Preoperative risk assessment and optimization of older patients undergoing oncological abdominal surgery
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CHAPTER 11
Discussion and future perspectives
This thesis has focused on identifying methods to improve preoperative risk assessment in older oncological-surgical patients as well as on evaluating approaches to preoperative physical optimization. In the following paragraphs, the findings and implications of the preceding chapters are discussed further.

**IMPROVING PREOPERATIVE RISK ASSESSMENT**

**Identifying the high-risk patient**

In an ideal world with unlimited time and resources, all older patients with cancer would undergo an in-depth geriatric evaluation (such as Comprehensive Geriatric Assessment (CGA)). Comprehensive geriatric evaluation can be used to facilitate shared decision-making (for instance, opting for less intensive or delayed therapy in vulnerable patients) and to direct management of geriatric conditions. However, a CGA is not feasible in all older patients which is why a screening step to identify the potentially frail patients has been introduced in many surgical treatment pathways. The current Dutch guidelines recommend frailty screening in all older patients for whom surgery is considered.

Ideally, a frailty screening instrument such as the Groningen Frailty Indicator (GFI) (as discussed in Chapter 4) would determine which patients are at risk for worse outcomes and direct them for a more in-depth assessment. However, it remains a challenge to distill the heterogeneous concept of frailty into a concise screening tool. The various frailty screening instruments that have been proposed so far have been shown to have inadequate discriminatory value for the frail patient, leading to under- or over-detection (when compared to the CGA). This likely stems from the fact that, although the CGA is the gold standard for diagnosing frailty, it does not provide a clear cut-off to definitively assign a patient to the frail or non-frail category. Insisting on a hard cut-off point in a screening instrument to define the at-risk patient can therefore also feel arbitrary. For example, a patient who reports poor physical fitness, polypharmacy and memory problems on the GFI-questionnaire comes one point short of being considered at risk for frailty, although a further geriatric evaluation is likely indicated based on memory complaints alone.

An attempt to dichotomize frailty inevitably results in a loss of information. Compared to instruments that produce an overall frailty score, the VMS-questionnaire (as discussed in Chapter 3) is an example of a more practical screening instrument as it consists of four geriatric domains that also stand on their own as risk prediction tools for certain outcomes. Identifying specific impairments in separate geriatric domains helps to generate an individual risk profile for each patient. This allows for the implementation of targeted interventions immediately after the initial screening step. In Chapter 3, we showed that the three-item questionnaire on delirium risk significantly improved risk
prediction for postoperative delirium and that physical impairment as measured with the KATZ-Activities of Daily Living (ADL) questionnaire predicted post-discharge institutionalization. The Short Nutritional Assessment Questionnaire (SNAQ) incorporated in VMS is also a validated tool to detect patients at risk for malnutrition. Patients who are at risk for delirium or with functional impairments should undergo an additional preoperative geriatric evaluation, and can be counseled on their individual risk of adverse outcomes. The identification of malnutrition risk should prompt a referral to a dietician. The VMS is currently applied during hospital admission, although it would have more impact if administered directly after diagnosis so that timely evaluations and interventions can take place in high-risk patients. Compared to an overall frailty screening instrument, this type of pragmatic screening for selected geriatric risk factors might be a preferable choice in a busy surgical setting.

The International Society for Geriatric Oncology (SIOG) currently has a light preference for the Geriatric 8 screening instrument (consisting of eight items), but no firm recommendations for a specific frailty screening tool in oncology have been made (as no single frailty screening instrument clearly outperforms the rest). The choice for a frailty screening tool is therefore often based on previous experience and preferences of clinicians as well as logistical factors (for example, the possibilities for integration in the electronic patient system). In any case, the implementation of preoperative frailty assessment in older patients is a welcome development in oncological surgery.

Identification of modifiable risk factors
Addressing geriatric risk factors in order to identify the high-risk patient and to improve shared-decision making is an important objective. Identifying potentially modifiable risk factors is at least as relevant a goal. Regarding patient-related risk factors, a successful surgical intervention chiefly depends on the patient having sufficient physical reserves to be able to cope with the surgery-induced stress. In the second part of this thesis, we showed that physical frailty was associated with negative outcomes in older patients undergoing major abdominal cancer surgery – regardless of whether it is manifested by poor aerobic fitness or slow walking speed (Chapter 5), or (progressive) sarcopenia (Chapter 7). In older surgical candidates, preoperative risk assessment should therefore include an evaluation of the patient’s physical status.

Physical fitness
The main goal of measuring physical fitness is to identify high-risk patients and to target preoperative exercise interventions. Low aerobic fitness (exercise intolerance) is a clear indicator of higher risk of postoperative complications and some measurement of aerobic capacity should be performed preoperatively. Cardiopulmonary Exercise Testing
Malnutrition and sarcopenia

Malnutrition is prevalent in patients with cancer and an important risk factor for postoperative complications. Malnutrition risk screening (with instruments such as SNAQ or Malnutrition Universal Screening Tool) should always be implemented early in the preoperative work-up of older patients to enhance the nutritional status of at-risk patients. However, it should be noted that the absence of overt signs of malnutrition (i.e., normal or high body mass index, no recent weight loss), does not always indicate a healthy status. In recent years, loss of lean body mass (sarcopenia) has emerged as a powerful risk factor for adverse outcomes across surgical specialties. In Chapter 7, we showed that progressive sarcopenia as measured on a CT-scan in older patients with colorectal cancer predicted higher mortality. The etiology of sarcopenia is multifactorial, but inadequate protein intake (especially when considering the increased protein requirement during illness) and low physical activity play a major role. As loss of lean body mass is not always evident, especially in the case of sarcopenic obesity, more sensitive instruments than traditional nutritional questionnaires are required to detect it. In patients undergoing abdominal cancer surgery, a preoperative CT-scan is readily available and can be used for diagnosing low muscle mass. Poor result on a short physical test assessing muscle strength or function (e.g., hand grip strength, Short Physical Performance Battery, Timed Up & Go) can confirm the diagnosis. The identification of low muscle mass and strength in presurgical patients can then be used to target preoperative nutritional and exercise interventions.

Preoperative physical activity

Low physical activity is one of the hallmarks of physical frailty, and a potentially modifiable risk factor in the preoperative period. Objective measures of physical activity in surgical patients have become an exciting new area of research. In our cohort study in
Chapter 6, compared to the more active patients, patients who exhibited sedentary behavior had significantly worse objective and subjective physical functioning. Previous studies have shown that less physically active patients as defined by a low step count (using wrist-worn activity trackers) have a higher risk of negative postoperative outcomes after colorectal surgery\(^\text{295,296}\) or hepato-pancreato-biliary surgery\(^\text{297}\). Inactive individuals with poor functional capacity are likely to benefit the most from preoperative exercise interventions.\(^\text{27}\)

Thigh-worn accelerometry is a novel approach in onco-geriatric medicine. Whereas counting steps is a relatively rough measure of activity levels, accelerometers can integrate data on body postures (sedentary vs upright), activity intensities and time spent doing specific activities which results in a more robust estimate of activity levels and energy expenditure.\(^\text{298}\) Compared to wrist- or hip-worn accelerometry, thigh-worn accelerometry has the additional benefit in that it can more accurately identify sedentary postures.\(^\text{299,300}\) Furthermore, the use of a cane or a walker does not affect the measurement if the accelerometer is placed on the thigh (as compared to the wrist). The MOX1 accelerometer used in our study also has the ability to detect low, moderate and vigorous physical activity, and algorithms to differentiate between these intensity thresholds are currently in development for the older patient population. Thigh-worn accelerometry is therefore an attractive alternative for a continuous measurement of sedentary behavior and physical activity in older patients.

Besides identifying patients with low activity levels, accelerometry could be used to monitor the effects of exercise interventions on changes in physical activity patterns and to track progress. Activity trackers also have the potential to be implemented as a motivational tool to increase physical activity. Pedometers have been shown to increase physical activity in adult patients\(^\text{301,302}\) and in the postoperative period in patients undergoing knee or hip replacement surgery\(^\text{303}\) or abdominal surgery\(^\text{304}\). Whether wearing an activity tracker can increase preoperative physical activity levels in older patients undergoing cancer surgery should be investigated further.

**OPTIMIZING OUTCOMES IN ONCOLOGICAL ABDOMINAL SURGERY**

**Prehabilitation in older oncological-surgical patients**

**Patient selection**

For prehabilitation to succeed, appropriate patient selection is essential. A criticism of prehabilitation trials has been that most studies so far have not focused on frail older patients although these patients may have the most to gain from prehabilitation.\(^\text{271}\) Preoperative exercise or nutritional interventions in low-risk patients will probably not lead to significant reductions in adverse outcomes which in turn results in the (possibly
erroneous) conclusion that these interventions are ineffective. For example, in our review on preoperative nutritional interventions in patients with colorectal cancer (Chapter 9), we noted that most patients receiving the intervention were not at risk for malnutrition and measures of sarcopenia (to identify a relative protein deficit) were largely absent. Directing prehabilitation interventions at high-risk patients based on low activity levels, poor performance on physical tests and/or presence of sarcopenia is therefore advisable.

**Compliance is key**

In exercise and nutritional therapy, compliance to the intervention is an absolute necessity. The results of our cohort study in Chapter 6 demonstrated that sedentary patients were less motivated to move or exercise and their motivation for prehabilitation was lower compared to the rest of the group. Sedentary patients who are not used to exercise might not be able to or might not want to participate in a training program. This lack of motivation can create an important barrier for participation in prehabilitation programs. Next to motivation, previous studies have shown that common barriers to participation in prehabilitation include limited time, limited information received, physical complaints, and accessibility. Important facilitators or motivators include being able to physically prepare for surgery, social support, and home-based interventions. There is no “one size fits all” solution for physical activity interventions or to nutritional interventions (as discussed in Chapter 9). An individualized approach to prehabilitation that takes into account the patient's needs, baseline capabilities, but also motivational triggers will therefore yield the highest returns. The Fit4Surgery program presented in Chapter 10 attempted to tackle some of the issues with compliance by offering at-home prehabilitation for frail older patients at a moment of the patient's own choosing. The feedback was largely positive as patients appreciated the ability to perform the exercises at home and the duration of the exercises (seven minutes) was considered appropriate. The compliance to the program was high, implying that such a program could potentially be implemented on a larger scale.

**Emerging evidence for prehabilitation in high-risk patients**

Two recent randomized controlled trials studying the efficacy of outpatient prehabilitation in high-risk patients undergoing abdominal oncological surgery have shown promising results. In a randomized controlled study in a group of patients aged 60 years and older with colorectal cancer and with poor baseline exercise capacity (low anaerobic threshold), the intervention group received a supervised, personalized three-week exercise program consisting of a moderate-to-high intensity interval training on a cycle ergometer and resistance training three times per week. The control group received usual care. Postoperative complications were significantly fewer in the group that underwent exercise prehabilitation. A second randomized controlled study in patients >70 years
and/or with ASA-classification III-IV undergoing major abdominal surgery (including upper gastrointestinal surgery and colorectal surgery) showed that exercise prehabilitation significantly reduced postoperative complications. In this study, patients in the intervention group received personalized high intensity endurance training on a cycle ergometer 1-3 times per week for six weeks and the control group received a pedometer and home-based functional exercises. However, another randomized controlled trial showed contradictory results: exercise and nutritional prehabilitation in frail patients (Fried frailty score 2 or higher) before colorectal cancer surgery did not result in fewer complications. In this study, patients in the intervention group performed moderate intensity exercise on a stepper and resistance training once per week for four weeks and received protein supplements whereas the control group received the same program postoperatively. It is thus likely that personalized high-intensity exercise for a longer duration and/or of a higher frequency would be required to improve outcomes, perhaps even necessitating postponing the surgery. In light of these findings, a relatively short bout of unsupervised exercise (such as the ‘Senior 7-minute Workout’ in our Fit4Surgery study) may not be a sufficient stimulus to increase physical resilience and to improve outcomes. On the other hand, having to undergo frequent supervised high-intensity training may deter patients from participating and result in suboptimal compliance. A digital and customizable home-based tool such as the Fit4SurgeryTV combined with supervision at a distance (eHealth or telemedicine) might offer a solution and should be explored further. Development of prehabilitation programs in frail older patients requires balancing on a fine line between efficacy and adherence: a clear-cut recipe is yet to be written.

Prehabilitation as a patient empowerment tool

The time window between diagnosis and surgery may be brief but it nevertheless provides an opportunity to enhance the patients’ physical resilience before surgery. And in line with adopting a more patient-centered approach in oncological surgery, prehabilitation has the ability to transform the passive preoperative waiting period into a phase of empowerment wherein the patient is provided with the tools to potentially influence their own treatment outcome. At the same time, patients who are unable to perform exercise prehabilitation will likely not be able to participate in postoperative rehabilitation either. These patients can thus be counseled on their high risk of postoperative functional decline. Cancer diagnosis and having to undergo major surgery could even be seen as triggers to prompt a permanent lifestyle change (not unlike smoking cessation and physical exercise following a myocardial infarction). Positive and negative perceptions of what it means to become older, personal motivation, and confidence in one’s own ability to change health behavior have been reported to have influence on adopting healthy eating and exercise habits in older adults. In our Fit4Surgery trial, some participants indicated that they would like to continue exercising with the Fit4Surgery-TV after surgery, suggesting that patients
experienced prehabilitation as a positive stimulus. Exercise interventions are notorious for their poor long-term adherence \( ^{310} \), but their effects in the setting of cancer surgery on persisting lifestyle changes have not been evaluated yet. This would certainly be an interesting area of research, especially in the older population with long-standing habits and a lower life expectancy.

**Modifying surgical risk**

The preoperative period is a salient opportunity to tackle modifiable patient-related risk factors before surgery. However, taking a step back to study the bigger picture is warranted. Optimal preparation for surgery may be wasted labor if the surgical procedure itself is not optimized. In Chapter 8, we approached surgery as a modifiable risk factor, specifically in patients who would undergo high-risk gastric cancer resections. Our aim was to facilitate shared decision-making with patients facing this major surgery by evaluating the current evidence base regarding the outcomes of different surgical treatment options. Although there were several encouraging findings, especially with respect to the feasibility of minimally invasive surgery in older patients, we had to conclude that most of the cohort studies included in the review were methodologically weak, resulting in low level evidence. The randomized controlled trials were not designed specifically for the older patient population, permitting analyses only in small subgroups of patients. Worldwide, less than 10% of randomized controlled trials target older patients which highlights the need for stronger evidence specifically in these patients.\(^ {251} \) We also noted the absence of baseline frailty screening and patient-reported outcome measures despite that knowledge of these factors would benefit shared decision-making. Although we focused on gastric cancer surgery, these areas for improvement are not unique to just this cohort. There are gaps in the knowledge regarding the optimal treatment strategy of cancer in the older patient population across surgical specialties.\(^ {311,312} \) Future studies investigating outcomes of cancer surgery in older patients should be transparent on study eligibility criteria and patient selection, report on preoperative geriatric parameters, report on any perioperative interventions (such as geriatric co-management and prehabilitation), and address patient-reported outcome measures next to standard surgical parameters.

**CONCLUSIONS**

Perhaps the most encouraging finding of this thesis is the confirmation that older age alone is indeed not a contraindication for major oncological abdominal surgery. An early identification of geriatric impairments following diagnosis is required to enhance prognostication and to guide timely preoperative referrals for additional evaluation and/or interventions. Focus on potentially modifiable risk factors (poor physical performance, sarcopenia and low physical activity) is especially warranted to target the
high-risk patient. Emerging evidence on the efficacy of prehabilitation interventions in frail patients is promising, but the optimal content, setting and motivational triggers need to be further elucidated. High-quality research specifically in older oncological-surgical patients regarding prehabilitation and surgical treatment options is required to continue improving outcomes for this population.