ANNUAL REVIEWS

Annual Review of Nutrition

Contemporary Perioperative Nutritional Care

Olle Ljungqvist,[1,2] Arved Weimann,[3] Marta Sandini,[4] Gabriele Baldini,[5] and Luca Gianotti[6,7]

[1]Department of Surgery, School of Medical Sciences, Orebro University Hospital and Orebro University, Orebro, Sweden; email: olle.ljungqvist@oru.se

[2]Department of Molecular Medicine and Surgery, Karolinska Institute, Stockholm, Sweden

[3]Department of General, Visceral, and Oncologic Surgery, Saint George Hospital, Leipzig, Germany

[4]Department of Medicine, Surgery, and Neuroscience and Unit of General and Oncologic Surgery, University of Siena, Siena, Italy

[5]Section of Anesthesia and Critical Care, Department of Anesthesia and Critical Care, Azienda Ospedaliero-Universitaria Careggi, University of Florence, Florence, Italy

[6]School of Medicine and Surgery, University of Milano-Bicocca, Monza, Italy

[7]HPB Surgery, Foundation IRCCS San Gerardo Hospital, Monza, Italy

Annu. Rev. Nutr. 2024. 44:231–55

The *Annual Review of Nutrition* is online at nutr.annualreviews.org

https://doi.org/10.1146/annurev-nutr-062222-021228

Keywords

surgery, nutrition, enhanced recovery after surgery, prehabilitation

Abstract

Over the last decades, surgical complication rates have fallen drastically. With the introduction of new surgical techniques coupled with specific evidence-based perioperative care protocols, patients today run half the risk of complications compared with traditional care. Many patients who in previous years needed weeks of hospital care now recover and can leave in days. These remarkable improvements are achieved by using nutritional stress-reducing care elements for the surgical patient that reduce metabolic stress and allow for the return of gut function. This new approach to nutritional care and how it is delivered as an integral part of enhancing recovery after surgery are outlined in this review. We also summarize the new and increased understanding of the effects of the routes of delivering nutrition and the role of the gut, as well as the current recommendations for artificial nutritional support.

Contents

1. INTRODUCTION

Providing nutritional care to the surgical patient has traditionally had specific challenges. Surgery and injuries cause major stress reactions with insulin resistance and marked inflammatory responses. In addition, traditional pain management with opioids and intravenous (IV) fluids, which are often given in large volumes, causes postoperative ileus. However, over the last two decades, new research has drastically changed the care of surgical patients. This has had a major impact on patient stress reactions to surgery and on the possibility to use the gastrointestinal (GI) tract and normal food. Enhanced Recovery After Surgery (ERAS) protocols recommend evidence-based perioperative care that has two distinct effects on nutritional care: Insulin resistance is minimized, and the return of gut function is much faster. ERAS programs are complemented by prehabilitation programs that aim to make the patient as fit as possible for the surgery. During prehabilitation, the patient develops improved resilience to the stress of surgery. By combining these novel developments, most of the previous challenges in delivering nutritional care to surgical patients are minimized. An abundance of literature has reported that because of these programs, outcomes are vastly improved with fewer complications and a shorter length of hospital care after surgery. At the core of these improvements is the management of metabolism and nutrition. Still, despite these improvements, a poor nutritional status remains a highly relevant risk for patients that should not be neglected. In this review, we present an update on the management of nutrition for the surgical patient in the era of ERAS and prehabilitation.

2. IDENTIFYING NUTRITION RISK BEFORE SURGERY

A poor nutritional status represents a well-recognized risk for complications in major surgery. Malnutrition before oncologic and nononcologic major surgery is frequent, and it can be due to several reasons (136). GI abnormalities (e.g., malabsorption of nutrients and mechanical obstruction), treatment-related side effects (e.g., neoadjuvant therapy and steroids), and patient-related factors (e.g., comorbidities, socioeconomic status, and anorexia) contribute to impair the preoperative nutritional status of surgical patients (54). Moreover, preoperative malnutrition frequently occurs with other morbid conditions such as impaired functional capacity, frailty, and sarcopenia (10, 87), and it is associated with poor mental health (53). A recent meta-analysis including 18,039 medical and surgical patients demonstrated that among those who were malnourished, 49.7% were also sarcopenic and 41.6% were prefrail (47). Notably, the odds of being sarcopenic or prefrail

Table 1 Critical nutritional and nonnutritional parameters implicated in increasing the risk of complications after major abdominal surgery

Nutritional parameters	Body mass index (both low and high)
	Unintentional body weight loss
	Low muscle mass and reduced muscle function (sarcopenia)
	Visceral obesity
	Sarcopenic obesity
	Reduced food intake
Nonnutritional parameters	Malignancy
	Age (>70 years)
	Sex (male)
	Ethnicity (non-Caucasian)
	Decompensated diabetes
	Chronic organ dysfunction (heart, lung, kidney, liver, pancreas, intestine, blood, etc.)
	Charlson Comorbidity Index
	Drug/alcohol dependency
	Chronic corticosteroid use
	American Society of Anesthesiologists physical status classification
	Bleeding disorders
	Active smoking
	Frailty
	Intraoperative blood loss
	Perioperative blood transfusion
	Duration and complexity of surgery
	Emergency operations
	Intravenous fluid overload
	Surgical field contamination
	Open surgery
	Persistent postoperative hyperglycemia (>180 mg/dl or 10 mmol/L)
	Low phase angle at bioimpedance analysis
	Albumin (<30 g/L)

among malnourished surgical patients was 16 and 4 times higher than among nonmalnourished surgical patients, respectively.

However, a deranged nutritional status is only one element in the assessment of the risk of a complicated postoperative course. Surgery is a treatment that causes an injury to the body that results in specific stress responses, which are outlined in Section 4. These reactions put pressure on vulnerable organs and systems in the body. Several reactions to surgical stress can be modified, and many nonnutritionally related risk factors may contribute to postoperative morbidity. **Table 1** summarizes the critical variables for evaluating the nutritional and nonnutritional risks of having complications after major abdominal surgery. This broader spectrum of risk factors should also be kept in mind when the current recommendations for the management of nutritional risk are discussed.

It is important to identify modifiable risk factors as early as possible to enhance the chances of an uneventful postoperative course, both in the early and late postoperative periods, and of a high quality of life (61, 136). A poor nutritional status is a modifiable factor that increases the risk of postoperative complications and a prolonged hospital stay (19, 74, 136). This metabolic risk may not always be clinically apparent and is often likely to be underestimated in a society where obesity is prevalent.

Therefore, standardized screening for malnutrition should be mandatory for all major surgeries and, if indicated, followed by full nutritional assessment. A well-validated tool for surgical patients is Nutrition Risk Screening (NRS-2002) (78). A NRS $\geq$ 3 indicates a risk for malnutrition. Parameters of the NRS are body mass index (BMI), unintended weight loss, reduced food intake, and severity of disease.

Malnutrition is often accompanied by sarcopenia. While sarcopenia is a decrease in muscle mass and function, malnutrition is characterized by a decrease of body cell mass. Especially in geriatric patients, sarcopenia may occur without malnutrition (143). This sarcopenic obesity is a special risk factor, since an increased amount of fat may hide an undetected decrease in muscle mass (5, 8, 57). The diagnosis of sarcopenic obesity requires altered skeletal muscle function parameters and altered body composition with increased fat mass plus reduced muscle mass. A staging for the severity of sarcopenia has related it to the presence of complications (30, 135). In esophageal cancer, sarcopenia is associated with more overall complications, major complications, and delayed hospital discharge (67, 135). In gastric cancer patients, preoperative sarcopenia has been shown to be associated with reduced overall survival (81). Preoperative poor muscle function along with impaired nutritional status has a negative impact on postoperative mobilization and pulmonary function.

For these reasons, muscle mass measurement has been incorporated into a consensus through the Global Leadership Initiative on Malnutrition (GLIM) criteria for malnutrition. The GLIM criteria have been endorsed by the major medical nutritional societies and adopted worldwide (21). A two-stage procedure is recommended, starting with one of the usual screenings, such as the NRS. One phenotypic and one etiological criterion must be fulfilled for the diagnosis of malnutrition. Phenotypic criteria are involuntary loss of body weight, diminished BMI, and low muscle mass. Etiological criteria are low food intake or absorption and the disease burden/inflammation (6, 21). Malnutrition, according to GLIM criteria, was associated with postoperative complications in patients with abdominal resections in a Norwegian registry study (126). In several studies, the prevalence of malnutrition was higher when using GLIM criteria than when previous definitions were used (27).

In line with the GLIM criteria, the use of computed tomography (CT) scans for body composition analysis and muscle mass can be recommended (57, 65, 116, 140). Alternatively, bioelectrical impedance analysis may be used (35). Measurement of muscle function such as hand grip strength has not been widely implemented in clinical routines but can be performed very easily.

When scanning is performed for diagnostic reasons in patients with cancer, CT-based measurement of body composition has been introduced for the assessment of muscle mass and the calculation of the skeletal muscle index (SMI). Impaired radiodensity is considered a parameter of muscle quality. In the axial scan at lumbar level 3, skeletal muscle area and density can be calculated (55). A new risk classification according to BMI and SMI has been recently proposed: Patients with high SMI, excluding those with BMI $\geq$ 35 kg/m^2, are considered low-risk, and those with low SMI and/or BMI $\geq$ 35 kg/m^2 are considered high-risk (94). In numerous studies, CT-derived reduced muscle mass (i.e., sarcopenia) has shown prognostic impact (67, 97, 98). Using CT-determined reduced muscle mass, the GLIM criteria have been reported to be correlated with surgical outcomes in patients undergoing major abdominal surgery (20).

If body composition analysis from computerized tomography is not available, the ESPEN surgery guideline provides a definition of high metabolic risk if one of the following criteria is fulfilled: weight loss > 10–15% in six months, BMI < 18.5kg/m^2, NRS > 5, and preoperative albumin level < 30 g/L without coexisting liver or kidney failure (136). Serum albumin is no longer considered a parameter reflecting nutritional status per se but has been shown to have prognostic value when evaluating the risk for postoperative complications (34, 139).

The current ESPEN guidelines (137) provide a good clinical practice recommendation for nutrition therapy without delay (*a*) in patients with malnutrition and those at a nutritional risk, (*b*) in patients anticipated to be unable to eat for more than 5 days postoperatively, and (*c*) in patients anticipated to have low oral intake who cannot maintain more than 50% of the recommended intake for more than 7 days.

In cancer patients undergoing neoadjuvant treatment before major abdominal surgery, nutritional support is recommended to prevent weight loss and deterioration of the nutritional status.

3. PREOPERATIVE NUTRITIONAL SUPPORT IN THE CONTEXT OF PREHABILITATION

Prehabilitation aims at improving the patient's resilience to withstand surgical stress. It represents a multimodal preoperative treatment where patients are prepared to better withstand surgical stress with specific nutritional, exercise, and psychological interventions with the overarching aim of recovering better after surgery. More specifically, preoperative nutritional support in the context of prehabilitation has several goals: (*a*) to correct malnutrition when present, (*b*) to support protein anabolism to better withstand the catabolic response of surgery, (*c*) to support the energetic cost of prehabilitation exercise interventions, and (*d*) to increase the anabolic effect of resistance exercise.

As outlined above, it is now well recognized that preoperative malnutrition leads to adverse outcomes and increases health-care resources and costs (139). Furthermore, poor preoperative nutritional status can negatively influence the response to prehabilitation (49, 50). In fact, severely malnourished patients did not respond to a 4-week prehabilitation program as they were not able to significantly improve their functional capacity (measured as a 6-min walking distance change). Fortunately, if identified in time, malnutrition can frequently be corrected before surgery and postoperative outcomes can be improved (17, 147) by identifying barriers to food intake and acting to ensure patients receive the recommended caloric (around 25 kcal/kg/day) and protein (around 1.5 g/kg/day) intake. This is preferably achieved through balanced meals and oral nutritional supplements (ONSs) and, in selected cases, through enteral feeding (136) or even by parenteral nutrition (see Section 9).

Support of protein anabolism in preparation for surgery is another important goal of prehabilitation. A catabolic state with high protein turnover, with or without the requirement of specific amino acids, is frequently observed preoperatively accompanying severe illness, inflammation, and oncologic disease and independently from the presence of malnutrition (54). This metabolic state is inevitably aggravated by the catabolic response induced by surgical stress, leading to insulin resistance and loss of muscle mass (48). Clinically, this is manifested by fatigue and loss of function and strength that, even in healthy patients or in the absence of postoperative complications, can require several weeks to return to preoperative states (37, 48). Therefore, implementing preemptive nutritional anabolic strategies that can attenuate surgical catabolism, in malnourished as well as in nonmalnourished patients, has shown to facilitate surgical recovery (48, 51). In a pooled analysis of two randomized controlled trials, trimodal prehabilitation and trimodal postoperative rehabilitation in colorectal surgical patients (both programs including aerobic and resistance exercise, nutritional optimization, and 20 g of whey proteins) were compared. Prehabilitation attenuated the loss of lean body mass compared to that observed in patients treated with a rehabilitation intervention (51). This benefit might be particularly valuable for patients whose reserve is already reduced, such as frail and sarcopenic patients (112), or in those experiencing a significant loss of muscle mass with neoadjuvant therapy (28, 69). In elderly patients or those with malignant disease, anabolic resistance might prevent an anabolic state before surgery (33, 103). Still the metabolic benefits of prehabilitation interventions can appear in the postoperative period, even if not manifested preoperatively (51).

Owing to the increased energetic cost of exercise, and the high prevalence of malnutrition in the surgical population, ensuring adequate nutritional support during the entire prehabilitation period is essential. It may be speculated that energy and protein intake should be higher during prehabilitation than that recommended by the current guidelines to better sustain exercise interventions. Particular attention should be paid to severely malnourished patients who might not respond to prehabilitation (49, 50) or even deteriorate if they do not have sufficient energetic reserves to sustain exercise. By contrast, moderately malnourished patients have been shown to respond to prehabilitation even better than nonmalnourished patients (49). These findings suggest that nutritional interventions should be combined with exercise training (131), as studies have shown that preoperative exercise alone fails to improve the functional capacity of colorectal surgical patients (20). In fact, a subsequent study demonstrated that a 4-week trimodal prehabilitation program including exercise and nutritional and psychological interventions improved the preoperative functional capacity (with a mean 6-min walking distance change of 40 ± 40 m) of colorectal patients (85). Further support for the important role of nutrition in the context of a multimodal prehabilitation program is provided by the results of a meta-analysis evaluating the efficacy of nutritional prehabilitation interventions with and without exercise in patients undergoing colorectal surgery (47). It was shown that both strategies were effective in reducing length of hospital stay by about 2 days (47).

Finally, nutritional support during prehabilitation aims at enhancing the anabolic effect of resistance exercise, as it exerts an independent and additive effect on muscle protein synthesis (61, 94). To obtain this goal, it is necessary to achieve a positive protein balance, with protein synthesis (favored by dietary protein consumption, protein ingestions, and resistance exercise) exceeding protein breakdown (induced by fasting states, concomitant disease, treatments, or resistance exercise) (54, 110). This is possible by spreading protein intake equally across all meals and after exercise (i.e., the equal distribution hypothesis). Maximal muscle protein synthesis plateaus with the ingestion of 20–35 g of protein (i.e., the muscle full effect). However, more than 35 g of protein per meal might be required to also sustain nonmuscle protein synthesis (i.e., whole-body protein). In addition, supplementation with a high dose of omega-3 fatty acids (2.0–2.2 g/day) and vitamin D might further potentiate the anabolic response of patients with reduced muscle mass (113). Whey proteins, which are rapidly digestible, are particularly advantageous to stimulate protein synthesis after resistance exercise (111); a clinically meaningful improvement of functional capacity before colorectal surgery has been observed after their administration (52).

While there is ample evidence demonstrating that prehabilitation improves preoperative functional capacity and optimizes functional recovery, some recent studies have also shown better postoperative outcomes, such as fewer complications (7, 8). A very recent multicenter randomized clinical trial (RCT; the PREHAB trial) conducted in colorectal cancer patients waiting for surgery, which compared multimodal prehabilitation (including nutritional intervention) with standard preoperative care, reported less severe and fewer medical postoperative complications in patients treated with prehabilitation. A better postoperative functional recovery was also observed (101).

4. THE STRESS RESPONSE TO SURGERY

Any injury to the body causes a series of reactions locally and systemically. In particular, the systemic reactions caused by an injury of any magnitude, such as in hospital surgeries, have profound effects on body metabolism (120). This in turn affects many key bodily functions: It sets off healing processes but also reactions that influence many other functions in the body that will interfere

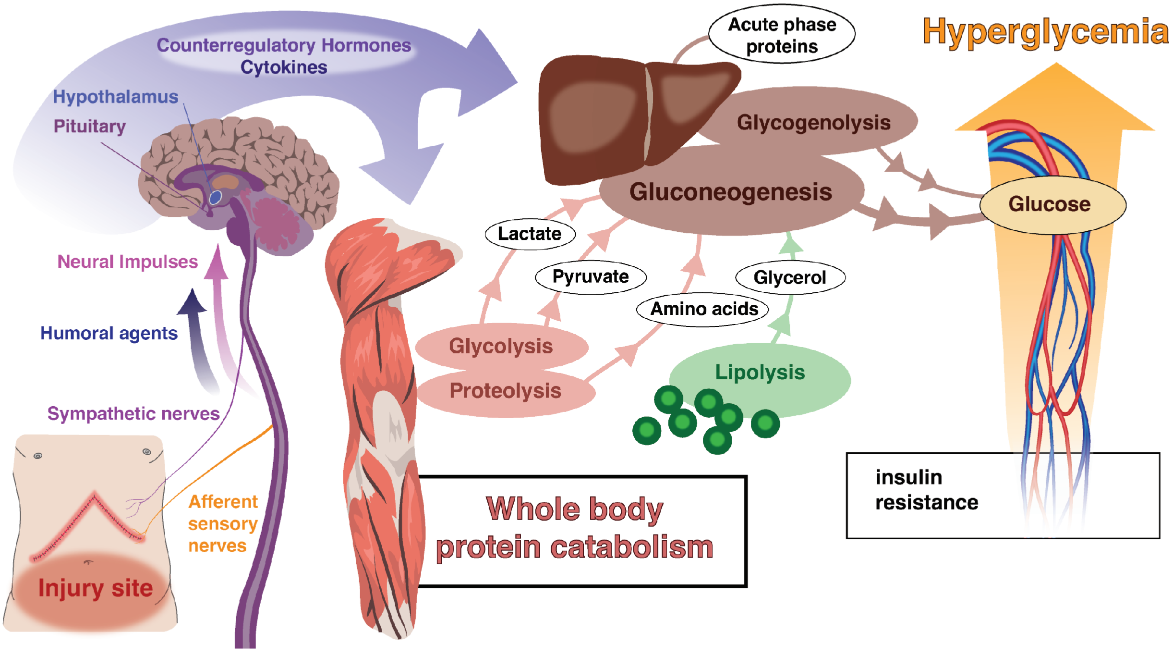

Figure 1

The stress reactions to surgical injury. Tissue damage induced by major surgical operations sets off several neural and humoral impulses, including cytokines that are initiated at the site of injury to activate the hypothalamic–pituitary–adrenal axis. This elicits an almost immediate response in catecholamines, shortly followed by releases of cortisol and glucagon. This cascade of stress hormone release causes a drastic and rapid change in body metabolism. Energy reserves are mobilized, and the entire body is set to a state of catabolism. Because of the overwhelming release of stress hormones, insulin actions are overruled, and a state of insulin resistance is instituted. Clinically, this is often recorded as the development of hyperglycemia that is associated with proteolysis and lipolysis to supply the liver with substrates for gluconeogenesis as well as amino acids as building blocks for acute phase proteins. Figure reproduced with permission from Reference 48.

with recovery. Here, we provide a broad description of these reactions followed by an overview of how modern surgical practice protocols can modify these reactions for the benefit of the patient.

As shown in **Figure 1**, the injury induced by a surgical operation sets off immediate neural and humoral impulses, including cytokines that are initiated at the site of injury to activate the hypothalamic–pituitary–adrenal axis. This elicits an almost immediate response in catecholamines, shortly followed by releases of cortisol and glucagon. This cascade of stress hormone release very quickly causes changes in body metabolism. Energy reserves are mobilized, and the entire body enters a state of catabolism. Because of the overwhelming release of stress hormones, a state of insulin resistance is instituted. As a result, hyperglycemia develops alongside proteolysis and lipolysis to supply the liver with substrates for gluconeogenesis as well as amino acids as building blocks for acute phase proteins.

There is growing evidence that hyperglycemia following surgery is harmful. Postoperative elevations of glucose have been associated with higher mortality, need for a longer stay, more infections, and other complications. Because of the shift in endocrine milieu to catabolism after surgery, glucose metabolism is drastically changed. In the nonstressed state when hyperglycemia develops after a meal, insulin elevations activate GLUT4 transporters in primarily muscle to store the glucose in muscle glycogen. This keeps glucose levels in control. Very quickly during surgery, this pathway is blocked, and at the same time gluconeogenesis in the liver is activated to produce more glucose to cause a rise in glucose levels that persists for days. In this situation, cells that are not sensitive to insulin, including blood cells and those in the endothelium and the brain, start to take up much more glucose. These cells take up glucose, depending on the prevailing level of glycemia, using other types of transporters of glucose (GLUT1). When the normal pathway for glucose storage is not functioning, these cells have no protection against increased glucose influx and are overwhelmed by it. This renders them dysfunctional, and they start to produce excess superoxide radicals that eventually cause apoptosis.

Protein metabolism is also changed after surgery. Muscle proteins are mobilized to provide amino acids for gluconeogenesis and as building blocks for protein synthesis in the liver and at the site of the injury for healing. Whole-body protein breakdown and amino acid oxidation are increased. A normal person undergoing surgery has been estimated to lose between 1.2 and 2.4 kg of wet muscle. In the case of septic complications, daily losses may amount to as much as 800 g of muscle mass. This loss of muscle mass in combination with the loss of energy sources from glycogen has a major impact on muscle function, hampers mobilization, and affects breathing capacity. If immobilization is added, there will be further muscle atrophy. While these effects apply to everyone, in the elderly and patients with malnutrition, they present an especially significant risk.

5. ERAS PROTOCOLS MODIFY STRESS RESPONSES

ERAS was initiated by a small group of surgeons in northern Europe in 2001 (91). The work with ERAS was inspired by the multimodal approach to recovery presented by Henrik Kehlet (72) and shown to be very effective. The hypothesis studied by the ERAS group tested whether building care protocols based on all elements of care throughout the perioperative period that were reported to enhance the recovery of patients undergoing major operations could improve outcomes (120). After reviewing the literature, the group created a perioperative guide to the care of the patient undergoing colonic resections (36) that proved to be highly effective (59). Today ERAS is one of the most important developments in surgery (91). Multiple studies in just about all types of surgeries have shown that adhering to the ERAS protocol has major effects on outcomes (60). Early reports by Kehlet (72) showed substantial reductions in length of stay (LOS). Later, ERAS reported up to 40% to 50% reductions in complications (56, 133) and, more recently, associations with long-term survival after cancer surgery (60, 108). Reductions in bed days and complications have yielded major savings for health-care providers and society in general (130).

Because ERAS involves all aspects of care and the entire care pathway, it also cuts across the traditional boundaries of specialties and professions (120). ERAS is built on a group concept of multidisciplinary and multiprofessional collaboration, from the very start of the formation of the guidelines to the implementation and operation of care on the hospital floor. Surgical specialists, anesthesiologists, intensivists, nurses, nutritionists, and physiotherapists all come together as the clinical team to run ERAS. It is also important to involve decision-makers and managers in the process.

It is essential that all the care elements of ERAS are integrated, as shown in **Figure 2**. It is by working together and seeing the entire pathway that each individual caregiver can reach a better understanding of her/his specific role in the bigger picture. A key to keeping track of the care delivered is to have the entire local ERAS team audit both processes and outcomes continuously because it is impossible to implement and follow an ERAS protocol unless the practice is known in detail at all times (89, 120). Making shortcomings in care obvious to the care team is often the best trigger to institute change and reach major improvements fast.

ERAS has been adopted and endorsed by many organizations around the world. Still, national outcomes data (where available) indicate that the true practice of ERAS is still not widespread in

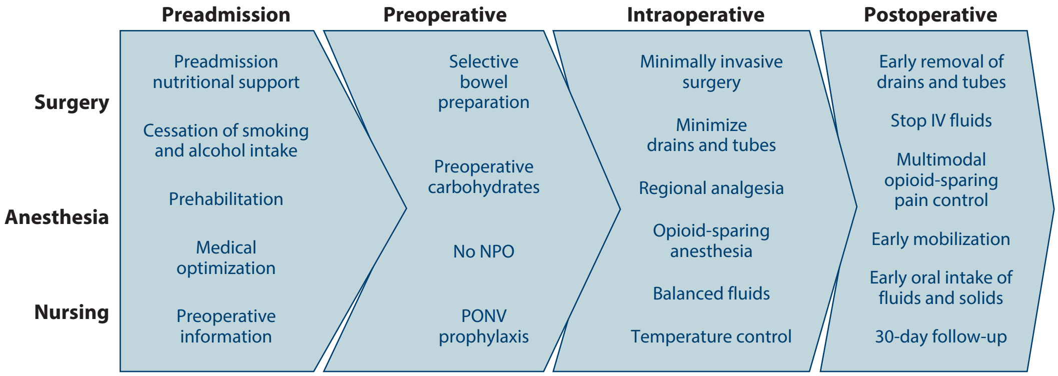

Figure 2

The integrated care pathway of an ERAS protocol. By working together and seeing the entire pathway, each individual caregiver can reach a better understanding of her/his specific roles in the bigger picture. A key to keeping track of the care delivered is to have the entire local ERAS team audit both processes and outcomes continuously. This is important since it is impossible to implement and follow an ERAS protocol unless the practice is consistently known in detail. Abbreviations: ERAS, Enhanced Recovery After Surgery; IV, intravenous; NPO, *nil per os* (nothing by mouth); PONV, postoperative nausea and vomiting. Figure adapted with permission from Olle Ljungqvist.

most countries, and the delivery of care is extremely variable and far from evidence based (90). As can be seen in **Table 2**, the care to be delivered in ERAS consists of simple care elements that are not hard to implement. Many of them have a direct impact by dampening stress reactions and maintaining normal homeostasis to support the return of normal functions.

Several of the elements of care have direct relevance to nutrition and metabolism, which play important roles for the effectiveness of ERAS. The specific roles of nutritional care per se are discussed in Section 6. Here, we discuss the role of some key elements that allow the best possible circumstances for nutritional care to reach its aims. In **Table 1**, all basic elements of ERAS are listed, and many of them have effects on metabolism and nutritional care.

Several elements of care contribute to and interact with two sought-after outcomes: One is to have normal gut function return as fast as possible, allowing the patient to drink, eat, and move bowels. This avoids some of the most common problems after surgery: postoperative nausea and vomiting and ileus. These complicating factors are often the effects of care delivered in more traditional settings and thus are effectively reduced by the employment of ERAS elements. The other important aspect for recovery is to ensure that the nutrition received by the patient is managed appropriately. For this to happen, insulin resistance must be minimized. Many of the treatments in the ERAS protocol have several effects and can act positively for both of the above objectives.

In the preoperative phase, avoiding fasting and giving a preoperative carbohydrate drink specifically designed for the occasion have several effects. Preoperative thirst, hunger, and anxiety are improved; less IV fluid is needed during surgery; and glucose levels are much better maintained both during and after surgery because of improved insulin sensitivity and reduced insulin resistance. The latter also improves whole-body protein balance (107).

The use of mid-thoracic epidural analgesia is an effective way to block the release of both catecholamines and cortisol (142). Epidurals also affect gut motility by supporting the vagal nerves and blocking the sympathetic nerves, and they give very effective basic pain relief. This helps minimize the use of opioids both during and after surgery. Opioids have several disadvantageous effects on nutritional care. They are a main cause of postoperative nausea and vomiting (100), they slow down gut motility, and they cause dizziness that hampers mobilization. In addition, the

Table 2 Basic care elements of ERAS and their role in management of nutritional care (based on the colorectal guidelines from the ERAS Society)

Timing	Basic care elements of ERAS	Aim(s) related to nutrition
Preadmission items	Preadmission information and counseling	Patient involvement
	Preoperative medical optimization	NA
	Prehabilitation	Nutrition and exercise
	Preoperative nutritional screening and care as needed	Nutrition for at-risk patients
	Anemia screening and treatment as needed	NA
Preoperative items	Prevention of PONV	Supporting oral intake
	Avoidance of long-acting sedatives	Reducing PONV
	Antimicrobial prophylaxis (IV) and skin preparation	NA
	Avoidance of oral bowel preparation in colonic surgery	Avoiding dehydration
	Preoperative carbohydrate loading	Reducing insulin resistance
Intraoperative items	Standard anesthetic protocol	Pain management
	Balanced fluid and electrolyte therapy	Keeping euvolemia and supporting GI function
	Minimally invasive surgery	Reducing pain and ileus
	Avoidance of surgical site drains	NA
	Maintaining temperature control	Avoiding protein losses
Postoperative items	Avoidance of nasogastric tubes	Allowing oral intake
	Multimodal standardized analgesia to minimize opioid use	Minimizing opioids and reducing PONV and ileus
	Thromboprohylaxis	NA
	Balanced fluid and electrolyte therapy	Keeping euvolemia and supporting GI function
	Early removal of urinary catheter	Supporting mobilization
	Prevention of postoperative ileus	Supporting GI function
	Postoperative nutritional care	Oral and IV support as needed
	Early mobilization	Building strength/stimulating appetite

Abbreviations: ERAS, Enhanced Recovery After Surgery; GI, gastrointestinal; IV, intravenous; NA, not applicable; PONV, postoperative nausea and vomiting.

use of opioids in surgery is one of the most common ways patients get caught up in addiction (83). The use of epidurals has some drawbacks, with occasionally reported high failure rates and problems with maintaining blood pressure both during and after surgery. Today, epidurals are primarily recommended for open surgery, while for laparoscopic surgery the use of spinals and other blocking techniques has been showing similar or better results.

Fluid overload is another common cause for postoperative ileus (15). In traditional care, patients often gain 4–6 kg in weight after the operation simply due to excess IV fluids. Not only does this cause a delay in the return of GI function, but fluid overload has also been shown to be a cause of several common complications (16). Modern guidelines suggest that keeping within 0–2 kg weight gain the day after surgery is a good target to minimize these problems. Dehydration is also bad for the patient, so the target is to keep a fluid balance.

In the traditional setting, surgeons considered their domains and anesthesiologists covered their own. No one had an overview of the entire care pathway. There was little or no insight as to how a problem caused by a single decision early in the patient's journey could cause further problems down the road. If, for instance, the surgeon ordered oral bowel cleansing preoperatively, the patient would be dehydrated when arriving to surgery. During induction of anesthesia, the patient's blood pressure would fall due to the dehydration, and this would typically trigger the anesthesiologist to give a lot of fluids to raise the blood pressure, thus causing an overload of fluids. The surgeon might then find the patient edematous with ileus on the day after surgery. If ERAS guidelines are followed, the patient would receive the carbohydrate drink and no bowel preparation and thus would remain more normal in terms of blood pressure and fluid balance at the start of surgery. This is one example of how following the ERAS model where everyone is made aware of how their care decision affects the next in line can help avoid unnecessary problems.

Nutritional care, however, should start well before the onset of the operation itself by the identification of poor nutritional status, as outlined in Section 3. Studies have shown that it is quite possible to improve adherence to the nutritional care elements of ERAS very quickly (96). This in turn is associated with a series of improvements for postoperative nutritional aspects of the care, GI function, and daily activities as well as improved clinical outcomes. It is also striking to find that these effects are not only seen in younger patients but almost equally effective in the old and frail. The only difference found between these effects in young and fit and old and frail patients was a one-day delay in the resumption of daily activities.

6. NUTRIENTS WITH SPECIFIC EFFECTS

In surgical patients, the traditional rationale behind the use of nutritional support has been the desire to prevent or correct nutritional derangements and, consequently, the malnutrition-associated risk of postoperative morbidity and mortality. In addition to the risks of poor nutritional status, it is well recognized that the tissue trauma induced by major surgery and general anesthesia generates homeostatic disorders, immunosuppression, generalized inflammation, and gut dysfunction. Therefore, targeting nutritional therapy for the simple maintenance of nutritional and metabolic needs may be inadequate. Instead, the target may be shifted to the preservation of a trophic gut mucosa through enteral nutrition, the boosting of the immune response, and the minimization of hyperinflammation. These goals have been attempted through the administration of specialized nutrients. The term immunonutrition (IMN) or pharmaconutrition encompasses the use of specific nutritional substrates that have the ability to modulate specific mechanisms involved in several immune and inflammatory pathways. To achieve these goals, these substrates must be administered in supraphysiologic doses. Moreover, the expected effects may be obtained even if the overall goal of calorie and nitrogen support is not met. Thus, the effects of these nutrients are ascribed more to pharmacological activity than to nutritional repletion (12). This phenomenon is defined as the effect of nutrients dissociated from nutrition, and as such the benefits should also be observed in patients without nutritional imbalances.

The first formulations reaching the market were enteral feeds containing several immunonutrients such as arginine, omega-3 fatty acids, and ribonucleic acid with or without glutamine. Although several multiple-component formulas are now available, only a few of them have been tested in RCTs to prove efficacy. The development of such enteral formulas started in the 1980s with extensive in vitro experiments first and then gradually in animal models of burn injury, sepsis, and bacterial translocation. Clinical use, with the first phase II RCTs focusing on surrogate endpoints such as nutritional, immune, and inflammatory mediators (43, 122), became available in the mid-1990s. Since then, dozens of RCTs have been published and their results pooled in meta-analyses and systematic reviews (44).

In the most recent meta-analysis by Khan et al. (75), 37 RCTs were included (22 preoperative IMN studies, 11 perioperative IMN trials, and 9 postoperative IMN trials; 4 trials had multiple IMN protocols) and reported on 3,793 patients. The main outcome, postoperative infectious complications, was reduced with IMN compared to placebo/control [odds ratio (OR) 0.58, 95% confidence interval (CI) 0.47–0.72]. This association was significant in a subgroup analysis only for preoperative and perioperative administration and in trials including upper GI cancers, colorectal cancer, and mixed GI cancer populations, and the effect was independent of nutritional status. IMN in a pooled analysis reduced surgical site infection (OR 0.65, 95% CI 0.52–0.81), anastomotic leak (OR 0.67, 95% CI 0.47–0.93), and LOS by 2 days (95% CI −3 to −0.87).

Very few other products in the field of clinical nutrition have been tested in such an extensive way. Overall, the results suggest that IMN should be the preferred strategy in abdominal cancer patients. However, most of the RCTs included in the abovementioned meta-analysis were performed when the ERAS protocols were not or only partially in use. ERAS pathways per se have been repeatedly shown to significantly reduce postoperative morbidity after colorectal surgery (56, 128) and across many other types of surgical interventions (134). Thus, it might be that the benefits of IMN are no longer evident when a full ERAS is implemented. Moya et al. (104) addressed this issue and designed an RCT to test the on-top effect of IMN in patients undergoing colorectal resection under an established ERAS protocol. The results showed that the patients who received IMN presented with fewer complications and, in particular, a significant decrease in infectious complications. In the near future, the role of pharmaconutrition should be tested in two other emerging fields of oncologic surgery: neoadjuvant treatments and prehabilitation.

Hyperglycemia is a widely acknowledged risk factor for postoperative morbidity in several surgical settings (71). The presence of chronic alterations of glucose metabolisms have been associated with both an increased rate of unfavorable outcomes following surgery and perioperative dysglycemia. Even in the absence of diagnosed diabetes mellitus (DM), hyperglycemia is reported to increase the occurrence of overall, severe, infectious, and procedure-related complications, as well as longer hospitalization and failure to rescue (76). It is now established that postoperative hyperglycemia is mainly caused by the occurrence of peripheral insulin resistance and enhanced further by prolonged preoperative fasting (32). Because of the deleterious effects of hyperglycemia, blood glucose levels should be strictly monitored so that hyperglycemia may be promptly treated or avoided (32). Yet, in clinical practice, this is not followed for all patients unless they are under intensive care, are receiving a high dose of IV glucose, or suffer from diabetes. Therefore, the real incidence of postoperative hyperglycemia and its potentially harmful consequences may be largely underestimated in nondiabetic or low-risk patients. Normal postoperative blood glucose levels may be achieved with several strategies. Continuous insulin infusion is commonly used in critically ill patients because of its protective effect on outcome. However, there is a concern that intensive glucose control with insulin without rigorous monitoring may result in hypoglycemia with subsequent severe complications (106). In patients who are candidates for elective major surgery, a safe and effective method to minimize postoperative hyperglycemia is the administration of oral preoperative carbohydrate (CHO)-rich beverages (42). The preoperative carbohydrate drink must be designed and proven to have certain effects (not all marketed drinks do), including a rapid passage from the stomach for safety reasons, and to elicit an insulin response at the level of a normal meal (i.e., approximately 5–6 times the basal fasting level) to set off the change of metabolism from a fasted to a fed state. Finally, the drink should have a proven effect on postoperative insulin sensitivity as measured by the hyperinsulinemic normoglycemic clamp tested at physiological levels of insulin (127). The drinks shown to achieve these goals are composed of mainly maltodextrins with some glucose, fructose, and salts.

A large body of recent literature (45) endorses the use of a preoperative carbohydrate drink taken up to 2 h before the operation as a safe treatment. This simple treatment is effective in reducing perioperative insulin resistance and hyperglycemia. In a large RCT, preoperative maltodextrin-enriched drinks significantly reduced the rate of insulin administration. Insulin was administered to 8 (2.4%) patients in the CHO group and 53 (16.0%) patients in the placebo group for treating blood glucose levels >180 mg/dl [relative risk (RR) 0.15, 95% CI 0.07–0.31] (42).

Carbohydrate oral solutions have also been shown to improve patient well-being and comfort. In particular, the treatment, when compared with fasting or placebo, was effective in reducing nausea and vomiting, hunger, thirst, dry mouth, tiredness, fatigue, weakness, malaise, anxiety, and depression. However, CHO loading does not affect postoperative pain, duration of hospitalization, or surgery-related morbidity (18).

Hence, the routine administration of an oral CHO-rich solution to nondiabetic patients who are candidates for a major abdominal operation could be an alternative strategy to prevent serial and repeated blood glucose measurements performed to strictly monitor the kinetics of glucose metabolism, thus reducing the risk of unidentified, potentially dangerous hyperglycemia episodes in most patients. Drinks containing complex carbohydrates are relatively cheap and easy to administer. Moreover, they have been proven to be safe even when given up to 2 h before general anesthesia since the rate of regurgitation and aspiration is not significantly different from nil-by-mouth treatment (42).

So far, there is limited evidence on the efficacy and safety of preoperative CHO loading in patients suffering from DM. Up to now, most research included patients with well-controlled DM (typically defined by an HbA1c < 7%). Because carbohydrate loading aims to increase insulin secretion, the use of carbohydrate loading is not recommended for those with type 1 DM (139). A recent scoping review (87) on the use of CHO-rich solutions in patients with well-controlled type 2 DM concluded that the benefits of preoperative carbohydrate loading outweighed the risks of glucose variability in most patients. However, the level of evidence was low given the paucity of well-designed RCTs in this specific cohort of patients.

A further unexplored use of CHO-loading is in major pancreatic resections where postoperative severe hyperglycemia is frequently observed owing to the combined effect of surgery-related injury and removal of beta cells.

7. MODULATION OF THE GUT MICROENVIRONMENT

Probiotics are defined by the World Health Organization as live microorganisms that confer beneficial effects to the host when given in sufficient quantities. They survive transit through the GI tract, with most of their activity being in the colon. Prebiotics are food ingredients that escape digestion in the upper GI tract and stimulate the growth and activity of selective bacterial genera in the colon. When prebiotics and probiotics are combined in a single preparation, they are known as synbiotics. The mechanisms of action for probiotics include competitive exclusion of potentially pathogenic bacteria and direct antimicrobial effects (105). The proliferation of probiotic bacteria can be enhanced by the coadministration of prebiotics, and certain bacterial genera are stimulated selectively by these compounds that supply nutrients for their growth (114).

Analysis of pooled data from RCTs demonstrates that the perioperative administration of probiotics and synbiotics significantly reduces the risk of infectious complications following abdominal surgery, with the magnitude of this risk reduction approaching 50% (RR 0.56; 95% CI 0.46–0.69). The reduction in risk of infection was greater with synbiotic preparations than with probiotics alone, confirming that the beneficial effects of probiotics can be enhanced by the addition of prebiotic substrates. In addition, there was a reduction in LOS in the synbiotic group but not the probiotic group. There was no impact on noninfectious complications or mortality (26).

Probiotics and synbiotics are safe in the setting of elective abdominal surgery and associated with few adverse effects. Both probiotics and synbiotics reduce the risk of postoperative infection. However, at present, there is no standardized probiotic preparation, duration of treatment, or route of administration, making a comparison of the trials challenging. In addition, some studies have used multispecies preparations, and it is unclear which strain is the best and what role it has. Furthermore, control groups in some studies received only standard care, whereas other studies employed a placebo.

8. POSTOPERATIVE NUTRITIONAL SUPPORT

The restoration of an adequate caloric intake in the postoperative period is fundamental for patient recovery. There are two main obstacles for the resumption of normal intake of food: the triad of nausea, vomiting, and postoperative ileus hindering the return of normal gut function and the patient metabolic capacity to make use of substrates administered.

Overcoming these obstacles is key since prolonged starvation postoperatively enhances the activation of a hormonal cascade with increased gluconeogenesis and release of proinflammatory cytokines, leading to protein wasting, peripheral insulin resistance, and, consequently, impaired wound healing and increased risk of complications (72). The risk of postoperative undernutrition is even more detrimental in patients who present with malnutrition at admission, a frequent condition, especially in oncological surgery settings (4).

For most patients undergoing elective surgery, except for those undergoing upper GI and pancreatic procedures, no contraindications to resumption of oral diet on the afternoon of or the morning after surgery have been reported (82). Especially when ERAS protocols are followed, free food at will is typically well tolerated and associated with shortened time to first flatus, as well as reduced length of hospitalization (3, 96). The basis for postoperative feeding in most surgeries is normal food. When food intake alone does not meet energy and protein needs, it should be supplemented by ONSs.

However, previous reports from nutritionDay, a cross-sectional audit screening and monitoring for malnutrition worldwide, showed that nearly half of hospitalized patients do not eat their full meals, and that decreased food intake was associated with increased hospital mortality (11). Preliminary data from nutritionDay focusing on surgical patients showed that merely one-third of postoperative patients tolerated a full meal and around 25% ate nothing, either because of a *nil per os* prescription or despite being allowed to eat.

There are several reasons why normal food is not tolerated postoperatively. The most common reason is that traditional treatments are still being delivered to patients. Several factors can lead to postoperative GI dysfunction, identified as nausea, vomiting, abdominal distension, and absence of bowel motility, thus limiting the routine practice of early food resumption. First, despite the recommendation of drinking as soon as patients are awake and nausea-free after the surgical procedure, several patients still receive IV fluid administration for a few postoperative days. The use of IV fluid therapy after surgery should be reserved for specific cases of hypovolemia, ongoing losses (e.g., high-output stoma or vomiting), or fluid shift to the extracellular compartment. The risk of these deficits, or more commonly of overload, remains nonnegligible and associated with an increased rate of postoperative morbidity, impaired microvascular perfusion with tissue edema and prolonged ileus, and longer hospitalization, as well as higher costs (92, 124, 132).

The type of anesthesia used affects bowel recovery and may condition postoperative GI dysfunction. Despite current evidence suggesting opioid-sparing anesthesia, epidural analgesia, and peripheral μ antagonists for prevention of primary ileus, the incorporation of such interventions into clinical practice remains inconsistent (22). In addition, emergency settings may represent a limitation of resumption of early oral intake of liquids and food. Patients undergoing emergency surgery are more likely to have open surgery than minimally invasive operations (115). These patients are at increased risk of fluid and electrolytic imbalance and may present at admission with ileus or gastric outlet and be in need of a nasogastric tube (123). All these elements prevent the early resumption of oral intake (121). Lastly, several surgery-related or intrinsic patient factors may reduce compliance to early oral feeding. In a large series of patients undergoing minimally invasive esophagectomies, being female and having a high risk score according to the America Society of Anesthesiologists (ASA) were predictive of failure of direct oral feeding (70). Similarly, advanced age, high ASA score, frailty, duration of surgery, the type of colonic anastomosis, and the onset of major complications have generally been recognized as risk elements for the failure of enhanced recovery pathways following abdominal surgery (79, 141, 144, 145). Yet, it has been shown that by implementing a full ERAS program, most of the impediments to early food tolerance are easily overcome (46).

The next paragraphs provide the rationale for the need for early feeding and how to preserve and restore gut function. Finally, alternative approaches for nutritional support when daily caloric intake cannot be successfully achieved through the physiological oral route are outlined.

Several reasons account for potential gut dysfunction in postoperative surgical patients. Perioperative starvation implies the progressive absence of luminal nutrients, and consequently the loss of structural and functional integrity of intestinal mucosa. Subsequent opening of intercellular channels in the intestinal epithelium occurs, directly related to the degree of surgery-related inflammatory response (79). Both the underlying disorder and the surgical procedure itself provoke a proinflammatory status leading to fluid shift to the extracellular compartment, causing mucosal edema, impaired gut motility ileus, and a defective mucosal barrier (79). Cytokine release may ultimately provoke cell apoptosis (2) and affect the microvascular environment of the intestinal wall, with ischemia/reperfusion injury and damage to intestinal epithelium. In this setting, early feeding plays a key role in maintaining the functional and structural integrity of the gut epithelium. The presence of nutrients in the intestinal lumen stimulates intestinal motility and favors the release of trophic elements (80). Early oral feeding has also been associated with reduced postoperative inflammatory response (129). All these aspects can directly affect the gut wall, preventing the occurrence of bacterial translocation (68) (**Figure 3**).

A possible modulation of the brain–gut axis deriving from early oral feeding has been postulated. The brain–gut peptides, namely gastrin, motilin, substance P, cholecystokinin, and somatostatin, are regulators of gut function (23, 109, 117, 118). They act on the GI tract through the neuroendocrine and brain–gut axis, regulate gastric emptying and intestinal transit, and affect satiety and appetite (109). In a recent study, patients receiving early oral feeding after esophagectomy reported higher levels of ghrelin, motilin, and substance P compared to patients not receiving early feeding (24). These hormones initiate the migrating motor complex in the stomach and stimulate GI motility, thus favoring gastric emptying and inducing hunger (117).

Other beneficial effects of early feeding have also been observed in experimental models, suggesting that adequate oral intake may positively affect the healing of GI anastomoses (38). The resumption of early oral food contributes to minimize catabolic activation and protein wasting associated with impaired wound healing. In addition, the restoration of oral food intake may help preserve the normal gut microbiome and reduce the risk of postoperative complications (146). The commensal microbiota create a balance with the immune system of the host (88) and play an active role in the digestive process (77). Moreover, the microbiome contributes to maintaining epithelial mucosal barrier function by providing a functional layer against pathogen infection, and its perturbation increases the risk of infectious complications and anastomotic leakage (31). Recent results in murine models showed a strong correlation between some bacterial strains in the gut microbiome, the inflammatory intestinal microenvironment, and the capability of anastomotic healing (62).

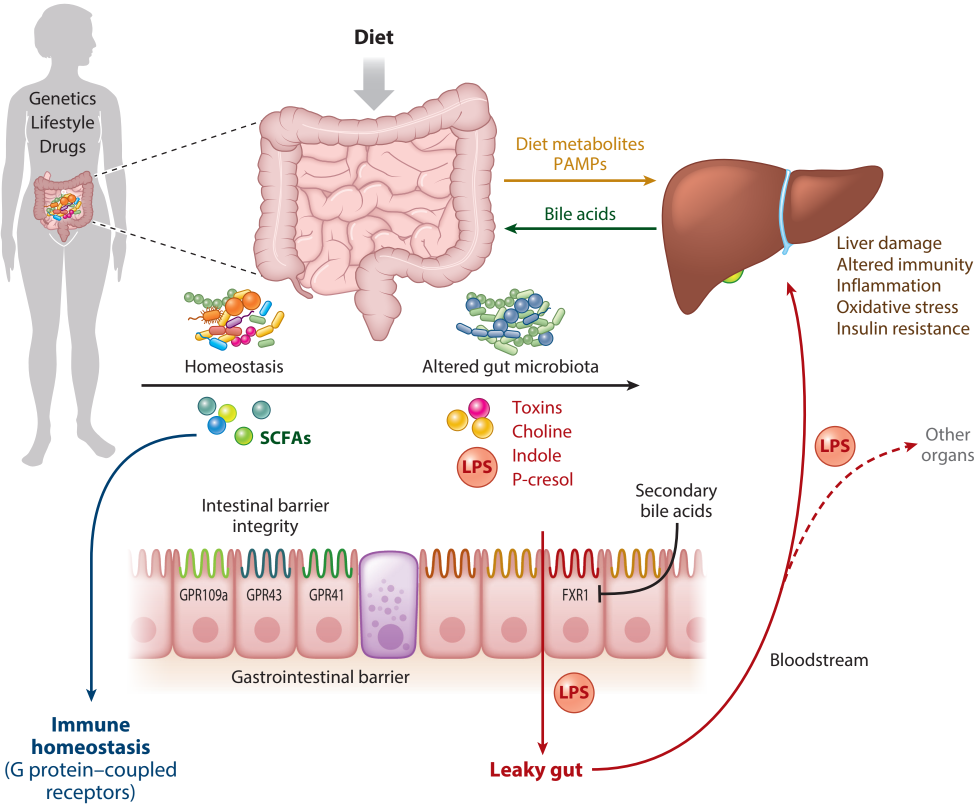

Figure 3

The gut–liver axis and consequences related to metabolic derangements. Exposure factors such as diet, drugs, and stressful events may provoke an important modulation of gut microbiota and microbial metabolite production. In physiological situations, SCFAs promote gut homeostasis. Alterations in the gut microbial environment potentially favor a leaky gut condition. Increased permeability of the intestinal barrier allows translocation of bacteria and their metabolites, such as LPS, further impairing the gut–liver axis and potentially hampering distant organ and system organ functions. In this setting, early feeding plays a key role in maintaining the functional and structural integrity of the gut epithelium. Early oral feeding is also associated with reduced postoperative inflammatory response. All these aspects can directly affect the gut wall, preventing the occurrence of bacterial translocation. Abbreviations: LPS, lipopolysaccharide; PAMP, pathogen-associated molecular pattern; p-cresol, para-cresol (4-methylphenol); SCFA, short-chain fatty acid. Figure adapted from Reference 102 (CC BY 4.0).

9. ROUTES OF FEEDING IN DIFFERENT SURGERIES

Accordingly, the most recent guidelines suggest that oral nutritional intake should be continued after surgery without interruption. Oral intake, including clear liquids, should be initiated within hours following a procedure (137). Normal hospital food is the basis for postoperative nutrition. If insufficient, the first line of additional nutritional support is the use of ONSs given to patients who do not meet energy and protein requirements with normal food.

The poor tolerance to oral intake is more often observed after complex upper GI and proximal pancreatic surgery. The occurrence of postoperative complications, such as anastomotic failure, surgical site infections, the need for reintubation, and organ failure, will often severely affect the resumption of postoperative oral intake (14).

There are no high-level scientific data available to inform when and to whom artificial nutrition, that is, enteral tube feeding or parenteral nutrition, should be initiated postoperatively. However, ESPEN expert recommendations suggest that in patients who are unable to resume oral intake for more than 5 postoperative days, artificial nutritional support should be initiated (93). Similarly, artificial nutrition is also indicated in those patients not expected to reach above 50% of recommended daily caloric intake for more than one week.

A lingering issue has been about the best route for administering artificial nutrition: enteral or parenteral. Several systematic reviews and meta-analyses definitively proved the superiority of oral nutrition and enteral nutrition over parenteral nutrition (1, 40, 64, 138). Whenever possible, this route should be used either alone or supplemented with parenteral nutrition if needed. Enteral nutrition provides similar beneficial effects on gut function as oral food. Enteral nutrition promotes the role of commensal bacteria that help degrade bacterial toxins and prevent colonization of pathogenic organisms (68, 119). Commensal bacteria produce short-chain fatty acids that play a role in the downregulation of the inflammatory response and oxidative stress in the colon (125). Moreover, beneficial effects of enteral nutrition on the gut immune microenvironment and epithelium have been described (68, 80). By contrast, the use of parenteral nutrition has been associated with impaired gut and liver function, poor control of glucose metabolism, and increased risk of infectious complications, as well as increased in-hospital mortality and duration of hospitalization (1, 25, 29, 84, 99). However, enteral nutrition is not always well tolerated because of abdominal swelling, ileus, or impaired gastric emptying after abdominal surgery (73). Patients undergoing major surgery for head, neck, or abdominal cancer surgery—mainly esophageal resection, gastrectomy, or proximal pancreatectomy—have a higher risk of developing morbidity, and any postoperative complications may delay oral and enteral feeding and diminish predefined caloric uptake (9). In those cases, supplemental parenteral nutrition or total parenteral nutrition is needed to achieve the daily caloric intake.

Three routes of tube feeding enteral nutrition are mainly used following surgery: via a nasogastric tube, via a nasoduodenal/jejunal tube, or via a needle catheter jejunostomy tube. For upper GI surgery, evidence suggests the benefit of a tube inserted distal to the anastomosis, either a needle catheter jejunostomy or nasojejunal tube (13, 58). Placement of a jejunostomy, preferably using the laparoscopic approach over the open jejunostomy placement, is associated with a risk of complications ranging from 1.5% to 6% (66). Because of the risks associated with its placement, routine placement of a feeding jejunostomy is not recommended. In addition, since the introduction of the ERAS programs, only about 50% of patients undergoing pancreatoduodenectomy require nutritional support in the postoperative period. For these reasons, jejunostomies should be reserved for high-risk cases, especially malnourished patients undergoing major upper GI and proximal pancreatic resections. However, the issue of indications for the selection of candidates for this type of feeding tube is still under debate and needs to be better supported by further evidence (41). In favor of its wider use is a recent retrospective analysis in more than 700 patients undergoing gastrectomy that showed that early enteral nutritional support by a feeding jejunostomy improved the nutritional status of the patients without increasing the rate of postoperative complications (86). As an alternative to jejunostomies, nasogastric or nasojejunal tubes can be used. An RCT showed no significant differences between nasoduodenal tube and feeding jejunostomy for the development of catheter-associated complications following esophagectomy (63). However, the use of nasogastric/jejunal tubes has other drawbacks and has been associated with a significant rate of dislodgement, with a consequent risk of vomiting and aspiration pneumonia (39, 95).

In brief, when the resumption of oral intake cannot be successfully achieved, early enteral nutrition is recommended. Whether it is better to administer enteral nutrition via nasogastric/jejunal tube or via jejunostomy remains inconclusive. Further evidence is needed to select those patients who could benefit from the intraoperative placement of a feeding jejunostomy, according to the type of surgical procedure and nutritional risk profile.

10. SUMMARY AND CONCLUSIONS

Surgical practice has changed drastically in the last couple of decades. New surgical techniques and the evidence-based perioperative care program, ERAS, have revolutionized the care of the surgical patient. These improvements have reduced complication rates and length of hospital stay by 30–50% in many types of surgeries. Several of the evidence-based care elements in ERAS protocols have a direct impact on the metabolic responses to surgery by reducing stress reactions. They also allow for much faster resumption of functions, including those of the GI tract. These improvements have opened up opportunities for changes in nutritional care. Instead of receiving low-caloric glucose IV fluids, patients can and should eat and drink almost immediately after surgery as an integral part of their recovery. A further development is the prehabilitation programs where patients preparing to undergo major operations are given specific protein-rich nutrition, perform specific exercise programs, and receive mental preparation to increase their resilience to the stress of surgery. In parallel to these advances, specific immunomodulating nutrients in pharmacologic doses have been shown to effectively reduce complications, primarily infectious complications in abdominal cancer patients. Pre- and probiotics affecting the gut microbiota also show promising effects on outcomes, while the simple use of carbohydrates preoperatively is an effective way of controlling postoperative glucose. Still, malnutrition remains a major risk for severe complications for many patients undergoing major surgery, especially for cancer. These patients need to be identified before surgery by screening and assessment and given proper nutritional care before and after surgery to help avoid complications. Nutritional care in the surgical patient should be based on normal food supplemented by ONSs if the GI tract is working. The previously very common modes of feeding—tube feeding and parenteral nutrition—are secondary choices either alone or in combination and reserved for patients where the normal oral routes are insufficient to fulfil the needs of the patients.

DISCLOSURE STATEMENT

O.L. is the founder and past chairman of the ERAS Society. He is the founder and a minority shareholder of Encare AB, Sweden, and received travel support and honoraria from Encare for training events and teaching. He has given advice to Nutricia AS, The Netherlands, and received speaker fees and travel support from B. Braun, Germany. G.B. received an honorarium and consultant fee from Abbott Nutrition Canada, Merck Inc., Fresenius Kabi, Aristea Education, and Baxter. A.W. received lecture fees from Abbott, Baxter, B. Braun, and Fresenius Kabi and grants from B. Braun, Mucos, and Seca. L.G. received lecture fees from Baxter.

LITERATURE CITED

1. Adiamah A, Ranat R, Gomez D. 2019. Enteral versus parenteral nutrition following pancreaticoduodenectomy: a systematic review and meta-analysis. *HPB* 21(7):793–801
2. Alverdy J, Zaborina O, Wu L. 2005. The impact of stress and nutrition on bacterial–host interactions at the intestinal epithelial surface. *Curr. Opin. Clin. Nutr. Metab. Care* 8(2):205–9
3. Andersen HK, Lewis SJ, Thomas S. 2006. Early enteral nutrition within 24h of colorectal surgery versus later commencement of feeding for postoperative complications. *Cochrane Database Syst. Rev.* 2006(4):CD004080.pub2
4. Arends J, Baracos V, Bertz H, Bozzetti F, Calder PC, et al. 2017. ESPEN expert group recommendations for action against cancer-related malnutrition. *Clin. Nutr.* 36(5):1187–96

5. Barazzoni R, Gortan Cappellari G. 2020. Double burden of malnutrition in persons with obesity. *Rev. Endocr. Metab. Disord.* 21(3):307–13
6. Barazzoni R, Jensen GL, Correia MITD, Gonzalez MC, Higashiguchi T, et al. 2022. Guidance for assessment of the muscle mass phenotypic criterion for the Global Leadership Initiative on Malnutrition (GLIM) diagnosis of malnutrition. *Clin. Nutr.* 41(6):1425–33
7. Barberan-Garcia A, Ubré M, Roca J, Lacy AM, Burgos F, Risco R, et al. 2018. Personalised prehabilitation in high-risk patients undergoing elective major abdominal surgery: a randomized blinded controlled trial. *Ann. Surg.* 267(1):50–56
8. Berkel AEM, Bongers BC, Kotte H, Weltevreden P, de Jongh FHC, Eijsvogel MMM, et al. 2022. Effects of community-based exercise prehabilitation for patients scheduled for colorectal surgery with high risk for postoperative complications: results of a randomized clinical trial. *Ann. Surg.* 275(2):e299–306
9. Berkelmans GHK, Kingma BF, Fransen LFC, Nieuwenhuijzen GAP, Ruurda JP, van Hillegersberg R, et al. 2020. Feeding protocol deviation after esophagectomy: a retrospective multicenter study. *Clin. Nutr.* 39(4):1258–63
10. Bicakli DH, Uslu R, Güney SC, Coker A. 2020. The relationship between nutritional status, performance status, and survival among pancreatic cancer patients. *Nutr. Cancer* 72(2):202–8
11. Böhne SEJ, Hiesmayr M, Sulz I, Tarantino S, Wirth R, Volkert D. 2020. Recent and current low food intake–prevalence and associated factors in hospital patients from different medical specialities. *Eur. J. Clin. Nutr.* 76(10):1440–48
12. Bozzetti F, Gianotti L, Braga M, Di Carlo V, Mariani L. 2007. Postoperative complications in gastrointestinal cancer patients: the joint role of the nutritional status and the nutritional support. *Clin. Nutr.* 26(6):698–709
13. Braga M, Gianotti L, Gentilini O, Liotta S, Di Carlo V. 2002. Feeding the gut early after digestive surgery: results of a nine-year experience. *Clin. Nutr.* 21(1):59–65
14. Braga M, Pecorelli N, Ariotti R, Capretti G, Greco M, Balzano G, et al. 2014. Enhanced recovery after surgery pathway in patients undergoing pancreaticoduodenectomy. *World J. Surg.* 38(11):2960–66
15. Bragg D, El-Sharkawy AM, Psaltis E, Maxwell-Armstrong CA, Lobo DN. 2015. Postoperative ileus: recent developments in pathophysiology and management. *Clin. Nutr.* 34(3):367–76
16. Brandstrup B, Tønnesen H, Beier-Holgersen R, Hjortsø E, Ørding H, et al. 2003. Effects of intravenous fluid restriction on postoperative complications: comparison of two perioperative fluid regimens: a randomized assessor-blinded multicenter trial. *Ann. Surg.* 238(5):641–48
17. Burden S, Todd C, Hill J, Lal S. 2012. Pre-operative nutrition support in patients undergoing gastrointestinal surgery. *Cochrane Database Syst. Rev.* 2012(11):CD008879
18. Canelli R, Louca J, Hartman C, Bilotta F. 2023. Preoperative carbohydrate load to reduce perioperative glycemic variability and improve surgical outcomes: a scoping review. *World J. Diabetes* 14(6):783–94
19. Cao Y, Han D, Zhou X, Han Y, Zhang Y, Li H. 2022. Effects of preoperative nutrition on postoperative outcomes in esophageal cancer: a systematic review and meta-analysis. *Dis. Esophagus* 35(3):doab028
20. Carli F, Charlebois P, Stein B, Feldman L, Zavorsky G, et al. 2010. Randomized clinical trial of prehabilitation in colorectal surgery. *Br. J. Surg.* 97(8):1187–97
21. Cederholm T, Jensen GL, Correia MITD, Gonzalez MC, Fukushima R, et al. 2019. GLIM criteria for the diagnosis of malnutrition—a consensus report from the global clinical nutrition community. *Clin. Nutr.* 38(1):1–9
22. Chapman SJ, Pericleous A, Downey C, Jayne DG. 2018. Postoperative ileus following major colorectal surgery. *Br. J. Surg.* 105(7):797–810
23. Chen CY, Tsai CY. 2012. Ghrelin and motilin in the gastrointestinal system. *Curr. Pharm. Des.* 18(31):4755–65
24. Chen X, Wang P, Leng C, Sun H, Liu X, et al. 2022. Early oral feeding after esophagectomy accelerated gut function recovery by regulating brain-gut peptide secretion. *Surgery* 172(3):919–25
25. Cheung NW, Napier B, Zaccaria C, Fletcher JP. 2005. Hyperglycemia is associated with adverse outcomes in patients receiving total parenteral nutrition. *Diabetes Care* 28(10):2367–71
26. Chowdhury AH, Adiamah A, Kushairi A, Varadhan KK, Krznaric Z, et al. 2020. Perioperative probiotics or synbiotics in adults undergoing elective abdominal surgery: a systematic review and meta-analysis of randomized controlled trials. *Ann. Surg.* 271(6):1036–47

27. Clark AB, Reijnierse EM, Lim WK, Maier AB. 2020. Prevalence of malnutrition comparing the GLIM criteria, ESPEN definition and MST malnutrition risk in geriatric rehabilitation patients: RESORT. *Clin. Nutr.* 39(11):3504–11
28. De Luca R, Gianotti L, Pedrazzoli P, Brunetti O, Rizzo A, et al. 2023. Immunonutrition and prehabilitation in pancreatic cancer surgery: a new concept in the era of ERAS® and neoadjuvant treatment. *Eur. J. Surg. Oncol.* 49(3):542–49
29. Denton C, Price A, Friend J, Manithody C, Blomenkamp K, et al. 2018. Role of the gut–liver axis in driving parenteral nutrition-associated injury. *Children* 5(10):136
30. Donini LM, Busetto L, Bischoff SC, Cederholm T, Ballesteros-Pomar MD, et al. 2022. Definition and diagnostic criteria for sarcopenic obesity: ESPEN and EASO consensus statement. *Obes. Facts* 15(3):321–35
31. Ducarmon QR, Zwittink RD, Hornung BVH, van Schaik W, Young VB, Kuijper EJ. 2019. Gut microbiota and colonization resistance against bacterial enteric infection. *Microbiol. Mol. Biol. Rev.* 83(3):10.1128/mmbr.00007-19
32. Dungan KM, Braithwaite SS, Preiser J-C. 2009. Stress hyperglycaemia. *Lancet* 373:1798–807
33. Engelen MP, van der Meij BS, Deutz NE. 2016. Protein anabolic resistance in cancer: Does it really exist? *Curr. Opin. Clin. Nutr. Metab. Care* 19(1):39–47
34. Evans DC, Corkins MR, Malone A, Miller S, Mogensen KM, et al. 2021. The use of visceral proteins as nutrition markers: an ASPEN position paper. *Nutr. Clin. Pract.* 36(1):22–28
35. Famularo S, Donadon M, Roccamatisi L, Di Lucca G, Angrisani M, et al. 2023. Association of indirect measurement of cell function by bioimpedance analysis with complications in oncologic hepatic surgery. *HPB* 25(3):283–92
36. Fearon KC, Ljungqvist O, Von Meyenfeldt M, Revhaug A, Dejong CH, et al. 2005. Enhanced recovery after surgery: a consensus review of clinical care for patients undergoing colonic resection. *Clin. Nutr.* 24(3):466–77
37. Feldman LS, Kaneva P, Demyttenaere S, Carli F, Fried GM, Mayo NE. 2009. Validation of a physical activity questionnaire (CHAMPS) as an indicator of postoperative recovery after laparoscopic cholecystectomy. *Surgery* 146(1):31–39
38. Fukuzawa J, Terashima H, Ohkohchi N. 2007. Early postoperative oral feeding accelerates upper gastrointestinal anastomotic healing in the rat model. *World J. Surg.* 31(6):1234–39
39. Gerritsen A, Besselink MG, Cieslak KP, Vriens MR, Steenhagen E, et al. 2012. Efficacy and complications of nasojejunal, jejunostomy and parenteral feeding after pancreaticoduodenectomy. *J. Gastrointest. Surg.* 16(6):1144–51
40. Gerritsen A, Besselink MG, Gouma DJ, Steenhagen E, Borel Rinkes IH, Molenaar IQ. 2013. Systematic review of five feeding routes after pancreatoduodenectomy. *Br. J. Surg.* 100(5):589–98; discuss. 599
41. Gerritsen A, Wennink RAW, Busch ORC, Borel Rinkes IHM, Kazemier G, et al. 2015. Feeding patients with preoperative symptoms of gastric outlet obstruction after pancreatoduodenectomy: early oral or routine nasojejunal tube feeding? *Pancreatology* 15(5):548–53
42. Gianotti L, Biffi R, Sandini M, Marrelli D, Vignali A, et al. 2018. Preoperative oral carbohydrate load versus placebo in major elective abdominal surgery (PROCY): a randomized, placebo-controlled, multicenter, phase III trial. *Ann. Surg.* 267(4):623–30
43. Gianotti L, Braga M, Fortis C, Soldini L, Vignali A, et al. 1999. A prospective, randomized clinical trial on perioperative feeding with an arginine-, omega-3 fatty acid-, and RNA-enriched enteral diet: effect on host response and nutritional status. *JPEN J. Parenter. Enter. Nutr.* 23(6):314–20
44. Gianotti L, Nespoli L, Sandini M. 2024. Pharmaconutrition: which substrates? *Eur. J. Surg. Oncol.* 50(5):106798
45. Gianotti L, Sandini M, Hackert T. 2020. Preoperative carbohydrates: What is new? *Curr. Opin. Clin. Nutr. Metab. Care* 23(4):262–70
46. Gianotti L, Sandini M, Romagnoli S, Carli F, Ljungqvist O. 2020. Enhanced recovery programs in gastrointestinal surgery: actions to promote optimal perioperative nutritional and metabolic care. *Clin. Nutr.* 39(7):2014–24

47. Gillis C, Buhler K, Bresee L, Carli F, Gramlich L, et al. 2018. Effects of nutritional prehabilitation, with and without exercise, on outcomes of patients who undergo colorectal surgery: a systematic review and meta-analysis. *Gastroenterology* 155(2):391–410.e4
48. Gillis C, Carli F. 2015. Promoting perioperative metabolic and nutritional care. *Anesthesiology* 123:1455–72
49. Gillis C, Fenton TR, Gramlich L, Keller H, Sajobi TT, et al. 2022. Malnutrition modifies the response to multimodal prehabilitation: a pooled analysis of prehabilitation trials. *Appl. Physiol. Nutr. Metab.* 47(2):141–50
50. Gillis C, Fenton TR, Gramlich L, Sajobi TT, Culos-Reed SN, et al. 2021. Older frail prehabilitated patients who cannot attain a 400 m 6-min walking distance before colorectal surgery suffer more postoperative complications. *Eur. J. Surg. Oncol.* 47(4):874–81
51. Gillis C, Fenton TR, Sajobi TT, Minnella EM, Awasthi R, et al. 2019. Trimodal prehabilitation for colorectal surgery attenuates post-surgical losses in lean body mass: a pooled analysis of randomized controlled trials. *Clin. Nutr.* 38(3):1053–60
52. Gillis C, Loiselle SE, Fiore JF Jr., Awasthi R, Wykes L, et al. 2016. Prehabilitation with whey protein supplementation on perioperative functional exercise capacity in patients undergoing colorectal resection for cancer: a pilot double-blinded randomized placebo-controlled trial. *J. Acad. Nutr. Diet.* 116(5):802–12
53. Gillis C, Richer L, Fenton TR, Gramlich L, Keller H, et al. 2021. Colorectal cancer patients with malnutrition suffer poor physical and mental health before surgery. *Surgery* 170(3):841–47
54. Gillis C, Wischmeyer PE. 2019. Pre-operative nutrition and the elective surgical patient: why, how and what? *Anaesthesia* 74(Suppl. 1):27–35
55. Gomez-Perez SL, Haus JM, Sheean P, Patel B, Mar W, et al. 2016. Measuring abdominal circumference and skeletal muscle from a single cross-sectional computed tomography image: a step-by-step guide for clinicians using National Institutes of Health ImageJ. *JPEN J. Parenter. Enter. Nutr.* 40(3):308–18. Corrigendum. 2016. *JPEN J. Perenter. Enter. Nutr.* 40(5):742–43
56. Greco M, Capretti G, Beretta L, Gemma M, Pecorelli N, Braga M. 2014. Enhanced recovery program in colorectal surgery: a meta-analysis of randomized controlled trials. *World J. Surg.* 38(6):1531–41
57. Gruber ES, Jomrich G, Tamandl D, Gnant M, Schindl M, Sahora K. 2019. Sarcopenia and sarcopenic obesity are independent adverse prognostic factors in resectable pancreatic ductal adenocarcinoma. *PLOS ONE* 15(12):e0244896
58. Gupta V. 2009. Benefits versus risks: a prospective audit. Feeding jejunostomy during esophagectomy. *World J. Surg.* 33(7):1432–38
59. Gustafsson UO, Hausel J, Thorell A, Ljungqvist O, Soop M, et al. 2011. Adherence to the enhanced recovery after surgery protocol and outcomes after colorectal cancer surgery. *Arch. Surg.* 146(5):571–77
60. Gustafsson UO, Oppelstrup H, Thorell A, Nygren J, Ljungqvist O. 2016. Adherence to the ERAS protocol is associated with 5-year survival after colorectal cancer surgery: a retrospective cohort study. *World J. Surg.* 40(7):1741–47
61. Gustafsson UO, Scott MJ, Hübner M, Nygren J, Demartines N, et al. 2019. Guidelines for perioperative care in elective colorectal surgery: Enhanced Recovery After Surgery (ERAS) Society recommendations. *World J. Surg.* 43:659–95
62. Hajjar R, Gonzalez E, Fragoso G, Oliero M, Alaoui AA, Calve A, et al. 2023. Gut microbiota influence anastomotic healing in colorectal cancer surgery through modulation of mucosal proinflammatory cytokines. *Gut* 72(6):1143–54
63. Han-Geurts IJ, Hop WC, Verhoef C, Tran KT, Tilanus HW. 2007. Randomized clinical trial comparing feeding jejunostomy with nasoduodenal tube placement in patients undergoing oesophagectomy. *Br. J. Surg.* 94(1):31–35
64. Herbert G, Perry R, Andersen HK, Atkinson C, Penfold C, et al. 2018. Early enteral nutrition within 24 hours of lower gastrointestinal surgery versus later commencement for length of hospital stay and postoperative complications. *Cochrane Database Syst. Rev.* 2018(10):CD004080
65. Hruby W, Stellamor K. 1988. Behavior of contrast media in liver tumors in computerized tomography—correlation between pharmacokinetics and histological structure. *Rontgenblatter* 41(4):133–39
66. Hsiung T, Chao WP, Chai SW, Chou TC, Wang CY, Huang TS. 2023. Laparoscopic versus open feeding jejunostomy: a systemic review and meta-analysis. *Surg. Endosc.* 37(4):2485–95

67. Ishida T, Makino T, Yamasaki M, Yamashita K, Tanaka K, et al. 2021. Quantity and quality of skeletal muscle as an important predictor of clinical outcomes in patients with esophageal cancer undergoing esophagectomy after neoadjuvant chemotherapy. *Ann. Surg. Oncol.* 28(12):7185–95
68. Jabbar A, Chang WK, Dryden GW, McClave SA. 2003. Gut immunology and the differential response to feeding and starvation. *Nutr. Clin. Pract.* 18(6):461–82
69. Jang MK, Park C, Hong S, Li H, Rhee E, Doorenbos AZ. 2020. Skeletal muscle mass change during chemotherapy: a systematic review and meta-analysis. *Anticancer Res.* 40(5):2409–18
70. Janssen HJB, Gantxegi A, Fransen LFC, Nieuwenhuijzen GAP, Luyer MDP. 2021. Risk factors for failure of direct oral feeding following a totally minimally invasive esophagectomy. *Nutrients* 13(10):3616
71. Kao LS, Phatak UR. 2013. Glycemic control and prevention of surgical site infection. *Surg. Infect.* 14:437–44
72. Kehlet H. 1997. Multimodal approach to control postoperative pathophysiology and rehabilitation. *Br. J. Anaesth.* 78(5):606–17
73. Kehlet H. 2000. Postoperative ileus. *Gut* 47(Suppl. 4):iv85–86
74. Kenny E, Samavat H, Touger-Decker R, Parrott JS, Byham-Gray L, August DA. 2022. Adverse perioperative outcomes among patients undergoing gastrointestinal cancer surgery: quantifying attributable risk from malnutrition. *JPEN J. Parenter. Enter. Nutr.* 46(3):517–25
75. Khan A, Wong J, Riedel B, Laing E, Beaumont A, et al. 2023. The impact of peri-operative enteral immunonutrition on post-operative complications in gastrointestinal cancer surgery: a meta-analysis. *Ann. Surg. Oncol.* 30(6):3619–31
76. Kiran RP, Turina M, Hammel J. 2013. The clinical significance of an elevated postoperative glucose value in nondiabetic patients after colorectal surgery: evidence for the need for tight glucose control? *Ann. Surg.* 258:599–604
77. Kolodziejczyk AA, Zheng D, Elinav E. 2019. Diet–microbiota interactions and personalized nutrition. *Nat. Rev. Microbiol.* 17(12):742–53
78. Kondrup J, Allison SP, Elia M, Vellas B, Plauth M, et al. 2003. ESPEN guidelines for nutrition screening 2002. *Clin. Nutr.* 22(4):415–21
79. Kudsk KA. 2001. Importance of enteral feeding in maintaining gut integrity. *Tech. Gastrointest. Endosc.* 3:2–8
80. Kudsk KA. 2002. Current aspects of mucosal immunology and its influence by nutrition. *Am. J. Surg.* 183(4):390–98
81. Kuwada K, Kikuchi S, Kuroda S, Yoshida R, Takagi K, et al. 2023. Survival impact of postoperative skeletal muscle loss in gastric cancer patients who underwent gastrectomy. *Anticancer Res.* 43(1):223–30
82. Lassen K, Kjaeve J, Fetveit T, Trano G, Sigurdsson HK, et al. 2008. Allowing normal food at will after major upper gastrointestinal surgery does not increase morbidity: a randomized multicenter trial. *Ann. Surg.* 247(5):721–29
83. Levy N, Quinlan J, El-Boghdadly K, Fawcett WJ, Agarwal V, et al. 2021. An international multidisciplinary consensus statement on the prevention of opioid-related harm in adult surgical patients. *Anaesthesia* 76(4):520–36
84. Lewis SR, Schofield-Robinson OJ, Alderson P, Smith AF. 2018. Enteral versus parenteral nutrition and enteral versus a combination of enteral and parenteral nutrition for adults in the intensive care unit. *Cochrane Database Syst. Rev.* 2018(6):CD012276
85. Li C, Carli F, Lee L, Charlebois P, Stein B, et al. 2013. Impact of a trimodal prehabilitation program on functional recovery after colorectal cancer surgery: a pilot study. *Surg. Endosc.* 27(4):1072–82
86. Li K, Zeng Z, Zhang Z, Ye X, Yu J, Kang W. 2023. Comparisons of nutritional status and complications between patients with and without postoperative feeding jejunostomy tube in gastric cancer: a retrospective study. *J. Gastrointest. Oncol.* 14(1):97–109
87. Ligthart-Melis GC, Luiking YC, Kakourou A, Cederholm T, Maier AB, de van der Schueren MAE. 2020. Frailty, sarcopenia, and malnutrition frequently (co-)occur in hospitalized older adults: a systematic review and meta-analysis. *J. Am. Med. Direct. Assoc.* 21(9):1216–28
88. Littman DR, Pamer EG. 2011. Role of the commensal microbiota in normal and pathogenic host immune responses. *Cell Host Microbe* 10(4):311–23

89. Ljungqvist O, Gustafsson U, de Boer HD. 2023. 20 + years of enhanced recovery after surgery: What's next. *World J. Surg.* 47(5):1087–89
90. Ljungqvist O, Nelson G, Demartines N. 2020. The post COVID-19 surgical backlog: Now is the time to implement Enhanced Recovery After Surgery (ERAS). *World J. Surg.* 44(10):3197–98
91. Ljungqvist O, Scott M, Fearon KC. 2017. Enhanced recovery after surgery: a review. *JAMA Surg.* 152(3):292–98
92. Lobo DN. 2009. Fluid overload and surgical outcome: another piece in the jigsaw. *Ann. Surg.* 249(2):186–88
93. Lobo DN, Gianotti L, Adiamah A, Barazzoni R, Deutz NEP, Dhatariya K, et al. 2020. Perioperative nutrition: recommendations from the ESPEN expert group. *Clin. Nutr.* 39(11):3211–27
94. López-Rodríguez-Arias F, Sánchez-Guillén L, Lillo-García C, Aranaz-Ostáriz V, Alcaide MJ, et al. 2021. Assessment of body composition as an indicator of early peripheral parenteral nutrition therapy in patients undergoing colorectal cancer surgery in an enhanced recovery program. *Nutrients* 13(9):3245
95. Markides GA, Al-Khaffaf B, Vickers J. 2011. Nutritional access routes following oesophagectomy—a systematic review. *Eur. J. Clin. Nutr.* 65(5):565–73
96. Martin L, Gillis C, Atkins M, Gillam M, Sheppard C, et al. 2019. Implementation of an enhanced recovery after surgery program can change nutrition care practice: a multicenter experience in elective colorectal surgery. *JPEN J. Parenter. Enter. Nutr.* 43(2):206–19
97. Martin L, Gioulbasanis I, Senesse P, Baracos VE. 2020. Cancer-associated malnutrition and CT-defined sarcopenia and myosteatosis are endemic in overweight and obese patients. *JPEN J. Parenter. Enter. Nutr.* 44(2):227–38
98. Mayanagi S, Tsubosa Y, Omae K, Niihara M, Uchida T, et al. 2017. Negative impact of skeletal muscle wasting after neoadjuvant chemotherapy followed by surgery on survival for patients with thoracic esophageal cancer. *Ann. Surg. Oncol.* 24(12):3741–47
99. Mazaki T, Ebisawa K. 2008. Enteral versus parenteral nutrition after gastrointestinal surgery: a systematic review and meta-analysis of randomized controlled trials in the English literature. *J. Gastrointest. Surg.* 12(4):739–55
100. Mc Loughlin S, Terrasa SA, Ljungqvist O, Sanchez G, Garcia Fornari G, Alvarez AO. 2019. Nausea and vomiting in a colorectal ERAS program: impact on nutritional recovery and the length of hospital stay. *Clin. Nutr. ESPEN* 34:73–80
101. Molenaar CJL, Minnella EM, Coca-Martinez M, ten Cate DWG, Regis M, et al. 2023. Effect of multimodal prehabilitation on reducing postoperative complications and enhancing functional capacity following colorectal cancer surgery: the PREHAB randomized clinical trial. *JAMA Surg.* 158(6):572–81
102. Montanari C, Parolisi S, Borghi E, Putignani L, Bassanini G, et al. 2021. Dysbiosis, host metabolism, and non-communicable diseases: trialogue in the inborn errors of metabolism. *Front. Physiol.* 12:716520
103. Moore DR, Churchward-Venne TA, Witard O, Breen L, Burd NA, et al. 2015. Protein ingestion to stimulate myofibrillar protein synthesis requires greater relative protein intakes in healthy older versus younger men. *J. Gerontol. Ser. A Biol. Sci. Med. Sci.* 70(1):57–62
104. Moya P, Soriano-Irigaray L, Ramirez JM, Garcea A, Blasco O, et al. 2016. Perioperative standard oral nutrition supplements versus immunonutrition in patients undergoing colorectal resection in an Enhanced Recovery (ERAS) protocol: a multicenter randomized clinical trial (SONVI Study). *Medicine* 95(21):e3704
105. Ng SC, Hart AL, Kamm MA. 2009. Mechanisms of action of probiotics: recent advances. *Inflamm. Bowel Dis.* 15:300–10
106. NICE-SUGAR Study Investig. 2009. Intensive versus conventional glucose control in critically ill patients. *N. Engl. J. Med.* 360:1283–97
107. Nygren J, Thorell A, Ljungqvist O. 2015. Preoperative oral carbohydrate therapy. *Curr. Opin. Anaesthesiol.* 28(3):364–69
108. Pang Q, Duan L, Jiang Y, Liu H. 2021. Oncologic and long-term outcomes of enhanced recovery after surgery in cancer surgeries—a systematic review. *World J. Surg. Oncol.* 19(1):191
109. Pappas TN, Tache Y, Debas HT. 1985. Opposing central and peripheral actions of brain-gut peptides: a basis for regulation of gastric function. *Surgery* 98(2):183–90

110. Phillips SM. 2004. Protein requirements and supplementation in strength sports. *Nutrition* 20(7–8):689–95
111. Phillips SM. 2011. The science of muscle hypertrophy: making dietary protein count. *Proc. Nutr. Soc.* 70(1):100–3
112. Prado CM, Ford KL, Gonzalez MC, Murnane LC, Gillis C, et al. 2023. Nascent to novel methods to evaluate malnutrition and frailty in the surgical patient. *JPEN J. Parenter. Enter. Nutr.* 47(Suppl. 1):S54–68
113. Prado CM, Purcell SA, Laviano A. 2020. Nutrition interventions to treat low muscle mass in cancer. *J. Cachexia Sarcopenia Muscle* 11(2):366–80
114. Roberfroid M. 2007. Prebiotics: the concept revisited. *J. Nutr.* 137:830S–37S
115. Roulin D, Blanc C, Muradbegovic M, Hahnloser D, Demartines N, Hubner M. 2014. Enhanced recovery pathway for urgent colectomy. *World J. Surg.* 38(8):2153–59
116. Sandini M, Patino M, Ferrone CR, Alvarez-Pérez CA, Honselmann KC, et al. 2018. Association between changes in body composition and neoadjuvant treatment for pancreatic cancer. *JAMA Surg.* 153(9):809–15
117. Sanger GJ, Furness JB. 2016. Ghrelin and motilin receptors as drug targets for gastrointestinal disorders. *Nat. Rev. Gastroenterol. Hepatol.* 13(1):38–48
118. Schmidt PT, Holst JJ. 2000. Tachykinins in regulation of gastric motility and secretion. *Cell Mol. Life Sci.* 57(4):579–88
119. Schorghuber M, Fruhwald S. 2018. Effects of enteral nutrition on gastrointestinal function in patients who are critically ill. *Lancet Gastroenterol. Hepatol.* 3(4):281–87
120. Schricker T, Latterman R, Carli F. 2020. Physiology and pathophysiology of ERAS. In *Enhanced Recovery After Surgery: A Complete Guide to Optimizing Outcomes*, ed. O Ljungqvist, NK Francis, RD Urman, pp. 11–22. Cham, Switz.: Springer Nature
121. Scott MJ, Aggarwal G, Aitken RJ, Anderson ID, Balfour A, et al. 2023. Consensus guidelines for perioperative care for emergency laparotomy Enhanced Recovery After Surgery (ERAS®) Society recommendations part 2—emergency laparotomy: intra- and postoperative care. *World J. Surg.* 47(8):1850–80
122. Senkal M, Kemen M, Homann HH, Eickhoff U, Baier J, Zumtobel V. 1995. Modulation of postoperative immune response by enteral nutrition with a diet enriched with arginine, RNA, and omega-3 fatty acids in patients with upper gastrointestinal cancer. *Eur. J. Surg.* 161(2):115–22
123. Shafi S, Aboutanos MB, Agarwal S Jr., Brown CV, Crandall M, et al. 2013. Emergency general surgery: definition and estimated burden of disease. *J. Trauma Acute Care Surg.* 74(4):1092–97
124. Shin CH, Long DR, McLean D, Grabitz SD, Ladha K, et al. 2018. Effects of intraoperative fluid management on postoperative outcomes: a hospital registry study. *Ann. Surg.* 267(6):1084–92
125. Singh N, Gurav A, Sivaprakasam S, Brady E, Padia R, et al. 2014. Activation of Gpr109a, receptor for niacin and the commensal metabolite butyrate, suppresses colonic inflammation and carcinogenesis. *Immunity* 40(1):128–39
126. Skeie E, Tangvik RJ, Nymo LS, Harthug S, Lassen K, Viste A. 2020. Weight loss and BMI criteria in GLIM's definition of malnutrition is associated with postoperative complications following abdominal resections—results from a National Quality Registry. *Clin. Nutr.* 39(5):1593–99
127. Soop M, Nygren J, Myrenfors P. 2001. Preoperative oral carbohydrate treatment attenuates immediate postoperative insulin resistance. *Am. J. Physiol. Endocrinol. Metab.* 280:E576–83
128. Spanjersberg WR, van Sambeeck JD, Bremers A, Rosman C, van Laarhoven CJ. 2015. Systematic review and meta-analysis for laparoscopic versus open colon surgery with or without an ERAS programme. *Surg. Endosc.* 29(12):3443–53
129. Sun HB, Li Y, Liu XB, Wang ZF, Zhang RX, et al. 2019. Impact of an early oral feeding protocol on inflammatory cytokine changes after esophagectomy. *Ann. Thorac. Surg.* 107(3):912–20
130. Thanh N, Nelson A, Wang X, Faris P, Wasylak T, et al. 2020. Return on investment of the Enhanced Recovery After Surgery (ERAS) multiguideline, multisite implementation in Alberta, Canada. *Can. J. Surg.* 63(6):E542–50
131. Thomas G, Tahir MR, Bongers BC, Kallen VL, Slooter GD, van Meeteren NL. 2019. Prehabilitation before major intra-abdominal cancer surgery: a systematic review of randomised controlled trials. *Eur. J. Anaesthesiol.* 36(12):933–45

132. Varadhan KK, Lobo DN. 2010. A meta-analysis of randomised controlled trials of intravenous fluid therapy in major elective open abdominal surgery: getting the balance right. *Proc. Nutr. Soc.* 69(4):488–98
133. Varadhan KK, Neal KR, Dejong CH, Fearon KC, Ljungqvist O, Lobo DN. 2010. The enhanced recovery after surgery (ERAS) pathway for patients undergoing major elective open colorectal surgery: a meta-analysis of randomized controlled trials. *Clin. Nutr.* 29(4):434–40
134. Visioni A, Shah R, Gabriel E, Attwood K, Kukar M, Nurkin S. 2018. Enhanced recovery after surgery for noncolorectal surgery? A systematic review and meta-analysis of major abdominal surgery. *Ann. Surg.* 267(1):57–65
135. Wang P-Y, Chen X-K, Liu Q, Yu Y-K, Xu L, et al. 2020. Highlighting sarcopenia management for promoting surgical outcomes in esophageal cancers: evidence from a prospective cohort study. *Int. J. Surg.* 83:206–15
136. Weimann A, Braga M, Carli F, Higashiguchi T, Hübner M, et al. 2017. ESPEN guideline: clinical nutrition in surgery. *Clin. Nutr.* 36(3):623–50
137. Weimann A, Braga M, Carli F, Higashiguchi T, Hübner M, et al. 2021. ESPEN practical guideline: clinical nutrition in surgery. *Clin. Nutr.* 40(7):4745–61
138. Willcutts KF, Chung MC, Erenberg CL, Finn KL, Schirmer BD, Byham-Gray LD. 2016. Early oral feeding as compared with traditional timing of oral feeding after upper gastrointestinal surgery: a systematic review and meta-analysis. *Ann. Surg.* 264(1):54–63
139. Wischmeyer PE, Carli F, Evans DC, Guilbert S, Kozar R, et al. 2018. American Society for Enhanced Recovery and Perioperative Quality Initiative joint consensus statement on nutrition screening and therapy within a surgical enhanced recovery pathway. *Anesth Analg*. 126(6):1883–95. Erratum. 2018. *Anesth. Analg.* 127(5):e95
140. Wobith M, Herbst C, Lurz M, Haberzettl D, Fischer M, Weimann A. 2022. Evaluation of malnutrition in patients undergoing major abdominal surgery using GLIM criteria and comparing CT and BIA for muscle mass measurement. *Clin. Nutr. ESPEN* 50:148–54
141. You K, Sohn DK, Park SS, Park SC, Oh JH, et al. 2022. Factors associated with diet failure after colon cancer surgery. *Surg. Endosc.* 36(5):2861–68
142. Young-Fadok TM, Cramer RC. 2020. Regional Anestehsia Techniques for abdominal operations. In *Enhanced Recovery After Surgery: A Complete Guide to Optimizing Outcomes*, ed. O Ljungqvist, NK Francis, RD Urman, pp. 149–62. Cham, Switz.: Springer Nature
143. Zhang X, Tang M, Zhang Q, Zhang KP, Guo ZQ, et al. 2021. The GLIM criteria as an effective tool for nutrition assessment and survival prediction in older adult cancer patients. *Clin. Nutr.* 40(3):1224–32
144. Zhang XY, Zhang XZ, Lu FY, Zhang Q, Chen W, et al. 2020. Factors associated with failure of enhanced recovery after surgery program in patients undergoing pancreaticoduodenectomy. *Hepatobiliary Pancreat. Dis. Int.* 19(1):51–57
145. Zhang Y, Xin Y, Sun P, Cheng D, Xu M, et al. 2019. Factors associated with failure of Enhanced Recovery After Surgery (ERAS) in colorectal and gastric surgery. *Scand. J. Gastroenterol.* 54(9):1124–31
146. Zheng Z, Hu Y, Tang J, Xu W, Zhu W, Zhang W. 2023. The implication of gut microbiota in recovery from gastrointestinal surgery. *Front. Cell Infect. Microbiol.* 13:1110787
147. Zhong JX, Kang K, Shu XL. 2015. Effect of nutritional support on clinical outcomes in perioperative malnourished patients: a meta-analysis. *Asia Pac. J. Clin. Nutr.* 24(3):367–78