Determinants of health-related quality of life in colon cancer patients include stoma and smoking habits, but not type of surgery

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Abstract

Background: Health-related quality of life (HRQoL) has gained increased attention in cancer care. Studies have shown that poor QoL might worsen the cancer related prognosis. The aim of this study was to investigate HRQoL in patients with colon cancer and to compare data with reference values from the general population in Sweden at diagnosis (baseline) and at six months of follow-up. Methods: This was a prospective population-based study of colon cancer patients from Västmanland County, Sweden, included between March 2012 and September 2016. HRQoL was measured using the cancer-specific EORTC QLQ-C30 questionnaire. Data on HRQoL was compared with Swedish population reference values. Multiple linear regression analysis adjusted for age, sex, body mass index (BMI), American Society of Anaesthesiology (ASA) physical status classification, emergency/elective surgery, and resection with/without a stoma and tumour stage (TNM), was used. Results: A total of 67% (376/561) of all incident colon cancer patients (196 [52.1%] females) were included. Mean (range) age was 73 (30-96) years. The univariate analysis showed that patients with colon cancer had worse QoL (8/15 parameters) compared with a Swedish reference population both at baseline and at 6 months follow-up. Furthermore, linear regression analysis showed that patients with more comorbidity (ASA 3 and 4), smokers and patients planned to be operated on with a stoma, were at higher risks for poor QoL than the other included patients. Conclusions: The reported determinants of HRQoL may be used to identify risk groups and enable individualized care for patients that need more support from health care.

Background

Colorectal cancer is the third most common cancer and the fourth most common cause of death worldwide [1], equally distributed between men and women. The incidence rates vary throughout the world, but colorectal cancer is mainly a disease of developed countries with a Western culture [2]. Survival has increased since the 1960s mainly because of improvements in early detection and treatment [3,4]. Recently, increased attention has been given to the cancer patient's health-related quality of life (HRQoL), because improved surgical and oncological treatments have prolonged the life expectancy of a significant number of patients.

A diagnosis of colon cancer has a major impact on the lives of patients. They have functional impairments and other adverse effects related to the cancer. Therefore, it is important to identify their needs and the major predictors of HRQoL.

The term 'HRQoL' is multifactorial and subjective [5] and therefore difficult to quantify. It refers to information about the patient's perceived physical, emotional and social functioning. The well-validated colorectal cancer-specific European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C30 (EORTC QLQ-C30) has been developed to capture cancer-specific symptoms and is widely used [6,7].
Several factors are known to be associated with HRQoL in patients with colorectal cancer, such as socio-demographic characteristics, treatment-related factors and lifestyle-related factors such as smoking, physical activity, diet and alcohol intake [8,9].

Many studies on colon cancer focus on short-term effects, i.e., they compare the effects on HRQoL of different treatments such as open versus laparoscopic surgery [10] or chemotherapy [11,12], which has been shown to reduce HRQoL early after treatment. In patients with advanced disease, fatigue seems to be the most damaging factor [13]. Long-term follow-up studies from Germany and the Netherlands that used EORTC QLQ-C30 reported that younger patients have more adverse symptoms than older patients [14,15].

Studies of HRQoL have been performed in colorectal cancer patients in several countries at a national level, but there are no data available for colon cancer patients in Sweden. Therefore, this study aimed to investigate the HRQoL in a well-defined population of patients with colon cancer at diagnosis and at the six-month follow-up, and to compare these data with those of a Swedish reference population. Further, we aimed to identify risk factors associated with poor reported outcomes for HRQoL in colon cancer survivors that could be used to support enhanced aftercare.

Methods

Study population

This was a prospective cohort study consisting of all patients diagnosed with colon cancer between March 2012 and September 2016 at Västmanland Hospital Västerås, Sweden. Västmanland is located about 100 km west of Stockholm and is a medium-sized Swedish county with approximately 270,000 inhabitants. Västmanland Hospital Västerås is the only hospital in the county that treats patients with colon cancer. Västmanland is considered representative of Swedish society because of its distribution of educational, income and employment levels, and urban and rural areas [16]. In total, 376 patients were enrolled in the study, representing 67% (376/561) of all incident colon cancer cases in the county (Fig. 1). All included patients provided written informed consent to participate. At the six-month follow-up, 20 patients had died and 34 did not return the questionnaire.

Measurements

Demographic and tumour stage characteristics

Clinical data for age (years), sex and tumour location were recorded. Body mass index (BMI) was calculated as an individual’s weight divided by their height squared, kg/m². The American Society of Anaesthesiology (ASA) physical status classification (1–4) was used as a surrogate marker for morbidity. We compared patients with less co-morbidity (ASA 1, 2) with patients with more co-morbidity (ASA 3, 4).
Pathological staging (tumour–node–metastasis, TNM) (I–IV) was recorded. We compared patients with metastases (TNM IV) with patients with non-metastatic disease (TNM I–III).

**Smoking status**

Patients were asked about their smoking habits (non-smoker, former smoker and current smoker). A former smoker was defined as having smoked during the previous 10 years. We compared current smokers with former and non-smokers.

**Treatment**

Both surgically and non-surgically treated patients were included. Patients entered the hospital through the emergency ward or were referred to the outpatient clinic (elective). Patients who were treated surgically underwent a right, left or total colectomy with (stoma w/resection) or without a stoma. Left-sided surgery included both left-sided and high-anterior resections. One group of patients were treated only with a stoma (stoma wo/resection).

**Data collection**

The data were collected prospectively before treatment using a predefined local quality registry form, and the information was compared with data from the Swedish Colon Cancer registry [17]. Decisions about treatment for individual patients were made in multidisciplinary meetings and followed the processes of the National Colorectal Cancer follow-up program.

Patients who agreed to participate were asked to complete the EORTC QLQ-C30 questionnaire at diagnosis and at the six-month follow-up. Inability to understand the questionnaire or severe illness were exclusion criteria (Fig. 1). The time window to complete the baseline form was within a month after diagnosis and before surgery or the start of palliative treatment. At the six-month follow-up, the QoL questionnaire was sent to all participating patients. Non-responders were mailed up to two reminder letters.

**HRQoL questionnaire**

The EORTC QLQ-C30 is a HRQoL questionnaire developed by the EORTC Quality of Life Study Group to assess quality of life in cancer patients in clinical trials [18]. It consists of 30 items comprising five functional scales (physical, role, emotional, cognitive and social) and three symptom scales (fatigue, nausea and vomiting and pain). Six single items are also included (dyspnoea, insomnia, appetite loss, constipation, diarrhoea and financial difficulties). The final two items in the questionnaire assess global health and overall QoL. Raw data were transformed to standardized scores ranging from 0 to 100 using
the EORTC scoring manual. A high score on the functional scale represents a high level of functioning (i.e., higher is better), whereas a high score on the symptom scale represents a high level of symptoms (i.e., lower is better). Differences in mean QoL scores >10 points were considered clinically meaningful [19].

The population reference values used in this study were downloaded from a Swedish reference study including a total of 4008 age-stratified individuals from a population-based registry (SEMA) born between 1918 and 1979 who completed the EORTC QLQ-C30 questionnaire who represented a random sample of the population in Sweden [20].

Statistical methods

Categorical data are presented as frequencies and percentages, \( n (\%) \), while ordinal and continuous data are given as means with accompanying standard deviations (SDs). Pearson’s \(^2\) test and Welch’s independent samples \( t \)-test were used for categorical and continuous variables, respectively, to evaluate the significance of differences in demographics, lifestyle and clinical risk factors between included and non-included patients. Tests of differences in HRQoL between the participating patients and a Swedish reference population were performed using Welch’s independent samples \( t \)-test separately for men and women. Sex-specific EORTC QLQ-C30 data for individuals aged 70–79 years reported by Michelson et al. [20] were used as the reference (standard). Tests of differences between patient data at baseline and follow-up were performed using Welch’s paired samples \( t \)-test.

The associations between demographics, lifestyle and clinical risk factors (independent variables) and the change in HRQoL from baseline to follow-up (dependent variable) were examined using separate complete-cases multiple linear regression analyses for each EORTC QLQ-C30 scale/item. Male sex, age (years), smoking, BMI (kg/m\(^2\)), ASA classification 1 or 2 (patients with fewer co-morbidities), emergency surgery, TNM stages I–III (patients with non-metastatic disease) and stoma (with resection, without resection or no stoma [reference]) were included as independent variables in the multiple regression analyses, together with the baseline values of the EORTC QLQ-C30 scale/item in question. Results from the linear regression analyses are presented as the coefficient (i.e., the coefficient of the slope giving the magnitude of the linear association between the independent and dependent variable) with accompanying 95% confidence intervals (CIs).

All statistical analyses were performed using IBM SPSS Statistics software (v. 24; IBM, Armonk, NY, USA), with \( P \)-values < 0.05 considered significant.

Results

The baseline characteristics of the colon cancer study population and the non-included patients are presented in Table 1. There were no major differences between included and non-included patients with respect to age, sex or BMI. The non-included patients had more co-morbidities and a more advanced
tumour stage (TNM). More included patients had undergone surgery and fewer received a stoma than in the non-included group.

Table 2 presents a comparison of HRQoL in the included colon cancer patients with that in a Swedish reference population [20]. In the colon cancer patients at baseline, there was a decrease in 11/15 and 10/15 parameters of HRQoL for men and women, respectively, compared with the Swedish reference population. At the six-month follow-up, men had less dyspnoea and less constipation and women had better role and emotional functioning and were less constipated compared with the respective sex in the Swedish reference population (Table 2). Except for a non-significant increase in pain in women, all other symptom scores were numerically higher in the colon cancer group than in the Swedish reference population (Table 2).

The univariate analysis of differences between status at baseline and status at the six-month follow-up showed that global health status and emotional function improved in both men and women, and that symptoms of constipation and appetite loss decreased. At the six-month follow-up, men had improved social function and decreased pain and insomnia, and women had less nausea/vomiting and diarrhoea (Table 2).

Multiple linear regression analyses (Table 3) showed that at baseline, patients whose planned surgery included a stoma (with or without resection) had a decrease in 4 of 5 functional scales, worse Global Health Status and significantly more symptoms (fatigue, nausea/vomiting and pain) as compared to patients not receiving a stoma. They also had a decrease in global QoL, more appetite loss and diarrhoea. Most of these changes persisted at the six-month follow-up in patients treated with a stoma without resection, while patients treated with a stoma with resection had worse social function (Table 2).

Table 4 shows the results of multiple linear regression analyses of the change in HRQoL in colon cancer patients from diagnosis to the six-month follow-up. Older patients had a greater improvement in role, emotional and physical function than younger patients. They also showed a greater decrease in fatigue, nausea/vomiting, appetite loss and diarrhoea between baseline and follow-up. Smokers had a greater deterioration in role, emotional and social function compared with other patients. They also had a greater increase in nausea/vomiting, diarrhoea symptoms and financial difficulties. Compared with those patients treated surgically without a stoma, patients treated with a stoma combined with colon resection had improved general health, while patients treated with a stoma without colon resection had increased levels of nausea/vomiting, pain, constipation and financial difficulties at the six-month follow-up compared with baseline. Type of surgery (right- or left-sided or total colectomy) did not influence HRQoL (data not shown).

**Discussion**

The EORTC QLQ-C30 questionnaire was used to investigate HRQoL in patients with colon cancer in this population-based study. The univariate analysis showed that patients with colon cancer had a worse HRQoL compared with a Swedish reference population both at baseline and at the six-month follow-up as
indicated by changed scores for 3/5 functional (role, emotional and social), and 4/9 symptom scales (fatigue, nausea/vomiting, appetite loss and diarrhoea). Furthermore, the major findings of this study, identified using linear regression analyses, were that patients whose planned surgery included a stoma (with or without resection), patients with more co-morbidities (ASA III and IV) and smokers were at higher risk of a lower HRQoL than the other included patients.

It is difficult to compare our findings with those of other studies that used a reference population because these vary in methodology and the reference values used [21]. However, consistent with our results, a study [22] of Finnish patients with colorectal cancer compared their data with reference data using the EORTC QLQ-C30 questionnaire, and found that pain, fatigue and financial difficulties were the main drivers of poor health. Another study conducted in Germany by Jansen et al. [14] also compared colorectal cancer patients with controls from the general population, and showed that diarrhoea and financial difficulties were worse in patients with colorectal cancer.

Several countries have assessed HRQoL in colon cancer patients, but only one randomized study comparing the effects of open and laparoscopic surgery in Sweden has been published [10]. Apart from that study, there is no published information regarding HRQoL in Swedish colon cancer patients.

Contradicting results have been presented regarding whether the presence of a stoma in surgically treated colorectal cancer patients has a negative effect on HRQoL. Most of these studies have been performed on patients with rectal cancer [23,24]. Of note, the patients in our study completed the questionnaire before they underwent surgery to create a stoma. This implies that it was the patients’ risk factors (as judged by the surgeon) or the advanced stage of their cancers that were related to the observed lower HRQoL in these patients. They might also have had poor expectations of life with a stoma, or it may have been that it was the information that they were to receive a stoma per se that contributed to their poor scores. Although this study included very few patients who were treated with a stoma alone, this group showed significantly worse functional scores and increased symptom scores compared with patients treated with a stoma plus colon resection. However, a recent study of colon cancer patients who answered questions postoperatively reported that 78% considered not having a permanent stoma as the most important factor analysed (76% stated that “being cured” was most important) [25].

This study found that HRQoL was not affected by whether the patients underwent right-sided, left-sided or total colectomy (data not shown), and that patients with an advanced tumour stage (TNM IV) did not have significantly worse HRQoL than other patients. However, 10 of the 14 patients who were treated with a stoma without resection had metastatic disease (TNM IV), and these patients had very low functional scores and high symptom scores, indicating worse HRQoL at both baseline and at the six-month follow-up.

Our study also found that younger patients had worse emotional and social functional QoL and more bowel problems (nausea/vomiting and diarrhoea) than older patients. This has also been observed by others and suggests that data presented for HRQoL should use age-matched groups [26,27].
In our study, co-morbidity as assessed by ASA grade had a negative impact on global QoL, physical function, fatigue, dyspnoea and constipation, both at baseline and at the six-month follow-up. These data are also consistent with the results of other studies of colorectal cancer and other cancer types such as head and neck, lung, and prostate cancer [28]. In breast cancer, the effect of co-morbidity explained most of the variance in nearly all subscales comparing demographic and clinical variables [29].

Our data also showed that patients with a higher BMI had worse physical function and more nausea and vomiting, pain and financial difficulties. This observation has also been reported by others [30]. Considering several different lifestyle factors, Schlesiger et al. [31] found that being non-obese had the strongest association with a high HRQoL, while another study reported decreased HRQoL in Dutch patients with high BMI [30].

The present study also showed that smokers had worse QoL than other patients at the six-month follow-up compared with baseline. These data are consistent with the findings of studies of the general population [32] and of colorectal cancer patients [33]. It has also been reported that survivors of colon cancer and melanoma had higher age-adjusted smoking rates than survivors of other cancers [34].

The main strengths of this study were its prospective design and that it was population based. The patient data were compared with those from a Swedish reference population [20]. We also used one of the most widely used cancer-specific validated analysis instruments and analysed the data from non-included patients. In addition, we performed multiple regression analyses of medically important parameters, including lifestyle factors, such as BMI and smoking.

Analysis of data from the non-included patients showed that these had higher co-morbidity, were less often treated surgically, had more advanced-stage tumours and where surgical treatment more often included stoma creation. Thus, presumably if these patients had been included, our results would have shown a worse outcome for HRQoL because these non-included patients had risk factors for lower HRQoL [35]. However, a possible limitation is that some patients were too ill to complete the questionnaire, implying a possible selection bias.

Other limitations were that this was a single-centre study, the reference data for the Swedish general population were from 2000 [20] and we did not measure social and psychological factors known to influence HRQoL [36]. A small study by Siassi et al. [37] showed that personality affects HRQoL more than clinical variables after major surgery. A study of Turkish colorectal cancer patients demonstrated a clear association between anxiety/depression symptoms and HRQoL [38]. We did not include data on the effect of chemotherapy, but others have shown that it is a major factor affecting HRQoL [12,15].

**Conclusion**

In conclusion, this study showed that at baseline, many colon cancer patients have low HRQoL compared with that of a reference population, but that HRQoL improved at the six-month follow-up. We identified several risk groups: i.e., younger patients, patients with higher BMI, smokers and patients who underwent
planned stoma surgery. These patients need enhanced support and identifying them would enable targeted early intervention and development of methods to facilitate rehabilitation, which could in turn enhance their HRQoL.

**Abbreviations**

HRQoL: Health-related quality of life, BMI: body mass index, ASA: American Society of Anaesthesiology, TNM: tumour-node–metastasis.

**Declarations**

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*Availability of data and materials*

Any request for data and materials should be made in writing to the corresponding author, and these will be considered.

*Authors' contributions*

Conception and design: CT, KS, AR. Collection and assembly of data: CT, ES. Analysis and interpretation: CT, AR. Manuscript writing: CT, AR, KS. All authors read and approved the final manuscript.

*Ethical approval and consent to participate*

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable standards. The study was approved by the Regional Ethics Committee of Uppsala University (Dnr 2011/417). Clinical trials ID: NCT 03910894.

Informed consent was obtained from all individual participants included in this study.

*Consent for publication*

Not applicable.

*Competing interests*
The authors declare that they have no competing interests.

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Tables

Table 1. Descriptive characteristics for HRQoL study group (n = 376) and those not included (n = 185).

| Variable                          | Included (n = 376) | Not included (n = 185) | P-value |
|-----------------------------------|-------------------|------------------------|---------|
|                                   | Value             | Missing, n (%)         | Value   | Missing, n (%) |       |
| Male sex, n (%)                  | 180 (47.9)        | -                      | 89 (48.1)| 0.858          |
| Age (years), mean (SD)           | 73.3 (10.9)       | -                      | 73.6 (13.2)| 0.777          |
| Current smoker, n (%)            | 34 (9)            | 16 (4.3)               | 12 (6.5) | 55 (29.7)      | -      |
| BMI (kg/m²), mean (SD)           | 26.6 (4.37)       | 4                      | 25.8 (5.60)| 11             | 0.120 |
| ASA level, n (%)                 |                   |                        |         |                |        |
| - 1                               | 43 (11.4)         | 10 (5.5)               | 4       | <0.001         |
| - 2                               | 186 (49.5)        | 76 (42.0)              | <0.001  |
| - 3                               | 134 (35.6)        | 78 (43.1)              |         |
| - 4                               | 143 (3.5)         | 17 (9.4)               |         |
| Operated, n (%)                  | 343 (91.2)        | -                      | 135 (73.0)| <0.001         |
| Acute surgery (%)                | 190 (50.5)        | -                      | 94 (50.8)| 0.634          |
| Operation type                   |                   |                        |         | <0.001         |
| - None                            | 49 (13.0)         | 75 (40.5)              |         |
| - Right sided operation          | 190 (50.5)        | 59 (31.9)              |         |
| - Left sided operation           | 119 (31.6)        | 36 (19.5)              |         |
| - Colectomy                      | 18 (4.8)          | 14 (7.6)               |         |
| - Laparotomy                     | 0                 | 1 (0.5)                |         |
| Stoma                            |                   |                        |         | <0.001         |
| - Yes, with resection            | 87 (23.1)         | 51 (27.6)              |         |
| - Yes, without resection         | 15 (4.0)          | 28 (15.1)              |         |
| - No                             | 274 (72.9)        | 106 (57.3)             |         |
| TNM stadium, n (%)               |                   |                        |         | <0.001         |
| - 1                              | 38 (10.1)         | 20 (10.8)              |         |
| - 2                              | 155 (41.2)        | 45 (24.3)              |         |
| - 3                              | 130 (34.6)        | 40 (21.6)              |         |
| - 4                              | 53 (14.1)         | 79 (42.7)              |         |
| - x                              | 1                 | 0                      |         |

Table 2. Comparison of the included colon cancer patient’s HRQoL with Swedish reference population (standard) at baseline and six months follow-up, univariate analyses.
| Scale                      | n  | Mean (SD) | n  | Mean (SD) | Pstandard | n  | Mean (SD) | Pstandard | n  | Mean (SD) | Pdiff |
|----------------------------|----|-----------|----|-----------|-----------|----|-----------|-----------|----|-----------|-------|
| **Global health status**   |    |           |    |           | <0.001    |    |           |           |    |           |       |
| **Functional scales**      |    |           |    |           |           |    |           |           |    |           |       |
| **Physical functioning**   | 224| 81.6 (22.7)| 178| 79.0 (20.8)| 0.232     | 130| 80.5 (18.5)| 0.629     | 129| 0.083     |
| **Role functioning**       | 224| 82.6 (29.7)| 178| 67.2 (34.7)| <0.001    | 130| 72.7 (31.4)| 0.004     | 129| 0.577     |
| **Emotional functioning**  | 223| 88.2 (17.3)| 178| 74.7 (21.1)| <0.001    | 132| 81.1 (22.3)| 0.002     | 131| 0.006     |
| **Cognitive functioning**  | 228| 85.2 (16.9)| 178| 85.3 (17.3)| 0.954     | 132| 83.1 (20.4)| 0.313     | 131| 0.074     |
| **Social function**        | 230| 89.1 (21.1)| 178| 77.9 (25.0)| <0.001    | 132| 73.3 (28.9)| <0.001    | 131| 0.020     |
| **Symptom scales/items**   |    |           |    |           |           |    |           |           |    |           |       |
| **Fatigue**                | 227| 21.5 (23.1)| 178| 39.0 (25.7)| <0.001    | 132| 33.7 (24.0)| <0.001    | 131| 0.350     |
| **Nausea and vomiting**    | 234| 2.5 (10.0)| 178| 9.5 (18.4)| <0.001    | 132| 5.6 (12.5)| 0.017     | 131| 0.527     |
| **Pain**                   | 226| 19.2 (25.0)| 178| 23.0 (26.9)| 0.144     | 132| 14.8 (22.2)| 0.084     | 131| 0.013     |
| **Dyspnoea**               | 232| 23.7 (29.4)| 178| 29.2 (29.8)| 0.062     | 130| 27.4 (26.4)| 0.216     | 129| 0.525     |
| **Insomnia**               | 231| 11.8 (22.5)| 178| 26.7 (29.7)| <0.001    | 132| 21.0 (29.8)| 0.002     | 131| 0.017     |
| **Appetite loss**          | 233| 2.7 (11.9)| 178| 21.2 (32.2)| <0.001    | 132| 10.9 (23.8)| <0.001    | 131| 0.036     |
| **Constipation**           | 234| 6.7 (17.7)| 178| 12.8 (25.6)| 0.007     | 131| 6.4 (16.6)| 0.855     | 129| 0.049     |
| **Diarrhoea**              | 231| 4.2 (13.1)| 177| 24.1 (31.2)| <0.001    | 131| 18.6 (24.9)| <0.001    | 130| 0.422     |
| **Financial difficulties** | 230| 5.4 (16.0)| 175| 6.5 (18.5)| 0.539     | 132| 8.8 (23.6)| 0.138     | 129| 0.015     |
| Women | Scale                        | n     | Mean (SD) | Baseline Vås | P<sup>b</sup>  | n     | Mean (SD) | Follow-up | P<sup>c</sup> | n<sup>d</sup> | P<sup>e</sup> |
|-------|-----------------------------|-------|-----------|--------------|----------------|-------|-----------|-----------|---------------|-------------|--------------|
|       | Global health status        | 285   | 69.9 (25.0) | 192          | 59.2 (22.9)    | <0.001 | 157       | 66.5 (23.7) | 0.152         | 153         | 0.001        |
|       | Functional scales           |       |           |              |                |        |           |           |               |             |              |
|       | Physical functioning        | 283   | 74.2 (23.6) | 190          | 72.0 (21.0)    | 0.296  | 157       | 73.6 (20.9) | 0.010         | 151         | 0.477        |
|       | Role functioning            | 280   | 80.4 (29.6) | 191          | 67.9 (32.6)    | <0.001 | 156       | 72.8 (29.7) |              |             |              |
|       | Emotional functioning       | 277   | 80.4 (22.0) | 192          | 69.0 (22.6)    | <0.001 | 156       | 76.9 (23.6) | 0.133         | 153         | <0.001       |
|       | Cognitive functioning       | 282   | 85.6 (19.5) | 192          | 81.3 (22.2)    | 0.032  | 157       | 81.6 (23.9) | 0.077         | 153         | 0.686        |
|       | Social functioning          | 272   | 89.9 (21.3) | 191          | 76.8 (24.5)    | <0.001 | 157       | 75.4 (28.4) | <0.001        | 152         | 0.406        |
|       | Symptoms/scales/items       |       |           |              |                |        |           |           |               |             |              |
|       | Fatigue                     | 285   | 28.2 (25.0) | 192          | 39.7 (25.3)    | <0.001 | 157       | 36.0 (26.4) | 0.003         | 153         | 0.265        |
|       | Nausea and vomiting         | 298   | 3.7 (12.4)  | 192          | 9.5 (18.4)     | <0.001 | 157       | 6.8 (26.4)  | 0.038         | 153         | 0.033        |
|       | Pain                        | 280   | 26.7 (30.5) | 192          | 24.9 (28.7)    | 0.518  | 157       | 22.5 (29.0) | 0.155         | 153         | 0.448        |
|       | Dyspnoea                    | 295   | 22.3 (27.5) | 189          | 22.9 (26.5)    | 0.802  | 156       | 20.1 (26.1) | 0.401         | 149         | 0.456        |
|       | Insomnia                    | 295   | 26.4 (31.2) | 191          | 30.1 (31.6)    | 0.216  | 156       | 34.6 (32.1) |              |             |              |
|       | Appetite loss               | 299   | 7.4 (18.5)  | 191          | 27.2 (32.5)    | <0.001 | 155       | 16.8 (27.5) | <0.001        | 151         | <0.001       |
|       | Constipation                | 298   | 8.6 (19.6)  | 190          | 16.7 (29.6)    | <0.001 | 155       | 11.2 (23.2) | 0.238         | 150         | 0.014        |
|       | Diarrhoea                   | 287   | 5.0 (14.8)  | 187          | 24.4 (31.0)    | <0.001 | 155       | 20.0 (27.3) | <0.001        | 147         | 0.046        |
|       | Financial difficulties      | 284   | 8.1 (21.2)  | 192          | 8.0 (21.1)     | 0.954  | 155       | 9.7 (25.5)  | 0.512         | 151         | 0.160        |

<sup>a</sup> Values in the standard population were from sex-specific data for ages 70-79 years given by Michelson et al. (2000)

<sup>b</sup> P-values for difference between values at baseline and values in the standard population.

<sup>c</sup> P-values for difference between values at follow-up and values in the standard population.

<sup>d</sup> Number of individuals with answers at both baseline and follow-up.

<sup>e</sup> P-values for difference between values at baseline and follow-up.

Table 3. Multiple linear regression analysis of HRQoL of patients with stoma with or without colon resection at baseline and at 6 months follow-up, according to stoma status before operation, adjusted for age, sex, BMI,
smoking, ASA classification, acute/elective surgery, and TNM stadium.

| Scale                           | Baseline Stoma with resection (n=89)a | Baseline Stoma without resection (n=14)a | 6 months follow-up Stoma with resection (n=68)a | 6 months follow-up Stoma without resection (n=4)a |
|---------------------------------|--------------------------------------|------------------------------------------|-----------------------------------------------|-----------------------------------------------|
|                                 | β         | P         | β         | P         | β         | P         | β         | P         |
| Global health status            | -7.4      | 0.014     | -22.5     | 0.002     | 1.39      | 0.690     | -23.4     | 0.091     |

Functional scales

- Physical functioning: -6.2, 0.015, -25.0, <0.001, -4.33, 0.140, -20.5, 0.077
- Role functioning: -14.0, 0.002, -39.2, <0.001, -0.67, 0.884, -30.9, 0.148
- Emotional functioning: -7.6, 0.011, -8.6, 0.219, -5.74, 0.095, -29.0, 0.033
- Cognitive functioning: -2.4, 0.384, -3.1, 0.632, -5.62, 0.095, -38.7, 0.004
- Social function: -9.7, 0.004, -9.8, 0.229, -10.4, 0.013, -50.0, 0.002

Symptom scales/items

- Fatigue: 10.5, 0.002, 10.7, 0.183, 2.40, 0.519, 25.3, 0.092
- Nausea and vomiting: 6.1, 0.005, 9.5, 0.065, 3.12, 0.132, 43.5, <0.001
- Pain: 7.8, 0.037, 21.8, 0.013, 1.65, 0.673, 62.0, <0.001
- Dyspnoea: 0.49, 0.893, 3.6, 0.671, -2.10, 0.592, 7.13, 0.642
- Insomnia: 2.9, 0.505, 2.2, 0.823, 3.69, 0.449, 25.3, 0.190
- Appetite loss: 16.5, <0.001, 46.3, <0.001, 0.476, 0.901, 47.6, 0.002
- Constipation: -0.7, 0.861, -9.3, 0.287, -8.4, 0.007, 26.7, 0.028
- Diarrhoea: 1.0, 0.808, 24.8, 0.016, 2.67, 0.502, 17.3, 0.268
- Financial difficulties: 2.6, 0.343, 4.4, 0.488, 3.81, 0.299, 26.5, 0.068

Reference category: No stoma

Table 4. Results from multiple linear regression of change in QLQ from baseline to follow-up at 6 months. Adjusted for value of each scale at baseline. $\beta$ is the regression coefficient.
| Scale                                      | Global Health Status | Physical Function | Role Function |
|--------------------------------------------|----------------------|-------------------|---------------|
| Male sex                                  | 0.79(-4.41;5.99)     | 0.765             | 0.191         |
| Age (years)                                | 0.10(-0.19;0.38)     | 0.511             | 0.293         |
| Smoker                                    | -6.0(-15.0;2.9)      | 0.184             | 0.072         |
| BMI (kg/m²)                                | -0.34(-0.94;0.26)    | 0.260             | 0.040         |
| ASA 1-2                                    | 5.5(-0.42;11.4)      | 0.069             | 0.579         |
| Acute                                     | 2.5(-2.67;7.62)      | 0.345             | 0.904         |
| TNM 1-III                                  | 1.7(-7.22;10.66)     | 0.705             | 0.969         |
| Stoma w/ resection                        | 6.6(0.051;13.1)      | 0.048             | 0.843         |
| Stoma wo/ resection                        | -6.4(-32.0;19.2)     | 0.624             | 0.983         |

| Scale                                      | Emotional Function | Cognitive Function | Social Function |
|--------------------------------------------|--------------------|--------------------|-----------------|
| Male sex                                  | 1.83(-3.20;6.85)   | 0.474              | 0.890           |
| Age (years)                                | 0.32(0.038;0.598)  | 0.026              | 0.270           |
| Smoker                                    | -9.5(-18.0;9.0)    | 0.030              | 0.101           |
| BMI (kg/m²)                                | -0.17(-0.74;0.40)  | 0.562              | 0.073           |
| ASA 1-2                                    | 4.6(-1.0;10.2)     | 0.107              | 0.715           |
| Acute                                     | 0.89(-4.02;5.80)   | 0.722              | 0.263           |
| TNM 1-III                                  | -3.7(-12.2;4.85)   | 0.395              | 0.638           |
| Stoma w/ resection                        | -1.1(-7.28;10.17)  | 0.730              | 0.226           |
| Stoma wo/ resection                        | -14.2(-38.5;10.17) | 0.253              | 0.005           |

| Scale                                      | Fatigue            | Nausea Vomiting    | Pain |
|--------------------------------------------|--------------------|--------------------|------|
| Male sex                                  | -1.63(-7.26;4.00)  | 0.570              | 0.630|
| Age (years)                                | -0.35(-0.66;-0.03) | 0.028              | 0.011|
| Smoker                                    | 9.33(-0.49;19.2)   | 0.063              | 0.009|
| BMI (kg/m²)                                | 0.23(-0.42;0.88)   | 0.481              | 0.016|
| ASA 1-2                                    | -6.27(-12.7;0.145) | 0.055              | 0.946|
| Acute                                     | 2.45(-3.13;8.04)   | 0.388              | 0.491|
| TNM 1-III                                  | -9.03(-18.8;0.70)  | 0.069              | 0.480|
| Stoma w/ resection                        | -2.26(-9.35;4.84)  | 0.532              | 0.538|
| Stoma wo/ resection                        | 9.92(-17.7;37.5)   | 0.479              | <0.001|

| Scale                                      | Dyspnoea           | Insomnia           | Appetite loss |
|--------------------------------------------|--------------------|--------------------|---------------|
| Male sex                                  | 3.75(-2.11;9.62)   | 0.209              | 0.001         |
| Age (years)                                | -0.26(-0.59;0.06)  | 0.110              | 0.124         |
| Smoker                                    | 2.42(-7.85;12.7)   | 0.643              | 0.139         |
| BMI (kg/m²)                                | 0.58(-0.12;12.7)   | 0.103              | 0.127         |
| ASA 1-2                                    | -6.6(-13.5;0.27)   | 0.060              | 0.646         |
| Acute                                     | -4.78(-10.6;1.05)  | 0.108              | 0.253         |
| TNM 1-III                                  | -5.78(-15.8;4.27)  | 0.259              | 0.446         |
| Stoma w/ resection                        | -3.47(-10.8;3.86)  | 0.352              | 0.984         |
| Stoma wo/ resection                        | 6.34(-21.8;34.5)   | 0.658              | 0.678         |

| Scale                                      | Constipation       | Diarrhoea          | Financial    |
|--------------------------------------------|--------------------|--------------------|--------------|
| Male sex                                  |                    |                    |              |
| Age (years)                                |                    |                    |              |
| Smoker                                    |                    |                    |              |
| BMI (kg/m²)                                |                    |                    |              |
| ASA 1-2                                    |                    |                    |              |
| Acute                                     |                    |                    |              |
| TNM 1-III                                  |                    |                    |              |
| Stoma w/ resection                        |                    |                    |              |
| Stoma wo/ resection                        |                    |                    |              |
| Scale                      | $\beta$ (95% CI) | $P$  | $\beta$ (95% CI) | $P$  | $\beta$ (95% CI) | $P$  |
|----------------------------|------------------|------|------------------|------|------------------|------|
| Male sex                   | -2.4(-7.02;2.74) | 0.389| -0.064(-11.0;1.59) | 0.143| -0.4(-5.02;4.21) | 0.863|
| Age (years)                | -0.26(-0.5;-0.011) | 0.060| -0.53(-0.88;-0.183) | 0.003| -0.17(-0.43;0.087) | 0.194|
| Smoker                     | 1.81(6.59;10.2)  | 0.671| 14.0(3.21;24.9)   | 0.011| 8.5(0.42;16.6)   | 0.039|
| BMI (kg/m$^2$)             | -0.052(-0.61;0.508) | 0.856| 0.49(0.23;1.22)   | 0.180| 0.54(0.006;1.07) | 0.048|
| Smoker                     | 1.81(6.59;10.2)  | 0.671| 14.0(3.21;24.9)   | 0.011| 8.5(0.42;16.6)   | 0.039|
| ASA 1-2                    | -5.60(-11.1;-0.066) | 0.047| -4.0(-11.1;3.01)  | 0.260| 0.48(-3.33;7.08) | 0.480|
| Acute                      | 3.15(1.66;7.95)  | 0.198| -3.0(-9.23;3.14)  | 0.333| -1.59(-6.13;2.96)| 0.493|
| TNM 1-III                  | 2.87(-5.43;11.1) | 0.497| 3.09(-7.96;14.1)  | 0.582| -0.13(-8.02;7.76)| 0.974|
| Stoma w/ resection         | -8.38(-14.4;-2.33) | 0.007| 4.15(-3.68;11.9)  | 0.298| -0.05(-5.77;5.67)| 0.986|
| Stoma wo/ resection        | 24.6(1.41;47.9)  | 0.038| -18.0(-53.6;17.5) | 0.319| 28.6(6.53;50.7)  | 0.011|

**Figures**
Figure 1

Flow chart of study patients diagnosed with colon cancer at baseline and at the six-month follow-up.