Laparoscopic total mesorectal excision for rectal cancer
Breukink, Stéphanie Olga

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CHAPTER 6

PROSPECTIVE EVALUATION OF QUALITY OF LIFE AND SEXUAL FUNCTIONING FOLLOWING LAPAROSCOPIC TOTAL MESORECTAL EXCISION

SO Breukink¹, HJ van der Zaag-Loonen², EMC Bouma³, JPEN Pierie⁴, C Hoff⁴, T Wiggers¹, WJHJ Meijerink⁴.

¹Department of Surgery, ²Department of Radiology, ³Department of Social Psychiatry, University Medical Centre Groningen, University of Groningen, Groningen, The Netherlands. ⁴Department of Surgery, Medical Centre Leeuwarden, Leeuwarden, The Netherlands.

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Abstract

Purpose: The aim of the present study was to investigate how the Quality of Life of patients with rectal cancer changes over time after laparoscopic Total Mesorectal Excision.

Methods: Patients completed the Medical Outcomes Study Short Form 36, and the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire and a colorectal specific European Organisation for Research and Treatment of Cancer quality of life questionnaire before laparoscopic Total Mesorectal Excision, on discharge from hospital and at 3, 6 and 12 months postoperatively. Patients were treated by laparoscopic low anterior resection or laparoscopic abdominoperineal resection.

Results: Fifty-one patients (mean age: 64 years, 29 (57 percent) male) participated in this study, of whom 38 (75 percent) underwent laparoscopic low anterior resection and 13 (25 percent) laparoscopic abdominoperineal resection.

Compared with preoperative scores on the Medical Outcomes Study Short Form 36, patients reported a deterioration in physical functioning (74 vs. 80, p=0.009), and improved mental functioning (76 vs. 70, p=0.007) at 3 months. Improvement in emotional wellbeing was reported both on the Medical Outcomes Study Short Form 36 (78 vs. 53, p=0.006) and the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (84 vs. 69, p<0.001). At one year, improvements in global Qualify of Life (82 vs. 68, p=0.001) and symptoms like fatigue (18 vs. 32, p<0.001), pain (5 vs. 12, p=0.009) and appetite loss (3 vs. 13, p=0.01) were reported.

However, sexual functioning was worse from 3 months onward until one year after surgery (47 vs. 66, p=0.004). Patients who underwent low anterior resection experienced less sexual dysfunction than patients after abdominoperineal resection (21 vs. 56, p=0.004).

Conclusion: One year after laparoscopic Total Mesorectal Excision for rectal cancer, patients reported improvement in some important Quality of Life outcomes, including global Quality of Life, despite a decrease in sexual functioning.
Introduction

Because of improvements in treatment and early detection, 5-year survival after curatively intended resection for rectal cancer is now 63 percent. It is known that next to surgical trauma, radiotherapy can damage the autonomous pelvic nerve plexus which can result in bowel, bladder and sexual dysfunction with great impact on quality of life (QoL). The advantage of any treatment, i.e. improved survival, should outweigh the negative impact on patients’ functioning and QoL in the remainder of his life.

Therefore QoL assessment is regarded an important outcome in addition to traditional endpoints such as survival, tumour recurrence and complication rates.

Several cross-sectional studies were published describing QoL after open rectal. The first randomized study describing the effects of short-term preoperative radiotherapy on QoL and sexual functioning after open surgery shows that, next to the known beneficial effect of decrease in local recurrence rate, preoperative radiotherapy leads to more sexual dysfunction, which is not reflected in a worse QoL. However, little is known about QoL changes over longer periods of time after open or laparoscopic surgery. To our knowledge, this is the first prospective longitudinal study describing QoL changes over time after laparoscopic TME (LTME).

With respect to objective outcomes, LTME is associated with improved short-term results compared to open TME (OTME) with respect to morbidity, recovery period and postoperative pain. Long-term outcome data of LTME are not available yet. We however know that the long-term survival of laparoscopic colectomy for colonic cancer is at least equal to open surgery.

This prospective study describes the QoL of patients with rectal cancer undergoing LTME. The main objective was to determine how the QoL of patients undergoing LTME changes over time. A secondary aim was to determine how factors like surgical procedures, low anterior resection (LAR) or abdominoperineal resection (APR), age and gender influence QoL in these patients. Finally, we compared QoL of patients who underwent LTME one year postoperatively with that of a general healthy population.

Materials and methods

Patients and methods

Between May 2002 and August 2004, 56 patients with rectal cancer were scheduled for elective LTME at Medical Centre Leeuwarden. The patients were considered to be eligible for our study if the operation had a curative intention. Patients with advanced T3 and T4 carcinomas, or patients with locally recurrent cancer were excluded. All patients received short course 5 x5 Gy radiotherapy preoperatively according to national protocol. Surgery took place within 10 days of the start of the first radiotherapy.

All patients were asked to participate in the QoL study and 51 agreed. Patients were given QoL questionnaires in the week before treatment, on discharge home (early postoperative assessment), and at 3, 6, and 12 months after surgery. Preoperative questionnaires were filled in before start of radiotherapy. Patients completed the further questionnaires through the mail. A reminder was sent after two weeks if no reply was received.
Details regarding age, gender, TNM classification, operation type were collected. Patients with Dukes B or Dukes C rectal cancer received adjuvant chemotherapy according to Mayo Clinic Schedule; intravenous bolus 5-fluorouracil (5-FU, 450 mg/m²) with leucovorin (LV, 20 mg/m²) for 5 days. This schedule was repeated for 6 times every 4 weeks.

For the study the patients were followed for one year with respect to recurrent / metastatic disease and death. Survival was measured in days from the time of surgery to death.

The study was approved by the Committee on Medical Research Ethics and all patients provided written informed consent.

Study instruments
We used a generic QoL questionnaire (Dutch version of the Medical Outcomes Study Short-Form (SF-36)\textsuperscript{17}, a cancer specific instrument (the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30)\textsuperscript{18} and a colorectal specific QoL questionnaire (the EORTC Colorectal Quality of Life Questionnaire QLQ-CR38)\textsuperscript{19}).

The SF-36 is a multidimensional questionnaire consisting of 36 questions, organized in nine multi-item scales: physical functioning, physical role functioning, pain, general well-being, vitality, social functioning, emotional role functioning, mental functioning and health change. The SF-36 has been validated for use in postoperative patients\textsuperscript{20} and its reliability and validity has been proven both in the Netherlands\textsuperscript{21}. The raw scores are linearly transformed to fit in a score range from 0 to 100; a higher score indicating a better health status.

The EORTC QLQ-C30 contains 30 questions and it is subdivided into five functional levels (physical, role, emotional, cognitive, and social), nine symptom scales (fatigue, nausea and vomiting, pain, dyspnoea, insomnia, appetite loss, constipation, diarrhea and financial difficulties) and one global quality of life scale. Scores are summed and transformed to a score range from 0 to 100. A high score for a functional scale represents a high level of functioning, and a high score for the global health status and quality of life represents a high quality of life. On the other hand, a high score for a symptom scale or item represents a high level of symptomatology and problems.

The EORTC QLQ-CR38 consists of 38 questions: 19 questions are completed by all patients while the remaining 19 questions are divided into groups of questions relevant for subsamples of patients only (i.e., male or female, patient with or without a stoma). The EORTC QLQ-CR38 is subdivided into four functional scales (i.e. body image, sexual functioning, sexual enjoyment and future perspective), eight symptom scales (micturition problems, gastrointestinal tract symptoms, chemotherapy side effects, defecation problems, stoma-related problems, male and female sexual problems and weight loss). Validity and reliability has been described in Dutch patients with colorectal cancer. Scoring is equal to that for the EORTC QLQ-C30.

According to the questionnaire manuals missing values were dealt with as follows: if at least half of the items on a scale were completed, the scale score was divided by the number of items present. If less than half of the items were completed the scale was considered missing.
Measures and statistical analysis

Scale scores are presented as means, medians with ranges. Changes in QoL over time were analyzed with the Wilcoxon signed rank test, comparing follow up scores to baseline scores.

To determine how age affects QoL at time of surgery we divided patients into two age groups; one younger group (≤ 65 years; 29 patients) and one older group (> 65 years). Differences in QoL between the two age groups were analysed with Mann-Whitney U tests.

Comparisons in QoL between the two groups of surgery (low anterior vs. abdominoperineal resection) or between men and women were also analysed with Mann-Whitney U tests.

We compared the SF-36 scale scores one year postoperative with those from a Dutch reference population, adjusted for age. Differences between study group and Dutch reference population were analysed with one sample t-tests.

As multiple testing was employed in this study we considered only P values < 0.01 statistically significant. Data were analyzed in SPSS for windows (version 12.0; SPSS, Chicago, IL, USA).
Results
The patient characteristics are displayed in Table 1. There were no conversions. In four patients defunctioning loop ileostomy was performed. Two patients died during follow-up (4 percent); one as a result of the disease and one died of another cause. One patient developed metachronous liver metastasis six months after the operation.

<table>
<thead>
<tr>
<th>Table 1. Patients, treatment and tumour characteristics</th>
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<tbody>
<tr>
<td>Total</td>
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</tr>
<tr>
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<tr>
<td>(100%)</td>
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<td>1</td>
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<td>2</td>
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</table>

Data are numbers with percentages in parentheses unless otherwise indicated.
LAR: low anterior resection
APR: abdominoperineal resection
T1: Tumour invades submucosa
T2: Tumour invades muscularis propria;
T3: Penetration through muscularis propria into subserosa, or into perirectal fat;
T4: Invasion of other organs or involvement of free peritoneal cavity.
N0: No nodal metastasis;
N1: 1-3 perirectal lymph nodes involved;
N2: 4 or more perirectal lymph nodes involved.
SF-36 (Fig. 1)
Physical functioning, social functioning, physical role functioning, vitality and pain were all worse on discharge home compared with preoperative scores. After 3 months, only physical functioning was still lower (74 vs. 80, p=0.009), while mental functioning improved (76 vs. 70, p=0.007). One year after surgery all scores had returned to preoperative levels, but patients reported better emotional role functioning (78 vs. 53, p=0.006).

Figure 1. Mean scale scores on the Medical Outcomes Study Short Form 36 preoperative, 3 months postoperative and 1 year postoperative.
* Wilcoxon signed rank test between scores preoperatively; P value < 0.01.
EORTC QLQ-C30 (Fig. 2)
Patients reported an improvement in emotional functioning at three months compared with baseline scores (83 vs. 69, p<0.001) which persisted until one year postoperatively (84 vs. 69, p<0.001). Six months after treatment, patients had less diarrhea (9 vs. 28, p=0.001). One year after treatment, patients reported an improvement in global quality of life (82 vs. 68, p=0.001) and suffered less from symptoms as fatigue (18 vs. 32, p<0.001), pain (5 vs. 12, p=0.009), appetite loss (3 vs. 13, p=0.01) and diarrhea (8 vs. 28, p=0.001).

EORTC QLQ-C38 (Table 2)
Sexual functioning significantly decreased from 3 months (47 vs. 66, p=0.004) until one year postoperatively (41 vs. 66, p=0.001). At one year, patients suffered less from weight loss (2 vs. 20, p=0.002).

<table>
<thead>
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<th>Table 2. EORTC QLQ-CR38 descriptives</th>
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<td>Function scales</td>
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<td>Body Image (n=46)</td>
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<td>Sexual functioning (n=31)</td>
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<td>Gastrointestinal symptoms (n=46)</td>
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<tr>
<td>Stoma-related problems (n=23)</td>
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<tr>
<td>Female sexual problems (n=6)</td>
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<td>Weight loss (n=46)</td>
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EORTC QLQ-CR 38: a colorectal specific European Organisation for Research and Treatment of Cancer quality of life questionnaire

*: Of the 46 patients 27 (64%) underwent chemotherapy.
Prospective evaluation of quality of life and sexual functioning

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<td>13</td>
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<td>0-100</td>
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</tbody>
</table>

**Figure 2.** Mean scale scores of the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire with significant changes over time. Error bars indicate one standard deviation from the mean. * Wilcoxon signed rank test between scores preoperatively; P value < 0.01.
Type of surgery (LAR OR APR)

There was no difference in age, gender distribution and tumour stage between the two treatment groups pre-operatively (Table 1). There was no difference between the LAR and the APR-group on either the SF-36 nor the EORTC QLQ-C30 at any time. On the colorectal specific questionnaire there were some significant differences between the two groups. First, patients who underwent a LAR had better sexual functioning (56 vs. 21, p=0.004) than patients who underwent an APR, three months postoperatively. Second, one year postoperatively patients who underwent LAR had a better body image (94 vs. 67, p=0.003) and sexual functioning (51 vs. 12, p=0.001) than patients who underwent APR.

Impact of age

There were no differences in the distribution of surgical procedures, tumour stage or gender between the two groups. Again, on the SF-36 and EORTC QLQ-C30 no differences between the two groups were observed at any time. However, on the colorectal specific questionnaire the older patients experienced more micturition problems (39 vs. 21, p=0.001) and chemotherapy side effects (24 vs. 9, p=0.009) 3 months postoperatively. One year after surgery complaints about micturition sustained in the elder group (36 vs. 19, p=0.001).

Impact of gender

The only difference in QoL between men and women was observed on the colorectal specific instrument: women reported better body image (93 vs. 82, p<0.004) one year postoperatively.

Comparison with normative populations

The SF-36 scores did not differ from the Dutch normative data, except for the symptom pain. After LTME patients had less pain than the general Dutch population one year postoperatively.

Discussion

In this prospective study we observed a significant decrease in QoL of patients after LTME in the first months, which returned to preoperative levels or even improved one year postoperatively. However, sexual functioning remained impaired and was worse in patients undergoing APR than in those with LAR.

The finding that QoL was equal or better one year postoperatively than preoperatively after LTME may be explained by a combination of presenting symptoms and distress preoperatively and the so called “response shift” or “reframing” phenomenon one year after operation. This response shift means that patients who have survived a life-threatening disease, like rectal cancer, seem to develop a conscious awareness that leads to new internal standards and a positive appreciation of everyday life and thereby often better QoL. It has also been described in patients with colon cancer after surgery.

We have found very few reports on QoL after LTME to compare our results with.
Studies in patients undergoing open colorectal surgery showed a decreased QoL during the first few months after TME, followed by an improvement after 3 to 6 months. Open rectal surgery resulted in a temporary reduction of QoL mainly because of reduced physical functioning. This is in accordance with our results; it is not surprising that especially physical functioning and sexual functioning decreases in the first 6 months.

However, sexual dysfunction persisted until one year postoperatively. Again little is known about sexual functioning after laparoscopic surgery, but open studies focusing on male sexual function also report sustained impairment of sexual functioning. We could not evaluate sexual functioning in women because only 4 of the women preoperatively answered questions regarding sexual functioning.

The present study demonstrates that patients who underwent laparoscopic LAR were better off: they had better sexual functioning and were more satisfied about their body image. The latter feature could well be caused by the absence of a stoma in the laparoscopic LAR group. Again these findings are in line with QoL data from open surgery for rectal cancer.

Lower mean scores of male sexual functioning following APR compared with LAR has been described previously in studies describing open TME. Impairment of sexuality in patients after an APR might be caused by a combination of higher proportion of low tumours and/or to the extended resection in the pelvis causing damage to the pelvic autonomic nerves and the pelvic floor.

However, we did not observe a difference in global QoL or social functioning between LAR and APR patients, although sexuality comprises a substantial part of patients’ subjective well-being. Hendren, as well as others, have also described the phenomenon of good overall QoL despite high rates of sexual dysfunction in open rectal surgery.

Cancer cure appears to be more important in determining overall QoL than sexual functioning.

Unlike other studies in which next to type of surgery, age was related to impaired sexuality, we did not find a relation between patients’ age and sexuality. In our study older patients had more micturition problems than younger patients at 3 months and one year postoperatively. Besides, at 3 months, higher chemotherapy side effects, i.e. a combination of 3 items; dry mouth, hair problems and taste changes were scored by the older group.

Our results are in accordance with the few laparoscopic studies reporting on rectal cancer. In a cross-sectional study comparing laparoscopic with open colorectal resection Sokolovic et al. described better long term QoL using the SF-36. However, no short term QoL differences in any of the scales or symptoms of the EORTC QLQ-C30 or CR38 were recorded in a multicentre, randomized controlled trial (the CLASICC trial). In the CLASSIC trial short-term endpoints were compared between laparoscopic-assisted versus open surgery in patients with colorectal cancer.

We found worse sexual function from 3 months until one year postoperative. Only two studies reported data on sexual dysfunction after LTME. One described a higher rate of male sexual dysfunction after laparoscopic resection compared to open resection. The sample size of Quah et al. was small; 15 patients underwent a LTME and 22 patients an OTME. The second study reporting on sexual dysfunction after
LTME found a nonsignificant trend towards male sexual dysfunction after laparoscopic rectal resection. More sexual dysfunction is also seen after OTME. Based on the little information in the literature it is difficult to draw any meaningful conclusions regarding sexual function after LTME yet.

When comparing QoL results in our group with normative data general QoL one year after LTME was comparable to a Dutch healthy population except for the symptom pain: patients in our study experienced less pain postoperatively.

For the EORTC QLQ-C30 and EORTC QLQ-CR38 no reference data were available for the Dutch general population. Rauch et al. compared QoL of 121 disease-free survivors of rectal cancer patients who underwent open rectal surgery with controls drawn from the general population and found the survivors to have a similar or even better QoL. They explained this effect may to the previously mentioned response shift. Compared with their results of patients who underwent open rectal surgery, we found better global quality of life (82 vs. 72) and less pain (5 vs. 16).

There are some limitations to our study. First our results are based on validated questionnaires and the drawback of such an analysis is that complications are not recorded which in theory could influence quality of life. Second, because this is a nonconsecutive study, results should be treated with caution because of a possible selection bias. Although the present study was prospective, it has potential limitations because of the small sample size, especially when performing subgroup analysis. Furthermore, this was a single-institution study, and results from one hospital may not be translated to a general surgical population.

Thus, our results may require prospective confirmation in larger series with an open control group in a multicentre randomized controlled trial. Meanwhile, thorough pretreatment information regarding good QoL prospective with probably worse sexual functioning after LTME is necessary. This may help patients to cope better with postoperative recovery, as symptoms may be better tolerated if they can be anticipated upon.
Reference List


