Targets for improving patient outcomes after major gastrointestinal cancer surgery: the value of perioperative care

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Chapter 10

Summary

Part I: Identification of Prognostic Factors for Postoperative Complications

Major gastrointestinal surgery is associated with high rates of postoperative complications, leading to increased length of hospitalization, morbidity and healthcare costs [1-3]. **Chapter 2**, shows a comprehensive overview of the literature describing prognostic factors which are associated with major postoperative complications and 30-day mortality after upper- and lower-gastrointestinal cancer surgery. In total 207 studies were included, identifying 33 risk factors for major postoperative complications and 13 preoperative laboratory results associated with major postoperative complications. This study showed strong associations between age, male sex, comorbidities, malnutrition, sarcopenia and overweight/obesity, and the occurrence of major postoperative complications (Clavien-Dindo ≥IIIa) [4]. Additionally, strong evidence was shown supporting an association between male sex, comorbidity, obesity, malnutrition, smoking, decreased serum albumin, advanced tumor stages, neoadjuvant therapy, and the occurrence of anastomotic leakage. Furthermore, an association between 30-day mortality and male sex, higher ASA score, and cardiac comorbidity is shown. This overview may contribute to personalized preoperative care by searching for modifiable factors, such as poor physical performance, smoking, alcohol consumption, iron deficiency anemia and malnutrition [5-9]. These factors may be suitable for preoperative optimization during preoperative prehabilitation programs and thus reduce postoperative complications.

Additionally, in **Chapter 3** a meta-analysis was performed for prognostic factors for major complications and mortality after esophageal cancer surgery. This systematic review and meta-analysis included 39 studies and identified 37 prognostic factors that are associated with anastomotic leakage, major complications and mortality after esophageal cancer surgery. Of these prognostic factors renal disease, vascular comorbidity, diabetes, pulmonary, hypertension, cardiac comorbidity, ASA-score ≥ III, male sex and adenocarcinoma tumor histology were significantly associated with anastomotic leakage. Patients receiving neoadjuvant chemotherapy had a lower risk for anastomotic leakage. Male gender, cardiac comorbidity and diabetes were associated with major complications (Clavien-Dindo ≥IIIa) [4]. Furthermore, age >70 years, ASA-score ≥ III, cardiac comorbidity and a BMI of 18.5-20 were significantly associated with 90-day mortality, whereas a BMI of 25-30 appeared preventive of mortality.

However, in daily practice, it might be difficult to estimate the surgical risk of individual patients and subsequently make treatment decisions, based on individual prognostic factors found in population studies. Therefore incorporating multiple factors into a generalizable prediction model might offer a solution to combine the information in a simple and more useful manner [10]. Altogether, with the current more data-driven approach to healthcare and the availability of nationwide clinical audits, big data becomes available. In addition, with big data, the interest in machine learning for prediction models has increased. **Chapter 4** described the construction of machine learning-based prediction models to predict postoperative complications, anastomotic leakage and pulmonary complications, after esophageal- and gastric cancer surgery. The machine learning models that are most frequently described in literature were used: k-Nearest Neighbors (KNN), support vector machine (SVM), Neural Networks, Random Forest, AdaBoost and SuperLearner [11-14]. Additionally, a comparison between machine learning models and the current golden standard, regression model was performed. **Chapter 4** showed that machine-learning models were able to predict postoperative complications, anastomotic leakage and pulmonary complications, after esophageal- and gastric cancer surgery, however, machine-learning models did not outperform a linear regression model.

In search of a modifiable prognostic factor that is cheap and easily available, **Chapter 5** entailed an explorative study of the use of contrast-enhanced (CE) computed tomography (CT)-based muscle measurements in the prediction of anastomotic leakage after oncological sigmoid and rectal resections. Using Vitrea software preoperative transversal CE-CT scans of patients were analyzed and total abdominal muscle area (TAMA) and total psoas area (TPA) at the inferior level of the L3 vertebrae was measured. Subsequently, muscle areas were standardized using the patient's height into psoas muscle index (PMI) and skeletal muscle index (SMI) (cm2/m2). **Chapter 5** showed that a lower PMI and SMI are both associated with the occurrence of anastomotic leakage after oncological sigmoid or rectal resection. This association might be explained by the fact that a low muscle mass indicates frailty, which causes muscle depletion [15]. These results indicate that preoperative CT-based muscle measurements can be used as a prognostic factor for preoperative risk stratification for anastomotic leakage.

Part II: Consequences of Major Gastrointestinal Surgery

As major gastrointestinal surgery is an invasive procedure, long-term effects of these types of surgery are to be expected [16]. This poses the question of how (surgical) treatment of gastrointestinal cancer impacts the long-term quality of life and daily life. Knowledge of long-term quality of life is essential to be able to counsel patients and shared decision-making. To gain more insights into the long-term quality of life after colorectal cancer surgery, we performed a qualitative study (**Chapter 6**) evaluating the long-term consequences of resectable colorectal cancer treatment. Semi-structured interviews were conducted, guided by a predefined topic guide. A total of 16 patients were interviewed, these interviews entailed the predefined themes: daily

life and activities, psychological functioning, social functioning, sexual functioning and healthcare experiences. This study showed that patients who underwent colorectal cancer treatment for resectable colorectal cancer report minor interference with their daily life, although they face several challenges and treatment-related health deficits in the long-term. Which challenges patients face depend on the kind of treatment (e.g., (neo-)adjuvant therapy, type of resection) that they underwent and treatment outcomes (e.g., complications, stoma construction). Frequently reported factors influencing daily life were: poor bowel function, the presence of a stoma, chemotherapy-induced neuropathy, fear of tumor recurrence and sexual dysfunction. Even though patients reported a good quality of life, they reported several challenges and treatment-related health deficits, this suggests that cancer survivorship might have led to increased resilience and mechanisms to cope with these challenges and health deficits [17, 18]. Therefore, the results of this study offer enhanced insights into patient perspectives on the challenges after colorectal cancer treatment and provide leads for patient education, postoperative rehabilitation and patient guidance programs to further improve long-term patient outcomes.

Additionally, **Chapter 7** studied the impact of postoperative complications following rectal cancer surgery on quality of life. For this study, the Rotterdam Symptom Checklist was sent at 6 timepoints (preoperatively and 3, 6, 12, 18 and 24 months after surgery), additionally the EORTC QLQ-C30 and EORTC QLQ-CR29 questionnaires were sent 14 years postoperative. This study showed that survival and short-term quality of life were negatively affected by postoperative complications. However, twelve months after surgery quality of life returns to a level similar to before surgery, regardless of complications within 30 days after surgery. These results are comparable to the results reported in **Chapter 6**. Furthermore, in patients that survived 14 years, there was no long-term effect of postoperative complications from the peri-operative trajectory on quality of life detected. These results suggest that the negative effects of postoperative complications on the quality of life are temporary.

As shown in **Chapter 6**, the presence of a stoma and poor bowel functioning were both reported to be influential on daily life, therefor in **Chapters 8 and 9,** westudied the impact of a stoma and poor bowel functioning after rectal cancer surgery on the quality of life. **Chapter 8** is based on a retrospective cohort of 149 patients who underwent sphincter-sparing resection for rectal cancer between 2012 and 2016 were recruited from the LUMC and Reinier de Graaf Gasthuis. Whereas, **Chapter 9** was based on patients who underwent surgery for a primary tumor located in the rectosigmoid and rectum between 2013-2020. These patients were identified from the nationwide Prospective Dutch Colorectal Cancer cohort study (PLCRC). Poor bowel functioning was defined as major Low-Anterior Resection Syndrome (LARS) [19]. Frequently (≥35%) reported symptoms of major LARS are: clustering of bowel movement, incomplete evacuation, fecal incontinence, uncontrollable flatus and urgency [20]. Results of both **Chapters 8 and 9** showed that the presence of a stoma and major LARS were both associated with reduced quality of life, regardless of postoperative complications. Notwithstanding, a postoperative complication, such as anastomotic leakage is often the cause of the construction of a stoma. Patients with poor functional outcomes, defined as major LARS, reported a similar level of quality of life compared to patients with a stoma. An additional finding was that the quality of life following rectal cancer surgery did not change significantly after the first year post-surgery.

General Discussion

Gastro intestinal oncologic treatment and especially surgery is often a high impact and riskful trajectory. Finding ways to limit this impact and risk is of paramount importance in itself but even more since the number of patients with cancer is increasing. Additionally survival after major gastrointestinal cancer surgery goes up due to improved oncological care and patients live longer with the consequences, such as physical-, psychological- and societal impairments after surgery and (neo-)adjuvant therapy. Therefore gathering data on short and long-term outcomes such as postoperative complications as well as short- and long-term quality of life and functional outcomes, is becoming increasingly important [21-23]. The current thesis identifies multiple targets for the improvement of short-term and long-term patient outcomes.

Prognostic factors for postoperative complications

The identification of prognostic factors for postoperative complications and mortality after major gastrointestinal surgery may contribute to surgical risk assessment and subsequent patient selection. Patients with high surgical risk may require different treatment decisions, for instance, “watch-and-wait” or the use of a defunctioning ileostoma in case of colorectal surgery [24, 25]. Surgical risk assessment and subsequent adequate perioperative care could significantly decrease in-hospital mortality [26]. Therefore, surgical risk assessment might also offer leads for personalized perioperative care and shared decision-making [27]. Furthermore, the identification of prognostic factors for postoperative complications may provide targets for preoperative optimization and prehabilitation to reduce postoperative morbidity. Reduction of complications might lower the length of recovery time, length of hospital stay, readmission rates and hospital costs, and increase long-term quality of life [28, 29]. Therefore, the reduction of postoperative complications impacts healthcare on patient-, hospital- and national levels.

Modifiable prognostic factors

Identification of specific prognostic factors is important to weigh the pros and cons before engaging in high-risk surgery. Furthermore, prognostic factors, especially improvable/modifiable factors offer possibilities for augmentation of perioperative care and enrollment in prehabilitation programs, which might ultimately lead to improved patient outcomes [30, 31]. In particular, with the use of neoadjuvant therapy, a time window for preoperative optimization and prehabilitation programs is opened. An example of a modifiable prognostic factor is diabetes since adequate preoperative glycemic control may lead to fewer postoperative hyperglycemic events and therefore reduces the risk of infectious complications [32]. However, some prognostic factors might seem unmodifiable but may be modifiable after all, due to confounding factors. For instance, males have a higher risk of postoperative complications, but historically the incidence of smoking and alcohol consumption in the male population has been higher, these confounding factors are not being measured and corrected for in many studies, therefore, the effect of male gender on postoperative complications may be modifiable [9]. Another theory on why males are more at risk for postoperative complications is that their more narrow pelvic anatomy, makes surgery for tumors located in this region (e.g., rectum) technically more difficult [3, 33]. The latter might become less of an issue with the introduction of new techniques, such as robot-assisted surgery. Therefore, one should be critical towards prognostic factors and possible confounders.

Clinical use of prognostic factors

In daily practice, it might be difficult to estimate the surgical risk and make treatment decisions based on multiple individual prognostic factors. Therefore, clustering multiple factors into a prediction model might offer a solution in a simple and useful manner [10]. Altogether, with the current more data-driven approach to healthcare and the availability of nationwide clinical audits, big data becomes available. This has also led to a growing interest in machine learning. Whereas some studies have shown superior prediction models using machine learning models compared to conventional regression-based models, one could question publication bias [12, 34]. In our study, linear regression was superior to the machine learning models. Furthermore, several studies that have shown a positive outcome towards using machine learning often used a great number of preoperative variables and patients to build their models. One could question the use in daily clinical practice when using these extensive models, which subsequently leads to more administrative burden to include all variables unless extraction of variables is automated [34, 35]. An additional shortcoming of some machine learning models (e.g., neural networks) is that the influence of individual prognostic factors is not always known, in contrast to for instance linear regression, making the identification of modifiable prognostic factors impossible.

Furthermore, there is a need for easy-to-use clinical parameters that can be used in the prediction of postoperative complications. An example that is gaining interest in current research, is the preoperative contrast-enhanced computed tomography (CE-CT)-based muscle measurements [36, 37]. Since a CE-CT is standard in the routine preoperative work-up of gastrointestinal cancer patients, there are no extra examinations or costs associated with obtaining this prognostic factor. Furthermore, multiple studies, including this thesis, have shown a positive association between low muscle volume and postoperative complications (e.g., anastomotic leakage) [38]. The association between low muscle mass and anastomotic leakage might be explained by frailty since previous studies have shown an association between frailty and anastomotic leakage following colorectal surgery as well [38, 39]. Therefore, the identification of low muscle volume using CE-CT-based muscle measurements might offer a solution to determining frailty. In several studies, a clear correlation between low muscle mass and an increased inflammatory state due to tumor-cachexia and frailty has been shown [40, 41]. This might explain the association between low muscle mass and anastomotic leakage as well, hence a more katabolic and inflammatory state may negatively influence the healing capacity of bowel tissue resulting in anastomotic leakage [42, 43].

Complications and survival

Short-term mortality caused by complications is often defined as failure-to-rescue [44]. A high risk of failure-to-rescue may reflect a compromised physiological reserve for surviving critical illness inflicted by complications [45]. Additionally, long-term (recurrence-free) survival is negatively impacted by complications, due to an improved risk of tumor-recurrence [46]. On one hand, postoperative complications may increase the risk of omission and delay of adjuvant therapy and therefore increasing the risk of tumor-recurrence [47]. On the other hand, infectious complications are shown to be associated with tumor recurrence, most likely due to a pro-inflammatory response with the release of cytokines and growth factors [48]. Also, surgery itself leads to the suppression of cell-mediated immunity, and possible diffusion of tumors, therefore increasing the recurrence potential [49].

Long-term consequences of major gastrointestinal surgery

Long-term patient outcomes in terms of quality of life and treatment-related health deficits are gaining interest with the introduction of value-based healthcare, a new strategy to redefine healthcare. Value-based health care is a conceptual framework, with the founding principle of defining value by measuring patient outcomes relative to the total costs of care [50, 51]. To measure patient outcomes uniformly, a standard set of patient-centered outcomes was developed by The International Consortium for Health Outcomes Measurement (ICHOM), including survival and disease control, disutility of care, degree of health, and quality of death [52]. Another reason to proceed

into gaining more insights into long-term patient outcomes is that previous studies have suggested that patients are only willing to risk an inferior functional outcome for better survival to a certain extent [53]. This should be taken into consideration in shared decision-making and treatment decisions. Other treatments may be more preferred by patients, for example, watching and waiting after clinical complete response to neoadjuvant therapy [25, 54]. To make optimal treatment decisions, the anticipated quality of life after gastrointestinal cancer treatment has to be known, as well as the factors influencing this, both to inform patients and to gain insight into possible improvements in perioperative care. As a result of major gastrointestinal cancer treatment, patients may face various treatment-related health deficits. As shown in this thesis factors impacting the quality of life were postoperative complications, poor bowel functioning, the presence of a stoma, chemotherapy-induced neuropathy, fear of recurrence and sexual dysfunction. Which health-deficits patients depend on the type of treatment, but also treatment outcomes (e.g., complications, stoma presence) [55-58]. However, studies have also shown that in the long-term the overall quality of life after cancer treatment seems to be relatively unaffected [55]. Suggesting that, cancer survivorship might enhance resilience and coping strategies [17, 18]. This may lead to a relative underestimation of the impact of cancer treatment and treatment-related health deficits (e.g., poor bowel function, chemotherapy-induced neuropathy), when measuring the quality of life using conventional questionnaires [58, 59]. Since patients can live a modified life with the use of various strategies and self-management techniques to maintain their quality of life. However, there is considerable individual variation between patients on how these self-management strategies are undertaken, therefore personalized patient guidance and rehabilitation are recommended [60, 61].

Postoperative complications

Short-term outcomes, such as postoperative complications, may have an impact long-term outcomes, as a decrease in physical functioning after major complications has been shown [62, 63]. Furthermore, postoperative complications are significantly associated with anxiety and depression [64]. Additionally, complications, such as anastomotic leakage after colorectal surgery might lead to the construction of a stoma which influences postoperative quality of life as well [65]. Several studies on long-term (>1 year) postoperative quality of life showed no significant difference in global health status after postoperative complications or anastomotic leakage compared to an uncomplicated postoperative course [62, 63, 66].

Stoma and bowel functioning

Frequently reported challenges after colorectal surgery is bowel related, either due to the presence of a stoma or due to functional bowel complaints. Both poor functional bowel outcomes and the presence of a stoma have a negative impact on quality of life [65, 67, 68]. The decision to construct a (temporary) stoma after colorectal cancer surgery is based on three key factors, the location of the tumor, the risk of anastomotic leakage and the risk of poor functional bowel outcomes. If the tumor location is appropriate for sphincter-sparing resection, the risk of anastomotic leakage should be considered when deciding whether or not to construct a (temporary) stoma [69]. As anastomotic leakage may be a fatal insult to the patient, therefore preoperative surgical risk assessment has to be performed. The other important consideration is the risk of a poor bowel functional outcome. Poor bowel functioning in patients without a stoma is commonly described in literature as low-anterior resection syndrome (LARS) [19]. The general definition of LARS in literature is: "*A disorder of bowel function after rectal resection, leading to a detriment in quality of life*" [19, 70]. Of all patients who underwent sphincter-sparing surgical resection for rectal cancer approximately 41% experience complaints of major LARS.

Since a stoma has disadvantages, such as stoma-related complications (e.g., parastomal hernia, bulge) and decrease quality of life, routine use of a defunctioning stoma in colorectal surgery is debated [23]. As a solution, the selective use of defunctioning stoma in high-risk patients has been proposed and proven feasible [24, 71]. Furthermore, patient- and treatment characteristics (e.g., age, radiotherapy, tumor location) may be used, for instance by applying the Pre-Operative LARS score (POLARS), to predict the anticipated LARS-score, thus the functional bowel outcome [72]. Subsequently, the combination of the surgical risk prediction and the predicted functional bowel outcomes together may be used in shared decision-making to ultimately decide whether or not to construct a (temporary) stoma. Such decisions are usually not straightforward, caused by the lack of a clinically 'superior choice', making such treatment decisions particularly relevant for shared decision-making [27, 73].

Future Perspectives

Preoperative risk assessment

With the availability of nationwide clinical audits, big data comes available for the creation of generalizable prediction models [74, 75]. As will be the upcoming and further development of artificial intelligence and machine learning algorithms [12]. These prediction models can support clinical knowledge by making treatment decisions, especially detecting modifiable prognostic factors (e.g., frailty, malnutrition). Prediction models can identify high-risk patients, and for those patients, treatments might require adjustment, for instance using a (defunctioning) stoma or less invasive treatment strategies. Perioperative care needs to be adjusted in the case of high-risk patients since failure to identify high-risk surgical patients could significantly increase in-

hospital mortality rates, due to inappropriate perioperative care [26]. However, for this to work in daily practice without leading to an administrative burden, automatization of extracting important parameters, such as patient characteristics, laboratory and imaging results, is necessary. Also, combining various available data sources is currently still an obstacle in modern-day medical research and daily practice. The availability of information on a patient's longitudinal pre-disease health status and a patient's health care perspectives might give additional information to use in preoperative decision-making. Eventually, preoperative surgical risk assessment may also be used to enhance preoperative patient education and with the patient deciding on the treatment, which is most appropriate, considering the patient's individual preferences.

Frailty

With the current aging population and advancing surgical techniques, more surgeries on elderly patients are being performed and it's probable that this trend will continue in the future. While cancer survival has improved over the past few decades, larger survival improvements have been observed in younger adult patients (<75 years) than older adult patients (≥75 years) [76]. Age has also shown to be an important prognostic factor for postoperative adverse outcomes, postoperative complications and mortality [2]. Postoperative complications result in an increase of mortality in the first year after surgery [77]. However, as chronological age progresses, the heterogeneity in interindividual health status and biological age, increases [78, 79]. To address the biological health heterogeneity in clinical practice, the term "frailty" is used to distinguish between either end of the spectrum of clinically recognizable physical state. With the aging population, the preoperative detection of frailty becomes a crucial part of personalized risk assessment to facilitate optimal perioperative care. The current golden standard to define frailty, is by using the comprehensive geriatric assessment (GSA), an assessment of multiple geriatric domains (e.g., somatic, psychosocial, functional). However, this assessment suffers from a limited consensus regarding methodology and is very time-consuming [80]. Therefore, an easy-to-use preoperative risk assessment and detection of frail patients will be necessary. Several biological, routinely measured, parameters have been proposed as determinants of patient frailty, biochemical, radiologic, and histologic parameters have been proposed and have to be further investigated to implement in clinical practice [81-84]. As shown in this thesis, contrast-enhanced (CE)-CT-based muscle measurements might offer an easy-to-use clinical parameter to detect frailty.

Personalized perioperative care

This thesis offers targets, methods for the identification of (modifiable) prognostic factors for postoperative complications and insights in treatment consequences. This may be used to enhance and personalize perioperative care. Some studies have suggested that perioperative care dictates postoperative complications more than surgery itself [85]. Therefore, perioperative care is currently being standardized into enhanced recovery after surgery (ERAS) protocols [86]. ERAS protocols have been shown to be able to reduce postoperative complications up to 50% [87]. The preadmission phase of ERAS focuses on an improved physical state of a patient before surgery, for instance, by lifestyle interventions, such as alcohol- and smoking cessation and physical prehabilitation, which are currently introduced in daily practice [88-90]. However, using preoperative risk assessment with an explicit focus on the detection of modifiable prognostic factors may aid in personalizing and improving preoperative care further for high-risk patients.

Preoperative optimization of modifiable prognostic factors (e.g., poor physical fitness, malnutrition) in dedicated prehabilitation programs has been described in literature, such as physical resistance training, nutritional support, cessation of smoking and cessation of alcohol intake [6, 9, 90, 91]. In theory, these prehabilitation programs are assumed to lead to a reduction in postoperative complications, although there is limited evidence to support this [92, 93]. For instance, physical prehabilitation programs have been shown to objectively improve physical fitness, however, the effects on postoperative outcomes were less eminent [5, 92]. The lack of evidence to support the ability to reduce complications by prehabilitation programs might be the result of these programs do not specifically target specific (modifiable) prognostic factors associated with postoperative complications. When a preoperative physical fitness prehabilitation program was applied in a high-risk population, >70 years of age with ASA III-IV, this led to a 20% reduction in postoperative complications [6]. This suggests that preoperative care should be targeting modifiable prognostic factors and individualized prehabilitation programs are required to establish a significant and cost-effective reduction in postoperative complications. Along these lines, several studies report that well-designed randomized controlled trials on prehabilitation programs are needed in order to prove their beneficial effects on short-term postoperative outcomes [5, 94]. These studies need to focus on a multimodal approach toward modifiable prognostic factors (e.g., malnutrition or poor physical status). After detection of modifiable prognostic factors patients may need to be referred for tailored preoperative optimization to a specialist on that specific factor, for instance, a physiotherapist in case of poor physical fitness, a dietician in case of malnutrition and a psychologist in case of anxiety. In the Netherlands primary care and general practitioners might have a coordinating role in this, since they are already familiar with the patient, but it also offers convenience for the patients as it is often closer to home, which might enhance compliance.

Identification of high-risk patients may indicate the need for intensified and personalized postoperative care. For example, closer postoperative surveillance or delayed enteral feeding in high-risk patients. Closer postoperative surveillance might, for instance, be done by using wearable devices for continuous postoperative monitoring of vital signs, even on the regular surgical ward [95, 96]. This has been shown to lead to more timely recognition and identification of postoperative adverse events, subsequently leading to earlier goal-directed therapy, for instance, antibiotic treatment in case of septic complications, and lower failure-to-rescue rates [95, 97].

Rehabilitation programs

Patients who underwent gastrointestinal cancer treatment may face various treatment-related health deficits in multiple domains (e.g., phycological, social, physical) [55]. As shown in this thesis, patients who suffer from major postoperative complications do suffer from physical impairments leading to a lower level of self-care. Therefore, postoperative rehabilitation programs for these patients may have to be directed toward regaining activity level and physical fitness. Besides direct treatment-related health deficits (e.g., abdominal wound, stoma), patient with postoperative complications have an increased risk of other health issues too, including physical difficulties, sexual dysfunction and psychosocial challenges [98, 99]. Hence, post-treatment psychological-, sexual-, nutritional-, and cognitive functioning of cancer survivors need to be an integral part of the multidisciplinary rehabilitation programs. In order to improve long-term quality of life post-treatment rehabilitation has to be in place for gastrointestinal cancer survivors. Since patients learn to cope with certain treatment-induced health deficits, they still might benefit from rehabilitation programs [17, 18]. Therefore, close attention has to be paid to any health deficits that could occur during or after treatment to offer rehabilitation programs. However, some treatment-induced health deficits may not be treatable, this may result into important information to incorporate into preoperative patient education and shared decision-making.

Shared decision-making

The results described in this thesis offer insights into the impact of major gastrointestinal cancer surgery on quality of life. Information on patient outcomes, short- and long-term, has to be incorporated in treatment decision-making, shared-decision making and preoperative patient education. Healthcare professionals have to keep long-term patient outcomes, quality of life and functional outcomes in mind while proposing oncological treatment decisions. Additionally, these insights in treatment consequences may serve in optimizing patient information and be used during preoperative patient education and in shared decision-making [73, 100]. Using information about treatment consequences in pre-treatment patient education may lead to more understanding. Furthermore, explicit patient consideration of treatment decisions may lead to a higher quality of life post-treatment [101]. Preoperative education of patients has also been shown to reduce postoperative anxiety and postoperative pain [102, 103].

Conclusion

Improving patient outcomes is a challenging process encompassing multiple factors and a multimodal approach. First of all, the importance of improving short-term patient outcomes, reducing postoperative complications, is important in itself, but will also contribute to enhance overall survival and quality of life after surgery. An improvement in preoperative risk assessment and subsequent personalization of perioperative care may lead to a reduction of postoperative complications and mortality. Furthermore, preoperative risk assessment may support clinical knowledge in making treatment decisions and it can be used to identify (modifiable) prognostic factors for postoperative complications. Especially identification of modifiable prognostic factors may be important, because those are possibly optimizable before surgery. Preoperative optimization of modifiable prognostic factors can be done by enrolling patients in prehabilitation programs and should lead to an enhanced physical status, which may result in improved short-term patient outcomes. Moreover, high-risk patients might benefit from personalized or intensified postoperative care, such as closer postoperative surveillance. The complete omission of adverse treatment effects, such as postoperative complications and construction of (temporary) stomas, after major gastrointestinal cancer surgery seems like a utopia. Therefore, knowledge of treatment consequences and treatment-related health deficits remains of utmost importance. This knowledge on treatment consequences and treatment-related health deficits may be used in preoperative education and decision-making, both for patients and healthcare professionals. Especially, if multiple treatment options are available knowledge on treatment consequences of the treatment options is important for shared decision-making. Healthcare professionals can use knowledge of treatment consequences and treatment-related health deficits by making treatment decisions and in the development of new treatment strategies. Additionally, knowledge on postoperative treatment-related health deficits can facilitate the enhancement of postoperative patient guidance and rehabilitation programs. Some treatment-related health deficits may be (partly) treatable, whereas others are not treatable. Especially, those that are not treatable can become vital information in preoperative patient education and shared decision-making. In conclusion, the targets for improving perioperative care presented in this thesis may be used to further improve short- and long-term patient outcomes of resectable gastrointestinal cancer survivors.

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