CHAPTER

General introduction
CHAPTER 1

Increasing incidence of cancer

Thanks to improvements in healthcare and infrastructure (antibiotics, vaccinations, preventative medicine, sanitation, nutrition)\(^1,2\), we lead longer and healthier lives than ever before. However, concomitantly with the aging population, we are seeing an increase in the incidence in cancer diagnoses. Older patients make up a large proportion of the population undergoing some form of cancer treatment - for example, more than half of newly diagnosed colorectal tumors are found in patients aged 65 and older.\(^3\) It is no longer a rare sight to have an 80-year-old patient at the surgical outpatient clinic discussing treatment options to remove a colon tumor.

Oncological abdominal surgery anno 2021

Most solid (non-metastatic) cancers in the abdominal cavity are amenable to surgery. In oncological abdominal surgery with curative intent, the goal is to remove the tumor with clear resection margins with acceptable risks for morbidity and mortality. Advances in operative techniques have improved postoperative recovery without compromising oncological outcomes. For example, laparoscopic surgery as opposed to the traditional open surgery is now the preferred treatment option for colorectal cancer as it has been shown to reduce complications, shorter hospital stays and lead to better quality of life.\(^4,5\) From prostate surgery to pancreatic resections, minimally invasive techniques are gaining ground in all oncological surgical fields.\(^6\) We are moving towards even smaller and less invasive surgeries such as endoscopic submucosal dissections for early-stage gastric cancer\(^7\) or transanal microsurgery for T1 rectal carcinomas\(^8\).

Synchronously with improvements in surgical techniques, advancements in perioperative care have contributed to safer surgery and faster recovery in surgical patients. The idea behind ‘fast track’ programs such as Enhanced Recovery After Surgery (ERAS) is the patient-centered approach to minimize the effects of surgical stress on the body so that homeostasis can be maintained. The ERAS protocol proposed for colorectal surgery consists of more than 20 items (e.g., preoperative carbohydrate loading, minimal use of abdominal drains, multimodal analgesia, early enteral feeding and early mobilization)\(^9\) aimed at optimizing the perioperative course of the patient. Fast track protocols in abdominal surgery have been shown to improve outcomes also in older patients.\(^10,11\)

Surgical considerations in older patients

Advances in surgical techniques and the growing knowledge base from clinical trials have increased the number of available surgical options in abdominal surgery. However, even if optimized to current standards, surgery can still cause considerable morbidity. This is especially the case when considering high-risk abdominal surgery such as gastrectomy for gastric cancer which is associated with 40% morbidity and 8% mortality rates in
older patients. And even if surgery were to be considered a success from an oncological perspective, it may not be worth if there is a high risk of permanent functional decline or worsening quality of life. The risks and benefits of different surgical treatment options (or indeed if non-surgical treatment is preferred) need to be evaluated specifically in the older patient group. In addition, older patients place a higher emphasis on retaining quality of life and functional independence as treatment goals (as opposed to tumor recurrence or survival outcomes alone). These treatment goals need to be taken into account when evaluating the treatment options.

**Preoperative risk assessment in older patients**

Treatment guidelines in oncology are increasingly calling for attention for the geriatric patient who might require adjustments in the treatment pathway. Identification of the vulnerable patients who are at risk for negative outcomes is key, as it facilitates shared decision-making, e.g., whether to proceed with surgery in a high-risk patient or what type of surgery to opt for. In addition, preoperative risk assessment can also guide the implementation of perioperative interventions such as geriatric co-management, prescription of nutritional supplements, or physiotherapy.

Traditionally, preoperative risk screening before major abdominal surgery consists of addressing comorbidities known to be associated with worse outcomes (such as diabetes or cardiovascular diseases) and by assessing the physical status of the patient, for example with the American Society of Anesthesiologists (ASA) score or performance status. Although useful, these risk prediction parameters are not specifically made for the older surgical patient and do not address important geriatric deficits that are common in older patient population and can negatively impact the patient’s ability to withstand major surgery. There is a need to improve risk prediction in the older patient group.

Older patients are at an increased risk of frailty which is classically defined as an age-related decline across multiple physiological systems which decreases the individual’s ability to respond to stressors (such as surgery). It is this increase in biological age, rather than a higher chronological age, that puts patients at risk for adverse outcomes. Frailty has a complex etiology and presentation: it manifests itself in physical decline (inactivity, mobility problems, loss of muscle mass and strength, and diminished cardiopulmonary function), functional impairment (needing help with self-care or with daily tasks), higher comorbidity burden and polypharmacy, psychological and cognitive problems (cognitive decline, depression), and/or social problems (isolation, lack of social support). In recent years, frailty has been increasingly recognized as a risk factor for adverse outcomes in older patients undergoing treatment for cancer. Some form of frailty assessment may therefore be a valuable addition to evaluate surgical risk. In geriatric medicine, frailty assessment is usually performed with the Comprehensive Geriatric Assessment (CGA).
which is used to identify deficits in the physical, medical, cognitive, psychological and social domains. However, the CGA is time-consuming, costly, and can only be performed by a trained geriatrician. It is therefore not feasible to perform it in all older surgical patients. In the busy preoperative period, a short frailty screening instrument may be a more suitable alternative to detect at-risk patients.

Preoperative risk assessment is not only useful for risk prediction purposes, but also for identifying factors that are possibly amenable to interventions in the preoperative phase (so-called modifiable risk factors). A specific focus on modifiable risk factors provides immediate targets for preoperative optimization. Poor cardiopulmonary capacity, low muscle mass and strength (sarcopenia) and physical inactivity are indicators of diminished physical reserves and have therefore negative implications for recovery from the stress induced by surgery. It may be useful to incorporate some form of assessment of the patient’s physical performance in the preoperative work-up to determine which patients would benefit from physical optimization.

Low physical activity is one of the hallmarks of frailty. Therefore, insight in the patient’s activity level can give valuable information on their health status. At the same time, knowledge of baseline activity patterns can guide the implementation of tailor-made exercise interventions as training should lead to an increase in activity levels compared to baseline. Time spent doing physical activities has been traditionally quantified with questionnaires, but recently also objective measures of physical activity patterns (pedometers, accelerometers) have been added to the repertoire.

The various methods that are used to address the patient’s physical fitness measure different physical constructs and different cut-off points for impaired results are used. Data specifically in older patients are still scarce. There is a need to determine which physical assessment methods should be implemented when evaluating surgical risk in older patients.

**Risk modification through prehabilitation**

Undergoing abdominal surgery has some parallels with that of a major sports challenge. Just like an athletic feat, surgery requires that the cardiopulmonary system be able to increase the heart-minute volume and ventilation to meet the increased oxygen demands of tissues. Skeletal muscle tissue must be able to provide the body with amino acids that are needed during recovery, and muscles are needed for mobilization after the operation. Just like an athlete who is not at the top of their game, a patient with insufficient physical capacity to rise up to the challenge (of surgery) is at risk for negative outcomes.

To counter adverse postoperative outcomes and to minimize the risk of permanent functional decline, the preoperative period between diagnosis and surgery is increasingly
seen as a window of opportunity to optimize the patient’s physical status before surgery. This preoperative optimization has been coined prehabilitation. The implication is that patients who undergo prehabilitation increase their functional capacity before surgery so that they are able to return faster to their preoperative levels of functioning and have a higher chance to return to their basic level of physical performance after surgery.24

Prehabilitation can include any intervention that increases the patient’s physical, medical or psychological resilience so that postoperative complications can be avoided and recovery can start sooner. Although there is no consensus on what the intervention should consist of, most programs incorporate some form of exercise (aerobic training, high-intensity training, inspiratory muscle training or muscle strengthening exercises), and often also offer nutritional supplements (extra protein). Prehabilitation in abdominal surgery has recently been examined in several randomized controlled trials and meta-analyses with evidence for improved outcomes in the intervention group.25,26 Due to lower baseline level of functioning (lower muscle mass, mobility problems, lower cardiopulmonary fitness, higher risk of malnutrition), frail older patients may have the most to gain from preoperative physical optimization.27,28

Even though the few weeks before surgery can be seen as a salient opportunity to address poor functional status, it is also a hectic period in the patients’ lives who have to come into terms with the diagnosis, manage extra visits to the hospital and prepare for surgery and its aftermath. At the same time, having the opportunity to be an active participant in their own cancer treatment and to be able to influence outcome can be considered motivating for patients.29,30 A successful prehabilitation program in older patients depends on understanding the needs of the patients and adjusting the intervention to the abilities of the participants. Few studies in abdominal oncological surgery have evaluated preoperative optimization programs specifically in the older patient population. It is unclear what type of preoperative interventions would be feasible in frail older patients.