Preoperative Preparations for Enhanced Recovery After Surgery Programs

A Role for Prehabilitation

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KEYWORDS

• ERAS • Preoperative assessment • Preoperative optimization • Prehabilitation

KEY POINTS

- Preoperative risk assessment, stratification, and optimization require a multidisciplinary approach, and should not be exclusively focused on patients' comorbidities.
- Preoperative risk assessment and stratification are valuable only if subsequent targeted optimization of patient care is allowed.
- Preoperative optimization requires time; early assessment of high-risk surgical patients is essential to facilitate appropriate optimization.
- The process of enhancing functional capacity of the individual to enable the patient to withstand the incoming surgical stressor has been termed prehabilitation.
- Multidisciplinary programs, such as prehabilitation, can address modifiable risk factors that may impact treatment outcomes.

INTRODUCTION

Almost 20 years ago, the concept of "fast track" was proposed with the understanding that it was necessary to revise surgical practice in view of the long hospital stay, high postoperative morbidity, and increasing health costs.[1,2] It was necessary to move forward from unimodal to multimodal interventions if surgical recovery was to be accelerated and morbidity reduced. In subsequent years, the Enhanced Recovery After Surgery (ERAS®) society was formed[3] with the intention to promote a multimodal and systematic approach to perioperative management and decrease postoperative

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morbidity as a result of standardized surgical care.[4] Surgeons began developing the infrastructure of ERAS and realized that it was necessary to involve other health providers if ERAS was going to achieve its goals. Clearly anesthesiologists, surgical nurses, physiotherapists, and nutritionists were needed to develop a sustainable program that would cover the whole surgical trajectory, from the preoperative clinic to hospital discharge. Many of the elements of the program, to name a few, carbohydrate drink, opioid-sparing analgesia, and intravenous fluid administration, are part of the anesthesia practice.[5,6] Knowledge on the underlying mechanisms of the stress response to surgery (endocrine, metabolic, and immunologic) and how to attenuate this response to prevent some of its negative effects (eg, increased oxygen consumption, cardiac demands, decreased gastrointestinal motility, pain) can facilitate the recovery process if integrated in the whole ERAS program. The anesthesiologist needs to be involved in various aspects of the ERAS program, for example, in the preoperative evaluation and optimization of preexisting organ dysfunction, the revision of fasting policy, the explanation to the patients and their families about the type of anesthesia and analgesia to be administered, the choice of perioperative care specific to the planned surgical procedure and with optimal intraoperative homeostasis and minimal organ dysfunction, thus facilitating rapid emergence and return of organ functions.

The implementation of procedure-specific ERAS protocols needs “champions” in various perioperative disciplines who need to meet regularly and review practice guidelines within the institution.[7] The anesthesiologist, as part of the group, must be aware of the continuous innovations in perioperative care and, as such, be flexible enough to make some changes in clinical practice and facilitate the implementation of the fast-track program. The present article has been written with the intention of addressing specific issues related to preoperative care, specifically in the context of ERAS programs. It provides evidence-based clinical approaches to best care starting in the preoperative clinic, where patients are informed about anesthesia and analgesia techniques, their health status is evaluated, and suggestions are given on how to improve functional capacity before surgery.

MINIMIZING THE SURGICAL STRESS RESPONSE: GENERAL CONSIDERATIONS

Surgery elicits a cascade of events that are broadly referred to as the stress response. This response is characterized by an increased release in neuroendocrine hormones and activation of the immune system via the upregulation of various cytokines. The combination of both a systemic inflammatory response and hypothalamic-sympathetic stimulation acts on target organs, including the brain, heart, muscle, and liver.[8] Central to the physiologic changes characterized by the inflammatory response is the relatively acute development of insulin resistance, which represents the main pathogenic factor modulating perioperative outcome, and it can be defined as an abnormal biological response to a normal concentration of insulin.[9] Insulin controls glucose, fat, and protein metabolism, and a change in insulin sensitivity by the cell, later the metabolic response. Hyperglycemia and protein breakdown represent the 2 main consequences of the low insulin sensitivity initiated by surgical insult.

Besides metabolic states such as cancer, obesity, diabetes, frailty, and sarcopenia, which characterize a preoperative state of insulin resistance, some intraoperative and postoperative elements that lead to a decrease in insulin sensitivity need to be mentioned: fasting, pain, bed rest, and fatigue.

As the pathophysiology of the stress response is multifactorial, it would make sense to plan a series of interventions aimed at attenuating the initiation of an insulin-resistant state. To that extent, the anesthesiologist, working as a team with the surgeon and the rest of the perioperative group, should consider a multimodal interventional strategy that could include the following: preoperative optimization and carbohydrate drink, neural de-afferentation, physiologic homeostasis, achievement of optimal nutritional and metabolic status, and enhancement of physical mobility.

PREOPERATIVE RISK ASSESSMENT, STRATIFICATION, AND CLINICAL OPTIMIZATION

Preoperative risk assessment and stratification are valuable only if subsequent, targeted optimization of patient care is allowed. The ultimate goal is to reduce postoperative morbidity and mortality, and facilitate surgical recovery. Surgery and organ-specific preoperative scoring systems can be integrated into preoperative clinical assessment to identify high-risk patients.[10] Similarly, biomarkers such as brain natriuretic peptide (BNP) and pro-BNP can also be used to estimate postoperative morbidity, further enhancing risk assessment and stratification.[11]

Poor preoperative functional status has been associated with increased morbidity and mortality, and prolonged surgical recovery.[12–15] Preoperative assessment of functional capacity can identify patients with poor functional status (low cardiopulmonary reserve) at high risk of developing postoperative complications and who are likely to benefit from preoperative prehabilitation and optimization.[16,17] It is commonly estimated by measuring metabolic equivalents or alternatively by using several functional tests, such as the 6-minute walking test (6MWT).[14–16]

Cardiopulmonary exercise testing (CPET) is a low-risk, noninvasive preoperative test that can more precisely and objectively determine functional capacity by measuring maximum oxygen consumption (VO_{2max}) and anaerobic threshold (AT). Peak oxygen consumption (VO_{2peak}), which is considered essentially similar to VO_{2max}, is more frequently used in clinical practice because surgical patients are not often able to achieve or are not sufficiently motivated to reach maximum oxygen uptake. AT should always be expressed as a percentage of the VO_{2max}, as oxygen consumption physiologically declines with aging.[18] Other parameters, such as pulmonary gas exchange and lactate, also can be obtained to interpret CPET main results. The results of the CPET can adequately inform perioperative physicians about the patient's ability to cope with the increased metabolic demand induced by surgical stress. Its use to stratify preoperative risk and identify high-risk patients requiring preoperative optimization, or to better allocate medical resources for the most vulnerable patients (ie, intensive care unit admission) has increased in the past 30 years. In fact, several observational studies in patients undergoing cardiovascular, thoracic, and abdominal surgery have shown that oxygen consumption at the AT less than 10 to 11 mL/kg per minute or VO_{2peak} less than 15 mL/kg per minute[19] can identify patients at high risk of developing postoperative complications.[20–26] Similarly, reduced AT has also been associated with increased mortality in the immediate postoperative period.[27–32] Moreover, in a large prospective observational study (n = 1725), the addition of CPET variables derived at AT improved the accuracy of other clinical (vital capacity), demographic (gender), and surgical variables (type of surgery) predicting long-term survival after thoraco-abdominal surgery[33] (**Table 1**). Candidates for CPET can be identified based on the presence of clinical risk factors or based on the results of functional tests, such as the 6MWT.[14] Interpretation of its results requires a team of experts and trained caregivers, as determination of AT can be influenced by several factors and therefore produce misleading results.[18] Variation of CPET protocols, interobserver and intraobserver variation of CPET results, learning effect, and preoperative

Table 1
Preoperative CPET and association with postoperative outcomes

Study	Type of Study, n	Surgery	Preoperative CPET Variables	Postoperative Outcome	Clinically Relevant Results
Older et al,[27] 1993	Observational, 187	Major abdominal Age >60 y	AT	Mortality	Higher mortality (18% vs 0.8%) if AT <11 mL/kg/min
Older et al,[28] 1999	Interventional, 548	Intra-abdominal Age >60 y	AT	Mortality	11% mortality[a] in patients with AT < 15 mL/kg/min 0% mortality in patients with AT > 14 mL/kg/min
McCullough, et al,[20] 2006	Observational, 109	Laparoscopic RGB	Vo_{2max}	Morbidity	Vo_{2max} <16 mL/kg/min
Snowden et al,[21] 2010	Major abdominal (colorectal excluded)	AT	Morbidity LOS	Morbidity LOS	AT <10.2 mL/kg/min predicted >1 postoperative complications
Wilson et al,[29] 2010	Observational, 847	Elective colorectal, nephrectomy, or cystectomy Age >59 y	AT	Mortality	AT <10.9 mL/kg/min Overall: RR = 6.8, 95% CI 1.6–29.5) Patients without cardiac risk factors RR = 10.0, 95% CI 1.7–61.0
West et al,[22] 2014	Observational, 136	Colorectal surgery	AT VO_{2peak} VE/VCO2[b]	Morbidity	Patients with at least 1 complication had a median AT = 9.9 mL/kg/min; VO_{2peak} = 15.2 mL/kg/min; VE/VCO2 = 31.3 mL/kg/min, significantly lower than patients without complications (P < .005)

Grant et al,[30] 2015	Observational, 506	EVAR	AT VO_{2peak} VE/VCO2[b] at AT > 42	1 and 3-y survival	VE/VCO2 at AT > 42, and VO_{2peak} < 15 mL/kg/min independently predict reduced survival; reduction in AT independently predicts complications
Carlisle et al,[31] 2007	Observational, 130	Open AAA repair	AT VE/VCO2	Midterm survival	AT HR = 0·84 (0·72–0·98) VE/VCO2 HR = 1.13 (95% CI 1.07–1.19)
Epstein et al,[32] 2004	Observational, 59	Liver transplantation	VO_{2peak} AT	Mortality	AT independently associated with mortality (adjusted OR = 14.1, *P* = .03)
Forshaw et al,[23] 2008	Observational, 78	Esophagectomy	AT VO_{2peak}	Morbidity	VO_{2peak} lower in patients with cardiopulmonary complications (19.2 mL/kg/min vs 21.4 mL/kg/min, *P* = 04)
Nagamatsu et al,[24] 2001	Observational, 91	Esophagectomy	Vo_{2max} AT	Morbidity	Vo_{2max} independently predicts postoperative complications (*P* = .001)
Nugent et al,[25] 1998	Observational, 30	Open AAA repair	VO_{2peak}	Morbidity	VO_{2peak} < 20 mL/kg/min in 70% patients who had complications vs 50% in those who had not

Abbreviations: AAA, abdominal aortic aneurysm; AT, anaerobic threshold; CI, confidence interval; CPET, cardiopulmonary exercise training; EVAR, endovascular abdominal aortic aneurism repair; HR, hazard ratio; LOS, length of stay; OR, odds ratio; RGB, Roux-en-Y gastric bypass; RR, relative risk of non-survival; Vo_{2max}, maximum oxygen consumption; VO_{2peak}, peak oxygen consumption.

[a] Estimated by the reported figure.

[b] Ventilatory equivalent for CO_2.

medications (beta-blockers) can all affect the measurement of AT.[18] Awareness of such pitfalls is crucial to avoid taking wrong preoperative clinical decisions.

Reestablishing baseline levels (eg, after neoadjuvant chemo-radiation therapy), or even improving baseline functional capacity before surgery, can be particularly important to increase physiologic reserve, to attenuate the impact of surgical stress, and to ensure a rapid and safe recovery. Interestingly, the results of a pilot study showed that the response to neo-adjuvant chemo-radiation therapy in patients treated with an intense exercise program before surgery was more effective than in patients in the control group, as demonstrated by a better MRI tumor staging 9 weeks after surgery.[34]

Surgical patients are frequently anemic preoperatively. In patients undergoing noncardiac surgery, the prevalence of preoperative anemia is estimated at approximately 30%[35] and has been reported as high as 90% in oncologic patients.[36] The pathogenesis of preoperative anemia is multifactorial: iron deficiency, chronic inflammation, myelosuppression, and renal impairment are the most common causes of anemia in surgical patients. Several studies have demonstrated an association between preoperative anemia and adverse outcomes.[37] Considering that allogeneic blood transfusion also has been independently associated with increased morbidity, mortality, and worse oncologic outcomes,[37] early identification of anemic patients is crucial to facilitate optimization of hemoglobin levels before surgery, without necessarily relying on blood transfusion. However, allogeneic blood transfusions remain essential to rapidly restore physiologic hemoglobin levels of severely anemic patients. Correction of preoperative anemia takes time and it can require a multidisciplinary approach, including anesthesiology and internists, hematology, transfusion medicine, gastroenterology, and education of all caregivers responsible for surgical patients.[38,39] Despite studies consistently demonstrating an association between preoperative anemia and postoperative morbidity and mortality, evidence suggesting that correcting preoperative hemoglobin levels improves postoperative outcomes is scarce.[39–41] A recent large prospective multicenter cohort study including 129,719 surgical patients showed that implementation of a patient blood management program, combining multidisciplinary perioperative interventions to increase and preserve autologous erythrocyte volume, is feasible and safe, and it significantly reduces the number of red blood cells and the incidence of acute renal failure.[42] Finally, it must be considered that anemic patients struggle to be compliant with exercise programs because of generalized fatigue. Optimizing preoperative hemoglobin levels in such patients might be beneficial to increase adherence to prehabilitation.

Preoperative screening of nutritional risk, and preoperative nutritional assessment and optimization also should be part of preoperative evaluation, as poor nutritional status not only increases the risk of postoperative complications,[43,44] but it has also been associated with worse oncologic outcomes.[45] It has been reported that the prevalence of malnutrition in patients with cancer ranges between 20% and 70%, depending on patient age and on the type and stage of cancer.[46] In fact, loss of appetite, metabolic rearrangements induced by the tumor, nausea and vomiting associated with oncologic treatments, and physical limitations induced by the cancer (eg, gastrointestinal obstruction) can significantly compromise the nutritional status of oncologic patients.[44] Identification of malnourished patients or patients at nutritional risk is crucial, and several validated scoring systems and questionnaires can be used.[44] Surgical patients should be routinely screened for malnutrition, and nutritional interventions should be given to malnourished patients and patients at nutritional risk. Preoperative nutritional interventions, preferably using the enteral route, should be given for at least 7 days before surgery.[44] If the energy and nutrient requirements cannot be met by oral and enteral intake alone (<50% of caloric requirement), parenteral nutrition also should be initiated. In patients in whom enteral nutrition is contraindicated or not feasible (eg, bowel obstruction), parenteral nutrition should be commenced as soon as possible.[44] Nutritional supplementation might be recommended in non-malnourished patients, as it helps to prevent serious postoperative complications and to maintain nutrition during the postoperative period.[44,47] Although the role of immunonutrition is controversial, guidelines recommend the administration of specific formula enriched with immunonutrients in malnourished patients undergoing major cancer surgery.[44] It is well established that optimizing nutritional status of malnourished patients scheduled for surgery decreases postoperative complications[44,48]; however, the impact of nutritional interventions on oncologic outcomes remains to be further investigated. A small randomized clinical trial suggested that in surgical patients with head and neck cancer, preoperative and postoperative arginine supplementation reduced the infection rate and impact on survival.[49] Moreover, a large retrospective study conducted in the context of an ERAS program demonstrated that high adherence to ERAS interventions, including those to optimize the nutritional status of malnourished patients with colorectal cancer scheduled for surgery, was associated with an improvement of cancer-specific survival and a reduction of cancer-specific death by 42% (hazard ratio = 0.58, 95% confidence interval = 0.39–0.88).[50]

The preoperative period also should be considered as an opportunity to change unhealthy lifestyle behaviors, such as smoking, and improve long-term outcomes.[51] Preoperative intense smoking cessation programs, including nicotine replacement therapy and patient counseling, have been associated with fewer postoperative infectious complications and long-term smoking abstinence, but only if initiated 4 weeks before surgery.[52] Alternatively, shorter interventions, such as preoperative treatment with Varenicline in association with patient counseling, can be prescribed.[53]

Psychological evaluation also should be part of the preoperative assessment, especially for oncologic patients. Despite animal and clinical trials suggesting that psychological stress can potentiate the stress response associated with surgery and facilitate cancer metastasis, implementation of psychological strategies in patients with cancer have failed to improve oncologic outcomes.[51] Nevertheless, it has been suggested that intervening throughout the entire perioperative period might be more beneficial than treating these patients solely in the postoperative period.[51] Moreover, psychological optimization has been associated with better postoperative analgesia and less analgesic consumption.[54]

Finally, with an aging population that continues to grow, elderly oncologic patients are more frequently scheduled for surgery. In this population, risk assessment is complex and it should require a multidisciplinary approach. It should not only include the risk associated with concomitant comorbidities, but also the risk of postoperative delirium, cognitive impairment, risk of falls, and the patient's frailty.[55]

FACILITATORS, BARRIERS, CHALLENGES

Optimal preoperative risk assessment, stratification, and optimization require a multidisciplinary approach, including anesthesiologists, internists, nurses, nutritionists, and smoking cessation facilitators. Implementation of a multidisciplinary preoperative clinic can facilitate risk assessment and optimization, and it has been associated with a reduction in postoperative morbidity and mortality.[56] It is also a great opportunity to inform patients about their surgical journey, the enhanced perioperative pathway, and seek for anesthesia consent after detailed discussion of most common anesthesia techniques.

Preoperative optimization might be challenging, as patients are frequently scheduled to be operated within a few weeks of the surgical diagnosis, leaving little or no time to optimize high-risk patients. This approach leaves high preoperative risk unmodified. This is particularly true for patients with cancer who in addition to the risk associated with their concomitant diseases[11,57–61] have specific oncologic conditions that further increase their risk of developing postoperative complications[62] (Fig. 1). If on the one hand it is commonly believed that immediate surgical resection of the tumor is crucial to avoid cancer recurrence and dissemination, on the other hand it must also be acknowledged that operating nonoptimized, high-risk patients significantly increases the risk of morbidity and mortality.[63] The decision to eventually delay surgery to optimize high-risk patients should consider the biology of the tumor, tumor staging, patients' physical status, and the effectiveness of preoperative interventions aimed at reducing the surgical risk. Evidence suggesting that postponing elective oncologic procedures to permit preoperative optimization of high-risk patients does not negatively affect oncologic outcomes is lacking, but urgently needed. In the meantime, preoperative evaluation of high-risk oncologic patients should be scheduled as early as possible, to permit medical and functional optimization.

PREHABILITATION TO INCREASE FUNCTIONAL CAPACITY BEFORE SURGERY

Surgery and Recovery

There is strong evidence that many of the negative immediate effects of surgery and cancer treatment, such as pain, fatigue, fluid overload, and weakness, can be

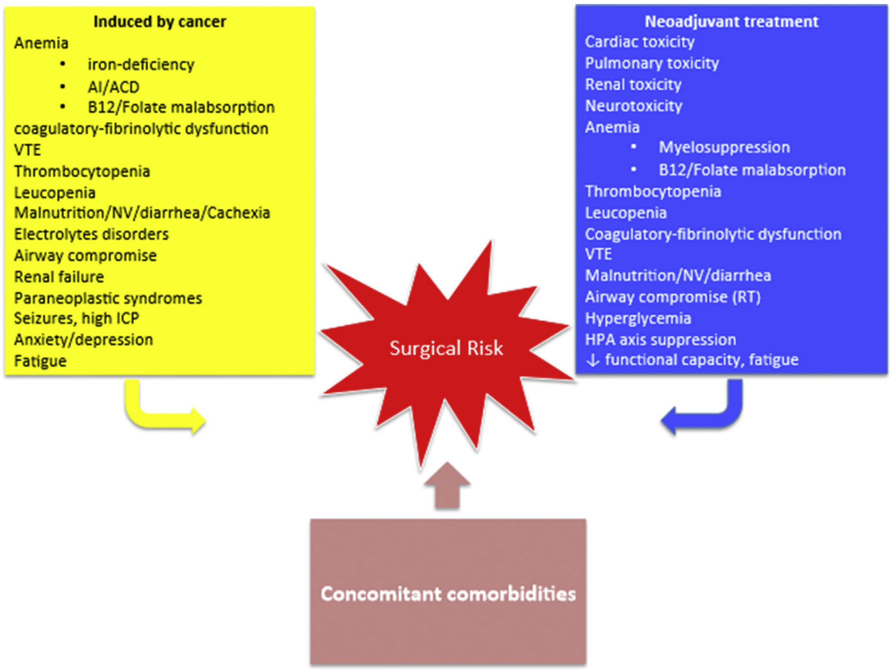

Fig. 1. Preoperative determinants of surgical risk in oncologic surgical patients. Surgery. related factors are not reported. AI/ACD, anemia if inflammation/anemia of chronic diseases; HPA, hypothalamic, pituitary, adrenal; ICP, intracranial pressure; NV, nausea and vomiting; RT, radiation therapy; VTE, venous thrombus embolism.

attenuated if adequate interventions are carried out, thus facilitating a faster recovery and early hospital discharge.[64] It would be of practical benefit if ways of improving postsurgery physical function and quality of life could be identified. Unfortunately, efforts are made to improve the recovery process by intervening in the postoperative period, which is not the most opportune time to introduce interventions to accelerate recovery because patients are tired, depressed, and anxious about further treatment they might receive. The preoperative period may be, then, a more emotionally opportune time to intervene while patients are scheduled for extra tests, and are anxiously waiting for surgery.

Increasing Functional Capacity by Prehabilitation

In the preoperative assessment of patients presenting for surgery, functional capacity is measured to estimate surgical risk and the need for intervention. As previously described, low functional capacity is correlated with an increase in postoperative complications.[21,29,65] It would therefore make sense if functional capacity can be increased before surgery, thus attenuating the postoperative risk. The process of enhancing functional capacity of the individual to enable him or her to withstand the incoming surgical stressor has been termed prehabilitation.[66,67] The concept of prehabilitation began in the orthopedic population (hip and knee arthroplasty) in which the impact of physical activity/exercise on postoperative outcome following surgery was addressed. The study of prehabilitation has since expanded to cardiac, vascular, and abdominal surgery. There is increasing evidence from the literature that preoperative exercise enhances physiologic reserve before and after surgery, with earlier return to baseline values. Recent systematic reviews reported that compared with standard care, prehabilitation reduced length of hospital stay and postoperative complication rate, and improved postoperative pain and physical and physiologic function[68–70]; however, interventions based on exercise alone may not be sufficient to enhance functional capacity. A randomized controlled trial in 112 patients undergoing colorectal surgery who received either a sham intervention of basic recommendations to walk daily and perform breathing exercises (control group) or a home-based high-intensity training program (aerobic and resistance exercises) demonstrated that patients in the control group experienced greater improvements in functional walking capacity compared with the intervention group.[71] Compliance to the high-intensity training program was only 16%, indicating that the prescribed exercise could not be maintained. Thus, a multimodal prehabilitation program has been recently proposed that includes structured aerobic and resistance exercise that is complemented by nutritional counseling, protein supplementation, and relaxation strategies to attenuate anxiety. This intervention is based on the understanding of the synergistic effect achieved by exercise in conjunction with protein administration to maximize muscle protein synthesis and therefore increase muscle strength.[72] The multimodal intervention was conducted in a pilot study[73] followed by a randomized controlled trial[74] in 164 patients undergoing colorectal resection. Results showed that more than 80% of patients were able to return to preoperative functional capacity by 8 weeks after surgery compared with only 40% in the control group.

Exercise Before Surgery

There is overwhelming evidence on the role of exercise in disease prevention, in fact, regular exercise has been shown to decrease the incidence of ischemic heart disease, diabetes, stroke, cancer progression, and fractures in the elderly. These achievements are a result of the various benefits associated with participating in regular physical activity, such as improvements in aerobic capacity, increased ratio of lean body mass to body fat, antioxidant capacity, better insulin sensitivity, and decreased sympathetic hyperactivity. Therefore, engaging surgical patients in physical activity and structured exercise programs to improve functional capacity in preparation for surgery is worth exploring; however, the literature on surgical prehabilitation is limited.

The traditional approach to the preoperative timeframe is to encourage rest to best prepare the patient for the upcoming surgery and initiate exercise only postoperatively as rehabilitation. However, bed rest has deleterious effects on lean muscle mass, physical function, lower extremity strength/power, aerobic capacity, and homeostasis.[75–77] Contrary to this standard, an exercise-mediated intervention initiated preoperatively, such as prehabilitation, has shown to result in greater improvements in functional walking capacity throughout the whole perioperative period when compared with rehabilitation started after surgery[72] (**Fig. 2**). These improvements are even more meaningful in patients with poorer fitness levels. Patients with lower baseline walking capacity experienced greater improvements in functional status with prehabilitation compared with patients with higher fitness.[78] However, such programs are only as effective as the adherence to them. The most commonly reported barriers for patients with cancer enrolled in a supervised prehabilitation program were parking (finding and paying for parking), transportation, and time.[79] Last, patient safety is a priority when participating in an exercise program. Prehabilitation programs have shown to be safe, even for elderly patients, whether they were delivered as home-based or center-based programs.[34] However, exercise performed under the supervision of an exercise specialist provides an added safety benefit. Careful considerations must be taken when developing a prehabilitation program to maximize adherence and ensure safety, as they can significantly influence the effectiveness of the program.

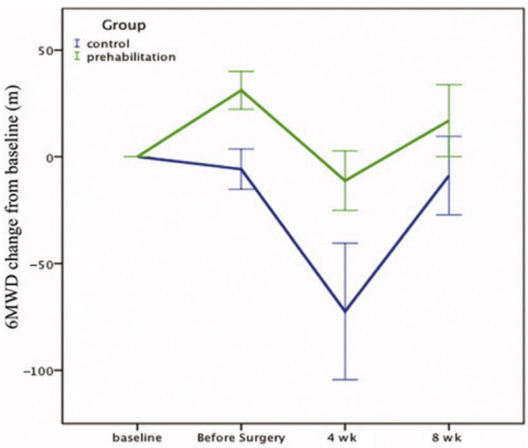

Fig. 2. The trajectory of the changes in functional capacity through the perioperative period in the prehabilitation and the control groups. Patients in the prehabilitation group received the trimodal intervention (exercise, nutrition, and relaxation strategies) before surgery. Patients in the control group started the same trimodal intervention (rehabilitation) after surgery. Error bars represent the 95% confidence interval. 6MWD = 6-minute walk distance. (*From* Minnella EM, Bousquet-Dion G, Awasthi R, et al. Multimodal prehabilitation improves functional capacity before and after colorectal surgery for cancer: a 5-year research experience. Acta Oncol 2017;56(2):298; with permission.)

Exercise Prescription

The term exercise refers to regular physical activity that is planned and structured for the specific goal of improving or maintaining fitness.[80] To better prepare for surgery, a preoperative exercise program should incorporate the 4 main types of exercise training: aerobic, strength, balance, and flexibility. Aerobic training stimulates the cardiovascular system by augmenting ventilator capacity and heart rate. It has been shown to be effective in improving physical fitness in patients awaiting intracavity surgery,[81] as well as improving cancer-related fatigue and quality of life.[82] An inexpensive and easy-to-perform test to assess functional exercise capacity is the 6MWT. The 6MWT has been validated in patients with cancer and is commonly used as a predictor for postoperative morbidity and mortality; however, it also can be used in the prescription of aerobic training, such as a walking program.[83]

Strength training focuses on resistance exercises to induce muscular contractions, promoting muscle anabolism, mass, and strength. Increasing lean muscle mass before surgery is key, given that muscle wasting is a typical phenomenon resulting from the catabolic effects of surgery in addition to the progressive muscle loss associated with aging.[84,85] Emphasis should be placed on exercises that reflect functional movements of daily living (ie, standing up from a seated position, which predominantly uses quadriceps muscular strength). Strengthening such muscles is particularly important for older adults, as they are associated with fall risk. Functional fitness tests, such as the 30-second sit-to-stand and arm curl test, can be used to predict muscular strength of the lower and upper limbs, respectively.[86]

In addition to aerobic and strength training, it is equally important to consider balance and flexibility training as necessary components of exercise prescription, particularly for the elderly population that is at an increased risk for falls and has limited range of motion. Given the relatively condensed period in which prehabilitation is being performed, careful monitoring of the program is of importance.

Just as the prescription of medication requires a specific dosage, delivery form, and frequency, the prescription of exercise should be given the same degree of precision. According to the American College of Sports Medicine (ACSM), the prescription of an exercise program should be tailored to the needs and desired outcomes of the patient by using the FITT principle[87]: frequency, intensity, timing, and type. Frequency refers to how often, usually the number of days per week, the patient should engage in exercise. The ACSM recommends healthy individuals to engage in aerobic training 3 to 5 days per week, resistance training 2 to 3 days per week, and flexibility/balance training most days of the week, especially following resistance training.[87] Intensity is the level of exertion experienced during exercise, which can be monitored using the 6 to 20 Borg scale (**Fig. 3**), a well-validated index of perceived exertion[88,89] or by tracking heart rate. The intensity recommended for aerobic exercise is moderate to vigorous intensity that is equivalent to 12 to 16 on the Borg scale (somewhat hard to hard) or a target heart rate between 40% and 85% of heart rate reserve (HRR).[87] Target heart rate is calculated by the Karvonen method: target heart rate = {[(220 − age) − resting heart rate] × percent intensity} + resting heart rate. For resistance exercise, 50% to 70% of 1 repetition maximum (maximal weight that can be lifted 1 time) in 2 or 3 sets with 8 to 12 repetitions per set has shown to be effective.[87] Time refers to the duration of the exercise, which should be between 20 and 60 minutes for aerobic training and 30 minutes for resistance training.[87] For flexibility training, each stretch should be held for 15 to 30 seconds and repeated 2 to 4 times.[87] Finally, type refers to exercise modality and can be any of the 4 types of exercise mentioned previously. A guide for a FITT exercise prescription is shown in **Table 2**.

6	No exertion at all
7	
8	Extremely light
9	
10	
11	Light
12	
13	Somewhat hard
14	
15	Hard (heavy)
16	
17	Very hard
18	
19	Extremely hard
20	Maximal exertion

Fig. 3. The Borg scale rating of perceived exertion. The scale values range from 6 to 20 and can be used to denote heart rates ranging from 60 to 200 beats per minute. Moderate intensity exercise registers 11 to 14, whereas vigorous exercise rates 15 or higher on the Borg scale. (*Data from* Borg G. Perceived exertion as an indicator of somatic stress. Scand J Rehabil Med 1970;2(2):92–8.)

Table 2
FITT exercise prescription

FITT Principle Components	Frequency	Intensity	Time	Type
Aerobic training	3–5 d per wk.	Moderate: 40%–60% of HRR or 11–14 RPE. Vigorous: 60%–85% of HRR or ≥15 on Borg scale.	20–60 min.	Dynamic use of large muscle groups.
Strength training	2–3 d per wk.	2–3 sets of 8–12 repetitions. 12–16 RPE.	30 min.	8–10 exercises targeting major muscle groups.
Flexibility	Most days of the week.	Stretch to tightness but not to pain.	15–30 seconds/ stretch. Repeat 2–4 times.	Static stretches targeting major muscle groups.

Abbreviations: FITT, frequency, intensity, time, type; HRR, heart rate reserve; RPE, rate of perceived exertion according to 6–20 Borg scale.

Another principle that is not included in the FITT acronym is exercise progression. Progressions to exercise must be considered when adaptations occur and the patient becomes accustomed to the demands of the exercise performed. This basic training principle is necessary to ensure that the body is continuously stressed, allowing for optimal improvements.[90] Overloading or progressing the exercise program accordingly can be achieved by increasing either one of the FITT variables; however, it is recommended to increase frequency and duration before intensity.[91]

Although there are yet to be specific exercise guidelines for patients awaiting surgery, there is evidence that preoperative exercise improves functional and cardiorespiratory fitness, strength, quality of life, and more. However, it is not clear if this improvement in fitness translates into reduced perioperative risk or improved postoperative outcomes.[92,93]

Role of Nutrition to Increase Muscle Strength

The nutritional status of patients scheduled for surgery is directly influenced by the presence of cancer, which has an impact on all aspects of intermediary metabolism. The primary goal of nutrition therapy is to optimize nutrient stores preoperatively and provide adequate nutrition to compensate for the catabolic response of surgery postoperatively.[94–97] To be successful, a nutrition intervention requires a timeline that needs to start with preoperative assessment and extend into the postoperative period. The greater sensitivity of protein catabolism to nutritional support, in particular to amino acids, could have important implications for the nutritional management of these patients during periods of catabolic stress, with particular emphasis on substrate utilization and energy requirement during the healing process. Protein intake is calculated as 20% of total energy expenditure, determined individually, using a stress factor of 1.3 for major surgery and an appropriate activity factor.[44] Protein requirements are elevated in stressed states, such as cancer, to account for added demands of hepatic acute phase proteins synthesis, and the synthesis of proteins involved in immune function and wound healing. Nonsurgical nutrition oncology guidelines on enteral nutrition suggest that patients with cancer should consume at least 1.2 to 2.0 g protein/kg per day.

Dietary protein increases whole body protein synthesis by increasing systemic amino acid availability. After exercise, the ingestion of amino acids is recommended because of the stimulatory effect that amino acids have on muscle protein synthesis[98,99] (Fig. 4). In fact, protein ingestion post resistance exercise has been found to stimulate rates of myofibrillar protein synthesis above fasting rates for 24 hours.[100]

Psychological Distress Before Surgery

The presence of psychological distress, specifically anxiety and depression, is very common in patients with cancer. In fact, Hellstadius and colleagues[101] found that 34% and 23% of patients with esophageal cancer waiting for surgery were considered

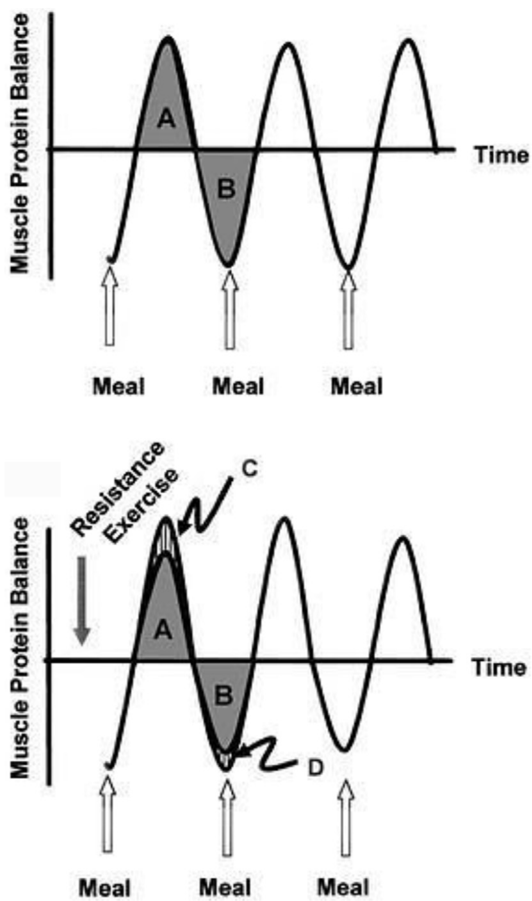

Fig. 4. Top: Normal fed–state protein synthesis and fasted-state protein breakdown. The area under the curve in the fed state (A) is equivalent to the fasted loss area under the curve (B); hence, skeletal muscle mass is maintained by feeding. Bottom: Fed-state protein synthesis and fasted-state protein breakdown in skeletal muscle with performance of resistance exercise. Fasted-state gains are enhanced by an amount equivalent to the stimulation of protein synthesis brought about by exercise (C). Additionally, fasted-state losses appear to be less (D), due to persistent stimulation of protein synthesis in the fasted state. (*Adapted from* Phillips SM. Protein requirements and supplementation in strength sports. Nutrition 2004;20(7):691; with permission.)

anxious and depressed, respectively. Such mental states have shown to negatively impact surgical and clinical outcomes, such as wound healing, postoperative pain relief, hospital stay, and functional recovery even after known physiologic factors were accounted for.[102] There is evidence in breast, colon, and prostate cancer supporting the role of psychological interventions implemented before surgery to alleviate distress, improve quality of life,[103] reduce anxiety and depression,[103,104] and reduce pain severity and fatigue.[105] These interventions include relaxation techniques (deep breathing, progressive muscle relaxation, and meditation), guided imagery, and/or problem-solving and coping strategies. However, these strategies did not affect traditional surgical outcomes, including length of hospital stay, complications, analgesic use, or mortality.[106]

Further Steps

The increasing interest in prehabilitation for surgical cancer patients stems from growing, however limited, evidence that such multidisciplinary programs can address modifiable risk factors that may impact treatment outcomes.[107] Additionally, in the patient perspective, prehabilitation shows promising effects on preoperative functional capacity in anticipation of surgery, and with more research could mitigate the pathophysiological burden associated with cancer and surgical stress, thus accelerating the recovery process. Patients with limited reserve can potentially benefit more from a structured personalized prehabilitation program, as shown recently.[72] Although the prehabilitation approach has the potential for diagnosing reversible limitations in the preoperative period and targeting intervention strategies to ameliorate postoperative outcomes, there are still gaps in our understanding of how to identify those patients who would benefit from the prehabilitation program, select the appropriate interventions, determine the effectiveness in the context of a definite type if surgery, and examine the impact on patient-centered and clinical outcomes. More needs to be done and knowledge to be acquired with respect to the prescription of exercise and the role of immunonutrition within the context of ERAS programs for each specific type of surgery. This patient-centered, multidisciplinary, and integrated medical care program should start in the preoperative clinic where vulnerable patients can be identified, risk stratified adequately by an interdisciplinary team with the aim of improving surgical outcome, and promoting healthy behaviors throughout the continuum of care.

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