

# The treatment of elderly patients with colorectal cancer

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## **CHAPTER 12**

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Summary, general discussion,  
and future perspectives

## SUMMARY

The aims of this thesis were: I) to gain insights into the treatment outcomes of elderly patients with colorectal cancer, in order to improve patient selection and counselling, and thereby, improve shared decision-making; II) to explore improvements in the care for elderly patients with colorectal cancer. The introduction (**chapter 1**) provided an overview of the available evidence and current status with regard to the aims of the thesis.

### **Part I: Treatment outcomes of elderly patients with colorectal cancer**

**Chapter 2** evaluated whether the postoperative outcomes of elderly patients ( $\geq 75$  years) with colorectal cancer have improved over the years, and compared the outcomes in elderly patients to those of younger patients ( $< 75$  years) in a single-centre, retrospective cohort. Among 1037 colon cancer and 981 rectal cancer patients, the 30-day and 90-day mortality rates of elderly patients improved from 5.8% and 9.1%, respectively, in the period 2006–2012, to 1.2% and 4.6%, respectively, in the period 2013–2017. In addition, the 1-year relative survival rates in the elderly improved from 88.4% in the period 2006–2012 to 94.3% in the period 2013–2017. In the most recent time period, the 30-day and 90-day mortality rates, and the 1-year relative survival rates were no longer different in elderly when compared to younger patients.

**Chapter 3** evaluated the developments in postoperative outcomes in a single-centre, retrospective cohort of elderly patients ( $\geq 75$  years) with clinical T4 rectal cancer (cT4RC) and locally recurrent rectal cancer (LRRC) over time, and compared the outcomes in the elderly to those of younger patients ( $< 75$  years). Elderly patients suffered more often from postoperative complications when compared to younger patients (cT4RC: 76.4% vs. 61.7%,  $p = 0.02$ ; LRRC: 96.2% vs. 77.1%,  $p = 0.001$ ), mostly due to non-surgical complications. The 30-day mortality rate of elderly patients improved over time and was no longer significantly different between both age groups in the most recent time period (2012–2017) (cT4RC: 3.1% in  $\geq 75$  years vs. 1.5% in  $< 75$  years,  $p = 0.46$ ; LRRC: 0.0% in  $\geq 75$  years vs. 1.4% in  $< 75$  years,  $p > 0.99$ ). However, the 90-day (cT4RC: 9.4% in  $\geq 75$  years vs. 2.1% in  $< 75$  years,  $p = 0.06$ ; LRRC: 9.1% in  $\geq 75$  years vs. 2.2% in  $< 75$  years,  $p = 0.09$ ) and 1-year (cT4RC: 28.1% in  $\geq 75$  years vs. 6.2% in  $< 75$  years,  $p = 0.001$ ; LRRC: 27.3% in  $\geq 75$  years vs. 13.8% in  $< 75$  years,  $p = 0.06$ ) mortality rates were still worse in the elderly population. About one in four elderly with cT4RC and LRRC died in the first postoperative year, mostly due to treatment-induced or other non-cancer related causes after the

period of hospitalisation. On the contrary, relapsing disease was the main cause of death in younger patients.

**Chapter 4** evaluated the prevalence of functional bowel complaints and the impact on quality of life in elderly patients ( $\geq 70$  years) after colorectal cancer surgery in a large, regional, multicentre cohort study. The LARS score was used to assess functional bowel complaints, and the EORTC QLQ-C30 and QLQ-CR29 were used to assess quality of life. Elderly patients reported major LARS in 40.6% after rectal cancer surgery and in 22.2% after colon cancer surgery, while younger patients ( $< 70$  years) reported major LARS in 57.3% after rectal cancer surgery ( $p = 0.001$ ) and in 20.4% after colon cancer surgery ( $p = 0.41$ ). Patients who suffered from major LARS reported significantly worse quality of life outcomes on almost all domains of the EORTC QLQ-C30 and EORTC QLQ-CR29.

**Chapter 5** investigated the diverting ostomy-related outcomes in elderly patients ( $\geq 70$  years) with more advanced rectal cancer in a single-centre, retrospective cohort. The majority (91.5%) of elderly patients with rectal cancer underwent primary or secondary ostomy creation. A total of 72.5% underwent diverting ostomy reversal after a median time of 3.2 (IQR 2.3–5.0) months. Non-reversal was mostly related to relapsing disease. Ostomy reversal was associated with no or minor complications in 84.0% of patients (95%-CI 75.3–90.6%). During follow-up, 15.0% of patients underwent ostomy recreation. The ostomy-free survival was 69.5% (95%-CI 61.6–76.6%) at 1 year after primary surgery, and 65.8% (95%-CI 57.8–73.2%) after the median follow-up of 3.8 years.

## Part II: Towards improved care in elderly patients with colorectal cancer

**Chapter 6** comprised of an overview of the developments that have been made over the years to improve the care of elderly patients with colorectal cancer, and which elements require additional attention when treating the elderly. Several developments in the treatment of elderly patients have probably contributed to the improved outcomes, including the implementation of minimal invasive surgery, improved perioperative care and enhanced recovery protocols, increased expertise due to colorectal differentiation, and high-volume care. When treating the elderly, attention should be paid for adequate staging protocols, frailty screening and assessment, preoperative optimisation of the patient's health status, a standardised evaluation by a multidisciplinary team including a geriatrician, and specific protocols to deal with problems like acute bowel obstruction.

**Chapter 7** investigated the postoperative outcomes of a single-centre, retrospective cohort of elderly patients ( $\geq 70$  years) with colorectal cancer who were screened positive for frailty, and evaluated the changes in treatment after frailty screening and geriatric assessment. A total of 43.5% of patients were screened positive for frailty ( $G8 \leq 14$ ) by the Geriatric-8 (G8) score. In those with a  $G8 \leq 14$  who underwent geriatric assessment, frailty and intermediate frailty were observed in 28.6% and 50.0%, respectively. Based on geriatric assessment, the oncological treatment plan was altered to a less intensive regimen in 8.9% of patients due to frailty, and to a more intensive regimen in 1.8%. Surgery was performed in 87.8% of patients with  $G8 \leq 14$  and 96.9% of patients with  $G8 > 14$  ( $p = 0.03$ ). The overall postoperative complication (46.2% vs. 47.3%,  $p = 0.89$ ) and Clavien-Dindo  $\geq III$  (13.8% vs. 18.3%,  $p = 0.46$ ) rates did not differ between patients with  $G8 \leq 14$  and  $G8 > 14$ . Postoperative delirium occurred in 7.7% of patients with  $G8 \leq 14$  and 1.1% of patients with  $G8 > 14$  ( $p = 0.08$ ). No differences were observed between patients with  $G8 \leq 14$  and  $G8 > 14$  with regard to 30-day mortality rates (1.1% vs. 1.5%,  $p > 0.99$ ), and 1-year and 2-year overall survival rates (log-rank,  $p = 0.26$ ).

**Chapter 8** presented a prospective, regional, multicentre cohort study to investigate the outcomes of continuous wound infusion (CWI) of local analgesics in a strictly adhered to enhanced recovery protocol after colorectal cancer surgery. Within the already existing ERAS protocols, the use of CWI was implemented in VieCuri Medical Centre since May 2019 and in the Catharina Hospital since March 2020. On the day of surgery, 61.5% (95%-CI 52.6–69.9%) of patients treated with CWI used opioids postoperatively, which decreased to 21.5% (95%-CI 14.8–29.6%), 20.8% (95%-CI 14.2–28.8%), and 13.8% (95%-CI 8.4–21.0%) on postoperative day 1, 2, and 3, respectively. The median pain scores were  $< 4$  on all postoperative days. A postoperative delirium was observed in 0.8% of patients. The median time until the first passage of stool was 1.0 (IQR 1.0–2.0) day and the median length of hospital stay was 3.0 (IQR 2.0–5.0) days.

**Chapter 9** presented an evaluation of the implementation of the colorectal ERAS protocol in a single-centre, retrospective cohort of rectal cancer patients who underwent TME surgery. In addition, ERAS related outcomes and compliance were compared between rectal cancer patients who underwent TME surgery, and LARC and LRRC patients who underwent beyond TME surgery. Specific modifications that are warranted to suit the complexity and needs of patients who undergo beyond TME surgery for LARC and LRRC were identified. In rectal cancer patients who underwent TME surgery, the mean overall compliance to ERAS improved from 54.7% before ERAS implementation, to 85.6% after ERAS implementation ( $p < 0.001$ ). This resulted in significantly shorter median times until

the first passage of stool (2.0 vs. 1.0 days,  $p = 0.04$ ) and discharge (4.0 vs. 3.0 days,  $p < 0.001$ ), without compromising postoperative complications (52.1% vs. 37.3%,  $p = 0.077$ ). In patients with LARC and LRRC who underwent beyond TME surgery, compliance to ERAS was significantly less when compared to the TME group before and after ERAS implementation (44.4% vs. 54.7% vs. 85.6%,  $p < 0.001$ ), in particular for the postoperative period (25.4% vs. 42.5% vs. 75.4%,  $p < 0.001$ ). In addition, longer median times until passage of stool (3.0 days) and discharge (9.0 days), and increased major postoperative complication rates (40.0% in bTME vs. 21.9% in pre-ERAS TME vs. 12.2% in post-ERAS TME,  $p < 0.001$ ) were observed in the beyond TME group. Based on compliance rates and outcomes in LARC and LRRC patients, a tailored, multimodal ERAS protocol with specific modifications is warranted for LARC and LRRC patients undergoing beyond TME surgery, which is currently being developed in the Catharina Hospital Eindhoven.

**Chapter 10** presented a literature overview on the Dutch perspectives and recent developments of organ preservation in the treatment of rectal cancer. Due to the promising outcomes in recent studies, there is a growing interest in organ preserving treatment approaches among both patients and clinicians. Currently, several ongoing studies investigate the value of different organ preserving treatment modalities to further improve tumour responses and increase the chance for successful organ preservation in early and advanced rectal cancer cases. Contact X-ray brachytherapy (CXB) is a promising treatment modality, and seems especially relevant for elderly and frail patients unable or refusing to undergo TME surgery.

**Chapter 11** discussed a multidisciplinary treatment approach to personalise the non-operative management of elderly and frail patients unable to undergo TME surgery. Patients unable to undergo TME surgery are at risk of undertreatment. Advancements in non-operative treatment modalities (e.g. systemic chemotherapy, (chemo)radiotherapy, endoluminal radiotherapy, and local excision) may provide alternative treatment options if surgery is not possible, aiming for optimal local control of the primary tumour. Due to the complexity of treating the elderly and frail, dedicated multidisciplinary clinical care pathways are warranted to personalise the non-operative management of these patients. This chapter also provided a short overview of the currently ongoing RESORT study, a prospective observational cohort study. The RESORT study aims to gain insights into the decision-making, treatment, and outcomes of elderly and frail rectal cancer patients who are unable to undergo surgery.