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Colorectal Anastomoses

Bakker, IIsalien

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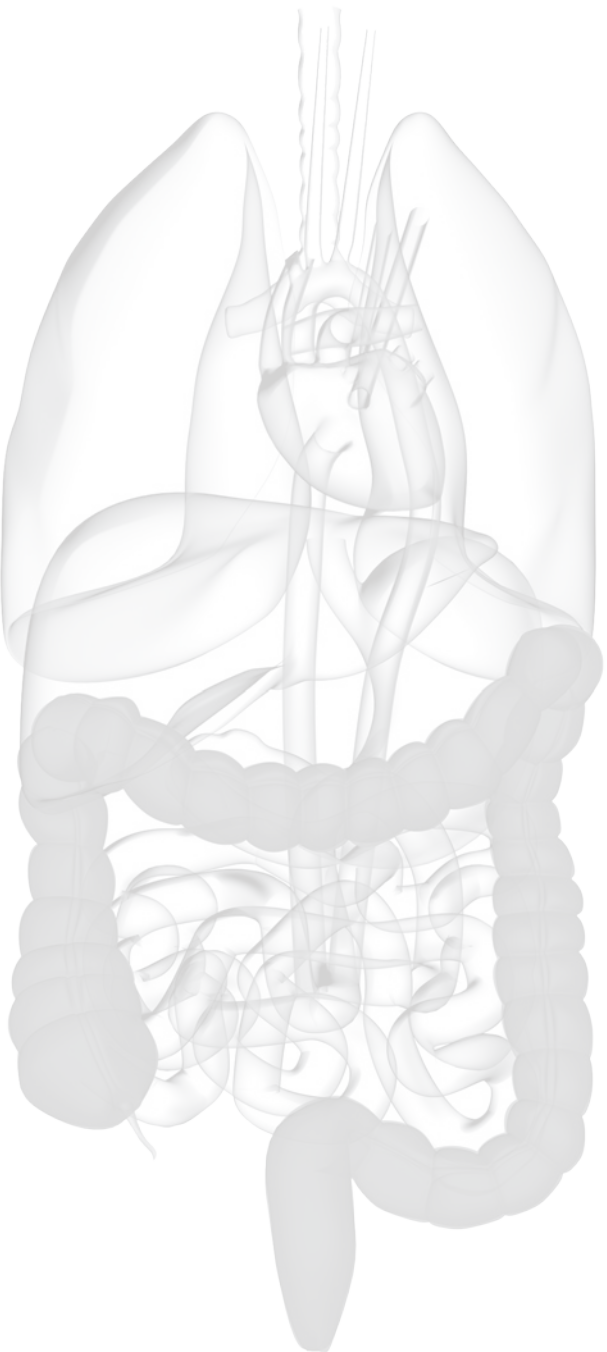
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SUMMARY



Chapter 6

SUMMARY

Colorectal cancer is the third most common cancer in the world, with in the Netherlands nearly 10.000 annual resections. The first part of this thesis focused on surgical outcome after colorectal cancer resection in the Netherlands. Present results are based on nationwide data from the Dutch Surgical Colorectal Audit. In chapter two and three, surgical outcome of colon cancer resection is described. Surgical resection is the cornerstone of treatment for patients with colon cancer. Anastomotic leakage is the most serious complication after colon resection with restoration of bowel continuity, resulting in high morbidity, high re-intervention rate, prolonged hospital stay and even mortality.

COLON SURGERY

In *CHAPTER 2* risk factors for anastomotic leakage and subsequent mortality after colon cancer surgery were described. All patients operated on for colon cancer in the Netherlands between 2009 and 2011 were included for analysis. From all included patients 7.5 percent developed clinical anastomotic leakage requiring a re-intervention. Male gender, high American Society of Anesthesiologists score, transverse resection, left sided or subtotal colectomy, and emergency surgery were identified as independent risk factors for anastomotic leakage. Also patients with preoperative tumour complications as tumour perforation and obstruction were at risk for postoperative leakage. Construction of a defunctioning stoma led to a lower leakage rate. There was a 4.1 percent overall mortality rate within thirty days of surgery, with a significant higher mortality rate in patients diagnosed with anastomotic leakage. Older age, high American Society of Anesthesiologists score, high Charlson score and emergency surgery were independent risk factors for postoperative death among patients diagnosed with anastomotic leakage. Although the anastomotic leakage incidence is higher after left sided colectomy, the risk of death associated with anastomotic leakage was lower after left sided resections compared to right sided resections, probably due to anatomical differences and relatively fitter patients. The present results showing high mortality after colon cancer resection emphasized the importance of adequate preoperative patient selection and intensive postoperative monitoring.

CHAPTER 3 further focused on outcome after non-elective colon cancer surgery in the Netherlands. From 2009 to 2013, 30.907 patients underwent colon cancer resection in the Netherlands. Nineteen percent of these patients were operated in non-elective setting. Surgical resection in non-elective setting was associated with significant more postoperative deaths. Elderly, male gender, patients with comorbidity, advanced tumours, perforated tumours and a

tumour located in the right or transverse colon were at risk for postoperative mortality. Also patients with anastomotic leakage had a higher death risk. In non-elective surgery especially patients undergoing right-sided colectomy, patients with perforated tumours and postoperative anastomotic leakage had the highest mortality rates. Non-elective colon cancer surgery remains a challenging clinical problem. Optimization of patients prior to surgery and resection by a dedicated surgical team might contribute to improved surgical outcome. High rates of postoperative mortality suggest that surgical resection shortly after diagnosis is the best option to prevent colon tumours to become symptomatic and thereby avoiding non-elective surgery. The recently implemented national colon screening programme could contribute to this, due to early tumour detection.

RECTAL SURGERY

While chapter two and three described outcome of colon cancer surgery, chapter four and five focused on rectal cancer surgery. In the Netherlands more than 2.500 rectal cancer resections are performed each year. When tumour size, stage and location allow a sphincter preserving procedure, there are three surgical options including bowel continuance by means of a primary anastomosis, an anastomosis with a defunctioning stoma and avoidance of bowel continuance with construction of an end-colostomy. *CHAPTER 4* described the surgical outcome of these three resection types for mid and high rectal cancer based on the national data of the Dutch Surgical Colorectal Audit. From January 2011 to December 2012 2.585 patients undergoing rectal cancer resection were included. Twentyfive percent of patients received a primary anastomosis, 51% of patients had an anastomosis with defunctioning stoma and in 24% of patients an end-colostomy was constructed. There was a high overall postoperative complication rate. Patients with a primary anastomosis had the most favourable postoperative results. Construction of defunctioning stomas led to a somewhat lower clinical anastomotic leakage rate, but was associated with more postoperative complications, longer hospital stay and higher postoperative mortality. An end-colostomy was associated with less invasive re-interventions. Knowledge of the outcome of the different surgical strategies is of great importance in shared decision making. The trade-offs of each surgical strategy together with patients preference should lead to tailored decision making for the individual patient resulting in the best postoperative outcome. Less defunctioning stomas, intensive postoperative surveillance with early re-interventions and creation of end-colostomies in high risk patients leads to the most optimal short term outcome. Furthermore knowledge of long term outcome after rectal cancer resection is important for the individual treatment plan and in order to properly inform patients preoperatively. In *CHAPTER 5*

the long term results of the aforementioned three surgical strategies for rectal cancer were analyzed. From January 2009 to June 2011, 388 patients undergoing rectal cancer resection in seven hospitals in the Netherlands, were analyzed according short term complications within thirty days postoperative and 1 year outcome. One third of all patients developed short term postoperative complications. There was a ten percent anastomotic leakage rate in patients with a primary anastomosis. Although patients with a defunctioning stoma had a slightly lower leakage rate on the short term, there was a higher readmission rate and more re-interventions were performed in these patients, mostly as a result of late anastomotic leakage. Besides, after secondary surgery to create bowel continuity these patients had an additional high risk for postoperative complications including anastomotic leakage. In one fifth of patients the stoma was not reversed at all. One year outcomes of patients with a primary anastomosis were favourable, probably caused by adequate patient selection. Despite the fact that the patient group with an end-colostomy was older and had more comorbidity it was associated with a comparable postoperative complication rate and a lower invasive intervention rate on the short term. On the long term however, these patients had a high unplanned readmission rate due to stoma problems and pelvic abscesses. Translating the results on both short term and long term outcome after rectal cancer surgery for clinical implication results in the importance of adequate patient selection and the avoidance of routine use of defunctioning stomas. Thorough preoperative counseling, taken patients preference and the postoperative morbidity risk into account, is required in the process of clinical decision making.

ANASTOMOTIC LEAKAGE

National data of the Dutch Surgical Colorectal Audit presented in the first part of this thesis showed persistent high morbidity and mortality rates after colorectal surgery. The anastomotic leakage risk, the most serious complication after colorectal resection with subsequent bowel continuity, remains unaltered throughout the years. The Second part of this thesis focused on prevention of anastomotic leakage in colorectal surgery. In *CHAPTER 6* the study protocol of the multi-center randomized controlled C-seal trial was described. The C-seal is a biodegradable intraluminal drain, which is fixed to the proximal side of the anastomosis with the circular stapler. Due to intraluminal application of the drain, the newly made anastomosis is protected against leakage of intestinal contents in case of anastomotic dehiscence. The study population consists of patients with a minimal age of eighteen years, undergoing elective colorectal resection with a circular stapled anastomosis. Preoperative mechanical bowel preparation is mandatory. Patients will be equally randomized to the C-seal and the control group, stratified by center, anastomotic

height and the intention to construct a defunctioning stoma. After fifty and seventy-five percent of patient inclusion an interim analysis will be performed by an independent data safety committee. The C-seal trial is aimed to evaluate the efficacy of the C-seal in reducing clinical anastomotic leakage. The primary endpoint is the incidence of anastomotic leakage leading to invasive treatment within thirty days after surgery.

In *CHAPTER 7* the results of the randomized controlled C-seal trial were presented. From December 2011 to December 2013 eligible patients were included in 41 hospitals in the Netherlands, Germany, France, Hungary and Spain. After the interim analysis, performed after the inclusion of fifty percent of the patients, the trial was terminated due to futility. At that point 402 patients were included for analysis. All included patients were equally randomized to the C-seal and the control group. Both groups were similar according baseline characteristics. There was a 7.7 percent overall anastomotic leakage rate with 10% leakages in the C-seal group compared to 5% in the control group. More anastomoses were dismantled in the C-seal group. Defunctioning stomas were equally created in both groups. There was no difference in interval between primary surgery and the occurrence of clinical anastomotic leakage and there was no difference in hospital stay between the groups. After correction for confounders construction of a defunctioning stoma led to a lower leakage rate. Male gender and C-seal application were independent risk factors for postoperative clinical anastomotic leakage. Feasibility of the C-seal was demonstrated in previous studies. In the present study however, problems related to the C-seal were reported in 32 patients, both including application problems as complications expressed by participating patients.

Unfortunately we could not demonstrate the previous presented promising results of the C-seal in leakage preventions. The randomized results of the C-seal trial did not show a leakage reducing effect of C-seal application in circular stapled colorectal anastomoses. Therefore there seems to be no future role for the C-seal in clinical anastomotic leakage prevention in colorectal surgery.

Influence of treatment factors and intraoperative surgical techniques on surgical outcome are focus of scientific interest. *CHAPTER 8* described results of a study on the influence of surgical strategies on postoperative clinical anastomotic leakage development in stapled colorectal anastomoses. All patients included in the control group of the C-seal trial and operated in the Netherlands were included for analysis. The C-seal student team collected detailed intraoperative information concerning patients and procedures. Male gender, high Body Mass Index, high blood loss, long course neoadjuvant chemoradiation and construction of end-to-end anastomoses showed increased clinical leakage rates. Performed surgical strategies concerning anastomosis

construction showed a great heterogeneity among surgeons in the Netherlands, not leading to a difference in anastomotic leakage rate. However, results of the present study showed some interesting findings. Insertion of pelvic drains did not influence the leakage rate. Defunctioning stomas showed a tendency to a lower leakage rate and air leak testing of the anastomosis, with subsequent management resulted in less anastomotic leakages. Combination of particular surgical techniques might lead to the most optimal anastomosis, resulting in the best surgical outcome. Standardization of surgical procedures and prospective data collection in national audits might identify the perfect colorectal anastomosis.

