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Current approach to perioperative nutrition in the ERAS age

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ABSTRACT

Enhanced recovery after surgery (ERAS) is a multidisciplinary and multimodal program designed to minimize the response to surgical trauma and normalize the patient as early as possible. While managing the perioperative process of the patient, ERAS protocols a change from classical and dogma-based treatments to modern concepts with a radical change. Its basic philosophy is to provide early recovery by supporting mobilization and gastrointestinal functions without causing complications. This protocol consists of many different elements, and when they are applied together, they support each other. Nutrition is an important part of ERAS protocols, and it directly affects clinical outcomes. The recommended perioperative nutritional management algorithm for patients to be operated with ERAS protocols starts with a routine nutritional assessment and aims at early oral/enteral feeding at each stage. The aim of this compilation is to review current perioperative nutritional recommendations in the period in which ERAS protocols are adapted to all areas of surgery.

Keywords: Accelerating postoperative recovery, enteral and parenteral nutrition, ERAS, perioperative nutrition

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Introduction

Of the patients who are admitted to general surgery clinics, 10%-35% are malnurished (1-7). Although the primary diseases such as cancer, trauma, acute inflammation, obstruction, or fistulas are the leading causes of this condition, advanced age, a previous chronic disease, and low socioeconomic status are additional risk factors. Moreover, the issue of iatrogenic malnutrition should not be forgotten. The malnutrition that develops during hospitalization is called "iatrogenic malnutrition," and it is reported to be seen at a rate between 10% and 50% by various researchers (3, 8). Knowing the causing factors (Table 1) plays an important role in preventing the worsening of the nutritional problem, which already exists at the time of hospitalization, and in the regulation of appropriate treatment. Malnutrition rates at the time of hospitalization in surgical clinics dealing with patients with cancer range between 50% and 80% (2, 9-14).

The effect of malnutrition on postoperative complications and mortality rates has long been known (Table 2). In the study published by Studley et al. (15) in JAMA in 1936, it was shown that the mortality increased with the increase of preoperative weight loss in patients undergoing peptic ulcer surgery, and this became a classic book knowledge, with the results of many subsequent studies parallel to this research (16, 17). Malnutrition increases not only mortality, but also all infectious complications, total morbidity, a prolonged hospital and intensive care unit stay, and costs (Figure 1). In a study published in 2011, it was shown that the health expenditures required for the treatment of patients with malnutrition were as twice as high as those without malnutrition and that malnutrition acted as an independent risk factor on mortality (18).

The basic philosophy of enhanced recovery after surgery (ERAS) protocols, defined as the multimodal and evidence-based perioperative care concept, is to reduce metabolic stress due to surgical trauma and to enable the return to normal activity as soon as possible by supporting normalization of functions in a short time. Preoperative optimization, prehabilitation, perioperative modern nutritional management, standard anesthesia and analgesia regimens, and early mobilization are the main components of ERAS protocols (19-24).

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A proper and safe nutritional support during the perioperative period can solve many problems that may arise due to malnutrition. In the period when ERAS protocols are on the agenda, the nutritional needs of patients who will undergo major surgeries are included in the guidelines of many associations (25-29).

Nutrition is one of the main elements of ERAS protocols since it includes important issues such as preoperative fasting, oral carbohydrate loading, optimizing preoperative nutritional status, and early oral feeding. Therefore, the issue of perioperative nutrition management for patients to be operated with ERAS protocols should be reviewed in the light of current information.

Table 1. Iatrogenic malnutrition factors
Lack of recording the body weight
Lack of a clear description of responsibilities
Lack of nutritional knowledge
Frequent fasting of the patient for examination purposes
Continuous blood-letting for examinations
Poor documentation of food intake
Loss of appetite due to environmental changes
Surgery in a malnourished patient
Postoperative long-term use of glucose and saline solutions
Delayed nutritional support leading to irreversible depletion

Table 2. Effects of malnutrition on surgical outcomes
• Impaired wound healing o Opening of incision o Leakage from the anastomosis
• Decreased resistance to infections o Postoperative pneumonia o Postoperative wound infection o Increase in intraabdominal infections o Postoperative urinary infection
• Impairment of adaptability o Insufficiency in adaptation after intestinal resections o Prolonged paralytic ileus
• Delay in recovery
• Pressure ulcers

Importance of ERAS Protocols

ERAS recommends changes for the whole patient's journey, starting from the outpatient clinic before the operation and ending up at home after being discharged (Figure 2).

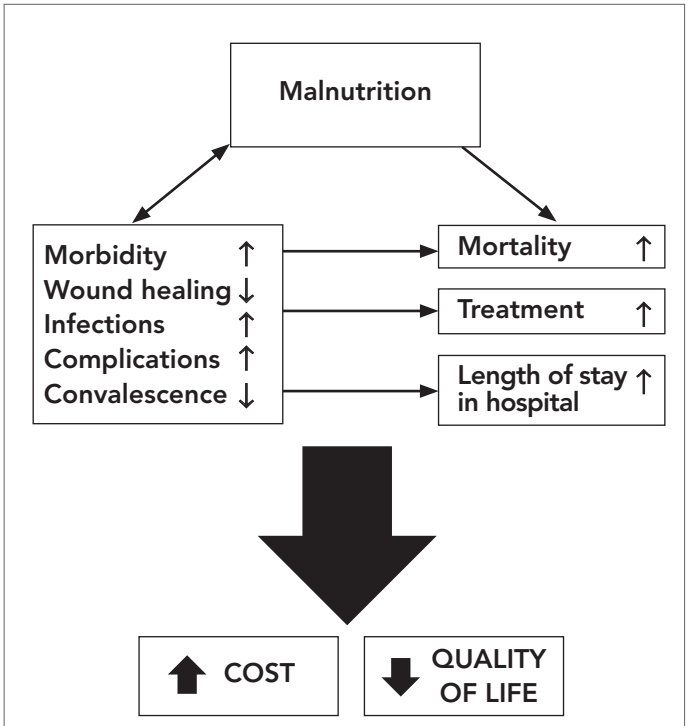

Figure 1. Results of malnutrition

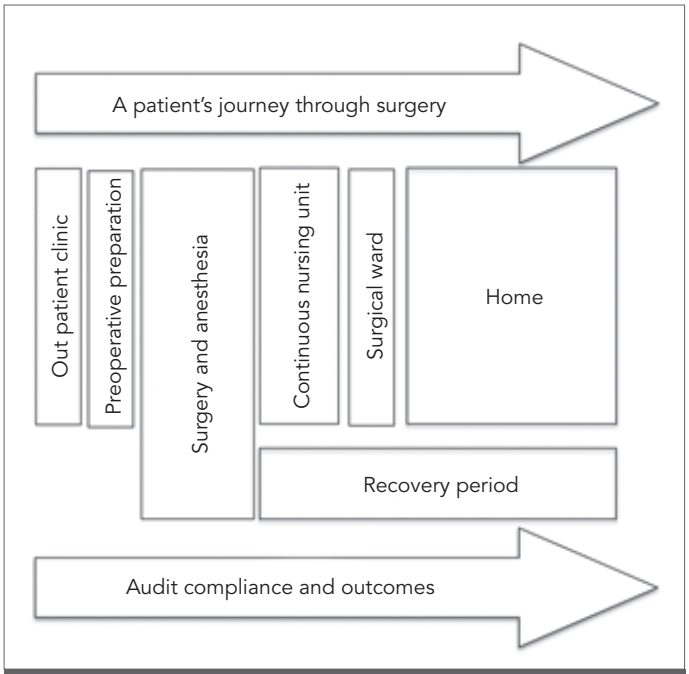

Figure 2. The journey of a surgical patient

One of the most important factors in the improvement after surgery is to fight against the metabolic trauma caused by surgery. ERAS aims to reduce the metabolic response to trauma thanks to modern surgery, anesthesia, analgesia, and some support applications. Thus, the process will end up with less damage and a quick recovery. The important point to note is that ERAS are not only surgeon's non-traditional practices, but also the performance of a trained team (23, 24, 26). Although there are the contributions of different team members in the process from the hospital admission to full recovery, surgeons, anesthesiologists, and nurses come to the forefront as the main actors. Under the leadership of these basic members of the team, all health professionals who will take part in the process should audit at least once in 15 days and evaluate the results and conduct training activities.

ERAS protocols go beyond the traditional and even dogmatic surgical and anesthetic applications, and they bring innovations that can be described as radical. The protocol includes more than 20 evidence-based elements to be applied in the perioperative period (Table 3) (23, 24, 26, 30, 31). These elements are grouped together by the ERAS Association in a way to include minor differences in guidelines prepared according to systems (http://erassociety.org/guidelines/list-of-guidelines/).

It is not possible to obtain good results by using one or more of the elements included in ERAS protocols. When all of the recommendations are implemented by a trained team, the contributions to the postoperative recovery process are seen. Each element has a synergical effect on another. The key issues such as proper management of pain, early mobilization, and providing early oral feeding through the proper management of gastrointestinal motility are supported by the use of many other elements.

In all recently published meta-analyses, it has been shown that the duration of hospitalization is reduced by 2-3 days, and the complications decrease by 30%-50% by applying ERAS protocols in major surgeries (32-35). The effect of adherence to protocols on the results is very clear. Mortality decreases by 42%-50% when the compliance to ERAS is higher than 70% (36, 37). As the cost analysis of ERAS protocols was puplished, it was understood that it also provided a very important advantage in this sense (38, 39). In particular, the cost analysis from the Canadian Alberta hospital chain was impressive, and it showed a profit of $2800-5900 per patient with ERAS protocols (40).

Prehabilitation

The necessity of medical optimization before surgery has gained a general acceptance. There have been many improvements in preoperative cardio-pulmonary preparation in the last 30 years, and as a result of this, mortality rates have been reduced (41). However, the same success could not be achieved with the complication rates arising with the coexisting problems such as obesity, diabetes, modern lifestyle, hypertension, and old age. In this sense, all patients who are to undergo major surgery should be operated after their general conditions are maximized to achieve success. In the recent years, the concept of prehabitation that is recommended to be performed in the preoperative period has been developed instead of the concept of postoperative rehabilitation (42).

Patients with diabetes should be well prepared preoperatively and should be closely monitored in the postoperative period. Patients with high levels of glycosylated hemoglobin (HBA1c) preoperatively remain approximately 1 mmol/L higher than patients with normal preopera-

Table 3. Components of ERAS protocol

Preoperative	Intraoperative	Postoperative
Preadmission counseling	Surgical incisions	Blood sugar management
Preoperative mechanical bowel preparation	Prevention of intraoperative hypothermia	Postoperative non-opioid analgesia
No prolonged fasting preoperatively	Mid-thoracic epidural analgesia	Early removal of urinary catheter
Preoperative oral carbohydrate loading	Short-acting anesthesia protocol	Stimulation of gut motility
Assessment of nutritional status and nutritional support if necessary	Prevention of postoperative nausea and vomiting	Early feeding / early enteral nutrition if necessary
Preoperative optimization	Perioperative fluid management	Early mobilization
Prehabilitation	No drains	Early discharge criteria
No premedication	Laparoscopic and robotic surgery	Audit of compliance and outcomes
Thromboprophylaxis	No nasogastric tubes	
Antimicrobial prophylaxis		

tive HbA1c levels, and additionally, more complications develop in these patients (43). As recommended in many guidelines, the blood glucose level should be aimed at around 140-180 mg/dL. Patients should be operated after the preparations are completed in the areas such as quitting cigarette smoking and alcohol consumption 4 weeks prior to the operation, exercise programs, reducing the risk of co-morbid diseases by conducting required consultations, and many other similar subjects.

Preoperative Nutritional Management

Surgical trauma results in significant endocrine and metabolic changes that increase catabolism. It also disrupts the immune response and reduces insulin resistance. In addition, inadequate food intake over 14 days causes an increase in morbidity and mortality (25). Planned or unplanned fasting along with surgical trauma results in an increased nutritional risk. With the widespread use of neoadjuvant chemo-radiotherapy in cancer patients, an additional burden to the deterioration of the nutritional status has emerged for patients receiving these treatments (44).

The European "NutritionDay" data of approximately 15,000 patients indicated the metabolic risk as a factor affecting hospital mortality, especially in the elderly (45). The high-risk patients in hospitals are mostly in the surgical, oncology, and geriatric clinics, and in intensive care units. The factors affecting the complication rates in hospitals are the severity of the disease, age over 70 years, surgery, and cancer. Considering the demographic developments in the Western world, surgeons must also deal with the risk in elderly patients undergoing major cancer surgery. Nutritional management is therefore an interdisciplinary field and has become a "necessity" for resource savings in the period of limitations in the health economy. Nutritional risk screening should definitely be performed at the time of hospitalization, and it should also involve the metabolic aspect of the surgery. There are many screening tools, but the Nutrition Risk Screening (NRS-2002) method is the one that has been officially proposed and validated by the European Society for Parenteral, Enteral Nutrition (ESPEN) (46). High complication rates were found in patients who were determined to be at risk with NRS. Preoperative tomography has been proven to be a valuable method in the detection of sarcopenia in patients with sarcopenic cancer (47).

Serious metabolic risk should be considered in the presence of one or more of the following criteria:

- Weight loss >10%-15%
- Body mass index <18.5 kg/m^2
- Serum albumin <30 g/L

However, it should always be kept in mind that serum albumin levels alone are not indicator of the nutritional status (48). Although albumin is a good laboratory parameter for postoperative morbidity, it does not give a clear information about the nutritional status due to its distribution in a large pool in the body, long half-life, and due to its changing levels in many diseases.

There is an indication of a nutritional plan in a patient who is unable to take 60% of his or her normal food for longer than 10 days in the preoperative period (29). In addition, even if no specific malnutrition is detected, there is an indication for perioperative nutritional support in a patient who is expected not be able to take food orally for more than 7 days.

There are different approaches to preparing the patient for surgery in terms of nutrition, which can be used in combination (25, 29, 49):

- Nutritional support if severe metabolic risk exists,
- Metabolic preparation (oral carbohydrate administration),
- Immunological modulation.

Postponement of the operation to complete the energy-protein deficiency or at least stop the hypercatabolic process is discussed only when there is a serious malnutrition or metabolic risk. If there is an indication of nutritional support, enteral route should be preferred. Enteral nutrition should be performed before hospitalization to prevent nosocomial infections. At this point, oral nutritional supplements (ONS) have an important role (29, 50, 51).

In severe malnutrition, parenteral nutrition is recommended in patients who can not be fed orally or enterally enough (52, 53). There is an indication of parenteral nutrition in patients with malnutrition, for whom enteral nutrition is not appropriate or in whom there is intolerance, including patients who have an impaired gastrointestinal system (GIS) function due to postoperative complications and who cannot receive and absorb adequate oral/enteral nutrition. Combined enteral-parenteral nutrition should be considered in patients who cannot meet 60%-75% of their energy requirement by enteral route (29, 54). Oral or parenteral nutrition support is usually maintained for approximately 7-14 days (14, 29, 48).

Obese patients constitute another group that is often neglected by surgeons. Many physicians think these patients are an energy and protein store and believe that there is no need for an aggressive nutritional therapy in the preoperative period. However, most these patients have sar-

copenic obesity, and their dry body masses are very low. This poses a serious risk for postoperative complications. In fact, when mortality is considered in surgical intensive care patients, morbid obesity is an independent predictor (55).

Keeping patients hungry at the preoperative night affects postoperative insulin resistance and negatively affects the results (56). The metabolic burden provided by perioperative hypoglycemia due to one-night fasting was clearly demonstrated, and the dogmatic information about preoperative fasting has changed completely (56, 57). Consumption of oral solid foods at night and liquids up to 2-3 h prior to surgery does not increase the risk of aspiration during anesthesia. Oral use of sugary fluids can be recommended for many patients because it does not prevent gastric emptying. It was shown that the oral solution containing 12.5% maltodextrin as the main substance decreases preoperative thirst, hunger, anxiety (58), and postoperative insulin resistance (56). Oral carbohydrate administration reduces postoperative nitrogen and protein loss (59), resulting in improved preservation of lean body mass and muscle strength (60). Patients who will undergo surgery should be given 800 mL of carbohydrate-rich liquid food until midnight preoperatively and 400 mL 2-3 h before the operation to ensure metabolic toughness. This practice has also been shown to significantly shorten the duration of hospital stay after surgery (57). Intravenous glucose infusion may be used in very few patients who cannot take food orally or enterally.

Postoperative Period

In the majority of patients after major abdominal surgery, the stomach returns to normal myoelectric functions within 24-48 h, the small intestines return to propulsive function within 12-24 h, and the colon returns to normal contractility within 48-72 h. Therefore, cessation of oral food after surgery in many patients is unnecessary, and it can be resumed within a few hours after surgery. It was shown[48] that a 75%-90% success rate was achieved when the feeding was started within 6-24 h postoperatively. It is now information based on clear evidence that early oral/enteral nutrition reduces infectious complications, regulates the metabolic response to surgery, and shortens hospital stay (61-63). It was also shown that the anastomotic leakage did not increase after GI tract operations with early feeding. Therefore, there is no valid reason for fasting for a long time after surgery. Oral feeding can be started without delay even after the operations with GIS anastomosis. In patients undergoing upper GI anastomosis, enteral nutrition can be performed via a tube placed distal to the anastomosis, and these patients may also drink ONS. In these patients, the nasojejunal tube or needle catheter jejunostomy (NCJ) placement as an enteral access is also suitable (64). After surgery, enteral tube feeding is started within 24 h and at a low rate (5-10 mL/h). The rate of administration is increased 10-20 mL/h per day. GI tolerance should be monitored carefully by performing abdominal examination. The most important issue that distresses clinicians is that it is not easy to distinguish GI intolerance due to early feeding and the early postoperative complications of major abdominal surgery. In such a situation, taking the easy ways such as interrupting feeding does not solve the problem. There are two critical moves to achieve optimal bowel functions. Early delivery of nutrients to the intestines and early correction of the changes in the pH or electrolytes (potassium>4 mEq/L, magnesium>2 mEq/L) are very important.

Postoperative early feeding, which is one of the most important components of achieving the targeted result with ERAS protocols, is supported by the combined use of some other elements included in the application. Thus, while long-term ileus is prevented, it is also possible to increase tolerance to early oral food intake. Early oral food intake is facilitated by many applications, such as avoiding preoperative fasting, analgesia at the mid-thoracic level, modern anesthesia management, target-specific perioperative fluid therapy, and early mobilization.

However, oral nutrition is unfortunately still delayed for some reasons (Table 4) (48). By changing a number of traditional, harmful, and unnecessary routines, the factors that prevent the transition to normal nutrition can be solved in the early period.

Parenteral Nutrition

While emphasizing the most important aims of ERAS protocols as giving oral food as soon as possible, using the digestive tract effectively, and early discharge, a question such as "Does parenteral nutrition still exist in this algorithm?" may come to mind. However, it is seen that it holds its own position in the recommendations made for perioperative period in the current guidelines (25, 29). There is a need for preoperative parenteral nutrition in patients with malnutrition who cannot receive oral feeding for 7 days for various reasons, and postoperative parenteral nutrition is needed in patients in whom oral/enteral feeding cannot be started within 7 days due to complications. In addition, in the daily practice, there are many patients in whom it is required to use both enteral and parenteral nutrition.

Discharge and Follow-Up

The follow-up of the nutritional status, including written monitorization of oral food intake, after major abdominal

Table 4. Factors that prevent early oral feeding
• Lack of understanding well the potential benefits of early feeding
• Poor understanding the postoperative ileus
• Unnecessarily waiting for the markers that are thought to show bowel activity
• Concern about complications o Aspiration o Bowel ischemia o Fear that feeding may cause anastomotic leakage
• Lack of feeding tube placement protocols
• Lack of communication among team members

surgery is a very important responsibility. Diet counseling, which is to be performed clearly enough for the patient, is also recommended. Oral calorie intake will be insufficient for months in most patients who undergo GI tract and pancreatic surgery. Reduction in appetite, deterioration of enteral tolerance due to "dumping" symptoms, bloating, and diarrhea are reasons that can cause this situation. If NCJ is placed during surgery, it should not be removed during discharge from the hospital. If necessary, 500-1000 kcal/day supplementary enteral nutrition may be given to patient through NCJ, even if he or she is able to receive oral food. After being trained, many patients will be able to do this on their own. Although it is not possible to prevent more weight loss, it has been proved that it can be reduced with oral supplementation. Even if patients with malnutrition in the preoperative period (especially those operated for upper GIS cancer) are managed without any problems during the period at the hospital, they should be discharged with ONS prescription, after explaining the correct and appropriate usage, and with the recommendations that they should be consumed as a supplement to normal food for 4-8 weeks. The quality of life is also significantly better in patients in whom supplementation is administered.

The Role of Pharmaconutrition

In recent years, the effects of some nutrients used for nutrition support in the perioperative period on the immune system have been investigated and discussed more seriously. There are different views on terminology, but when mentioning the effects of nutrients on the immune system, "pharmaconutrition" may be a more appropriate nomenclature.

The main nutritional elements that affect the immune system in various ways and about which investigations are made are arginine, glutamine, nucleotides, omega-3 fatty acids, fiber, prebiotics, probiotics, various antioxidants, and glutathione. The prominent biochemical effects of these formulas are increasing the cell membrane stability, supporting gastrointestinal mucosal integrity, enhance cellular immune response, and increase the blood flow in ischemic tissues. Thus, it is aimed to decrease postoperative infective complications and general morbidity as clinical results. Regardless of the nutritional status of the patient, there is strong evidence that preoperative pharmaconutrition reduces the length of hospital stay and postoperative complications (66-70). The SONVI study showed that postoperative complications could be reduced by the combined use of ERAS protocols and immune nutrients (71). In a recently published meta-analysis, the effect of different combinations of immune nutrients on mortality, morbidity, and the length of hospitalization in patients undergoing major abdominal surgery was investigated (72). The results of a total of 7116 patients in 83 randomized controlled trials were evaluated. It was found that immune nutrients decreased morbidity, mortality, and the duration of hospital stay. In the ESPEN and ASPEN guidelines, it is strongly suggested that pharmaconutrition should be administered for 5-7 days preoperatively and for 1 week postoperatively in patients who are to undergo major cancer surgery (25, 73). It is recommended that these products be used in patients who have a serious risk and will have a major operation (esophagectomy, gastrectomy, pancreatoduodenectomy) due to neck (laryngectomy, pharyngectomy) and abdominal cancer.

In a recent meta-analysis that examined many aspects of pharmaconutrition, 19 randomized controlled trials were evaluated, and with the conclusion that it reduced wound infections and hospital stay, it was suggested to be a part of the ERAS program in the upper GI cancer surgery (74).

The subject of the recent discussion is related to the timing of pharmaconutrition. It is examined whether the results are affected by its administration in the preoperative, postoperative, or perioperative period. While the benefits of perioperative pharmaconutrition were supported in a recent meta-analysis, it was shown that only preoperative administration did not affect the outcomes (68). In another meta-analysis published in the same year, it was found that there was no difference between standard oral supplements and immune nutrients in terms of the effect on outcomes, when they remained limited within the preoperative period (75).

The impacts of these specific products on the cost were also discussed and evaluated in many studies. Contrary to popular belief, these formulas have been shown to be cost-effective in many studies. In a systematic review of

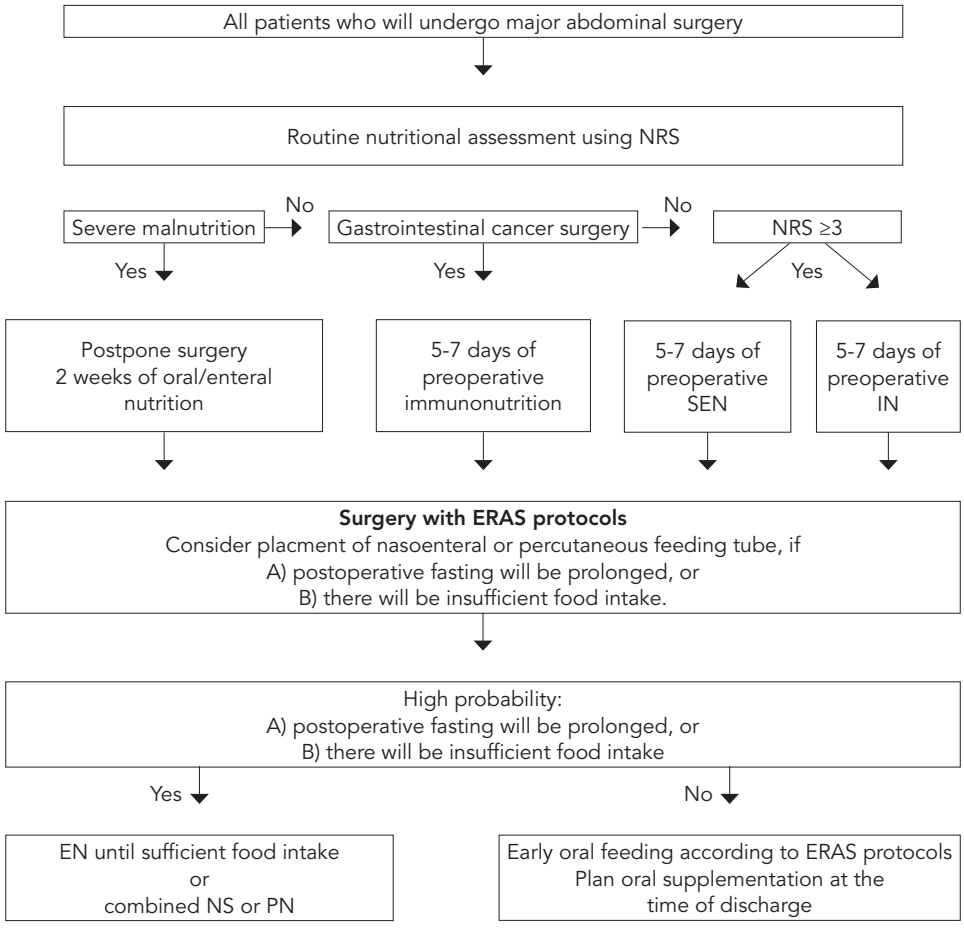

Figure 3. Perioperative nutritional planning algorithm

cost analysis of perioperative pharmaconutrition in patients undergoing GI cancer surgery, there were six prospective, randomized, controlled trials evaluated (76). Compared to standard oral supplements, it was shown that special products were more advantageous in terms of the total costs.

Conclusion

Nutrition is an important part of ERAS protocols, and nutritional status is an independent predictor of clinical outcomes. The perioperative nutritional management algorithm proposed for patients to be operated according to ERAS protocols starts with a routine nutritional evaluation and proceeds by targeting oral/enteral nutrition at each stage (Figure 3). Patients included in ERAS, especially the ones with malnutrition, nutrition should be integrated into the protocol to ensure an optimal perioperative management.

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