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European Journal of Surgical Oncology 44 (2018) 1261–1267

Contents lists available at ScienceDirect

European Journal of Surgical Oncology

journal homepage: www.ejso.com

Bowel dysfunction after sigmoid resection underestimated: Multicentre study on quality of life after surgery for carcinoma of the rectum and sigmoid☆

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ARTICLE INFO

Article history:
Accepted 3 May 2018
Available online 9 May 2018

Keywords:
Health-related quality of life
Bowel dysfunction
Low anterior resection syndrome
Rectal cancer
Sigmoid cancer
Sigmoid resection

ABSTRACT

Aim: The Low Anterior Resection Syndrome (LARS) severely affects quality of life (QoL) after rectal cancer surgery. There are no data about functional complaints after sigmoid cancer surgery. We investigated LARS and QoL in patients with a resection for sigmoid cancer versus patients who had surgery for rectal cancer.

Methods: 506 patients after resection for rectal or sigmoid cancer who were at least one year colostomy-free were included between January 2008 and December 2013. Bowel function was assessed by the LARS-Score. QoL was assessed by the EORTC QLQ-C30 and -CR29 questionnaires. QoL was compared between the LARS score categories and tumour height categories.

Results: 412 respondents (81.5%) could be included for the analyses. The median interval since treatment was 5 years, and the median age at the follow-up point was 72 years. Major LARS increased significantly with decreasing tumour height from one fifth in sigmoid carcinoma to 90% in low rectum carcinoma. Female gender (OR = 2.162; 95% CI: 1.349–3.467), postoperative temporary diverting stoma (OR = 3.457; 95% CI: 2.019–5.919) and tumours located in the middle (OR = 3.193; 95% CI: 1.696–6.010) or lower rectum (OR = 8.247; 95% CI: 1.672–40.678) were independently associated with the development of major LARS. Patients with major LARS fared significantly worse in most QOL domains.

Conclusions: For the first time, we found that functional abdominal complaints after sigmoid surgery are a major problem, with a negative effect on QoL, even 5 years after treatment. Patients need to be adequately informed about these long-term complaints.

Introduction

There is progress in the opportunity to perform sphincter-preserving surgery in patients with rectal cancer. This has led to a decrease in abdominoperineal resections in which the anal sphincter cannot be preserved and avoids the construction of a permanent stoma [1]. Despite this benefit, previous research from our hospital accentuates an on-going discussion between performing a colorectal anastomosis versus a lifelong stoma [2]. A recent publication has shown that rectal cancer survivors with a stoma have a poorer Quality of Life (QoL), worse illness perceptions, and a higher health care consumption, but fewer bowel symptoms like diarrhoea and constipation [3]. Other publications have also demonstrated bothersome changes in bowel habits like faecal incontinence, frequent bowel movements, urgency and emptying difficulties after low anterior resection (LAR) with an anastomosis. This cluster of symptoms is referred to as Low Anterior Resection

☆ The paper is not based on a previous communication to a society or meeting.

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https://doi.org/10.1016/j.ejso.2018.05.003
0748-7983/

Syndrome (LARS) [4]. With a prevalence up to 60–90%, LARS severely affects QoL, even years after treatment [5].

Previous studies have shown that not only patients with low rectal cancer had a worse bowel function after sphincter preserving surgery, but also patients with high rectal resection might have functional abdominal complaints [6,7]. [8], Concordant with these findings the height of the anastomosis, i.e. the length of the residual rectal stump, is an important predictive factor for gastrointestinal functional results [9,10]. The occurrence of functional abdominal complaints and the effect on QoL has been investigated extensively for rectal cancer. Few data are available describing these complaints after sigmoid resections [11,12].

Colorectal surgeons do not have a thorough understanding of which bowel dysfunctions truly matter to the patient nor how it affects QoL [13]. Therefore, it is of high clinical relevance to assess the presence of these complaints after sigmoid resection in order to counsel patients adequately before surgery.

The aim of our study was to investigate the prevalence of symptoms and quality of life including possible risk factors in patients with a high rectal anastomosis for sigmoid cancer versus a low anastomosis in patients with rectal cancer without a permanent stoma.

Patients and methods

Data collection

All patients who underwent low anterior resection (LAR) for rectal cancer or sigmoid resection for sigmoid cancer in three general hospitals in the Netherlands between January 2008 and December 2013 were included. Patients aged >18 years and at least 1 year free of stoma were included. Exclusion criteria were: presence of a stoma; disseminated or recurrent disease; intellectual disability; patients with inconsistent pre- and postoperative tumour height measures (difference >1 cm between two successive exams). Demographic and clinical information were obtained from patient records. Participants were approached via a letter explaining the aim of the study together with the questionnaires and a prepaid return envelope. The letters were sent between September 2015 and April 2016 to ensure a minimum duration of 1 year after stoma reversal to allow their bowel function to have regained stability [14]. The study was approved by the hospitals' ethical committees.

Measures

The LARS score, an internationally validated tool, was used to assess bowel dysfunction [15]. It consists of 5 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), Major LARS (30-42 points) [16]. Additionally the European Organization for the Research and Treatment of Cancer (EORTC) QLQ-C30 and -CR29 questionnaires were used. The EORTC QLQ-C30 questionnaire consists of 30 questions on functional scales, a global QoL measure and symptom assessment [17]. The EORTC QLQ-CR29 questionnaire is designed specifically for colorectal cancer, and consists of 29 items addressing gastrointestinal symptoms, chemotherapy side effects, defecation problems, pain and problems with micturition, and separate items addressing sexual function for men and women [18]. For both questionnaires a high functional score represented a high level of function while a high symptom score represented a high level of symptoms.

Statistical analysis

Comparisons between treatment groups (Rectum vs. Sigmoid) were performed using x^2 test or Fisher's exact test for categorical data and the Mann–Whitney *U* test for continuous data. The following factors with a possible association with major LARS were first tested in univariate analysis: gender, age at surgery (categorized as ≤ 75 vs. > 75 years), marital status, time since operation (years), tumour height (rectal cancer: measured by MRI; sigmoid cancer: measured by colonoscopy (Lower Rectum: <5 cm, Mid Rectum 5–9.9 cm, High Rectum: 10–14.9 cm, Sigmoid: >15 cm), postoperative tumour stage (TNM 0, I, II, III), neo-adjuvant therapy (radiotherapy, chemoradiotherapy, no neo-adjuvant therapy), adjuvant therapy (chemotherapy, no adjuvant therapy), surgical technique (laparoscopic vs. open), temporary diverting stoma (Yes vs. No), operative complication (Clavien-Dindo scale) and ASA-classification (1-6)). The independent association of potential risk factors with major LARS were tested using a multiple logistic regression analysis. Only the variables that were possible risk factors in univariate analyses ($p < 0.10$) were included in a stepwise multivariate analysis to derive a final model of the variables that had a significant relationship with major LARS. To add or remove a variable from the model, the corresponding *P*-value had to be respectively smaller than 0.05 and greater than 0.10. The EORTC HRQL instrument was scored according to the guidelines. EORTC HRQL scores were compared between tumour height groups as well as between LARS score categories using x^2 test or the Mann-Whitney *U* test where appropriate. A recent study showed both clinical and significant differences in QoL between the major LARS and no LARS groups, and between the major LARS and minor LARS groups, but not between the no LARS and minor LARS groups [19]. Based on these findings we compared QoL scores for patients with 'major LARS' versus 'no or minor LARS'. All statistical analyses were performed using IBM® SPSS® Statistics, version 22.

Results

A total of 1441 patients underwent surgery for rectal or sigmoid cancer between January 2008 and December 2013. 935 Patients were excluded: died prior to the start of study (N = 452), presence of a stoma (N = 291), disseminated (N = 46) or recurrent (N = 13) disease, intellectual disability/dementia (N = 10), other operations than LAR or sigmoid resection for rectal or sigmoid cancer (N = 103) and inconsistent pre- and postoperative tumour height measures (difference >1 cm between two successive exams) (N = 20). Finally 506 patients were eligible for inclusion. 458 patients (90.5%) returned the questionnaire, of whom 46 patients returned a blank or incomplete questionnaire, leaving 412 (81.5%) for analyses (Fig. 1).

At inclusion, characteristics of rectum (N = 163) and sigmoid (N = 249) cancer patients were similar, except for surgical approach with a higher frequency of laparoscopy in the sigmoid group ($p = 0.008$), more temporary diverting stoma creations in the rectum group ($p < 0.01$) and a lower complication rate in the sigmoid group ($p < 0.01$). The median interval since treatment was 4.9 years (range 2.3–8.4) in the rectum group vs. 5.2 years (range 2.3–8.3) in the sigmoid group. Median age was 72 years for both groups (range rectum 47-86; range sigmoid 31-94). (Table 1).

Bowel dysfunction

'Major LARS' was observed in 34% (N = 141) of all patients, increasing significantly with decreasing tumour height from 21.7% in sigmoid cancer patients to 83.3% in lower rectum cancer patients (Fig. 2). 'Minor LARS' was observed in 18.9% of sigmoid cancer patients vs. 8.3% of lower rectum cancer patients while 'No LARS' was observed in 59.4% and 8.3%, respectively.

The following factors were independently associated with the development of Major LARS after surgery for both rectum and

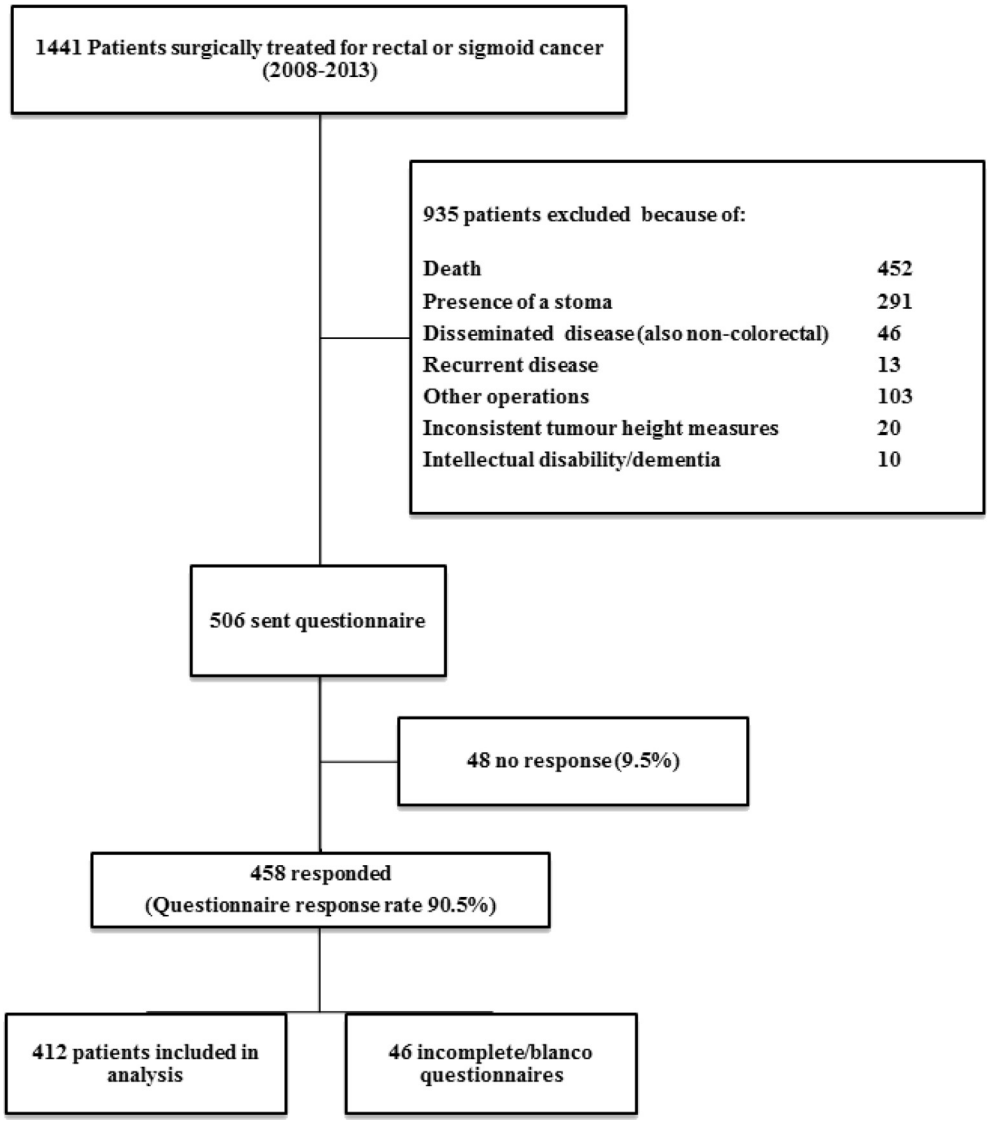

Fig. 1. Flow chart of study patients.

sigmoid tumours: Female gender (OR = 2.16 95% CI: 1.35–3.47), postoperative temporary diverting stoma (OR = 3.46; 95%CI: 2.02–5.92), tumours located in the middle (OR = 3.19; 95%CI: 1.70–6.01) and lower rectum (OR = 8.25; 95%CI: 1.67–40.68) (Table 2).

LARS and quality of life

Major LARS was significantly associated with a reduced QoL. Patients with major LARS fared significantly worse compared with patients with no/minor LARS in all "general" QoL domains (QLQ-C30 questionnaire), except for physical functioning where statistical significance was not reached at the $p < 0.05$ level ($p = 0.065$) and dyspnoea where no significant difference between the groups was observed ($p = 0.491$) (Fig. 3). Patients suffering major LARS also scored significantly worse in all functional and symptom scales of the QLQ-CR29 questionnaire, except for: dysuria ($p = 0.138$), dry mouth ($p = 0.066$), worry about weight ($p = 0.124$), sexual interest in women ($p = 0.813$) and dyspareunia ($p = 0.922$) (Fig. 4).

Rectum vs. sigmoid carcinoma

Among patients with major LARS, no statistically significant differences in general QoL (QLQ-C30 questionnaire) were observed between rectum and sigmoid cancer patients. When analysing the colorectal cancer specific (QLQ-CR29 questionnaire) among patients with major LARS, sigmoid cancer patients suffered significantly less often from blood and mucus in their stool ($p = 0.016$), faecal incontinence ($p = 0.002$), sore skin ($p = 0.036$) and an increased stool frequency ($p = 0.001$) than rectal cancer patients.

Discussion

To the best of our knowledge, our study is the first demonstrating minor and major LARS in almost 41% of patients after a sigmoid resection for cancer. Although the prevalence of major LARS significantly decreased with increasing tumour height, still one fifth of all patients with sigmoid carcinoma suffered from major functional bowel complaints resulting in a severely affected quality

Table 1
Comparison of patient characteristics between tumour height groups.

Characteristic	Rectum (n=163)	Sigmoid (n=249)	*P* Value
Age (Years)			0.119
Median	72	72	
Range	47–86	31–94	
Gender			0.950
Male	99 (60.7%)	152 (61.0%)	
Female	64 (39.3%)	97 (39.0%)	
Marital status			0.590
Single/Widowed	30 (18.4%)	51 (20.5%)	
Married	133 (81.6%)	198 (79.5%)	
TNM stage			0.503
0	8 (4.9%)	3 (1.2%)	
I & II	104 (63.8%)	157 (63.1%)	
III & IV	51 (31.3%)	89 (35.7%)	
Tumor height (cm from anal verge)			
Low rectum: <5 cm	12 (7.4%)	0 (0%)	
Mid rectum: 5 cm–9.9 cm	82 (50.3%)	0 (0%)	
High rectum: 10 cm–14.9 cm	69 (42.3%)	0 (0%)	
Sigmoid: ≥15 cm	0 (0%)	249 (100%)	
Interval since treatment (Years)			0.362
Median	4.9	5.2	
Range	2.3–8.4	2.3–8.3	
Surgical approach			0.008
Laparoscopy	74 (45.4%)	146 (58.6%)	
Laparotomy	89 (54.6%)	103 (41.4%)	
Temporary diverting stoma			<0.001
Yes	128 (78.5%)	55 (22.1%)	
No	35 (21.5%)	194 (77.9%)	
Stoma days (Days)			0.119
Median	136	154	
Range	6–497	7–529	
ASA grade			0.103
Grade I–II	149 (93.7%)	216 (88.9%)	
Grade III–IV	10 (6.3%)	27 (11.1%)	
Complication (Clavien-Dindo)			<0.001
Grade 0 (No complication)	94 (57.7%)	184 (73.9%)	
Grade I–II	48 (29.4%)	42 (12.9%)	
Grade III–IV	21 (12.9%)	33 (13.3%)	

of life. Female gender, a temporary stoma and tumours located in the middle and lower part of the rectum were significantly associated with increased prevalence of major LARS. Patients with major LARS fared significantly worse compared with patients with no/minor LARS in almost all "general QoL" and "symptom-related QoL" domains. These results are in consonance with previous studies that have shown a decrease in bowel dysfunction with increasing tumour height for rectal cancer. Although previous studies have shown that patients experience long-lasting functional complaints after sigmoid resection for diverticulitis [12,20], evidence for these complaints after sigmoid cancer resection is scarce [21,22]. Our study confirmed previous results demonstrating an association between female gender and major LARS after surgery, hypothesizing that besides a different pelvic anatomy other concomitant risk factors such as obstetric trauma and pelvic floor dysfunction might account for this association [23]. In line with recent publications, our study found an association between a diverting stoma in the past and the presence of major LARS even after adjustment for tumour height [8,24]. The decision to create a protective stoma relies on peri-operative risk estimation, especially regarding the risk of anastomotic leakage, which could be an indirect causal relation. Another explanation might be the presence of an altered gastro-intestinal microbioma in the excluded part of the colon with possible mucosal changes [25,26]. The current study demonstrates an impaired QoL for patients with bowel dysfunction after sigmoid and rectum resection. There was a significant decrease in almost all "general" QoL domains in patients with major LARS. The greatest differences between major and no/minor LARS were found in: role functioning, social functioning and diarrhoea [27,28], which confirms a persisting influence of abdominal complaints on regular daily activities and social withdrawal as has been shown for rectal cancer previously [24]. Patients suffering from major LARS also scored significantly worse on practically all colorectal-specific QoL items (QLQ-CR29). The most striking differences were observed in the typical abdominal function subscales like abdominal and buttock pain, bloating, blood and mucus in stool, flatulence, faecal incontinence, sore skin, stool frequency and embarrassment, which were all significantly more common among patients with major LARS. The fact that the subscales that have the highest consistency with the LARS-score are also most significantly different in our patient population contributes to the presumption that there also is a high correlation between the EORTC QLQ-CR29 questionnaire and LARS score in a sigmoid cancer population, which had not been described previously. The fact that lower

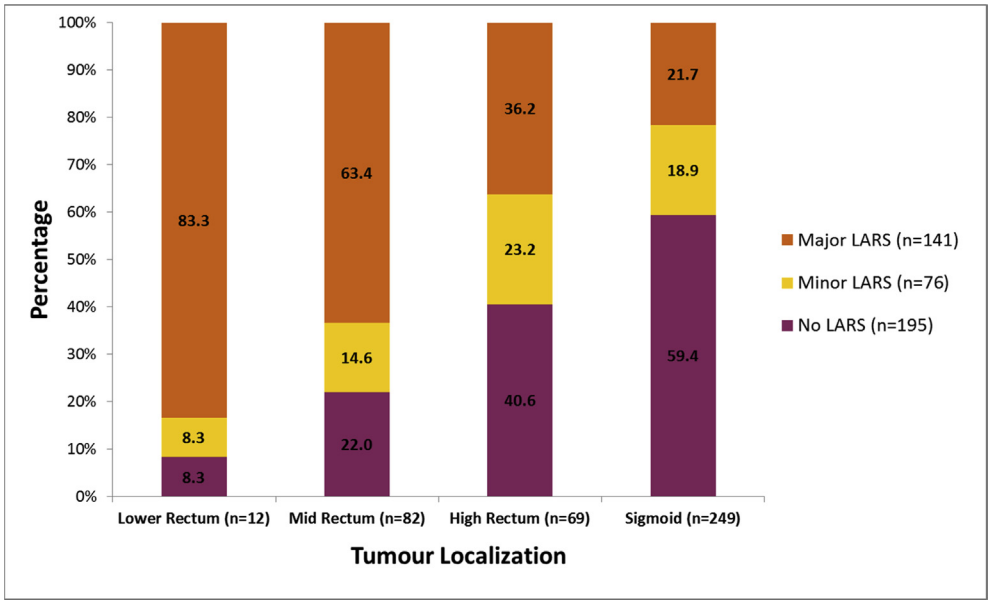

Fig. 2. LARS score severity categories according to tumour localization.

Table 2
Potential risk factors for major LARS.

Associated factor	Patients (n = 412)	Unadjusted OR (95% CI)	*P*-value	Adjusted OR (95% CI)	*P*-value
Age at follow-up (years)					
≥75	147	*Reference*		*n.s.*	
<75	265	1.49 (0.96–2.3)	0.072		
Gender					
Male	251	*Reference*		*Reference*	
Female	161	1.78 (1.18–2.70)	0.006	2.16 (1.35–3.47)	0.001
Marital status					
Married	331	*Reference*		*n.i.*	
Single/Widowed	81	1.06 (0.63–1.77)	0.837		
TNM stage					
III–IV	140	*Reference*		*n.s.*	
I–II	261	5.63 (1.43–22.23)	0.014		
0	11	1.07 (0.69–1.66)	0.750		
Tumour height (distance from anal verge)					
Sigmoid (≥15 cm)	249	*Reference*		*Reference*	
High rectum (10–14.9 cm)	69	2.05 (1.15–3.65)	0.014	1.25 (0.66–2.37)	0.497
Mid rectum (5–9.9 cm)	82	6.26 (3.64–10.75)	<0.001	3.19 (1.70–6.01)	<0.001
Low rectum (<5 cm)	12	18.06 (3.84–84.88)	<0.001	8.25 (1.67–40.68)	0.010
Neo-adjuvant therapy					
No neo-adjuvant therapy	277	*Reference*		*Reference*	
Radiotherapy	96	4.10 (2.51–6.69)	<0.001	1.29 (0.49–3.43)	0.607
Chemoradiotherapy	39	5.33 (2.64–10.76)	<0.001	1.20 (0.40–3.65)	0.745
Adjuvant therapy					
No adjuvant therapy	271	*Reference*		*n.i.*	
Chemotherapy	141	1.19 (0.88–1.59)	0.250		
Surgical approach					
Laparoscopy	220	*Reference*		*n.i.*	
Laparotomy	192	0.97 (0.65–1.46)	0.883		
Temporary diverting stoma					
No	229	*Reference*		*Reference*	
Yes	183	5.25 (3.37–8.18)	<0.001	3.46 (2.02–5.92)	<0.001
ASA grade					
Grade I–II	365	*Reference*		*n.i.*	
Grade III–VI	37	0.59 (0.27–1.29)	0.188		
Complication (Clavien-Dindo)					
Grade 0 (No complication)	278	*Reference*		*n.s.*	
Grade I–II	80	2.74 (1.64–4.56)	<0.001		
Grade III–IV	54	1.34 (0.73–2.49)	0.347		

Variables with a *P*-value >0.10 in univariate analysis were not included (n.i.) in the stepwise multivariate analysis. Variables that were not added to the model (p-in >0.05) or were removed from the model (p-out > 0.10) were defined as not significant (n.s.).

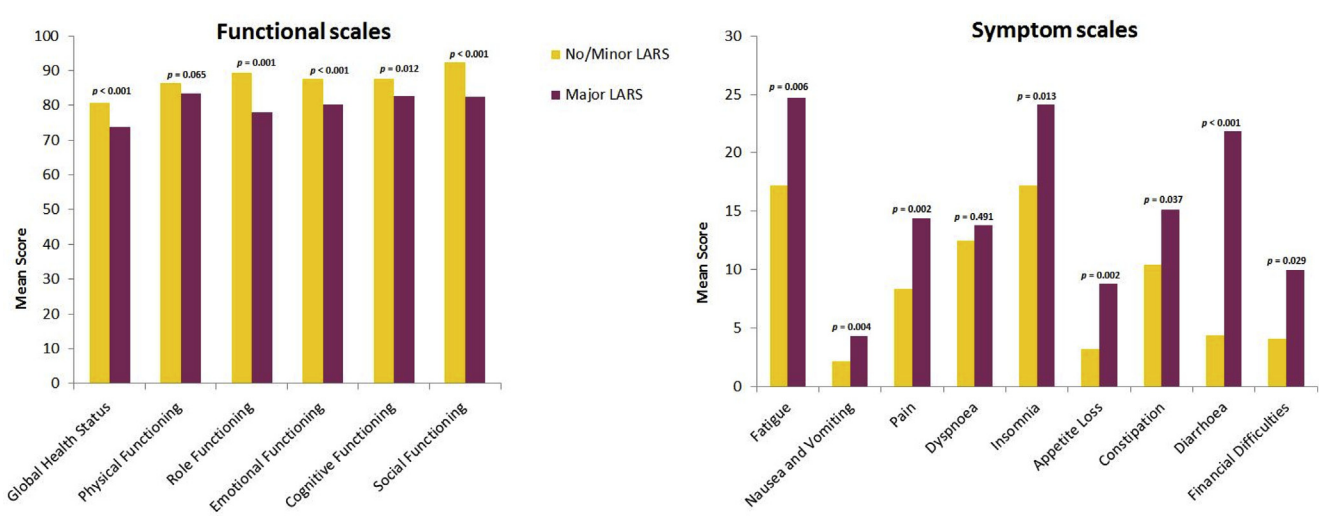

Fig. 3. Mean scores of EORTC QLQ-C30 subscales by LARS groups. Functional scales: A higher score represents a better level of functioning. Symptom scales: A higher score represents a higher level of symptoms.

tumours are associated with a higher degree of bowel dysfunction suggests that rectum cancer patients have a potential lower quality of life compared with sigmoid cancer patients. However, when we compared QoL between rectal and sigmoid cancer patients with major LARS, we found no difference in terms of general quality of life (QLQ-C30). These data suggest a similar effect of bowel dysfunction on general quality of life in both cancer groups. However, colorectal cancer-specific quality of life was significantly

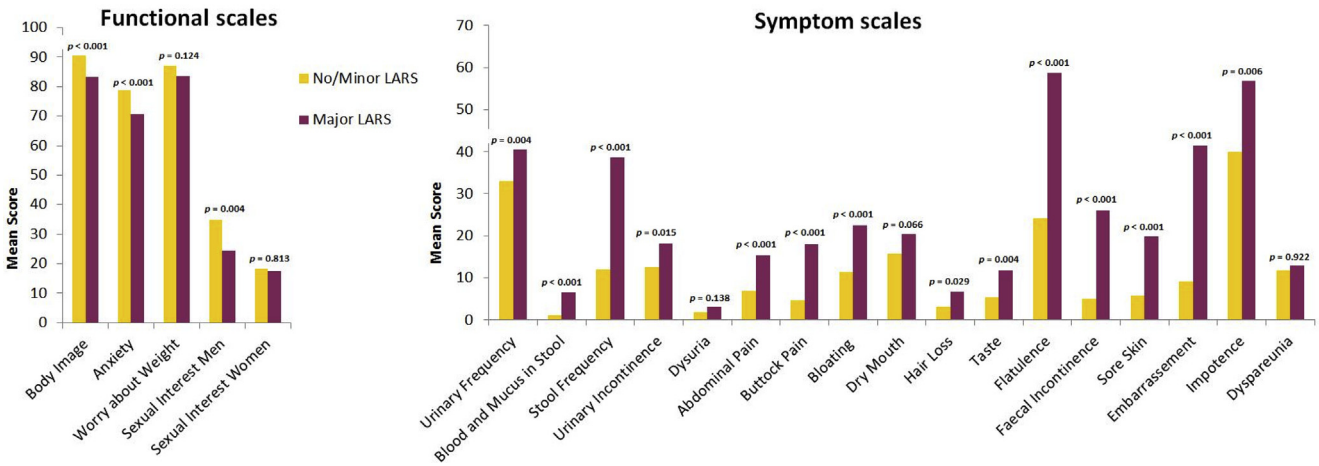

Fig. 4. Mean scores of EORTC QLQ-CR29 subscales by LARS groups. Functional scales: A higher score represents a better level of functioning. Symptom scales: A higher score represents a higher level of symptoms.

better in sigmoid cancer patients with major LARS than in rectum cancer patients with major LARS. This is most likely explained by the higher risk of direct surgical and radiotherapy induced nerve damage in treatment of rectal tumours compared with sigmoid tumours [4,29,30]. In line with these findings we found an association between the incidence of major LARS and receiving neo-adjuvant therapy in univariate analysis. Nevertheless, after adjustment for confounders such as tumour height no significant association could be found. The relative high amount of sigmoid cancer patients compared to rectal cancer patients included was mainly due to the higher stoma-rate in the rectal cancer group. The high response rate together with the use of comprehensive, validated questionnaires in a sufficiently large cohort is crucial to the strength of our study. New in our study is the analysis of the association between tumour height (e.g. sigmoid) and the development of bowel dysfunction. As bowel dysfunction after resection for tumours in the sigmoid is relatively unknown, this information is necessary for pre-operative counselling. The use of the LARS score may be a potential limitation. Knowing that the LARS score is specifically designed to evaluate bowel symptoms after surgery for rectal cancer, it may sound contradictory to use this in sigmoid cancer patients [15]. However, as one fifth of patients with sigmoid cancer reported major LARS, functional problems as described in the LARS-score also seem to be of clinical relevance in these patients. Another possible limitation is the cross-sectional design. Functional abdominal complaints and the decline in QoL are most prominent in the first twelve months after colorectal surgery [31,32]. Therefore, performing a prospective study, with the inclusion of relevant control groups to investigate changes in QoL within the first year after treatment, can yield more information on the evolution of bowel dysfunction. Another valuable addition to the study design could be the determination of a pre-operative LARS score to evaluate bowel dysfunction before surgery although the reliability of this preoperative measurement could be biased by the presence of a tumour, influencing the patients' bowel Despite the recognition of LARS as a cluster of invalidating complaints, there is still much uncertainty about the underlying pathophysiology. Future studies should focus on pathophysiological mechanisms that cause functional complaints in patients who underwent resection for colorectal cancer. Recent studies emphasize the importance of interrupted colonic migrating motor complexes and their influence on bowel motility and recto-anal coordination [33,34]. This might partially explain functional complaints after surgery for sigmoid cancer.

In conclusion, our study is the first to demonstrate the prevalence of long-term LARS and a decreased quality of life, not only in rectal cancer patients but also in a considerable proportion of patients who underwent resection for sigmoid cancer. Patients need to be adequately informed about these long-term complaints.

Funding

Except for patients' letters, paid by the local department of surgery in each participating hospital, funding was not applicable.

Conflict of interest statement

None declared.

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