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From preoperative assessment to preoperative optimization of frail older patiens

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ABSTRACT

Physiological and mental reserve decreases with age and the ability to mount a response to a stress like surgery can represent a burden to the frail and sarcopenic patient. It is necessary to evaluate the cardiorespiratory capacity and muscle strength before surgery in the older persons and prepare adequately to the same extent the marathon runner prepares before a full marathon. Assessment and stratification of risk are necessary for decision-making, but also for planning interventions aimed at improving the functional and emotional status in anticipation of surgery. Prehabilitation can improve the physiological reserve by optimizing cardiorespiratory capacity, muscle strength, and mental resiliency. Patients with low reserve and chronic medical conditions at high risk can benefit.

Frail patient and physiological reserve

Frail patients are vulnerable to adverse health outcomes and even minor illnesses can lead to substantive declines in health, and in this context surgery represents an exceptional challenge for the frail older cancer patient. Several physiological adaptions are required to maintain cardiac output, to cope with fluid shifts, and to endure the metabolic demands of substrate utilization. Frail older patients have limited functional reserve to support this response, and as a result they become susceptible to the negative effects of surgery, thus leading to postoperative complications and prolonged hospital stay [1]. The presence of chronic medical comorbidities and other risk factors such as poor physical status, malnutrition and depression can, in presence of surgical stress, accelerate the catabolism with a significant impact on short and long-term aspects of recovery and quality of life in older patients undergoing pancreatic surgery [2,3].

The preoperative assessment of the older population includes an evaluation of physiological status and identification of age related diseases. Functional reserve has to be assessed within the specific disease process and each organ system, and includes physical, nutritional, metabolic, and mental components. Functional reserve represents a safety margin that may be needed to meet increased demands for cardiac output, carbon dioxide excretion, tissue healing, immune responsiveness, etc. Since the functional reserve decreases with age, any organ system dysfunction places the elderly population at risk. There is strong evidence that older adults who are physically active, in good nutritional state and with adequate mental function have higher levels of functional health and lower postoperative complications.

Poor physical fitness may well influence access to surgery in this age group, and a steep decline in survival rates after the age of 70 years has been seen in most cancers [4]. Denying older frail patients access to surgery could be prevented if they are adequately assessed and their clinical conditions optimized.

Preoperative assessment and risk stratification

Preoperative assessment and risk stratification of elderly patients should take into account not only their age, comorbidities, and invasiveness of surgery, but also their functional capacity and age-related conditions such as depression, frailty, functional independence, cognitive impairment malnutrition and polypharmacy (Fig. 1). However, despite the well proven negative prognostic value of the latter variables, preoperative assessment is frequently and exclusively based on the presence of patients' comorbidities and invasiveness of surgery. Notably, while certain chronic medical conditions could be ameliorated only to a certain degree, age related diseases can be frequently optimized before surgery. Indeed, preoperative assessment is valuable not only to stratify

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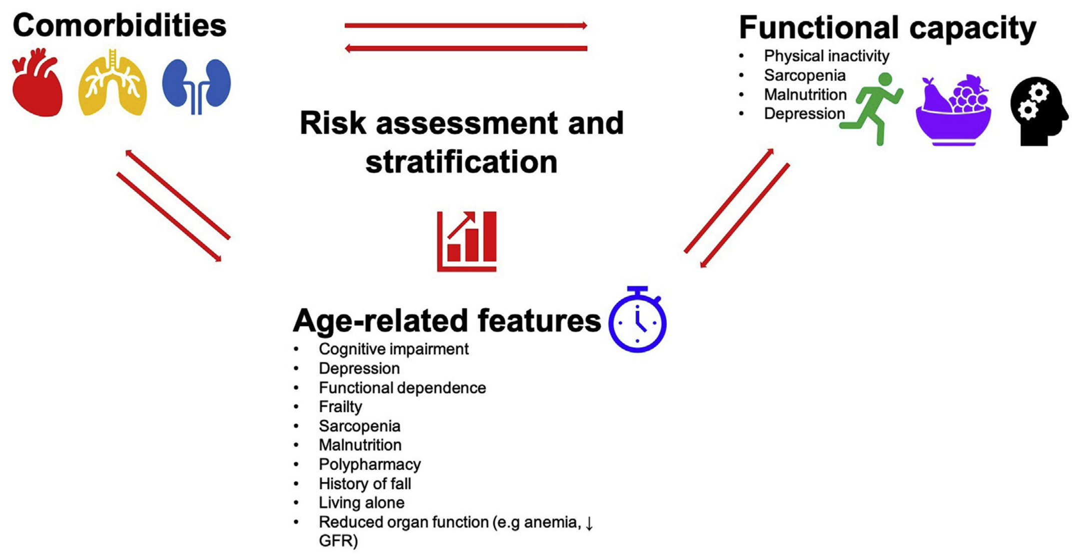

Fig. 1. Influence of chronic conditions, functional capacity, and age-related issues on risk assessment and evaluation.

surgical risk and adequately allocate medical resources (i.e high dependency unit or intensive care unit admission, intensified monitoring) but most importantly to allow preoperative optimization to reduce the risk of complications and facilitate recovery. With these purposes in mind, a multidisciplinary approach, including surgeons, anesthesiologists, internists and whenever possible a geriatrician is recommended [5].

The presence of concomitant comorbidities and the physiologic reduction of organ function increase the risk of postoperative complications and prolong hospital stay. Several general and organ-specific scoring systems are available to estimate overall morbidity and mortality or specific risks (e.g cardiovascular, respiratory, renal).

It is well established that reduced preoperative functional capacity is associated with higher morbidity and mortality, prolonged hospital stay, poor quality of life and loss of independence [1]. Recently, the American College of Surgeon National Surgical Quality Improvement Program (ACS NSQIP) Surgical Risk Calculator has incorporated the level of functional dependency and basic geriatric assessment measures to predict not only complications, but also functional decline, postoperative delirium, the use of a mobility aid and the probability to be discharged to a nursing or rehabilitation facility (https://riskcalculator.facs.org/RiskCalculator/). Ageing, functional capacity declines, and perioperative risk increases. Nevertheless, elderly patients with poor functional capacity have shown a greater improvement in functional capacity, before and after surgery, than younger and fitter patients when treated with a multimodal prehabilitation program [6]. This suggests that routine preoperative measurement of functional capacity provides a great opportunity to identify and thus to optimize high-risk elderly surgical patients to facilitate their surgical recovery [1,7]. Several methods are available to estimate functional capacity. The Cardiopulmonary Exercise Test (CPET) is considered the gold standard for measuring cardiorespiratory capacity, but it might not be always feasible, or provide valuable information (sub-maximal effort) in elderly frail patients. Subjective assessment of functional capacity by estimating metabolic equivalents (METs) is the most common method used in daily practice. METs less than 4 (i.e inability of climbing more than 2 flights of stairs) has been used as discriminator for many years to identify "unfit" patients, as this threshold has been associated with poor outcomes [8,9]. However, the accuracy of this measure in estimating preoperative functional capacity and in predicting outcomes has been recently questioned by the finding of a large multicenter prospective trial [10]. In fact, the results of the METs trial have demonstrated that 84% of patients with peak oxygen consumption ($VO_{2\ peak}$) < 14 ml/kg/min (which is consistent with less than 4 METs) had physicians rating METs ≥ 4 (sensitivity of 19%). Moreover, METs< 4 did not predict any complications or 30-day mortality [10]. These important findings are supported by another recent study, demonstrating that preoperative physicians correctly identify patients reporting poor fitness (positive likelihood ratio 3.8). However, among those rating adequate exercise tolerance they frequently miss subjects with poor cardiopulmonary fitness (negative likelihood ratio 0.85) [11]. Alternately, dynamic tests, such as the 6 and 2-min walking tests (6MWT, 2MWT) the shuttle walking test, the time up and go, and the gait speed have been successfully used to estimate preoperative functional capacity and predict surgical risk and postoperative recovery [12]. The 6MWT moderately correlates with $VO_{2\ peak}$ and predicts cardiopulmonary complications [13], disability free survival (DFS) (AUROC = 0.63), 30-day death or myocardial infarction (AUROC = 0.70), and 1-year mortality (AUROC = 0.66) [14]. Similarly, even simpler tests easy to perform in elderly and frail patients such as the Timed Up and Go test (TUG) can be used to estimate functional capacity (this timed test starts with the subject standing from a chair, walking 10 feet, returning to the chair, and ends after the subject sits). In fact, patients with a slow preoperative TUG ($\geq$15 s) have an increased risk of 1-year mortality and postoperative complications [15]. The Duke Activity Status Index (DASI), a self-administered questionnaire, is also a well validated and accurate measure of functional capacity (Spearman's correlation coefficient for with VO_{2peak}, ρ, ranges between 0.41 and 0.58) [10,16]. In contrast, to the 6MWT or to the CPET, where the assessment of functional capacity depends on the patient's performance during the test, the DASI includes measures of physical and emotional fitness covering a period of time, thus better reflecting overall patient functional capacity. A DASI >46 has been reported as good threshold to screen out high-risk patients (PPV = 1.00) [17]. However, a DASI $\leq$46 underestimates functional capacity of 2/3 of low-risk patients (NPV = 0.40), suggesting that it should not be used as single test to identify high-risk patients. In fact, a recent larger study has shown that a lower threshold (DASI < 34) predicts MINS, MI, 30-day and 1-year mortality, and DFS [14]. Finally, biomarkers such the NT-pro BNP weakly correlates with objective measure of functional capacity (Spearman's correlation coefficient $\rho = -0{\cdot}21$, $p < 0{\cdot}0001$). NT-pro BNP predicts 30-day death or myocardial injury (adjusted odds ratio 1.78, 95% CI 1.21 to 2.62; $p = 0{\cdot}003$), 1 year death (adjusted odds ratio 2.91, 95% CI1.54 to 5.49; $p = 0{\cdot}001$), but not disability free survival (AUC 0.56, 95%CI 0.49 to 0.63, $p = 0.08$) [10,14].

Frailty is a syndrome characterized by an accelerated decrease in physiological reserve that is not compensated by homeostatic mechanisms, and that it occurs mainly, but not exclusively, in elderly patients [18]. This results in a rapid decline of physical, psychological and cognitive status, exposing surgical patients to a higher perioperative risk, including mortality and morbidity, prolonged recovery, poor quality of life and loss of independence or development of new disability [19,20]. Notably, the presence of concomitant comorbidities such as dementia, Chronic Pulmonary Obstructive disease and heart failure aggravates the association between frailty and survival after elective noncardiac surgery [21]. Several clinical tools have been developed to measure frailty. Although they measure the same syndrome, certain frailty scales are better than others in predicting specific postoperative outcomes [22]. In a recent prospective trials comparing 3 different frailty measures, the Clinical Frailty Scale, a simple and easy scale to use in the preoperative setting, better predicts death or new disability, prolonged length of stay, and adverse discharge (death or non-home discharge) than the Fried Phenotype (FP) or the Frailty Index (FI) [23]. Poor nutritional intake leading to sarcopenia is also common in elderly and frail surgical patients and should be systematically assessed when evaluating patients with poor functional capacity [24]. Several methods are available to identify nutritional risk. The American Society for Enhanced Recovery and Perioperative Quality Initiative Joint Consensus Statement on Nutrition Screening and Therapy Within a Surgical Enhanced Recovery Pathway recommends the perioperative nutrition screen (PONS) as simple tool to screen for malnutrition that includes BMI, recent significant changes in body weight, and decrease in dietary intake [24].

Preoperative cognitive impairment and depression are important risk factors of postoperative functional decline and delirium [5]. A recent study found that depressive symptoms were more frequent in patients with poor functional capacity [25]. The Mini-Mental State Exam (MMSE), the Hospital Anxiety and Depression Scale (HADS) or the Geriatric Depression Scale (GDS) have been used as screening tools to identify elderly patients at risk of such complications, and whom might benefits from optimization strategies [25,26]. Finally, geriatric-specific variables such as the use of mobility aid, living alone, consent signed by a surrogate, and fall history, have been identified as predictors to discharge to a facility [27].

Preoperative optimization

The preoperative period can be an opportune time to increase the physiological reserve in anticipation of surgery with the intention to improve outcomes and accelerate recovery. The main determinants of poor functional capacity are the physical, nutritional and psychological status, and these represent risk factors for poor surgical outcomes. However, there is sufficient evidence that these factors can be modified in anticipation of surgery. This implies that we move from restoring functional capacity after surgery to preoperative preventative strategies [7].

To this extent, prehabilitation represents a multidisciplinary intervention that uses the preoperative period to prevent or mitigate the surgery-related functional decline and its consequences [28,29]. Prehabilitation involves specific individualized assessments and interventions that are likely to improve outcomes. For example, frail older patients known at high risk of postoperative complications often present with low muscle strength, decreased lean body mass, lower protein reserve, anemia, depression, and they might not tolerate excessive exercise without sufficient protein and energy intake. This high-risk group can benefit from preoperative intervention [30]. However, the interventions must be structured and personalized, and the progress evaluated. Beside the medical interventions three elements characterize multimodal prehabilitation: exercise training, nutritional counselling and supplementation, and psychological support. These three elements are integrated as part of mind body unit.

Exercise training

A structured exercise program is the central component of prehabilitation

The United State Department of Health and Human Services Guidelines recommend that older adults should perform at least 150 min per week of moderate-intensity or 75 min of vigorous-intensity physical activity to have substantial health benefits [31]. It is also recommended that aerobic activity should be spread throughout the week with sessions of at least 10 min and be accompanied with muscle strengthening exercises.

For optimal results, a presurgical exercise programme for older frail patients should consist of both resistance and aerobic training and be supplemented by flexibility and balance exercises [32,33]. Aerobic and resistance training in elderly patients increases muscle strength and endurance, favors weight loss, reduces incidence of falls, and increases range of motion in a number of joints. Personalization of the exercise intervention is necessary to achieve success without harm [34].

Also it is necessary to define specific exercise requirements of an effective prehabilitation program, in fact physical activity is different from exercise: physical activity is defined as any body movement that results in quantifiable energy expenditure, while exercise incorporates a planned and structured program with a specific goal of improving fitness [35,36]. In the case of prehabilitation, a structured program that specifies exercise intensity, frequency and modality is the goal. The aerobic exercise prescription is based on the American College of Sports Medicine (ACSM) Guidelines for Exercise Testing and Prescription [37]. Training intensities are based on percentage of heart rate reserve (HRR) calculated with the Karvonen formula (Target Heart Rate = [(Heart Rate_{max} − Heart Rate_{rest}) x %intensity]+ HR_{rest}. Individuals who are classified as having low initial fitness will show improvements in functional capacity with training intensities that raises their heart rate higher than their resting heart rate. It is recommended for them to start exercising at an intensity of 55% of Heart Rate Reserve (HRR), which, in a 75-year-old adult with a resting heart rate of 55 would correspond to a target heart rate of 105 beats per minute. Another tool to assess exercise intensity is the Borg scale, or Rating of Perceived Exertion (RPE) scale [38]. It is a visual scale on which patients are asked to rate how intense they felt their effort from 6 − being no perceived effort − to 20 − being maximal exertion. Moderate-intensity would be quantified as 12 to 14 on the RPE or 50%−70% of HRR and vigorous-intensity 15 to 17 or 70%−85% of HRR. Patients can choose the type of exercise they feel comfortable, like walking, jogging, biking, dancing. Strength training can be done with any device that generates resistance to movement, such as elastic bands, dumbbells free weights, machines or own body-weight (calisthenics). Resistance exercises should target all major muscle groups of the arms, shoulders, chest, back, abdomen, hips and legs. Additionally, it is recommended that older adults perform balance exercises such as sit-to-stands and backward, side, heel and toe walking. The choice of exercise modality should be tailored to patient preference and comorbidities.

Another important element in the implementation of a personalized exercise program is to identify when and how exercise progression should occur to maximise functional status improvement over a short period of time. Exercise intensity should be increased to match the increase in fitness, for instance, when a patient doesn't reach their target heart rate or RPE target when performing the prescribed exercises. For example, walking speed or incline and resistance exercises weight or number of sets and repetitions could be increased. As for balance exercises, they could initially be done with the help of a stable support with progression to no support.

Step counting devices (accelerometers and pedometers) offers an opportunity to monitor and encourage daily ambulatory activity, particularly in the elderly, although it is not clear what amount is required according to the public health guidelines. It is recommended that with a daily background of 5000 steps/day (which can be too high for some older adults and special populations), 7000 steps will include a target of achieving 30 min of moderate-to vigorous physical activity.

Nutritional optimization

Muscle wasting in the older patients is the result of decreased basal rates of muscle protein synthesis, elevated rates of muscle protein breakdown, or a combination of the two processes resulting in a negative protein balance [39,40]. It is not clear whether the changes in protein metabolism are due to high degree of systemic inflammation and associated co-morbidities, or a reduction in protein intake or to decreased physical activity. There is suggestion that these patients are less able to utilize amino acids for muscle protein synthesis, anabolic resistance of older's muscle to a physiological dose of amino acids. Even in response to resistance exercise, the older muscle is not able to mount a response similar to the one elicited by a young person [41]. This might explain the reason for greater protein requirements in the older. A nutrition program that includes high quality proteins per meal will provide sufficient essential amino acids, particularly leucine, which is needed to elicit muscle protein synthetic response and accretion of muscle protein. The addition of resistance exercise to an intake of high dose of proteins favors muscle mass buildup and will improve strength and physical function [42].

Malnutrition in the older patient needs to be identified and possibly corrected because of the significant impact on postoperative complications [43]. The primary goal of perioperative nutritional care is thus to promote GI tolerance, enhance immunity, support normoglycemia, provide sufficient protein to achieve anabolism and sufficient energy to maintain body weight. A combination of both individualized nutrition counselling and oral nutrient supplementation (ONS) has proven to be effective in building functional capacity [44].

Emotional support

The burden of cancer and surgery is linked to high levels of emotional distress, and anxiety and depression at baseline are associated with poorer recovery [45]. This is particularly true even for older patients. Therefore there is a need to address the importance of incorporating mental strategies to attenuate the stress response and enhance the effect of prehabilitation [46]. In a recent prehabilitation study conducted in patients who underwent colorectal resections [47], those who improved in functional capacity showed also positive changes in mental health and some aspects of the Short Form 36 subscale vitality [48]. The belief that fitness aids recovery represents a strong predictor of improvement [49]. Reducing psychological stress provides further evidence of the impact of psychological and behavioral factors in wound repair [50].

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 [51]. 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.

Summary

Surgical prehabilitation is an emerging innovative concept that has recently attracted the attention of clinicians and health administrators because of the potential impact on patients' recovery and health costs. Prehabilitation is part of the perioperative care that starts with patient preparation for surgery and includes, beside clinical and pharmacologic interventions, preoperative physical, nutritional, and mental optimization. With an increase in aging populations, additional concerns are directed to include quality of life, community reintegration, and physical and mental performance after surgery and cancer treatment. The published data on prehabilitation in the old frail persons is still insufficient to demonstrate a positive impact of the multimodal interventions on clinical outcome [52–54]. Several reason such as heterogeneity of outcome measured and different intensity of surgical stress, difficulty to distinguish frailty classifications and inconsistency of compliance to the protocols by the patients, can explain some of the negative results.

Multidisciplinary prehabilitation programs incorporate innovative and comprehensive preoperative risk evaluation and stratification accompanied by structured and personalized interventions with particular attention for those patients at risk. The integrated role of preoperative exercise training, adequate nutrition, and psychosocial balance within the perioperative medical and surgical care deserves to receive more attention in the future for our older frail patients.

Declaration of competing interest

The authors declare no conflicts of interest.

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