Prehabilitation to Enhance Perioperative Care

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KEYWORDS

• Surgery • Elderly • Cancer • Prehabilitation • Exercise • Nutrition

KEY POINTS

- Despite advances in surgical care, there remain patients with suboptimal recovery; elderly patients, especially those with cancer and limited protein reserve are at highest risk for negative postsurgical outcomes.
- Although more traditional approaches have targeted the postoperative period for rehabilitation, it has been shown that the preoperative period is most effective for intervention.
- Surgical prehabilitation is an emerging concept, deriving from the realization that effective perioperative care must include in addition to the clinical and pharmacological preparation of the surgical preparation, preoperative physical, nutritional and psychological optimization.

THE STRESS OF SURGERY AND TRAJECTORY OF RECOVERY

Tissue trauma, physical inactivity, quasi-starvation and psychological distress represent major stresses to the body. In turn, immediate systemic changes are initiated, resulting in both short- and long-term effects on the capacity to perform activities of daily living and on overall quality of life.

Despite advances in surgical technology, anesthesia and perioperative care, which have made surgery safer and more accessible to a variety of patients potentially at risk, there remains a group of patients who still have suboptimal recovery. Almost 30% of patients undergoing major abdominal surgery have postoperative complications,[1] and, even in absence of morbid events, major surgery is associated with a 40% reduction in functional capacity.[2] After surgery, patients experience physical fatigue, disturbed sleep, and a decreased capacity to concentrate for up to 9 weeks after discharge.[3] Long periods of physical inactivity induce loss of muscle mass, deconditioning, pulmonary complications, and decubitus. Postoperative fatigue and

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complications have been found to be correlated with preoperative health status, functional capacity, and muscle strength.[4] The elderly, persons with cancer, and persons with limited protein reserve are the most susceptible to the negative effects of surgery.

There is mounting evidence that many of the negative immediate effects of surgery such as pain, fatigue, and weakness, are potentially amenable to intervention. If proper interventions are carried out, these symptoms may be readily controlled, allowing for a faster recovery and early hospital discharge. However, the effects of surgery are felt far beyond the immediate convalescent period and patients can feel fatigued for many weeks; fatigue delays return to usual function and reduces quality of life. Thus, it would be of practical benefit if ways of improving postsurgery physical function and quality of life could be identified.

Traditionally, efforts have been made to improve the recovery process by intervening in the postoperative period. However, the postoperative period may not be the most opportune time to introduce interventions to accelerate recovery. Many of these surgical patients are concerned about perturbing the healing process as well as being depressed and anxious as they await extra treatment of the tumor and, therefore, are unwilling to be engaged in the process.

The preoperative period may be, then, a more emotionally opportune time to intervene in the factors that contribute to recovery. Patients are often scheduled for extra tests, anxiously waiting for surgery, and searching for explanation and reassurance. In the face of the powerlessness and diminished self-esteem that often follow a health threat, active engagement of the individual in the preparation process may have benefits beyond the physical and alleviate some of the emotional distress surrounding the anticipation of surgery and the recovery process.

SURGICAL PREHABILITATION AND THE PUBLISHED EVIDENCE

The process of enhancing functional capacity of the individual to enable them to withstand an incoming stressor has been termed prehabilitation.[5] Although several programs have attempted to prepare patients for the postoperative recovery through education and positive reinforcement, little has been developed to systematically enhance functional capacity before surgery.

The theory of prehabilitation was initially supported in animal models. To investigate the effect of voluntary exercise on the tolerance to trauma, female rats, kept in cages with running wheels for periods of 3 to 7 weeks (exercise group), were subjected to trauma and compared with rats kept in cages without running wheels for the same period (sedentary group).[6] Mortality was significantly decreased in rats kept in cages with running wheels for 5 weeks or 7 weeks, but not those in the 3-week group. These results indicated that voluntarily exercising rats showed increased resistance to trauma compared with rats kept under sedentary conditions.

Although the benefits of physical activity have been shown in many disabling conditions, there are limited clinical data on the role of exercise before surgery. However, the evidence of the role of exercise in disease prevention is overwhelming. In medicine, regular exercise has been shown to decrease the incidence of ischemic heart disease, diabetes, stroke, and fractures in the elderly as a result of improved balance and strength. As a result of exercise, there is an increase in aerobic capacity, decreased sympathetic overreactivity, increased antioxidant capacity, improved insulin sensitivity, and increasing ratio of lean body mass to body fat.[7] Exercise training, particularly in sports medicine, has been used as a method of preventing a specific injury or facilitating recuperation. Thus, one would assume that by increasing the patient's aerobic and muscle strength capacity through increased physical activity before surgery, physiologic reserve would be enhanced and postoperative recuperation would be facilitated.

In 2002, Topp and colleagues[5] proposed that, by applying an exercise program before the stress of surgery, postoperative recovery would occur more rapidly compared with patients who remained sedentary. Since then, several studies have been undertaken, using different types of exercise programs.

The first systematic review of fair to good methodological quality was published in 2011 and included 12 studies.[8] The effect of preoperative exercise therapy on postoperative complication rate and length of hospital stay was studied, and it showed that preoperative exercise therapy can be effective for reducing postoperative complication rates and accelerate discharge from hospital in patients undergoing cardiac and abdominal surgery. Conversely, the outcome after joint arthroplasty was not significantly affected by preoperative exercise therapy.

All 4 studies that investigated cardiac and abdominal surgery included inspiratory muscle training as an intervention. The results showed that the risk of developing postoperative pulmonary complications was significantly higher in the group not receiving inspiratory muscle training. The interventions included in the review varied with respect to the type of exercise, frequency, duration, and intensity and lacked detailed about the precise implementation of the programs. In the orthopedic groups, the prehabilitation lasted up to 6 weeks, whereas in the cardiac and abdominal group, the average was 3 to 4 weeks. Also, some interventions were home based, whereas others were partly supervised or fully supervised by a physiotherapist. Functional measures such as exercise capacity and muscle strength were not included as outcome measures. In the studies involving joint replacement surgery, there was a large variety of physical exercises, with different emphasis on either joint mobility or muscle strength. The results of these studies indicated that preoperative exercise therapy does not affect length of hospital stay or complication rate after surgery.

Santa Mina and colleagues[9] reviewed 15 studies and concluded that total-body prehabilitation improved postoperative pain, length of stay, and physical function, but it was not consistently effective in improving health-related quality of life or aerobic fitness in the studies that examined these outcomes.

More recently, another systematic review of 8 studies[10] reported that exercise confers some physiologic improvement with limited clinical benefit. However, the data analyzed were limited, with great heterogeneity between the studies because of the differences in surgery type. Also, the exercise regimens were not uniformly reported with regard to the individual components of exercise (eg, the duration and the intensity), and the lack of adherence to high-intensity exercise. Although some physiologic improvement during the preoperative period was reported by most of the studies, this change did not translate into improved clinical outcomes.

A previous randomized controlled trial (RCT), conducted by our group,[11] in patients undergoing colorectal surgery compared the effects of a home-based program, which included a sham intervention (basic recommendation to walk daily and do breathing exercises), and a high-intensity training program, which consisted of both aerobic and resistance exercise. We found that, unexpectedly, a third of the patients in the intense exercise group deteriorated in their functional walking capacity (a measure of functional exercise capacity) during the presurgical period. Their compliance was recorded at a mere 16%, thus indicating that the prescribed exercise regimen could not be maintained. Only 33% improved during prehabilitation, and 29% deteriorated despite the intervention. Predictors of poor surgical outcome included deterioration while waiting for surgery, age greater than 75 years, and high anxiety, thus supporting the need to better identify which factors, such as disease progression, catabolic state, poor compliance, and psychological stress, in addition to exercise, contributed to functional deterioration before surgery. These results suggest that an intervention based on exercise alone may not have been sufficient to enhance functional capacity if factors such as nutrition, anxiety, and perioperative care were not taken into consideration during the program. Also, the intensity of the exercise program should be carefully considered as well. Although physical activity has undoubtedly several benefits in restoring physiologic reserve in preparation for abdominal surgery, the role played by other modalities cannot be excluded, such as pharmacologic optimization, smoking cessation, alcohol reduction, dietetic counseling, nutritional supplementation, cognitive enhancement, and psychosocial support beside education.

In a recent pilot study[12] followed by an RCT,[13] a multimodal prehabilitation program composed of moderate-intensity physical exercise and complemented by nutritional counseling and protein supplementation, and anxiety and reduction strategies within the context of the ERAS (enhanced recovery after surgery) protocol, showed that more than 80% of patients with cancer undergoing colorectal resection were able to return to preoperative functional capacity by 8 weeks, compared with 40% of a control group who did not receive the prehabilitation program.

Although some components of a prehabilitation program are common to all types of surgery, specific interventions need to be tailored on a personal basis to improve definite body functions. For instance, the requirement of prehabilitation for someone going for lung surgery concentrates on the aerobic component, whereas peripheral and core muscle strengthening are needed for those undergoing hip and knee surgery. In addition, the timing of prehabilitation in relationship to the time of surgical intervention needs to be appropriately evaluated. In most studies, the time interval for prehabilitation has been proposed to be between 4 and 8 weeks, with short periods for patients with lung or abdominal cancer, and long periods for more chronic conditions, such as spine surgery or arthroplasty.

INCREASING PHYSIOLOGIC RESERVE WITH PHYSICAL EXERCISE: HOW DOES EXERCISE BENEFIT?

The participation in an acute bout of strenuous exercise is met with the need for the body to compensate for potentially major systemic perturbations. For example, blood volume can be quickly recruited and flow redirected to active muscle groups from less metabolically active tissue. Depending on the intensity and duration of exercise performed, cardiac output and systolic blood pressure increase to adequately perfuse blood to the working tissue. Breathing rate and the depth of each breath also increase, to ensure adequate oxygenation of the blood. Metabolism increases and shift nutrient source to reflect the availability of oxygen to the mitochondria and need for adenosine triphosphate, the primary energy source of the human body. Motor units that control skeletal muscle fiber recruitment become activated, and neural pathways fire to reflect the work undertaken. Many other body systems also adjust to minimize the stress of physical activity. As with other events that disrupt homeostasis, the body attempts to compensate for these perturbations to reestablish its natural environment.[14,15]

When exercise is undertaken on a regular basis, the body becomes more efficient in its adaptation to the stress of exercise. Physiologic systems, such as cardiovascular, respiratory, muscular, neural, and endocrine, all become more adept at both the anticipation and the compensation for each individual bout of exercise. As the body is exposed to repeated bouts of exercise, the systems become trained to adapt to the stress of work, and the body resets what is considered to be in its normal range for daily living. Trained individuals are able to tax a greater percentage of their functional range, or maximal physiologic capacity, during periods of physical stress.[15] For example, if a sedentary person is required to run for a bus, their body is not accustomed to performing the acute bout of activity. They are able to use only a smaller portion of their potential functional capacity, thus resulting in a limited ability for adaptation to that particular stress. Heart racing, sweating, feeling slightly ill, with shaky legs, and out of breath, they might be unable to speak with a bus driver or have difficulty climbing stairs. In the case of someone who performs regular exercise, they encounter a similar situation and are better able to adapt to the stress by means of their ability to tap into a greater percentage of their physiologic reserve. Although they run the same amount to catch up with a bus, their bodies are better able to cope with the bout of activity undertaken.

Physiologic reserve is the overall range of functional capacity in an individual, defined by genetics, and including all organ systems in the human body. The aging process is associated with some degree of diminishment, which starts in early adulthood.[16] Depending on the degree of loss of physiologic reserve, there may be negative consequences on the ability to perform activities of daily living, and, in more severe cases, frailty and increased morbidity/mortality may ensue. Although the aging process itself compromises physiologic reserve, the effects are compounded by sedentary behavior. Regular physical exercise can attenuate the degree of physical decline associated with aging.[17] Despite the known benefits of active living, only 30% of individuals older than 65 years participate in some form of daily exercise.[18] Despite increasing efforts to promote physical activity in this population, the figures remain consistent.[19]

The ability to adapt to physical stress and the preservation of physiologic reserve are both relevant concepts for prehabilitation. Functional capacity, as determined by cardiopulmonary exercise testing, has been associated with surgical outcomes in noncardiopulmonary procedures: patients who are less fit have been shown to have a higher incidence of postsurgical morbidity and mortality.[20] In addition, impaired handgrip strength before surgery, as assessed by dynamometry, also seems to be related to poorer postoperative outcomes in patients undergoing nonemergency, cardiac and noncardiac procedures.[21] The goal of prehabilitation is to improve these fitness parameters, among others such as flexibility, to optimize postsurgical recovery and maintain physical function.

A critical aspect of improving physiologic reserve lies in the postsurgical healing process. There is a decrease in functional decline in the period after surgery (**Fig. 1**).[22] Although the functional decline is primarily caused by surgical trauma, inflammation, or the cancer itself, it can be further amplified by the effects of bed rest or a need to take it easy. The health of physiologic systems quickly diminish as a result of inactivity, with the process beginning in as little as the first week after cessation of activity.[23] This factor is also important during the presurgical time frame, where diminished physical activity can directly affect surgical outcomes. Bed rest, in as little as 7 days, has been shown to decrease insulin-mediated glucose extraction.[24] The vasodilator effects of insulin diminish with 10 days of bed rest, even in healthy populations.[25] Those at risk for developing type 2 diabetes are subject to a disproportionate aggravation of existing systemic low-grade inflammation during periods of physical inactivity.[26] These effects of physical inactivity are critical for the surgical process, when inflammation is already of concern.

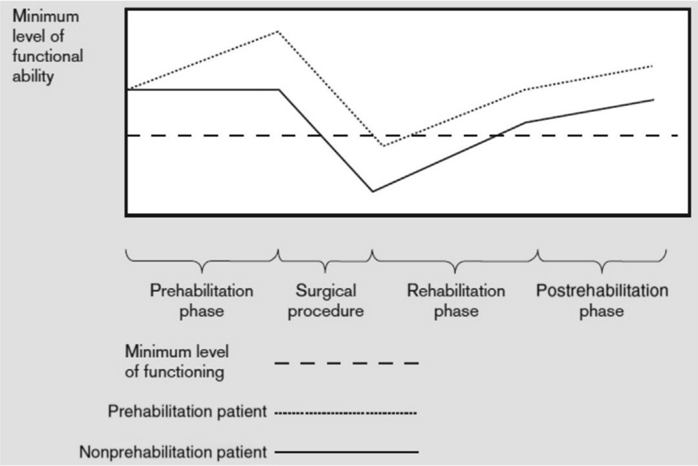

Fig. 1. Trajectory of functional capacity throughout the surgical process. (*From* Sultan P, Hamilton MA, Ackland GL. Preoperative muscle weakness as defined by handgrip strength and postoperative outcomes: a systematic review. BMC Anesthesiol 2012;12:1.)

As rapid as the physiologic decline caused by sedentary behaviors, the effects of training also occur quickly. For example, cardiovascular improvements can be seen within 3 weeks on commencement of physical training, even in older individuals.[27] The effective use of strength training programs is also not exclusive to younger populations: regular resistance training can reverse the age-related declines in skeletal muscle strength and function, even in frail, elderly individuals.[28] The limited time between diagnosis and surgery also seems to be an adequate time frame to obtain objectively measurable training effects.[29]

In 2007, the American College of Sports Medicine and the American Heart Association issued exercise recommendations specifically for the older adult, taking into consideration their heterogeneous health status and individual needs/goals for performing physical activity.[19] Other organizations have also released similar guidelines (eg, 2008 Physical Activity Guidelines for Americans, Canadian Society for Exercise Physiology, World Health Organization). A summary of the comprehensive guidelines published by the US Department of Health and Human Services (2008 Physical Activity Guidelines for Americans) has been presented in **Box 1**. Considering that the older adult is the least likely to regularly exercise,[19] it is important that their physical activity be meaningful, feasible, and something that they enjoy to maximize adherence. The main message is that the elderly should be encouraged to maintain a lifestyle as active as possible to promote and maintain good health practices.[30]

EXERCISE: WHAT TO DO?

Current recommendations include a combination of moderate and vigorous exercise, if deemed appropriate for the individual (see **Box 1**). What does moderate and vigorous represent for the patient? On a scale of 1 to 10 (1 representing a resting activity with no effort and 10 representing all-out, exhaustive exercise), moderate activity can be thought of as being a 5 to 6. Vigorous exercise falls within the range of 7 to 8. This scale, otherwise known as Rating of Perceived Exertion (RPE) or Borg Scale, is

Box 1
Physical activity guidelines for older adults.

Key Guidelines for Older Adults (2008 Physical Activity Guidelines for Americans)

The following Guidelines are the same for adults and older adults:

- All older adults should avoid inactivity. Some physical activity is better than none, and older adults who participate in any amount of physical activity gain some health benefits.
- For substantial health benefits, older adults should do at least 150 minutes (2 hours and 30 minutes) a week of moderate-intensity, or 75 minutes (1 hour and 15 minutes) a week of vigorous-intensity aerobic physical activity, or an equivalent combination of moderate- and vigorous-intensity aerobic activity. Aerobic activity should be performed in episodes of at least 10 minutes, and preferably, it should be spread throughout the week.
- For additional and more extensive health benefits, older adults should increase their aerobic physical activity to 300 minutes (5 hours) a week of moderate-intensity, or 150 minutes a week of vigorous-intensity aerobic physical activity, or an equivalent combination of moderate- and vigorous-intensity activity. Additional health benefits are gained by engaging in physical activity beyond this amount.
- Older adults should also do muscle-strengthening activities that are moderate or high intensity and involve all major muscle groups on 2 or more days a week, as these activities provide additional health benefits.

The following Guidelines are just for older adults:

- When older adults cannot do 150 minutes of moderate-intensity aerobic activity a week because of chronic conditions, they should be as physically active as their abilities and conditions allow.
- Older adults should do exercises that maintain or improve balance if they are at risk of falling.
- Older adults should determine their level of effort for physical activity relative to their level of fitness.
- Older adults with chronic conditions should understand whether and how their conditions affect their ability to do regular physical activity safely.

From US Department of Health and Human Services. Physical Activity Guidelines for Americans. Available at: http://www.health.gov/paguidelines/guidelines/. Accessed November 5, 2014.

easy to use and gives a rough indication of the intensity of activity performed (**Fig. 2**). It can easily be transferred onto an easy to read poster (large print) and hung up within view of the patients while exercising. This strategy allows for a common reference point for both the tester and testee. Although it does not represent a perfect representation of exercise intensity, it is commonly used in many populations of patients chronic disease (eg, American Thoracic Society). There are other scales, such as the Modified Borg Scale, which work on the same concept but use different numbers to represent perceived exertion. The use of a simple RPE scale is especially relevant for patients who have been prescribed medications that affect the heart rate response to exercise (eg, β-blockers), therefore limiting the use of heart rate as an indication of intensity. The benefit of the RPE scale is that it reflects the perceived intensity of the activity on a given day, taking into consideration any fatigue, illness, or other condition that negatively affects the individual's health status at a given moment. Conversely, it also takes into consideration positive adaptations caused by training, and the patient must increase their work intensity to maintain the same range of RPE values.

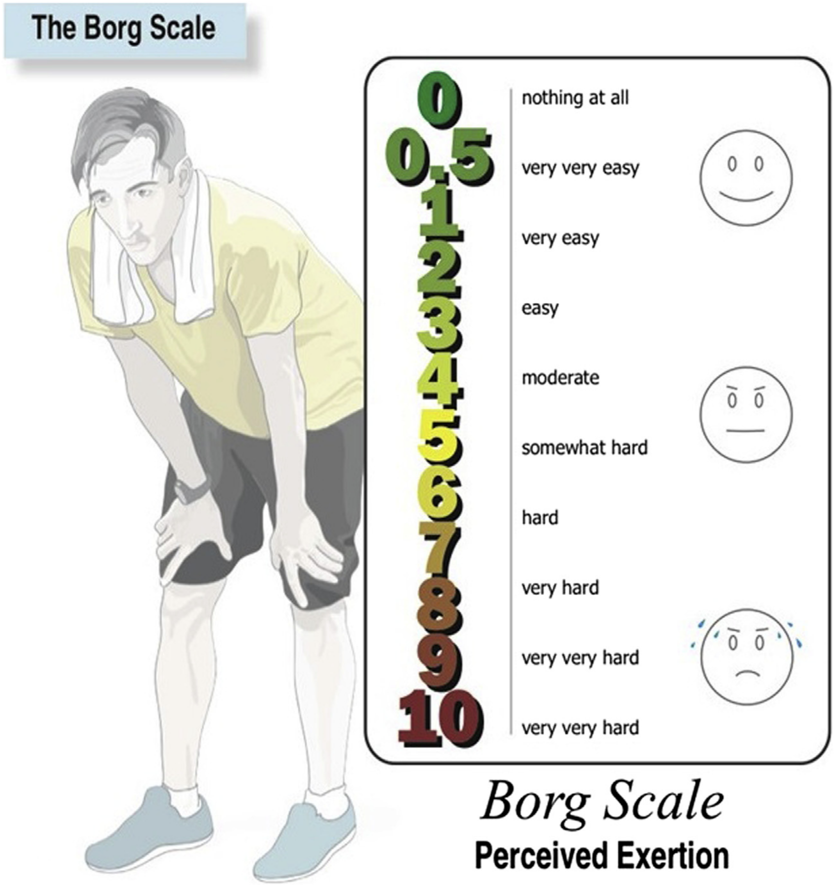

Fig. 2. Sample of the RPE (Borg) Scale. A scale such as this may be transferred onto a large poster board and mounted within view of the exercising patient. Often the RPE is color coded (from *green* or *blue* at rest to *red* at maximal efforts) or has cartoons representing effort. Key words represent exercise intensity.

Another important point raised in the more recent guidelines is that aerobic exercise does not have to take place in continuous bouts but has been shown to be of benefit in smaller sessions of at least 10 minutes. In patients with type 2 diabetes, 3 x 10 minutes of aerobic exercise during the day had more desirable effects on glycemic control than performing a single session of 30 minutes. The multiple short daily sessions may be associated with a higher energy expenditure than occurs during a single bout.[31] Besides possible physiologic benefits, the 10-minute sessions may be more feasible in this patient population, because of perceived time restraints, fatigue, or motivational factors.

Regarding exercise in general, it can be said that more is better but something is better than nothing.[32] In terms of exercise prescription, there is a clear dose response, with more health benefits occurring with higher amounts of physical activity.[30] However, when considering the prehabilitation patient, there are 2 issues to keep in mind: first, there is a clearly defined period between diagnosis and surgery, which depends on individual health care programs and, second, the presurgical patient may have a host of health conditions, including anxiety, depression, malnutrition, concurrent conditions, and the cancer itself, which might affect how they perform physical activity. For these reasons, encouraging the patient to do as much as they can in the period that is available may be the most efficient and effective approach. This strategy is especially important for the patient who has been previously sedentary or who has engaged in very low levels of physical activity. Programming for prehabilitation should introduce exercise that is more than what the individual already partakes in, so that the body experiences the stress of additional work, but avoiding an exercise protocol that is too intense, which may result in fatigue, injury, or (in our previous experience) poor adherence.[11] Prehabilitation in a 4-week period (diagnosis to surgery) has been shown to be sufficient to improve distance in the 6-minute walk test, decrease heart rate/oxygen consumption at submaximal workloads, and improve peak power output.[33] In addition, the program should be varied, touching on the various components outlined in **Box 1** (ie, aerobic and muscle strengthening exercises) and reflecting the needs of the individual. A sample exercise program from our laboratory is presented in **Box 2**. Allowing adequate rest between bouts of exercise is also important, both for physical recovery and to reap the physiologic benefits from the previous activity bout.[34] To continue physical improvements, the program must progress by slowly increasing the challenge of the exercise intensity. The concept of specificity should also be addressed when designing an exercise program for prehabilitation: an individual improves their functional capacity according to the type of stress delivered.[15] For instance, someone who trains on a bicycle may not achieve a higher peak oxygen consumption if evaluated on a treadmill. For that reason, the method of evaluation should reflect the type of training prescribed. Specificity may also be evident when the exercise testing occurs at intensities higher than training values (ie, measuring peak oxygen consumption [VO_2peak] after training at values 50%–60% of VO_2peak). In this instance, submaximal evaluation may be reflective of training and more appropriate to detect improvements in the elderly population.[35]

In general, individuals who have been the least fit and the most sedentary show the most improvements when they commence an exercise program.[32] Since the ratio of actual physiologic reserve to total physiologic reserve is small, even small amounts of physical training are remarkable. Patients following simple walking and breathing exercise guidelines have made marked improvements in walking capacity, as measured by the 6-minute walk test.[11] Older adults are particular susceptible to bed rest and physical inactivity, because of their already low functional capacity, this is a patient population who particularly benefit from targeted intervention.[22] In addition, prehabilitation programs that are multimodal (including physical, nutritional, and psychological components) seem to be more effective than programs that are unimodal.[36] As indicated by systemic reviews, preoperative exercise intervention before cardiac or abdominal surgery has been shown to reduce postoperative complications.[8] For these reasons, a multimodal prehabilitation program, with the aim of improving physical capacity before cancer surgery, seems to be an efficient and cost-effective method to ameliorate patient outcome after surgery.[22]

OPTIMIZING NUTRITION FOR PREHABILITATION

The nutritional status of patients scheduled for abdominal surgery is directly influenced by the presence of cancer or other chronic conditions, such as inflammatory bowel disease, which have an impact on all aspects of intermediary (protein,

Box 2
Example of 4-week prehabilitation program including physical activity and nutrition and relaxation exercises

Aerobic exercise

- Start a slow walk to adequately warm up
- 30 minutes minimum of aerobic activity (walking/biking) 3 times per week at moderate intensity (4–6 on the Borg Scale). If the participant finds the activity to be easier (2–3 on the Borg Scale), then, the walking pace or duration should be gradually increased. It is recommended not to surpass 7 to 8 on the Borg Scale. Example: walk at a normal pace for 5 minutes and then walk at a quicker pace for 2 minutes and repeat for the duration of time.

Resistance exercise

- All exercises are to be performed starting with 1 set of about 10 to 12 repetitions. Number of sets and repetitions gradually increase to 2 sets and 12 to 15 repetitions.
  - Use of a resistance band/handheld weights and some body weight exercises
  - Body weight exercise involve the following:
    - Push-ups (wall, modified, or full)
    - Squats with the use of a chair
    - Hamstring curls
    - Calf raises
    - Abdominal crunches (chair or floor)
  - Theraband/handheld weight exercises involve the following
    - Chest exercise
    - Deltoid lifts
    - Bicep curls
    - Triceps extension

Flexibility

- Flexibility exercises are given for the following muscles (each exercise should be performed twice and held for a minimum of 20 seconds).
  - Chest
  - Biceps
  - Triceps
  - Quadriceps
  - Hamstring
  - Calf

Breathing Relaxation Exercise

- Abdominal breathing (15 minutes twice daily)
- Use of relaxation CD (nature sounds and breathing instructions)

It is instructed to take protein within 30 minutes on completion of the exercise regimen.

carbohydrate, lipid, trace element, vitamin) metabolism, and by other factors, such as age, adjuvant cancer therapy, and stage of the disease. In addition, a patient who is undernourished before surgery has a greater risk of morbidity and mortality.[37] 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.[38,39]

The purpose of nutritional prehabilitation is therefore to prepare (or optimize) the patient for surgery, not necessarily to replace nutritional deficits. To be successful, nutrition intervention requires a timeline that needs to start with preoperative assessment and extend into the postoperative period. The shift to preemptive preoperative nutritional therapy (which is focused on prevention) is strongly considered if the patient meets risk criteria.[40]

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. The European Society for Clinical Nutrition and Metabolism recommends 1.2 to 1.5 g protein/kg, for surgical patients. 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.[41]

The benefits of an interaction between nutrition and physical exercise have been studied in elderly patients, in whom it been shown that a minimum of 140 g of carbohydrate taken 3 hours before exercise increases liver and muscle glycogen and facilitates the completion of the exercise session.[42] Also, the time of ingesting a protein meal after surgery is of importance; elderly individuals who consume 10 g proteins immediately after weight training have their mean quadriceps fiber area increased by 24% as well as their dynamic muscular strength.[43,44]

With regard to the type of nutrients, administration of a pharmaconutrition formula containing arginine, fish oil, and nucleotides has been shown to reduce infection, other complications, and hospital length of stay in patients undergoing major upper or lower gastrointestinal surgeries, regardless of preexisting nutritional status.[45,46] A synergistic effect may exist between arginine and fish oils, and therefore, a combination of the 2 agents should be used. Timing of delivery is optimized by starting 5 to 7 days preoperatively (500–1000 mL per day) and continuing postoperatively. No prehabilitation studies have been performed with administration of immunonutrition coupled with physical activity/exercise.

Whey protein is another nutritional component that has attracted the interest of exercise physiologists, because it is a protein that is highly bioavailable, is rapidly digested, and contains all the indispensable amino acids.[47,48] Compared with casein, whey protein is also associated with an increase in protein synthesis.[49] In addition, when whey protein is compared with other sources of complete proteins, whey is found to score highest on the quality assessments used to assess protein quality, such as net protein utilization, biological value, and the protein digestibility corrected amino acid score (a measure of how well a particular protein provides indispensable amino acids).[50] Whey protein plays a role in oxidative stress defense, by increasing the content of intracellular stores of the antioxidant glutathione (GSH). The mechanism of GSH is believed to be related to the in vivo synthesis of GSH being limited by the availability of the amino acid cysteine, found in rich supply in whey protein. GSH is a major intracellular antioxidant that neutralizes reactive oxygen species (ROS) by donating its sulfridryl proton.[51] Because ROS is involved in cytokine signaling during the acute phase response, the consumption of whey protein and resultant increase in GSH levels, which neutralize ROS, may aid in blunting the inflammatory processes characteristic of the stress induced by surgery. In a recent prehabilitation nutrition (no physical exercise) RCT, patients who had undergone colorectal cancer surgery were given a daily whey protein supplement (10–20 g) for 4 weeks before surgery and the functional walking capacity (assessed by the 6-minute walk test) increased more than 20 m (minimal clinically important difference for the measure of surgical recovery) in more than 50% of the subjects (C Gillis, personal communication, 2014).

STRATEGIES TO MINIMIZE THE EMOTIONAL BURDEN OF SURGERY

The physical burden of surgery is closely linked to the emotional one. Increased levels of psychosocial distress seen in patients undergoing abdominal surgery are related to the diagnosis (eg, cancer), the treatment (chemotherapy), and most often to the disability (stoma siting). Several studies have identified that anxiety and depression can affect postoperative outcome (eg, those who were more stressed on the third day after surgery stayed longer in hospital, and those who were more optimistic were not often hospitalized).[52] Depression was associated with more infection-related complication and poor wound healing.[53–55] In a recent prehabilitation study conducted in patients who underwent colorectal resections,[56] those who improved in functional capacity showed also positive changes in mental health and some aspects of the Short Form 36 subscale vitality. Anxiety at baseline was also associated with poorer recovery. The belief that fitness aided recovery was a strong predictor of improvement. Stress management before prostate surgery has been shown to affect immune function.[57]

These observations indicate that there is a need to address the importance of incorporating mental strategies to attenuate the stress response and enhance the effect of prehabilitation. Interventional studies that improve healing outcomes by reducing psychological stress provide further evidence of the impact of psychological and behavioral factors in wound repair.

Physical exercise can reduce psychological distress in addition to improving cardiovascular function. Older adults were randomized to an exercise intervention (1-hour aerobic exercise session, 3 times per week) or a nonintervention control group. One month after the beginning of the intervention, participants received a 3.5-mm punch biopsy on the back of their nondominant upper arm. Older adults who exercised healed their wounds on average 18 days earlier than those in the control group.[58]

Another aspect inherent to prehabilitation is related to the benefits of informing patients of all aspects of the perioperative process. The benefits of giving preoperative information to patients include decreased length of stay, less demand for analgesia postoperatively, and increased patient satisfaction.[59] The use of information booklets and tailored messages on how to promote personal health help to empower patients in the control of their own health and become more involved in the healing process. The prehabilitation program can provide adequate information that is made to suit individual-level psychological characteristics, such as motivational orientation or cognitive processing style. This process can elicit motivation and participation.

Although there has been great effort in studying the impact of physical exercise on postoperative outcome, little has been done to address patient and caregiver's emotional burden of surgery. There is a growing interest in mind-body interventions, with the intent to attenuate the stress of anxiety and sleep deprivation. Therefore, it makes sense that a multimodal prehabilitation program includes all these aspects of care in a multidisciplinary fashion.

WHO BENEFITS FROM PREHABILITATION?

Because people are living well in their late 70s, they are more likely to undergo surgery. Morbidity and mortality associated with surgery increase with advancing age once individuals are older than 75 years. There is a large heterogeneity in this population, with frail and cognitively impaired on one side and highly functional and robust on the other side. There has also been a shift in the comorbidity of this population, with an increase in cancer, obesity, diabetes, cognitive impairment, and osteoarthritis.[36,60]

Comprehensive preoperative assessments that take into consideration functionality, comorbidity, cognition, social support, nutrition, and medical assessment could help identify those who are at risk of adverse events and formulate a treatment plan before surgery.

Although there have been several studies emphasizing the benefit of long-term endurance training in patients with chronic heart failure and the positive effect of rehabilitation physical exercise after reconstructive surgery, few studies have focused on surgical prehabilitation in the elderly and patients with cancer with the intent to increase physiologic reserve and enhance functional capacity in preparation for surgery. It is assumed that elderly, frail patients with medical comorbidities, poor functional and social status, at risk of malnutrition need some attention.[61–63]

The appropriate time for the development of a prehabilitation program is during the preoperative assessment period for elective operations. At this time, the multidisciplinary team, which should include internal medicine, geriatrics, anesthesia, surgery, dietetics, kinesiology/physiotherapy, and nursing, would devise a risk stratification model and identify the type and duration of prehabilitation needed to balance the potential benefit of such intervention versus the potential harms of delaying surgery.

RECOVERY AND EVALUATION OF PREHABILITATION

Traditionally, successful recovery from surgery has been identified with the patient leaving the hospital and without complications during the first 30 postoperative days. However, length of hospital stay may be affected by external elements, such as socioeconomic, cultural, and institutional factors, and complications and mortality are uncommon and often inconsistently measured.[64] These measures are important to clinicians and administrators but may not be relevant to the patient, who wants to go back to baseline activities and to be able to function socially. This situation implies that recovery is a more complex construct, because it includes physiologic, social, functional, and economic domains.[65] For example, with the trend of declining 30-day morbidity and mortality as a result of better perisurgical and anesthesia care, advances in cancer therapy, and pharmacologic optimization, patients who have cancer live longer, and, therefore, emphasis has shifted to cancer survivorship and community reintegration.[36]

This situation shifts the paradigm from addressing short-term health issues to considering long-term functional and psychosocial capacity and improving patient-centered longitudinal outcome. The measures used to assess the impact of prehabilitation intervention on recovery need to be relevant in the context of the time chosen. For example, in the first 3 weeks after surgery, the recovery trajectory focuses on mobility, pain relief, and coping with side effects of medications, whereas at 6 to 8 weeks, the focus is more on quality of life and reintegration in the community and the workplace.[66]

Outcome measures to evaluate the impact of prehabilitation need to take into consideration 2 aspects of this program: the preoperative period, during which the prehabilitation program is implemented, and the postoperative period, during which the impact of the prehabilitation program is evaluated. The scope of the preoperative period is to increase physiologic, physical, nutritional, and mental reserve. It is during this time that the multidisciplinary interventions aimed at making patients stronger for surgery are chosen, taking into consideration the type of surgery and the patient's physiologic and metabolic conditions. In the second period, after surgery, the increased reserve obtained during the prehabilitation phase is available to provide sufficient energy and sustain the recovery process, which, in cases of cancer, might facilitate earlier administration of adjuvant therapy.

Because recovery is a complex phenomenon to assess, it is clear that a single outcome measure is not able to capture the evolution of the healing trajectory. Preferably, a composite of objective performance measures together with self-reported measures assessing functional status, independence, and feelings would help the clinician to follow the progress.[67]

SUMMARY

Surgical prehabilitation is an emerging concept that derives from the realization that perioperative care must include, beside clinical and pharmacologic preparation of the surgical patient, preoperative physical, nutritional, and mental optimization. As the population ages and mortality decreases, additional concerns in patients who undergo surgery and other treatment include quality of life, community reintegration, and physical and mental performance after surgery and cancer treatment. Multidisciplinary prehabilitation programs that incorporate innovative comprehensive preoperative risk evaluation need to be developed, tested, implemented, and directed to patients, especially those at risk. The integrated role of physical exercise, adequate nutrition, and psychosocial balance, together with medical and pharmacologic optimization, deserves to receive more attention by clinicians.

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