Health-related quality of life after laparoscopic and open surgery for rectal cancer in a randomized trial

J. Andersson1,2, E. Angenete1, M. Gellerstedt1, U. Angerås1, P. Jess3, J. Rosenberg4, A. Fürst5, J. Bonjer6 and E. Haglind1

1Scandinavian Surgical Outcomes Research Group (SSORG), Department of Surgery, Sahlgrenska University Hospital/Östra, Gothenburg, and 2Department of Surgery, Alingsås Hospital, Alingsås, Sweden, Departments of Surgery, 3Roskilde Hospital, Roskilde, and 4Herlev Hospital, University of Copenhagen, Copenhagen, Denmark, 5Department of Surgery, Caritas Clinic St Josef, Regensburg, Germany, and 6VUmc University Medical Centre, Amsterdam, The Netherlands

Correspondence to: Professor E. Haglind, SSORG, Department of Surgery, Sahlgrenska University Hospital/Östra, SE-416 85 Gothenburg, Sweden (e-mail: eva.haglind@vgregion.se)

**Background:** Previous studies comparing laparoscopic and open surgical techniques have reported improved health-related quality of life (HRQL). This analysis compared HRQL 12 months after laparoscopic versus open surgery for rectal cancer in a subset of a randomized trial.

**Methods:** The setting was a multicentre randomized trial (COLOR II) comparing laparoscopic and open surgery for rectal cancer. Involvement in the HRQL study of COLOR II was optional. Patients completed the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 and QLQ-CR38, and EuroQol – 5D (EQ-5D) before surgery, and 4 weeks, 6, 12 and 24 months after operation. Analysis was done according to the manual for each instrument.

**Results:** Of 617 patients in hospitals participating in the HRQL study of COLOR II, 385 were included. The HRQL deteriorated to moderate/severe degrees after surgery, gradually returning to preoperative values over time. Changes in EORTC QLQ-C30 and QLQ-CR38, and EQ-5D were not significantly different between the groups regarding global health score or any of the dimensions or symptoms at 4 weeks, 6 or 12 months after surgery.

**Conclusion:** In contrast to previous studies in patients with colonic cancer, HRQL after rectal cancer surgery was not affected by surgical approach. Registration number: NCT0029779 (http://www.clinicaltrials.gov).

Presented in part to the Annual Meeting of the European Society for Coloproctology, Vienna, Austria, September 2012

Paper accepted 7 March 2013

Published online in Wiley Online Library (www.bjs.co.uk). DOI: 10.1002/bjs.9144

**Introduction**

There have been extensive studies of laparoscopic resection for colonic cancer, including randomized clinical trials showing short-term advantages for a minimally invasive approach. Some have also studied health-related quality of life (HRQL), reporting the superiority of laparoscopic surgery. Laparoscopic surgery for rectal cancer has been studied less extensively. The impact of a permanent stoma on HRQL has been described, as has the change of HRQL over time in patients treated for rectal cancer. In a prospective comparison of the effects of laparoscopic versus open surgery, Li and colleagues found improved HRQL 1 week after laparoscopic surgery, but not after 1 year. The present study compared HRQL 1 year after laparoscopic or open surgery for rectal cancer in a subset of patients from the international multicentre randomized clinical trial COlorectal cancer Laparoscopic or Open Resection (COLOR) II.

**Methods**

The COLOR II trial

The patients in this HRQL study constituted a subset of the COLOR II trial cohort. Thirty hospitals in eight countries (Belgium, Canada, Denmark, Germany, the Netherlands, South Korea, Spain and Sweden) participated in COLOR
II, but inclusion in the HRQL study was optional. The primary endpoint of the trial is local recurrence rate, and the trial was designed as a non-inferiority study. Patients were randomized between laparoscopic and open surgery in the ratio 2:1, and the trial was stratified according to centre, preoperative radiation and type of operation. The inclusion criteria focused on selection of patients undergoing elective surgery for potentially curable rectal cancer, T1–T3, best treated by partial mesorectal excision, total mesorectal excision or abdominoperineal resection. Exclusion criteria included transanal resection. The protocol of the COLOR II trial was approved by the appropriate ethics committees, and registered at ClinicalTrials.gov (NCT0029779).

Patients

Twelve hospitals in five countries (Canada, Denmark, Germany, the Netherlands and Sweden) participated in the HRQL component of the COLOR II trial. Inability to understand the questionnaires was an exclusion criterion. Patients who agreed to participate were asked to complete the preoperative questionnaire within 5 days before the operation, then 4 weeks, 6, 12 and 24 months after surgery. In Dutch hospitals, patients were also asked to complete EuroQol – 5D questionnaires 3, 7 and 14 days after operation. The results at 24 months will be published separately.

Demographic details, data on complications, tumour stage as classified in the pathology report on the resected specimen, reoperations, postoperative adjuvant chemotherapy, sexual function, and urinary and faecal continence, as recorded in clinical record forms at follow-up outpatient visits, were retrieved from the COLOR II database in Halifax, Canada. An analysis of sexual and urinary function will be presented separately, including European Organization for Research and Treatment of
Table 1 Demographics for health-related quality-of-life study and for those not included in this study

| Not included in HRQL study (n = 199) | Included in HRQL study (n = 385) | Laparoscopic (n = 260) | Open (n = 125) | P[j] |
|-------------------------------------|----------------------------------|-----------------------|----------------|------|
| Age [years]*                        | 67 (66.0, 69.4)                  | 67 1 (66.1, 68.1)     | 0.696[j]       | 67 4 (66.4, 68.4) |
| Sex ratio [M : F]                   | 123 : 76                         | 239 : 146             | 0.949          | 162 : 98 |
| Body mass index [kg/m²]*            | 25 9 (25.3, 26.5)                | 26 0 (25.6, 26.5)     | 0.750[j]       | 26 1 (25.3, 26.8) |
| ASA fitness grade                  |                                  |                       |                | 0.624 |
| I                                  | 37 (18.9)                        | 103 (26.8)            | 0.008          | 69 (26.5) |
| II                                 | 101 (50.8)                       | 224 (58.2)            | 0.632          | 149 (57.3) |
| III                                | 48 (24.1)                        | 55 (14.3)             | 0.091†         | 40 (15.4) |
| IV                                 | 1 (0.5)                          | 2 (0.5)               | 0.087†         | 2 (0.8) |
| Unknown                            | 12 (6.0)                         | 1 (0.3)               | 0.632          | 0 (0) |
| Tumour stage†                      |                                  |                       |                | 0.552 |
| I                                  | 8 (4.0)                          | 22 (5.7)              | 0.262          | 18 (6.9) |
| II                                 | 71 (35.7)                        | 135 (35.1)            | 0.898†         | 93 (35.8) |
| III                                | 101 (50.8)                       | 207 (53.8)            | 0.956          | 135 (51.9) |
| IV                                 | 7 (3.5)                          | 12 (3.1)              | 0.898†         | 9 (3.5) |
| Unknown                            | 12 (6.0)                         | 9 (2.3)               | 0.898†         | 5 (1.9) |
| Type of resection                  |                                  |                       |                | 0.961 |
| Partial mesorectal excision        | 15 (7.5)                         | 42 (10.9)             | 0.632          | 27 (10.4) |
| Total mesorectal excision          | 112 (56.3)                       | 219 (66.9)            | 0.552          | 147 (56.5) |
| Abdominoperineal excision          | 64 (32.2)                        | 116 (30.1)            | 0.409          | 80 (30.8) |
| Other                              | 3 (1.5)                          | 6 (1.6)               | 0.091†         | 4 (1.5) |
| Unknown                            | 5 (2.5)                          | 2 (0.5)               | 0.091†         | 2 (0.8) |
| Preop. radiotherapy‡               | 133 (66.8)                       | 216 (66.1)            | 0.001          | 150 (57.7) |
| Short                              | 110 (55.3)                       | 157 (40.8)            | 0.816†         | 110 (42.3) |
| Long                               | 23 (11.6)                        | 40 (10.4)             | 0.816†         | 27 (10.4) |
| None                               | 60 (30.2)                        | 168 (43.6)            | 0.816†         | 110 (42.3) |
| Unknown                            | 6 (3.0)                          | 1 (0.3)               | 0.816†         | 0 (0) |
| Preop. chemotherapy                |                                  |                       |                | 0.895 |
| Yes                                | 31 (15.6)                        | 64 (16.6)             | 0.087†         | 44 (16.9) |
| No                                 | 145 (72.9)                       | 290 (75.3)            | 0.816†         | 195 (75.0) |
| Unknown                            | 23 (11.6)                        | 31 (8.1)              | 0.816†         | 21 (8.1) |
| Conversion                         | –                                | –                     |                | 65 (25.0) |

Values in parentheses are percentages unless indicated otherwise;*values are mean (95 per cent confidence interval). †Stage in the pathology report of the resected specimen. ‡Stage regimen comprised 5 × 5 Gy or less, and long programmes more than 5 days. Among those included in the health-related quality-of-life (HRQL) study, the dose specification was missing for 13 patients (5-0 per cent) in the laparoscopic group and six (4-8 per cent) in the open group. ASA, American Society of Anesthesiologists. §χ² test, except †Student’s t test.

Cancer (EORTC) QLQ-PR25 together with data from clinical follow-up.

Health-related quality-of-life instruments

The instruments used and reported here were EQ-5D™, EORTC QLQ-C30 and EORTC QLQ-CR38. Validated Swedish, Dutch, Danish, English and German translations of the instrument were used⁶.

EuroQol – 5D

The EQ-5D™ is a generic measure of health status. It is a standardized non-disease-specific (generic) instrument for assessing self-reported health status, allowing for comparisons across disease groups⁶. It comprises a description of the patient’s health in five dimensions (mobility, self-care, daily activity, pain/discomfort and anxiety/depression). One of three levels is chosen for each dimension; the first level denotes no problems or a low level of symptoms, whereas the third level denotes severe problems or a high level of symptoms. Also included in the instrument is a vertical ‘thermometer’ (EQ-VAS) in which the patient is asked to assess their global health on a visual analogue scale from 0 (worst imaginable health state) to 100 (best imaginable). Respondents were requested to assess their health status on the day they filled out the questionnaire.

European Organization for Research and Treatment of Cancer QLQ-C30 and QLQ-CR38

The EORTC QLQ-C30 is a questionnaire developed to assess the quality of life of patients with cancer. The instrument available at the start of the study (2004)
Table 2  EuroQol – 5D global health scores

|                  | Preop.     | 4 weeks    | 6 months   | 12 months  |
|------------------|------------|------------|------------|------------|
| Mean(s.d.) EQ-5D score |            |            |            |            |
| Laparoscopic     | 77(16.6)   | 64(20.8)   | 77(16.2)   | 79(15.9)   |
| Open             | 74(16.6)   | 62(20.4)   | 75(18.0)   | 78(15.1)   |
| Mean change*     | 2.4(–1.5, 6.3) | 1.6(–3.3, 6.5) | 1.7(–2.4, 5.9) | 0.6(–3.4, 4.7) |
| P†               | 0.228      | 0.981      | 0.615      | 0.646      |

Table 3  Results for the five health dimensions of the EuroQol – 5D

|                  | % of patients |            |            |            |
|------------------|--------------|------------|------------|------------|
|                  |              | Preop.     | 4 weeks    | 6 months   | 12 months  |
|                  |              | Laparoscopic | Open     | Laparoscopic | Open       | Laparoscopic | Open       | Laparoscopic | Open     |
| Mobility         |              |            |            |            |            |
| Level 1          | 91           | 88         | 68         | 65         | 85         | 82         | 87         | 88         |
| Level 2          | 9            | 12         | 30         | 34         | 14         | 18         | 13         | 11         |
| Level 3          | 0            | 0          | 2          | 1          | 1          | 0          | 0          | 1          |
| Self-care        |              |            |            |            |            |
| Level 1          | 99           | 98         | 87         | 85         | 96         | 92         | 96         | 97         |
| Level 2          | 1            | 2          | 12         | 13         | 4          | 7          | 4          | 3          |
| Level 3          | 0            | 0          | 1          | 2          | 0          | 1          | 0          | 0          |
| Daily activity   |              |            |            |            |            |
| Level 1          | 89           | 80         | 40         | 37         | 73         | 72         | 80         | 80         |
| Level 2          | 10           | 15         | 43         | 48         | 24         | 23         | 18         | 17         |
| Level 3          | 1            | 5          | 17         | 15         | 3          | 5          | 2          | 2          |
| Pain/discomfort  |              |            |            |            |            |
| Level 1          | 58           | 49         | 28         | 30         | 49         | 53         | 59         | 55         |
| Level 2          | 40           | 49         | 66         | 68         | 49         | 44         | 40         | 44         |
| Level 3          | 2            | 2          | 6          | 2          | 2          | 3          | 1          | 1          |
| Anxiety/depression|             |            |            |            |            |
| Level 1          | 60           | 51         | 55         | 52         | 68         | 68         | 72         | 68         |
| Level 2          | 37           | 42         | 42         | 47         | 29         | 32         | 26         | 32         |
| Level 3          | 3            | 7          | 3          | 1          | 3          | 0          | 2          | 0          |

Level 1, no problems; level 2, low level of symptoms; level 3, severe problems or high level of symptoms. The only significant difference between groups was in daily activity before treatment (P = 0.024, χ² test).

was version 3.0, a 30-item instrument designed for self-administration. The validated Swedish, English, Dutch, Danish and German translations were used[10,11]. This instrument has cross-cultural validity and the psychometric properties are considered satisfactory[12]. Normative data are available for German[13] and Swedish[14] patients as well as reference values[15].

The QLQ-C30 questionnaire consists of 30 questions[16]. Both multi-item and single-item scales are constructed from the questions. There are five functional scales (physical, role, emotional, cognitive and social functioning), three symptom scales (fatigue, nausea/vomiting and pain), six single-item questions (about dyspnoea, insomnia, loss of appetite, constipation, diarrhoea and financial difficulties) and a global health/quality-of-life index. The latter assesses overall health and overall quality of life on a seven-point scale, where 1 indicating very poor and 7 indicating excellent. All other questions have four possible answers: ‘not at all’, ‘a little’, ‘quite a bit’ and ‘very much’. The time frame was ‘during the past week’.

The EORTC QLQ-CR38 questionnaire is used to measure more specific information about quality of life in patients with colorectal cancer. It is constructed in a similar manner to QLQ-C30. Thirty-eight questions cover four functional scales/single items (body image, sexual functioning, sexual enjoyment, future perspective) and eight symptom scales/items (micturition problems, chemotherapy side-effects, gastrointestinal symptoms, male sexual problems, female sexual problems, defaecation problems, stoma-related problems and weight loss). At the
Table 4 Changes in function and symptom scores on European Organization for Research and Treatment of Cancer QLQ-C30

|                          | 4 weeks       | Adjusted mean difference (laparoscopic – open) | 6 months       | Adjusted mean difference (laparoscopic – open) | 12 months      | Adjusted mean difference (laparoscopic – open) |
|--------------------------|---------------|-----------------------------------------------|----------------|-----------------------------------------------|----------------|-----------------------------------------------|
|                          | Mean preop.   | Mean change from preop.                        |                | Mean change from preop.                        |                | Mean change from preop.                        |
| Global quality of life*  | 72.8 (70.2, 75.3) | -14.8                                         |                | -1.9                                          |                | 2.1                                          |
| Laparoscopic             | 68.6 (64.7, 72.6) | -11.9                                         |                | 3.0                                           |                | 3.0                                          |
| Open                     |               |                                               |                |                                               |                |                                               |
| Physical function*       | 88.7 (86.8, 90.6) | -21.6                                         |                | -6.7                                          |                | -3.4                                         |
| Laparoscopic             | 88.8 (86.0, 91.9) | -21.8                                         |                | -6.0                                          |                | -3.3                                         |
| Open                     |               |                                               |                |                                               |                |                                               |
| Role function*           | 80.9 (77.5, 84.4) | -34.9                                         |                | -4.9                                          |                | -0.8                                         |
| Laparoscopic             | 81.9 (76.8, 87.0) | -33.7                                         |                | 1.7                                          |                | 0.6                                          |
| Open                     |               |                                               |                |                                               |                |                                               |
| Emotional function*      | 77.2 (74.4, 80.0) | -2.5                                          |                | 6.1                                           |                | 7.1                                          |
| Laparoscopic             | 74.2 (70.1, 78.3) | 12                                             |                | 10.2                                          |                | 12.0                                         |
| Open                     |               |                                               |                |                                               |                |                                               |
| Cognitive function*      | 88.9 (86.8, 91.0) | -8.4                                          |                | -0.8                                          |                | -3.5                                         |
| Laparoscopic             | 89.3 (86.5, 92.0) | -7.1                                          |                | 3.5                                           |                | -1.2                                         |
| Open                     |               |                                               |                |                                               |                |                                               |
| Social function*         | 87.0 (84.4, 89.5) | -22.4                                         |                | 5.2                                           |                | -1.0                                         |
| Laparoscopic             | 84.4 (80.4, 88.5) | -20.7                                         |                | 4.7                                           |                | -0.1                                         |
| Open                     |               |                                               |                |                                               |                |                                               |
| Fatigue†                 | 22.8 (19.8, 25.7) | 25.0                                          |                | 5.2                                           |                | 4.7                                          |
| Laparoscopic             | 25.8 (21.9, 29.6) | 21.0                                          |                | 4.7                                           |                | -1.6                                         |
| Nausea and vomiting†     | 4.9 (3.3, 6.5) | 2.7                                          |                | -1.4                                          |                | -2.6                                         |
| Laparoscopic             | 4.1 (2.4, 5.9) | 6.0                                          |                | 0.4                                           |                | -3.3                                         |
| Pain†                    | 14.3 (11.6, 17.1) | 18.5                                          |                | 1.8                                           |                | 0.3                                          |
| Laparoscopic             | 13.9 (9.9, 17.9) | 18.5                                          |                | 3.5                                           |                | 0.1                                          |
| Nausea and vomiting†     | 10.8 (8.4, 13.2) | 10.0                                          |                | 1.8                                           |                | -1.1                                         |
| Dyspnoea†                | 12.8 (8.2, 17.5) | 9.4                                          |                | 2.5                                           |                | 0.0                                          |
| Insomnia†                | 26.1 (22.5, 29.8) | 4.5                                          |                | -5.0                                          |                | 2.3                                          |
| Appetite loss†           | 28.8 (21.6, 32.0) | 5.1                                          |                | -8.6                                          |                | 2.3                                          |
| Constipation†            | 9.7 (7.0, 12.5) | 17.1                                          |                | -4.3                                          |                | -3.9                                         |
| Financial difficulties†  | 10.3 (6.3, 14.2) | 21.1                                          |                | -2.3                                          |                | -1.6                                         |

Values in parentheses are 95 per cent confidence intervals.*A high value is positive to the patient; †a high value is negative to the patient.

The start of the study in 2004, QLQ-CR38 was available in the appropriate languages.

For both instruments individual scores were converted to a score ranging from 0 to 100, according to the EORTC scoring manuals. A high score for the symptom/item scales represents a high level of symptoms/problems, whereas a high score for the functional scales and the global/general quality-of-life index represents a high level of functioning, overall health and quality of life.
Table 5  Changes in scores on European Organization for Research and Treatment of Cancer QLQ-CR38

|                      | Mean preop. score | Mean change from preop. | Adjusted mean difference (laparoscopic − open) | Mean change from preop. | Adjusted mean difference (laparoscopic − open) | Mean change from preop. | Adjusted mean difference (laparoscopic − open) |
|----------------------|-------------------|-------------------------|-----------------------------------------------|-------------------------|-----------------------------------------------|-------------------------|-----------------------------------------------|
| Body image†         |                   |                         |                                               |                         |                                               |                         |                                               |
| Laparoscopic         | 90.3 (88.2, 92.4) | −17.8                   | 0.4 (−5.9, 6.6)                               | −13.8                   | −2.0 (−7.9, 3.9)                               | −11.5                   | −2.8 (−8.7, 3.0)                               |
| Open                | 87.4 (83.8, 90.9) | −17.1                   |                                               | −10.1                   |                                               | −6.6                     |                                               |
| Future perspective† |                   |                         |                                               |                         |                                               |                         |                                               |
| Laparoscopic         | 57.1 (53.5, 60.7) | 5.6                     | 2.0 (−4.5, 8.4)                               | 10.2                    | −2.4 (−8.6, 3.8)                               | 11.8                    | −2.7 (−8.9, 3.6)                               |
| Open                | 54.0 (48.2, 59.8) | 5.7                     |                                               | 14.3                    |                                               | 16.7                     |                                               |
| GI symptoms‡        |                   |                         |                                               |                         |                                               |                         |                                               |
| Laparoscopic         | 17.6 (15.7, 19.4) | 6.9                     | 2.6 (−11.1, 6.3)                              | −0.6                    | 0.5 (−2.7, 3.7)                                | −0.8                    | 0.1 (−3.0, 3.2)                                |
| Open                | 17.1 (14.6, 19.6) | 4.5                     |                                               | −0.5                    |                                               | −1.1                     |                                               |
| Defaecation problems‡|                   |                         |                                               |                         |                                               |                         |                                               |
| Laparoscopic         | 26.5 (24.1, 29.0) | 7.2                     | 2.7 (−5.7, 11.0)                              | 2.4                     | 5.9 (0.2, 11.6)                                | −1.2                    | 4.2 (−0.4, 8.7)                                |
| Open                | 26.0 (22.2, 29.8) | 6.7                     |                                               | −3.4                    |                                               | −5.8                     |                                               |
| Weight loss‡        |                   |                         |                                               |                         |                                               |                         |                                               |
| Laparoscopic         | 14.7 (11.7, 17.7) | 22.8                    | −3.7 (−11.2, 3.9)                             | −0.7                    | −1.6 (−7.3, 4.2)                               | −5.6                    | 1.6 (−2.8, 6.0)                                |
| Open                | 14.5 (10.2, 18.9) | 26.5                    |                                               | −0.4                    |                                               | −8.0                     |                                               |
| Chemotherapy side-effects‡|     |                         |                                               |                         |                                               |                         |                                               |
| Laparoscopic         | 8.8 (7.2, 10.5)   | 13.8                    | −0.9 (−5.8, 4.0)                              | 6.8                     | −0.8 (−5.0, 3.5)                               | 2.7                     | 0 (−3.7, 3.6)                                 |
| Open                | 10.5 (7.3, 13.7)  | 13.5                    |                                               | 6.6                     |                                               | 1.3                      |                                               |
| Stoma-related problems‡|                |                         |                                               |                         |                                               |                         |                                               |
| Laparoscopic         | −                  | 30.6                    | −1.0 (−6.7, 4.7)                              | 25.2                    | −4.8 (−11.0, 1.4)                              | 27.5                    | −13 (9.4, 6.7)                                |
| Open                | −                  | 31.6                    |                                               | 30.0                    |                                               | 28.8                     |                                               |

Values in parentheses are 95 per cent confidence intervals. *Only six patients had a stoma before surgery. Values at 4 weeks, 6 months and 12 months are mean scores instead of mean change in score. †A high value is positive to the patient; ‡a high value is negative to the patient. GI, gastrointestinal.

Statistical analysis

Because the study was piggy-backed on to a randomized trial with power calculated for the primary endpoint, no power calculation was performed for the HRQL component. Missing data were handled as instructed in the EORTC scoring manual. All statistical analysis of demographic data, relevant clinical outcome measures and differences between study groups was carried out using SPSS® 20 software (IBM, Armonk, New York, USA).

Comparisons of groups at baseline were made using Student’s t test, χ² test and, where appropriate, Fisher’s exact test. EQ-5D™ global health was analysed at each assessment by means of the independent t test and repeated-measurement ANOVA was used for analysis over time. Proportions of patients reporting each level of the five dimensions were analysed by χ² test or Fisher’s exact test. As few patients reported problems at level 3 (severe problems), levels 2 and 3 were pooled in most analyses. QLQ-C30 and QLQ-CR38 global quality-of-life, functional and symptom scales were analysed using ANCOVA with baseline (preoperative score) as a co-variable and surgical procedure as a factor. The results are presented as mean changes, adjusted for baseline, with 95 per cent confidence intervals.

All statistical analyses were carried out on the basis of intention to treat. P < 0.050 was considered statistically significant. Owing to the explorative nature of this study, significant P values should be interpreted with care, and considered as interesting findings rather than conclusive evidence.

Results

The COLOR II trial included 1103 patients between 2004 and 2010. In all, 617 patients were eligible for the HRQL study (Fig. 1). Thirty-three patients were excluded from the COLOR II trial after randomization as they did not conform to the inclusion criteria, and another 199 were primarily eligible but were not included owing to logistical difficulties in retrieving preoperative HRQL data, organizing preoperative radiation, language difficulties, patients’ cognitive disabilities or lack of consent. Thus, 385 patients were included in the study (260 laparoscopic and 125 open). The included patients had a lower American Society of Anesthesiologists grade and fewer had undergone preoperative radiation compared with
eligible patients who were not included. Basic demographic characteristics and clinical data did not differ between the laparoscopic and open groups (Table 1).

The intention was to analyse the change in HRQL from baseline (preoperative data) over time and compare the groups. Analysis of stoma-related problems was therefore excluded from this part of the study. The actual results at 4 weeks, 6 months and 12 months regarding these problems, with comparisons between groups, are presented, but for obvious reasons without comparison with preoperative data (see Table 5).

Compliance in answering the questionnaires was generally around 90 per cent at baseline and diminished over time to around 80 per cent at 12 months (Fig. 1). The compliance for EQ-5D™ was lower than this in the open group, being around 80 per cent at baseline and 70 per cent at 12 months. Compliance with the EQ-5D™ global health part was lower than for EQ-5D™ dimensions or EORTC questionnaires. For EORTC QLQ-C30 and QLQ-CR38 the answer rates were between 88 and 85 per cent at 4 weeks and 6 months, and 76–78 per cent at 12 months.

There were no significant differences between the two groups at any time in overall health measured by EQ-5D™ (Table 2), nor was the repeated-measurement analysis significant \( (P = 0.171–0.966) \). Regarding the five dimensions, the only significant difference was in ‘daily activity’; a higher proportion of patients in the open group reported problems before treatment (level 2–3) (Table 3).

HRQL measured by the cancer-specific EORTC QLQ-CR30 showed no statistically significant differences between groups in any dimension (global quality of life, five functional scales and three symptom scales) either before, or 4 weeks, 6 months and 12 months after surgery (Table 4). There were changes in most functional scales and symptoms between baseline and 4 weeks after surgery within both treatment groups. Global quality of life was restored by 12 months after both types of surgery, as were scores on most functional scales and symptoms, whereas emotional function had improved by 12 months.

There were no differences between groups in EORTC QLQ-CR38 data at any time point measured (Table 5). Future perspective scores improved over time in both groups, with no difference between the two surgical techniques.

Discussion

This study has shown no difference in the changes to HRQL within 12 months after laparoscopic and open surgery for rectal cancer. It is important to evaluate what constitutes a clinically significant difference. In regard to EORTC QLQ-C30, several studies have examined the minimal important change (MID) implicating a change that is clinically meaningful to the patient. Osoba\(^{17}\) has suggested that the MID is in the range of 5–10 points on the 100-point scale, whereas over 20 points indicates a substantial change. In the present study, the changes reported for most functional scales and symptoms, in both the EORTC QLQ-C30 and QLQ-C38, were substantial or moderate after 4 weeks, and gradually diminished over time. All results were within narrow confidence intervals, which supports the validity of the results, and also excludes any ‘clinically relevant’ differences between the groups.

Physical functioning, role functioning, social function and fatigue measured by QLQ-C30 showed substantial deterioration 4 weeks after surgery. All of these functional/symptom scales improved after 6 months and were fully recovered at 12 months. The time frame differed from that in laparoscopic surgery for colonic cancer, where physical function and role function were reduced after 2 weeks, but partially recovered within 4–6 weeks\(^{12}\). It appears that patients with rectal cancer require a longer time to recover after curative surgery.

There was a selection bias in the present study cohort as participants were somewhat healthier in general than the entire COLOR II trial cohort. This could be the result of logistics related to radiotherapy treatment. For patients with a high level of co-morbidity the ability and/or inclination to answer questionnaires might be reduced. This was, however, true for both groups and the authors suggest that the lack of difference between laparoscopic and open surgery is valid.

There is no obvious explanation for the difference in compliance between the laparoscopic and open groups at baseline (Fig. 1). It is also intriguing that the compliance varied for the different instruments as they were sent out as a complete booklet at each time point. In particular, compliance in completion of EQ-5D™ at baseline differed, with lower compliance in the open group. The trial was not blinded so the patients were aware of which technique they had been randomized to. It could be speculated that, having agreed to participate in a randomized trial testing a new and presumably less invasive surgical technique, patients would be more ‘positive’ to the new technique and so those randomized to laparoscopy would also comply with the demands of this substudy. Baseline clinical data in the two groups were similar and, if the difference in compliance had represented a systematic difference in recruitment, differences in the results would have been expected. It is therefore argued that this difference most probably arose by chance.

HRQL assessment is important when evaluating new treatments. Patients today have a longer life expectancy,
and the overall improved results of rectal cancer treatment, with 5-year survival rates of more than 60 per cent, indicate that there will be many survivors. The present results are therefore of interest as they reflect patients’ experience after rectal cancer surgery. As the surgical technique resulted in no difference in HRQL, other factors, such as reduction in the risk of small bowel obstruction\textsuperscript{18,19} or the amount of perioperative bleeding or postoperative pain\textsuperscript{20}, may influence the choice of surgical technique for rectal cancer.

The fact that HRQL after rectal cancer surgery is substantially reduced for a prolonged period is noteworthy, indicating the need for a high level of healthcare support for several months after operation. This is in agreement with the finding of Wilson and co-workers\textsuperscript{21}, who reported a substantial reduction of HRQL for several months after operation. This is in agreement with the finding of Wilson and co-workers\textsuperscript{21}, who reported that HRQL was impaired for up to 6 months after rectal cancer surgery. The present study showed clinically meaningful changes at 4 weeks after surgery, regardless of the surgical technique and for most functional scales, but these returned to, or were close to, preoperative values by 6 months. The findings in this HRQL study do not mirror the improved short-term clinical outcomes reported after laparoscopic colonic surgery, such as reduced pain and earlier restoration of bowel function. This could possibly be explained by the time points chosen for HRQL measurements, the first of the questionnaires being completed at 4 weeks after operation.

A previous study of patients who had surgery for inflammatory bowel disease found that body image was rated more highly after laparoscopic than open surgery\textsuperscript{22}. This was not demonstrated here and, although speculative, body image may have been less important to the older patients in this trial.

Acknowledgements

The authors are grateful to K. Ingles, E. Lindholm, K. Druhan (data manager), S. Skullman, Z. Läckberg, G. Kurlberg and M. Cuesta for their help with the study.

The HRQL study was supported by research grants from the Swedish Cancer Foundation (2010/593), Region Västra Götaland, Sahlgrenska University Hospital (ALF grant 138751, agreement concerning research and education of doctors) and the Alice Swenson Foundation. Ethicon EndoSurgery provided financial support for the administration of the COLOR II trial.

Disclosure: The authors declare no other conflict of interest.

References

1 Janson M, Lindholm E, Anderberg B, Haglind E. Randomized trial of health-related quality of life after open and laparoscopic surgery for colon cancer. \textit{Surg Endosc} 2007; 21: 747–753.

2 Weeks J, Nelson H, Gelber S, Sargent D, Schroeder G; Clinical Outcomes of Surgical Therapy (COST) Study Group. Short-term quality-of-life outcomes following laparoscopic-assisted colectomy vs open colectomy for colon cancer: a randomized trial. \textit{JAMA} 2002; 287: 321–328.

3 Fucini C, Gattai R, Urena C, Bandettini L, Elbetti C. Quality of life among five-year survivors after treatment for very low rectal cancer with or without a permanent abdominal stoma. \textit{Ann Surg Oncol} 2008; 15: 1099–1106.

4 Kasparek MS, Hassan I, Cima RR, Larson DR, Gullerud RE, Wolff BG. Quality of life after coloanal anastomosis and abdominoperineal resection for distal rectal cancers: sphincter preservation vs quality of life. \textit{Colorectal Dis} 2011; 13: 872–877.

5 Gervaz P, Bucher P, Konrad B, Morel P, Beyeler S, Lataillade L \textit{et al.}. A prospective longitudinal evaluation of quality of life after abdominoperineal resection. \textit{J Surg Oncol} 2008; 97: 14–19.

6 Li J, Chen R, Xu YQ, Wang XC, Zheng S, Zhang SZ \textit{et al.}. Impact of a laparoscopic resection on the quality of life in rectal cancer patients: results of 135 patients. \textit{Surg Today} 2010; 40: 917–922.

7 Buunen M, Bonjer HJ, Hop WC, Haglind E, Kurlberg G, Rosenberg J \textit{et al.}; Color II Study Group. COLOR II. A randomized clinical trial comparing laparoscopic and open surgery for rectal cancer. \textit{Dan Med Bull} 2009; 56: 89–91.

8 EuroQol Group. \textit{EQ-5D-3 L Translations}, 2011. http://www.euroqol.org/eq-5d/eq-5d-products/eq-5d-3l-translations.html [accessed 1 January 2013].

9 Brooks R, Charro F, Rabin R. \textit{The Measurement and Valuation of Health Status Using EQ-5D: a European Perspective}. Kluwer Academic Publishers: Dordrecht, 2003.

10 Hjermstad MJ, Fayers PM, Bjordal K, Kaasa S. Health-related quality of life in the general Norwegian population assessed by the European Organization for Research and Treatment of Cancer Core Quality-of-Life Questionnaire: the QLQ-C30 (+ 3). \textit{J Clin Oncol} 1998; 16: 1188–1196.

11 Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ \textit{et al.}. The European Organization for Research and Treatment of Cancer Core Quality-of-Life Questionnaire: the QLQ-C30 (+ 3). \textit{J Clin Oncol} 1993; 11: 311–321.

12 Bjordal K, Kaasa S. Psychometric validation of the EORTC Core Quality of Life Questionnaire, 30-item version and a diagnosis-specific module for head and neck cancer patients. \textit{Acta Oncol} 1992; 31: 311–321.

13 Schwarz R, Hinz A. Reference data for the quality of life questionnaire EORTC QLQ-C30 in the general German population. \textit{Eur J Cancer} 2001; 37: 1345–1351.

14 Michelson H, Bolund C, Nilsson B, Brandberg Y. Health-related quality of life measured by the EORTC QLQ-C30 – reference values from a large sample of Swedish population. \textit{Acta Oncol} 2000; 39: 477–484.

15 Scott NW, Fayers PM, Aaronson NK, Bottomley A, de Graeff A, Groenvold M \textit{et al.}; EORTC Quality of Life
Group; Quality of Life Cross-Cultural Meta-Analysis Group. The relationship between overall quality of life and its subdimensions was influenced by culture: analysis of an international database. *J Clin Epidemiol* 2008; 61: 788–795.

16 Sprangers MA, te Velde A, Aaronson NK. The construction and testing of the EORTC colorectal cancer-specific quality of life questionnaire module (QLQ-CR38). European Organization for Research and Treatment of Cancer Study Group on Quality of Life. *Eur J Cancer* 1999; 35: 238–247.

17 Osoba D. Interpreting the meaningfulness of changes in health-related quality of life scores: lessons from studies in adults. *Int J Cancer Suppl* 1999; 12: 132–137.

18 Angenete E, Jacobsson A, Gellerstedt M, Haglind E. Effect of laparoscopy on the risk of small-bowel obstruction: a population-based register study. *Arch Surg* 2012; 147: 359–365.

19 Burns EM, Currie A, Bottle A, Aylin P, Darzi A, Faiz O. Minimal-access colorectal surgery is associated with fewer adhesion-related admissions than open surgery. *Br J Surg* 2013; 100: 152–159.

20 van der Pas MH, Haglind E, Cuesta MA, Fürst A, Lacy AM, Hop WC et al.; COlorectal cancer Laparoscopic or Open Resection II (COLOR II) Study Group. Laparoscopic versus open surgery for rectal cancer (COLOR II): short-term outcomes of a randomised, phase 3 trial. *Lancet Oncol* 2013; 14: 210–218.

21 Wilson TR, Alexander DJ, Kind P. Measurement of health-related quality of life in the early follow-up of colon and rectal cancer. *Dis Colon Rectum* 2006; 49: 1692–1702.

22 Eshuis FJ, Slors JF, Stokkers PC, Sprangers MA, Ubbink DT, Cuesta MA et al. Long-term outcomes following laparoscopically assisted versus open ileocolic resection for Crohn’s disease. *Br J Surg* 2010; 97: 563–568.

If you wish to comment on this, or any other article published in the *BJS*, please visit the on-line correspondence section of the website (www.bjs.co.uk). Electronic communications will be reviewed by the Correspondence Editor and a selection will appear in the correspondence section of the Journal. Time taken to produce a thoughtful and well written letter will improve the chances of publication in the Journal.