Optimizing strategies in gastrointestinal surgery

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General introduction

Surgery for Ulcerative Colitis and Familial Adenomatous Polyposis (part I)

Ulcerative Colitis
Ulcerative colitis (UC) is a chronic inflammatory bowel disease of the colon and rectum, and is characterized by episodes of remission and relapses.\(^1\) In Europe incidence ranges from 1.5 to 20.3 cases per 100 000 person years.\(^2\) The incidence of UC has been increasing, but appears to be stabilizing nowadays.\(^3\) At this moment, around 30 000 people are diagnosed with UC in the Netherlands. Yearly, approximately 500 patients are newly diagnosed.\(^4\) Average age of onset is between 15 and 40 years of age, and slightly more men are affected by this disease.\(^1\)

Initially UC is treated with medications; during an exacerbation patients need remission-induction therapy, once regained, prophylactic therapy is given. The recommended method of treatment is the ‘step-up approach’. However, some patients are refractory to all medications and need surgical treatment.\(^5;6\) If surgery can be done in an elective setting, a proctocolectomy with ileal pouch anal anastomosis (IPAA) will be performed with or without temporary defunctioning loop ileostomy.\(^7\) This is decided by the surgeon depending on the perceived risks for an anastomotic leakage, like use of steroids and nutritional status.\(^8\) If surgery has to be done in an acute setting, a subtotal colectomy with an end ileostomy will be performed. In a later phase, a completion proctectomy with IPAA will be performed. The number of patients that require an operation because of refractory UC vary from 7.5% after 5 years of onset of the disease to 24% after 10 years of onset.\(^9;10\)

Colorectal dysplasia and colorectal cancer are, besides refractory colitis, other indications for a proctocolectomy with IPAA. Longstanding UC increases the risk of developing colorectal dysplasia and cancer.\(^11\) Eaden et al. even showed cumulative risks of 2% after 10 years, 8% after 20 years, and 18% after 30 years of disease.\(^12\) Therefore, UC patients are advised to undergo colonic surveillance to detect dysplasia or colorectal cancer at a surgical curable stage.\(^13;14\)

Familial Adenomatous Polyposis
Familial adenomatous polyposis (FAP) is a rare autosomal dominant disease. Incidence is 1 case per approximately 100 000 individuals.\(^15\) This syndrome is characterized by the development of hundreds to thousands colorectal adenomas and is diagnosed between the age of 10 and 40 years. In the end more than thousands of adenomas will be present in the colon and rectum. The adenomas develop via the ‘adenoma-carcinoma pathway’ into a carcinoma. An untreated FAP will result in colorectal carcinoma in nearly 100% of the patients. FAP patients also have an increased risk of extracolonic manifestations.\(^16\)

Endoscopic surveillance is advised twice per year but, once multiple polyps have developed, endoscopic surveillance is unreliable. In those cases a patient is advised to undergo surgery; a proctocolectomy with IPAA will be performed.\(^17\)
**Proctocolectomy with ileal pouch anal anastomosis**

During the 1970s this procedure has been developed by Parks and Nicholls. They described an ileal pouch reservoir using a S configuration following distal rectal mucosectomy.\(^8\) This technique, however, was associated with impaired pouch emptying, and in 1980 Utsunomiya developed the J pouch.\(^9\) At present, most surgeons favour this type of reservoir.

The operation can be performed both open and laparoscopically. The first laparoscopic assisted proctocolectomy with IPAA has been described in 1992.\(^10\) A recently published meta-analysis showed that the laparoscopic approach is safe and feasible.\(^11\) An additional advantage of laparoscopy, especially in this relatively young patient group, is better cosmesis.\(^12;13\)

The operation consists of three parts: colectomy, rectal extirpation and formation of the IPAA. The construction of the pouch can be performed by a double-stapling technique, which is done in most cases, or by a mucosectomy, in order to prevent recurrence. Stapling devices have simplified the procedure. Nevertheless, it is still a very complex operation with potential morbidity.\(^14\) Stool frequency and continence are the two main factors that will determine optimal pouch function; average stool frequency at day time is about 6-7 times, at night time 1-2 times.\(^11\)

**Enhanced Recovery After Surgery (part II)**

**Colorectal cancer**

Worldwide, colorectal cancer is the second most common cancer. Its incidence is expected to rise with the increasing longevity and obesity of the Western population. In 2009, 11 450 people were newly diagnosed with colorectal cancer in the Netherlands. Yearly, about 4 500 patients die from this disease, which makes colorectal cancer, after lung cancer (9 414) the second highest cancer-related death. Overall 5-year survival is 60%, but differs dramatically between patients that have been diagnosed at an early stage (5-year survival 93%) or those that have been diagnosed with metastasis to other organs (5-year survival 9%).\(^15\)

Screening programs for colorectal cancer are implemented and will probably further increase the number of patients requiring treatment. The first line strategy to treat colorectal cancer is surgery.\(^16\)

**Laparoscopy and fast track perioperative care**

Over the past twenty years there have been two important developments in elective major abdominal surgery; the introduction of laparoscopic surgery and the implementation of an Enhanced Recovery After Surgery program, also referred to as ‘fast track’ perioperative care, both focusing on accelerated recovery resulting in shorter hospital stay.\(^17;18\)

Laparoscopic resection of bowel cancer was first described in 1991.\(^19\) Randomized clinical trials have shown that this technique is safe and effective for malignant disease, results in a hospital stay shorter by about 1-4 days, and less morbidity and postoperative pain than open colorectal surgery.\(^20;21\)

During the mid-nineties fast track perioperative care was pioneered by Henrik Kehlet.\(^22;23\)
Fast track programs consist of a multidisciplinary approach, involving dieticians, nurses, surgeons and anesthesiologists and are aimed at reducing surgical stress response, organ dysfunction and morbidity, thereby promoting a faster recovery after surgery.\textsuperscript{33,35-37} Fast track perioperative care comprises extensive preoperative counseling, no bowel preparation, no sedative premedication, carbohydrate-loaded liquids up to two hours before surgery, effective multimodal pain management, short acting anesthetics, adequate perioperative fluid management, small incisions, and no routine use of drains and nasogastric tubes. Postoperative care includes early oral feeding, enforced mobilization, early removal of urinary catheter and standard laxation.

Similar or even faster rates of recovery have been reported for fast track and open colectomy on comparison with laparoscopic colectomy in a standard perioperative care setting.\textsuperscript{38-41} Due to the implementation of fast track programs, the leading trials\textsuperscript{28-30}, comparing laparoscopic with open surgery with respect to recovery, are presently outdated as in these trials standard perioperative care was given. There are no trials to be found in literature addressing the four combinations of standard or fast track care with laparoscopic or open surgery.

It is hypothesized that fast track and/or laparoscopy are associated with less attenuation of the patient’s condition after surgery, resulting in a shorter postoperative stay and faster recovery to full activity. A faster postoperative recovery, i.e. shorter hospital stay, might have enormous consequences for hospital resources and costs of healthcare.

At present, it is still a matter of debate whether to apply either laparoscopy, fast track or a combination of both. So, now these new developments have proved their feasibility and safety and, as colorectal resections are one of the most common operations in the Netherlands, time has come to evaluate its use in colorectal surgery.\textsuperscript{42}

\textit{Implementation and costs}

The introduction of fast track care and laparoscopy in daily practice is not simple. Both programs are costly and require extensive expertise. In order to make the fast track program work, the medical and nursing staff needs additional training how to implement the fast track elements. Up to now, full implementation seems troublesome, which is most likely explained by the need to break with longstanding traditions.\textsuperscript{34,43,44} Laparoscopic surgery is costly due to expensive disposables, additional operating time, and a considerable learning curve must be mastered.

The higher costs for laparoscopy and fast track care, might be counterbalanced by shorter hospital stay. In addition, the reduced hospital stay will increase hospital bed utilisation, thereby increasing the capacity to treat colorectal cancer patients resulting in shorter waiting lists. If waiting lists for malign colorectal surgery can be shortened, the patient deteriorates less, subsequently resulting in; less preoperative complications like acute colectomy due to an obstruction; less postoperative complications due to better preoperative condition, and; less tumour progression. Obviously, all this will lead to fewer costs.
**Aim of the thesis**

In this thesis several aspects of abdominal surgery for benign and malign diseases are highlighted. The aim of part I is to evaluate the clinical and functional outcome of surgery in patients with ulcerative colitis (UC) and familial adenomatous polyposis (FAP). In part II, the aim is to critically appraise the effects of the two new major developments in elective abdominal surgery, i.e. laparoscopy and fast track.

**Outline of the thesis**

**Surgery for Ulcerative Colitis and Familial Adenomatous Polyposis (part I)**

The standard treatment for patients with UC and FAP is a proctocolectomy with IPAA via an open or laparoscopic approach. In laparoscopic surgery mostly a medial to lateral approach is applied, instead of the more commonly used lateral to medial approach in open surgery. In laparoscopic colectomy devascularisation can be started on the left side at the inferior mesenteric artery or at the right side at the ileocolic artery. The aim of chapter 1 is to determine whether the type of approach, open or laparoscopic, and the order of devascularisation in laparoscopic colectomy, affects intestinal barrier function, local inflammatory response and clinical outcome.

After a proctocolectomy with IPAA, UC patients with dysplasia or cancer in the resection specimen are still at risk for developing dysplasia or cancer in their IPAA. Since there is a considerable discrepancy in prevalence of dysplasia in the pouch, there is no surveillance guideline. In chapter 2 the prevalence of dysplasia in the IPAA is assessed in patients with UC who have undergone IPAA and demonstrated dysplasia in their resection specimen.

One of the complications seen after open and laparoscopic IPAA is sexual dysfunction. Up to date, little is known about sexual dysfunction after IPAA and the contribution of damage to the pelvic autonomic nerves. Aim of chapter 3 is to assess whether IPAA is associated with autonomic pelvic nerve damage and changes in subjective indices of sexual function in women.

Another complication after pouch surgery is the lower fertility rate in women. Fortunately many patients do become pregnant. However, there is no consensus about the optimal mode of delivery. The effect of vaginal delivery and its potential complications both before and after proctocolectomy on the function of the pouch is evaluated in chapter 4.

**Enhanced Recovery After Surgery (part II)**

There is accumulating evidence that short-term outcomes of laparoscopic surgery are better compared to open surgery. Up to date it is unclear whether this can be extrapolated to quality of life. In chapter 5, a systematic review of studies comparing quality of life in patients that underwent open or laparoscopic colorectal surgery is presented.

After the introduction of fast track care the question raised, whether or not laparoscopic surgery was still of added benefit. In chapter 6 all studies comparing laparoscopic surgery with open surgery within a fast track program are evaluated. In addition, we aimed to deter-
mine in a multicenter randomized trial, which form of perioperative treatment, laparoscopic or open surgery combined with fast track or standard care (LAFA-study), was the most optimal combination for patients undergoing segmental resection for colon cancer. The results are described in chapter 7.

The major determinant of recovery after colorectal surgery is a postoperative ileus characterized by delayed gastrointestinal transit. A side study of the LAFA-study is presented in chapter 8, in which it is evaluated whether fast track care and laparoscopic surgery lead to faster recovery of the gut after colonic surgery.

A major factor in the development of morbidity is the surgical stress response with subsequent increased demand on the patient’s reserves and immune competence. In chapter 9 the effect of laparoscopic or open colectomy with fast track or standard perioperative care on a patient’s immune status and stress response after surgery is evaluated.

Implementation of fast track care appears to be difficult. It remains questioned whether all separate fast track elements are actually essential for the enhanced postoperative recovery. The aim of chapter 10 is to determine which baseline characteristics or fast track elements are independent predictors of faster postoperative recovery in patients undergoing a colonic resection for colon cancer.

Finally, in chapter 11 the ultimate level of fast track care, day-care surgery, is evaluated. In this study the feasibility and desirability of a 360° laparoscopic Nissen fundoplication in day-care is compared to laparoscopic cholecystectomy in day-care.
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General introduction and outline of the thesis

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