



## Samenvatting van het proefschrift

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*"Complications and salvage surgery following restorative and non-restorative rectal cancer resection"*

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Patients should be well informed of possible complications following rectal cancer resection. With the introduction of new, less invasive techniques, the question arises whether these techniques are associated with fewer complications, or if the complication rate is equal to the techniques that are still considered the golden standard for rectal cancer resection. Therefore, Part I and Part II address complications, reinterventions and reoperations following rectal cancer resection. Part I focusses on restorative rectal cancer resection with creation of an anastomosis. Part II focusses on non-restorative rectal cancer resection without restoration of bowel continuity, by creation of an end colostomy. Part III of this thesis focusses on redo surgery following the most dreaded complication in restorative rectal cancer resection; anastomotic leakage. We have looked at the success of redo anastomosis for anastomotic leakage when considering bowel continuity, the complication rate and the functional outcomes following redo surgery.

### Part I - Restorative rectal cancer resection

In Chapter 1, a cross-sectional overview of anastomotic leakage and chronic presacral sinus formation following low anterior resection (LAR) in the Netherlands is presented. These are results of a snapshot study on rectal cancer resection performed in 71 hospitals in the Netherlands, comprising 2095 patients. The study showed that in 13.4% of 998 included patients

undergoing LAR for rectal cancer, anastomotic leakage was diagnosed within 30 days. This number increased to 20.0% beyond 30 days. Of all patients with anastomotic leakage, nonhealing of the anastomosis was observed in 48%, resulting in an overall proportion of chronic presacral sinus of 9.5%. Independent predictors for anastomotic leakage at any time during follow-up were neo-adjuvant therapy (OR 2.85; 95% CI 1.00-8.11) and a distal tumour location, defined as a tumour  $\leq 3$ cm from the anorectal junction on MRI (OR 1.88; 95% CI 1.02-3.46). The study also shows that the long-term anastomotic leakage rate is similar, with or without the creation of a diverting stoma.

This last finding forms an important base for the next chapter, since from a historical perspective, a diverting ileostomy is thought to reduce anastomotic leakage rates and urgent reoperations. Chapter 2 compares patients who underwent laparoscopic TME and were routinely diverted to a group of patients who underwent only highly selective diversion in combined laparoscopic and transanal TME with reinforcement of the anastomosis with a continuous suture. Anastomotic leakage occurred in 20% following routine diversion, compared to 8% following highly selective diversion after a median follow-up of 36 and 19 months respectively. This difference was not significantly different. There was however, a significant difference in one-year stoma-related readmission and reoperation rate (stoma reversal included); 84% and 86% respectively following routine diversion compared to 17% and 17% respectively following highly selective diversion.

## **Part II - Non-restorative rectal cancer resection**

Chapter 3 aimed to evaluate current practice regarding rectal cancer resection without restoration of bowel continuity. Surgeons from 37 Dutch hospitals responded to an online survey with questions addressing low Hartmann's resection (LHR) and intersphincteric abdominoperineal (iAPR) as non-restorative treatment options. Of 42 responding surgeons, 36% indicated not to distinguish between a high or low Hartmann's resection based upon the estimated length of the rectal remnant. Overall, in 86% iAPR was the preferred technique and 62% indicated that they would consider a different technique in tumours at 1cm from the pelvic floor compared to tumours at 5cm. The incidence of pelvic abscesses after LH was thought to be higher, equal or lower than after iAPR in 36%, 36% and 21% respectively.

In Chapter 4, the actual incidence of pelvic abscess formation following LHR and iAPR was assessed in a small retrospective comparative cohort study including 40 patients undergoing LH and 12 patients after iAPR. There were no significant differences in major complications within 30 days postoperative (18% vs 33% respectively,  $P=0.253$ ) or overall pelvic abscess formation

(10% vs 17% respectively,  $P=0.612$ ). Limiting factor of this study was the small number of patients, therefore a study with a similar design, but within a larger cohort from a collaborative snapshot study is displayed in Chapter 5. We included 139 patients after LHR and 46 patients after iAPR. Overall, a pelvic abscess occurred in 17% of patients following LHR and 11% after iAPR. This showed not to be a significant difference, also when censored for mortality or loss to follow-up. Nevertheless, after iAPR significantly more abscesses were diagnosed beyond 30 days postoperative. The study also revealed a high number of surgical reinterventions and readmissions for any reason, with only a minority occurring within 30 days postoperative.

### **Part III – Salvage surgery following rectal cancer resection**

In Chapter 6 the results of a systematic review on outcomes following redo surgery with the creation a new (redo) anastomosis after anastomotic leakage is presented. We included nine studies, comprising 291 patients. It showed a pooled success rate of 79% (95% CI 69-86), with a pooled incidence of major postoperative morbidity of 16% (95% CI 10-24) and a pooled pelvic sepsis rate of 16% (95% CI 9-27).

Clinical success and morbidity after the construction of a redo coloanal anastomosis (CAA) because of anastomotic leakage after LAR in a cohort of 59 cases is presented in Chapter 7. It revealed that anastomotic leakage was the most frequent complication following redo CAA (41%). In 66% of patients, bowel continuity was restored at the end of follow-up and in 24% of patients, a definitive end colostomy was constructed. In a multivariate model, leakage of the redo CAA was the only risk factor for a permanent stoma (OR 0.022; 95% CI 0.004-0.122). This cohort study also showed that 97% of all procedures is performed through an open approach. This is thought to be caused by poor visibility and accessibility of the deep pelvis due to location, prior surgery and inflammation. In Chapter 8, the use of transanal minimally invasive surgery (TAMIS) for redo surgery is described, because of its possible ability to overcome these obstacles encountered in conventional redo surgery. Both salvage surgery with creation of a redo anastomosis as well as intersphincteric completion proctectomy (ICP) with end colostomy through TAMIS were described and compared to series of patients undergoing conventional redo anastomosis or ICP. By extending the transanal dissection further upwards by using a TAMIS approach, the abdominal part could be performed using laparoscopy in two-thirds of the patients. There were no significant differences between TAMIS and conventional approach in intra-operative complications and 90-day postoperative outcomes and a stapled redo anastomosis could be done in 62% of the TAMIS procedures, while all conventional redo anastomosis were hand-sewn.

Finally, Chapter 9 focusses not on the surgical outcomes, but on the patient reported functional outcomes and quality of life following redo anastomosis. Outcomes were compared to patients who underwent uncomplicated total mesorectal excision (TME) for rectal cancer. In total, 52 redo anastomosis patients were included, of whom 83% had radiotherapy. Outcomes were assessed using the low anterior resection syndrome (LARS) score and the EORTC QLQ-C30 and QLQ-CR29 questionnaires and revealed comparable major LARS scores between groups; 73% after redo anastomosis compared to 68% following uncomplicated TME. The redo group had significantly worse EORTC QLQ-CR29 mean scores for faecal incontinence and flatulence, but there were no differences in urinary or sexual dysfunction neither in men nor in women. Global health, role-, and social function, body image and anxiety were scored significantly worse in the redo group. We therefore concluded that although redo anastomosis is associated with a negative impact on quality of life, considering the comparable LARS scores and thus ano(neo)rectal function after uncomplicated TME, it might still be a valid treatment option in patients highly motivated for restoration of bowel continuity.