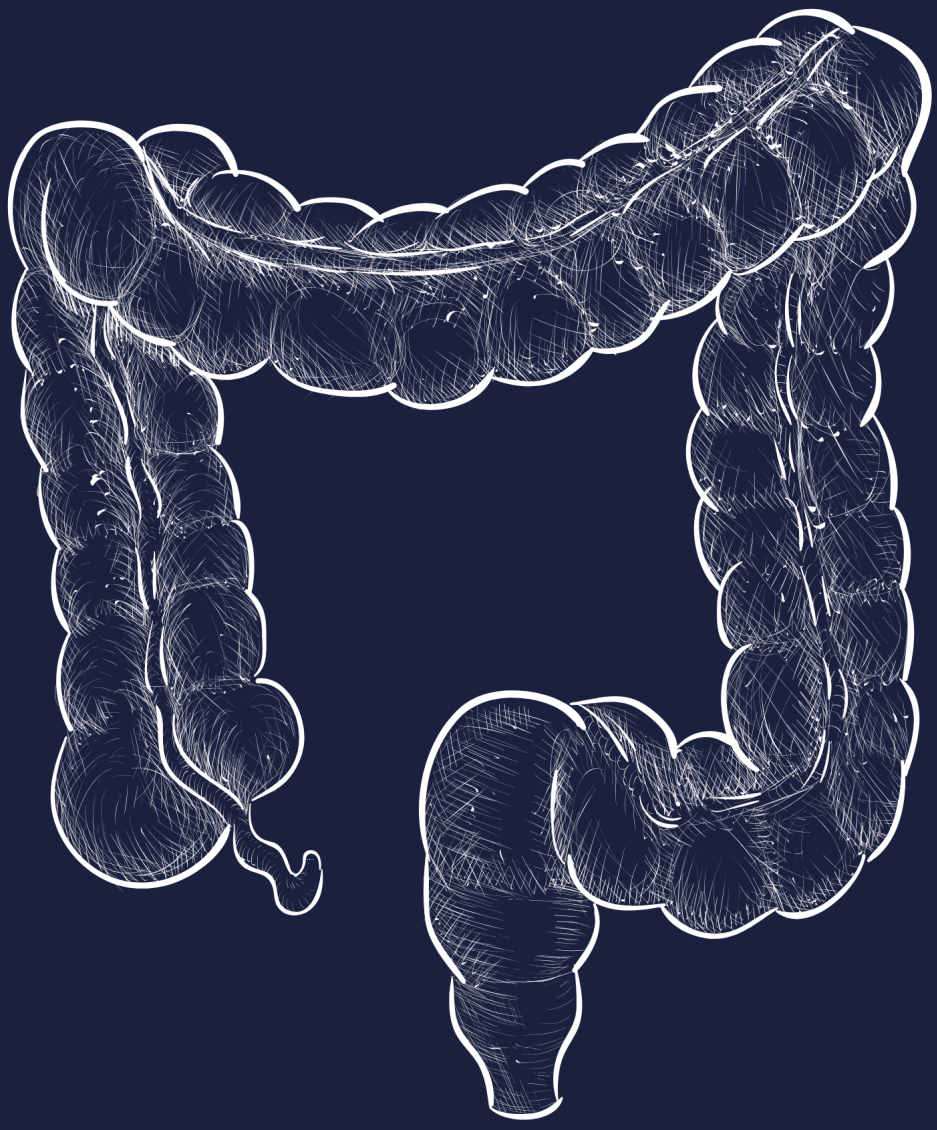
The treatment of elderly patients with colorectal cancer



CHAPTER 13

Impact paragraph

This thesis focused on the treatment of elderly patients with colorectal cancer. Over half of patients with colorectal cancer are 70 years or older at the time of diagnosis. Elderly patients suffer more often from comorbidities, physical impairments, dependency in activities of daily living, or frailty when compared to younger patients. This may challenge the treatment of colorectal cancer in this specific population.

The standard treatment of colon cancer consists of a surgical resection, while in stage III colon cancer, surgery may be followed by adjuvant (i.e. after surgery) chemotherapy. The current standard to treat early stage rectal cancer consists of surgery. Although, improvements in the non-operative treatment of early stage rectal cancer are currently being made. More advanced rectal cancer is treated with neoadjuvant radiotherapy (i.e. before surgery), followed by a surgical resection of the rectum. In case of locally advanced rectal cancer (LARC) and locally recurrent rectal cancer (LRRC), the tumour often extends the rectal wall and involves surrounding pelvic structures (e.g. bladder or reproductive organs). In LARC and LRRC, intensive treatment regimens are often required to downsize the tumour before surgery. Neoadjuvant therapy for LARC standardly consists of chemoradiotherapy (i.e. radiotherapy combined with oral chemotherapy). The surgical procedure for LARC and LRRC often comprises of an extended surgical resection with removal of the affected organs in the pelvis (i.e. resection of rectum, bladder, reproductive organs).

The surgical treatment of colorectal cancer is associated with a risk of complications. In addition, it may affect bowel, bladder, and sexual function. Since earlier studies have reported that elderly patients are at increased risk of postoperative complications and mortality, it has been believed that elderly patients could not withstand intensive treatment. This has resulted in a concern for overtreatment, and, thereby, a reluctance to offer elderly patients guideline-based treatment. However, due to improvements in the care and outcomes of elderly patients, it may be unnecessary to deny elderly patients an optimal curative treatment nowadays. This illustrates that there is much to gain in improving the care for elderly patients with colorectal cancer. Therefore, the main objective of this thesis was to gain insights into the treatment and outcomes of elderly patients with colorectal cancer, in an effort to further improve and personalise treatment. Challenges and improvements regarding patient selection, perioperative treatment, and non-operative management were identified and addressed.

In this thesis, we concluded that the postoperative outcomes of elderly patients with colorectal cancer have improved over the years. Elderly patients who are eligible for surgery can withstand curative treatment, and no longer have an increased risk of

postoperative complications or mortality. This underlines that elderly patients should not be deprived of optimal treatment, based on age or comorbidities alone. However, we found that there are still some areas of concern. Although perioperative care have improved, elderly patients with LARC and LRRC still face high postoperative mortality rates. In particular in these patients, further improvements in patient selection and perioperative care are warranted.

An important part of shared-decision making is adequate patient counselling, which also contributes to better patient selection. Patients should be informed about the treatment options, risks, and consequences. We observed that elderly patients were not at an increased risk to develop functional bowel complaints after colorectal surgery when compared to younger patients. However, we found that half of elderly patients with rectal cancer and one in five with colon cancer developed severe functional bowel complaints after surgery that profoundly impaired their quality of life. Furthermore, we observed that the diverting ostomy reversal rates in elderly patients with more advanced rectal cancer were relatively high and comparable to other studies among younger patients. Nevertheless, one in four did not reverse their diverting ostomy, whereas ostomy recreation was performed in about 15%. These studies underlined that the treatment of colorectal cancer also affects quality of life and functional outcomes. Although many aspects may influence these outcomes, this thesis showed that functional bowel complaints and ostomy-related outcomes should be considered as an essential part of the decision-making process, especially when balancing a restorative procedure versus a non-restorative procedure.

The findings of the first part of this thesis have changed our view on the role of age and comorbidities on the treatment of elderly patients. The outcomes of the first part of this thesis may benefit clinicians during patient selection, counselling, and decision-making. Clinicians should be encouraged to incorporate these aspects and outcomes when different treatment options are balanced and discussed. In addition, these outcomes may benefit elderly patients themselves, since they support the improvements in care and may provide them with insights to optimise shared-decision making, and weigh the benefits and risks of different treatment options. The outcomes have also resulted in novel research questions and efforts to further improve and personalise the treatment and outcomes of elderly patients. These include improvements in patient selection, perioperative care, and whether prehabilitation and rehabilitation programmes will benefit the outcomes of the elderly. Some of these efforts and novel research questions were investigated in the second part of this thesis.

In the second part of this thesis, we investigated which elements required additional attention in the treatment of elderly patients with colorectal cancer. We found that frailty screening and assessment may provide important insights to improve patient selection and outcomes in elderly patients, in particularly in the more frail. The study in **chapter 7**, unveiling the changes in treatment after frailty screening and assessment, as well as the favourable postoperative outcomes of elderly patients at risk of frailty nowadays, was selected for an oral presentation at the 2022 European Society of Surgical Oncology (ESSO) conference in Bordeaux. More importantly, the outcomes have resulted in a closer alignment of care between the geriatrician and the rest of the multidisciplinary team in our hospital. In particular when treating patients with a doubtful health status or those who clearly suffer from frailty, geriatric co-management has become standard in our hospital.

We also investigated whether and how the perioperative care of elderly patients could be improved. We found that the implementation of continuous wound infusion (CWI) of local analgesics (i.e. continuous infusion of pain-reducing agents that act locally on the surgical wound by a small wound catheter) as part of the postoperative pain management in patients that were treated within enhanced recovery protocols (i.e. perioperative protocol to optimise all elements during treatment to improve the recovery after surgery and reduce the risk of complications) resulted in beneficial outcomes. Patients used low amounts of opioids and quickly recovered after surgery, while adequate pain control was maintained. Not only the elderly patient will greatly benefit from reduced opioid consumption, but all patients will. Based on the outcomes of the study and the clinical advantages that were observed, CWI has become standard of care after colorectal surgery in both hospitals that participated in the study in **chapter 8**. Hopefully, the outcomes of the study can support the transition of CWI to become standard of care in more centres. Thereby, our study may contribute to further improvements in the postoperative recovery of patients after colorectal surgery. Furthermore, we identified the need for a modified enhanced recovery protocol with specific elements to improve perioperative care for patients after more extensive surgery for LARC and LRRC (**chapter 9**). Based on the identified elements that needed specific adaptations for LARC and LRRC patients, a perioperative protocol is being developed and implemented in the Catharina Hospital. Hopefully, this will benefit the outcomes of patients after undergoing major rectal cancer surgery.

The non-operative management of rectal cancer has gained interest over the recent years, which may be especially beneficial for elderly patients who refuse surgery or who

are unable to undergo surgery, e.g. due to frailty. The beneficial outcomes that were observed have resulted in the set-up of a Papillon facility (i.e. contact X-ray brachytherapy, which is a technique in which radiotherapy is directly administered to the tumour in the rectum) in our hospital to complete the spectrum of non-operative treatment strategies. Since the non-operative treatment of elderly and frail patients requires a multidisciplinary onco-geriatric approach to personalise treatment, we have implemented a dedicated multidisciplinary clinical care pathway for the treatment of elderly and frail rectal cancer patients unable or refusing to undergo surgery. The multidisciplinary team consists of a surgical oncologist, radiation oncologist, medical oncologist, geriatrician, and, if applicable, an anaesthesiologist. By implementing the multidisciplinary onco-geriatric pathway, we have aimed to improve patient selection, align care between different medical specialties, and optimise the treatment and follow-up of elderly patients. Likely, this will further improve decision-making, in an effort to better meet the needs, and, thereby, improve the outcomes of elderly patients with colorectal cancer.

Since the optimal treatment and outcomes of patients unable to undergo surgery are unknown, we have initiated a single centre, prospective observational cohort study, the RESORT study. Due to the observational character, the study will also provide insights into the decision-making process. Hopefully, the insights of the RESORT study with regard to decision-making, treatment, and outcomes will contribute to improved patient selection and counselling of patients with a doubtful physical condition or willingness to undergo surgery. Thereby, the RESORT study may serve clinicians who are often confronted with elderly and frail rectal cancer patients who are unable to undergo surgery.

The outcomes of this thesis have changed our view on the treatment of elderly patients with colorectal cancer. The studies in this thesis have shown that the majority of elderly patients can be treated safely with standard approaches. However, we found that additional attention may be needed in those undergoing major surgery or those at risk of frailty to optimise their health status or to personalise treatment. In addition, this thesis provides insights on the non-operative treatment of elderly patients unable or refusing surgery. Based on the findings of this thesis, several important changes have been made in the current care for these patients in our hospital. For example the implementation of multidisciplinary onco-geriatric treatment pathways to improve patient selection, the improved perioperative care protocols, and the exploration of personalised non-operative treatment strategies. This thesis will also stimulate follow-up studies to further improve the care for elderly patients with colorectal cancer.

In this thesis, studies were included that could benefit several people that are involved in the treatment of elderly patients. Apart from patients and surgeons, the results of the studies in this thesis provide relevant data and knowledge that is applicable for the decision-making of all members of the multidisciplinary team. In addition, from a societal point of view, the results of this thesis show that delivering appropriate care to elderly patients is beneficial. Most elderly patients benefit as much from adequate treatment as younger patients. Therefore, this thesis underlines that efforts should be made to achieve optimal treatment in the elderly.