Targets for improving patient outcomes after major gastrointestinal cancer surgery: the value of perioperative care

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Chapter 9

The Impact on Health-Related Quality of a Stoma or Poor Functional Outcomes After Rectal Cancer Surgery in Dutch Patients: a Prospective Cohort Study

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List of Abbreviations

APR; abdominoperineal resection, ASA; American Society of Anesthesiologists, EORTC; European Organization for Research and Treatment of Cancer, HRQoL; health-related quality of life, LARS; Low-Anterior Resection Syndrome, NKR; Netherlands Cancer Registry, POLARS; Pre-Operative LARS score, PLCRC; Prospective Dutch Colorectal Cancer, PROFILES; Patient Reported Outcomes Following Initial treatment and Long-term Evaluation of Survivorship

Abstract

Background: As the survival of patients with rectal cancer has improved in recent decades, more and more patients have to live with the consequences of rectal cancer surgery. An influential factor in long-term Health-related Quality of Life (HRQoL) is the presence of a stoma. This study aimed to better understand the long-term consequences of a stoma and poor functional outcomes.

Methods: Patients who underwent curative surgery for a primary tumor located in the rectosigmoid and rectum between 2013 and 2020 were identified from the nationwide Prospective Dutch Colorectal Cancer (PLCRC) cohort study. Patients received the following questionnaires: EORTC-QLQ-CR29, EORTC-QLQ-C30, and the LARS-score at 12 months, 24 months and 36 months after surgery.

Results: A total of 1,170 patients were included of whom 751 (64.2%) had no stoma, 122 (10.4%) had a stoma at primary surgery, 45 (3.8%) had a stoma at secondary surgery and 252 (21.5%) patients that underwent abdominoperineal resection (APR). Of all patients without a stoma, 41.4% reported major low-anterior resection syndrome (LARS). Patients without a stoma reported significantly better HRQoL. Moreover, patients without a stoma significantly reported an overall better HRQoL.

Conclusion: The presence of a stoma and poor functional outcomes were both associated with reduced HRQoL. Patients with poor functional outcomes, defined as major LARS, reported a similar level of HRQoL compared to patients with a stoma. In addition, the HRQoL after rectal cancer surgery does not change significantly after the first year after surgery.

Introduction

In recent decades, the 5-year survival of rectal cancer patients has increased to approximately 80%, leading to more patients having to deal with the consequences of rectal cancer treatment [1]. The cornerstone of rectal cancer treatment is still surgical resection [2]. These consequences of rectal cancer surgery are, for instance, stoma presence, bowel dysfunction, psychological and physical stress [3-5]. Of all the surgically treated rectal cancer patients in the Netherlands, 63.6% receive a (temporary) stoma [6]. The decision on whether or not to make a stoma during rectal surgery can be difficult [7]. This decision between an anastomosis or a stoma is mainly based on two considerations. Firstly, the risk of postoperative complications (e.g., anastomotic leakage) as can lead to morbidity and mortality [8, 9]. A (temporary) stoma has been shown to reduce the rate of symptomatic anastomotic leakage and re-operations Secondly, dysfunctional bowel functions, often defined as major Low-anterior Syndrome (LARS), may have a detrimental effect on the quality of life and should therefore be taken into account [10-12]. Major LARS is reported in 42 % of the patients one year after rectal surgery [13]. Several patient characteristics (e.g., age, gender) and treatment characteristics (e.g., low tumor, neoadjuvant radiotherapy) are prognostic factors for major LARS [14].

The presence of a stoma and poor bowel functions in patients can both affect the quality of life after rectal cancer surgery, therefore the trade-off between the formation of a (temporary) stoma or anastomosis should be explored further [15]. This study aims to determine the influence of a stoma and poor functional outcomes on the health-related quality of life (HRQoL) after rectal cancer surgery in a nation-wide population-based study.

Methods

Study population and treatment

Patients who underwent surgical resection for a primary carcinoma in the rectosigmoid and rectum between 2013 and 2020 were retrieved from the ongoing nationwide Prospective Dutch Colorectal Cancer (PLCRC) cohort study [16]. this study collected clinical data and patient-reported outcome measurements (PROMs) from colorectal cancer patients; a total of 59 centers in The Netherlands participated. PROMs were retrieved within the Patient Reported Outcomes Following Initial treatment and Long-term Evaluation of Survivorship (PROFILES) registry [17]. Patients were included at any time during their rectal cancer treatment, therefor a cross-sectional study design was used. Three separate cohorts of 1-, 2- and 3-years after surgery were constructed and

analyzed separately. Clinical data were obtained from the Netherlands Cancer Registry (NKR). All patients signed an informed consent form before their medical records were reviewed and sending questionnaires were sent. Inclusion criteria were: patients with a primary tumor of stage I-III located in the rectosigmoid and rectum treated with surgical resection. Patients who underwent emergency surgery or palliative intended surgery were excluded.

Health-related quality of life assessment

The following PROMs were completed by the patients: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core (EORTC) questionnaires: cancer-specific QLQ-C30 and colorectal- cancer-specific QLQ-CR29 and Low-Anterior Resection Syndrome (LARS)-questionnaire at 12 months, 24 months and 36 months after surgery [18-20]. A four-point Likert scale was used in all questionnaires after which all responses were linearly converted to 0–100 scales.

Statistical analyses

Patients were divided into four groups, patients without a stoma 1 year after surgery, patients with a stoma 1 year after surgery constructed during primary surgery, patients with a stoma 1 year after surgery constructed during secondary surgery and patients who underwent an APR resection. The chi-square test was used for categorical variables, the Mann-Whitney U test was used for numeric variables, a post-hoc Bonferroni test was used to correct for multiple testing. For sub-analysis, patients with a stoma were divided into a group of patients with- and without major-LARS. Major LARS was defined as a LARS-score ≥30.

Results

Patient characteristics

A total of 1,545 patients were identified from the PLCRC registry of whom 355 (23.0%) were excluded because they had not filled-out any questionnaire (Fig. 1). In addition, 20 (1.3%) patients were excluded because essential variables were missing. Patients were divided into four groups; patients without a stoma (64.2%), patients with Low Anterior Resection (LAR) and a stoma constructed at primary surgery (10.4%), patients with a stoma constructed at secondary surgery or a temporary stoma present at 1-year (3.8%) and patients that underwent an APR (21.5%) (Table 1).

Patient with a stoma constructed during primary surgery were older than the other groups, including patients that underwent APR. Furthermore, patients with a stoma and APR had a lower located tumor, compared to patients without a stoma, and received significantly more neo-adjuvant therapy. In addition, patients with a stoma constructed during secondary surgery were significantly more affected by anastomotic leakage.

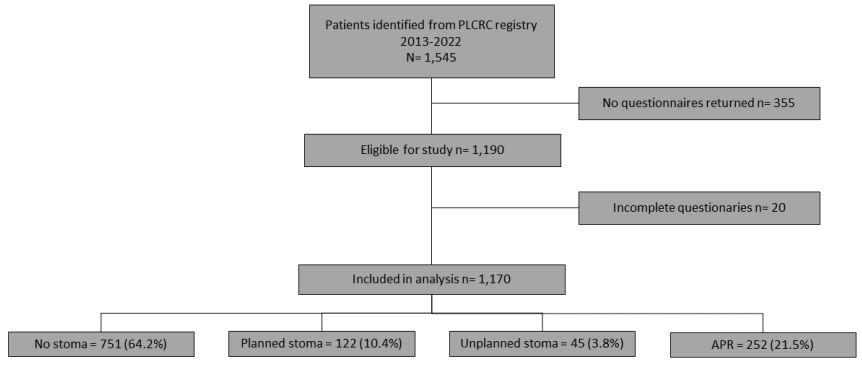

Figure 1 – Flowchart of patient selection

Health-Related Quality of Life (12 months)

Patients without a stoma reported an overall better HRQoL compared to patients with a stoma measured by the EORTC qlq-C30 questionnaire (Fig. 2, Table S.1). Furthermore, stoma patients who underwent APR reported better HRQoL outcomes than stoma patients after LAR. No significant differences were seen in HRQoL when comparing patients with a stoma constructed during primary or during secondary surgery. Witnessed by the EORTC qlq-CR29 questionnaire, patients with a stoma constructed during secondary surgery reported more problems in stoma care compared to patients with a stoma constructed during primary surgery (Table S.2). Another significant finding was that the body image is worse in patients with a stoma compared to patients without a stoma.

Table 1 – Patient characteristics

		No stoma	Stoma at primary surgery	Stoma at secondary surgery	APR	p-value
		n=751 (64.2%)	n=122 (10.4%)	n=45 (3.8%)	n=252 (21.5%)	
Age (years)	**Mean**	63.2	69.3	62.7	64.7	**<0.01**
Gender %	**Male**	484 (64.4%)	85 (69.7%)	32 (71.1%)	167 (66.3%)	0.39
	Female	267 (35.6%)	37 (30.3%)	13 (28.9%)	85 (33.7%)	
BMI	**Mean**	26.1	26.6	28.5	26.3	0.07
ASA	**I-II**	638 (85.0%)	96 (78.7%)	34 (75.6%)	213 (84.5%)	0.20
	III-IV	101 (13.4%)	23 (18.9%)	9 (20.0%)	36 (14.3%)	
	Unknown	12 (1.6%)	3 (2.5%)	2 (4.4%)	3 (1.2%)	
Tumor location	**0-5cm**	165 (22,0%) β γ δ	69 (56,6%)	17 (37,8%)	223 (88,5%)	**<0.01**
	5.1-10cm	277 (36,9%)	36 (29,5%)	20 (44,4%)	18 (7,1%)	
	10.1-15cm	145 (19,3%)	12 (9,8%)	5 (11,1%)	3 (1,2%)	
	>15cm	27 (3,6%)	0 (0,0%)	1 (2,2%)	0 0,0%	
	Unknown	137 (18,2%)	5 (4,1%)	2 (4,4%)	8 (3,2%)	
pT-score	**0**	52 (6,9%)	11 (9,0%)	4 (8,9%)	36 (14,3%)	0.64
	I	124 (16,5%)	10 (8,2%)	6 (13,3%)	27 (10,7%)	
	II	239 (31,8%)	42 (34,4%)	9 (20,0%)	88 (34,9%)	
	III	304 (40,5%)	57 (46,7%)	24 (53,3%)	90 (35,7%)	
	IV	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
	Unknown	32 (4,3%)	2 (1,6%)	2 (4,4%)	11 (4,4%)	
Neoadjuvant therapy	**Radiotherapy**	170 (22.6%) β γ δ	30 (24.6%)	15 (33.3%)	47 (18.7%)	**<0.01**
	Chemoradiation	146 (19,4%)	48 (39.3%)	15 (35.6%)	146 (57.9%)	
	None	435 (57.9%)	44 (36.1%)	14 (31.1%)	59 (23.4%)	
Approach	**Open**	15 (2.0%)	6 (4.9%)	0 (0.0%)	22 (8.7%)	0.96
	Laparoscopic	564 (75.1%)	74 (60.7%)	31 (68.9%)	146 (57.9%)	
	Robot-assisted	166 (22.1%)	42 (34.4%)	14 (31.1%)	83 (32.9%)	
	Unknown	6 (0.8%)	0 (0.0%)	0 (0.0%)	1 (0.4%)	
Anastomotic leakage	**Yes**	44 (5.9%) β γ δ	0 (0.0%)	17 (37.8%)	0 (0.0%)	**<0.01**

ASA, American Society of Anesthesiologists,
α: statistically different from group no stoma
β: statistically different from group stoma at primary surgery
γ: statistically different from group stoma at secondary surgery
δ: statistically different from group APR

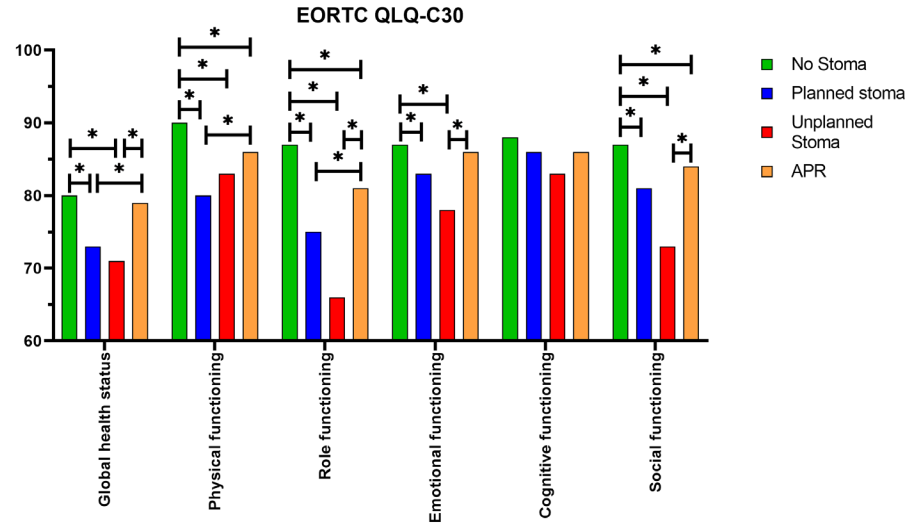

Figure 2 – Health-related quality of life over time 12 months after surgery, measured using EORTC QLQ-C30 and EORTC QLQ-CR29. Complete overview of data is shown in Table S.1 and Table S.2.

Functional outcome and health-related quality of life

Patients without a stoma were divided into two groups based on their LARS-score, patients with a LARS-score ≥30 (33.1%) were defined as major LARS (Table S.3). Major LARS patients had a tumor located lower in the rectum and received more neoadjuvant therapy compared with patients without or with minor LARS. Overall, patients without a stoma reported a better HRQoL (Fig. 3, Table S.4). Patients with major LARS did not report a significantly better HRQoL, expect for physical functioning, compared to patients with a stoma. Body image was significantly worse in patients with a major LARS than in patients without major LARS, but significantly better compared to stoma patient (Table S.5).

Health-related quality of life (HRQoL) over time (12-36 months)

The group of patients (n=311) who completed all questionnaires, at time-points: 12 months, 24 months and 36 months after surgery, were analyzed (Table S.6). As shown in Figure 4, the HRQoL does not change significantly between 12months and 36 months after surgery.

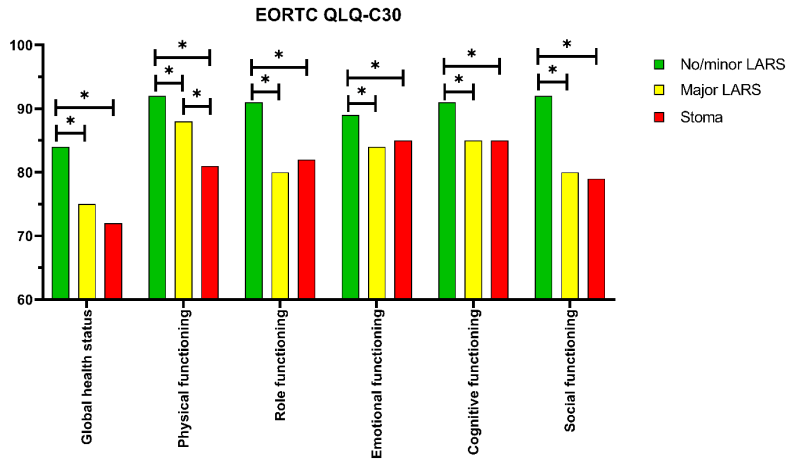

Figure 3 – Health-Related Quality of Life (HRQoL) 12 months after surgery, using the EORTC QLQ-C30 questionnaire, patients were divided into three groups. Patient characteristics are shown in Table S.3 and the complete overview of HRQoL data is shown in Tables S.4 and S.5.

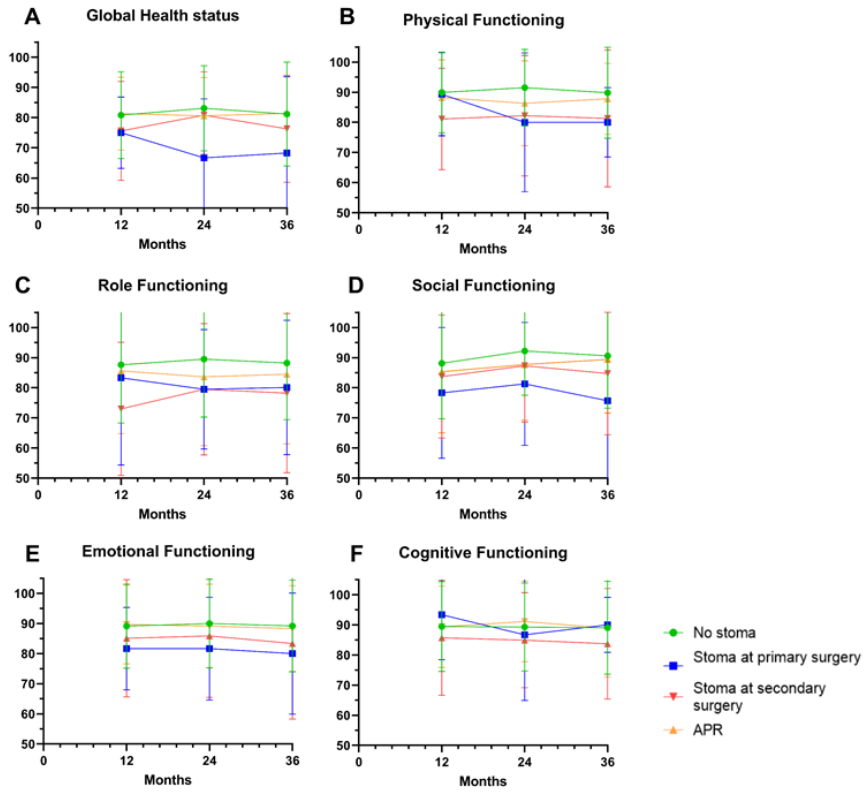

Figure 4 – Health-related quality of life (HRQoL), using the EORTC-QLQ-C30 questionnaire, over time in the first 36 months after surgery in patients who filled out all three questionnaires (t=12, t=24, t=36), patient characteristics are shown in (Table S.6)

Discussion

This study presents a comparison in the HRQoL between patients with and without a stoma and poor functional outcome after rectal cancer surgery. The presence of a stoma and poor functional outcomes were both associated with a reduced HRQoL. A primary colostoma, can be constructed after APR and after LAR. Reported physical functioning was better in patient with a colostoma after APR. HRQoL after rectal cancer surgery did not change significantly after the first year postoperatively over the next two years.

Previous studies have also shown a reduced HRQoL in patients with a stoma or major LARS [15, 21]. However, some studies reported ambiguous results for the influence of a stoma on HRQoL. A Cochrane review by Pachler et al. included 26 studies, of which only 10 reported a significantly reduced HRQoL in patients with a permanent colostoma [22]. Moreover, as shown, patients without a stoma can be divided into two groups based on the functional outcomes measured by LARS score. Outcomes of this study were in line with other studies, as these studies agree that poor bowel function is associated with reduced HRQoL [19, 23, 24]. The differences between patients with a stoma during primary or secondary surgery stoma have not been widely studied. It has been shown that postoperative complications and anastomotic leakage can affect postoperative HRQoL [25, 26]. Additionally, there is a direct independent association between postoperative complications, a permanent stoma and failure to close a (temporary) stoma [27, 28]. Additionally, postoperative distant metastasis are associated with failure to close a (temporary) stoma [27, 28]. The differences in HRQoL between patients with a LAR and stoma and patients that underwent an APR, might be the result of an APR reducing the risk of pelvic abscesses, persisting mucus production and diversion proctitis and therefore impacting HRQoL, however an APR is associated with increased morbidity and a perineal wound [29, 30]. Furthermore, Bakker et al. showed that patients that underwent a LAR with primary stoma, were significantly older and had more comorbidities, therefore differences in HRQoL might be subjected to worse patient characteristics [31].

Knowledge of postoperative HRQoL after the rectal cancer surgery provides essential information regarding treatment options to aid in shared decision-making. Since explicit patient consideration regarding treatment options is positively associated with long-term quality of life and improved acceptance [32]. An important treatment option is whether to construct a stoma, which is usually not a foregone conclusion [7, 33]. When deciding between an anastomosis and a (temporary) stoma in rectal cancer surgery, two factors are being considered. Firstly, the risk of postoperative complications, especially anastomotic leakage and secondly the expected functional outcomes [8, 9, 14, 34]. The risk of poor functional outcomes can be estimated using the POLARS score, based on prognostic factors, such as: age, gender, tumor location, stoma and preoperative

radiotherapy [14, 35]. In addition, anastomotic leakage can be estimated as well using patient- and treatment characteristics (e.g., comorbidity, gender, tumor location) [9, 36, 37]. Better information to improve postoperative patient education on stoma care leads to an increased HRQoL and lower healthcare costs [38, 39].

Limitations

Although this study reports valuable results, it has some limitations. First, due to the lack of patients with more than 1 year of follow-up in the database, a cross-sectional approach was used. This hampers an accurate analysis of the development of HRQoL overtime. Second, the data on considerations and subsequent decision on when to construct a stoma and why a stoma was not reversed were not available. A prospective study might be needed to further investigated the decision towards stoma construction and their consequences. Moreover, comparison of patients with and without a stoma is subjected to confounding by indication, as the choice to construct a (planned) stoma is based on patient- and treatment characteristics. This effect is apparent by the differences in age, tumor location and neoadjuvant therapy between these groups. These factors may also influence HRQoL and thereby inherently bias comparisons [40]. There is an ongoing debate about the indication to perform an APR as alternative to a low Hartmann resection, therefore indication for APR might differ from other countries [29, 30]. Unfortunately, we had no information on whether APRs were intersphincteric or extralevator APRs.

Conclusion

This study shows the impact of a stoma and poor functional outcomes on HRQoL after rectal cancer surgery. The presence of a stoma and poor functional bowel outcomes were both associated with a decreased HRQoL. Patients with poor functional bowel outcomes, defined as major LARS, report a similar level of HRQoL compared to patients with a stoma. Additionally, HRQoL after rectal cancer surgery does not change significantly after the first year post surgery. Information on the effect of treatment decisions and surgical outcomes on the long-term HRQoL of patient undergoing rectal cancer surgery is essential for patient education and shared-decision making.

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Supplementary Information

Table S.1 - Health-related quality of life (HRQoL) 12 months after surgery measured using EORTC-QLQ-C30.

EORTC-QLQ-C30	No stoma	Stoma at primary surgery	Stoma at secondary surgery	APR	p-value
	n= 751 (64.2%)	n= 122 (10.4%)	n= 45 (3.8%)	n= 252 (21.5%)	
Global Health status	80.1 β,γ	73.4 δ	71.9 δ	79.0	**<0.01**
Physical functioning	90.9 β,γ,δ	80.1 δ	83.0	86.0	**<0.01**
Role Functioning	87.6 β,γ,δ	75.1 δ	66.3 δ	81.5	**<0.01**
Emotional functioning	87.4 β,γ	83.4	78.2 δ	86.9	0.08
Cognitive functioning	88.8	86.7	83.7	86.3	0.09
Social functioning	87.6 β,γ,δ	81.7	73.9 δ	84.2	**<0.01**
Fatigue	17.4 β,γ,δ	25.1	27.0	20.5	**<0.01**
Nausea and vomiting	2.4 δ	2.5	4.5	1.3	0.24
Pain	9.0 δ	12.7	14.8	12.3	**<0.01**
Dyspnea	8.1	10.1	12.1	9.7	0.37
Insomnia	17.7	18.3	23.5	19.2	0.68
Appetite loss	4.1 β	8.7 δ	8.3	3.3	**<0.01**
Constipation	9.4 β,γ,δ	4.4	2.3	3.7	**<0.01**
Diarrhea	11.6 γ,δ	9.6 δ	4.7	4.6	**<0.01**
Financial difficulties	4.2 β,δ	8.2	8.3	6.8	**0.02**

α: statistically different from group No stoma
β: statistically different from group stoma at primary surgery
γ: statistically different from group stoma at secondary surgery
δ: statistically different from group APR

Table S.2 – Health-related quality of life (HRQoL) 12 months after surgery measured using EORTC-QLQ-CR29.

EORTC-QLQ-CR29	No stoma	Stoma at primary surgery	Stoma at secondary surgery	APR	p-value
	n= 751 (64.2%)	n= 122 (10.4%)	n= 45 (3.8%)	n= 252 (21.5%)	
Urinary frequency	26.9 β	32.0 γ	21.9 δ	31.7	**<0.01**
Urinary incontinency	7.8 β	12.0	9.6	13.7	**<0.01**
Dysuria	1.7	2.7	5.9	2.8	0.09
Abdominal pain	9.8	10.4	5.9 δ	10.8	0.42
Buttock pain	13.2	15.3	13.3	18.4	**<0.01**
Bloating	15.4 γ,δ	15.6 γ	5.9 δ	12.2	**<0.01**
Blood and mucus in stool	3.7	4.0 δ	4.4	1.5	**<0.01**
Dry mouth	14.1	14.8	16.3	13.4	0.80
Hair loss	2.5	4.4	9.6	2.2	**0.01**
Taste	4.1 β	8.5	8.9	5.3	**<0.01**
Flatulence (no stoma)	40.0	-	-	-	-
Fecal incontinence (no stoma)	12.9	-	-	-	-
Sore skin (no stoma)	13.8	-	-	-	-
Stool frequency (no stoma)	29.9	-	-	-	-
Embarrassment (no stoma)	24.5	-	-	-	-
Flatulence (stoma)	-	27.3	20.7 δ	28.9	0.08
Fecal incontinence/leakage (stoma)	-	10.9	15.6	9.4	0.40
Sore skin (stoma)	-	13.9 γ	25.9 δ	14.9	**0.02**
Stool Frequency/ bags change (stoma)	-	12.1	14.8	11.8	0.94
Embarrassment stoma)	-	24.0	24.4	20.7	0.58
Stoma care problems	-	4.9	8.9 δ	3.5	**<0.01**
Impotence	32.8 β, δ	46.2 γ, δ	28.1 δ	61.4	**<0.01**
Dyspareunia	17.9 δ	45.8	45.5	34.5	**<0.01**
Anxiety	24.7 β,γ,δ	30.3	34.8 δ	25.5	**0.02**
Weight	14.1	14.6	21.5	14.7	0.60
Body image	11.9 β,γ,δ	23.4	27.3	23.2	**<0.01**
Sexual interest Men	47.0 β, δ	31.2	39.6	36.0	**<0.01**
Sexual interest Women	30.4	19.5	20.3	26.2	**<0.01**

α: statistically different from group No stoma
β: statistically different from group stoma at primary surgery
γ: statistically different from group stoma at secondary surgery
δ: statistically different from group APR

Table S.3 - Patient characteristics.

		No/minor LARS	Major LARS	Stoma	p-value
		n=447 (48.7%)	n=304 (33.1%)	n=167 (18.2%)	
Age (years)	**Mean**	63.61	62.53	67.5 α β δ	**<0.01**
Gender %	**Male**	300 (68.2%)	184 (59.2%)	117 (70.1%)	**0.04**
	Female	140 (31.8%)	127 (40.8%)	50 (29.9%)	
BMI	**Mean**	26.06	26.26	27.1	0.07
ASA*	**I-II**	373 (85.6%)	265 (86.0%)	130 (77.8%)	0.99
	III-IV	60 (13.8%)	41 (13.3%)	32 (19.2%)	
	Unknown	3 (0.8%)	2 (0.7%)	5 (3.0%)	
Tumor location	**0-5cm**	63 (14.3%) β γ δ	102 (32.8%)	86 (51.5%)	**<0.01**
	5.1-10cm	162 (36.8%)	115 (37.0%)	56 (33.5%)	
	10.1-15cm	86 (19.5%)	59 (19.0%)	17 (10.2%)	
	>15cm	20 (4.5%)	7 (2.3%)	1 (0.6%)	
	Unknown	109 (24.8%)	28 (9.0%)	6 (3.6%)	
pT-score	**0**	16 (3.6%) β	36 (11.6%)	15 (9.0%)	**0.02**
	I	69 (15.7%)	55 (17.7%)	16 (9.6%)	
	II	138 (31.4%)	101 (32.5%)	54 (30.5%)	
	III	196 (44.5%)	108 (34.7%)	81 (48.5%)	
	IV	0 (0.0%)	0 (0.0%)	0 (0.0%)	
	Unknown	21 (4.8%)	11 (3.5%)	4 (2.4%)	
Neoadjuvant therapy	**Radiotherapy**	83 (18.9%) β γ δ	87 (28.0%)	71 (42.5%)	**<0.01**
	Chemoradiation	58 (13.1%)	88 (28.3%)	48 (28.7%)	
	None	299 (68.0%)	136 (43.7%)	48 (28.7%)	
Approach	**Open**	10 (2.3%)	5 (1.6%)	6 (3.6%)	0.29
	Laparoscopic	337 (76.6%)	227 (73.0%)	105 (62.9%)	
	Robot-assisted	91 (20.7%)	75 (24.1%)	56 (33.5%)	
	Unknown	2 (0.5%)	4 (1.3%)	0 (0.0%)	
Anastomotic leakage	**Yes**	19 (4.3%) γ δ	25 (8.0%) γ δ	55 (32.9%)	**<0.01**

*ASA, American Society of Anesthesiologists
α: statistically different from group No/minor LARS
β: statistically different from group Major LARS
γ: statistically different from group Stoma

Table S.4 – Health-related quality of life (HRQoL) 12 months after surgery in patients with no or minor Low-Anterior Syndrome (LARS) and patients with major LARS, measured using EORTC-QLQ-C30.

EORTC-QLQ-C30	No/minor LARS	Major LARS	Stoma	p-value
	n=447 (59,5%)	n=304 (40.5%)	n= 167 (14.2%)	
Global Health status	84.1 β,γ	75.0	73.0	**<0.01**
Physical functioning	92.6 β γ	88.8 γ	80.9	**<0.01**
Role Functioning	91.3 β,γ	80.5 δ	72.7	**<0.01**
Emotional functioning	89.6 β,γ	84.4	82.0	**<0.01**
Cognitive functioning	91.3 β,γ	85.	85.9	**<0.01**
Social functioning	92.9 β,γ	80.5	79.6	**<0.01**
Fatigue	13.6 β,γ	22.6	25.6	**<0.01**
Nausea and vomiting	1.6	3.3	3.0	**0.17**
Pain	6.7 β,γ	12.0	13.3	**<0.01**
Dyspnea	7.7	8.8	10.6	**0.40**
Insomnia	14.1 β	22.3	19.7	**<0.01**
Appetite loss	2.6 β,γ	6.0	8.6	**<0.01**
Constipation	8.5 γ	11.0 γ	3.8	**<0.01**
Diarrhea	5.7 β,γ	20.2 γ	8.3	**<0.01**
Financial difficulties	2.5 β,γ	6.0	8.2	**<0.01**

α: statistically different from group No/minor LARS
β: statistically different from group Major LARS
γ: statistically different from group stoma at primary surgery
δ: statistically different from group stoma at secondary surgery

Table S.5 – Health-related quality of life (HRQoL) 12 months after surgery, measured using EORTC-QLQ-CR29.

EORTC-QLQ-CR29	No/minor LARS	Major LARS	Stoma	p-value
	n=447 (59,5%)	n=304 (40.5%)	n= 167 (14.2%)	
Urinary frequency	24.0 β,γ	30.5	29.2	**<0.01**
Urinary incontinency	6.5 β,γ	9.3	11.4	0.05
Dysuria	1.1 β	2.5	3.6	0.05
Abdominal pain	7.3 β	13.4	9.2	**<0.01**
Buttock pain	7.2 β,γ	21.7 γ	14.8	**<0.01**
Bloating	11.0 β,γ	22.0 γ	13.0	**<0.01**
Blood and mucus in stool	2.3 β	5.7	4.1	**<0.01**
Dry mouth	11.7 β	17.4	15.2	**0.01**
Hair loss	1.9 δ	3.3	5.8	0.03
Taste	2.4 β,γ	6.1	8.6	**<0.01**
Flatulence (no stoma)	31.3	52.5	-	**<0.01**
Fecal incontinence (no stoma)	4.9	23.9	-	**<0.01**
Sore skin (no stoma)	8.3	21.6	-	**<0.01**
Stool frequency (no stoma)	21.1	42.4	-	**<0.01**
Embarrassment (no stoma)	13.2	40.2	-	**<0.01**
Flatulence (stoma)	-	-	25.5	0.06
Fecal incontinence (stoma)	-	-	12.2	0.30
Sore skin (stoma)	-	-	17.2	**0.01**
Stool frequency (stoma)	-	-	12.9	0.43
Embarrassment (stoma)	-	-	24.2	0.93
Stoma care problems	-	-	5.9	0.13
Impotence	29.2 β,γ	38.8	40.9	**<0.01**
Dyspareunia	18.2	17.7	45.7	0.05
Anxiety	21.9 β,γ	28.5	31.5	**<0.01**
Weight	12.2 β	16.3	16.5	0.08
Body image	7.8 β,γ	17.2 γ	24.5	**<0.01**
Sexual interest Men	49.2 γ	44.3 γ	33.5	**<0.01**
Sexual interest Women	37.1 β,γ	23.7	19.7	**<0.01**

α: statistically different from group No/minor LARS
β: statistically different from group Major LARS
γ: statistically different from group Stoma

Table S.6 – Patient characteristics of those who completed all questionnaires at t=12, t=24 and t=36

		No stoma	Stoma at primary surgery	Stoma at secondary surgery	APR	p-value
		n=205 (65.9%)	n=43 (13.8%)	n=5 (1.6%)	n=58 (18.6%)	
Age (years)	**Mean**	64.69	68.63	59.00	64.88	**0.02**
Gender %	**Male**	142 (69.3%)	29 (67.4%)	3 (60.0%)	35 (60.3%)	0.63
	Female	63 (30.7%)	14 (32.6%)	2 (40.0%)	23 (39.7%)	
BMI	**Mean**	26.01	27.21	23.89	25.86	0.47
ASA	**I-II**	179 (87.3%)	33 (76.7%)	3 (60.0%)	53 (91.4%)	0.16
	III-IV	23 (11.2%)	7 (16.3%)	2 (40.0%)	3 (5.2%)	
	Unknown	3 (1.5%)	3 (7.0%)	0 (0.0%)	2 (3.4%)	
Tumor location	**0-5cm**	36 (17.6%) β ,	19 (44.2%)	0 (0.0%)	51 (87.9%)	**<0.01**
	5.1-10cm	77 (37.6%)	15 (34.9%)	3 (60.0%)	4 (6.9%)	
	10.1-15cm	51 (24.9%)	5 (11.6%)	1 (20.0%)	2 (3.4%)	
	>15cm	4 (2.0%)	1 (2.3%)	0 (0.0%)	0 (0.0%)	
	Unknown	37 (18.0%)	3 (7.0%)	1 (20.0%)	1 (1.7%)	
pT-score	**0**	22 (10.7%)	4 (9.3%)	0 (0.0%)	11 (19.0%)	0.07
	I	32 (15.6%)	5 (11.6%)	0 (0.0%)	5 (8.6%)	
	II	58 (28.3%)	16 (37.2%)	0 (0.0%)	22 (37.9%)	
	III	84 (41.0%)	17 (39.5%)	4 (80.0%)	18 (31.0%)	
	IV	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
	Unknown	9 (4.4%)	1 (2.3%)	1 (20.0%)	2 (3.4%)	
Neoadjuvant therapy	**Radiotherapy**	42 (20.5%) δ	14 (32.6%)	1 (20.0%)	8 (13.8%)	**<0.01**
	Chemoradiation	52 (25.4%)	14 (32.6%)	1 (20.0%)	37 (63.8%)	
	None	111 (54.1%)	15 (34.9%)	3 (60.0%)	13 (22.4%)	
Approach	**Open**	4 (2.0%)	1 (2.3%)	1 (20.0%)	1 (1.7%)	0.06
	Laparoscopic	162 (79.0%)	25 (58.1%)	2 (40.0%)	41 (70.7%)	
	Robot-assisted	39 (19.0%)	17 (39.5%)	2 (40.0%)	16 (27.6%)	
	Unknown	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Anastomotic leakage	**Yes**	10 (4.9%)	10 (23.3%)	0 (0.0%)	0 (0.0%) α β γ	**<0.01**

α: statistically different from group No stoma
β: statistically different from group stoma at primary surgery
γ: statistically different from group stoma at secondary surgery
δ: statistically different from group APR