Enteric physiology, neuropathology, and bowel function following colorectal resections in adults and children

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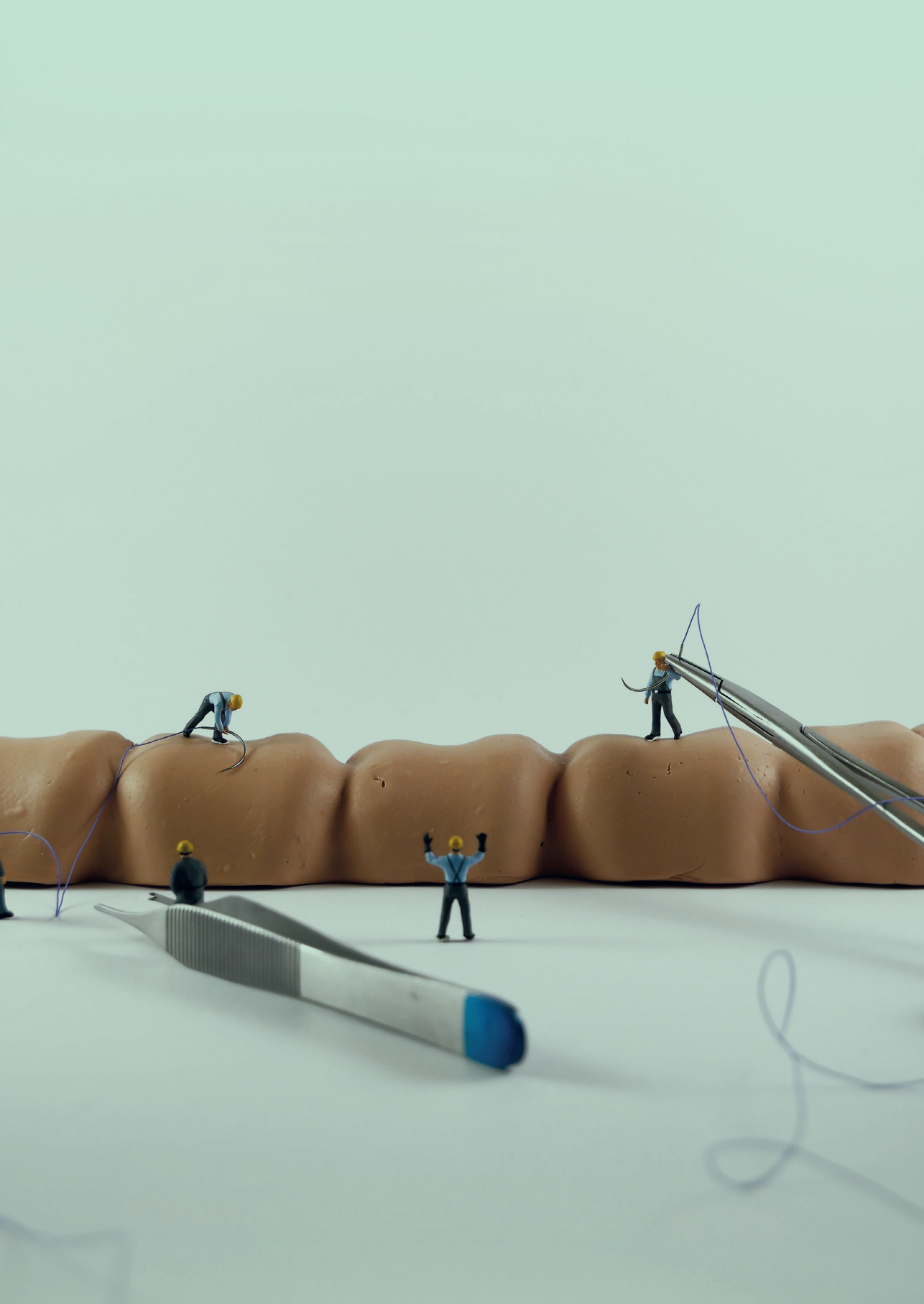

Video abstract

Chapter 10

Long-term bowel dysfunction and decline in quality of life following surgery for colon cancer: call for personalized screening and treatment

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Abstract

Background
Differences in long-term outcomes regarding types of colon resections are inconclusive, precluding preoperative patient counseling and effective screening and personalized treatment of postoperative bowel dysfunction during follow-up.

Objective
To compare long-term bowel function and quality of life in patients who underwent right or left hemicolectomy, or sigmoid colon resection.

Design
A multicenter cross-sectional study.

Settings
Seven Dutch hospitals participated.

Patients
Included patients underwent right or left hemicolectomy, or sigmoid colon resection without construction of a permanent stoma between 2009 and 2015. Deceased, mentally impaired, or patients living abroad were excluded. Eligible patients were sent the validated Defecation and Fecal Continence and Short-Form 36 questionnaires.

Main outcome measures
Constipation, fecal incontinence (both Rome IV criteria), separate bowel symptoms, and generic quality of life were assessed.

Results
Included were 673 right hemicolectomy, 167 left hemicolectomy, and 284 sigmoid colon resection patients. Median follow-up was 56 months (IQR 41-80). Sigmoid colon resection increased the likelihood of constipation compared to right and left hemicolectomy (ORs, 2.92, 95%CI,1.80-4.75, $p<0.001$ and 1.93, 95%CI,1.12-3.35, $p=0.019$). Liquid incontinence and fecal urgency increased following right hemicolectomy compared to sigmoid colon resection (ORs, 2.15, 95%CI,1.47-3.16, $p<0.001$ and 2.01, 95%CI,1.47-2.74, $p<0.001$). Scores on quality of life domains were significantly lower following right hemicolectomy.

Limitations
Due to the cross-sectional design, longitudinal data is still lacking.

Conclusions
Different long-term bowel function problems occur following right or left hemicolectomy, or sigmoid colon resection. The latter seems to be associated with more constipation than right or left hemicolectomy. Liquid incontinence and fecal urgency seem to be associated with right hemicolectomy, which may explain the decline in physical and mental generic quality of life of these patients.

Introduction

Worldwide, more than one million patients are diagnosed with colonic cancer every year.[1] Developments in surgical techniques and adjuvant chemotherapy regimens resulted in a current five-year survival rate of 64%.[2] This implies that the long-term effects of surgery for colon cancer are becoming important to a growing number of people.

The three most commonly performed resections for colon cancer, depending on the location of the tumor, are right hemicolectomy, left hemicolectomy, and sigmoid colon resection. A recent meta-analysis emphasized the magnitude of both constipation-associated and fecal incontinence-associated symptoms following surgery for colon cancer.[3] More detailed knowledge of the long-term presence of specific bowel symptoms after the three different types of colectomies would not only enhance tailored preoperative patient counseling but would also provide the clinician with practical indications for more direct screening and personalized treatment during regular follow-up.

Extreme heterogeneity of the available studies, small cohorts, and the use of many non-validated bowel function scores previously precluded comparison of the different types of colon resections.[3] Such knowledge could possibly improve our understanding of the functioning of different parts of the colon.

The hypothesis was that sigmoid colon resection will lead to more constipation given previous reports on difficult emptying and/or straining.[4,5] Patients who underwent right hemicolectomy are expected to suffer frequently from diarrhea or loose stools,[6] possibly predisposing them to fecal incontinence. Given the negative influence of constipation and/or fecal incontinence on generic quality of life,[7,8] there may also be differences in generic quality of life. The aims of this study were therefore to determine and compare long-term bowel function and generic quality of life between patients who had undergone right hemicolectomy, left hemicolectomy, or sigmoid colon resection.

Materials & Methods

Study design

Between October 2017 and December 2019, this cross-sectional study was performed at seven Dutch hospitals. The mandatory Dutch ColoRectal Audit (DCRA) registry was searched for patients ≥18 years, without a previous colectomy, who had undergone either right hemicolectomy, left hemicolectomy, or sigmoid colon resection for colon cancer with curative intention between 2009-2015. Excluded were patients who had either died, were mentally impaired, had a permanent stoma, whose address was unknown, or who lived abroad.

Patients who had signed an informed consent form were invited to complete two validated questionnaires: the Defecation and Fecal Continence (DeFeC) questionnaire and the Short-Form (SF) 36 (Supplemental Digital Content 1).[9,10] A link to the digital questionnaires was provided, unless the patient preferred to receive a hard copy. The patient data were acquired by one investigator who screened all medical records. Adjuvant chemotherapy was administered according to one of the following standard regimens: FOLFOX, CAPOX, or Capecitabine as a single agent. Radiotherapy in the pelvic region had been administered mainly for previous prostate cancer. The Medical Ethical Review Board of University Medical Center Groningen approved the study (Approval code METc 2017/245) and it was performed in accordance with the guidelines on Strengthening the Reporting of Observational Studies in Epidemiology (STROBE).

Questionnaires

The DeFeC questionnaire contains questions from widely used scoring systems and criteria for various bowel function problems, for example, the Rome IV criteria for constipation and fecal incontinence, the symptoms of the LARS score, and the Bristol Stool Scale (Supplemental Digital Content 1).[11-13] The SF-36 is a generic quality of life questionnaire containing 36 questions covering eight domains. The scores range from 0 (bad quality of life) to 100 (good quality of life).[10]

Definitions

To be diagnosed with constipation according to the Rome IV criteria patients had to report ≥2 of the following symptoms: straining, lumpy or hard stools, incomplete defecation, anorectal blockage, manual maneuvers to facilitate defecation, and <3 spontaneous bowel movements per week.[11] Additionally, the regular use of laxatives had to be needed to loosen stool. Fecal incontinence was also defined according to the Rome IV criteria and included any involuntary loss of stool at least twice a month.[12] Besides, different subtypes of fecal incontinence were distinguished: soiling (loss of small amounts of feces), urge incontinence (unable to reach the toilet in time), solid

incontinence (loss of solid feces without urge), and liquid incontinence (loss of watery feces). The five very disabling bowel symptoms of the LARS score (any flatus or liquid incontinence, altered stool frequency, fecal clustering, and fecal urgency) were also analyzed, because of their known negative influence on quality of life.[13] To define stool consistency the Bristol Stool Scale was used.

Sigmoid colon resection was defined as the surgical resection of a sigmoid tumor with an anastomosis of >15 cm above the anal verge. Surgical resection of a tumor in the descending colon or distal transverse colon was defined as left hemicolectomy. Follow-up time was defined as the time between completion of the questionnaires and primary surgery or reversal of the temporary stoma. Tumor stage was defined according to the Union for International Cancer Control (UICC) classification. The Charlson Comorbidity Index was used to score the severity of comorbidities.[14] The European Perioperative Clinical Outcome definitions were used to specify postoperative complications other than anastomotic leakage or a reoperation.[15]

Statistical analysis

Continuous data were reported as means (SD) or medians (IQR) and were compared using either analysis of variance (ANOVA) or the Kruskal-Wallis test. For categorical data, counts and percentages were given and compared using the chi-square test. To account for multiple testing, subgroup chi-square tests were added. Univariable and multivariable binary logistic regression analyzes were performed to identify associations between bowel dysfunction and the three types of colon resections. Results were presented as odds ratios (OR) with 95% confidence intervals (CI). Only relevant univariable variables (p value <0.10) or variables with a theoretical confounding effect based on an extensive literature search were included in the multivariable models. Possible interactions were checked. A p value of <0.05 was considered statistically significant. Missing data were omitted from statistical analyses. All statistical analyses were performed with IBM SPSS Statistics, Version 23.0 (Armonk, NY, USA:IBM Corp.).

Results

Between 2009-2015, a total of 3023 patients underwent right or left hemicolectomy or sigmoid colon resection for colonic cancer without construction of a permanent stoma. After excluding 1372 patients who had either died, had a mental impairment, or an unknown or foreign address, questionnaires were sent to 1651 patients, 1124 of whom completed the questionnaires (Figure 1). Ten of the 1114 included patients (0.9%) had one or more missing variable for the definition of constipation or fecal incontinence.

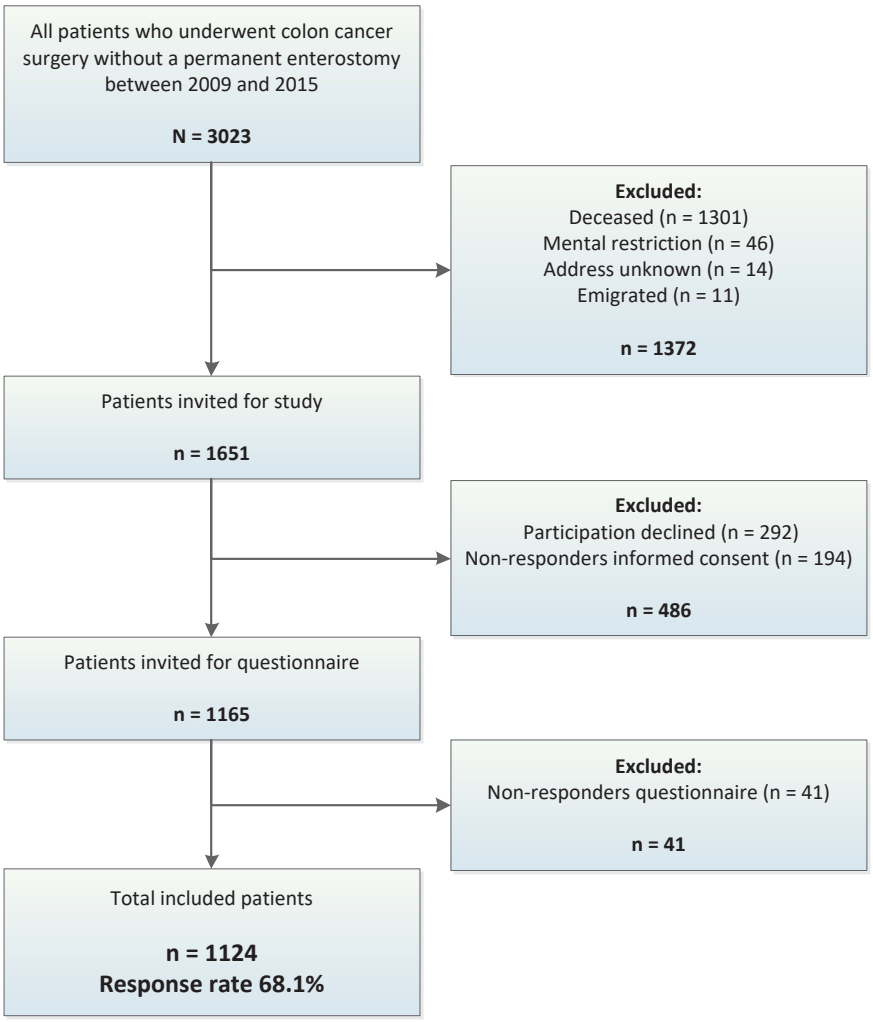

Figure 1 | Flow chart of inclusion and exclusion

Patient characteristics

There were 673 patients who had undergone right hemicolectomy, 167 had undergone left hemicolectomy, and 284 patients had undergone sigmoid colon resection. Taken together, the median follow-up time was 56 (IQR 41-80) months. Patient characteristics according to the type of colon resection are shown in Table 1. A drop-out analysis revealed that more non-responders had undergone sigmoid

Table 1 | Patient characteristics according to the type of colon resection

	Right hemicolectomy No. (%)	Left hemicolectomy No. (%)	Sigmoid colon resection No. (%)	*p* value [a]
Overall	673 (100.0)	167 (100.0)	284 (100.0)	
Basic characteristics				
Men	314 (46.7)	99 (59.3)	181 (63.7)	*<0.001***
Age at surgery (years) [b]	68.5 (9.7)	65.8 (9.5)	66.2 (9.5)	*<0.001***
Follow-up (months) [c]	57.0 (42-79)	52.0 (38-79)	58.0 (41-83)	*0.121*
BMI at surgery (kg/m^2) [c]	26.5 (4.2)	26.6 (4.3)	27.6 (4.3)	*0.001***
ASA score at surgery				*0.016**
I	106 (16.2)	34 (21.0)	63 (23.2)	
II	403 (61.6)	96 (59.3)	172 (63.2)	
III	140 (21.4)	32 (19.8)	34 (12.5)	
IV	5 (0.8)	0 (0.0)	3 (1.1)	
Charlson comorbidity index at surgery	2.0 (2-2)	2.0 (2-2)	2.0 (2-2)	*0.218*
Previous lower abdominal surgery	239 (35.5)	56 (33.5)	80 (28.2)	*0.089*
Previous upper abdominal surgery	45 (6.7)	9 (5.4)	20 (7.0)	*0.780*
Smoking				*0.596*
No	497 (81.5)	128 (82.6)	211 (83.7)	
Yes	87 (14.3)	19 (12.3)	35 (13.9)	
Recently quit	26 (4.3)	8 (5.2)	6 (2.4)	

Table 1 | Continued

	Right hemicolectomy No. (%)	Left hemicolectomy No. (%)	Sigmoid colon resection No. (%)	*p* value [a]
Oncologic characteristics				
Tumor stage (UICC)				*<0.001***
I	145 (21.7)	37 (22.2)	102 (36.2)	
II	315 (47.2)	65 (38.9)	88 (31.2)	
III	188 (28.1)	61 (36.5)	85 (30.1)	
IV	20 (3.0)	4 (2.4)	7 (2.5)	
Distant metastasis				*0.111*
No	645 (96.1)	155 (92.8)	264 (93.3)	
Liver	16 (2.4)	6 (3.6)	11 (3.9)	
Lung	5 (0.7)	1 (0.6)	5 (1.8)	
Multiple locations	5 (0.7)	5 (3.0)	3 (1.1)	
Adjuvant treatment				
Previous radiotherapy in pelvic region	14 (2.1)	4 (2.4)	8 (2.8)	*0.793*
Adjuvant therapy				*0.013**
No	470 (72.6)	97 (60.2)	196 (71.3)	
CAPOX	78 (12.1)	38 (23.6)	44 (16.0)	
FOLFOX	63 (9.7)	16 (9.9)	22 (8.4)	
Capecitabine	36 (5.6)	10 (6.2)	12 (4.4)	
Years since last chemotherapy	4.0 (3.0-6.0)	5.0 (4.0-7.0)	5.0 (3.0-7.0)	*0.498*
Surgical characteristics				
Setting				*0.032**
Elective	605 (91.1)	138 (84.1)	248 (89.5)	
Emergency	59 (8.9)	26 (15.9)	29 (10.5)	

Surgical approach				*<0.001***
Open	391 (58.7)	82 (49.1)	112 (39.6)	
Laparoscopic	219 (32.9)	70 (41.9)	145 (51.2)	
Conversion	56 (8.4)	15 (9.0)	26 (9.2)	
Method of anastomosis				*<0.001***
Handsewn	398 (61.9)	107 (71.3)	113 (41.1)	
Stapled	245 (38.1)	43 (28.7)	162 (58.9)	
Reconstruction				*<0.001***
Side-to-end	26 (4.0)	17 (10.8)	127 (51.8)	
Side-to-side	600 (92.2)	87 (55.4)	59 (24.1)	
End-to-end	25 (3.8)	53 (33.8)	59 (24.1)	
Temporary stoma	15 (2.2)	29 (17.4)	35 (12.3)	*<0.001***
Postoperative characteristics				
Anastomotic leakage	24 (3.6)	13 (7.8)	12 (4.2)	*0.057*
Reoperation	43 (6.4)	16 (9.6)	23 (8.1)	*0.305*
Other types of complications				*0.024**
No	446 (66.3)	116 (69.5)	215 (75.7)	
One complication	152 (22.6)	40 (24.0)	50 (17.6)	
More than one complication	75 (11.1)	11 (6.6)	19 (6.7)	

[a] *p* value for comparison of the three groups.
[b] Values expressed as median (IQR)
[c] Values expressed as mean (SD)
* Statistical significance of $p < 0.05$
** Statistical significance of $p < 0.005$
Abbreviations: ASA, American Society of Anesthesiologists; UICC, Union for International Cancer Control.

colon resections in comparison to responders (31.5% versus 25.3%, p=0.021, Supplemental Digital Content 2). In addition, non-responders were older than responders and had a higher ASA score (both p<0.001).

Stool consistency and frequency

Figure 2 shows the stool consistency after the three types of colon resections. On comparing stool consistency it was found that the stools of patients who had undergone right hemicolectomy were more liquid compared to patients who had undergone left hemicolectomy and sigmoid colon resection (p<0.001, Figure 2A). No differences were found for stool frequency (Figure 2B).

Individual bowel symptoms

The prevalence of the different investigated bowel symptoms after the three types of colon resections is shown in Figure 3. The prevalence of straining was significantly higher in patients who had undergone sigmoid colon resection compared to patients who had undergone left or right hemicolectomy (45.2% versus 29.9% and 28.9%, p<0.001, Figure 3A). Regarding fecal incontinence-associated symptoms, liquid incontinence and urge incontinence were both significantly more prevalent following right hemicolectomy, compared to left hemicolectomy and sigmoid colon resection (6.6% versus 1.8% and 2.5%, p=0.004 and 6.6% versus 2.4% and 3.2%, p=0.021, Figure 3B). Likewise, liquid incontinence and fecal urgency were the only symptoms of the LARS score that showed a statistically significant difference between patients who had undergone right or left hemicolectomy, or sigmoid colon resection (31.9% versus 17.4% and 16.2%, p<0.001 and 55.2% versus 39.5% and 36.7%, p<0.001, Figure 3C).

Use of defecation treatment

Enemas and laxatives were used to treat constipation in less than 16.9% of the patients, without significant differences between the types of colon resections (Figure 3D). Rectal irrigations and antidiarrheals were used in less than 3.7% of the patients for all types of resections. Antidiarrheals were used most often following right hemicolectomy, compared to left hemicolectomy and sigmoid colon resection (3.7% versus 1.8% and 0.7%, p=0.023).

Constipation and fecal incontinence

Overall, the prevalence of constipation was significantly higher in patients who had undergone sigmoid colon resection compared to patients who had undergone right or left hemicolectomy (31.1% versus 17.7% and 21.0% p<0.001), while the prevalence of fecal incontinence was not significantly different (12.7% versus 18.5% and 16.8%, p=0.088).

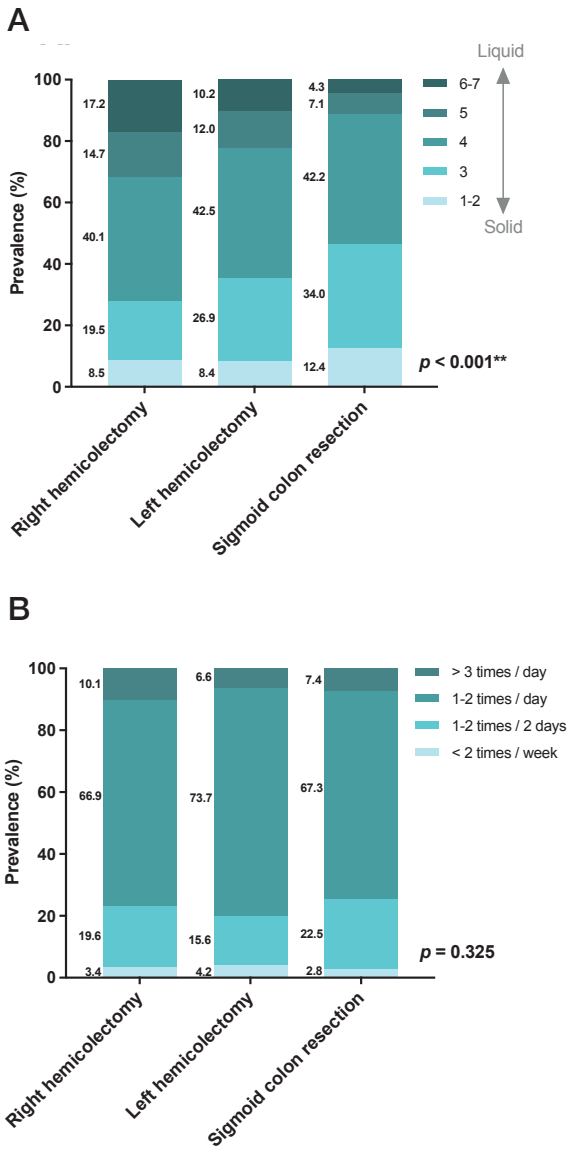

Figure 2 | Stool frequency and stool consistency according to the type of colon resection
(A), stool consistency following the Bristol Stool Chart. (B), stool frequency.

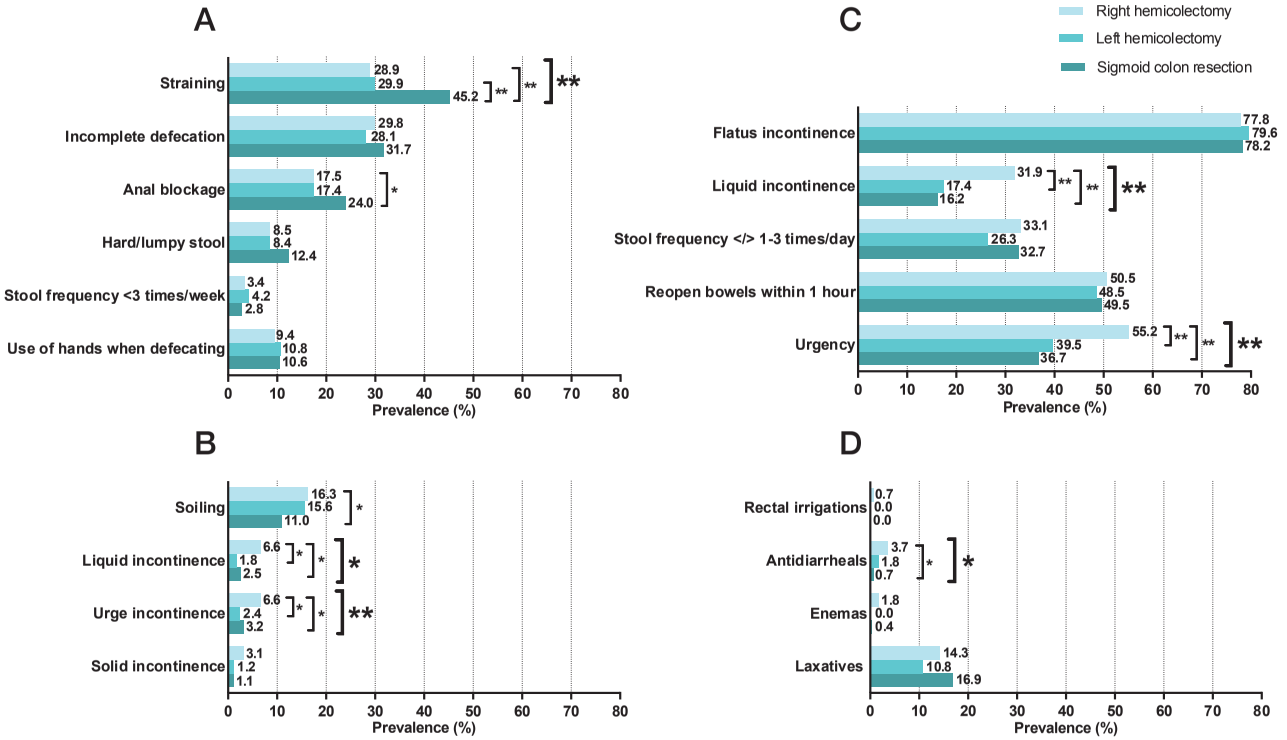

Figure 3 | The prevalence of bowel symptoms and defecation treatment according to the type of colon resection

(A), symptoms of constipation. (B), symptoms of fecal incontinence. (C), symptoms of the low anterior resection syndrome score. (D), use of defecation treatment.

In accordance with these differences in prevalence, a multivariable model of constipation showed an increased likelihood of constipation in patients who had undergone sigmoid colon resection if right hemicolectomy was taken as the reference category (OR 2.92, 95%CI, 1.80-4.75, $p<0.001$). There was no significant association between fecal incontinence and any specific type of colon resection. Additionally, the same univariable and multivariable analyses were performed with left hemicolectomy as the reference category. They also revealed a statistically significant increase of the likelihood of constipation in patients who had undergone sigmoid resection (OR 1.93, 95%CI, 1.12-3.35, $p=0.019$, Supplemental Digital Content 3). A direct comparison between patients who had undergone left hemicolectomy versus sigmoid colon resection did not show significant associations for fecal incontinence.

All univariable and multivariable associations between different characteristics and constipation and fecal incontinence are presented in Figure 4. The exact outcomes of these analyses can be found in Supplemental Digital Content 4. Women were more likely to suffer from both constipation and fecal incontinence (OR 1.43, 95%CI, 1.02-1.99, $p=0.038$ and OR 1.46, 95%CI, 1.03-2.07, $p=0.036$, respectively). Likewise, increasing age was also associated with increased odds of constipation (OR 1.02, 95%CI, 1.00-1.04, $p=0.037$). Previous upper abdominal surgery was associated with a decreased likelihood of constipation (OR 0.31, 95%CI, 0.13-0.75, $p=0.009$). Finally, smoking and radiotherapy were found to be significantly associated with fecal incontinence (OR 1.68, 95%CI, 1.10-2.56, $p=0.017$ and OR 2.92, 95%CI, 1.20-7.08, $p=0.018$, respectively).

Additionally, using the same multivariable logistic regression model as for overall fecal incontinence, an increased likelihood of liquid incontinence was found in patients who had undergone right hemicolectomy, compared to patients who had undergone sigmoid colon resection (OR 2.15, 95%CI, 1.47-3.16, $p<0.001$). A similar multivariable logistic regression model of fecal urgency yielded a comparable result (OR 2.01, 95%CI, 1.47-2.74, $p<0.001$).

Generic quality of life

The quality of life scores after the three different types of colon resections are shown in Figure 5. The scores on different physical domains of quality of life (physical functioning, role-physical, and bodily pain) as well as on different mental domains (social functioning and role-emotional) were significantly lower in patients who had undergone right hemicolectomy (Figure 5). Sub analysis performed in patients without fecal incontinence still showed a worse quality of life on the domains physical functioning and role-physical after right hemicolectomy, while no significant difference for the psychosocial domains was observed (Supplemental Digital Content 5).

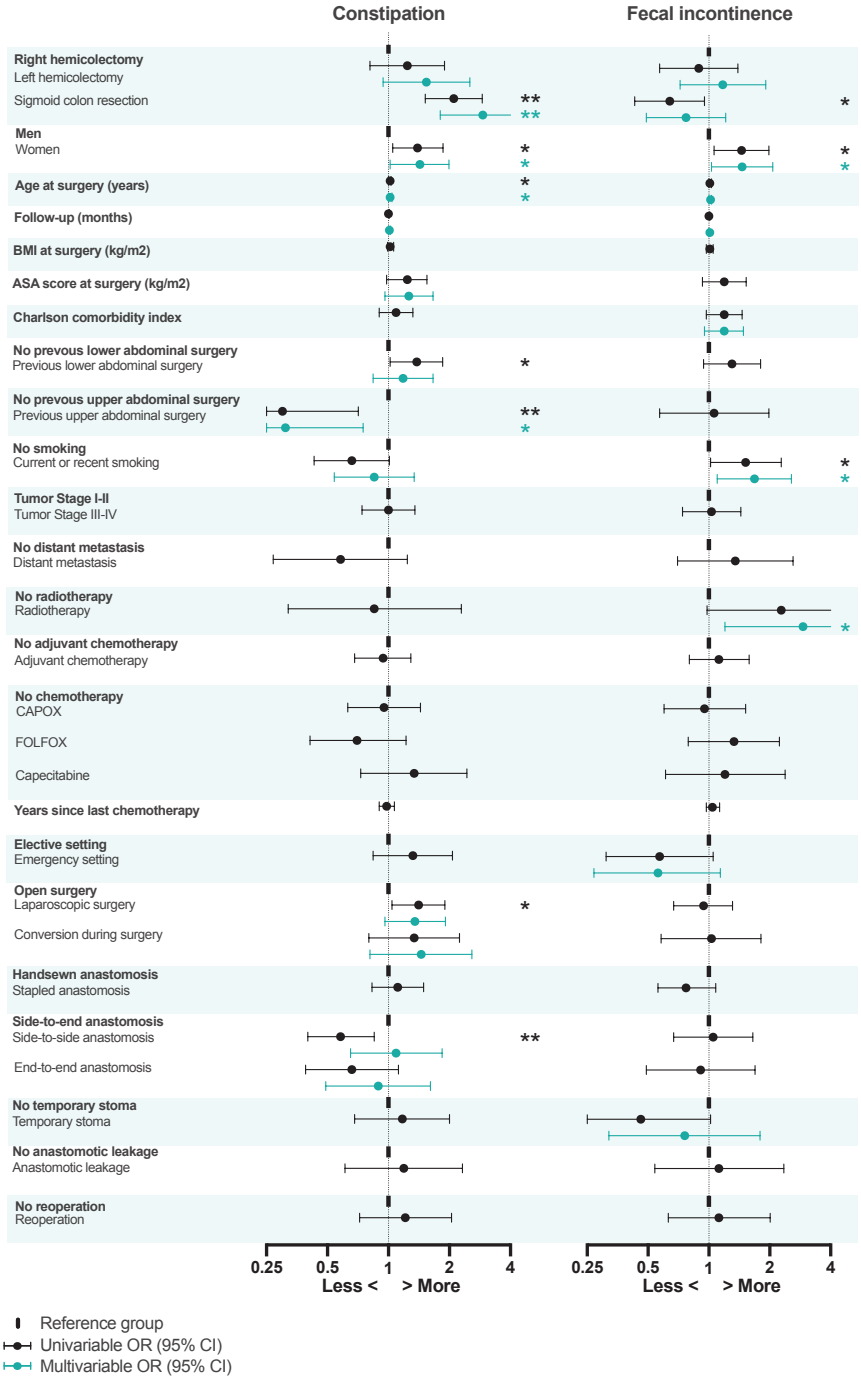
Constipation
Fecal incontinence
Right hemicolectomy
Left hemicolectomy
Sigmoid colon resection
Men
Women
Age at surgery (years)
Follow-up (months)
BMI at surgery (kg/m2)
ASA score at surgery (kg/m2)
Charlson comorbidity index
No prevous lower abdominal surgery
Previous lower abdominal surgery
No prevous upper abdominal surgery
Previous upper abdominal surgery
No smoking
Current or recent smoking
Tumor Stage I-II
Tumor Stage III-IV
No distant metastasis
Distant metastasis
No radiotherapy
Radiotherapy
No adjuvant chemotherapy
Adjuvant chemotherapy
No chemotherapy
CAPOX
FOLFOX
Capecitabine
Years since last chemotherapy
Elective setting
Emergency setting
Open surgery
Laparoscopic surgery
Conversion during surgery
Handsewn anastomosis
Stapled anastomosis
Side-to-end anastomosis
Side-to-side anastomosis
End-to-end anastomosis
No temporary stoma
Temporary stoma
No anastomotic leakage
Anastomotic leakage
No reoperation
Reoperation
0.25
0.5
1
2
4
Less <
> More
Reference group
Univariable OR (95% CI)
Multivariable OR (95% CI)

Figure 4 | Univariable and multivariable logistic regression analysis of constipation and fecal incontinence

Abbreviations: CI, Confidence Interval; OR, odds ratio.

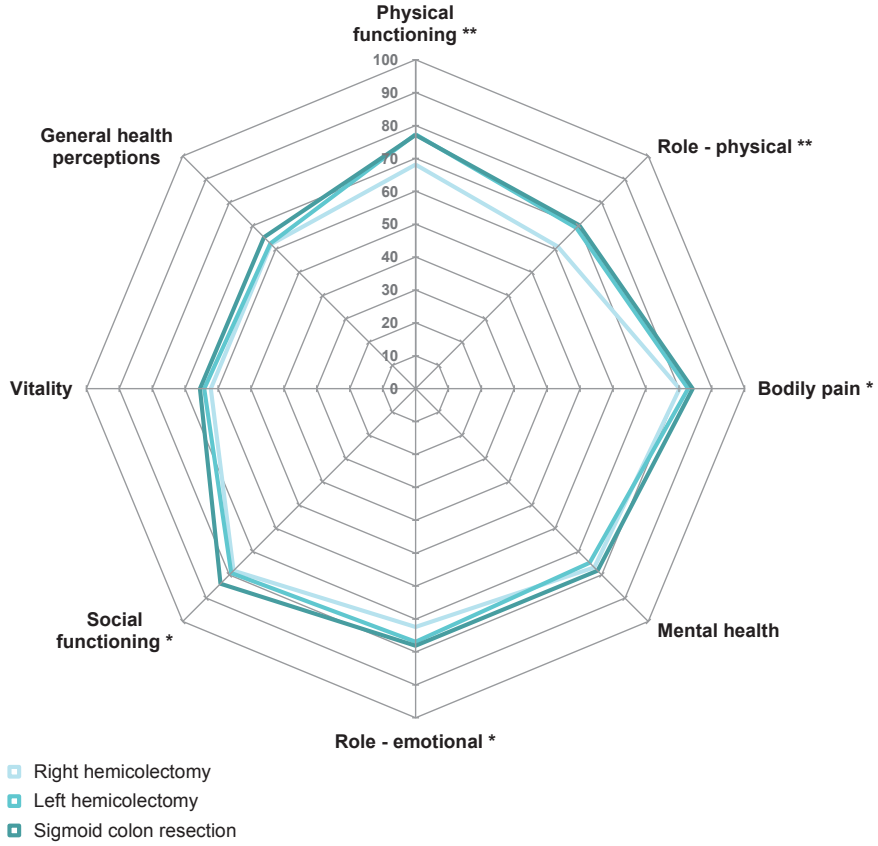

Figure 5 | Generic quality of life scores according to the type of colon resection

Discussion

This study shows that patients who underwent sigmoid colon resection are three times more likely to suffer from constipation in the long-term than patients who underwent right or left hemicolectomy. This finding corroborates with others who found more constipation-associated problems following sigmoid colon resection compared to patients who underwent a hemicolectomy[16] or a polypectomy.[17] Nevertheless, this study is the first to use a validated constipation score to assess patients who underwent a resection for colon cancer. Patients who underwent sigmoid colon resection suffered from constipation one and a half times more often than the general Dutch population of comparable age (19.8% versus 31.1%).[18]

Various pathophysiological factors have been postulated for the association between sigmoid colon resection and constipation. First, following colonic mobilization, the sensory and motor function of the colon might be reduced because of denervation and fibrosis.[5,16] Decreased activity of the descending colon and a prolonged transit time were found in patients following surgery for rectal cancer and were attributed to autonomic denervation.[19,20] These mechanisms are likely to occur after surgery for colon cancer as well. Second, an animal study showed that after twelve weeks levels of nitric oxide synthesis increased in rats with a denervated distal colon compared to rats that had not undergone colon surgery.[21] Nitric oxide might down-regulate the contractile activity of the colon and lead to constipation, but this warrants further research.

Right hemicolectomy was associated with twice as much liquid incontinence and fecal urgency compared to sigmoid colon resection. Liquid incontinence was probably linked to the more liquid stool consistency that was found in patients following right hemicolectomy, which had also been reported in previous long-term studies.[22,23] Comparing stool consistency in patients following right hemicolectomy versus the general population of comparable age, illustrates the true increase of liquid to mushy stool following right hemicolectomy (17.2% versus 4.8%, respectively).[24] Liquid incontinence and fecal urgency were also the two symptoms of the LARS score that showed a significantly higher prevalence following right hemicolectomy.

From a pathophysiological point of view, two main issues can be distinguished that predispose patients who underwent right hemicolectomy to more liquid stool. First, the absence of the proximal colon that is known as the part of the colon that absorbs most of the water from the stool.[25] Second, the absence of or damage to the terminal ileum and/or ileocolic valve may lead to bile acid malabsorption, which causes chronic diarrhea.[6,26,27] In addition, small-bowel bacterial overgrowth on account of the absence of the ileocecal valve that acts as a barrier between the flora of the small and large intestine, was proposed as liquifying the stool.[6,27] Next to that, some hypothesize that injury to the superior mesenteric nerve plexus could result

in neurogenic diarrhea,[28] although more recent studies could not prove this association.[29,30]

Despite the differences in outcomes, personalized treatment after the different types of colon resections appears to be lacking. This may be caused by a lack of awareness among physicians regarding the bowel function problems after colon resections. For the rectum resections, the postoperative low anterior resection syndrome is receiving more and more attention, but the postoperative bowel function problems after colectomies have not been widely investigated. In the current study, only 16.9% of the patients who underwent sigmoid colon resection use laxatives, while 31.1% suffer from constipation. Similarly, also treatment for fecal incontinence was uncommon. Only 3.7% of the patients who underwent right hemicolectomy are using an antidiarrheal, while no less than 6.6% suffer from liquid incontinence more than once a month. As bile acid malabsorption is likely to play a role in liquid incontinence following right hemicolectomy, a bile acid sequestrant might relieve these complaints.[27] Less than 10% of the patients in this study, however, who suffered from liquid incontinence following right hemicolectomy, reported using a bile acid sequestrant – a situation that leaves room for improvement.

All multivariable models were adjusted for sex, age, and follow-up time, as these factors are well-known to influence bowel functioning, also in the context of surgery for colon cancer.[5,17,31-33] The current study shows no effect of follow-up time on constipation and fecal incontinence. This is in contrast with the general consensus that the colon structurally adapts over time after surgery.[6] These findings imply that prompt treatment of constipation and fecal incontinence is required, because the complaints are not likely to resolve spontaneously and might even worsen the more time passes between surgery and follow-up. Concerning smoking, this study shows that smoking seems to be associated with more fecal incontinence following a resection for colon cancer. This might by related to the direct stimulating effect of nicotine on colonic motor activity.[34] Finally, the current study provides evidence of a three-fold increase in fecal incontinence in patients who previously received radiotherapy in the pelvic region for other conditions. This emphasizes the detrimental effect of radiotherapy on fecal incontinence, which has been attributed to structural changes of the irradiated tissue.[35]

Remarkably, it seems that adjuvant chemotherapy following surgery for colon cancer does not worsen constipation or fecal incontinence in the long term, which has been noted by others as well.[17,23,32] However, this is the first study that compares the long-term effects of different chemotherapy regimens and the time since the last chemo treatment, which were both not associated with any of the bowel function problems. It therefore seems that the direct cytotoxic effect of chemotherapeutic agents on the mucosa of the gastrointestinal tract do not have a chronic debilitating impact on patients' bowel functions, as was suggested previously.[36] However, future

research is required to establish the exact effects of chemotherapy on long-term bowel function.

In line with the findings of more liquid incontinence and fecal urgency following right hemicolectomy, most physical and mental generic quality of life domains were worse in these patients. This observation is corroborated by other long-term studies showing impaired quality of life following right hemicolectomy, especially in patients with loose stools.[22,23] Comparable generic quality of life between patients who had undergone right-sided and left-sided colectomies had been found previously, although shorter questionnaires were used that did not distinguish domains.[37,38]

The large study population, in combination with the validated bowel function scores strengthen this multicenter study. Although the used scores were not validated for patients who had undergone resection for colon cancer, together they provide a thorough examination of bowel function that can be compared to other patients and/or to the general population. Furthermore, longitudinal data is lacking. Lastly, including long surviving patients without a permanent stoma, combined with the higher age and worse ASA score of the non-responders, may have caused selection bias, because this would imply that the 'most healthy' patients were included in this study. This would, however, only reinforce our findings on the large amount of bowel function problems following surgery for colon cancer.

Conclusion

This study shows clear differences in long-term bowel function problems following right hemicolectomy, left hemicolectomy, or sigmoid colon resection for colon cancer. Sigmoid colon resection seems to be associated with constipation, with alarmingly low treatment ranges. On the contrary, liquid incontinence and fecal urgency seem to be associated with right hemicolectomy, which may explain the decline in physical and mental generic quality of life of these patients. Hopefully, the current results will provide the clinician with a tool to personalize screening and lead to prompt treatment of both constipation and fecal incontinence during the follow-up of surgery for colon cancer.

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Supplementary files

Supplemental Digital Content 1 | The Groningen Defaecation & Faecal Continence questionnaire

Supplemental Digital Content 2 | Dropout analysis

	Responders No. (%)	Non-responders [a] No. (%)	*p* value
Overall	1124 (100.0)	527 (100.0)	
Type of colectomy			*0.021**
Right hemicolectomy	673 (59.9)	297 (56.4)	
Left hemicolectomy	167 (14.9)	64 (12.1)	
Sigmoid colon resection	284 (25.3)	166 (31.5)	
Men	594 (52.8)	235 (44.6)	*0.002***
Age at surgery (years) [b]	67.0 (62 – 75)	72.0 (64 – 78)	*<0.001***
Follow-up (months) [b,c]	55.0 (40 – 78)	61.0 (42 – 80)	*0.079*
ASA score at surgery			*<0.001***
I	203 (18.7)	62 (12.1)	
II	671 (61.7)	279 (54.6)	
III	206 (18.9)	164 (32.1)	
IV	8 (0.7)	6 (1.2)	
Previous abdominal surgery	330 (29.4)	178 (33.8)	*0.070*
Tumor stage (UICC)			*0.466*
I	284 (25.4)	133 (25.4)	
II	468 (41.9)	238 (45.5)	
III	334 (29.9)	139 (26.6)	
IV	31 (2.8)	13 (2.5)	

[a] The clinical data of the non-responders was obtained from the Dutch ColoRectal Audit (DCRA) registry.
[b] Values expressed as median (IQR)
[c] Follow-up since primary rectum or rectosigmoid cancer surgery
* Statistical significance of $p < 0.05$
** Statistical significance of $p < 0.005$
Abbreviations: ASA, American Society of Anesthesiologists; UICC, Union for International Cancer Control.

Supplemental Digital Content 3 | Univariable and multivariable logistic regression analysis of constipation and fecal incontinence with left hemicolectomy as the reference category

	Constipation				Fecal incontinence			
	Univariable		Multivariable [a]		Univariable		Multivariable [b]	
Variables	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Type of colectomy								
Left hemicolectomy	Reference		Reference		Reference		Reference	
Sigmoid colon resection	1.70 (1.08–2.67)	*0.021**	1.93 (1.12–3.35)	*0.019**	0.72 (0.42–1.23)	*0.231*	0.67 (0.38–1.20)	*0.177*

[a] The same variables were used as for the multivariable model of constipation with right hemicolectomy as the reference category (see Supplementary Digital Content 3): sex, age at surgery, follow-up, ASA score at surgery, previous lower abdominal surgery, previous upper abdominal surgery, smoking, surgical approach, and type of anastomosis.

[b] The same variables were used as for the multivariable model of fecal incontinence with right hemicolectomy as the reference category (see Supplementary Digital Content 3): sex, age at surgery, follow-up, Charlson comorbidity index at surgery, smoking, radiotherapy, setting, and temporary stoma.

* Statistical significance of $p < 0.05$

** Statistical significance of $p < 0.005$

Abbreviations: CI, confidence interval.

Supplemental Digital Content 4 | Univariable and multivariable logistic regression analysis of constipation and fecal incontinence

	Constipation				Fecal incontinence			
	Univariable		Multivariable		Univariable		Multivariable	
Variables	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Type of colectomy								
Right hemicolectomy	Reference		Reference		Reference		Reference	
Left hemicolectomy	1.24 (0.81–1.89)	*0.326*	1.54 (0.94–2.52)	*0.090*	0.89 (0.57–1.39)	*0.602*	1.17 (0.72–1.91)	*0.532*
Sigmoid colon resection	2.10 (1.52–2.90)	*<0.001***	2.92 (1.80–4.75)	*<0.001***	0.64 (0.43–0.95)	*0.028**	0.77 (0.49–1.21)	*0.259*
Sex								
Men	Reference		Reference		Reference		Reference	
Women	1.39 (1.05–1.86)	*0.023**	1.43 (1.02–1.99)	*0.038**	1.45 (1.06–1.98)	*0.021**	1.46 (1.03–2.07)	*0.036**
Age at surgery (years)	1.02 (1.00–1.03)	*0.036**	1.02 (1.00–1.04)	*0.037**	1.01 (1.00–1.03)	*0.150*	1.02 (1.00–1.03)	*0.123*
Follow-up (months)	1.00 (1.00–1.01)	*0.559*	1.01 (1.00–1.02)	*0.050*	1.00 (1.00–1.01)	*0.348*	1.01 (1.00–1.01)	*0.203*
BMI at surgery (kg/m^2)	1.02 (0.99–1.06)	*0.162*	-	-	1.01 (0.97–1.05)	*0.631*	-	-
ASA score at surgery	1.24 (0.98–1.55)	*0.068*	1.26 (0.96–1.66)	*0.089*	1.19 (0.93–1.53)	*0.175*	-	-
Charlson comorbidity index at surgery	1.09 (0.90–1.32)	*0.396*	-	-	1.19 (0.97–1.46)	*0.088*	1.19 (0.95–1.48)	*0.128*
Previous lower abdominal surgery							-	-
No	Reference		Reference		Reference			
Yes	1.38 (1.02–1.85)	*0.035**	1.18 (0.84–1.66)	*0.333*	1.30 (0.94–1.80)	*0.110*		

Supplemental Digital Content 4 | Continued

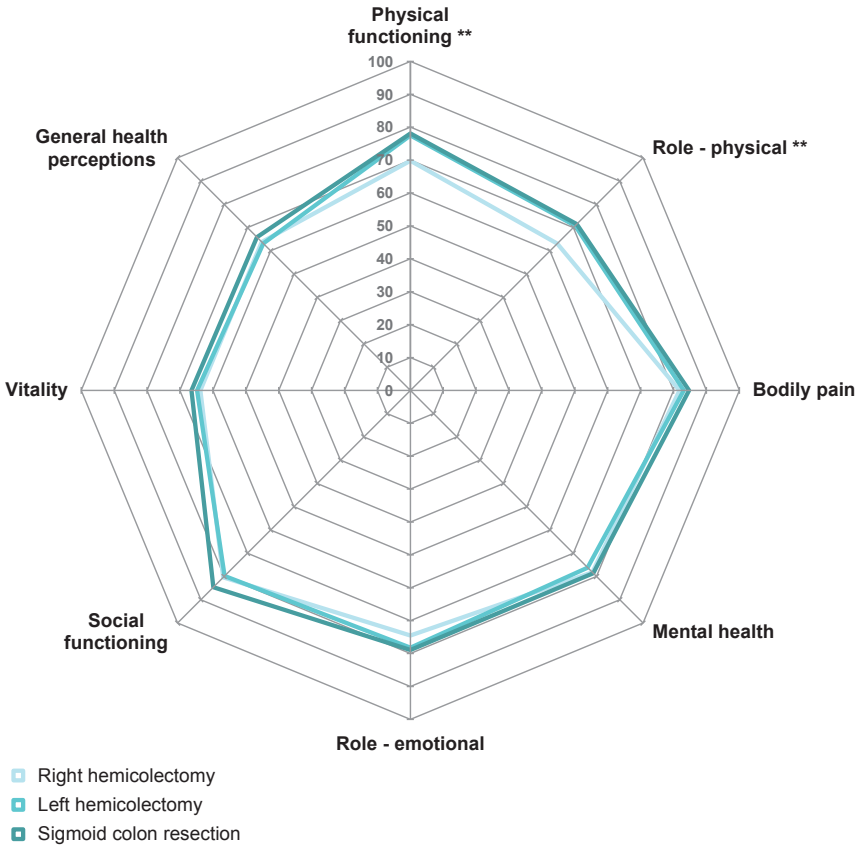
	Constipation				Fecal incontinence			
	Univariable		Multivariable		Univariable		Multivariable	
Variables	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Previous upper abdominal surgery							-	-
No	Reference		Reference		Reference			
Yes	0.30 (0.13–0.71)	*0.006**	0.31 (0.13–0.75)	*0.009**	1.06 (0.57–1.98)	*0.849*		
Smoking								
No	Reference		Reference		Reference		Reference	
Yes or recently quitted	0.66 (0.43–1.01)	*0.057*	0.85 (0.54–1.34)	*0.484*	1.52 (1.02–2.28)	*0.039**	1.68 (1.10–2.56)	*0.017**
Tumor stage (UICC)								
I - II	Reference		-	-	Reference		-	-
III - IV	1.00 (0.74–1.35)	*0.992*			1.03 (0.74–1.44)	*0.856*		
Distant metastasis								
No	Reference		-	-	Reference		-	-
Yes	0.58 (0.27–1.24)	*0.160*			1.35 (0.70–2.61)	*0.371*		
Radiotherapy								
No	Reference		-	-	Reference		Reference	
Yes	0.85 (0.32–2.29)	*0.754*			2.28 (0.98–5.32)	*0.057*	2.92 (1.20–7.08)	*0.018**
Adjuvant chemotherapy								
No	Reference		-	-	Reference		-	-
Yes	0.94 (0.68–1.29)	*0.690*			1.12 (0.80–1.58)	*0.509*		
Type of chemotherapy			-	-			-	-
No	Reference				Reference			
CAPOX	0.95 (0.63–1.44)	*0.803*			0.95 (0.60–1.52)	*0.829*		
FOLFOX	0.70 (0.41–1.22)	*0.208*			1.33 (0.79–2.23)	*0.280*		
Capecitabine	1.34 (0.73–2.44)	*0.341*			1.20 (0.61–2.38)	*0.601*		

Years since last chemotherapy	0.98 (0.90–1.07)	*0.654*	-	-	1.04 (0.97–1.13)	*0.269*	-	-
Setting			-	-				
Elective	Reference				Reference		Reference	
Emergency	1.32 (0.84–2.07)	*0.225*			0.57 (0.31–1.05)	*0.073*	0.56 (0.27–1.14)	*0.108*
Surgical approach							-	-
Open	Reference		Reference		Reference			
Laparoscopic	1.41 (1.0–1.90)	*0.027**	1.35 (0.96–1.91)	*0.087*	0.94 (0.67–1.31)	*0.698*		
Conversion	1.34 (0.80–2.24)	*0.263*	1.45 (0.81–2.58)	*0.207*	1.03 (0.58–1.81)	*0.922*		
Method of anastomosis								
Handsewn	Reference		-	-	Reference		-	-
Stapled	1.11 (0.83–1.49)	*0.488*			0.77 (0.56–1.08)	*0.127*		
Type of anastomosis							-	-
Side-to-end	Reference		Reference		Reference			
Side-to-side	0.58 (0.40–0.85)	*0.005***	1.09 (0.65–1.84)	*0.734*	1.05 (0.67–1.65)	*0.816*		
End-to-end	0.66 (0.39–1.12)	*0.120*	0.89 (0.49–1.61)	*0.697*	0.91 (0.49–1.69)	*0.769*		
Temporary stoma								
No	Reference		-	-	Reference		Reference	
Yes	1.17 (0.68–2.00)	*0.571*			0.46 (0.21–1.02)	*0.056*	0.76 (0.32–1.79)	*0.758*
Anastomotic leakage								
No	Reference		-	-	Reference		-	-
Yes	1.19 (0.61–2.32)	*0.606*			1.12 (0.54–2.35)	*0.760*		
Reoperation			-	-			-	-
No	Reference				Reference			
Yes	1.21 (0.72–2.05)	*0.472*			1.12 (0.63–2.01)	*0.702*		

* Statistical significance of $p < 0.05$

** Statistical significance of $p < 0.005$

Abbreviations: CI, Confidence Interval; ASA, American Society of Anesthesiologists; UICC, Union for International Cancer Control.



Supplemental Digital Content 5 | Generic quality of life scores of all patients without fecal incontinence according to the type of colon resection

Part IV

Long-term bowel function following colorectal resections in children