



Effects of low anterior resection syndrome after colorectal cancer resections on health-related quality of life: a systematic review and meta-analysis

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Abstract

Background Low anterior resection syndrome (LARS) is a term that encompasses multidimensional bowel dysfunction that typically occurs following resections of rectum and distal parts of the colon. We aimed to systematically assess the available literature on the effects of bowel dysfunction after colorectal cancer (CRC) surgeries on health-related quality of life (HRQOL) and conduct a meta-analysis.

Methods Studies were included if they assessed patients who had undergone sphincter-preservation surgeries for CRC. Studies were eligible if they assessed bowel dysfunction using the LARS score and HRQOL using the European Organization for Research and Treatment Core Quality-of-Life Questionnaire (EORTC QLQ-C30).

Results Of 1410 reports, 28 studies were included. According to the analyses, patients with major LARS had lower global health status [weighted mean differences (WMD) = − 10.98; 95% confidence interval (CI) − 13.18, − 8.79], physical functioning (WMD = − 5.96; 95% CI − 7.40, − 4.52), role functioning (WMD = − 10.59; 95% CI − 12.54, − 8.63), emotional functioning (WMD = − 11.09; 95% CI − 14.34, 7.84), cognitive functioning (WMD = − 9.27; 95% CI − 12.22, − 6.32), and social functioning (WMD = − 15.73; 95% CI − 18.82, − 12.63) and higher scores of symptoms compared to patients with minor/no LARS.

Conclusions The study findings suggest that patients with major LARS experience worse HRQOL compared to those with minor/no LARS.

Registration PROSPERO, CRD42023479657.

Keywords Colorectal neoplasms · Low anterior resection syndrome · Meta-analysis · Quality of life · Systematic review

Background

Colorectal cancer (CRC) is considered the second most prevalent cancer and the second leading cause of cancer-related mortality worldwide in 2020 [1]. Surgical management, involving tumor removal and lymph node dissection, is generally recognized as the primary curative treatment for patients with CRC [2]. Given the advancements in detection and treatment strategies, as well as improved overall survival rates, there has been growing interest among clinicians and researchers in assessing the long-term side effects of treatment strategies and their impact on health-related quality of life (HRQOL) [3].

Multidimensional bowel dysfunction commonly occurs following surgeries for both colon and rectal cancers, often persisting over time. It frequently manifests as liquid and solid stool incontinence, urgency, and constipation-related

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symptoms such as incomplete or difficult evacuation and obstruction [3]. These symptoms are particularly prevalent in patients with rectal cancer who have undergone low anterior resection with anal sphincter preservation, collectively known as low anterior resection syndrome (LARS) [4]. According to a previous meta-analysis, the incidence of LARS 1 year following sphincter-preserving surgeries for rectal cancer was relatively high, reported at 44% (95% confidence interval [CI] 40–48%) [5]. Major risk factors for LARS include being female, total mesorectal excision, protective transient ileostomy or colostomy, chemoradiotherapy (neoadjuvant or adjuvant therapy), tumors and anastomosis placed near to the anal verge, and postoperative anastomotic leakage [6, 7].

Several studies have reported a detrimental impact of LARS on various dimensions of HRQOL [8, 9]; however, the data on this issue remain conflicting [10]. According to a recently published systematic review, bowel dysfunction primarily affects the social and emotional functional domains of HRQOL in patients with rectal cancer who have undergone sphincter-preserving surgery [11]. However, this finding was not according to a pooled effect meta-analysis. In this study, the LARS score and the European Organization for Research and Treatment Core Quality-of-Life Questionnaires (EORTC QLQ-C30) were identified as the most commonly used instruments for assessing bowel dysfunction and HRQOL, respectively. The LARS score, a self-administered questionnaire, has been developed and validated as a straightforward tool for evaluating bowel function following an anterior rectal resection [12]. However, recently, this score has also been utilized in other CRC surgeries [13].

No previous study has systematically reviewed and statistically combined the current literature on how bowel dysfunction following surgery affects the HRQOL of patients with CRC. Therefore, the primary objective of the present study was to systematically assess the available literature on the effects of bowel dysfunction after CRC surgeries, as measured by the LARS score, on HRQOL, as assessed by the EORTC QLQ-C30, and estimate the pooled effect for different domains. Understanding the impact of LARS on HRQOL is crucial for effective preoperative counseling of patients.

Methods

The current systematic review and meta-analysis has been reported in line with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) [14] and AMSTAR (A Measurement Tool to Assess systematic Reviews) [15] guidelines. The protocol is registered in PROSPERO (CRD42023479657).

Study eligibility criteria

Population

Patients from all age groups, ethnicities, and both sexes were included in this study. The included studies were evaluated patients who had undergone sphincter-preserving surgeries for rectal cancer (AR, LAR, intersphincteric resection, transanal endoscopic microsurgery) or sigmoid resection and colectomy for sigmoid and colon cancer. Studies were excluded if the exposure was evaluated in a group of subjects without any previous CRC surgeries or who underwent surgeries without a history of CRC.

Exposure

Studies were eligible if they assessed bowel dysfunction in the postoperative periods, when patients did not have a stoma, using the LARS score questionnaire categorized as major, minor, or/and no LARS. The LARS score questionnaire consists of five items that assess various aspects such as flatus incontinence, liquid stool incontinence, frequency, clustering, and urgency. Each item carries its own weighting, and a cumulative score ranging from 0 to 42 is calculated. The severity of bowel dysfunction is categorized into three levels: no LARS (score range 0–20), minor LARS (score range 21–29), and major LARS (score range 30–42) [12]. Studies that assessed bowel dysfunction using questionnaires other than the LARS score or reported LARS as a continuous variable were excluded.

Comparison

In this study, we assessed the effects of major compared to minor or/and no LARS on different domains of QOL. This assessment is crucial for identifying which specific domains of QOL are impacted by varying severities of LARS symptoms, thereby facilitating the tailoring of clinical interventions and enhancing patient care.

Outcome

Our primary outcome of interest was the mean score of domains in the EORTC QLQ-C30 questionnaire across different levels of LARS. The EORTC QLQ-C30 is a generic questionnaire designed to assess the HRQOL of patients with cancer consists of 30 questions assessing global health status, functional scales (physical, roles, emotional, cognitive, and social) and symptom scales (fatigue, nausea and vomiting, pain, dyspnea, insomnia,

loss of appetite, constipation, diarrhea, and financial difficulties) [16].

Study design

The present study included original observational studies (published or preprint) such as cohort, cross-sectional, and case-control studies (both population-based and hospital-based). However, trials, reviews, conference abstracts, case reports, case series, notes, and letters did not meet the inclusion criteria.

Search strategy and literature sources

Relevant studies were searched for in the PubMed, Scopus, and Web of Science databases using a combination of MeSH keywords related to “LARS” and “QOL” (Supplementary Box 1). The search covered eligible studies published from January 1, 1970 to July 20, 2023 without any language restrictions. Furthermore, a manual search in recent systematic review studies was conducted along with reviewing references and citations of included studies. Contact with experts was also made to ensure a comprehensive search.

Study screening and selection

All identified studies were exported to Endnote X8 and duplicates were removed. Then, a pilot phase of screening on a random sample of studies was conducted by two reviewers to ensure consistency in interpreting the studies. They independently screened the title and abstract of all studies according to the eligibility criteria. The full texts of certain studies also were assessed to make a final decision. In case of any discrepancies between reviewers, a meeting was scheduled to reach a consensus.

Data extraction

Two independent reviewers designed a pilot table to extract related data independently from five randomly selected studies. Subsequently, the reviewers shared their ideas regarding the data extraction sheet with each other and finalized the format of the table. These two independent reviewers then performed data extraction for all included studies, and any discrepancies were resolved through discussion.

A summary of the data that were extracted includes first author's name, study country, publication year, study period, study design, setting, mean age and sex ratio of participants, sample size, type of surgery, location and stage of tumor, history of chemotherapy or radiotherapy, time from surgery to LARS and QOL assessment, and a history of stoma

following CRC surgery. Furthermore, the following data were extracted for meta-analysis: number of patients with major/minor/no LARS, and mean and standard deviation (SD) related to domains of EORTC QLQ-C30 questionnaire at each level of LARS. If these data were not reported in the primary study, we contacted the authors for additional information up to three times. If the authors did not respond, the study was excluded.

We converted median and interquartile range, 95% CI, or range to mean and SD in order to include them in the meta-analysis [17]. If no data is reported in limited studies for SD calculation and authors do not respond, SD was imputed on the basis of other studies according to Cochrane criteria [18]. If outcomes were assessed at multiple time points within one study, we selected either the last time point or the time that is most similar to other included studies. Some of the included studies reported the QOL in three categories of LARS score (major, minor, and no), while others reported on two categories (major and minor/no). In order to combine the studies in the meta-analysis, we pooled the means and SDs related to minor and no categories in studies that were on three categories according to the Cochrane formula [18].

Risk of bias (ROB) assessment

The ROB assessment was independently conducted by two authors using the Newcastle–Ottawa Scale (NOS) [19, 20]. This tool is specifically designed for observational studies and consists of three domains: selection, comparability, and exposure/outcome. The included studies were categorized into different tiers based on the total scores obtained: very high (0–3 points), high (4–6 points), and low ROB (7–10 points).

Statistical analysis

Statistical analyses were performed using Stata MP Version 17. Pooled effect sizes were calculated in a primary analysis for major compared to minor/no LARS for all studies, and a further analysis was conducted only on studies with three categories of major, minor, and no LARS to compare major vs. minor, major vs. no, and minor vs. no. The random-effect model was used as a result of methodological heterogeneities between studies. The results are expressed as weighted mean difference (WMD) with a 95% CI. Statistical heterogeneity was evaluated using Cochran's Q test and I^2 statistics, with interpretations based on Cochrane criteria [18].

Subgroup analyses were also conducted on the basis of the study region, location of tumor, and study quality. These analyses aimed to achieve our secondary objectives and identify potential sources of between-study heterogeneity.

Publication bias was assessed using funnel plot appearance and Egger's test. If publication bias was detected, the effect of missing studies on the pooled WMD was assessed using trim-and-fill analyses. Additionally, a sensitivity analysis was conducted to investigate the influence of each individual study on the pooled effect sizes. A *P* value less than 0.05 was deemed statistically significant for the pooled effect sizes, and less than 0.1 for Egger's test in detecting publication bias.

Results

Study selection

A total of 1982 records were identified from the databases PubMed, Web of Science, and Scopus. After removal of duplicates ($n = 257$), 1410 articles underwent title and abstract screening. Of these, 210 documents were selected for full-text screening. Subsequently, 182 articles were excluded for the reasons outlined in Fig. 1. Attempts were made to contact authors for missing data or further analysis,

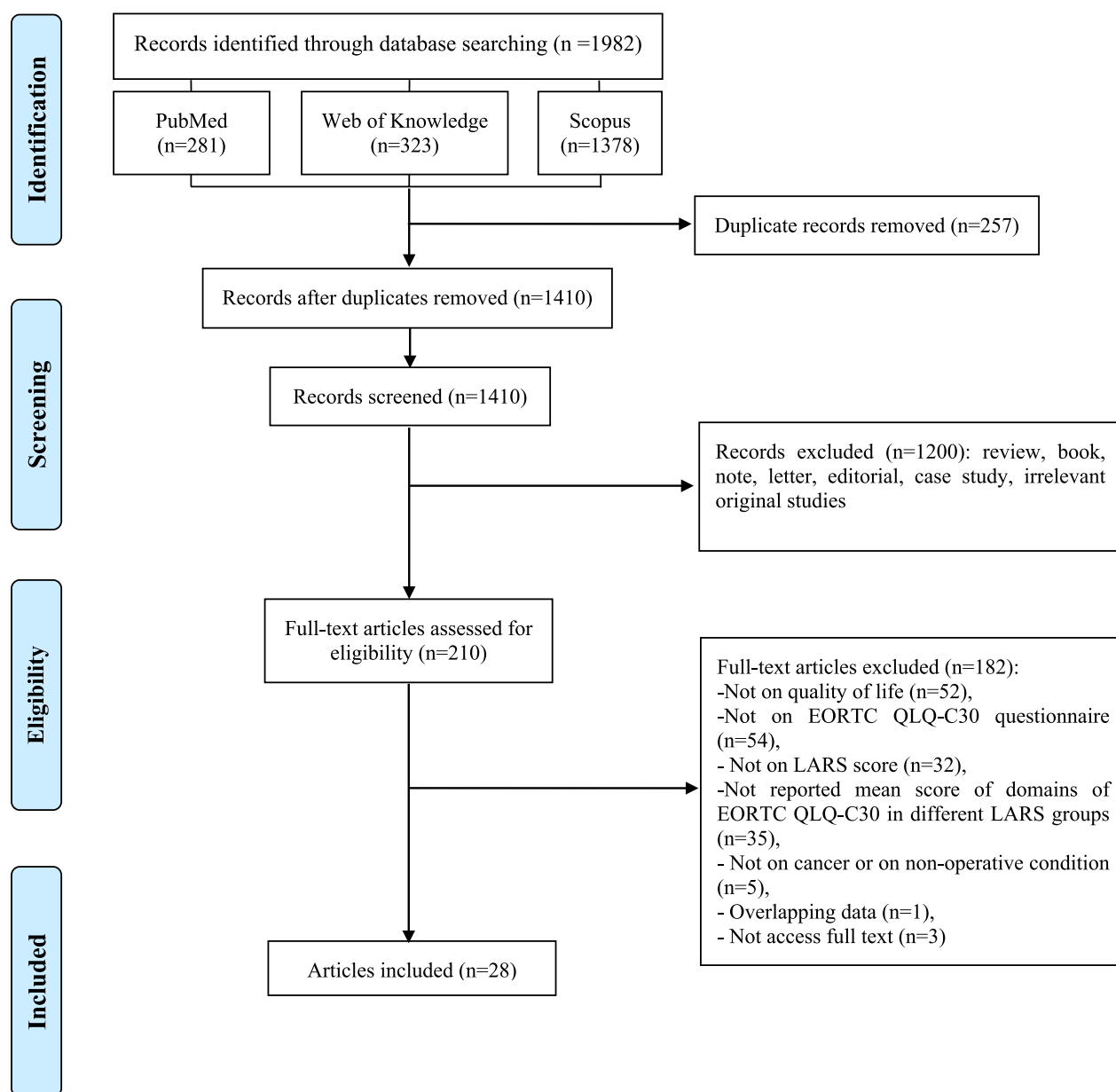


Fig. 1 PRISMA diagram

with some responding to our requests [8, 21–23]. Those who did not provide the necessary data or did not respond to our inquiries were excluded [24–26]. Ultimately, 28 eligible studies were included in the analysis, with no additional studies identified through forward and backward citation tracking.

Study characteristics

The characteristics of the included studies are reported in Table 1. Among these studies, 26 were cross-sectional [8, 10, 21–23, 27–47] and two were prospective cohort studies [9, 48]. They were published from 2013 to 2023 and were mostly conducted in Europe [8–10, 22, 23, 27–31, 33, 35–40, 42, 45–48]. The included patients had rectal cancer in most studies [8–10, 21–23, 29–31, 33–37, 39–46, 48], while some studies also included patients with cancer in the rectosigmoid, sigmoid, or colon [27, 28, 32, 38, 47]. The patients underwent several types of surgeries, including AR or LAR (by partial mesorectal excision, total mesorectal excision, or transanal total mesorectal excision) [8–10, 21–23, 28–36, 39–45, 47, 48], intersphincteric resection [22, 31, 32], transanal endoscopic microsurgery [46], sigmoid resection [47], and colectomy [28, 38] using laparoscopy or laparotomy methods. Some of the included studies investigated the effects of LARS on QOL only in patients with a previous history of temporary stoma [29, 30], some were focused on subjects without a history of defunctioning stoma [27, 46], while others included a combined sample. The included patients were predominately male in all but one study [29]. The sample sizes of the included studies ranged from 55 [29] to 1623 [28].

ROB assessment

The results of the ROB assessment are reported in Supplementary Table 1. According to the NOS, eight studies were tiered as low ROB [9, 30, 31, 33–35, 43, 48] and others as high risk.

Meta-analysis of effects of LARS score on domains of EORTC QLQ-C30

According to the first analysis (Supplementary Figs. 1–4), patients suffering from major LARS had significantly lower scores of global health status (WMD = − 10.98, 95% CI − 13.18 to − 8.79, $P < 0.001$), physical functioning (WMD = − 5.96, 95% CI − 7.40 to − 4.52, $P < 0.001$), role functioning (WMD = − 10.59, 95% CI − 12.54 to − 8.63, $P < 0.001$), emotional functioning (WMD = − 11.09, 95% CI − 14.34 to 7.84, $P < 0.001$), cognitive functioning (WMD = − 9.27, 95% CI − 12.22 to − 6.32, $P < 0.001$), and social functioning (WMD = − 15.73, 95% CI − 18.82

to − 12.63, $P < 0.001$) and also higher scores of fatigue (WMD = 10.28, 95% CI 8.03–12.53, $P < 0.001$), nausea and vomiting (WMD = 2.50, 95% CI 1.50–3.50, $P < 0.001$), pain (WMD = 8.47, 95% CI 5.46–11.49, $P < 0.001$), dyspnea (WMD = 4.69, 95% CI 2.51–6.86, $P < 0.001$), insomnia (WMD = 9.99, 95% CI 7.58–12.40, $P < 0.001$), loss of appetite (WMD = 4.46, 95% CI 2.54–6.39, $P < 0.001$), constipation (WMD = 4.12, 95% CI 2.20–6.03, $P < 0.001$), diarrhea (WMD = 19.15, 95% CI 14.39–23.92, $P < 0.001$), and financial difficulties (WMD = 7.52, 95% CI 4.29–10.74, $P < 0.001$) compared to patients with minor/no LARS (Table 2).

Considerable between-studies heterogeneity ($I^2 = 75–100\%$) was observed in the analyses of global health status, emotional functioning, cognitive functioning, social functioning, nausea and vomiting, pain, dyspnea, loss of appetite, diarrhea, and financial difficulties. Substantial heterogeneity was detected in other analyses ($I^2 > 50\%$). The heterogeneity was significantly reduced in the subgroups of study location (global health status, role functioning, nausea and vomiting, appetite loss, and constipation), site of tumor (pain, insomnia, appetite loss, constipation, and financial difficulties), risk of bias (global health status, role functioning, cognitive functioning, social functioning, fatigue, nausea and vomiting, and constipation), and time since surgery or stoma closure (constipation). Furthermore, the score of appetite loss was significantly higher in patients with shorter time since surgery or stoma closure (WMD = 8.95, 95% CI 3.86–14.05) than others (WMD = 2.87, 95% CI 0.83–4.92, P value for difference = 0.03). The cognitive functioning was also lower in the studies with a high risk of bias (WMD = − 10.79, 95% CI − 14.88 to − 6.69) compared to low risk studies (WMD = − 5.57, 95% CI − 7.18 to − 3.95, P value for difference = 0.02). No significant differences were detected between other subgroups (Table 2).

In the second analyses, we compared major vs. minor LARS; major vs. no LARS; and minor vs. no LARS (Supplementary Table 2). Significant differences were observed in the all domains of EORTC QLQ-C30 between patients with major compared to minor LARS as well as no LARS (P values < 0.05). In the comparison of minor with no LARS, except for emotional functioning ($P = 0.07$), cognitive functioning ($P = 0.10$), nausea and vomiting ($P = 0.06$), appetite loss ($P = 0.26$), and constipation ($P = 0.70$), other domains were significantly worse in the patients with minor LARS.

Publication bias and sensitivity analysis

We detected a significant publication bias in the first analyses related to the global health status (P value of Egger's test = 0.094), pain (P value of Egger's test = 0.002), insomnia (P value of Egger's test = 0.031), appetite loss (P value

Table 1 Characteristics of the included studies

First author	Year	Design	Country	Type of surgery	RT/CT (%)	Stage (%)	Location of tumor	Anastomosis (%)	Temporary ostomy (%)	Sex, male (%)	Age, year (mean)	Sample size (n)	LARS (%)			Mean time since surgery	Tumor distance from anal verge (mean, cm)
													No	Minor	Major		
Celisin	2023	Cross-sectional	Turkey (multicenter)	TME (70.7%); PME (29.3%); (LAR)	Neoadjuvant RT: 56.7; Neoadjuvant CT: 58.5; Adjuvant CT: 76.6	T0-2: 52.3 T3-4: 47.7	Rectum	–	73.4	58.1	59.7 (at surgery)	222	29.7	15.3	55	7.3 years	9.3
van Kooten	2023	Cross-sectional	Netherlands (multicenter, Prospective Dutch Colorectal Cancer cohort)	Laparoscopy: 75.1% Neoadjuvant RT: 22.6 Neoadjuvant CT: 19.4	Neoadjuvant RT: 22.6 Neoadjuvant CT: 19.4	0: 6.9, I: 16.5, II: 31.8, III: 40.5	Rectosigmoid, rectum	–	0	64.4	63.2	751	59.5	40.5	1 year	<5 cm: 22%, 5.1–10: 36.9%, 10.1–15: 19.3%, > 15: 3.6%	
De Simone	2022	Cross-sectional	Italy (single-center)	TME (77.6%); PME (22.4%); Laparoscopy (53.2%); (LAR)	Neoadjuvant RT: 42	–	Rectum	–	60	57.1	67.7	205	37.1	26.8	36.1	–	8.95
Ketelaers	2022	Cross-sectional	Netherlands (multicenter)	Laparoscopy: Colon: 55.8% Rectal: 43% Total: 52.3% LAR: Rectal: 96.1% Neoadjuvant RT: 34.8	Colon: Adjuvant CT: 32.5; Rectal: Neoadjuvant CT: 32.3; Neoadjuvant RT: 34.8	Colon: I-II: 68.5, III-IV: 31.4; Rectal: 0: 3.6, I-II: 65.7, III-IV: 30.7	Colon, rectum	–	Colon: 9.8; Rectal: 72; Total: 26.7	Colon: 55; Rectal: 62; Total: 57	Colon: 69.1; Rectal: 65.5; Total: 68.1 (at surgery)	Colon: 1183; Rectal: 440; Total: 1623	Colon: 58.6; Rectal: 28.6; Total: 50.5	Colon: 20.1; Rectal: 19.1; Total: 19.8	Colon: 21.2; Rectal: 52.3; Total: 29.6	Rectal: <5 cm: 13.6%, 5–9.9: 41.0%, 10–14.9: 34.3%, ≥15: 11.4	
Ribas	2022	Prospective cohort	Spain (double-center)	Laparoscopy: T0-1: 24.3, T2: 20.5, T3: 52.6, T4: 2.6; Laparotomy: T0: 70.5, T1: 23.1, T2: 5.1 PME: 38.5% (AR)	Neoadjuvant RT: 52.6; Neoadjuvant CT: 47.4; Adjuvant RT/CT: 9; Adjuvant CT: 37.2	T0-1: 24.3, T2: 20.5, T3: 52.6, T4: 2.6; N0: 70.5, N1: 23.1, N2: 5.1	Rectum	Straight colorectal/colanal: 84.6, Side to end: 15.4	69.2	70.5	65.1 (at surgery)	78	37.2	28.2	34.6	6.5 months (since stoma closure)	9.7
Algje	2022	Cross-sectional	Netherlands (double-center)	Minimally invasive surgery: 96.8% (LAR)	Neoadjuvant RT: 16.7 Neoadjuvant CT: 21.4	I: 11.1, II: 22.2, III: 65.1, IV: 0.8	Rectum	–	20.6	66.7	64.6	126	76.2	23.8	3.7 years	–	
Herzberg	2022	Cross-sectional	Germany (single-center)	Laparoscopy (87.2)	–	–	Rectum	End to end: 100	–	57.7	65.6	78	30	48	19.5 months	≤8 cm	
Dilke	2022	Cross-sectional	UK (multicenter)	TME (100%) (LAR)	Neoadjuvant RT: 18.6 Neoadjuvant CT: 4.5 Adjuvant RT: 1.3 Adjuvant CT: 33.8	I: 39.5, II: 25, III: 32.5, IV: 2.8	Rectum	–	100	63.3	71.8	311	23.1	23.5	53.4	6.5 years	–
Shen	2021	Cross-sectional	China (multicenter)	tdTME	Neoadjuvant CT: 9.2; Neoadjuvant RT/CT: 7; Adjuvant RT/CT: 7.6; Adjuvant CT: 34.2	0-I: 62, III-IV: 38	Rectum	–	36.7	63.3	62.9	316	39.9	28.2	31.9	11.7 months	5
Pape	2021	Cross-sectional	Belgium (single-center)	TME (94.2%); PME (5.8%); Laparoscopy (12.4%); (LAR)	Neoadjuvant CT: RT: 100	–	Rectum	–	–	69.4	66	121	14.04	16.5	69.4	52.4 months (since surgery or stoma closure)	<5 cm: 43.8%, 6–10: 38.8%, 11–15: 16.5%

Table 1 (continued)

First author	Year	Design	Country	Type of surgery	RT/CT (%)	Stage (%)	Location of tumor	Anastomosis (%)	Temporary ostomy (%)	Sex, male (%)	Age, year (mean)	Sample size (n)	LARS (%)		Mean time since surgery	Tumor distance from anal verge (mean, cm)
													No	Minor		
Lao	2021	Cross-sectional	China (single-center)	TME (45.5%); PME (54.5%); Laparoscopy (93.75%) (AR)	Neoadjuvant CT: 26.34	I: 37.05; II: 29.91; III: 23.21; IV: 9.82	Rectum	–	53.57	68.75	59.58	224	19.64	17.86	62.5	– –

Table 1 (continued)

First author	Year	Design	Country	Type of surgery	RT/CT (%)	Stage (%)	Location of tumor	Anastomosis (%)	Temporary ostomy (%)	Sex, male (%)	Age, year (mean)	Sample size (n)	LARS (%)		Mean time since surgery	Tumor distance from anal verge (mean, cm)	
													No	Minor			Major
Trenti	2018	Cross-sectional	Spain (double-center)	TME (100%) (AR, ISR)	Neoadjuvant RT: 83.6 Adjuvant RT: 2.6	I: 9.9, II: 11.2, III: 75, IV: 3.9	Rectum	End to end: 61.8, Side to End: 20.6, J pouch: 4, Transverse coloplasty: 4.6	88.8	69.1	62	152	12.5	25.7	61.8	4.3 years (since surgery or stoma closure)	–
Ribas	2017	Cross-sectional	Spain (single-center)	TME (70%); PME (30%); Laparoscopy (64%) (AR)	RT: 67.1	–	Rectum	Colonic J pouch: 6, Straight anastomosis: 94	70	67	65	70	30	15.7	54.3	55 months	–
Chen	2015	Cross-sectional	Netherlands (multicenter, TME trial)	TME (100%)	Neoadjuvant RT: 48.7	0: 2.9, I: 39.7, II: 26.8, III: 30.2, IV: 0.4	Rectum	Pouch: 28.1, End to side: 59.9, End to end: 10.7	–	55	71	242	32.2	22.3	45.4	14.6 years	<5 cm: 7%, 5–9.9: 49%, ≥10: 44%
Hou	2015	Cross-sectional	China (single-center)	TME (100%)	RT: 27.5	I: 32.6, II: 37.8, III: 29.6	Rectum	End to end: 100	21.6	57.8	66.5	102	23.5	21.6	54.9	17.9 months (since surgery or stoma closure)	11.2
Juul	2015	Cross-sectional	UK (multicenter)	TME (81.6%); PME (18.3%) (LAR)	Neoadjuvant RT: 31.3; Neoadjuvant CT: 18.9; Adjuvant CT: 32.2	T0–2: 53.2, T3–4: 46.8; N0: 69.2, N1: 30.8	Rectum	–	80.3	60.3	69.8	451	29.7	22.8	47.5	5.9 years	9
Juul	2014	Cross-sectional	Sweden, Spain, Germany, Denmark (multicenter)	TME (75%) (LAR)	RT: 54 CT: 44	T3–T4: 44%	Rectum	–	–	55	67.8	796	28.3	19.2	51.5	5.6 years	9.5
Emmertsen	2013	Prospective cohort	Denmark (multicenter)	TME (65.4%); PME (34.6%); Laparoscopy (33.5%) (LAR)	Neoadjuvant CT-RT: 19.6	I: 29.2, II: 35, III: 35.8	Rectum	Colonic J pouch: 6.5, Side to end: 49.2, End to end: 44.2	65.4	60	64	3 months: 203, 12 months: 193	3 months: 18.1, 12 months: 29	3 months: 23.8, 12 months: 25.1	3 months: 58, 12 months: 45.9	3 and 12 months	≤5 cm: 6.5%, 5–10: 48.4%, >10: 48.1%

CT chemotherapy, ISR intersphincteric resection, LAR low anterior resection, PME partial mesorectal excision, RT radiotherapy, TEM transanal endoscopic microsurgery, TME total mesorectal excision

of Egger's test = 0.018), diarrhea (P value of Egger's test = 0.012), and financial difficulties (P value of Egger's test = 0.009) (Supplementary Figs. 5–7). The trim-and-fill analyses imputed eight additional effect sizes into the pain, seven into the appetite loss, six into the global health status, and nine into the diarrhea and financial difficulties analyses that did not significantly change the pooled effect sizes in all analyses (global health status: WMD = -12.90, 95% CI -15.18 to -10.62; pain: WMD = 12.20, 95% CI 8.89–15.50; appetite loss: WMD = 7.22, 95% CI 3.65–10.79; diarrhea: WMD = 26.46, 95% CI 21.04–31.89; financial difficulties: WMD = 12.80, 95% CI 9.07–16.53).

The sensitivity analyses revealed that none of the included studies had a significant impact on the pooled effect sizes.

Discussion

Psychological and social impairments resulting from a cancer diagnosis, cancer-related symptoms, comorbidities, and adverse effects of specific treatment strategies impact the HRQOL of patients [49, 50]. Poor scores in all domains of the EORTC QLQ-C30, with the exception of cognitive functioning and diarrhea, have been linked to an increased risk of all-cause mortality in patients with CRC [51]. Therefore, it is imperative to provide greater attention and personalized healthcare programs to patients with CRC who are at risk of experiencing decreased HRQOL in order to enhance their response to treatment and overall survival.

On the basis of the current analysis, bowel dysfunction following CRC surgeries significantly deteriorated all domains of EORTC QLQ-C30. Specifically, major LARS demonstrated a large effect on social functioning, medium effects on global health status, cognitive functioning, and diarrhea, small effects on physical functioning, role functioning, fatigue, pain, dyspnea, insomnia, and financial difficulties, and trivial effects on nausea and vomiting, appetite loss, and constipation when compared to minor/no LARS. These findings were based on the minimal clinically important differences (MCID) for the EORTC QLQ-C30 [52]. Furthermore, major LARS resulted in large effects on global health status, cognitive functioning, and social functioning when compared to patients without LARS. The domain of global health status typically evaluates the overall health and QOL. Conversely, social functioning assesses the impact of physical conditions and medical treatment on family life and social activities. Cognitive functioning also evaluates difficulties in memory or concentration. In the present study, emotional functioning, which encompasses feelings of tension, irritability, worry, or depression, was also notably affected by major LARS; however, no MCID was established for direct comparison [52]. Collectively, patients with major LARS should be provided with targeted interventions, such

as counseling or support groups, to enhance their overall well-being and address the challenges they face in emotional regulation, social interactions, and family life. We also found that patients with a shorter time since surgery or stoma closure experienced higher levels of appetite loss than their counterparts. Factors such as study location, tumor site, risk of bias, and time since surgery or stoma closure were identified as potential sources of heterogeneity.

Our findings were consistent with a previous systematic review study that indicated social and emotional functioning as domains most affected by bowel dysfunction following sphincter-preserving rectal cancer surgeries [11]. The LARS score has also been reported to be negatively correlated with global health status, physical functioning, role functioning, emotional functioning, cognitive functioning, and social functioning, and positively correlated with diarrhea in patients who underwent sphincter-preserving rectal cancer surgeries [53, 54]. Several studies have also investigated the effects of bowel function on QOL using other tools [11]. The LARS score is reported to be negatively correlated with Fecal Incontinence Quality of Life (FIQL) summary score, as well as the sexual enjoyment and future perspective domains of EORTC QLQ-CR38 score among patients undergoing intersphincteric resection for ultralow rectal cancer. Furthermore, it was positively correlated with gastrointestinal symptoms and defecation problems domains of EORTC QLQ-CR38. The Wexner incontinence score (Cleveland Clinic Fecal Incontinence Severity Scoring System) and Kirwan's incontinence score were also assessed in this study, revealing a negative correlation with certain domains of the EORTC QLQ-C30 [54].

There is conflicting evidence regarding the long-term differences in QOL between abdominoperineal resection and sphincter-preservation surgeries. While some studies suggest that avoiding a stoma through sphincter-preserving surgeries may enhance QOL [55–57], a previous meta-analysis found no significant superiority in QOL between these two procedures [56]. The subjective nature of QOL assessments, the use of varying measurement tools, and differing demographic features and cultural attitudes toward stomas may contribute to these contrasting results. Therefore, additional studies, particularly large-sample long-term prospective cohort or interventional studies, should be conducted across diverse populations and cultural contexts. Qualitative studies could also yield valuable insights into patients' expectations, experiences, and preferences across various types of surgical procedures. Our data could provide valuable insights for both surgeons and patients regarding the anticipated HRQOL following sphincter-preservation surgeries for colorectal cancer, enabling informed decision-making between treatment options based on their associated risks and benefits. Additionally, it is crucial for patients who have experienced

Table 2 Stratified meta-analysis of the effects of major LARS on EORTC QLQ-C30 in comparison with minor/no LARS

Variable	Subgroups	Number of studies	Pooled WMD (95% CI)	<i>P</i> for difference	<i>P</i> for Cochran <i>Q</i> test	<i>I</i> ² (%)
Global health status						
All		28	− 10.98 (− 13.18, − 8.79)	<0.001	<0.001	80.93
Location	Europe/North America	23	− 10.49 (− 13.08, − 7.89)	0.28	<0.001	83.63
	Asia	5	− 12.53 (− 15.18, − 9.89)		0.28	21.19
Site of tumor	Rectum	23	− 10.97 (− 13.87, − 8.08)	0.70	<0.001	82.59
	Rectum/Rectosigmoid/Colon	5	− 10.21 (− 12.72, − 7.71)		0.03	62.06
Risk of bias	High	20	− 10.84 (− 13.89, − 7.79)	0.77	<0.001	85.32
	Low	8	− 10.28 (− 12.32, − 8.25)		0.18	31.59
Time since surgery or stoma closure	≥ 4 years	17	− 11.14 (− 14.11, − 8.17)	0.60	<0.001	84.68
	< 4 years	9	− 9.85 (− 13.61, − 6.09)		<0.001	73.02
Physical functioning						
All		27	− 5.96 (− 7.40, − 4.52)	<0.001	<0.001	63.87
Interventions	Europe/North America	22	− 6.03 (− 0.41, − 0.25)	0.99	0.01	48.04
	Asia	5	− 6.06 (− 0.63, − 0.05)		<0.001	86.10
Site of tumor	Rectum	22	− 6.05 (− 7.84, − 4.26)	0.88	<0.001	62.18
	Rectum/Rectosigmoid/Colon	5	− 5.80 (− 8.50, − 3.09)		<0.001	75.66
Risk of bias	High	19	− 6.40 (− 7.92, − 4.88)	0.48	<0.001	51.66
	Low	8	− 5.12 (− 8.28, − 1.96)		<0.001	75.95
Time since surgery or stoma closure	≥ 4 years	16	− 5.60 (− 7.11, − 4.09)	0.71	0.02	47.76
	< 4 years	9	− 6.35 (− 9.91, − 2.78)		<0.001	78.96
Role functioning						
All		27	− 10.59 (− 12.54, − 8.63)	<0.001	<0.001	66.57
Location	Europe/North America	22	− 10.86 (− 13.13, − 8.59)	0.46	<0.001	69.67
	Asia	5	− 9.31 (− 12.80, − 5.81)		0.14	41.69
Site of tumor	Rectum	22	− 11.21 (− 13.80, − 8.62)	0.30	<0.001	68.50
	Rectum/Rectosigmoid/Colon	5	− 9.25 (− 11.88, − 6.62)		0.05	58.74
Risk of bias	High	19	− 10.78 (− 13.40, − 8.16)	0.52	<0.001	74.17
	Low	8	− 9.68 (− 11.76, − 7.59)		0.41	2.11
Time since surgery or stoma closure	≥ 4 years	16	− 10.42 (− 12.53, − 8.31)	0.55	<0.001	54.91
	< 4 years	9	− 12.07 (− 17.06, − 7.08)		<0.001	80.49
Emotional functioning						
All		27	− 11.09 (− 14.34, 7.84)	<0.001	<0.001	91.74
Location	Europe/North America	22	− 10.07 (− 12.50, − 7.65)	0.66	<0.001	80.45
	Asia	5	− 13.64 (− 29.59, 2.31)		<0.001	97.99
Site of tumor	Rectum	22	− 9.83 (− 12.71, − 6.95)	0.33	<0.001	82.08
	Rectum/Rectosigmoid/Colon	5	− 15.16 (− 25.48, − 4.84)		<0.001	97.91
Risk of bias	High	19	− 11.55 (− 16.04, − 7.07)	0.50	<0.001	93.67
	Low	8	− 9.62 (− 12.99, − 6.24)		<0.001	73.41
Time since surgery or stoma closure	≥ 4 years	16	− 10.54 (− 14.87, − 6.20)	0.53	<0.001	92.56
	< 4 years	9	− 13.00 (− 19.46, − 6.54)		<0.001	92.08

Table 2 (continued)

Variable	Subgroups	Number of studies	Pooled WMD (95% CI)	<i>P</i> for difference	<i>P</i> for Cochrane <i>Q</i> test	<i>I</i> ² (%)
Cognitive functioning						
All		27	− 9.27 (− 12.22, − 6.32)	<0.001	<0.001	90.89
Location	Europe/North America	22	− 8.12 (− 0.35, − 5.90)	0.61	<0.001	79.52
	Asia	5	− 11.86 (− 25.90, 2.18)		<0.001	97.47
Site of tumor	Rectum	22	− 8.09 (− 10.69, − 5.49)	0.33	<0.001	79.71
	Rectum/Rectosigmoid/Colon	5	− 12.84 (− 22.01, − 3.67)		<0.001	97.69
Risk of bias	High	19	− 10.79 (− 14.88, − 6.69)	0.02	<0.001	93.32
	Low	8	− 5.57 (− 7.18, − 3.95)		0.88	0.00
Time since surgery or stoma closure	≥ 4 years	16	− 8.49 (− 12.41, − 4.56)	0.49	<0.001	92.22
	< 4 years	9	− 10.97 (− 16.80, − 5.15)		<0.001	90.39
Social functioning						
All		27	− 15.73 (− 18.82, − 12.63)	<0.001	<0.001	86.25
Location	Europe/North America	22	− 14.66 (− 17.28, − 12.04)	0.53	<0.001	75.38
	Asia	5	− 18.90 (− 32.04, − 5.77)		<0.001	95.60
Site of tumor	Rectum	22	− 15.00 (− 17.90, − 12.09)	0.55	<0.001	72.83
	Rectum/Rectosigmoid/Colon	5	− 17.94 (− 27.13, − 8.75)		<0.001	96.41
Risk of bias	High	19	− 15.72 (− 20.03, − 11.42)	0.92	<0.001	89.87
	Low	8	− 15.45 (− 18.08, − 12.83)		0.15	34.81
Time since surgery or stoma closure	≥ 4 years	16	− 15.01 (− 19.49, − 10.52)	0.62	<0.001	89.88
	< 4 years	9	− 16.69 (− 21.52, − 11.87)		<0.001	78.74
Fatigue						
All		23	10.28 (8.03, 12.53)	<0.001	<0.001	73.96
Location	Europe/North America	18	11.00 (8.65, 13.35)	0.33	<0.001	69.16
	Asia	5	7.94 (2.23, 13.65)		<0.001	79.65
Site of tumor	Rectum	18	10.72 (8.05, 13.39)	0.57	<0.001	66.81
	Rectum/Rectosigmoid/Colon	5	9.13 (4.37, 13.89)		<0.001	87.88
Risk of bias	High	17	10.67 (7.77, 13.57)	0.45	<0.001	78.21
	Low	6	9.10 (6.19, 12.00)		0.12	42.90
Time since surgery or stoma closure	≥ 4 years	14	9.04 (6.74, 11.33)	0.14	<0.001	60.35
	< 4 years	8	13.61 (7.93, 19.29)		<0.001	86.18
Nausea and vomiting						
All		23	2.50 (1.50, 3.50)	<0.001	<0.001	87.34
Location	Europe/North America	18	2.26 (1.16, 3.36)	0.18	<0.001	87.97
	Asia	5	3.38 (2.15, 4.61)		0.51	0.00
Site of tumor	Rectum	18	2.27 (1.10, 3.43)	0.38	<0.001	80.97
	Rectum/Rectosigmoid/Colon	5	3.01 (1.80, 4.22)		0.01	67.76

Table 2 (continued)

Variable	Subgroups	Number of studies	Pooled WMD (95% CI)	<i>P</i> for difference	<i>P</i> for Cochran <i>Q</i> test	<i>I</i> ² (%)
Risk of bias	High	17	2.28 (1.13, 3.43)	0.38	<0.001	88.66
	Low	6	2.99 (1.89, 4.08)		0.53	0.00
Time since surgery or stoma closure	≥ 4 years	14	2.12 (0.93, 3.31)	0.28	<0.001	86.82
	< 4 years	8	3.24 (1.58, 4.89)		<0.001	68.00
Pain						
All		23	8.47 (5.46, 11.49)	<0.001	<0.001	87.81
Location	Europe/North America	18	9.79 (6.54, 13.03)	0.09	<0.001	86.19
	Asia	5	3.74 (− 2.56, 10.04)		<0.001	86.68
Site of tumor	Rectum	18	9.58 (5.04, 14.12)	0.25	<0.001	90.21
	Rectum/Rectosigmoid/Colon	5	6.70 (4.73, 8.66)		0.15	40.26
Risk of bias	High	17	9.73 (6.26, 13.20)	0.19	<0.001	87.43
	Low	6	5.10 (− 0.85, 11.04)		<0.001	87.21
Time since surgery or stoma closure	≥ 4 years	14	7.84 (5.81, 9.87)	0.40	0.01	52.51
	< 4 years	8	11.62 (2.99, 20.25)		<0.001	95.16
Dyspnea						
All		23	4.69 (2.51, 6.86)	<0.001	<0.001	86.96
Location	Europe/North America	18	4.61 (2.16, 7.07)	0.89	<0.001	87.21
	Asia	5	5.04 (− 0.52, 10.61)		<0.001	82.31
Site of tumor	Rectum	18	4.08 (1.79, 6.38)	0.43	<0.001	75.97
	Rectum/Rectosigmoid/Colon	5	6.19 (1.47, 10.92)		<0.001	89.59
Risk of bias	High	17	4.62 (2.09, 7.16)	0.92	<0.001	87.88
	Low	6	4.91 (0.20, 9.62)		<0.001	77.19
Time since surgery or stoma closure	≥ 4 years	14	4.19 (1.70, 6.67)	0.54	<0.001	84.80
	< 4 years	8	6.04 (0.58, 11.51)		<0.001	86.61
Insomnia						
All		23	9.99 (7.58, 12.40)	<0.001	<0.001	64.51
Location	Europe/North America	18	10.53 (8.14, 12.92)	0.53	<0.001	53.93
	Asia	5	8.01 (0.59, 15.43)		<0.001	81.24
Site of tumor	Rectum	18	11.14 (7.55, 14.73)	0.20	<0.001	71.34
	Rectum/Rectosigmoid/Colon	5	8.51 (6.65, 10.38)		0.88	0.00
Risk of bias	High	17	10.08 (7.60, 12.56)	0.92	<0.001	54.64
	Low	6	9.71 (3.04, 16.39)		<0.001	80.72
Time since surgery or stoma closure	≥ 4 years	14	10.45 (7.84, 13.06)	0.77	0.01	53.59
	< 4 years	8	9.51 (3.74, 15.27)		<0.001	77.19
Appetite loss						
All		23	4.46 (2.54, 6.39)	<0.001	<0.001	89.66
Location	Europe/North America	18	4.18 (2.04, 6.32)	0.43	<0.001	90.42
	Asia	5	5.68 (2.68, 8.67)		0.14	42.63
Site of tumor	Rectum	18	4.18 (1.74, 6.61)	0.53	<0.001	88.02
	Rectum/Rectosigmoid/Colon	5	5.14 (3.43, 6.86)		0.11	46.58

Table 2 (continued)

Variable	Subgroups	Number of studies	Pooled WMD (95% CI)	<i>P</i> for difference	<i>P</i> for Cochrane <i>Q</i> test	<i>I</i> ² (%)
Risk of bias	High	17	4.97 (2.55, 7.39)	0.33	<0.001	91.69
	Low	6	3.09 (0.14, 6.04)		0.02	62.81
Time since surgery or stoma closure	≥ 4 years	14	2.87 (0.83, 4.92)	0.03	<0.001	85.75
	< 4 years	8	8.95 (3.86, 14.05)		<0.001	90.63
Constipation						
All		23	4.12 (2.20, 6.03)	<0.001	<0.001	72.03
Location	Europe/North America	18	4.06 (1.89, 6.24)	0.83	<0.001	74.23
	Asia	5	4.46 (1.55, 7.37)		0.45	0.00
Site of tumor	Rectum	18	3.91 (1.44, 6.37)	0.90	<0.001	68.67
	Rectum/Rectosigmoid/Colon	5	4.10 (2.38, 5.81)		0.65	0.00
Risk of bias	High	17	3.62 (1.44, 5.80)	0.33	<0.001	70.65
	Low	6	5.33 (2.66, 8.00)		0.31	15.57
Time since surgery or stoma closure	≥ 4 years	14	3.67 (1.19, 6.15)	0.79	<0.001	75.92
	< 4 years	8	4.11 (2.01, 6.21)		0.69	0.00
Diarrhea						
All		23	19.15 (14.39, 23.92)	<0.001	<0.001	93.09
Location	Europe/North America	18	21.57 (16.77, 26.36)	0.08	<0.001	91.29
	Asia	5	10.27 (− 1.59, 22.12)		<0.001	94.10
Site of tumor	Rectum	18	19.73 (12.65, 26.81)	0.77	<0.001	94.06
	Rectum/Rectosigmoid/Colon	5	18.45 (13.42, 23.48)		<0.001	86.91
Risk of bias	High	17	19.65 (14.55, 24.74)	0.77	<0.001	92.16
	Low	6	17.54 (4.67, 30.41)		<0.001	95.39
Time since surgery or stoma closure	≥ 4 years	14	18.93 (15.65, 22.21)	0.74	<0.001	75.38
	< 4 years	8	21.38 (7.22, 35.54)		<0.001	97.21
Financial difficulties						
All		23	7.52 (4.29, 10.74)	<0.001	<0.001	86.47
Location	Europe/North America	18	8.24 (4.98, 11.50)	0.53	<0.001	84.05
	Asia	5	4.61 (− 6.31, 15.53)		<0.001	91.94
Site of tumor	Rectum	18	8.56 (3.73, 13.39)	0.25	<0.001	88.98
	Rectum/Rectosigmoid/Colon	5	5.46 (3.36, 7.56)		0.19	34.31
Risk of bias	High	17	8.49 (4.84, 12.13)	0.40	<0.001	85.08
	Low	6	4.86 (− 2.71, 12.44)		<0.001	90.54
Time since surgery or stoma closure	≥ 4 years	14	7.26 (4.81, 9.70)	0.57	<0.001	61.25
	< 4 years	8	10.03 (0.83, 19.23)		<0.001	94.39

EORTC QLQ-C30 European Organization for Research and Treatment Core Quality-of-Life Questionnaire, *LARS* Low anterior resection syndrome, *WMD* weighted mean differences, *CI* confidence interval

major LARS following surgeries to receive close monitoring and support to mitigate potential declines in HRQOL domains that may be at risk.

The strength of our study, in comparison to previous systematic reviews, lies in its assessment of the effects of LARS at varying severities on QOL through meta-analysis, as well as the comparison of the results with the MCID. However, this study had several limitations. Firstly, we did not include data related to all available tools for assessing bowel dysfunction and QOL. Secondly, the majority of the included studies were cross-sectional and did not assess baseline QOL before surgeries. Thirdly, some of the included studies did not report data on certain domains of the EORTC QLQ-C30 questionnaire. Fourthly, publication bias was detected in some analyses. Fifthly, the studies examined tumors located at various sites within the colorectal region; although no significant differences were reported in the subgroup analyses, this variability may introduce biases into the overall analysis. Additionally, subgroup analysis according to tumor stage, type of surgery, location of anastomosis, sex, age, tumor distance from anal verge, chemotherapy, and radiotherapy could not be conducted because of incomplete data reported in the original articles. These factors undeniably influence LARS symptoms. Future research that offers more comprehensive data on the effects of LARS on QOL, stratified by these factors, will contribute significantly to the existing literature.

In conclusion, our study findings indicate that patients with CRC who experienced major LARS following resections exhibited significantly and clinically poorer HRQOL, particularly in the domains of global health status, cognitive functioning, social functioning, and emotional functioning, compared to their counterparts. Furthermore, our analysis revealed that patients with a shorter duration since surgery or stoma closure reported higher levels of appetite loss compared to those with longer intervals.

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Data availability Data described in the manuscript are available from the corresponding author (ARS), upon reasonable request.

Declarations

Conflict of interest The authors declare no competing interests.

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