Functional bowel complaints and quality of life after surgery for colon cancer

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Functional bowel complaints and quality of life after surgery for colon cancer: prevalence and predictive factors

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Abstract

Aim Low anterior resection syndrome (LARS) severely affects the quality of life (QoL) of patients after surgery for rectal cancer. There are very few studies that have investigated LARS-like symptoms and their effect on QoL after colon cancer surgery. The aim of this study was to investigate the prevalence of functional abdominal complaints and related QoL after colon cancer surgery compared with patients with similar complaints after rectal cancer surgery.

Method All patients who underwent colorectal cancer resections between January 2008 and December 2015, and who were free of colostomy for at least 1 year, were eligible (n = 2136). Bowel function was assessed by the LARS score, QoL by the EORTC QLQ-C30 and QLQ-CR29 questionnaires. QoL was compared between the LARS score categories and tumour height categories.

Results A total of 1495 patients (70.0%) were included in the analyses, of whom 1145 had a colonic and 350 a rectal tumour. Symptoms of LARS were observed in 55% after rectal cancer resection compared with 21% after colon cancer resection. Female gender (OR 1.88, CI 1.392–2.528) and a previous diverting stoma (OR 1.84, CI 1.14–2.97) were independently associated with a higher prevalence of LARS after colon cancer surgery. Patients with LARS after colon cancer surgery performed significantly worse in most QoL domains.

Conclusion The results of this study highlight the presence of LARS-like symptoms after surgery for colonic cancer. Patients suffering from major LARS-like symptoms after colon resection reported the same debilitating effect on their QoL as patients with major LARS after rectal resection. This should be addressed by colorectal cancer specialists in order to adequately inform patients.

Keywords Health-related quality of life, bowel dysfunction, low anterior resection syndrome, colorectal cancer, colonic resection

What does this paper add to the literature?
Low anterior resection syndrome (LARS) severely affects quality of life (QoL) after rectal cancer surgery. This is the first study to raise awareness of the presence of LARS-like symptoms after surgery for colon cancer, with patients having the same debilitating effect on their QoL as patients with major LARS after rectal resection.

Introduction

Survivors of colorectal cancer (CRC) often experience long-term side effects of the cancer and its treatment, such as troublesome abdominal complaints, depressive symptoms and fatigue, all of which may last for several years [1,2]. These persisting problems can have a

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negative impact on specific domains of health-related quality of life (HRQoL), such as physical and social functioning [3,4].

The burden of postoperative complaints has been extensively studied over the last decade in patients surgically treated for rectal cancer and are collectively known as low anterior resection syndrome (LARS), which has a prevalence of 60–90% [5]. A recently published cross-sectional study showed that posttreatment symptoms also occur in patients treated for sigmoid tumours, even years after the event [6]. Moreover, patients surgically treated for colonic cancer by right hemicolectomy seem to experience persisting diarrhoea in the first 3 months after surgery, resulting in a decreased quality of life (QoL) [7,8]. The presence of persisting functional abdominal complaints after sigmoid resection and right colectomy suggests that treatment for tumours in the remaining colon might also result in longstanding postoperative problems.

It has been suggested that that colorectal surgeons do not have a thorough understanding of postoperative problems after colonic surgery or how these affect QoL [1]. The aim of this study was to assess the prevalence of functional abdominal complaints and related QoL after colon cancer surgery compared with patients having similar complaints after rectal cancer surgery.

Method

A multicentre retrospective cross-sectional study was carried out on all patients who underwent surgery for Stage 1–3 CRC. Patients who had a temporary colostomy or ileostomy could participate if their stoma was closed more than a year previously (to allow their bowel function to have regained stability [9]). Patients were operated on between 2009 and 2015 in six hospitals in the south-east Netherlands (Viecuri Medical Centre Venlo, Laurentius Hospital Roermond, Zuyderland Hospital Sittard and Heerlen, Maxima Medical Centre Veldhoven, Maastricht University Medical Centre, Catharina Hospital Eindhoven). The exclusion criteria were: deceased, age below 18 years, disseminated or recurrent disease, inadequate Dutch language skills, and intellectual disability or dementia. Patients with irresectable disease or patients with locally excised tumours (e.g. transanal endoscopic microsurgery) were also excluded.

Clinical data from patients who underwent colorectal surgery between 2009 and 2015 were obtained from the electronic patient file. Participants who were eligible for inclusion based on information from their electronic patient file were approached via a patient letter.

This letter contained information on the research, an informed consent form and the questionnaires used within this study (see Measures). Patients independently filled in the questionnaires and informed consent at home and could send them back free of charge in a return-paid envelope. Patients who did not respond received a reminder after 8 weeks. This study was approved by the internal board of medical ethical commissions within each participating hospital and deemed not to be subject to the medical research (human subjects) legislative requirements as no intervention was applied.

Measures

Clinical data were derived from the electronic patient file. This included gender, age, marital status, body mass index (BMI), American Society of Anesthesiologists (ASA) score, complication types (according to the Clavien–Dindo classification), tumour stage and location, treatment and time since surgery.

The LARS score, an internationally validated tool, was used to assess bowel dysfunction [10,11]. It consists of five questions with a score that ranges from 0 to 42 points, with classification of patients into: no LARS (0–20 points), minor LARS (21–29 points) or major LARS (30–42 points) [12]. Additionally the European Organization for the Research and Treatment of Cancer (EORTC) QLQ-C30 and QLQ-CR29 questionnaires were used. The EORTC QLQ-C30 questionnaire consists of 30 questions on functional scales, a global QoL measure and symptom assessment [13]. The EORTC QLQ-CR29 questionnaire is designed specifically for CRC, and consists of 29 items addressing gastrointestinal symptoms, side effects of chemotherapy, defaecation problems, pain and problems with micturition, and separate items addressing sexual function for men and women [9]. For both questionnaires, a high functional score represents a high level of function while a high symptom score represents a high level of symptoms. The EORTC HRQoL instruments were scored in accordance with guidelines [13].

Statistical analysis

All statistical analyses were performed using SPSS® Statistics (version 25.0, IBM Corp. Released 2017, Armonk, New York, USA). Comparisons of patient and treatment characteristics between tumour location groups (rectum, colon) were performed using the chi-square test or Fisher's exact test for categorical data and the Mann–Whitney *U*-test for continuous data. The prevalence of the different LARS groups was determined using descriptive analyses. This article focuses on the association between colon tumours and major LARS,

because the association between major LARS and sigmoid/rectal tumours has already been investigated. The following factors having a possible association with major LARS-like symptoms in patients with colon tumours were first tested in univariate analysis: gender (female *vs* male), marital status (married *vs* unmarried), time since operation (years), age at surgery (categorized as < 75 years *vs* ≥ 75 years), tumour stage (TNM 0–1, 2, 3), resection type (right hemicolectomy, left hemicolectomy, sigmoid), surgical technique (laparoscopic, open), temporary stoma (no *vs* yes), operative complication (Clavien–Dindo scale), neoadjuvant therapy (radiotherapy, none), adjuvant therapy (chemotherapy, none) and ASA classification (ASA I, II, III–IV). Significant associations ($P \leq 0.10$) were further tested via binomial logistic regression to assess the independent association of patient, tumour and treatment characteristics with major LARS-like symptoms in patients with colon tumours.

For the association between major LARS and QoL in patients with colon tumours univariate testing was used (Mann–Whitney *U*-test) with binary logistic

Table 1 Baseline characteristics according to tumour location (rectum *vs* colon).

Characteristics	Rectum (n = 350)	Colon (n = 1145)	P-value
Age (years)			
Median	71	73	< 0.001*
Range	34–88	29–96	
Gender			
Male	215 (61.4%)	633 (55.3%)	0.042*
Female	135 (38.6%)	512 (44.7%)	
TNM stage			
Stage 0–1	157 (44.9%)	316 (27.6%)	< 0.001*
Stage 2	99 (28.3%)	493 (43.1%)	
Stage 3	94 (26.9%)	336 (29.3%)	
Time since treatment (years)			
Median	5	4	< 0.001*
Range	2–10	2–10	
Surgical approach			
Laparoscopy	156 (44.7%)	653 (57.0%)	< 0.001*
Laparotomy	193 (55.3%)	492 (43.0%)	
Anastomotic type			
End-to-end	67 (19.2%)	199 (17.4%)	< 0.001*
Side-to-end	252 (72.2%)	429 (37.5%)	
Side-to-side	6 (1.7%)	430 (37.6%)	
J-pouch	3 (0.9%)	6 (0.5%)	
Temporary diverting stoma			
No	74 (21.1%)	1018 (88.9%)	< 0.001*
Yes	276 (78.9%)	127 (11.1%)	
ASA grade			
Grade I	100 (29.2%)	271 (24.0%)	0.002*
Grade II	221 (64.6%)	716 (63.5%)	
Grade III–IV	21 (6.1%)	141 (12.5%)	
Clavien–Dindo			
Grade 0	201 (57.4%)	760 (66.4%)	0.009*
Grade I–II	93 (26.6%)	241 (21.1%)	
Grade III–IV	56 (16.0%)	143 (12.5%)	
Neoadjuvant therapy			
No	98 (28%)	1125 (98.3%)	< 0.001*
Yes	252 (72.0%)	20 (1.7%)	
Adjuvant therapy			
No	263 (75.1%)	821 (71.7%)	0.207
Yes	87 (24.9%)	324 (28.3%)	

All significant differences ($P < 0.05$) are indicated by an asterisk (*).
ASA, American Society of Anesthesiologists.

regression being used for the functional and symptom scales. Finally, the Mann–Whitney *U*-test was used for the comparison of QoL between major LARS and no/minor LARS in the colon and in the rectum.

Results

A total of 5824 patients were operated on for CRC between January 2008 and December 2015. Of these, 2136 were included in this study and received a patient invitation letter. Reasons for exclusion were death ($n = 850$), metastatic disease ($n = 1288$) or Stage 4 tumours ($n = 218$), presence of a colostomy or ileostomy ($n = 897$), local excision ($n = 120$), relapse of disease ($n = 192$), mental disability ($n = 84$) or other reasons, such as missing address ($n = 11$) or poor proficiency in the Dutch language ($n = 28$).

Of the 2136 patients included, 82.6% completed and returned the questionnaires and 12.6% returned an unfilled questionnaire and gave reasons for this. A total of 1495 patients were thus included for analysis. When looking at the distribution of baseline characteristics between the rectum ($n = 350$) and colon groups ($n = 1145$), almost all characteristics were significantly different (Table 1). Patients with a rectal tumour were younger (median 71 *vs* 73 years, $P < 0.001$), had more Stage 0–1 tumours (44.9% *vs* 27.6%, $P < 0.001$) and fewer comorbidities according to the ASA classification (ASA I; 29.2% *vs* 24.0%, $P < 0.001$). In addition, the time since surgery was longer (median 5 *vs* 4 years, $P < 0.001$), the presence of a temporary diverting colostomy/ileostomy was higher (78.9% *vs* 11.1%, $P < 0.001$), more patients had neoadjuvant therapy (72% *vs* 1.7%, $P < 0.001$) and the surgical approach was different (55.3% open surgery *vs* 43.0%, $P < 0.001$).

Prevalence of LARS

Major LARS was observed in 20.9% ($n = 237$) of the patients after surgery for a tumour in the colon, while 55.4% ($n = 194$) of the patients with a tumour in the rectum indicated having major LARS symptoms (Fig. 1). Minor LARS was distributed more evenly between the groups: 19.5% of patients with a colon tumour ($n = 221$) suffered from minor LARS and 20.7% of patients with a rectal tumour ($n = 73$).

When comparing all surgical resection types (rectal resection, sigmoid resection, left hemicolectomy and right hemicolectomy), the percentages of patients reporting major LARS were 51.2% after rectal resection, 20.4% after sigmoid resection, 14.3% after left hemicolectomy and 22.3% after right hemicolectomy (Fig. 2).

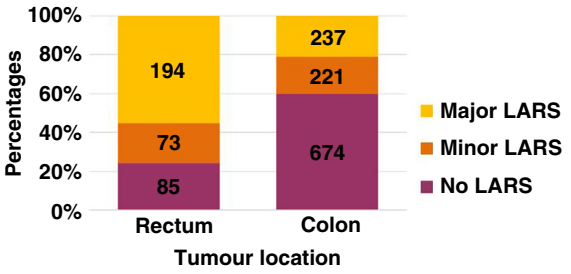

Figure 1 Prevalence of no, minor and major low anterior resection syndrome (LARS) in the rectum *vs* the colon.

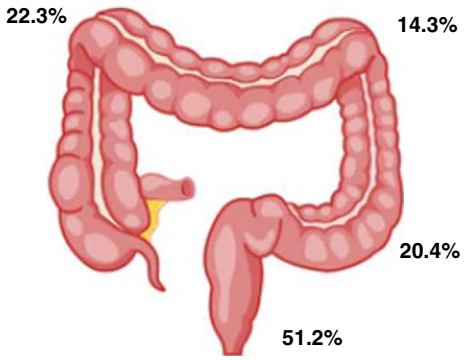

Figure 2 Prevalence of major low anterior resection syndrome (LARS) according to surgical colon resection type.

Factors associated with major LARS in the colon

In univariate analyses (Table 2), patients with colon tumours suffering from major LARS were more likely to be female ($P < 0.001$), had a previous temporary stoma ($P = 0.012$) and have mild postsurgical complications according to the Clavien–Dindo scale ($P = 0.037$). In addition, patients with a tumour in the transverse colon, splenic flexure or descending colon ($P = 0.061$) or patients who received adjuvant therapy ($P = 0.010$) reported fewer major LARS symptoms.

In the multivariate analyses, in patients with colon cancer, women were more likely to suffer from major LARS symptoms than men (OR = 1.9, CI 1.39–2.53), as were patients who had had a diverting stoma in the past (OR 1.8, CI 1.14–2.97). Patients who underwent a left hemicolectomy (OR 0.5, CI 0.31–0.97) or received adjuvant therapy (OR 0.6, CI 0.45–0.89) were less likely to suffer from major LARS symptoms (Table 2).

Association between major LARS and QoL

Quality of life was not normally distributed (skewness −0.97, kurtosis 1.19, Shapiro–Wilk $P < 0.001$). On average, patients with major LARS symptoms reported

Table 2 Independent associations between patient and treatment characteristics and major low anterior resection syndrome in colon cancer survivors.

Associated factors	Patients	Unadjusted OR (95% CI)	*P*-value	Adjusted OR (95% CI)	*P*-value
Age (years)					
< 75	606	0.845 (0.634–1.125)	0.249	NS	NS
≥ 75	526	Reference			
Gender					
Male	626	Reference			
Female	506	1.751 (1.312–2.337)	< 0.001**	1.876 (1.392–2.528)	< 0.001**
Marital status					
Married	817	Reference			
Single/widowed	305	0.976 (0.706–1.350)	0.884	NS	NS
TNM stage					
Stage 0–1	317	Reference			
Stage 2	484	0.904 (0.643–1.270)	0.559	NS	NS
Stage 3	331	0.755 (0.516–1.106)	0.149	NS	NS
Resection type					
Sigmoid	542	Reference			
Left hemicolectomy	118	0.582 (0.331–1.026)	0.061*	0.547 (0.307–0.974)	0.040**
Right hemicolectomy	452	1.068 (0.790–1.446)	0.668	1.051 (0.758–1.456)	0.765
(Sub)total colectomy	20	1.238 (0.441–3.477)	0.686	1.161 (0.402–3.357)	0.782
Surgical approach					
Laparoscopy	646	Reference			
Laparotomy	395	1.182 (0.874–1599)	0.277	NS	NS
Conversion	91	0.649 (0.35–1.203)	0.170	NS	NS
Temporary diverting stoma					
No	1011	Reference			
Yes	121	1.707 (1.122–2.596)	0.012**	1.841 (1.142–2.968)	0.012**
ASA classification					
Grade I	268	Reference			
Grade II	710	1.300 (0.910–1.857)	0.149	NS	NS
Grade III–IV	136	0.910 (0.528–1.569)	0.734	NS	NS
Complications (Clavien–Dindo)					
Grade 0	754	Reference			
Grade I–II	236	1.444 (1.023–2.039)	0.037**	1.415 (0.992–2.020)	0.056*
Grade III–IV	141	1.244 (0.806–1.919)	0.325	1.079 (0.674–1.729)	0.750
Neoadjuvant therapy					
No	1112	Reference			
Yes	20	2.065 (0.815–5.235)	0.127	NS	NS
Adjuvant therapy					
No	812	Reference			
Yes	320	0.658 (0.468–0.923)	0.015**	0.636 (0.450–0.899)	0.010**

Reference values are indicated, values that were not significant ($P > 0.1$) in the univariate analyses are denoted as NS in the multivariate analysis: **high significance ($P < 0.05$); *mild significance ($P \leq 0.1$).
ASA, American Society of Anesthesiologists.

a poorer global QoL (mean QoL 70.9, SD 19.4) compared with patients with no/minor LARS symptoms (mean QoL 80.8, SD 17.1).

The difference between the mean QoL score for patients with no/minor LARS symptoms and major LARS was most substantial in patients who had undergone a (sub)total colectomy (−26.8), followed by patients who had undergone a right hemicolectomy (−13.3) (Fig. 3).

In multivariate analyses, patients with colon tumours and major symptoms reported lower emotional functionality (OR 0.98, CI 0.98–0.99, $P = 0.006$) than patients with no/minor symptoms on the functional scales of the QLQ-C30. On the symptom scales, the same patient group also reported more pain (OR 1.01, CI 1.00–1.02, $P = 0.034$), insomnia (OR 1.006, CI 1.00–1.01, $P = 0.047$) and diarrhoea (OR 1.04, CI

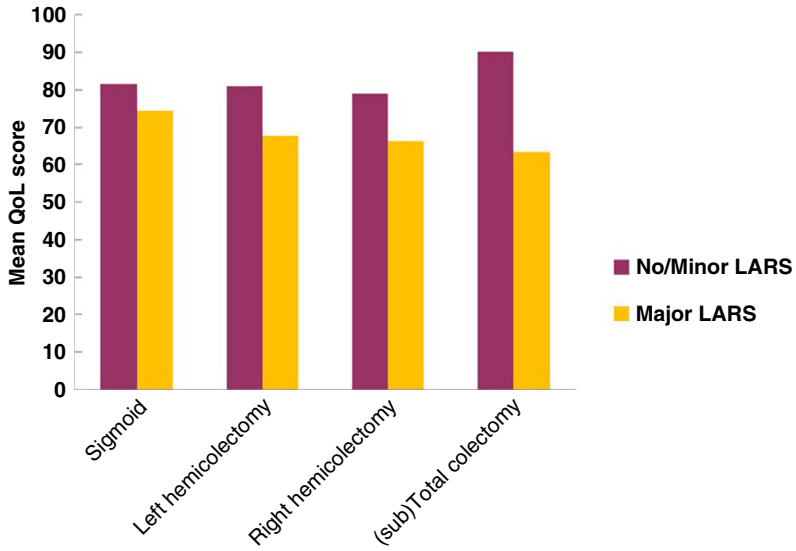

Figure 3 Mean quality of life (QoL) scores for each resection type between no/minor low anterior resection syndrome (LARS) and major LARS in colon cancer survivors.

1.03–1.05, $P < 0.001$) than the no/minor LARS group (Table 3).

With respect to colorectal-specific QoL (QLQ-CR29), patients with major symptoms reported less anxiety regarding the future (OR 1.016, CI 1.01–1.02, $P < 0.001$) than patients with no/minor LARS. Among the symptom scales, patients with major symptoms reported higher stool frequency (OR 1.05, CI 1.04–1.06, $P < 0.001$) and incontinence (OR 1.03, CI 1.02–1.04, $P < 0.001$), as well as more problems with controlling flatulence (OR 1.02, CI 1.01–1.03, $P < 0.001$; Table 4).

There was no difference in QoL between colon and rectal patients with major symptoms of LARS ($P = 0.138$).

Discussion

This study is the first to describe the prevalence of LARS-like complaints and the association with patients' QoL after resections at different levels of the colon and rectum. Although we found that the presence of major LARS symptoms remains most common among rectal cancer patients treated surgically, more than one-fifth of the patients who underwent surgical treatment for a tumour in the colon also declared abdominal LARS-like complaints. The patients suffering from LARS-like complaints in the colon reported the same debilitating effect of this on their QoL as patients with major LARS symptoms after rectal resection.

Previous studies have already reported a decrease in postoperative functional abdominal complaints with increasing tumour height among survivors of rectal cancer [14,15]. A recent publication from our group described major LARS-type symptoms after sigmoid resections [6]. Similarly, in the present study we found a 20.4% prevalence of major LARS symptoms after resection of a tumour in the sigmoid. Furthermore, by using the LARS score we were able to demonstrate the prevalence of troublesome functional bowel symptoms even years after resection for a tumour located above the sigmoid colon. We found the presence of major LARS symptoms in 14.3% and 22.3%, respectively, of patients after left and right hemicolectomy. Bowel complaints after surgery at different colonic levels have been described before with the use of the EORTC questionnaires [16]. These publications have shown significantly more abdominal complaints after right-sided than after left-sided colonic resections [17,18]. From a pathophysiological point of view a number of different mechanisms have been proposed, suggesting a multifactorial aetiology for LARS-type symptoms [19–21].

One important factor probably relates to water and electrolyte absorption, as this is a primary function of the colon. Inevitably, following resection there is less remaining absorptive capacity which will predispose to more liquid stool, increased bowel frequency, gas and a higher risk of faecal incontinence [22]. In this context we observed differences in the prevalence of LARS-like symptoms in relation to the site of colonic resection, with the highest prevalence of symptoms occurring after sigmoid and right colon resection. The higher prevalence of functional bowel complaints in patients who underwent a sigmoid resection may also be a consequence of a reduced reservoir function of the rectum when this is incorporated into an anastomosis [23,24]. As the anastomosis in a left-sided colonic resection is colo-colonic, the reservoir function of the rectum is spared and functional complaints are less likely to occur.

Table 3 The associations between the EORTC QLQ-C30 functional/symptom scale and no/minor *vs* major low anterior resection syndrome (LARS) in colon cancer survivors.

	Patients	Unadjusted OR (95% CI)	*P*-value	Adjusted OR (95% CI)	*P*-value
Physical function					
No/minor LARS	888	Reference			
Major LARS	232	0.979 (0.972–0.985)	< 0.001**	0.994 (0.984–1.004)	0.270
Role function					
No/minor LARS	885	Reference			
Major LARS	232	0.981 (0.976–0.986)	< 0.001**	0.992 (0.984–1.001)	0.086*
Emotional function					
No/minor LARS	881	Reference			
Major LARS	234	0.978 (0.972–0.984)	< 0.001**	0.988 (0.980–0.997)	0.006**
Cognitive function					
No/minor LARS	885	Reference			
Major LARS	235	0.981 (0.974–0.988)	< 0.001**	0.997 (0.988–1.006)	0.463
Social function					
No/minor LARS	884	Reference			
Major LARS	234	0.979 (0.973–0.985)	< 0.001**	0.995 (0.986–1.004)	0.316
Fatigue					
No/minor LARS	887	Reference			
Major LARS	232	1.025 (1.019–1.032)	< 0.001**	1.009 (0.999–1.020)	0.076*
Nausea/vomiting					
No/minor LARS	886	Reference			
Major LARS	233	1.029 (1.017–1.041)	< 0.001**	1.003 (0.9881–1.018)	0.723
Pain					
No/minor LARS	890	Reference			
Major LARS	234	1.024 (1.017–1.031)	< 0.001**	1.010 (1.001–1.020)	0.034**
Dyspnoea					
No/minor LARS	887	Reference			
Major LARS	231	1.015 (1.010–1.021)	< 0.001**	1.005 (0.997–1.012)	0.206
Insomnia					
No/minor LARS	886	Reference			
Major LARS	233	1.014 (1.010–1.019)	0.002**	1.006 (1.000–1.013)	0.047**
Appetite loss					
No/minor LARS	887	Reference			
Major LARS	232	1.017 (1.009–1.024)	< 0.001**	0.994 (0.984–1.005)	0.286
Constipation					
No/minor LARS	887	Reference			
Major LARS	229	1.008 (1.002–1.015)	0.014**	1.002 (0.994–1.010)	0.659
Diarrhoea					
No/minor LARS	884	Reference			
Major LARS	235	1.045 (1.038–1.053)	< 0.001**	1.042 (1.035–1.050)	< 0.001**
Financial problems					
No/minor LARS	879	Reference			
Major LARS	232	1.019 (1.012–1.027)	< 0.001**	1.000 (0.991–1.010)	0.962

Reference values are indicated, values that were not significant ($P > 0.1$) in the univariate analyses are denoted as NS in the multivariate analysis: **high significance ($P < 0.05$); *mild significance ($P \leq 0.1$).
Sex, resection type, temporary diverting stoma and adjuvant therapy were included as confounders in the multivariate analyses.

Nevertheless, with right-sided colonic resections the prevalence of abdominal complaints increases. An additional factor other than a reduction in absorptive capacity may be the consequences of loss of the ileocaecal valve [25–30].

Our results suggest that the survivors of colon cancer, female gender and a temporary stoma were independently associated with an increased prevalence of major LARS symptoms. The association between gender and LARS-type symptoms has already been

Table 4 The associations between EORTC QLQ-CR29 functional/symptom scales and no/minor *vs* major low anterior resection syndrome (LARS) in colon cancer survivors.

	Patients	Unadjusted OR (95% CI)	*P*-value	Adjusted OR (95% CI)	*P*-value
Body image					
No/minor LARS	872	Reference			
Major LARS	226	1.018 (1.011–1.026)	< 0.001**	1.004 (0.993–1.015)	0.480
Anxiety					
No/minor LARS	882	Reference			
Major LARS	232	1.021 (1.016–1.027)	< 0.001**	1.016 (1.008–1.023)	< 0.001**
Weight					
No/minor LARS	885	Reference			
Major LARS	232	1.013 (1.007–1.018)	< 0.001**	1.006 (0.99–1.013)	0.111
Sexual dysfunction					
No/minor LARS	695	Reference			
Major LARS	176	1.429 (0.990–2.063)	0.057*	1.199 (0.805–1.787)	0.372
Urinary frequency					
No/minor LARS	873	Reference			
Major LARS	228	1.024 (1.017–1.030)	< 0.001**	1.003 (0.994–1.012)	0.487
Blood and mucus in stool					
No/minor LARS	879	Reference			
Major LARS	233	1.051 (1.032–1.070)	< 0.001**	1.008 (0.981–1.035)	0.569
Stool frequency					
No/minor LARS	848	Reference			
Major LARS	227	1.071 (1.061–1.082)	< 0.001**	1.051 (1.038–1.064)	< 0.001**
Urinary incontinence					
No/minor LARS	882	Reference			
Major LARS	232	1.022 (1.016–1.028)	< 0.001**	1.009 (0.99–1.018)	0.066*
Dysuria					
No/minor LARS	879	Reference			
Major LARS	233	1.018 (1.006–1.030)	0.002**	0.989 (0.969–1.010)	0.313
Abdominal pain					
No/minor LARS	883	Reference			
Major LARS	231	1.021 (1.014–1.028)	< 0.001**	1.008 (0.997–1.019)	0.165
Buttock pain					
No/minor LARS	882	Reference			
Major LARS	233	1.025 (1.018–1.033)	< 0.001**	1.004 (0.991–1.018)	0.550
Bloating					
No/minor LARS	883	Reference			
Major LARS	232	1.025 (1.019–1.031)	< 0.001**	1.002 (0.992–1.012)	0.704
Flatulence					
No/minor LARS	850	Reference			
Major LARS	230	1.036 (1.030–1.042)	< 0.001**	1.022 (1.015–1.030)	< 0.001**
Faecal incontinence					
No/minor LARS	848	Reference			
Major LARS	229	1.056 (1.046–1.066)	< 0.001**	1.031 (1.018–1.043)	< 0.001**
Sore skin					
No/minor LARS	848	Reference			
Major LARS	228	1.026 (1.019–1.034)	< 0.001**	0.984 (0.987–1.013)	0.984

Reference values are indicated, values that were not significant ($P > 0.1$) in the univariate analyses are denoted as NS in the multivariate analysis: **high significance ($P < 0.05$); *mild significance ($P \leq 0.1$)

Sex, resection type, temporary diverting stoma and adjuvant therapy were included as confounders in the multivariate analyses.

described [6,31] and may be accounted for by a higher risk of pelvic floor dysfunction associated with obstetric trauma [31].

The association between major LARS symptoms and a history of a diverting stoma is more difficult to explain. An altered gastrointestinal microbiome in the

excluded part of the colon with possible permanent mucosal changes after restoration has been suggested but is unlikely to persist for more than a few weeks following closure [32,33] Surprisingly, adjuvant therapy seemed to have a protective effect for the development of long-term complaints after colon cancer surgery. This positive effect on patients' postoperative functioning was seen previously in a study investigating QoL after adjuvant chemotherapy for colon cancer [34]. This result could partly be due to selection bias, in which chemotherapy tends to be offered to the healthier patients. Another explanation could be the 'response shift' phenomenon which leads patients faced with cancer and its demanding treatment to adopt a more pragmatic attitude regarding their everyday life experiences and therefore to reduce their initial expectations regarding functional complaints, resulting in an improvement of perceived QoL [35].

In agreement with previous studies that have investigated LARS-type symptoms in both colon and rectal cancer patients, we have confirmed an association between QoL and major symptoms but no impairment with minor symptoms [36,37]. Patients with major LARS symptoms in our study scored worse on almost all domains that concern functional abdominal complaints (increased faecal frequency, incontinence and decreased flatulence control, abdominal pain). On the more general symptoms (QLQ-C30) and colorectal-specific (QLQ-CR29) questions, patients with major LARS reported an increase in insomnia, but the effect was small. The insomnia could be related to the abdominal issues, with nightly disruptions caused by the need to go to the bathroom. Interestingly, patients with major LARS tended to report fewer worries about the future and their psychological well-being than patients suffering from no/minor LARS. No differences were found when comparing QoL in patients with major LARS within the colon with patients with major LARS in the rectum. Even though there is a higher prevalence of major LARS symptoms after rectal resection, the association with QoL is as severe in patients with a colonic resection.

One of the strengths of our study is the high response rate in a sufficiently large population of CRC survivors. Another strength is the use of comprehensive validated questionnaires to determine both the prevalence of abdominal complaints and the concomitant QoL.

We recognize that the major limitation of this study is the use of the LARS score. This was originally developed for patients who had undergone an anterior resection, and application to patients who have had colonic resection may have drawbacks [10]. However, the use of the score is justified, as a significant proportion of patients have reported functional abdominal LARS-like complaints after colonic resection. The cross-sectional design of this study might have been a possible limitation as it is not the most reliable design and no causal relations between patient characteristics and the prevalence of postoperative complaints can be established. Another limitation might be the fact that only patients who were stoma free for at least 1 year were included. Since functional abdominal complaints are most prominent in the first year after treatment, a prospective study to investigate intra-patient changes could yield more information about certain causal relations.

Conclusion

LARS describes a well-known cluster of troublesome symptoms that not infrequently occur after surgery for rectal cancer. This is the first study aiming to raise awareness of similar symptoms after colonic resection. This study reveals LARS-like symptoms not only after surgical treatment for rectal cancer but also in a considerable proportion of patients after surgery for colon cancers. In addition, patients suffering from major LARS in the colon report the same debilitating effect on their QoL as patients with major LARS after rectal resection. The present study highlights an unknown problem that should be addressed by CRC specialists in order to adequately inform patients pre- and postoperatively about the symptoms they might experience.

Conflicts of interest

None declared.

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