Chapter 10

SUMMARY AND CONCLUSIONS
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Summary

Preventive or curative treatment modalities for pre-malignant or malignant rectal diseases has undergone fundamental changes in the last two decades. This has lead to prolonged survival and has decreased local recurrence. Good long-term functional outcome and a good quality of life is therefore becoming increasingly important. Although these topics have been addressed in various publications, only few studies have prospectively evaluated anorectal function and quality of life. Thus so far the underlying mechanisms responsible for the impaired anorectal function have not been clarified.

In Chapter 2, a prospective study is reported that investigates the relationship between clinical and functional outcome pre- and postoperatively in patients with rectal carcinoma who underwent rectum resection with Total Mesorectal Excision (TME). Patients were examined before, 4 and 12 months after surgery and compared with age matched healthy volunteers. Ano-(neo-)rectal function was examined by: clinical outcome questionnaire, anal manometry, anal and rectal mucosal electrosensitivity, and measurement of rectal compliance and sensation. Half of the volunteers also underwent compliance measurements in the sigmoid colon that is normally used for construction of the neo-rectum in patients. Soiling and passive incontinence increased significantly until 12 months after operation, whereas urgency and tenesmus increased only temporarily, returning to preoperative values at 12 months. Anal sphincter function was grossly preserved, whereas rectal-anal inhibitory reflex (RAIR) was decreased at 4 months but recovered after 1 year. Neo-rectal compliance in patients was similar to that of the healthy volunteers' sigmoid, increasing slightly after 12 months, but still significantly lower than that of normal rectum. Neo-rectal sensation to pressure distention was similar to that of normal rectum, however accompanied by smaller volumes. Neo-rectal distention induced contractions which were significantly larger in amplitude and more frequent at 4 months, returning to normal after 12 months.

It can be concluded from these results that the transient increase in urgency and tenesmus after surgery results from a temporary increase in neo-rectal “irritability” accompanied by some adaptation of compliance in time. In contrast, episodes of incontinence and soiling are increased after one year most likely because of reduced neo-rectal capacity and RAIR recurrence in the presence of a lowered basal anal sphincter pressure.
Rectum resection with TME and radiotherapy (RT) are the only two treatment modalities for rectal carcinoma that have been reported (independent of each other) to improve local control and survival although anorectal function is often comprised. The effect on anorectal function was studied in Chapter 3. By a prospective study the effect of RT and surgery on anorectal function and clinical outcome of patients with a rectal carcinoma was evaluated. As in Chapter 2 anorectal function was studied before surgery, 4 and 12 months postoperatively in patients that only underwent surgery (TME group) and compared to patients that also received radiotherapy (RT+TME group). Postoperatively, defaecation frequency increased in both patient groups, but significantly more in RT+TME than in the TME group. Urgency and the need to wear a pad tended to increase more in RT+TME patients than in TME patients. Blood loss was still reported by 33% of the RT+TME group and 7% of the TME group 12 months postoperatively. Anal mucosal electrosensitivity, resting anal pressure or squeeze pressure were not affected by either treatment. An obvious change in anal motility was noticed in the RT+TME group where in more than half of the patients, short bursts of slow waves were observed up to 12 months postoperatively. Recto-anal inhibition reflex testing provoked significantly higher neo-rectal contractions 12 months postoperatively in RT+TME patients than in TME patients and rectal compliance was significantly lower in the RT+TME group at both 4 and 12 months postoperatively. Pressure thresholds for first sensation and desire to defaecate did not differ, however at 30 mmHg above MDP 29% of the RT+TME group reached the sensation discomfort in comparison to 50% in the TME group. Finally, rectal mucosal electrosensitivity was higher in RT+TME patients 12 months postoperatively than in patients in the TME group.

Therefore it could be concluded that radiotherapy increases urgency, defaecation frequency, usage of pads and rectal blood loss, most likely due to decreased neo-rectal reservoir capacity (compliance) and increased neo-rectal contractility (distention induced contractions). In addition sensation to distention and to electrical stimuli was reduced by RT suggesting afferent nerve injury. When survival is prolonged after the combination of TME and RT it remains questionable whether this increase in survival is substantial enough to compensate for the considerable inferior functional outcome in this group.

Restorative proctocolectomy with an ileal pouch-anal anastomosis (IPAA) is a frequently performed surgical technique in patients with ulcerative colitis (UC) or familial adenomatous polyposis (FAP). IPAA is a safe procedure in clinics with experience. The aim of the study described in Chapter 4 was to evaluate the
morbidity, mortality and functional results in patients that had undergone a proctocolectomy with an IPAA during the last five years in a hospital where at least 25 of these procedures are performed yearly. Retrospective chart review on functional results and complications was performed for 100 patients who underwent an IPAA between 1994 and 1999. Median operating time was 2.3 hours, intraoperative blood- and fluid loss 500 ml and median hospital stay 15 days. There was no postoperative mortality. Ten patients had a loop ileostomy formation, in six because of postoperative complications. A total of 30 patients developed postoperatively or during follow-up postoperative complications, of which 10 patients needed a relaparotomy. One pouch had to be excised and two patients still have a loop ileostomy due to postoperative complications. In 56 patients with at least 12 months follow-up, median 24-hour stool frequency was 6. Eighty-nine percent of these patients were satisfied or highly satisfied with the overall long-term outcome.

It was concluded that in a hospital with experience with this technique, a restorative proctocolectomy with IPAA formation is a safe procedure, with very low mortality rate, acceptable morbidity, good functional results and can be performed in most cases without a diverting loop ileostomy. The overall outcome is perceived as satisfactory by the majority of the patients.

Patients with FAP develop hundreds of colorectal adenomas and will die of colorectal cancer if left untreated. The choice of operation lies between colectomy with an ileorectal anastomosis (IRA), and proctocolectomy with an IPAA. One factor crucial to decision-making is the functional outcome following either procedure. To date, studies on this issue have reported conflicting results and have been based on small series of patients. The objective of Chapter 5 was to compare the long-term functional results of IRA with those of IPAA in patients with FAP. A questionnaire was sent to 323 FAP patients with either IRA or IPAA who were registered at the Netherlands Foundation for the Detection of Hereditary Tumors. The overall response rate was 86%, and comprised 161 IRA patients and 118 IPAA patients. IRA patients scored significantly better for daytime and nighttime stool frequency, soiling, occasional passive incontinence, flatus and faeces discrimination, stool consistency and the need for anti-diarrheal medication. There was no difference with regard to perianal irritation, episodes of bowel discomfort or dietary restrictions. The functional results according to the aggregate score of the Gastro-Intestinal Functional Outcome Scale, where the items specified above were integrated (0 indicating a poor and 100 a good overall function), were significantly better in patients with an IRA (74.5), than in patients with an IPAA (66.0) (p < 0.01).
The conclusion of this study was that the functional outcome after IRA is significantly better than after IPAA. On the basis of these results IRA might still be considered in patients with a mild phenotypic expression of the disease in the rectum.

Knowledge of post-operative health status is another important argument in decision making about the type of operation necessary in patients with FAP. In Chapter 6 the quality of life (QOL) is compared between patients with IPAA, and those with an IRA. QOL was assessed with both a generic questionnaire, Short Form-36 Health Survey (SF-36), and a disease-specific questionnaire, Colorectal QOL Questionnaire (EORTC QLQ-CR38). The SF-36 consists of 36 items representing eight generic health domains, and the EORTC QLQ-CR38 comprises 38 items comprising disease-specific health domains. Both questionnaires were distributed among the same 323 FAP patients as discussed in Chapter 5 who had previously undergone IRA or IPAA. The results of the SF-36 were compared to the scores of age and sex-matched respondents from the general population. Generic and disease-specific QOL was the same for IRA and IPAA patients. The SF-36 scores of both groups were significantly lower than those of the general population. It was concluded in the present study that no differences regarding health status between patients with an IRA or IPAA could be shown. Therefore a preference for either procedure cannot be based on an expected better quality of life.

In patients with benign colorectal diseases undergoing a restorative proctocolectomy with an IPAA, semen cryopreservation (SC) seems rational to warrant the possibility of procreation in case pelvic surgery would have lead to sexual disorders or impotence. In Chapter 7, the pre- and post-operative semen quality in patients undergoing IPAA, and the incidence of surgery induced sexual dysfunction was determined in order to evaluate the economic efficiency of SC, as compared to recent developed alternatives like microsurgical epididymal sperm aspiration (MESA). Pre- and post-operative semen analyses were offered to 97 male IPAA patients with benign colorectal diseases since 1989. The direct costs of the SC program were determined and compared with those of alternatives. In 34 out of 40 consecutive IPAA patients who made use of pre-operative semen preservation, normal sperm concentrations, motility and morphology were found. The total number of spermatozoa was significantly decreased in all patients who returned for postoperative analysis, although all other semen characteristics had not changed. Postoperatively only two patients developed temporarily retrograde ejaculation. None of the preserved semen samples were used, SC therefore benefited none of these patients. The total costs
of SC were between 2.2 and 5 times higher than the costs for one MESA procedure.
In conclusion, this study showed that preoperative semen cryopreservation in patients undergoing IPAA because of benign colorectal diseases is feasible. However, most likely due to improved surgical techniques and the increasing number of effective alternatives, preoperative semen cryopreservation in IPAA patients is no longer cost-effective.

Restorative proctocolectomy with an IPAA is the operation of choice in an increasing number of patients with FAP. For reconstruction two techniques are currently used, i.e., (1) a double stapled (DS) anastomosis between pouch and anal canal and (2) a mucosectomy and handsewn (HS) ileoanal anastomosis at the dentate line. Although an IPAA is thought to abolish the risk of colorectal adenoma, an increasing number of case reports have been published on the development of adenomas at the anastomotic site. In Chapter 8, an evaluation has been made of the overall cumulative risk to develop adenomatous polyps after IPAA and both anastomotic techniques are compared. Consecutive groups of FAP patients undergoing an IPAA were identified from polyposis registries in The Netherlands, Denmark, Italy, Germany and New York. Life table analysis was used to calculate the cumulative risk for developing polyps in 97 patients with at least one year of endoscopic follow-up. A double stapled anastomosis was used in 35 patients, whereas in 62 patients a hand-sewn anastomosis with a mucosectomy was performed. Thirteen patients developed polyps at the anastomotic site. The cumulative risk to develop a polyp at the anastomotic site was 8% (95% C.I. 2 - 14%) at 3.5 years and 18% (95% C.I. 8 - 28%) at 7 years, respectively. The risk for developing a polyp at the anastomotic site within 7 years was 31% for patients with a double stapled versus 10% for patients with a hand-sewn anastomosis with mucosectomy.

It was concluded that although the risk is significantly lower in the group of patients with hand-sewn anastomosis, FAP patients with either a double stapled or a hand-sewn IPAA have both a substantial risk for developing adenomatous polyps at the anastomotic site. Therefore, lifelong endoscopic surveillance of the anastomosis is mandatory after both techniques.

The surgical options for patients with FAP includes proctocolectomy followed by IPAA or total colectomy and IRA. In the decision making between the two procedures the risk of developing rectal cancer after IRA is important but even more crucial is the risk of dying of rectal cancer. In Chapter 9, the risk of dying from rectal cancer after IRA was assessed and life expectancy between patients
with an IRA and those with an IPAA was compared. It was furthermore evaluated whether regular endoscopic examination leads to detection of cancer at an earlier stage. Clinical and pathological data on 659 patients who underwent total colectomy and ileorectal anastomosis were collected from four National Polyposis Registries in Denmark, Finland, Sweden and the Netherlands. The data were analyzed using survival analysis methods and a decision analysis was used to compare the life expectancy between patients with an IRA and those with an IPAA. A total of 47 patients developed rectal cancer after IRA and survival analysis showed that the risk of dying from rectal cancer was 12.5 percent by age 65 years. As compared to IRA, IPAA would have lead to an increased life expectancy of 1.8 years. Finally, it was shown that 75% of the patients with rectal cancer had a negative endoscopy within 12 month before the diagnosis.

It was concluded that the finding of a significant risk of dying from rectal cancer and the shortened life expectancy are arguments against performing IRA in patients also in those with a moderate or low number of rectal adenomas. Moreover, follow-up examinations of the rectum do not guarantee early detection of rectal carcinoma. Probably an IRA procedure in patients with FAP is only indicated in case of a very limited number or absence of rectal adenomas in a family with a mild phenotype of the disease.
Conclusions

In this thesis it is shown that anorectal function is hampered after rectal resection for rectal carcinoma most likely as a consequence of decreased neo-rectal reservoir capacity and increased neo-rectal contractility. Moreover, the combination of total mesorectal excision and radiotherapy that may lead to prolonged survival and additional reduction in local recurrence rates, carries the risk of a further worsened anorectal function, decreased neo-rectal reservoir capacity and increased neo-rectal contractility in combination with reduced rectal sensation for distention.

For patients with FAP, the reduced rectal function occurring after preventive rectal resection and restoration of the intestinal continuity by an ileal pouch-anal anastomosis is well tolerated at long term follow-up and does not to reduce long-term quality of life in comparison to patients who underwent an ileorectal anastomosis. The risk of loosing the ability of procreation after surgery seems to be very limited. Cryopreservation of semen in IPAA patients is therefore no longer cost-effective in view of improved surgical techniques and the increasing number of effective alternatives.

It has been shown that this preventative treatment by proctocolectomy does not guarantee absolute extirpation of all mucosa at risk, not even when mucosectomy of the anal canal is performed. Therefore lifelong endoscopic follow-up of the anastomosis is mandatory for patients with FAP after IPAA.

Preventive rectal resection tends to prolong life expectancy substantially as compared with rectal sparing surgery. Secondly up to three-quarter of the patients, who developed an adenocarcinoma in their conserved rectum had a negative endoscopy within one year prior to the diagnosis.

Considering these findings, the indication for IRA therefore, may be limited to patients with few or no rectal adenomas from a family with a similar mild phenotype of the disease.