Surgery for inflammatory bowel disease, crossing borders
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General introduction and outline of the thesis
GENERAL INTRODUCTION

Inflammatory bowel disease (IBD)

IBD is a chronic, idiopathic inflammatory disease of the gastrointestinal tract. Patients with IBD are diagnosed with either Crohn’s disease (CD) or ulcerative colitis (UC). A small portion of patients is classified as having unspecified disease (IBD-U). Incidence of IBD in the Western countries has risen in the past decades to 6-15 per 100,000 individuals for CD and 8-14 per 100,000 individuals for UC. In the Netherlands, yearly approximately 1000 patients with CD and 1500 patients with UC are newly diagnosed with an estimated prevalence of 20,000 and 30,000 patients respectively. In CD, the peak age of onset is in the 2nd or 3rd decade, while UC is most frequently diagnosed in patients between 15-40 years and the middle aged. Both CD and UC are characterized by episodes of relapse and remission.

Crohn’s disease

CD can occur throughout the entire gastrointestinal tract. It is characterized by transmural inflammation and a skip lesion pattern, and can present with structuring and penetrating complications. Patients with CD often present with a history of abdominal cramping, persistent diarrhoea, fever with or without anorexia and possibly nausea and vomiting as signs of obstructive intestinal disease. Smoking increases the risk for CD.

Patients with CD are commonly treated according to the step-up approach. Patients are initially treated with the least toxic, but also least potent drug. Treatment is intensified by using stronger medication (e.g. anti-tnf; anti-tumour necrosis factor) if necessary. Indications for surgery are obstructive disease, medical refractory disease, fistulas or complications such as abscesses, perforations or bleeding. Despite the current variety of available medications, more than two thirds of patients will require surgery during their lifetime, and nearly half of these patients will undergo repeat surgical interventions.

Ileocolic resection

In approximately 30-35% of all CD patients, the disease activity is confined to the terminal ileum. The ileocolic resection is the most performed resection in IBD. Many studies have established short and long term advantages of the laparoscopic ileocolic resection.

Ulcerative colitis

In UC, disease activity is confined to the colon, and typically involves the rectum. The disease diffusely affects the superficial mucosa of the colon. Patients with UC often present with a history of abdominal cramping, bloody diarrhoea, fatigue and weight loss. Smoking lowers the risk for UC.
Treatment of UC is primarily medical, according to the step-up approach. Colitis refractory to medical treatment requires surgery. Basically there are two procedures commonly applied, the emergency colectomy and (completion) proctocolectomy with ileoanal pouch reconstruction. Reported operation rates vary in the literature, but are between 20-30% after 25 years of UC.

Subtotal colectomy
In case of severe colitis refractory to medical therapy a subtotal colectomy is performed. In an elective setting, a completion proctectomy and ileal pouch anal anastomosis (IPAA) is performed.

Restorative (completion) proctocolectomy and pouch procedure
In an elective procedure, a restorative proctocolectomy (RPC) is performed. During this procedure the (remaining) colon is removed, followed by a proctectomy and IPAA. For creation of the IPAA, the J-pouch configuration is most commonly used. The J-pouch is created by stapling a folded loop of the terminal ileum. The pouch is subsequently stapled or sewn to the anal canal. In patients with an increased risk of anastomotic complications, such as preoperative high doses of steroids or technical difficulties during the procedure, a defunctioning loop ileostomy is created. An RPC can be performed as an open or laparoscopic procedure, in which the laparoscopic procedure has different advantages over the open approach. The quality of life increases after creation of a pouch, even to a level comparable to that of the general healthy Dutch population.

A restorative proctocolectomy is also performed in patients with familial adenomatous polyposis (FAP). In these patients hundreds of adenomas develop in the colon and rectum during childhood and adolescence. Without treatment, the colorectal cancer rate is 100% around age 40 to 50. Incidence of FAP is estimated 1 per 100,000 individuals. Indication for surgery is the presence of large numbers of adenoma’s over 5mm in size, including adenomas showing high grade dysplasia. This criterion is often reached between the age of 15 and 25 years.

Appendectomy
Although the trigger for the development of UC is still unknown, T-helper type II cells and their cytokines are suggested to enhance the development of UC. Over the past 20 years evidence has accumulated suggesting a role of the appendix in the development and disease course of UC. Cytokine production in the appendix has been proposed to trigger an immunological cascade in the colorectum. The appendix is suggested to be a potential priming site in the development of UC. Several studies show a beneficial effect.
of appendectomy on the disease course of UC\textsuperscript{26-29}. Therefore, the role of the appendix in UC is further evaluated.

Laparoscopic surgery
Laparoscopic techniques have transformed colorectal surgery in the last decades, and meanwhile numerous studies have shown the safety and advantages of laparoscopic surgery in Crohn’s disease and colitis\textsuperscript{30-36}.

Especially young patients and patients undergoing repeat surgery may benefit from bowel-sparing techniques and minimally invasive surgery with reduced adhesion formation. These minimally invasive procedures have further developed into even more minimal invasive techniques, e.g. single-incision laparoscopic surgery, natural orifice specimen extraction, close rectal dissection techniques and transperineal resectional surgery.

Complications after surgery
Surgery is inevitable associated with complications. The Achilles’ heel of ileoanal pouch surgery is anastomotic leakage. Leakage might result in a chronic presacral sinus precluding stoma closure or jeopardizing pouch function if the stoma can be closed. It is for debate whether creating a primary defunctioning ileostomy after IPAA benefits the patient.

The same applies to the influence of the type of proctectomy performed in ileoanal pouch surgery, e.g. total mesorectal excision or close rectal dissection, on the clinical significant anastomotic leaks. When an anastomotic leak after pouch surgery has developed there are only a few options other than a defunctioning ileostomy to solve the problem. A relatively new technique to take care of the leaking low anastomosis is applying the Endo-sponge technique. Weidenhagen et al. described a technique to treat the presacral sinus with vacuum assisted drainage\textsuperscript{37}. A modification of this technique is currently used in which the Endo-sponge is used to clean the cavity during two or three Endo-sponge\textsuperscript{®} placements. When the cavity is clean and is surrounded by healthy granulation tissue, the anastomotic defect is closed surgically. With the use of this novel technique a higher percentage of secondary healed anastomosis and a better long term pouch function is expected.

AIM OF THE THESIS
The aim of this thesis was to present recent developments in the surgical treatment of patients with CD, UC and FAP. Part I of the thesis presents the results of studies on the developments in surgical treatment and surgical techniques. Part II focuses on the appendix as a new and promising aspect in the (surgical) treatment of UC.
OUTLINE OF THE THESIS

The first part of this thesis focusses on the developments in the surgical treatment of patients with inflammatory bowel disease and familial adenomatous polyposis and it concentrates on new developments in surgical techniques. In Chapter 1 we perform a systematic review with meta-analysis to compare short-term outcomes after laparoscopic and open emergency colectomy for acute medically refractory colitis. In Chapter 2 the results of a series of patients who underwent emergency colectomy at the Academic Medical Centre are presented. In this chapter we have aimed to determine possible risk factors for postoperative complications. Chapter 3 describes different extraction techniques to remove the specimen from the abdominal cavity after emergency colectomy, such as the rectum or stoma site. The short term results of two surgical dissection techniques in the creation of an ileal pouch-anal anastomosis (IPAA) are compared in a randomized controlled trial presented in Chapter 4. Aim of the latter study is to compare morbidity and quality of life in patients having total mesorectal excision or close rectal dissection during proctectomy followed by IPAA for benign disease. In Chapter 5 we compared the results of 2 cohorts of patients undergoing IPAA surgery with or without primary defunctioning ileostomy. Both surgical outcomes, functional results and quality of life of these patients are analysed. A novel solution for the treatment of anastomotic leakage after IPAA is presented in Chapter 6 and compared to the conventional treatment of this challenging complication by investigating the effectiveness and direct medical costs of both treatment modalities. Chapter 7 discusses the most recent developments in the surgical techniques in the treatment of patients with CD. One of these developments, the single-port laparoscopic ileocolic resection, is explored in Chapter 8 by comparing short term surgical outcomes in two cohorts of patients undergoing either single-port or multi-port laparoscopic ileocolic resection for CD.

The second part of this thesis focuses on the appendix and its role in UC. There is evidence that appendectomy protects against development of UC and may influence the disease course of UC. Furthermore, the appendix is suggested to be a potential priming site in the development of UC. In Chapter 9, a systematic review of studies investigating the effect of appendectomy on the disease course of patients with UC is presented. Chapter 10 describes the study protocol of the ACCURE trial, an international multicentre randomised trial in patients with UC that will provide evidence on the role of appendectomy in the treatment of UC and the effects of appendectomy on the disease course. In depth analysis of the appendix is performed in Chapter 11. In this study T cell infiltration in the appendices of UC patients is analysed and compared to the appendices of patients with CD, acute appendicitis and non-inflammatory controls.
REFERENCES


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