Advances in colorectal surgery
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Summary and conclusions
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In this thesis, several aspects of colorectal surgery are highlighted. The aim of this thesis was to critically appraise colorectal surgery and to evaluate potential improvements in perioperative care (part I), complications (part II), and prognostication (part III).

Part I: Fast track colorectal surgery

In chapter 1 the application of fast track perioperative care in colonic surgery is described. Fast track perioperative care programmes have been introduced in several surgical procedures. In colonic surgery fast track perioperative care is defined as an intensive multimodal programme combining a number of perioperative elements with the purpose to preserve preoperative body composition and organ functions and to actively enhance postoperative recovery. The essence of fast track perioperative care consists of extensive preoperative counselling, no preoperative fasting but adequate nutrition, omission of oral bowel preparation, reducing the surgical trauma, no routine use of drains and nasogastric tubes, tailored anaesthesiology encompassing thoracic epidural, early and enhanced postoperative feeding and mobilisation and medicinal support with prokinetics and laxatives. Furthermore, it is highlighted that for some elements there is solid evidence that its implementation results in less morbidity and an enhanced postoperative recovery; e.g. removal of the nasogastric tube at the time of extubation and the omission of oral bowel preparation. For other elements the evidence is less robust, and the implementation into a fast track perioperative care programme is in those cases either based on “common sense” or on consensus interpretation of accumulating evidence. However, it should be noted that concerning all the individual elements the available evidence is derived from traditional perioperative care settings.

In chapter 2 a systematic review is performed of all randomised and clinical controlled trials on fast track perioperative care in colonic surgery. The main endpoints were the number of applied fast track perioperative care elements, postoperative hospital stay, readmission rate, morbidity and mortality. After a systematically performed search in several databases, six studies (three randomised and three clinical controlled trials) were eligible for analysis, including 512 patients. The fast track perioperative care programmes that were applied in the included studies contained an average of nine of the 17 fast track elements as defined in the literature. The pooled analysis showed that fast track perioperative care significantly reduced primary hospital stay (weighted mean difference: -1.56, 95% confidence interval [CI]: -2.61 to -0.50) and morbidity (relative risk 0.54, 95% CI: 0.42 to 0.69). Readmission rates were not significantly different and there was no increase in mortality. Based on this limited evidence, fast track perioperative care appears safe and enhances postoperative recovery after elective colorectal surgery. However, as the evidence is limited, a multi-centre randomised trial seems justified.

To investigate whether the demonstrated benefits of fast track perioperative care
could also be applied on our own patient population, a pilot study was initiated at the Academic Medical Centre. The results of this study are presented in chapter 3. All 55 patients, scheduled for elective segmental colorectal resection and treated in a fast track perioperative care programme were compared to a control-group of 52 patients treated in a traditional care setting. Successful implementation of the fast track care programme demonstrated to be difficult, since only 7.4 out of 13 predefined and evaluated fast track care elements were achieved per patient. Despite incomplete implementation and a potentially higher incidence of readmissions, primary and overall hospital stay were shorter after fast track perioperative care without affecting patient-satisfaction. Median primary hospital stay was 4.0 vs. 6.0 days and median overall hospital stay was 4.0 vs. 6.5 days. No robust conclusions could be drawn from a subgroup analysis in which open and laparoscopic surgery as well as traditional care and fast track perioperative care were compared, because the numbers of patients were too small. Nonetheless, the largest reduction in primary and overall hospital stay was observed in patients who had laparoscopic surgery and fast track perioperative care.

To further assess the optimal combination, in chapter 4 a systematic review was performed of all randomised and controlled clinical trials on laparoscopic and open surgery both incorporated within a fast track perioperative care programme. Main endpoints were primary and overall hospital stay, readmission rate, morbidity, and mortality. After a systematically performed literature search only two randomised and three controlled clinical trials were eligible for final analysis, which reported on a total of 400 patients. The extracted data of the individual studies could not be pooled because of clinical heterogeneity. Two studies of the five included studies reported a shorter primary hospital stay in the laparoscopic group of two and three days. In one study the readmission rate was lower after laparoscopic surgery (absolute risk reduction 21.4%, and a “numbers needed to treat” of 4.7 patients). One study showed a 23% difference in favour of the laparoscopic group with regard to morbidity, i.e. a “numbers needed to treat” of 4.4 patients. Concerning the main endpoints in the individual studies no further significant differences between open and laparoscopic surgery within a fast track perioperative care programme were found.

Despite some reported advantages of laparoscopic surgery, based on the lack of evidence, no robust conclusions can be made. A large randomised controlled trial is required to compare laparoscopic with open surgery within a fast track perioperative care setting.

In chapter 5 such a randomised controlled multi-centre trial is proposed. The LAFA-trial (LAparoscopy and/or FAst track multimodal management versus standard care) is conceived to determine whether laparoscopic surgery, fast track perioperative care or a combination of both is to be preferred over open surgery with traditional care in patients having segmental colectomy for malignant disease. The LAFA-trial is a double blinded, multicentre trial with a two by two balanced factorial design. Patients eligible for segmental colectomy for malignant colorectal disease i.e. right and left colectomy and anterior resection are randomised to either open or laparoscopic colectomy, and to either traditional care or fast track perioperative care. This factorial design produces
four treatment groups; open segmental colectomy with traditional care, open segmental colectomy with fast track perioperative care, laparoscopic segmental colectomy with traditional care, and laparoscopic surgery with fast track perioperative care. The primary outcome parameter is postoperative hospital stay including readmissions within 30 days. Secondary outcome parameters are quality of life two and four weeks after surgery, overall hospital costs, morbidity, patient satisfaction and readmission rate. The LAFA-trial has started in 2005 and will be finished in the beginning of 2009. Hopefully this trial will answer the question which combination of perioperative care and type of surgery is the most optimal combination.

Part II: Complications in colorectal surgery

In chapter 6 several techniques for the establishment of the pneumoperitoneum are described including the equipment that is used and the potential complications that can occur. Roughly entry techniques can be divided in two groups. The first group comprises introductions performed without direct visual control, the so called blind entry techniques (e.g. introductions with a Veress needle). The other group comprises of entry techniques performed under visual control. The latter includes the open entry technique and closed entry techniques with optical trocar devices. In this chapter it is demonstrated that concerning entry-related complications approximately one half of all intra-operative laparoscopic complications is caused during the establishment of the pneumoperitoneum and introduction of the trocars. The reported incidence of vascular and bowel injuries varies and is between approximately 0.05 and 0.5 complication per 100 laparoscopic procedures. The reviewed literature in this chapter, suggests that the open-entry technique is the safest introduction technique because an overshoot of the introduction, especially those resulting in retroperitoneal vascular injury can be avoided. However, open-entry techniques do not preclude bowel injury.

Chapter 7 describes a retrospective chart review including all malpractice claims concerning entry-related injuries filed at MediRisk, which is presently the largest medical liability mutual insurance company for institutions, mainly hospitals in health care in the Netherlands. From January 1993 to December 2005, 229 laparoscopy-related claims were filed of which 41 (18%) claims were identified as entry-related complications. Therefore, medical liability claims concerning laparoscopic entry-related complications comprise one fifth of all laparoscopy-related claims. Patients that filed a claim were mostly young females with a history of abdominal surgery who were operated on in a day-care setting or had short-stay surgery with severe consequences of the entry-related complication. In the investigated cases most claims involved the closed-entry technique. Vascular injury was exclusively associated with the closed-entry technique. In more than half of the complications, the entry-related injury was diagnosed with a delay. There was no mortality. Besides conversion, the majority of the patients filed a claim to compensate for the longer hospital stay and related costs. A payment was made in 17 (57%) of the 30 settled claims.
In chapter 8 the feasibility, safety, and potential benefits of a laparoscopic reintervention for anastomotic leakage after primary laparoscopic surgery was assessed. From January 2003 to January 2006, ten consecutive patients who underwent laparoscopic colorectal resection and subsequently developed anastomotic leakage, underwent a laparoscopic reintervention. Relaparotomy was performed in fifteen consecutive patients who had primary open surgery. In this chapter a laparoscopic reintervention after primary laparoscopic surgery for anastomotic leakage appears feasible and safe in terms of conversions, intraoperative morbidity, necessity of opening the minilaparotomy, and operating time. In addition, laparoscopic reintervention was associated with less postoperative morbidity (40% vs. 80%), shorter postoperative ileus (resumption of a normal diet; three vs. six days), and a faster recovery (hospital stay; nine vs. 13 days). Furthermore, the incidence of incisional hernia was zero percent in the laparoscopic group versus 33% in the open group. Nonetheless, this are preliminary data and, ideally a prospective trial, should confirm these data. To evaluate the effect of laparoscopic reintervention after primary laparoscopic surgery, it has to be part of a very large study randomising patients for a laparoscopic or open initial procedure.

In chapter 9 potential usage concerns regarding linear cutters are described. An incomplete linear staple line discovered during the stapling of an ileal pouch presented as a case report in this chapter indicated that malfunctioning might occur when using linear cutters. Subsequently, in an animal model three different lengths of linear cutters (Proximate®, Ethicon Endo-Surgery) were used to cross staple and transect the large bowel of one pig to check for the integrity of the proximal end of the staple line. The experiment demonstrated that when the tissue was advanced up to the highest number on the scale of the 100 mm stapling device an insufficient overlap between the proximal end of the staple line and the proximal end of the cut line occurred. Although a more than 100 mm staple line was delivered, the 100 mm cutter may not produce a double-staggered row of staples at the most proximal end of the staple line when the tissue is advanced past the 9.5 centimeters mark. Ethicon Endo-Surgery has agreed to add indicator markers to the scale label on the instrument to provide the user with additional guidance for tissue placement. Nevertheless, it remains important to routinely inspect the pouch after linear stapling, both anteriorly and posteriorly, by inversion of the pouch to check for insufficiency of the proximal staple line. On the posterior site, the hole is oversewn and at the anterior site of the pouch the hole is incorporated in the purse string of the anvil of the circular stapler. In case of a side-to-end colonic anastomosis, the proximal end of the cross stapling line should also be routinely checked and oversewn if necessary.

In chapter 10 literature regarding different strategies for open-abdomen treatment in terms of full fascial closure of the abdomen is systematically reviewed. The aim of this review was to investigate which temporary closure technique has the highest rate of full fascial closure. The results of this review suggest that temporary abdominal closure techniques that keep traction on the fascial edges, including Vacuum Assisted Closure (VAC®) result in high rates of fascial closure. Furthermore, techniques with high closure rates seemed to result in relatively low rates of fistula, abscesses, and mortality. After open-
abdomen management when full fascial closure during index admission is not possible, the fascial defect can be left to heal by secondary intention or an absorbable mesh can be used to close the abdomen. These planned ventral hernias are often associated with enterocutaneous fistula and stomas. Closure of enterocutaneous fistula and/or stomas and simultaneous management of a large abdominal defect is a difficult procedure. In chapter 11 the results of closure of enterocutaneous fistula and/or stomas and simultaneous abdominal wall repair using the components separation technique were described. All patients with enterocutaneous fistula and/or stomas in the presence of large abdominal wall defects (i.e. laparostomy of ventral hernia) who underwent a single-stage repair using the components separation technique in the period January 2000 to July 2007 were reviewed retrospectively. The study demonstrated that closure of enterocutaneous fistula or stomas in the presence of large abdominal wall defects is feasible using the components separation technique. This technique is one of the few options available to deal with this very difficult problem. Early recurrence of abdominal hernia (7/32) and fistula (4/15) was acceptable but morbidity (16/32) was considerable. Suggested modifications to preserve the blood supply of the skin and subcutaneous tissue, extended antibiotic therapy and changes in mesh repair might improve outcome.

Part III: Prognostication in colorectal cancer

The impact of extracapsular lymph node involvement has been studied for several malignancies, including gastrointestinal malignancies. In chapter 12 the literature on extracapsular lymph node involvement in gastrointestinal malignancies is systematically reviewed in order to assess the current evidence on extracapsular lymph node involvement as a prognostic factor for recurrence in gastrointestinal malignancies. Based on the limited evidence available it can be concluded that extracapsular lymph node involvement is a common phenomenon in patients with gastrointestinal malignancies. The pooled incidence of extracapsular lymph node involvement was 57% (95% CI: 53-61%) for oesophageal cancer, 41% (95% CI: 36-47%) for gastric cancer, and 35% (95% CI: 31-40%) for rectal cancer. Furthermore, extracapsular lymph node involvement identified a subgroup of patients with a significantly worse long-term survival. This systematic review highlighted the importance of assessing extracapsular lymph node involvement as a valuable prognostic factor. Pathologists and clinicians should be aware of this important feature. Further research is, however, warranted on the correlation of extracapsular lymph node involvement with different histological types and other important covariates, such as the recurrence pattern and the effect of (neo-) adjuvant therapy.

Since the prognostic significance of extracapsular lymph node involvement was not yet established in colonic cancer as demonstrated in the above mentioned systematic review, a retrospective study was undertaken which is described in chapter 13. Between January 1994 and May 2005, all patients who underwent resection for primary colonic cancer with lymph node metastasis were reviewed. In a multivariate analysis, pN-stage (hazard
ratio 3.50, 95% CI: 1.72–7.42) and extracapsular lymph node involvement (hazard ratio 1.98, 95% CI: 1.00–3.91) were the only significant factors, indicating that extracapsular lymph node involvement in colonic cancer is an independent negative prognostic factor, reflecting a particularly aggressive biological behaviour. Interestingly, among patients without extracapsular lymph node involvement, those receiving adjuvant chemotherapy had a significantly better survival. In contrast, chemotherapy did not improve disease free survival in patients with extracapsular lymph node involvement. Therefore, detection and quantification of extracapsular lymph node involvement in the surgical resection specimen might also be helpful in the future to individualize postoperative therapeutic strategies in the adjuvant setting.

Finally, in chapter 14 the presence and amount of circulating tumour cells was assessed in peripheral and portal blood of patients who had open or laparoscopic surgery for primary colonic cancer. Patients in the laparoscopic group were operated on in a medial to lateral approach (“vessels first”), in the open group a lateral to medial approach was applied. The enumeration of circulating tumour cells was performed with immuno-magnetic isolation and immuno-specific labelling. This technique not only counts complete cells instead of cellular fragments as done by RNA identification by Polymerase Chain Reaction (PCR) but also allows for evaluation of the morphology of the detected circulating tumour cells. It was shown that the presence of circulating tumour cells was significantly increased intra-operatively and was in general significantly higher in portal blood. Between 4-7% of the peripheral and 26-45% of the portal samples contained circulating tumour cells. Significantly less circulating tumour cells were detected during laparoscopic surgery possibly as result of the medial to lateral approach. Fluorescence In Situ Hybridization (FISH) was applied as an additional tool to determine the true signature of these cells with the different morphology. Both circulating tumour cells and primary tumour tissue were diploid. Although the primary tumour tissue and circulating tumour cells showed the same cytogenetic profile this does not provide a definite answer whether or not the detected circulating tumour cells were true tumour cells or if these were normal epithelial cells that were shed into the portal blood due to the surgical trauma.