patients who cannot maintain > 50% of the determined caloric intake [11, 51]. Establishing a pre-operative multimodal rehabilitation plan is also recommended to intervene against any potential adverse events [11]. In a previous systematic review, interventional nutrition lasting for ≥ 7 days (as part of a multimodal approach that includes other interventions, like psychological coaching and physiotherapy) and continued postoperatively can significantly shorten the hospital stay [52]. Moreover, it was shown that higher mortality is significantly associated with weight loss ≥ 10% in oesophageal cancer patients [53], further indicating the need to establish perioperative nutritional plans [11]. A previous study showed that in oesophageal cancer patients, less weight loss at 10 months postoperatively was associated with the administration of early nutrition during neoadjuvant treatment [54].

Extended nutrition after surgery

Catabolic stress is a characteristic event following any surgical procedure, due to increased systemic inflammation and catabolic processes. It can result in weight loss, which can significantly impact patient outcomes. Therefore, nutritional therapy in this stage should be aimed at adapting to the newly altered body composition and enhancing the patient's physical activity. In these events, it has been indicated that oral nutrition is the ideal strategy. However, studies indicate that continuing the plan through enteral jejunostomy is required in some cases. Many relevant investigations have reported the importance of early oral nutrition. For instance, a matched retrospective study compared early oral feeding with delayed oral intake after gastrectomy. Delayed onset of flatus and prolonged hospital stay were noticed in the delayed feeding group (3.1 versus 2.9 days, p = 0.013; 12.6 versus 8.9 days, p = 0.044). Moreover, delayed feeding was correlated with a more elevated rate of anastomotic leakage and abdominal infections (4.9% versus 1.5%, p = 0.048; 7.4% versus 3%, p = 0.044, respectively) [46]. Another investigation demonstrated that Clavien-Dindo III events were common among individuals who did not reach sufficient protein and energy intake [55]. Accordingly, it has been concluded that despite the feasibility of early postoperative oral intake, it might not be adequate to achieve nutritional requirements for these patients, leading to weight loss, which might adversely impact postoperative complications. Therefore, other routes of nutrition should be considered.

It should be noted that the small intestine undergoes a para-physiological transient dysfunction, significantly impacting the absorption of nutrients. Accordingly, it has been suggested that EN should be conducted 6 h postoperatively, giving enough time for the small intestine to recover from this state. Moreover, it is recommended that oral nutrition be continued during this phase to stimulate the functions of the small intestine. Various studies have investigated the role of oral and EN following surgeries for gastrointestinal tumours. A recent meta-analysis reported that early postoperative EN could significantly reduce mortality [56]. Moreover, an RCT compared early postoperative EN to PN in patients undergoing surgery for cholangiocarcinoma with obstructive jaundice [57]. The authors reported that EN was associated with more favourable outcomes regarding immune functions, length of hospital stay, and intestinal recovery. Another RCT reported the outcomes of PN compared to tropic EN via a nasogastric tube in patients having pelvic exenteration surgery. It was demonstrated that paralytic ileus was more significantly associated with PN, and the mean time to first bowel movement was similar between the 2 groups [58]. It was further demonstrated that postoperative complications and time to first bowel movement were significantly associated with time restriction from an oral diet. Another Dutch RCT studied the safety and feasibility of an early oral diet initiated postoperatively versus EN for 5 days in patients undergoing minimally invasive oesophagectomy with intrathoracic anastomosis [59]. The authors demonstrated that no significant differences were noticed between the 2 groups regarding pneumonia rate, anastomotic leakage, and time of postoperative recovery (24.6% versus 34.3%, 18.5% versus 16.4%, and 7 versus 8 days, respectively).

It should be noted that even after adequate perioperative management and proper application of the ERAS protocol, postoperative stress-related catabolism and related complications might still occur, indicating the need for additional care and nutritional therapy. According to the ESPEN guidelines, combined EN and PN is recommended in cases with failure to meet 50% of the nutritional requirements 7 days after oral or EN alone [25]. Special care should also be given to patients with gastrointestinal resection surgeries because of the risks of weight loss associated with the potential bariatric effect. This has been shown in a systematic review, which revealed that 6 months after the surgery, postoperative weight loss was documented in 5–12% of the study population. Moreover, > 10% loss of total body weight was reported in > 50% of their population at one year postoperatively, indicating the severe metabolic risk for these patients [60]. Accordingly, it is essential to continue follow-up and dietary counselling on the nutritional status of these patients, even after discharge.

Individual EN might not be adequate for reducing postoperative weight loss in patients with resection gastrointestinal surgeries. For instance, Koterazawa *et al.* [61] reported that EN did not have a favourable impact on severe weight loss within 3 postoperative months. However, it significantly impacted the 5-year survival rate. Therefore, some guidelines have recommended feeding jejunostomy in these patients to enhance their outcomes. However, a study that recruited patients undergoing oesophageal gastrectomy with partial pancreatoduodenectomy showed that 6 months after the surgery, 40% of patients had > 10% weight loss despite continuous postoperative use of jejunostomy nutrition [24]. The authors suggested that EN should be extended to prevent weight decline and enhance outcomes. A comparative investigation by Chen *et al.* [62] showed that home EN for ≥ 6 weeks for elderly patients undergoing oesophagectomy was associated with significantly improved immune parameters, serum albumin, PG-SGA score, and BMI. Another meta-analysis of patients undergoing surgical resection of gastrointestinal tumours compared the efficacy and safety of ONS and home EN [63]. Reducing the incidence of latent nutrition and malnutrition and weight loss prevention was more significantly associated with EN than with ONS. The authors furtherly observed a significant improvement in transferrin, pre-albumin, haemoglobin, and albumin in patients with EN. Moreover, home-based EN significantly enhanced the domains of quality of life in this cohort. Various clinical trials have also indicated the significant impact ONS might have in reducing weight loss and enhancing functional and immunological parameters, indicating its ability to enhance the patient's postoperative outcomes [25, 64–66].

Jejunostomy nutrition is another option for patients undergoing surgery for advanced-stage gastrointestinal diseases. Having a high risk for developing anastomotic leakage was considered a significant indication for jejunal nutrition. Many previous studies have investigated the efficacy and safety of this route for their patients. For instance, a previous Swedish registry-based investigation compared the outcomes of patients having oesophagectomy with and without the intraoperative application of a jejunal nutritional tube. The authors demonstrated that patients with jejunostomy nutrition had a more significant reduction in the risk of developing severe complications than patients without it, with no increased risk of developing procedure-related complications [67]. Another retrospective investigation compared the outcomes of oesophagectomy patients with and without jejunostomy application. The authors demonstrated that overall survival, short-term mortality, and length of hospital stay did not significantly differ between the 2 groups [68]. On the other hand, it has been shown that anastomotic leakage improved faster in patients with jejunal anastomosis (mean = 27.2 days) than in other patients without it (mean = 37.4 days), but the difference was not significant (p = 0.073) [68]. Therefore, it has been concluded that jejunostomy nutrition is safe and efficacious. However, it should only be considered with high-risk patients. These findings were indicated in a meta-analysis that compared the outcomes of patients with jejunostomy nutrition and others with naso-EN [69]. The authors found that more beneficial outcomes regarding tube dislocation, length of hospital stay, and postoperative pneumonia were associated with jejunostomy nutrition. In a more recent meta-analysis of 12 articles, Lee *et al.* [70] further showed that jejunostomy could reduce the risk of 30-day mortality with no impact on the risk of procedure-related complications. It should be noted that approaching this route is usually recommended on a highly selective basis for patients with severe conditions, and other perioperative surgical uses are controversial and still need further evidence for validation.

Comparing enteral and parenteral nutrition

The most appropriate nutrition route should be based on many factors, including mainly the advantages and disadvantages of the different routes (Table I). It should be noted that various investigations have indicated that using EN can significantly reduce the length of hospital stay and decrease the number of postoperative infectious complications [71, 72]. Moreover, comparing the safety of EN and PN shows that there are more complications with PN. It has been shown that the risk of postoperative adverse events and mortality is increased with PN, particularly for severely ill patients [72–75]. Moreover, continuing the nutritional intervention postoperatively is crucial to maintain enhanced postoperative outcomes. On the other hand, it has been demon-

Table I. Advantages and disadvantages of the different nutritional routes

Type	Description	Advantages	Disadvantages	Costs
Enteral nutrition	Delivered directly into the gastrointestinal tract through a tube or feeding tube	Can be used for long-term nutrition support, can help prevent malnutrition, and can provide specific nutrients that may be lacking in the diet	Can cause nausea, vomiting, diarrhoea, and abdominal discomfort; may require frequent monitoring; and can be expensive	Moderate
Oral nutrition	Consumed orally as part of a regular diet	Easily accessible and cost-effective; allows for variety in the diet; and can provide specific nutrients that may be lacking in the diet	May not provide enough calories or nutrients to meet nutritional needs; may require frequent monitoring; and can be difficult to swallow for some individuals	Less
Parenteral nutrition	Delivered directly into the bloodstream through an intravenous line or catheter	Can provide complete nutrition support; can help prevent malnutrition; and can provide specific nutrients that may be lacking in the diet	Can cause infection at the site of injection; requires frequent monitoring; and can be expensive	Highest

strated that caloric intake through the enteral route might be more difficult and time-consuming to fulfilling satisfaction than parenteral administration secondary to the issues reported with nutrient intake through the physiological route and reduced caloric value of food mixtures [76]. Accordingly, combining EN and PN might be the optimal way to overcome these limitations. For instance, a previous investigation of 308 intensive care unit patients by Heidegger *et al.* [77] compared EN with combined EN and PN, and with EN alone. On the fourth day of administration, the authors demonstrated that the required energy was achieved by 103% in the group indicated for the combined route and by 77% of the other group receiving EN. Moreover, 38% of patients in the combined group with supplemental PN had an infection rate significantly lower than the rate estimated for patients in the EN group. Accordingly, the authors suggested that reducing hospital infections in these patients can be successfully done by providing optimal coverage.

Various clinical trials have compared EN and PN in the settings of perioperative care for patients undergoing surgeries for gastrointestinal diseases. Di Carlo *et al.* [78] conducted a phase II randomized controlled trial (RCT) in 1999 to compare the length of hospital stay, bowel canalization to faeces and gases, infectious, non-infectious, and total complications, the severity of complications, and mortality for 100 patients undergoing pancreatoduodenectomy due to cancer of the head of the pancreas, and receiving either PN (n = 32), enteral immunonutrition (n = 33), or standard immunonutrition (n = 35). The authors reported that the length of hospital stay and infectious and non-infectious complications were not significantly different between the standard PN and EN groups (13.9 (8) versus 17.8 (6.9) days, 8/32 (25%) versus 6/35 (17.2%), and 11–32 (34.3%) versus 8/35 (22.8%), respectively). It has been furtherly demonstrated that the mortality rate, sepsis score, and total complications were higher in the standard parenteral group. Finally, resuming normal bowel habits was significantly faster in the EN than in the PN groups [78]. Another phase II trial concluded that EN is a feasible and safe alternative to PN after major abdominal surgical procedures. It has been estimated that the rates of infectious and non-infectious complications and the length of hospital stay did not significantly differ between patients receiving total PN versus standard EN during pancreatic and abdominal surgeries. The authors also conducted a subgroup analysis to investigate the outcomes of pre-operatively malnourished patients receiving omega-3, RNA, and arginine-enriched EN. They found that this approach significantly reduced the length of hospital stay and severity of infections compared to patients included in the total PN group. The authors further demonstrated the positive impact of immunomodulatory nutrition in a subgroup analysis of patients receiving a homologous blood transfusion [79].

In 2001, another phase II randomized clinical trial by Braga *et al.* [80] compared the length of hospital stay between EN (n = 126) and PN (n = 131) for patients undergoing oesophagectomy (n = 26), pancreatectomy (n = 110), and gastrectomy (n = 121). The authors demonstrated that the length of hospital stay did not significantly differ between the 2 routes of nutrition (mean (± SD) = 20.7 (8.8) versus 19.9 (8.2) days, respectively). Moreover, the overall complication rate was higher in the PN than in the EN group (52% versus 37.1%, p = 0.23). Accordingly, the authors' conclusions recommend using EN rather than PN, particularly in a malnourished population, due to their lower complication rate and reduced length of hospital stay. Similar findings were also reported in other clinical trials, indicating the safety and superiority of early EN over PN [81–85]. More recently, a Cochrane systematic review and meta-analysis of 25 studies, including 23 RCTs, demonstrated that patients receiving EN had reduced sepsis compared to others receiving PN, with no sufficient evidence to draw any conclusion between the 2 modalities regarding in-hospital mortality and mortality at 90 and 180 days. Moreover, it has been shown that combined PN and EN significantly reduces the risk of death among patients admitted to the intensive care unit [86]. More recent meta-analyses of critically-ill patients further indicated the significant potential of PN and EN in reducing the risk of mortality and hospital infections [87, 88], further indicating the positive effects of such combinations which can be associated with more favourable efficacy and safety outcomes.

Another vital factor to consider is the cost of these routes and the economic burden they might constitute on patients and healthcare facilities. Overall, evidence shows that PN is associated with higher costs [89]. This has been indicated in the phase II RCT by Braga *et al.*, which concluded that the mean cost per day for EN was significantly lower than that for PN ($25 versus 90.6$, *p*-value < 0.001, i.e. 4-fold lower) [80]. The elevated costs of PN might, therefore, suggest the need to use a combined nutrition route, whether oral or enteral, to reduce these costs and achieve nutritional requirements. This might also be a favourable option as we previously discussed the beneficial outcomes of combining EN and PN, particularly among critically ill patients.

Deficiencies in micronutrients have been reported even after minimally invasive surgeries for digestive tumours [90]. Accordingly, immunonutrition has been reported with many clinical applications due to their favourable advantages and their role in patient outcomes (Table II) [91–93]. Many research advances have been reported for the benefits of using immunonutrition, like omega-3 fatty acids, nucleotide, arginine, and glutamine for cancer patients during perioperative management. Evidence indicates that these modalities can significantly enhance inflammatory and host immune system responses [94, 95]. Moreover, more research shows the advantages of using immunonutrition with enteral and oral formulas. In this context, it has been shown that mixing these factors with EN can be associated with better outcomes more than using them alone, although current data are scarce. Various RCTs have evaluated the efficacy of combining nucleotides, omega-3 fatty acids, and arginine with oral and EN [96, 97]. These studies demonstrated that such combinations can remarkably reduce hospital costs, length of hospital stay, and infectious complications. However, the formula of other nutritional supplements with these immunonutrients is still controversial [10]. In this context, a recent meta-analysis showed that the pre-operative administration of immunonutrients by 5–7 days was associated with a significant reduction in the incidence of complications, and hospital stay among patients undergoing surgery for gastrointestinal diseases, compared to isonitrogenic standard drinking food and normal diet, with a non-significant heterogeneity among the included studies [98]. However, it should be noted that the impact of immunonutrition was non-significant on mortality and non-infectious complications. A meta-analysis of RCTs for patients undergoing gastric surgeries by Li *et al.* [99] showed that immunonutrition is associated with favourable outcomes and should be considered following the surgery to enhance patient prognosis. Another meta-analysis of patients having oesophagectomy showed that no significant impact on the postoperative complication rate was seen following the perioperative administration of immunonutrition [100]. However, evidence from guidelines indicate the preferred use of ONS and immunonutrition before the surgery by 5–7 days [25].

There are both physiological and immunological barriers in the digestive tract [101]. Tight junctions between epithelial cells constitute the physiological barrier [101]. Lamina propria lymphocytes, intraepithelial lymphocytes, and Peyer patches are all components of the gut-associated lymphoid tissue that creates an immunological barrier in the intestine [101]. The immune system is weakened, the gut flora is altered, and numerous problems arise after surgery [102, 103]. Reduced infection problems may

Table II. Advantages, disadvantages, and applications of the commonest elements used in immunonutrition

Element	Advantages	Disadvantages	Applications
Arginine	Stimulates immune system, increases wound healing, reduces inflammation and oxidative stress	High doses can cause gastrointestinal distress	Wound healing, sepsis, cancer, HIV/AIDS
Glutamine	Enhances immune function and helps to reduce inflammation	High doses can cause nausea and vomiting, expensive	Surgery, trauma, burns, cancer
N-acetylcysteine (NAC)	Antioxidant properties that help to reduce inflammation and improve immune system function	Can cause nausea and vomiting in some people	Chronic obstructive pulmonary disease (COPD), cystic fibrosis, HIV/AIDS
Zinc	Enhances immune system function and helps to reduce inflammation	High doses can cause nausea and vomiting in some people	Wound healing, HIV/AIDS, cancer treatment
Nucleotides	Boosts immune system; helps with cell growth and repair	Expensive; may cause nausea, vomiting, and diarrhoea in some people	Used to treat malnutrition, HIV/AIDS, cancer, and other conditions that weaken the immune system

be one benefit of immunonutrition. Its potential to improve immune response and decrease inflammation after gastrointestinal surgery may explain this. Patients with gastric cancer who had gastrectomy had larger CD4 cell counts and a better CD4/CD8 ratio in the immunonutrition group, as validated by Li *et al*. and Chen *et al*. [104, 105]. At the same time, TNF- levels dropped drastically [104, 105]. Immunonutrition also contains nutrients with distinct antimicrobial and immune-boosting functions. Wound healing, lymphocyte activity, and intestinal IgA levels were all positively affected by arginine treatment [106–108]. Glutamine is required for the synthesis of the endogenous antioxidant glutathione and for the maintenance of the gut barrier function [107–109]. By altering the composition of membrane phospholipids to generate the lipid mediators with reduced bio-activity, stabilizing the NFκB/IkB complex, and acting as agonists for peroxisome proliferator-activated receptors, omega-3 fatty acids decrease responsiveness to cytokines and the systemic inflammatory response [107, 108]. The expression of mature and phenotypically distinct T lymphocytes may be influenced by RNA [109].

One of the most serious consequences of gastrointestinal surgery is anastomotic leakage, which is linked to a higher risk of death and a longer length of stay in the hospital [110, 111]. Four stages – haemostasis, inflammation, proliferation, and remodeling – make up the normal healing process of an anastomosis. Infectious difficulties during anastomosis healing are caused by the presence of many gastrointestinal aerobic and anaerobic bacteria, as well as the function of elevated loads of collagenases and matrix metalloproteinase [112]. In addition, anastomotic leakage is significantly associated with malnutrition [113, 114]. Therefore, preventing anastomotic leakage requires adequate nutritional support. Therefore, immunonutrition helps improve patients' nutritional status on the one hand, and also helps maintain the function of gut-associated lymphoid tissue, stimulates tissue growth after infection, and modulates dysfunction of the intestinal barrier, promotes wound healing, and reduces anastomotic leakage on the other [107–109]. Anastomotic leakage is a common complication of gastrointestinal surgery; however, Yildiz *et al.* [115] discovered that immunonutrition helped prevent this problem.

Multiple variables, including those at the microbiological, patient, and procedural levels, contribute to the development of surgical site infection [116]. Endogenous infections are the most prevalent source of surgical site infections [116], with anastomotic leaking being a major contributor to this problem [117]. It is possible for the infected surgical site to disseminate either directly or haematogenously during anastomotic leakage, leading to abscess development and septic consequences from intraperitoneal spilling of feculent material and significant bowel leakage [117]. It was suggested that the ability of immunonutrition to sustain the quantity of gut-associated lymphoid tissue cells and IgA levels in the intestinal lumen may play a role in fighting infection [101, 109], which might explain why immunonutrition was found to reduce the incidence of surgical site infection. A leaky anastomosis or infection disseminated via the bloodstream are also possible causes of abdominal abscess [118]; for instance, pancreatic leakage or fistula, which leads to abdominal abscess following pancreaticoduodenectomy [119]. Contamination with bacteria, the bacterium's pathogenicity, and the patient's resistance and defensive mechanisms are all crucial factors in the development of abdominal abscesses [118]. The incidence of abdominal abscesses was shown to be drastically decreased in our research when immunonutrition was administered. The intestinal mucosal barrier, the spread of germs, and the immune system may all benefit from possible immunonutrition involvement [109].

Patients with colorectal cancer seem to benefit more from the ability of immunonutrition to pinpoint their cancer subtype. Colorectal cancer patients treated with immunonutrition have substantially lower rates of infection, infection at the surgical site, and duration of hospital stay. Because the majority of intestinal bacteria are found in the lower gastrointestinal tract [120], and the prevalence of infectious complications in the lower gastrointestinal tract is substantial [121, 122], immunonutrition may have a more pronounced impact on reducing postoperative infection for colorectal cancer. The varying amounts and durations of immunonutrition administration, as well as the small sample size in certain subgroups, may also play a role. Additional research on this subset of tumours is necessary. Perioperative immunonutrition outperformed preoperative and postoperative immunonutrition in lowering infection rates and length of hospital stay, respectively, in the intervention period study [123]. This agrees with the findings of Song *et al.* [124], who also found that patients with gastrointestinal cancer after surgery benefited most from perioperative immunonutrition treatment. Immunonutrition was more successful in lowering the incidence of postoperative complications when no supplement was administered, indicating the relevance of nutrition supplements, as compared to the regular diet in the control group [123].

Immunonutrition was shown to minimize overall problems, certain infectious complications, and duration of hospital stay in both well-nourished and malnourished patients when compared to controls when examining particular nutritional circumstances [123]. It is noteworthy that immunonutrition medication dramatically reduced mortality in malnourished groups, suggesting that immunonutrition was more effective for malnourished patients. Nutritional status may be greatly improved in malnourished patients with immunonutrition, which is important because malnutrition is a risk factor for surgical complications [10, 125]. Malnourished patients benefit from immunonutrition because it helps them recover faster from wounds, avoid more serious consequences, and live longer overall [101]. Most investigations, however, have failed to show that immunonutrition reduces mortality in surgical patients [126–128]. Unfortunately, there was not enough information for us to draw any firm conclusions on the difference in postoperative problems between the malnourished and the well-nourished groups when it came to immunonutrition. Thus, further research is needed to determine whether immunonutrition has an influence on mortality, and more randomized trials are required to examine the effects of immunonutrition on postoperative complications in patients of varying nutritional states.

Conclusions

Malnutrition is a frequent complication for patients with advanced stage gastrointestinal tumours and represents a significant risk for poor prognosis. Although minimally invasive procedures might reduce malnutrition in these patients, evidence shows that nutritional care is still needed to enhance the postoperative outcomes. However, the current literature review revealed that there is a need for further research and clinical trials to determine the optimal nutrition support for these patients. Evidence suggests that early oral nutrition can be initiated following minimally invasive surgeries (for instance oesophagectomy) with no impact on the postoperative functional outcomes and complications. Moreover, EN is beneficial in terms of improving outcomes, reducing complications, and improving quality of life. However, the optimal timing and composition of EN are still unclear. It is also essential to highlight the importance of individualized nutritional care for these patients. The patient's overall health status, comorbidities, and preferences should be considered when making decisions about nutrition support. In addition, it is important to consider the potential risks associated with EN such as aspiration risk, diarrhoea, and infection. Healthcare providers should be aware of the benefits associated with EN and should consider its use when managing these patients.

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Conflict of interest

The authors declare no conflict of interest.

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