International Journal of Colorectal Disease (2019) 34:747–762
https://doi.org/10.1007/s00384-019-03249-7

ORIGINAL ARTICLE

To what extent is the low anterior resection syndrome (LARS) associated with quality of life as measured using the EORTC C30 and CR38 quality of life questionnaires?

Juliane Kupsch[1] · Matthias Kuhn[2] · Klaus E. Matzel[3] · Joerg Zimmer[4] · Olga Radulova-Mauersberger[1] · Anja Sims[1] · Helmut Witzigmann[1] · Sigmar Stelzner[1]

Accepted: 15 January 2019 / Published online: 5 February 2019

Abstract

Purpose Treatment of rectal cancer often results in disturbed anorectal function, which can be quantified by the Low Anterior Resection Syndrome (LARS) score. This study investigates the association of impaired anorectal function as measured with the LARS score with quality of life (QoL) as measured with the EORTC-QLQ-C30 and CR38 questionnaires.

Methods All stoma-free patients who had undergone sphincter-preserving surgery for rectal cancer from 2000 to 2014 in our institution were retrieved from a prospective database. They were contacted by mail and asked to return the questionnaires. QoL was evaluated in relation to LARS and further patient- and treatment factors using univariate and multivariate analysis.

Results Of the eligible patients ($n = 331$), 261 (78.8%) responded with a complete LARS score. Mean score for global QoL according to the EORTC-QLQ-C30 questionnaire was 63 ± 21 for all patients. If major LARS was present, mean score decreased to 56 ± 19 in contrast to 67 ± 20 in patients with no/minor LARS ($p < 0.001$). In regression analysis, major LARS was furthermore associated with reduced physical, role, emotional, cognitive and social functioning as well as impaired body image, more micturition problems and poorer future perspective. It was not related to sexual function. The variance explained by major LARS in the differences of QoL was approximately 10%.

Conclusion The presence of major LARS after rectal resection for cancer is negatively associated with global health as well as many other aspects of QoL. Preserving anorectal function and treatment of LARS are potential measures to improve QoL in this patient group.

Keywords Rectal cancer · Sphincter-preserving surgery · Quality of life · Low anterior resection syndrome score

Introduction

Assessment of rectal cancer therapy has focused on oncologic outcomes for many years, and there have been major advances regarding local recurrence rates [1, 2] and overall survival [3, 4]. However, patients are often affected by sequelae of therapy, which may impact on their quality of life (QoL) [5, 6]. The European Organisation for Research and Treatment of Cancer (EORTC) has developed and validated a 30-item core questionnaire (QLQ-C30) that reflects global QoL in cancer patients [7]. It has been supplemented by a specific module for colorectal cancer patients comprising 38 questions (QLQ-CR38) [8]. For the specific alterations after low anterior resection, only recently a simple patient-reported five-item questionnaire, the Low Anterior Resection Syndrome (LARS) score was introduced. It addresses impairment of defaecation including incontinence for wind and liquid stool, frequency,

✉ Sigmar Stelzner
stelzner-si@khdf.de

[1] Department of General, Visceral and Thoracic Surgery, Dresden-Friedrichstadt General Hospital, Teaching Hospital of the Technical University of Dresden, Friedrichstr. 41, D-01067 Dresden, Germany

[2] Institute for Medical Informatics and Biometry, (Carl Gustav Carus) Faculty of Medicine, Technische Universität Dresden, Blasewitzer Str. 86, D-01307 Dresden, Germany

[3] Department of Surgery, Section Coloproctology, University Hospital Erlangen, Friedrich-Alexander University Erlangen-Nürnberg, Krankenhausstr. 12, D-91054 Erlangen, Germany

[4] Department of Radiation Therapy, Dresden-Friedrichstadt General Hospital, Teaching Hospital of the Technical University of Dresden, Friedrichstr. 41, D-01067 Dresden, Germany

urgency and clustering [9]. This questionnaire has also been translated and validated into German [10, 11]. There is growing evidence from a variety of studies using this score that more than 50% of patients suffer from LARS after sphincter-preserving treatment for rectal cancer [10, 12]. To which extent these functional disturbances affect various aspects of QoL, however, has not yet been fully elucidated.

The primary aim of this study was to correlate impairment of anorectal function as measured by the LARS score with quality of life determined by the QLQ-C30 and QLQ-CR38 questionnaires. Further patient-, tumour- and treatment-related factors that might also be associated with QoL were investigated as secondary endpoints.

Patients and methods

All patients treated at our institution for rectal cancer from 2000 to 2014 were retrieved from a prospective coloproctologic database. After exclusion of non-survivors, patients with local recurrence and patients with an ostomy, we contacted all eligible patients per mail in October 2015, explaining the purpose of the study and delivering the questionnaires. If no response was received, a second letter was sent out after 2 months as a reminder. Ethical approval was granted by the responsible institution (Saxon Physicians Chamber, No. EK-BR-92/15-1/134619).

The LARS score yields numerical values between 0 and 42. Scores from 0–20 are interpreted as "no LARS," 21–29 as "minor LARS" and 30–42 as "major LARS" [9]. After evaluation of each group, we dichotomised them, first into no LARS vs. any form of LARS, and second into no/minor LARS vs. major LARS. The dichotomisation that presented a better stratification of QLQ scores was chosen for further analysis.

Permission to use the QLQ-C30 (version 3.0) and the colorectal cancer module QLQ-CR38 questionnaires was obtained with the EORTC Data Centre. QLQ-C30 is a cancer-specific, multidimensional questionnaire designed for self-administration. It contains a scale for global health status, five functional scales (physical, role, emotional, cognitive and social functioning), three symptoms scales (fatigue, nausea/vomiting and pain), five single items (dyspnoea, insomnia, appetite loss, constipation and diarrhoea) and a single question concerning financial difficulties. Values for the scales and single items were linearly transformed into a score of 0–100 as stipulated by the EORTC manual [13]. For the functional scales including the global health status, higher values reflect a higher level of functioning, whereas for the symptoms scales and items, a higher value represents a higher level of problems. Missing data were imputed according to the instructions of the manual.

The colorectal cancer module QLQ-CR38 contains 19 questions that apply to all patients, four questions concerning either male or female sexual dysfunction and seven questions each for patients with or without a stoma. Since we excluded patients with a stoma, the latter questions were not applicable. Furthermore, no patient was on chemotherapy; hence, this scale was omitted. Questions related to sexual problems were only to be answered if the patient indicated sexual activity. Transformation of raw data and handling of missing values followed the same principles as described for the QLQ-C30 questionnaire.

Statistical analysis

Although some of the data shows a skewed distribution, we present means and standard deviation for all QLQ items as exemplified by the EORTC group [7, 8]. All values were calculated for the absence or presence of LARS as well as for each potentially relevant factor such as age, sex, type of operation, mode of reconstruction, anastomotic leak, radio(-chemo)therapy, T- and N- category and distant recurrence. To analyse differences between early and late impairment of QoL, we divided time since operation into up to 2 years and more than 2 years.

According to the suggestions of the EORTC research group, the differences between groups were rated as follows, 5–10—small, > 10–20—moderate and more than 20—large [14]. Intergroup comparisons were performed with the Mann-Whitney *U* test or Kruskal-Wallis test, as appropriate [15, 16]. Because of the association of partial mesorectal excision (PME) and straight anastomosis, PME was excluded for the comparison of reconstruction modes. The majority of reconstructions in total mesorectal excision (TME) or intersphincteric resection (IR) was done by fashioning a J-pouch. It was, however, at the surgeon's discretion to perform a side-to-end anastomosis or coloplasty. The latter types of reconstruction were small in number and were therefore combined into one group.

We evaluated the impact of all scales by linear regression analysis with a backward variable elimination at a threshold of $p = 0.05$. Histograms of the standardised residuals were checked and showed unimodal distribution with only few residuals beyond 2 in magnitude. Their distribution was deemed sufficiently close to normal although the data with discrete values do not fully comply with the assumptions of linear regression analysis. Single QLQ items with only few outcomes were modelled via an ordinal regression analysis. The extent to which the variance is explained by the models is reflected by the R^2 value (linear regression models) or by Nagelkerke's pseudo R^2 value (ordinal regression models). For the linear regression models, we display regression-coefficients with 99% confidence intervals (CI) to illustrate the estimated net difference in QoL if the independent factor

is present and other factors in the model held constant. For the ordinal regression models, location estimates, odds ratios (OR) and 99% CI for all retained factors were estimated. The OR for a factor describes the chances of having a higher outcome in a single QLQ-item of patients with a certain level of the given factor compared to patients at the reference level of that factor. Model fit was tested by displaying the normal P-P plot of regression standardised residuals. The proportional odds assumption in ordinal regression was tested. To account for multiple testing, we chose a significance level of $\alpha = 0.01$ (corresponding to $p < 0.01$) per test to indicate significant differences [15] and display 99% CI in the regression analysis. Statistical analysis was carried out with SPSS Version 21.0 (IBM Corp., Armonk, NY).

Results

Of 534 patients with an anastomosis, we excluded all patients with a permanent stoma ($n = 76$) and all who were known to have died ($n = 127$). There remained 331 eligible patients who were contacted by mail. Response was received from 264 patients; however, three patients did not completely fill in the LARS questionnaires. Thus, 261/331 (78.9%) of patients were counted as responders. The group of responders was comparable to the non-responders with respect to age, sex, operative details and tumour characteristics. Time since surgery was longer and rate of anastomotic leaks was higher in non-responders.

Of the responders, 162 (62.1%) patients were male and 99 (37.9%) were female with a median age at operation of 64 (range 28–87) years. Median tumour height measured from the anal verge by rigid rectoscopy was 9 cm. A PME was performed in 71 (27.2%) patients, a TME in 149 (57.1%) patients and an IR in 41 (15.7%) patients. A laparoscopic operation was carried out in only six (2.3%) patients. In 184 patients, a neoreservoir was constructed after TME or IR, 143 patients received a J-pouch, 17 a coloplasty pouch and 24 a side-to-end anastomosis. Anastomotic leakage occurred in 37 (14.2%) patients. Radio(chemo) therapy was administered in 144 (55.4%) patients, 125 of whom received preoperative and 19 postoperative therapy. Median time since operation was 6.5 years, and 17 (6.5%) patients experienced distant recurrence. In 206 (78.9%) patients, a diverting stoma was fashioned which was reversed after a median of 176 days.

LARS was distributed as follows, 117 (44.8%) reported no LARS, 51 (19.5%) minor LARS and 93 (35.6%) major LARS. A total of 73 patients were on antidiarrhoeal drugs, 55 of them on demand only. Forty-one patients took some laxatives or stool softeners, two patients used transanal irrigation and two patients were treated by sacral nerve stimulation (SNS). Patient numbers are displayed in Tables 1 and 3. Further details of the patient cohort and non-responders are published elsewhere [12].

QLQ-C30

Score of global health for the entire study population was 63 ± 21. The evaluation of the three LARS groups showed a score of 69 ± 20 for patients without LARS vs. 64 ± 22 and 56 ± 19 for minor and major LARS, respectively ($p < 0.001$). Dichotomisation into no LARS vs. minor and major LARS revealed an equal number of scales and single items with significant differences and was comparable to the dichotomisation into no and minor LARS vs. major LARS. However, differences were more pronounced and more often in the range of > 10 in no and minor LARS vs. major LARS; therefore, this dichotomisation was used throughout the study.

Patients with major LARS showed a moderate, but significant, difference in global health vs. patients without major LARS (56 ± 19 vs. 67 ± 20, $p < 0.001$). This difference was seen in all functional scales being large for social functioning (59 vs. 82, $p < 0.001$), moderate for role functioning (62 vs. 77, $p < 0.001$) and for emotional functioning (68 vs. 82, $p < 0.001$) and small for physical functioning (75 vs. 81, $p < 0.001$) and cognitive functioning (79 vs. 86, $p = 0.012$). In the symptom scales and single items, we found significant differences for fatigue (38 vs. 27, $p = 0.001$), insomnia (42 vs. 27, $p < 0.001$) and diarrhoea (41 vs. 16, $p < 0.001$). A moderate difference was also detected for financial difficulties (13 vs. 24, $p = 0.003$) (Table 1, Fig. 1).

None of the other factors investigated showed a significant difference in global health. However, anastomotic leak negatively correlated with fatigue (moderate), pain (moderate), appetite loss (moderate) and diarrhoea (large). Younger patients had a better physical functioning (small difference), but were faced with financial difficulties (moderate difference). Males exhibited a worse social functioning (moderate difference), and suffered less often from insomnia (moderate difference) than females. Radiotherapy (30 vs. 17, $p < 0.001$) and type of procedure (PME 14, TME 28, IR 34, $p < 0.001$) were only significantly related to diarrhoea. Patients with a history of distant recurrence more often reported financial difficulties (Table 1).

In regression analysis, major LARS remained as single significant factor associated with global health (11 [4 … 18] points [99% CI] less if major LARS was present). This was also true for all function scales, fatigue, insomnia and diarrhoea. For younger patients, better physical functioning but more financial problems were confirmed. Status after anastomotic leak was found to be related to appetite loss and diarrhoea, radiation therapy was coupled with better cognitive function and patients with distant recurrence more often exhibited financial difficulties. In general, R^2 values were rather

Table 1 Scores for EORTC QLQ-C30 by patient-, treatment- and tumour factors

	n (%)*	Global health	Physical functioning	Role functioning, *n* = 260	Emotional functioning	Cognitive functioning	Social functioning	Fatigue
Age								
≤ 64a	137 (52.5)	64 ± 20	83 ± 18	72 ± 31	75 ± 24	85 ± 20	71 ± 32	29 ± 26
> 64a	124 (47.5)	63 ± 21	75 ± 24	71 ± 31	79 ± 21	82 ± 24	76 ± 30	33 ± 26
		$p = 0.710$	$p = 0.007$	$p = 0.659$	$p = 0.320$	$p = 0.610$	$p = 0.142$	$p = 0.110$
Sex								
Female	99 (37.9)	66 ± 19	76 ± 23	74 ± 31	78 ± 22	84 ± 22	80 ± 29	32 ± 26
Male	162 (62.1)	62 ± 22	81 ± 20	71 ± 31	76 ± 23	83 ± 23	70 ± 31	30 ± 27
		$p = 0.195$	$p = 0.039$	$p = 0.290$	$p = 0.473$	$p = 0.738$	$p = 0.005$	$p = 0.359$
OP-Procedure[a]								
PME	71 (27.2)	64 ± 20	77 ± 24	68 ± 34	74 ± 26	80 ± 23	78 ± 28	34 ± 30
TME	149 (57.1)	64 ± 20	80 ± 21	73 ± 30	78 ± 21	84 ± 23	73 ± 32	31 ± 26
IR	41 (15.7)	61 ± 22	79 ± 20	73 ± 28	78 ± 23	87 ± 16	67 ± 32	26 ± 23
		$p = 0.701$	$p = 0.872$	$p = 0.625$	$p = 0.545$	$p = 0.052$	$p = 0.175$	$p = 0.513$
Reconstruction[b]								
J-pouch	143 (77.7)	63 ± 20	81 ± 18	75 ± 28	79 ± 21	86 ± 20	72 ± 31	28 ± 22
Side-to-end + colo-plasty	41 (22.3)	62 ± 24	75 ± 20	67 ± 33	77 ± 23	82 ± 28	70 ± 32	32 ± 32
		$p = 0.622$	$p = 0.460$	$p = 0.191$	$p = 0.760$	$p = 0.940$	$p = 0.663$	$p = 0.918$
Anastomotic leakage								
No	224 (85.8)	64 ± 20	79 ± 22	73 ± 30	78 ± 22	85 ± 22	74 ± 31	29 ± 26
Yes	37 (14.2)	59 ± 21	80 ± 19	62 ± 33	69 ± 24	76 ± 25	68 ± 28	40 ± 26
		$p = 0.215$	$p = 0.811$	$p = 0.039$	$p = 0.016$	$p = 0.020$	$p = 0.096$	$p = 0.009$
Time since operation								
< 2 years	44 (16.9)	63 ± 23	80 ± 23	74 ± 31	78 ± 20	85 ± 20	66 ± 32	29 ± 27
≥ 2 years	217 (83.1)	63 ± 20	79 ± 21	71 ± 31	77 ± 23	83 ± 23	75 ± 30	31 ± 26
		$p = 0.890$	$p = 0.475$	$p = 0.483$	$p = 0.888$	$p = 0.621$	$p = 0.055$	$p = 0.548$
Radiotherapy[c]								
No	116 (44.6)	63 ± 21	77 ± 25	73 ± 32	76 ± 25	80 ± 26	77 ± 30	33 ± 28
Yes	144 (55.4)	63 ± 20	81 ± 18	71 ± 30	78 ± 21	87 ± 19	71 ± 31	29 ± 24
		$p = 0.944$	$p = 0.409$	$p = 0.419$	$p = 0.806$	$p = 0.069$	$p = 0.092$	$p = 0.284$
pN-category								
Negative	198 (75.9)	62 ± 20	78 ± 22	71 ± 31	76 ± 23	83 ± 23	74 ± 30	31 ± 26
Positive	63 (24.1)	68 ± 22	83 ± 20	75 ± 29	78 ± 22	87 ± 19	74 ± 33	29 ± 28
		$p = 0.030$	$p = 0.087$	$p = 0.446$	$p = 0.473$	$p = 0.330$	$p = 0.663$	$p = 0.330$
pT-category								
0–2	178 (68.2)	63 ± 20	79 ± 21	73 ± 31	77 ± 23	84 ± 22	75 ± 30	30 ± 25
3–4	83 (31.8)	64 ± 21	79 ± 23	68 ± 31	77 ± 22	84 ± 22	70 ± 32	32 ± 29
		$p = 0.609$	$p = 0.889$	$p = 0.222$	$p = 0.919$	$p = 0.957$	$p = 0.210$	$p = 0.902$
Distant recurrence								
No	244 (93.5)	63 ± 20	79 ± 22	72 ± 31	77 ± 22	83 ± 22	74 ± 30	31 ± 26
Yes	17 (6.5)	62 ± 16	77 ± 17	65 ± 28	75 ± 26	85 ± 20	65 ± 33	33 ± 26

Table 1 (continued)

		$p = 0.640$	$p = 0.411$	$p = 0.164$	$p = 0.824$	$p = 0.792$	$p = 0.214$	$p = 0.638$
LARS[a]								
No	117 (44.8)	69 ± 20	82 ± 24	79 ± 28	83 ± 20	87 ± 20	85 ± 24	26 ± 26
Minor	51 (19.5)	64 ± 22	81 ± 19	72 ± 33	79 ± 19	84 ± 22	73 ± 31	30 ± 25
Major	93 (35.6)	56 ± 19	75 ± 19	62 ± 31	68 ± 24	79 ± 24	59 ± 32	38 ± 25
		$p < 0.001$	$p = 0.001$	$p < 0.001$	$p < 0.001$	$p = 0.029$	$p < 0.001$	$p = 0.002$

	Nausea and vomiting	Pain	Dyspnoea	Insomnia, $n = 260$	Appetite loss	Constipation, $n = 259$	Diarrhoea, $n = 260$	Financial difficulties, $n = 260$
Age								
≤ 64a	4 ± 13	21 ± 30	15 ± 25	32 ± 33	9 ± 21	11 ± 22	28 ± 32	24 ± 36
> 64a	3 ± 10	26 ± 30	21 ± 29	33 ± 34	11 ± 25	15 ± 27	21 ± 28	9 ± 22
	$p = 0.861$	$p = 0.118$	$p = 0.140$	$p = 0.894$	$p = 0.784$	$p = 0.191$	$p = 0.126$	$p < 0.001$
Sex								
Female	4 ± 14	26 ± 31	18 ± 28	42 ± 36	10 ± 22	17 ± 29	25 ± 32	14 ± 29
Male	3 ± 9	22 ± 28	18 ± 27	26 ± 31	10 ± 23	10 ± 21	24 ± 30	19 ± 31
	$p = 0.776$	$p = 0.668$	$p = 0.881$	$p = 0.001$	$p = 0.915$	$p = 0.074$	$p = 0.701$	$p = 0.074$
OP-Procedure[a]								
PME	4 ± 14	28 ± 32	21 ± 30	36 ± 37	13 ± 27	12 ± 21	14 ± 24	16 ± 31
TME	3 ± 10	21 ± 28	17 ± 26	30 ± 33	9 ± 21	13 ± 27	28 ± 31	18 ± 31
IR	4 ± 12	24 ± 31	16 ± 26	33 ± 32	8 ± 22	14 ± 22	34 ± 32	19 ± 28
	$p = 0.673$	$p = 0.253$	$p = 0.656$	$p = 0.652$	$p = 0.578$	$p = 0.515$	$p < 0.001$	$p = 0.463$
Reconstruction[b]								
J-pouch	3 ± 10	21 ± 28	16 ± 25	33 ± 33	8 ± 20	12 ± 25	31 ± 32	16 ± 28
Side-to-end + colo-plasty	2 ± 8	22 ± 30	20 ± 29	26 ± 32	12 ± 27	15 ± 29	20 ± 27	24 ± 36
	$p = 0.478$	$p = 0.856$	$p = 0.424$	$p = 0.231$	$p = 0.530$	$p = 0.680$	$p = 0.081$	$p = 0.382$
Anastomotic leakage								
No	3 ± 11	21 ± 29	17 ± 27	32 ± 34	8 ± 20	13 ± 25	22 ± 29	15 ± 29
Yes	7 ± 13	36 ± 29	23 ± 28	35 ± 31	21 ± 33	10 ± 22	42 ± 35	29 ± 37
	$p = 0.002$	$p = 0.001$	$p = 0.102$	$p = 0.435$	$p = 0.006$	$p = 0.465$	$p < 0.001$	$p = 0.014$
Time since operation								
< 2 years	3 ± 10	25 ± 30	14 ± 27	29 ± 33	9 ± 22	10 ± 21	21 ± 30	20 ± 31
≥ 2 years	4 ± 12	23 ± 30	19 ± 27	33 ± 34	10 ± 23	13 ± 25	25 ± 31	16 ± 31
	$p = 0.600$	$p = 0.532$	$p = 0.126$	$p = 0.419$	$p = 0.790$	$p = 0.378$	$p = 0.363$	$p = 0.222$
Radiotherapy[c]								
No	5 ± 14	24 ± 30	20 ± 29	34 ± 36	13 ± 26	14 ± 27	17 ± 28	15 ± 29
Yes	2 ± 8	22 ± 29	16 ± 25	31 ± 32	8 ± 20	11 ± 22	30 ± 31	19 ± 32
	$p = 0.026$	$p = 0.562$	$p = 0.506$	$p = 0.482$	$p = 0.148$	$p = 0.609$	$p < 0.001$	$p = 0.321$
pN-category								

Table 1 (continued)

Negative	4 ± 11	23 ± 29	18 ± 26	31 ± 32	11 ± 23	14 ± 25	25 ± 32	15 ± 28
Positive	3 ± 11	23 ± 32	18 ± 29	35 ± 38	8 ± 21	11 ± 23	24 ± 27	23 ± 37
	$p = 0.344$	$p = 0.687$	$p = 0.759$	$p = 0.696$	$p = 0.263$	$p = 0.309$	$p = 0.714$	$p = 0.259$
pT-category								
0–2	3 ± 11	23 ± 30	16 ± 24	34 ± 34	10 ± 23	14 ± 25	26 ± 31	15 ± 29
3–4	4 ± 12	24 ± 30	22 ± 33	29 ± 33	11 ± 23	10 ± 23	23 ± 28	22 ± 34
	$p = 0.493$	$p = 0.692$	$p = 0.320$	$p = 0.304$	$p = 0.551$	$p = 0.205$	$p = 0.649$	$p = 0.154$
Distant recurrence								
No	3 ± 12	23 ± 30	17 ± 26	32 ± 34	10 ± 23	13 ± 25	24 ± 30	15 ± 29
Yes	5 ± 10	31 ± 32	31 ± 32	35 ± 32	10 ± 20	8 ± 15	31 ± 30	45 ± 41
	$p = 0.124$	$p = 0.154$	$p = 0.031$	$p = 0.606$	$p = 0.740$	$p = 0.645$	$p = 0.238$	$p < 0.001$
LARS[a]								
No	3 ± 13	21 ± 29	16 ± 26	26 ± 33	10 ± 24	12 ± 24	11 ± 22	12 ± 26
Minor	2 ± 7	21 ± 30	17 ± 26	29 ± 34	8 ± 17	8 ± 20	26 ± 26	17 ± 30
Major	4 ± 12	28 ± 30	21 ± 28	42 ± 33	11 ± 24	16 ± 27	41 ± 34	22 ± 35
	$p = 0.577$	$p = 0.065$	$p = 0.301$	$p < 0.001$	$p = 0.501$	$p = 0.119$	$p < 0.001$	$p = 0.006$

Apart from *n*, cells give mean scores with standard deviation and *p* values for the Mann-Whitney *U* test, if not otherwise specified. In global health and functional scales including physical, role, emotional, cognitive and social functioning, higher scores reflect a higher level of functioning. In the remaining symptom scales and single items, higher scores reflect a higher level of problems

PME partial mesorectal excision, *TME* total mesorectal excision, *IR* intersphincteric resection, *LARS* low anterior resection syndrome

*$n = 261$ if not otherwise specified

[a] Kruskal-Wallis test

[b] $n = 184$, patients with PME or straight anastomosis excluded

[c] One patient missing

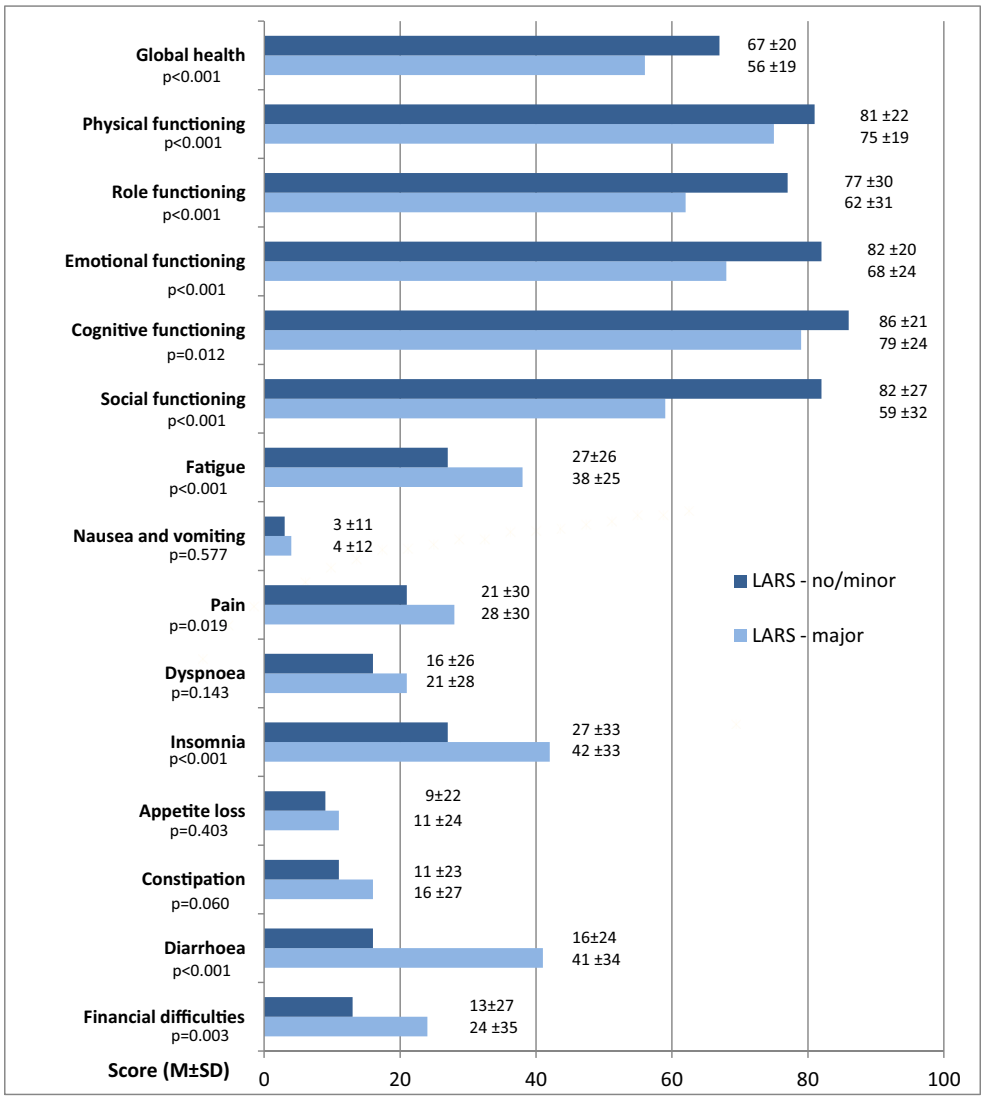

Fig. 1 EORTC QLQ-C30 mean scores, no/minor LARS versus major LARS. In global health and functional scales including physical, role, emotional, cognitive and social functioning, higher values reflect a higher level of functioning. In the remaining symptom scales and single items, higher values reflect a higher level of problems. $n = 261$, Mann-Whitney U test; *LARS* low anterior resection syndrome

low, indicating that the investigated factors explained only around 10% of the variance within the scales (Table 2).

QLQ-CR38

Dichotomisation of the three LARS categories again showed more pronounced differences if major LARS was compared to no and minor LARS. Body image, micturition problems, GI symptoms, problems with defaecation and future perspective were impaired if major LARS was present (Fig. 2). Anastomotic leakage was associated with reduced body image and GI symptoms. Radiation therapy exhibited more defaecation problems (small difference). Problems with defaecation scored higher for IR and TME as compared to PME.

Overall, sexual functioning was not significantly related to LARS, but showed low scores with a moderate difference for age (patients ≤ 64 years 30 vs. patients > 64 years 16, $p < 0.001$) and sex (females 14 vs. males 29, $p < 0.001$). Sexual enjoyment was indicated with higher scores by younger patients (70) than by older ones (38, $p = 0.003$); however, only 67 (25.7%) patients answered this question. Male sexual problems (response rate 129/162 (79.6%)) occurred with radiation therapy (moderate difference) and in tendency with major LARS (moderate difference) and higher age (moderate difference). Females were asked to answer questions related to sexual problems only if they were sexually active and had sexual intercourse; thus, only 23/99 (23.2%) patients responded to the questions. Irradiated females reported more difficulties (large difference) (Table 3).

Regression analysis revealed an association of LARS with body image, micturition problems, GI symptoms, problems with defaecation and future perspective. Regarding sexual function, we could only elicit a tendency towards more problems in men with LARS. Anastomotic insufficiency had a negative independent impact on body image and GI

Table 2 Regression analysis QLQ-C30

Dependent variable *Dependent variable*	Independent variable *Independent variable*	Coefficient (99% CI) *Odds ratio for higher outcome (99% CI)*	p *p*	R^2 *Pseudo* R^2
Global health	(constant)	66 (61 … 70)	< 0.001	0.08
	LARS no/minor	ref.		
	major	− 11 (− 18 … − 4)	< 0.001	
	N-pos. no	ref.		
	yes	7 (− 1 … 14)	0.021	
Physical functioning	(constant)	83 (77 … 90)	< 0.001	0.09
	LARS no/minor	ref.		
	major	− 8 (− 15 … − 1)	0.002	
	Age ≤ 64 years	ref.		
	> 64 years	− 10 (− 16 … − 3)	< 0.001	
	Radiotherapy no	ref.		
	yes	6 (− 1 … 13)	0.025	
Role functioning	(constant)	71 (62 … 81)	< 0.001	0.07
	LARS no/minor	ref.		
	major	− 16 (− 26 … − 6)	< 0.001	
	Procedure PME	ref.		
	TME/IR	8 (− 2 … 19)	0.044	
Emotional functioning	(constant)	78 (71 … 85)	< 0.001	0.11
	LARS no/minor	ref.		
	major	− 14 (− 21 … − 7)	< 0.001	
	Procedure PME	ref.		
	TME/IR	7 (− 1 … 15)	0.016	
	Anastomotic leak no	ref.		
	yes	− 8 (− 17 … 2)	0.050	
Cognitive functioning	(constant)	82 (77 … 88)	< 0.001	0.05
	LARS no/minor	ref.		
	major	− 9 (− 16 … − 1)	0.003	
	Radiotherapy no	ref.		
	yes	8 (1 … 15)	0.006	
Social functioning	(constant)	88 (80 … 96)	< 0.001	0.15
	LARS no/minor	ref.		
	major	− 21 (− 31 … − 12)	< 0.001	
	Sex female	ref.		
	Male	− 8 (− 17 … 2)	0.035	
	Time since operation			
	< 2 years	ref.		
	≥ 2 years	− 9 (− 22 … 3)	0.044	
Fatigue	(constant)	26 (21 … 31)	< 0.001	
	LARS no/minor	ref.		
	major	10 (1 … 18)	0.004	0.05
	Anastomotic leak no	ref.		
	yes	10 (− 2 … 22)	0.029	
Insomnia	*LARS no/minor*	*ref.*		*0.13*
	major	*2.7 (1.4 ... 5.2)*	*< 0.001*	
	Sex female	*ref.*		
	male	*0.4 (0.2 ... 0.8)*	*< 0.001*	
Appetite loss	*Anastomotic leak no*	*ref.*		*0.07*
	yes	*3.1 (1.1 ... 8.9)*	*0.006*	

Table 2 (continued)

Dependent variable *Dependent variable*	Independent variable *Independent variable*	Coefficient (99% CI) *Odds ratio for higher outcome (99% CI)*	p *p*	R^2 *Pseudo* R^2
Diarrhoea	*LARS no/minor*	*ref.*		*0.28*
	major	*4.4 (2.2 … 8.7)*	*< 0.001*	
	Sex female	*ref.*		
	male	*0.6 (0.3 … 1.1)*	*0.029*	
	Procedure PME	ref.		
	TME	*2.1 (0.9 … 5.1)*	*0.029*	
	IR	*2.9 (0.9 … 9.4)*	*0.021*	
	Anastomotic leak no	*ref.*		
	yes	*4.2 (1.6 … 10.6)*	*< 0.001*	
	Radiotherapy no	*ref.*		
	yes	*2.0 (0.9 … 4.1)*	*0.019*	
Financial difficulties	*LARS no/minor*	*ref.*		*0.15*
	major	*1.9 (0.9 … 4.0)*	*0.030*	
	Age ≤ 64 years	*ref.*		
	> 64 years	*0.4 (0.2 … 0.8)*	*0.002*	
	Distant recurrence no	*ref.*		
	yes	*3.9 (1.0 … 14.4)*	*0.008*	

All linear regression analyses including Coefficients and R^2 values are given in roman, all ordinal regression analyses including Odds Ratio for higher outcome and Pseudo R^2 are given in italics. In linear regression, all scales are out of 100. In functional scales, higher scores reflect a higher level of functioning. In the symptom scales and single items, higher scores reflect a higher level of problems

PME partial mesorectal excision, *TME* total mesorectal excision, *IR* intersphincteric resection, *LARS* low anterior resection syndrome

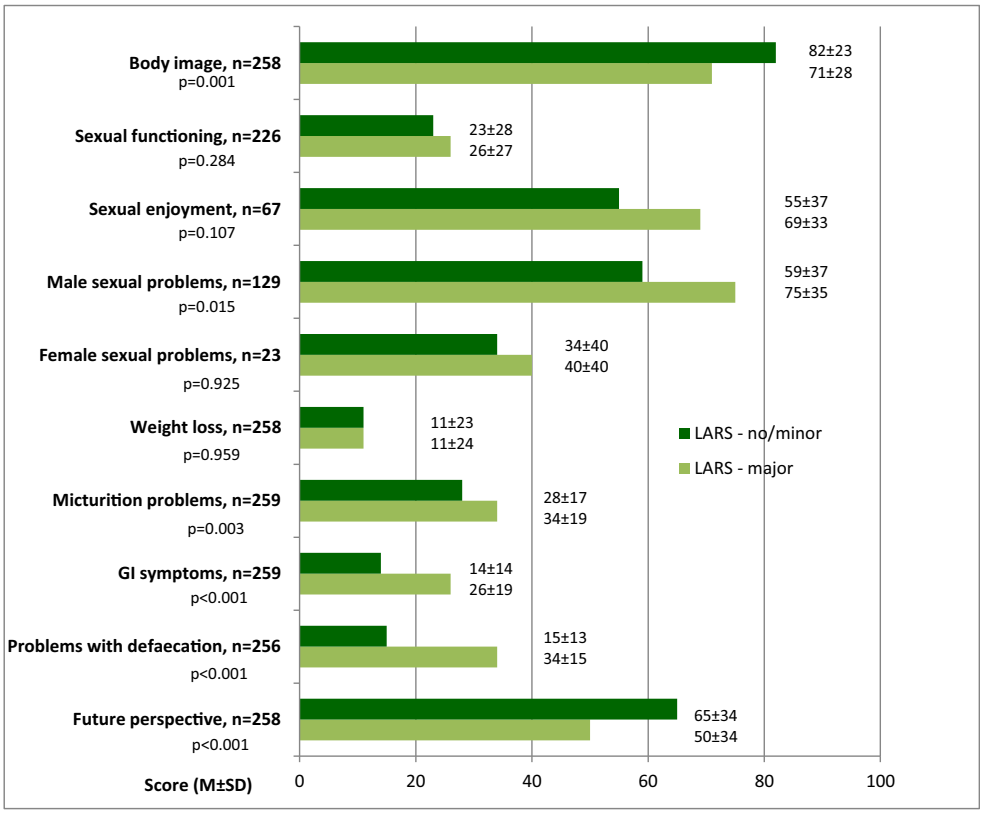

Fig. 2 EORTC QLQ-CR38 mean scores, no/minor LARS versus major LARS. In functional scales including body image, sexual functioning, sexual enjoyment and future perspective, higher values reflect a higher level of functioning. In symptom scales and single items, higher values reflect a higher level of problems. $n = 259$ if not otherwise specified, Mann-Whitney *U* test; *LARS* low anterior resection syndrome, *GI* gastrointestinal

Table 3 Scores for EORTC QLQ-CR38 by patient-, treatment- and tumour factors

	*n**	Body image, *n* = 258	Sexual functioning	Sexual enjoyment	Male sexual problems	Female sexual problems	Weight loss, *n* = 258	Micturition problems	GI symptoms	Problems with defaecation	Future perspective
			n = 226	*n* = 67	*n* = 129	*n* = 23				*n* = 256	*n* = 258
Age											
≤ 64a	137 (52.9)	76 ± 26	30 ± 28	70 ± 30	61 ± 36	47 ± 40	10 ± 22	28 ± 18	21 ± 18	22 + 16	59 ± 35
> 64a	124 (47.1)	80 ± 24	16 ± 25	38 ± 39	74 ± 37	6 ± 9	12 ± 24	32 ± 17	15 ± 14	20 ± 16	61 ± 34
		$p = 0.162$	$p < 0.001$	$p = 0.003$	$p = 0.027$	$p = 0.044$	$p = 0.393$	$p = 0.093$	$p = 0.007$	$p = 0.324$	$p = 0.686$
Sex											
Female	99 (85.7)	80 ± 26	14 ± 22	49 ± 41	p = not to calculate	36 ± 39	10 ± 25	31 ± 19	17 ± 17	19 ± 16	61 ± 35
Male	160 (14.3)	77 ± 25	29 ± 29	64 ± 32		p = not to calculate	11 ± 22	30 ± 17	19 ± 13	23 ± 16	59 ± 34
		$p = 0.207$	$p < 0.001$	$p = 0.124$	66 ± 37		$p = 0.412$	$p = 0.454$	$p = 0.087$	$p = 0.020$	$p = 0.671$
OP-Procedure[a]											
PME	69 (26.6)	81 ± 24	21 ± 26	55 ± 34	61 ± 40	17 ± 29	12 ± 25	30 ± 18	18 ± 16	16 ± 15	65 ± 33
TME	149 (57.5)	78 ± 26	24 ± 28	60 ± 35	67 ± 36	40 ± 41	12 ± 24	30 ± 16	18 ± 17	22 ± 15	56 ± 34
IR	41 (15.8)	74 ± 28	28 ± 30	67 ± 41	68 ± 37	50 ± 44	7 ± 16	32 ± 22	19 ± 17	29 ± 17	63 ± 36
		$p = 0.475$	$p = 0.561$	$p = 0.425$	$p = 0.810$	$p = 0.412$	$p = 0.837$	$p = 0.883$	$p = 0.997$	$p < 0.001$	$p = 0.133$
Reconstruction[b]											
J-pouch	143 (77.7)	78 ± 25	26 ± 28	64 ± 38	67 ± 36	42 ± 42	8 ± 19	31 ± 17	18 ± 17	23 ± 16	60 ± 35
Side-to-end + coloplasty	41 (22.3)	74 ± 30	20 ± 30	56 ± 29	70 ± 34	42 ± 59	18 ± 30	28 ± 18	19 ± 17	23 ± 18	52 ± 32
		$p = 0.783$	$p = 0.238$	$p = 0.343$	$p = 0.727$	$p = 0.933$	$p = 0.036$	$p = 0.251$	$p = 0.808$	$p = 0.949$	$p = 0.147$
Anastomotic leakage											
No	222 (85.7)	80 ± 24	23 ± 27	61 ± 36	65 ± 38	33 ± 27	10 ± 22	29 ± 18	17 ± 15	20 ± 16	62 ± 34
Yes	37 (14.3)	64 ± 28	30 ± 29	58 ± 37	68 ± 34	100	18 ± 29	34 ± 18	28 ± 23	28 ± 19	49 ± 36
		$p < 0.001$	$p = 0.131$	$p = 0.763$	$p = 0.783$	$p = 0.174$	$p = 0.030$	$p = 0.121$	$p = 0.010$	$p = 0.029$	$p = 0.045$
Time since operation											
<2 years	44 (17.0)	79 ± 25	20 ± 25	59 ± 34	70 ± 35	42 ± 40	8 ± 24	27 ± 18	21 ± 18	24 ± 17	53 ± 33
≥2 years	215 (83.0)	78 ± 26	25 ± 28	60 ± 37	65 ± 37	35 ± 40	11 ± 23	31 ± 18	18 ± 16	21 ± 16	61 ± 34
		$p = 0.819$	$p = 0.440$	$p = 0.791$	$p = 0.477$	$p = 0.725$	$p = 0.186$	$p = 0.147$	$p = 0.319$	$p = 0.272$	$p = 0.115$
Radiotherapy[c]											
No	114 (44.0)	81 ± 24	26 ± 29	56 ± 37	55 ± 39	10 ± 21	13 ± 26	30 ± 18	17 ± 15	18 ± 15	62 ± 35
Yes	144 (55.6)	76 ± 26	22 ± 26	66 ± 34	74 ± 33	56 ± 38	9 ± 21	30 ± 17	19 ± 17	24 ± 16	58 ± 34
		$p = 0.145$	$p = 0.394$	$p = 0.275$	$p = 0.004$	$p = 0.003$	$p = 0.177$	$p = 0.634$	$p = 0.399$	$p = 0.001$	$p = 0.397$
pN-category											
Negative	196 (75.7)	78 ± 25	24 ± 28	60 ± 35	65 ± 38	38 ± 41	11 ± 22	30 ± 16	18 ± 16	21 ± 16	61 ± 34
Positive	63 (24.3)	79 ± 26	24 ± 27	61 ± 38	69 ± 32	33 ± 37	12 ± 26	30 ± 21	20 ± 19	22 ± 16	56 ± 36
		$p = 0.655$	$p = 0.987$	$p = 0.824$	$p = 0.777$	$p = 0.769$	$p = 0.728$	$p = 0.943$	$p = 0.956$	$p = 0.516$	$p = 0.321$
pT-category											
0–2	176 (68.0)	79 ± 25	25 ± 28	62 ± 37	67 ± 36	40 ± 40	10 ± 22	31 ± 17	17 ± 15	22 ± 15	60 ± 34
3–4	83 (32.0)	77 ± 27	22 ± 24	56 ± 35	65 ± 38	25 ± 39	12 ± 25	28 ± 19	20 ± 19	21 ± 18	58 ± 34
		$p = 0.601$	$p = 0.568$	$p = 0.434$	$p = 0.837$	$p = 0.516$	$p = 0.725$	$p = 0.333$	$p = 0.469$	$p = 0.409$	$p = 0.699$

Table 3 (continued)

	*n**	Body image, *n* = 258	Sexual functioning	Sexual enjoyment	Male sexual problems	Female sexual problems	Weight loss, *n* = 258	Micturition problems	GI symptoms	Problems with defaecation	Future perspective
Distant recurrence											
No	242 (93.4)	71 ± 25	23 ± 28	59 ± 36	67 ± 36	37 ± 40	11 ± 23	30 ± 18	18 ± 16	21 ± 16	61 ± 34
Yes	17 (6.6)	65 ± 29	31 ± 23	67 ± 39	58 ± 42	17[d]	8 ± 19	27 ± 14	27 ± 19	24 ± 20	39 ± 38
		$p = 0.033$	$p = 0.100$	$p = 0.577$	$p = 0.511$		$p = 0.644$	$p = 0.353$	$p = 0.041$	$p = 0.656$	$p = 0.020$
LARS[a]											
No	115 (44.4)	84 ± 23	24 ± 29	53 ± 37	55 ± 38	38 ± 44	11 ± 23	27 ± 16	14 ± 15	13 ± 12	68 ± 33
Minor	51 (19.7)	77 ± 23	20 ± 27	60 ± 38	68 ± 32	25 ± 32	10 ± 22	29 ± 19	15 ± 12	18 ± 13	60 ± 34
Major	93 (35.9)	71 ± 28	26 ± 27	69 ± 33	75 ± 35	40 ± 40	11 ± 24	34 ± 19	26 ± 19	34 ± 15	50 ± 34
		$p < 0.001$	$p = 0.449$	$p = 0.235$	$p = 0.025$	$p = 0.817$	$p = 0.912$	$p = 0.013$	$p < 0.001$	$p < 0.001$	$p < 0.001$

Apart from *n*, cells give mean scores with standard deviation and *p* values for the Mann-Whitney *U* test, if not otherwise specified. In functional scales including body image, sexual functioning and sexual enjoyment and future perspective, higher scores reflect a higher level of functioning. In symptom scales and weight loss, higher scores reflect a higher level of problems

PME partial mesorectal excision, *TME* total mesorectal excision, *IR* intersphincteric resection, *LAR*S low anterior resection syndrome, *GI* gastrointestinal

*$n = 259$ if not otherwise specified (two patients missing)

[a] Kruskal-Wallis test

[b] $n = 184$, patients with PME or straight anastomosis excluded

[c] One patient missing

[d] Only one patient

symptoms. Younger age and male sex were independently associated with better sexual functioning, and younger patients indicated a higher sexual enjoyment. There was a tendency towards more male sexual problems with higher age and after irradiation. Female sexual problems showed only an independent adverse relationship with radio(chemo) therapy (Table 4).

Discussion

Our study provides a cross section of patient-reported QoL after surgery-preserving bowel continuity for rectal cancer in relation to patient- and treatment factors. Mean score for global health status (63) was almost identical to the score of a reference population (61) which comprised all cancer stages of colorectal cancer and was published by the EORTC [17]. This is remarkable because the reference population includes colon cancer patients in whom many functional problems that rectal cancer patients are faced with do not apply. Furthermore, global QoL of our patient cohort with a median age of 64 years was very similar to the 60–69 years age group of a randomly selected general German population [18]. Thus, a median 6.5 years after operation, global QoL as measured with the EORTC QLQ-C30 is almost equal to that of the general population in patients after anterior resection for rectal carcinoma.

Our study shows that global health in rectal cancer patients is associated with the absence or presence of bowel symptoms as reflected by LARS. Differences were more pronounced if patients with major LARS were compared to the other two groups. This tendency has already been shown by several authors [5, 19, 20]. Major LARS displays a moderate difference in QoL. Moreover, major LARS correlates independently and negatively with physical, role, emotional, cognitive and social functioning as well as body image and micturition problems. It is also related to insomnia and fatigue which can be explained by nocturnal bowel movements that interrupts and fragments sleep episodes. However, as only about 10% of variance is explained by major LARS, one may speculate that the impact of patient- and treatment factors on QoL is less important as hitherto assumed.

The second factor that showed changes in a variety of QoL aspects was anastomotic leak. It was associated with appetite loss, diarrhoea, GI symptoms, body image and in tendency with defaecation problems. Impairment of anorectal function after anastomotic leaks has been demonstrated before [21]. We could further detect a tendency towards lower scores of role, emotional and cognitive functioning as well as higher values for pain, fatigue and financial problems.

Both LARS and anastomotic leak are sequelae of surgery: LARS to a large extent [12] and anastomotic insufficiency exclusively. Although it is obvious that treatment has to first address the tumour with the goal of optimal tumour management, many treatment options exist nowadays to optimise functional outcome. These include autonomic nerve preservation during surgery twinned with a thorough knowledge of autonomic nerve anatomy in the small pelvis [22–25], pelvine intraoperative neuromonitoring (pIONM) [26] and possibly transanal total mesorectal excision (taTME) [27–29] as well as robotic surgery [30]. The laparoscopic approach, however, could not demonstrate superior results regarding QoL [31].

Our data are in line with previous reports that investigate the impact of LARS on QoL with the EORTC QLQ-C30. Emmertsen and Laurberg enrolled 260 patients in a prospective study and could demonstrate a negative impact of major LARS on global health and all functional scales except on cognitive function 3 and 12 months after surgery [20]. The international validation study of the LARS score [10] also co-investigated the association of LARS and selected scales of the EORTC QLQ-C30 [19]. The authors described a close association of major LARS and impairment for seven of the eight scales chosen for analysis, amongst them global QoL, role, emotional and social functioning, whereas they could not find a relevant difference for minor LARS as compared to no LARS.

Another study correlated LARS to an anchor question regarding bowel QoL which categorised patients in three groups with no, minor and major impairments. These three groups correlated well with the three LARS categories and the EORTC QLQ-C30 scales. Significant differences for bowel QoL were reported in a total of 462 patients for global health and all functional scales at a median 5 years after surgery. However, no direct comparison of LARS and QLQ-C30 was performed [5].

In our patient population, males reported a significantly worse social function but less symptoms with insomnia than females. Gender differences in QoL have been described for the general population by other groups which found generally higher functional and lower symptom scores for males [18, 32, 33]. In rectal cancer patients, it is conceivable that males cope less well with their situation and feel therefore socially more isolated than women.

Furthermore, the role of radio(chemo) therapy is often discussed as having an adverse impact on QoL [34–37]. We could neither detect a significant association of radio(chemo) therapy with global health nor with any functional scale. The vast majority of our patients was treated by preoperative radiochemotherapy, of whom a large number received either intensity-modulated radiotherapy (IMRT) or volumetric intensity-modulated arc therapy (VMAT), which might ameliorate the reported functional impairments attributed to radiotherapy [38]. In the linear regression models, radiotherapy was significantly associated with cognitive function by + 8 points, a finding which has no straightforward explanation.

Table 4 Regression analysis QLQ-CR38

Dependent variable *Dependent variable*	Independent variable *Independent variable*	Coefficient (99% CI) *Odds ratio for higher outcome (99% CI)*	p *p*	R^2 *Pseudo* R^2
Body image	(Constant)	84 (79 … 89)	< 0.001	0.9
	LARS no/minor	ref.		
	major	− 11 (− 19 … − 2)	0.001	
	Anastomotic leak no	ref.		
	yes	− 15 (− 27 … − 4)	0.001	
Sexual functioning	(Constant)	21 (12 … 29)	< 0.001	0.12
	Age ≤ 64 years	ref.		
	> 64 years	− 14 (− 23 … − 5)	< 0.001	
	Sex female	ref.		
	male	14 (4 … 23)	< 0.001	
Sexual enjoyment	*Age ≤ 64 years*	*ref.*		*0.27*
	> 64 years	*0.2 (0.0 ... 0.6)*	*0.001*	
Male sexual problems	(Constant)	45 (30 … 60)	< 0.001	0.12
	LARS no/minor	ref.		
	major	13 (− 4 … 29)	0.048	
	Age ≤ 64 years	ref.		
	> 64 years	13 (− 3 … 30)	0.037	
	Radiotherapy no	ref.		
	yes	16 (0 … 33)	0.011	
Female sexual problems	(Constant)	10 (− 19 … 39)	0.334	0.36
	Radiotherapy no	ref.		
	yes	46 (8 … 85)	0.002	
Micturition problems	(Constant)	28 (24 … 31)	< 0.001	0.03
	LARS no/minor	ref.		
	major	7 (1 … 12)	0.004	
GI symptoms	(Constant)	15 (11 … 19)	< 0.001	0.17
	LARS no/minor	ref.		
	major	11 (6 … 16)	< 0.001	
	Age ≤ 64 years	ref.		
	> 64 years	− 4 (− 9 … 1)	0.033	
	Anastomotic leak no	ref.		
	yes	9 (2 … 16)	0.001	
Problems with defaecation	(Constant)	11 (7 … 14)	< 0.001	
	LARS no/minor	ref.		
	major	18 (14 … 22)	< 0.001	0.35
	Anastomotic leak no	ref.		
	yes	6 (0 … 12)	0.012	
	Time since operation			
	<2 years	ref.		
	≥ 2 years	5 (− 1 … 10)	0.037	
	Radiotherapy no	ref.		
	yes	4 (0 … 8)	0.016	
Future perspective	*LARS* no/minor	*ref.*		*0.12*
	major	*0.4 (0.2 ... 0.7)*	*< 0.001*	
	Anastomotic leak no	*ref.*		
	yes	*0.5 (0.2 ... 1.2)*	*0.045*	
	Time since operation			

Table 4 (continued)

Dependent variable *Dependent variable*	Independent variable *Independent variable*	Coefficient (99% CI) *Odds ratio for higher outcome (99% CI)*	p *p*	R^2 *Pseudo* R^2
	<2 years	*ref*		
	≥2 years	*0.5 (0.2 … 1.1)*	*0.038*	
	Distant recurrence no	*ref.*		
	yes	*0.4 (0.1 … 0.8)*	*0.047*	

All linear regression analyses including Coefficients and R^2 values are given in roman; all ordinal regression analyses including Odds Ratio for higher outcome and Pseudo R^2 are given in italics. In linear regression, all scales are out of 100. In functional scales including body image, sexual function, sexual enjoyment and future perspectives, higher scores reflect a higher level of functioning. In symptom scales and weight loss, higher scores reflect a higher level of problems

PME partial mesorectal excision, *TME* total mesorectal excision, *IR* intersphincteric resection, *LARS* low anterior resection syndrome, *GI* gastrointestinal

In our study, we found a large difference in sexual function; females had more severe problems than men, when we compared patients with and without radio(chemo)therapy. The follow-up study of the Dutch trial confirmed more sexual dysfunction for males and females in the TME + short-course radiotherapy group. Erection difficulties were reported at a rate of 50.5% in the irradiated group compared to 29.9% in the surgery only group. Sexually active females reported dyspareunia in 20% after TME + radiotherapy as compared to 5.4% after TME only [39]. Stephens et al. were able to show in a randomised trial comparing short-course preoperative radiotherapy to selective postoperative chemoradiotherapy that scores of male sexual dysfunction rose from 28 at baseline to 59 after surgery [40]. At 2 years, the group with preoperative short-course radiotherapy indicated a score of 66 vs. 57 in the selective treatment group. On the contrary, other studies have also described deterioration of sexual function for both genders after rectal cancer treatment but could not or only in part document an association with radio(chemo) therapy [37, 41]. In general, women especially are reluctant to answer questions about sexual function. Therefore, our data have to be interpreted with caution especially with regard to female sexual function due to the limited number of patients reporting on sexual issues. Nevertheless, these functional impairments should be considered in patient counselling especially in sexually active patients.

The strength of our study is a thorough investigation of all aspects of QoL as expressed by both the EORTC QLQ-C30 and the bowel specific QLQ-CR38 questionnaires. We could demonstrate that overall QoL is associated with LARS. As expected, bowel-related symptoms also correlate with LARS, as do body image, micturition problems and future perspective. Sexual functioning and sexual problems are rather correlated with age, and the impact of other factors is difficult to judge, because the number of affected patients was restricted in a population with a median age of approximately 70 years.

Our study harbours some limitations that need to be addressed. In the group of responders, there were significantly more patients with a time interval since operation of <2 years and less patients who suffered an anastomotic leak after surgery. Despite these differences, we esteem the responders as representative for the investigated patient population. Furthermore, we neither evaluated the educational, socioeconomic or marital status of the patients nor co-morbidities. It was shown that these factors are associated with various aspects of QoL [33, 42, 43]. There is also evidence that personality has a strong impact on QoL after colorectal surgery [44] of which we also had no information. It is likely that these information would have explained a larger part of the variance than the available factors [44]. We indeed focused on patient-, tumour- and treatment aspects to analyse their respective associations as we could assume that the aforementioned factors are independent of tumour treatment.

Conclusion

This study thoroughly investigates the association of LARS with QoL as measured with the EORTC QLQ-C30 and CR38 questionnaires in rectal cancer patients. It reveals that major LARS is associated with many more aspects of QoL as compared to other patient- and treatment factors such as RCT, age and tumour characteristics. The differences in QoL that can be explained by LARS, however, are only in the range of 10%. Nevertheless, preservation of anorectal function as well as treatment of LARS are potential measures to improve QoL in this patient group.

Acknowledgments The authors are indebted to Lisa Domichowski, Medical Data Manager, for her support in data acquisition. The maintenance of the database at the Coloproctologic Unit of Dresden-Friedrichstadt General Hospital is supported by a grant from the Tumour Centre Dresden.

Compliance with ethical standards

Ethical approval was granted by the responsible institution (Saxon Physicians Chamber, No. EK-BR-92/15-1/134619).

References

1. Heald RJ, Moran BJ, Ryall RDH, Sexton R, MacFarlane JK (1998) The Basingstoke Experience of total mesorectal excision. Arch Surg 133:894–899
2. Merkel S, Klossek D, Göhl J, Papadopoulos T, Hohenberger W, Hermanek P (2009) Quality management in rectal carcinoma: what is feasible? Int J Color Dis 24:931–942
3. Birgisson H, Talbäck M, Gunnarsson U, Påhlman L, Glimelius B (2005) Improved survival in cancer of the colon and rectum in Sweden. Eur J Surg Oncol 31:845–853
4. Fischer J, Hellmich G, Jackisch T, Puffer E, Zimmer J, Bleyl D, Kittner T, Witzigmann H, Stelzner S (2015) Outcome for stage II and III rectal and colon cancer equally good after treatment improvement over three decades. Int J Color Dis 30:797–806
5. Battersby NJ, Juul T, Christensen P, Janjua AZ, Branagan G, Emmertsen KJ, Norton C, Hughes R, Laurberg S, Moran BJ, United Kingdom Low Anterior Resection Syndrome Study Group (2016) Predicting the risk of bowel-related quality-of-life impairment after restorative resection for rectal cancer: a multicenter cross-sectional study. Dis Colon Rectum 59:270–280
6. Hupkens BJP, Martens MH, Stoot JH, Berbee M, Melenhorst J, Beets-Tan RG, Beets GL, Breukink SO (2017) Quality of life in rectal cancer patients after chemoradiation: watch-and-wait policy versus standard resection—a matched-controlled study. Dis Colon Rectum 60:1032–1040
7. Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, Filiberti A, Flechtner H, Fleishman SB, de Haes JC et al (1993) The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst 85:365–376
8. Sprangers MA, te Velde A, Aaronson NK (1999) The construction and testing of the EORTC colorectal cancer-specific quality of life questionnaire module (QLQ-CR38). Eur J Cancer 35:238–247
9. Emmertsen KJ, Laurberg S (2012) Low anterior resection syndrome score: development and validation of a symptom-based scoring system for bowel dysfunction after low anterior resection for rectal cancer. Ann Surg 255:922–928
10. Juul T, Ahlberg M, Biondo S, Espin E, Jimenez LM, Matzel KE, Palmer GJ, Sauermann A, Trenti L, Zhang W, Laurberg S, Christensen P (2014) International validation of the Low Anterior Resection Syndrome Score. Ann Surg 259:728–734
11. Bittorf B, Matzel KE (2015) The LARS score for evaluation of low anterior resection syndrome. Coloproctology 37:262–265 **[in German]**
12. Kupsch J, Jackisch T, Matzel KE, Zimmer J, Schreiber A, Sims A, Witzigmann H, Stelzner S (2018) Outcome of bowel function following anterior resection for rectal cancer—an analysis using the Low Anterior Resection Syndrome (LARS) score. Int J Color Dis 33:787–798
13. Fayers PM, Aaronson NK, Bjordal K, Groenvold M, Curran D, Bottomly A, on behalf of the EORTC Quality of Life Group (2001) The EORTC QLQ-C30 Scoring Manual, 3rd edn. European Organisation for Research and Treatment of Cancer, Brussels
14. Osoba D, Rodrigues G, Myles J, Zee B, Pater J (1998) Interpreting the significance of changes in health-related quality-of-life scores. J Clin Oncol 16:139–144
15. Young T, de Haes H, Curran D, Fayers P, Brandberg Y, Vanvoorden V, Bottomley A, on behalf of the EORTC Quality of Life Group (2002) Guidelines for assessing quality of life in EORTC clinical trials. EORTC Quality of Life Group Publication, Brussels
16. Curran D, Aaronson N, Standaert B, Molenberghs G, Therasse P, Ramirez A, Koopmanschap M, Erder H, Piccart M (2000) Summary measures and statistics in the analysis of quality of life data: an example from an EORTC-NCIC-SAKK locally advanced breast cancer study. Eur J Cancer 36:834–844
17. Scott NW, Fayers PM, Aaronson NK, Bottomley A, de Graeff A, Groenvold M, Gundy C, Koller M, Petersen MA, Sprangers MAG (2008) EORTC QLQ-C30 Reference Values. European Organisation for Research and Treatment of Cancer, Brussels
18. Schwarz R, Hinz A (2001) Reference data for the quality of life questionnaire EORTC QLQ-C30 in the general German population. Eur J Cancer 37:1345–1351
19. Juul T, Ahlberg M, Biondo S, Espin E, Jimenez LM, Matzel KE, Palmer GJ, Sauermann A, Trenti L, Zhang W, Laurberg S, Christensen P (2014) Low anterior resection syndrome and quality of life: an international multicenter study. Dis Colon rectum 94: 1278–1284
20. Emmertsen KJ, Laurberg S, on behalf of the Rectal Cancer Function Study Group (2013) Impact of bowel dysfunction on quality of life after sphincter-preserving resection for rectal cancer. Br J Surg 100:1377–1387
21. Nesbakken A, Nygaard K, Lunde OC (2001) Outcome and late functional results after anastomotic leakage following mesorectal excision for rectal cancer. Br J Surg 88:400–404
22. Enker WE, Thaler HT, Cranor ML, Polyak T (1995) Total mesorectal excision in the operative treatment of carcinoma of the rectum. J Am Coll Surg 181:335–346
23. Havenga K, DeRuiter MC, Enker WE, Welvaart K (1996) Anatomical basis of autonomic nerve-preserving total mesorectal excision for rectal cancer. Br J Surg 83:384–388
24. Runkel N, Reiser H (2013) Nerve-oriented mesorectal excision (NOME): autonomic nerves as landmarks for laparoscopic rectal resection. Int J Color Dis 28:1367–1375
25. Stelzner S, Böttner M, Kupsch J, Kneist W, Quirke P, West N, Witzigmann H, Wedel T (2018) Internal anal sphincter nerves—a macroanatomical and microscopical description of the extrinsic autonomic nerve supply of the internal anal sphincter. Color Dis 20: O7–O16
26. Kneist W, Kauff DW, Juhre V, Hoffmann KP, Lang H (2013) Is intraoperative neuromonitoring associated with better functional outcome in patients undergoing open TME? Results of a case-control study. Eur J Surg Oncol 39:994–999
27. Aigner F, Hörmann R, Fritsch H, Pratschke J, D'Hoore A, Brenner E, Williams N, Biebl M, TAMIS TME Collaboration Group (2015) Anatomical considerations for transanal minimal-invasive surgery: the caudal to cephalic approach. Color Dis 17:O47–O53
28. Kneist W, Rink AD, Kauff DW, Konerding MA, Lang H (2015) Topography of the extrinsic internal anal sphincter nerve supply during laparoscopic-assisted TAMIS TME: five key zones of risk from the surgeon's view. Int J Color Dis 30:71–78
29. Koedam TWA, van Ramshorst GH, Deijen CL, Elfrink AKE, Meijerink WJHJ, Bonjer HJ, Sietses C, Tuynman JB (2017) Transanal total mesorectal excision (TaTME) for rectal cancer: effects on patient-reported quality of life and functional outcome. Tech Coloproctol 21:25–33
30. Luca F, Valvo M, Guerra-Cogorno M, Simo D, Blesa-Sierra E, Biffi R, Garberoglio C (2016) Functional results of robotic total intersphincteric resection with hand-sewn coloanal anastomosis. Eur J Surg Oncol 42:841–847

31. Andersson J, Angenete E, Gellerstedt M, Angerås U, Jess P, Rosenberg J, Fürst A, Bonjer J, Haglind E (2013) Health-related quality of life after laparoscopic and open surgery for rectal cancer in a randomized trial. Br J Surg 100:941–949
32. Hjermstad MJ, Fayers PM, Bjordal K, Kaasa S (1998) Using reference data on quality of life–the importance of adjusting for age and gender, exemplified by the EORTC QLQ-C30 (+3). Eur J Cancer 34:1381–1389
33. van de Poll-Franse LV, Mols F, Gundy CM, Creutzberg CL, Nout RA, Verdonck-de Leeuw IM, Taphoorn MJ, Aaronson NK (2011) Normative data for the EORTC QLQ-C30 and EORTC-sexuality items in the general Dutch population. Eur J Cancer 47:667–675
34. Parc Y, Zutshi M, Zalinski S, Ruppert R, Fürst A, Fazio VW (2009) Preoperative radiotherapy is associated with worse functional results after coloanal anastomosis for rectal cancer. Dis Colon Rectum 52:2004–2015
35. Loos M, Quentmeier P, Schuster T, Nitsche U, Gertler R, Keerl A, Kocher T, Friess H, Rosenberg R (2013) Effect of preoperative radio(chemo)therapy on long-term functional outcome in rectal cancer patients: a systematic review and meta-analysis. Ann Surg Oncol 20:1816–1828
36. Trenti L, Galvez A, Biondo S, Solis A, Vallribera-Valls F, Espin-Basany E, Garcia-Granero A, Kreisler E (2018) Quality of life and anterior resection syndrome after surgery for mid to low rectal cancer: a cross-sectional study. Eur J Surg Oncol 44:1031–1039
37. Contin P, Kulu Y, Bruckner T, Sturm M, Welsch T, Müller-Stich BP, Huber J, Büchler MW, Ulrich A (2014) Comparative analysis of late functional outcome following preoperative radiation therapy or chemoradiotherapy and surgery or surgery alone in rectal cancer. Int J Color Dis 29:165–175
38. Samuelian JM, Callister MD, Ashman JB, Young-Fadok TM, Borad MJ, Gunderson LL (2012) Reduced acute bowel toxicity in patients treated with intensity-modulated radiotherapy for rectal cancer. Int J Radiat Oncol Biol Phys 82:1981–1987
39. Wiltink LM, Chen TYT, Nout RA, Meershoek-Klein Kranenbarg E, Fiocco M, Laurberg S, van de Velde CJH, Marijnen CAM (2014) Health-related quality of life 14 years after preoperative short-term radiotherapy and total mesorectal excision for rectal cancer: report of a multicenter randomised trial. Eur J Cancer 50:2390–2398
40. Stephens RJ, Thompson LC, Quirke P, Steele R, Grieve R, Couture J, Griffiths GO, Sebag-Montefiore D (2010) Impact of short-course preoperative radiotherapy for rectal cancer on patients' quality of life: data from the Medical Research Council CR07/National Cancer Institute of Canada Clinical Trials Group C016 randomized clinical trial. J Clin Oncol 28:4233–4239
41. Adam JP, Denost Q, Capdepont M, van Geluwe B, Rullier E (2016) Prospective and longitudinal study of urogenital dysfunction after proctectomy for rectal cancer. Dis Colon rectum 59:822–830
42. Kobayashi K, Morita S, Shimonagayoshi M, Kobayashi M, Fujiki Y, Uchida Y, Yamaguchi K (2008) Effects of socioeconomic factors and cancer survivors' worries on their quality of life (QOL) in Japan. Psychooncology 17:606–611
43. Movsas B, Scott C, Watkins-Bruner D (2006) Pretreatment factors significantly influence quality of life in cancer patients: a Radiation Therapy Oncology Group (RTOG) analysis. Int J Radiat Oncol Biol Phys 65:830–835
44. Siassi M, Weiss M, Hohenberger W, Lösel F, Matzel K (2009) Personality rather than clinical variables determines quality of life after major colorectal surgery. Dis Colon rectum 52:662–668