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Chapter 2

A PROSPECTIVE EVALUATION OF ANO-RECTAL FUNCTION AFTER TOTAL MESORECTAL EXCISION IN PATIENTS WITH A RECTAL CARCINOMA

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Abstract

Background/Aims: Rectum resection with Total Mesorectal Excision (TME) and neo-rectal anastomosis often compromises anorectal function. Insight in the underlying mechanisms is lacking. Therefore, a prospective study was designed to investigate the relationship between clinical and functional outcome pre- and postoperatively.

Methods: Eleven patients were examined before, 4 and 12 months after surgery and compared with 11 healthy volunteers (HV). Ano-(neo-)rectal function was examined by: clinical outcome questionnaire, anal manometry, rectal compliance and sensation. Six HV also underwent barostat measurements in the sigmoid colon.

Results: Soiling and passive incontinence increased significantly until 12 months postoperatively, whereas urgency and tenesmus increased temporarily, returning to preoperative values at 12 months. Anal sphincter function was grossly preserved, however rectal-anal inhibitory reflex (RAIR) was decreased at 4 months but recovered after 1 year. Neo-rectal compliance was similar to that of HV 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 who were significantly larger in amplitude and more frequent at 4 months, returning to normal after 12 months.

Conclusions: Our results suggest 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.
Introduction

Anal sphincter function, rectal reservoir capacity and the ability to differentiate between rectal sensations are important features in maintaining faecal continence. Patients who have to undergo surgery for rectal carcinoma are at risk for reduced postoperative anorectal function. Improved surgical techniques, like total mesorectal excision (TME) who propagate rectal mobilization via sharp dissection under direct vision along the parietal pelvic fascia, have been reported to result in lower recurrence percentages and probably better 5-year survival. A good long-term functional outcome is therefore becoming increasingly important.

Yet, functional results remain suboptimal up to one year after surgery even in recent reports as illustrated by increased defaecation frequencies, soiling incidence and even, although less frequently, incontinence of liquid and or solid stools. There is an ongoing debate about the pathophysiology of this disturbed functional outcome. Explanations for impaired anorectal function include decreased internal and external anal sphincter function due to direct damage or injury of the nervous supply, the level of the colo-anal anastomosis, impaired neo-rectal capacity and or compliance, and the loss of rectal sensation. The substantial number of studies on anal sphincter function, however, give no absolute clarification for the impaired anorectal function. Therefore more emphasis must be put on the impact of impaired neo-rectal capacity, compliance, and the change in rectal sensation and motility, considering that the expanding characteristics of sigmoid or descending colon used for construction of a neo-rectum are very different from those of a normal rectum. At present, only few studies have prospectively evaluated rectal function, before and up to one year after surgery. Although manometry and neo-rectal compliance measurements were performed in all studies, they only correlated the outcome to bowel frequency or to an overall score of clinical bowel function. A comparison of neo-rectal compliance and sensation with that of a healthy volunteer sigmoid colon, which is used for neo-rectal construction, has not been performed. Moreover, a combination of early and late postoperative assessment to evaluate changes in time has not been performed. Therefore, a prospectively study was designed to evaluate the effects of TME on anal sphincter and ‘rectal’ function and to study the degree of adaptation in time. In addition, changes in functional outcome at different time points were evaluated in relation to the clinical outcome in order to gain more insight in the underlying pathophysiological mechanisms in these patients.
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Material and methods

Subjects
Fifteen consecutive patients with a rectal carcinoma who underwent a rectal resection with total mesorectal excision (TME) between August 1996 and November 1997 were studied. Only patients with a resectable rectal carcinoma below the level of S1/S2 were included, provided that the distal border of the tumor was within 15 cm of the anal verge. Clinical details of all subjects are shown in Table 1.

Eleven healthy volunteers (6 males; mean age 60.0 years; range 47 - 79 years) were recruited by advertisement. None had a history of an acute or chronic illness or abdominal surgery. There was no evidence of abdominal symptoms either by bowel symptom questionnaire or by personal history.

Table 1: Details of patients with rectal carcinoma and healthy volunteers (HV)

<table>
<thead>
<tr>
<th></th>
<th>patients</th>
<th>HV</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>15</td>
<td>11</td>
</tr>
<tr>
<td>Mean age (years (range))</td>
<td>66 (38-83)</td>
<td>60 (48-79)</td>
</tr>
<tr>
<td>Gender (Male / Female)</td>
<td>11/4</td>
<td>6/5</td>
</tr>
<tr>
<td>Tumor stage (Astler Coller classification A,BI,BII,CI,CII,D)</td>
<td>1,7,6,0,1,0</td>
<td></td>
</tr>
<tr>
<td>Median tumor height above anal verge (cm (range))</td>
<td>7.5 (3-15)</td>
<td></td>
</tr>
<tr>
<td>Median anastomotic height above anal verge (cm (range))</td>
<td>3 (2-7)</td>
<td></td>
</tr>
</tbody>
</table>

Study protocol
Patients and healthy volunteers answered a questionnaire regarding their anorectal function and were examined by means of anorectal manometry, rectal and anal mucosal electrosensory testing, Pudendal nerve terminal motor latency (PNTML) time and (neo-)rectal compliance and visceral sensation measurements. In patients, anorectal function was assessed one week before and 4 and 12 months after surgery. All subjects underwent bowel preparation by means of a sodium-phosphate enema either at home or at least one and a half our before onset of the anorectal function measurements.

Each subject answered a questionnaire to assess defaecation frequency during day and or night-time, stool consistency, blood loss per anum, the ability to differentiate between flatus and stools, soiling during day and night-time, anal incontinence score, urgency to defaecate, episodes of passive incontinence, loss of a large quantity, need to wear pads, sensation of incomplete evacuation, and tenesmus. The answers were characterized as never, occasional (less than once a week), frequent (at least once a week) or daily occurrence. The anal incontinence
score as described by Pescatori gives an indication of the type of incontinence, i.e., incontinent for flatus, liquid and or solid stools, and the frequency, ranging from never to every day.

Subjects were placed in left lateral position for anorectal manometry. After insertion of the catheter the recordings were allowed to stabilize for 15 min, after which the mean value of the resting pressure was measured for 2 min. Hereafter the subjects were instructed to maximally squeeze on three occasions. The terminal inflatable balloon was inflated with increasing volumes (10 to 50 mL) in order to assess a (neo)rectal-anal inhibitory reflex (RAIR). RAIR was defined as a reduction of internal anal sphincter pressure from baseline of at least 10 mmHg of 5 seconds' duration. After removal of the manometric assembly, a ring-electrode was inserted into the rectum approximately 10 cm above the anal verge to measure rectal mucosal electrosensitivity. A small pulsed electric current generated by a computer controlled stimulator (Dantec Keypoint, Skovlunde, Denmark) was applied and increased until subjects reported some rectal/abdominal sensation. The amperage of first sensation was recorded on three occasions. The electrode was then positioned into the mid-anal canal and the same measurements were done to estimate the anal mucosal sensation threshold.

Following these measurements the barostat-bag was inserted into the (neo-)rectum. To prevent curling-up of the bag and kinking of the catheter, the folded bag was placed into a non-flexible tube. After insertion of approximately 20 cm, the 'over' tube was withdrawn. The bag was slowly inflated with 80-125 mL to allow adequate unfolding and was then drawn back against the pelvic floor or in postoperative patients just above the anastomosis (Figure 1).

Figure 1: X-ray of the pelvis showing the unfolded bag just above the anastomosis.
The catheter was secured with tape to maintain its position. A recovery period of 15 min was allowed after which minimal distension pressure (MDP) was determined. Thereafter, an intermittent isobaric pressure controlled distention protocol, (pressure steps of 3 mmHg lasting 2 minutes) was started. Subjects were asked at the onset of the distension, at 30s and at 60s to score their sensation on a scale varying from (a) nothing, (b) first sensation, (c) a light desire to defaecate, (d) desire to defaecate, (e) urgent desire to defaecate, (f) intolerable discomfort. The experiment was stopped when subjects experienced intolerable discomfort or when 50 mmHg was reached.

After the barostat study, three reproducible PNTML recordings were taken from each side. All healthy volunteers underwent the same measurements. However, in six healthy volunteers, both the rectum and the sigmoid (at 30-35 cm from the anal verge, which is normally used for colo-anal anastomosis) were examined using the same intermittent isobaric pressure-controlled distention protocol. The barostat bag was positioned in the sigmoid colon by means of a sigmoidoscopy (Figure 2). The protocol was approved by the Hospital Ethics Committee and informed consent was obtained from all patients and healthy volunteers.

Figure 2: Abdominal x-ray showing the unfolded bag in the sigmoid of a volunteer.

**Equipment**

**Anorectal manometry**

Anorectal manometry was recorded using a multi-lumen 14.5 cm long, water-perfused sleeve catheter assembly, with a 4 cm long sleeve and 5 radially distributed side holes, positioned at 1, 2, 3, 4 and 6.5 cm and a terminal inflatable balloon at 8.5 cm from the anal verge (Dentsleeve Pty Ltd, Parkside, Australia). Each sidehole was perfused with degassed water at a rate of 0.3 ml/min and
intraluminal pressures were sensed by external transducers, connected to a polygraph (Synetics Medical, Stockholm, Sweden) and monitored and analyzed with commercially available software (Polygram for Windows, Synetics Medical).

Mucosal electrosensitivity / Pudendal nerve terminal motor latency
A 1-cm long bipolar ring-electrode (Dantec 21L10, Skovlunde, Denmark) mounted on a Foley-urine catheter was used to measure the rectal and anal mucosal electrosensitivity. For measuring the PNTML time, a St. Mark’s pudendal electrode (Dantec Medical, Denmark) was used.

Rectal barostat study
To measure compliance and rectal sensitivity, an electronic barostat (Synetics Medical, Stockholm, Sweden) was used. There was a fixed pressure limit that automatically triggered balloon deflation for pressures above 55 mmHg. A non-compliant polyethylene bag was hermetically fastened to a double-lumen 12F Salem polyvinyl tube (Sherwood medical, St. Louis, USA) and connected to the barostat. The maximum capacity of the bag was 350 ml and had a maximal diameter of 11 cm and a length of 14 cm. The balloon was inflated up to 20 mmHg, prior to and following completion of the experiment to rule out any leakage of air.

Data analysis
Two way analyses of variance were used for comparison of pre- and post operative data as well as for comparison of healthy volunteers with patients. The values reported for maximum squeeze pressure and mucosal electrosensitivity thresholds are the mean of three efforts. Non-parametric tests were used in case of ordinal data and proportions of events were compared by means of chi-square tests, values < 0.05 were considered statistically significant. Phasic volume-pressure curves for compliance calculation were obtained from mean volume values reached during each 120-second pressure step. The volume-pressure curves were described with the following equation: \[ V = A(1 - e^{-kp}) \], where \( V \) is the volume, \( A \) is the maximum volume, \( k \) is an expansion constant and \( p \) is pressure. Compliance is defined as \( \frac{dV}{dp} \) and computed at \( V_{50} \), which is half-way the maximum volume. A mixed non-linear model was used to estimate the mean compliance curves for patients (pre- and postoperatively) and volunteers by means of the restricted maximum likelihood method. In addition comparisons of the fixed effects estimations of the fitted compliance curves in time, and between patients and volunteers were performed using a Wald test on fixed effects.
Overall goodness of fit was assessed by the Bayesian Information Criterion. The influence of surgery on the perception of the (neo-)rectal sensation was evaluated by comparing the percentage of patients in whom a specific sensation was elicited at a certain pressure level. The cumulative percentages of patients at 4 and 12 months and the volunteers measured in either the rectum or sigmoid colon were analysed with Kaplan-Meier analysis and differences were compared by log-rank test. This analysis method was chosen because not every barostat procedure was terminated by the sensation intolerable discomfort, since measurements with the barostat-bag were also ceased at the maximum distention pressure of 50 mmHg. Kaplan-Meier analysis enabled us to take every measurement into account even if a certain sensation was not induced. The measurement was censored at the highest pressure at which this sensation could not be induced.

Results

Fifteen patients were enrolled in the study protocol. Eleven patients were re-evaluated at four and twelve months after surgery. Four patients were lost to follow-up for various reason. Two patients withdrew themselves from the study because the investigations were regarded too strenuous. In one patient it was decided intraoperatively to perform an abdomino-perineal resection whereas the fourth patient died from septic complications. None of the patients developed distant metastasis or local recurrence at the one-year follow-up and none received adjuvant radio- or chemotherapy. No complications were encountered in any of the studies. In none of the subjects, the duration of the experiments exceeded four hours.

Clinical characteristics
All but one patient presented with persistent blood loss per anum as principal symptom (Table 2). Forty-five percent of all patients experienced soiling at least once a month, which is in agreement with the anal incontinence score of 3. Before surgery, approximately one third of the patients, reported urgency and more than half of the patients had tenesmus and sensation of incomplete defaecation.

Postoperatively, the percentage of patients with soiling at night and with episodes of passive incontinence (at least once a month), increased significantly after 4 and 12 months. The defaecation frequency during day and the percentages of patients with soiling during the day, and patients with the need for pads showed an increase, although not significantly, 4 months after surgery and remained
<table>
<thead>
<tr>
<th>Clinical characteristics of healthy volunteers and patients with rectal carcinoma.</th>
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<tbody>
<tr>
<td>Healthy Volunteers</td>
</tr>
<tr>
<td>Defaecation frequency / day</td>
</tr>
<tr>
<td>Defaecation frequency / night</td>
</tr>
<tr>
<td>Stools consistency</td>
</tr>
<tr>
<td>Blood loss per anum</td>
</tr>
<tr>
<td>Ability to differentiate flatus from stools</td>
</tr>
<tr>
<td>Soiling during day-time</td>
</tr>
<tr>
<td>Soiling during night-time</td>
</tr>
<tr>
<td>Anal incontinence score 18</td>
</tr>
<tr>
<td>Urgency of defaecation</td>
</tr>
<tr>
<td>Episodes with passive incontinence</td>
</tr>
<tr>
<td>Loss of large quantities</td>
</tr>
<tr>
<td>Need to wear a pad</td>
</tr>
<tr>
<td>Sensation of incomplete defaecation</td>
</tr>
<tr>
<td>Tenesmus</td>
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</tbody>
</table>

Pts = patients; Pre-OP = preoperative; Post-OP = postoperative; * significantly different (p < 0.05) from patients preoperatively, † significantly different (p < 0.05) from healthy volunteers.
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elevated 12 months postoperatively. In contrast, the percentages of patients with urgency, tenesmus and sensation of incomplete defaecation showed an initial rise after 4 months but decreased after 12 months to values who were lower than preoperatively. Finally, there were no considerable changes in defaecation frequency during night, stool consistency, the ability to differentiate between flatus and faeces, anal incontinence score and the percentage of patients with loss of large faecal quantities.

Manometry, mucosal sensitivity and PNMLT outcome
The results of the anal manometry are shown in Table 3. Preoperative resting and squeezing pressures of patients were significantly lower than those of HV. Postoperatively, there was no significant decrease in either the resting pressure or the maximum squeezing pressure in comparison to preoperative values. The RAIR was present in all patients preoperatively as well as in all HV. The presence of RAIR was significantly decreased to 36% 4 months postoperatively, but recovered to 81% after 12 months. Remarkably, during the RAIR assessment strong neo-rectal contractions, with pressures up to 321 mmHg (mean 84 ± 31 mmHg, RAIR induced with 40 ml), were seen in patients 4 months postoperatively. These contractions decreased one year postoperatively (Table 4). Preoperative anal- and rectal mucosal sensitivity and PNTML data of patients did not differ from those of HV. There were also no postoperative changes in both mucosal sensitivity and PNTML data (Table 3). No data are given for PNTML data 4 months postoperatively, since this examination was experienced as too strenuous by eight patients.

(Neo-)Rectal and sigmoid colon compliance
Mean compliance curves for patients (pre- and postoperatively) and volunteers are shown in Figure 3. The preoperative rectal compliance in patients (Table 4.) was not different from that of HV’s rectum (8.9 ± 0.8 vs. 9.3 ± 0.8 ml/mmHg, respectively) but both were significantly higher than the postoperative patients neo-rectal compliance (4 months: 4.4 ± 0.8 ml/mmHg, 12 months: 5.5 ± 0.8 ml/mmHg).

The HV’s sigmoid colon compliance (4.9 ± 0.8 ml/mmHg) was significantly lower than the preoperative rectal compliance in patients and that of HV’s rectum, but was similar to that of the neo-rectum both 4 and 12 months postoperatively.
Figure 3: Volume-pressure curves obtained during isobaric distentions patients before and after surgery and in volunteers in the rectum and in the sigmoid colon. The compliance of the neorectum in patients 4 and 12 months postoperatively and of the volunteers sigmoid was significantly lower than that of the rectum in volunteers and preoperative patients (p < 0.05, ANOVA).

The neo-rectal compliance 4 months postoperatively was significantly lower than that of 12 months postoperatively, indicating that there was some adaptation 12 months postoperatively.

As described by Akervall et al., reactive rectal contractions were observed at the onset of every distention of the barostat-bag. In the neo-rectum, however, these contractions were followed by one or more extra contractions (median 2; range 1-6) both at 4 and 12 months postoperatively with increased amplitude (Figure 4). Four months postoperatively, the mean amplitude of these contractions was significantly larger than in the HV’s rectum, but the amplitude at 12 months was within the preoperative range (Table 4).

**Pressure thresholds to induce (Neo-)Rectal and sigmoid colon sensation**

The pressure threshold to induce first sensation in the rectum of HV was equal to that of the rectum in preoperative patients (Table 4). Similar agreement was shown for the thresholds for sensations desire to defaecate and intolerable discomfort. The pressure threshold for first sensation in the HV’s sigmoid was also not different from the values in the HV’s rectum and those of the preoperative patients’ rectum. However, the threshold for desire to defaecate was
significantly higher than those of the HV's rectum and those of the preoperative patients' rectum.

Figure 4: Representative tracings showing the intraballoon volume in (A) healthy volunteers rectum and (B) neo-rectum (4 months after surgery) at 15 mmHg above MDP. In contrast to HV rectum, distention induces neo-rectal contractions, shown as a decrease in volume.

Moreover, in the sigmoid of HV, sensation of intolerable discomfort could not be elicited, not even at 50 mmHg (Figure 5).

In contrast, when the sigmoid was used for neo-rectal construction and placed on the pelvic floor, the pressure thresholds to induce the sensations desire to defaecate and intolerable discomfort, both at 4 and 12 months postoperatively, dropped significantly and were similar to those of the normal rectum (Table 4).

Figure 5: Cumulative percentage of patients and volunteers who experienced the sensations desire to defaecate (upper panel) and intolerable discomfort (lower panel) during isobaric distentions. The curves for the sigmoid colon in healthy volunteers show a significant shift towards higher pressures as compared to those of the (neo-)rectum in patients and volunteers. (p < 0.05, Log rank test)
<table>
<thead>
<tr>
<th></th>
<th>Healthy Volunteers</th>
<th>Pts Pre-OP</th>
<th>Pts 4 months Post-OP</th>
<th>Pts 12 months Post-OP</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resting pressure (mmHg (SD))</td>
<td>74.6 * (18)</td>
<td>55.7 (26)</td>
<td>34.8 (18)</td>
<td>41.9 (22)</td>
</tr>
<tr>
<td>Maximum squeezing pressure (mmHg (SD))</td>
<td>196.2 * (62)</td>
<td>139.5 (55)</td>
<td>117.8 (60)</td>
<td>131.4 (59)</td>
</tr>
<tr>
<td>(neo)Rectal-Anal Inhibitory Reflex (RAIR)</td>
<td>100%</td>
<td>100%</td>
<td>36%†</td>
<td>82%</td>
</tr>
<tr>
<td>Anal mucosal electrosensitivity (SD)</td>
<td>5.2 (0.8)</td>
<td>8.0 (4.0)</td>
<td>6.5 (2.6)</td>
<td>6.3 (1.6)</td>
</tr>
<tr>
<td>Rectal mucosal electrosensitivity (SD)</td>
<td>22.0 (8)</td>
<td>26.7 (11)</td>
<td>35.3 (22)</td>
<td>29.4 (11)</td>
</tr>
<tr>
<td>PNTML (Left / Right (SD))</td>
<td>2.0 (0.1) / 2.2 (0.2)</td>
<td>2.5 (0.4) / 2.2 (0.2)</td>
<td>2.2 (0.4) / 2.2 (0.1)</td>
<td></td>
</tr>
</tbody>
</table>

Pts = patients; Pre-OP = preoperative; Post-OP = postoperative; * significantly different (p < 0.05, ANOVA) from patients; † significantly different (p < 0.05, χ² test) from patients preoperatively and 12 months Post-OP and healthy volunteers.
Volume thresholds to induce (Neo-)Rectal and sigmoid colon sensation

The volume at first sensation was similar in the rectum, sigmoid and neo-rectum of patients or HV (Table 4 & Figure 6). However, the volume at desire to defaecate in the sigmoid of HV and in the neo-rectum at 4 months, was significantly lower than that of the rectum of both HV and patients preoperatively. The volume at desire to defaecate in the neo-rectum at 12 months showed a significant increase in comparison to 4 months postoperatively, not different anymore from preoperative values and HV rectum. The volume at intolerable discomfort in the neo-rectum at 4 months was, like that at desire to defaecate, lower than that of the rectum of HV and patients preoperatively. At 12 months there was an increase in volume as compared to 4 months postoperatively, although not significant. The volume to induce intolerable discomfort at 12 months was still significantly lower than the volume at intolerable discomfort in the rectum of HV.

Data on the volume threshold for intolerable discomfort in the HV’s sigmoid are not available, since the intolerable discomfort sensation could not be elicited in the sigmoid of HV.

Figure 6: Mean barostat bag volumes at the sensations first sensation, desire to defaecate and intolerable discomfort. Pts = patients; * significantly different ($p < 0.05$, ANOVA) from patients preoperatively and healthy volunteers’ rectum; † significantly different ($p < 0.05$, ANOVA) from healthy volunteers’ rectum; ‡ significantly different ($p < 0.05$, ANOVA) from Pts 4 months postoperatively; § None of the volunteers reached sensation discomfort in the sigmoid colon.
Table 4: Compliance and median pressures to induce rectal sensation results in healthy volunteers and patients with rectal carcinoma.

<table>
<thead>
<tr>
<th></th>
<th>Healthy Volunteers Rectum</th>
<th>Healthy Volunteers Sigmoid</th>
<th>Pts Pre-OP</th>
<th>Pts 4 months Post-OP</th>
<th>Pts 12 months Post-OP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compliance (ml/mmHg (SE))</td>
<td>9.3 (0.8)</td>
<td>4.9 * (0.8)</td>
<td>8.9 (0.8)</td>
<td>4.4 * (0.8)</td>
<td>5.5 * (0.8)</td>
</tr>
<tr>
<td>(Neo-)Rectal Contractions during RAIR (mmHg (SE))</td>
<td>14 (5)</td>
<td>14 (4)</td>
<td>84 (31)</td>
<td>18 (4)</td>
<td></td>
</tr>
<tr>
<td>(Neo-)Rectal Contractions during barostat distention (ml (SE))</td>
<td>24 (6)</td>
<td>10 (4)</td>
<td>42* (10)</td>
<td>21* (8)</td>
<td></td>
</tr>
<tr>
<td>Median pressures inducing:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First sensation (mmHg (range))</td>
<td>3 (0-9)</td>
<td>4.5 (0-12)</td>
<td>6 (0-12)</td>
<td>3 (0-9)</td>
<td>3 (0-15)</td>
</tr>
<tr>
<td>Desire to defaecate (mmHg (range))</td>
<td>9 (6-50)</td>
<td>36* (24-50)</td>
<td>12 (3-30)</td>
<td>9 (3-50)</td>
<td>18 (3-50)</td>
</tr>
<tr>
<td>Discomfort (mmHg (range))</td>
<td>33 (18-50)</td>
<td>&gt;50*</td>
<td>21 (6-50)</td>
<td>30 (9-50)</td>
<td>36 (15-50)</td>
</tr>
<tr>
<td>Median volumes inducing:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First sensation (ml (range))</td>
<td>56 (27-93)</td>
<td>34 (15-50)</td>
<td>43 (14-68)</td>
<td>40 (2-101)</td>
<td>39 (6-109)</td>
</tr>
<tr>
<td>Desire to defaecate (ml (range))</td>
<td>152 (86-218)</td>
<td>95* (86-111)</td>
<td>147 (75-215)</td>
<td>57 * (28-157)</td>
<td>119* (30-199)</td>
</tr>
<tr>
<td>Discomfort (ml (range))</td>
<td>222 (201-251)</td>
<td>8</td>
<td>197 (119-286)</td>
<td>102 * (32-231)</td>
<td>139* (73-220)</td>
</tr>
</tbody>
</table>

Pts = patients; Pre-OP = preoperative; Post-OP = postoperative; RAIR = rectal-anal inhibitory reflex; * significantly different (p < 0.05, ANOVA) from patients preoperatively and healthy volunteers' rectum; † significantly different (p < 0.05, ANOVA) from patients 4 months Post-OP; ‡ significantly different (p < 0.05, Log rank test) from patients rectum and neo-rectum and healthy volunteers' rectum; § significantly different (p < 0.05, ANOVA) from healthy volunteers' rectum; § None of the volunteers reached sensation discomfort.
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Discussion

A growing number of publications report rising 5-year disease free survival rates and declining local recurrence rates.\textsuperscript{1,2} However, up to 60 percent of patients experience a decreased functional outcome one year postoperatively, ranging from soiling to episodes with faecal incontinence.\textsuperscript{3,26} Therefore, comprehension of the underlying patho-physiologic mechanism becomes increasingly important.

In this study anal and rectal function in combination with clinical outcome was assessed in patients before and after surgery for rectal cancer, and compared to that of age-matched healthy volunteers. It was presumed that the clinical outcome like in patients with an ileal pouch, would improve with an increase of neo-rectal compliance.\textsuperscript{27} However, similar to previous reports,\textsuperscript{3,26} anorectal function in this study was seriously diminished after TME surgery for rectal carcinoma with 1. increased urgency and tenesmus and 2. increased incidence of soiling and episodes with passive incontinence.

Tenesmus and urgency was present 4 months postoperatively in 55\% and 46\% of the patients respectively, both decreasing after one year to 36\% and 18\%. From a pathophysiological point of view, urgency and tenesmus most likely result from altered motility and reservoir function of the neo-rectum. It is indeed becoming increasingly clear that these components play a pivotal role in normal physiology and continence.\textsuperscript{16,26} As shown in healthy volunteers, the compliance of the sigmoid, which is used to construct the neo-rectum, is significantly smaller than that of the normal rectum, explaining a similar reduction of the compliance of the neo-rectum in patients. Although there was some degree of adaptation in time, compliance remained significantly reduced after one year as compared to that of a normal rectum, resulting in smaller volumes necessary to induce sensation of defecation and discomfort. Furthermore, as shown by the neo-rectal contractions observed during distension, the neo-rectum is much more 'irritable' than a normal rectum. These contractions will certainly contribute to the feeling of urgency and tenesmus, especially in the presence of decreased compliance. Interestingly, the volume at the threshold of desire to defecate and discomfort increased whereas the distention-induced contractions decreased after 12 months, most likely explaining the decrease in urgency and tenesmus percentages. Similar pathophysiological mechanisms are very likely involved in the urgency and tenesmus observed in patients with inflammatory bowel disease.\textsuperscript{28}

In contrast to urgency and tenesmus, the occurrence of soiling and episodes with passive incontinence increased in time. Although the underlying pathophysiological mechanisms of soiling and faecal incontinence are complex, it is clear that dysfunction of the internal anal sphincter is of crucial importance.\textsuperscript{4,5,7,9,12}
Compared to age-matched healthy volunteers, preoperative basal pressure was significantly lower in patients, with 45% of patients having a basal pressure below the normal value and therefore a higher risk for a less favourable functional outcome. Most interestingly, the percentage of patients with a positive recto-anal inhibitory reflex was decreased after 4 months, recovering in almost all patients after one year, similar to results reported by other groups.\(^{29,30}\) One might argue that this finding may explain in part why episodes with passive incontinence increases. As previously discussed, the neo-rectum is more irritable and thus generates contractions even when small amounts enter. When the RAIR is absent, this will not result in opening of the sphincter. However, when RAIR has recovered after 12 months, increased pressure in the neo-rectum and/or small amounts of stool will induce a RAIR with further reduction of the basal pressure resulting in passive faecal incontinence. This mechanism is somewhat alike to the transient sphincter relaxations described in patients with diabetes, where these spontaneous reductions in basal sphincter pressure are believed to contribute to the faecal incontinence in these patients.\(^{31}\)

Another interesting finding in this study was the change in visceral sensation to distension of the sigmoid when it was moved to the pelvic floor. Indeed, in healthy volunteers, the thresholds to induce sensations in the sigmoid were much higher compared to that of the rectum, including that of the patients before surgery. Even distension of the sigmoid to 50 mmHg was unable to induce a sensation of discomfort. However, when the sigmoid was transferred to the pelvic floor to function as a neo-rectum, sensation to pressure-controlled distension resembled that of a normal rectum, irrespective of the decreased compliance. These findings strongly suggest that receptors mediating these sensations are located in the pelvic floor, and not in the rectal wall, which was recently propagated in a study where a relationship between a simulataneous drop in rectal smooth muscle tension and rectal sensation was reported.\(^{32}\)

Based on our findings and the possible underlying pathophysiological mechanisms, one might hypothesise that the construction of a neo-rectum with a colo-anal anastomosis is not a good choice from a functional point of view. First of all, the reservoir function should be increased, for example by creating a colonic pouch. Clinical outcome of patients treated as such are reported to be better compared patients as in this study with a colo-anal anastomosis.\(^{33}\) Secondly, transsection of the rectal wall as is done during a pouch procedure should theoretically reduce the irritability and contractility of the neo-rectum. However, as we have shown that the distension-induced contractility diminishes in time, this issue may become of minor importance after some time as is
described in studies were patients with either procedure have been observed for 2 years. Further follow-up studies therefore are needed to confirm this.

In conclusion, anorectal function after TME surgery for rectal carcinoma is seriously hampered resulting in increased urgency, tenesmus, episodes with passive incontinence and soiling. Urgency and tenesmus most likely result from decreased compliance and increased contractility, both showing some degree of adaptation in time. This adaptation most likely explains the decrease in urgency and tenesmus after one year. In contrast, we showed that episodes with passive incontinence and soiling increase in time. Although we have no good explanation, the recurrence of the RAIR in the presence of a lowered basal anal pressure most likely contributes to these problems. Further studies are needed to investigate whether a larger more compliant reservoir will indeed increase functional outcome and eventually quality of life.

References