



University of Groningen

Functional outcomes of surgery for colon cancer

Verkuijl, Sanne J.; Jonker, Jara E.; Trzpis, Monika; Burgerhof, Johannes G.M.; Broens, Paul M.A.; Furnée, Edgar J.B.

Published in: European Journal of Surgical Oncology

DOI:

10.1016/j.ejso.2020.11.136

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version Publisher's PDF, also known as Version of record

Publication date:

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):

Verkuijl, S. J., Jonker, J. E., Trzpis, M., Burgerhof, J. G. M., Broens, P. M. A., & Furnée, E. J. B. (2021). Functional outcomes of surgery for colon cancer: A systematic review and meta-analysis. *European* Journal of Surgical Oncology, 47(5), 960-969. https://doi.org/10.1016/j.ejso.2020.11.136

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: https://www.rug.nl/library/open-access/self-archiving-pure/taverneamendment.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): http://www.rug.nl/research/portal. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Download date: 05-06-2022

\$30 ELSEVIER

Contents lists available at ScienceDirect

European Journal of Surgical Oncology

journal homepage: www.ejso.com



Functional outcomes of surgery for colon cancer: A systematic review and meta-analysis



Sanne J. Verkuijl ^{a, *}, Jara E. Jonker ^a, Monika Trzpis ^a, Johannes G.M. Burgerhof ^b, Paul M.A. Broens ^{a, c}, Edgar J.B. Furnée ^d

- a Department of Surgery, Anorectal Physiology Laboratory, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands
- ^b Department of Epidemiology, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands
- ^c Department of Surgery, Division of Pediatric Surgery, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands
- d Department of Surgery, Division of Abdominal Surgery, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands

ARTICLE INFO

Article history: Received 8 November 2020 Accepted 21 November 2020 Available online 26 November 2020

Keywords: Colon cancer Bowel dysfunction Postoperative Follow-up Meta-analysis

ABSTRACT

Introduction: As survival rates of colon cancer increase, knowledge about functional outcomes is becoming ever more important. The primary aim of this systematic review and meta-analysis was to quantify functional outcomes after surgery for colon cancer. Secondly, we aimed to determine the effect of time to follow-up and type of colectomy on postoperative functional outcomes.

Materials and methods: A systematic literature search was performed to identify studies reporting bowel function following surgery for colon cancer. Outcome parameters were bowel function scores and/or prevalence of bowel symptoms. Additionally, the effect of time to follow-up and type of resection was analyzed.

Results: In total 26 studies were included, describing bowel function between 3 to 178 months following right hemicolectomy (n=4207), left hemicolectomy/sigmoid colon resection (n=4211), and subtotal/total colectomy (n=161). In 16 studies (61.5%) a bowel function score was used. Pooled prevalence for liquid and solid stool incontinence was 24.1% and 6.9%, respectively. The most prevalent constipation-associated symptoms were incomplete evacuation and obstructive, difficult emptying (33.3% and 31.4%, respectively). Major Low Anterior Resection Syndrome was present in 21.1%. No differences between time to follow-up or type of colectomy were found.

Conclusion: Bowel function problems following surgery for colon cancer are common, show no improvement over time and do not depend on the type of colectomy. Apart from fecal incontinence, constipation-associated symptoms are also highly prevalent. Therefore, more attention should be paid to all possible aspects of bowel dysfunction following surgery for colon cancer and targeted treatment should commence promptly.

© 2020 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

Introduction

Annually, more than 1.8 million people are diagnosed with colorectal cancer, which makes it the third most common type of cancer worldwide [1]. Surgical resection of the tumor remains the cornerstone of its curative treatment [2,3]. Extensive research regarding curative oncological colorectal surgery and neoadjuvant therapy has contributed to a noteworthy increase in survival during

E-mail address: s.j.verkuijl@umcg.nl (S.J. Verkuijl).

the past decades and has led to a current overall five-year survival rate of 64% [4]. Therefore, clinicians are now able to extend their focus to long-term functional outcomes following surgery for colorectal cancer.

Despite the fact that the term 'colorectal cancer' is commonly used, neither the anatomic sites of rectal and colon cancer are similar, nor are etiology, treatment, and complications [5,6]. Functional outcomes of rectal cancer surgery have been studied extensively and are summarized in at least seven systematic reviews. It appears that even years after surgery one third of the patients still suffer from fecal incontinence [7–13]. Contrarily, reports on functional outcomes following surgery for colon cancer are scarce and are often conducted in relatively small study populations. This is

^{*} Corresponding author. Department of Surgery, Anorectal Physiology Laboratory, University of Groningen, University Medical Center Groningen, Hanzeplein 1, PO Box 30 001, 9700, RB Groningen, the Netherlands.

surprising, because colon cancer is more than twice as common as rectal cancer [4]. To date, a systematic review and/or meta-analysis of functional outcomes following surgery for colon cancer does not exist. This hinders the decision-making process surrounding colon cancer treatment because evidence-based knowledge of the expected postoperative bowel function is lacking. Such an overview would be invaluable and will direct attention towards the functional problems to be expected following surgery for colon cancer, thus enabling patients to develop optimal postoperative coping strategies [14,15].

The general opinion amongst physicians is that postoperative bowel function improves slightly over time. To the best of our knowledge, however, no systematic overview exists of bowel function during the years following surgery for colon cancer. A summary comparison between postoperative bowel function following different types of oncological colonic resections is also lacking.

Therefore, the primary aim of this systematic review and metaanalysis was to quantify the functional outcomes following surgery for colon cancer. Second, the functional outcomes were assessed according to the time to follow-up and the type of colectomy.

Materials and methods

This systematic review and meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Supplementary Table S1) [16].

Search strategy

We performed a comprehensive literature search of the PubMed, EMBASE, and Cochrane Library databases from January 1, 1995 up to November 1, 2020. The following keywords and/or Medical Subject Heading (MeSH) terms were used: "Colorectal Neoplasms", "Colorectal Surgery", "Colectomy", "Anastomosis, Surgical", "Colon/surgery", "Colonic Neoplasms/surgery", "Signs and Symptoms, Digestive", "Fecal Incontinence", and "Defecation", and in combination with free-text words related to bowel symptoms following different types of oncological colectomies. In addition, references of the included studies and relevant reviews were manually screened for additional studies not captured by the initial literature search.

Study selection

Independently of each other, two authors, S.J.V. and J.E.J., selected the eligible articles retrieved by the initial search on the basis of titles and abstracts. At this stage the reviewers were blinded as to authors, institutions, and journals. Once a study met the criteria for eligibility, the full text of the article was independently analyzed. Discrepancies were solved by discussion and consensus with a third author, E.J.B.F.

Studies were considered eligible if they met the following inclusion criteria: (1) the study contains data of adult colon cancer patients who underwent a colon resection with primary anastomosis, without construction of a pouch, with curative intention; (2) at least one postoperative bowel function score or bowel symptom is reported separately, with a time to follow-up of at least three months. Exclusion criteria were: (1) a sample size of less than ten patients, (2) the study only focuses on quality of life, (3) reviews, case reports, editorials, and commentaries, (4) non-English studies, (5) overlapping patient populations. If studies were based on the same patient population, the study with the longest postoperative time to follow-up was included. By including articles published

after January 1, 1995, we captured twenty-five years of modern oncologic surgery.

Outcomes of interest

The outcome focuses on bowel function, determined by either a bowel function score or prevalence of a bowel symptom, that is fecal incontinence, urgency, and stool frequency. A bowel function score was considered to be as validated if a validation report could be found in the literature. In addition, the outcomes were assessed according to the length of postoperative follow-up and the type of colon resection.

Quality assessment

The authors S.J.V. and J.E.J. assessed the methodological quality of the included studies independently by using the Jadad score for randomized studies and the Newcastle-Ottawa scale (NOS) for non-randomized studies [17,18]. The Jadad score appraises randomization, blinding, and withdrawals/dropouts of the individual study with a total score ranging from 0 to 5 points (from low to high quality). Using the NOS the domains patient selection, comparability, and outcome were assessed that has a total score ranging from 0 to 9 points (from poor to excellent quality). Additionally, the Oxford Center for Evidence-based Medicine's Levels of Evidence were determined for the individual studies [19].

Data extraction

The authors S.J.V. and J.E.J. independently carried out the data extraction by cross-checking all the results. A standard data extraction form was used to obtain the following details from each selected full-text study: general study characteristics (first author, year of publication, country of origin, study design, number of included patients, length of follow-up), clinical characteristics (sex, age), surgical characteristics (type of resection, surgical technique), and outcome measures (reported bowel function scores, prevalence of bowel symptoms). The symptoms stool fragmentation and stool clustering were taken together because previous studies stated that these definitions overlap [11,20].

Data synthesis and statistical analysis

Random-effect models according to the DerSimonian and Laird procedure were used to pool the most frequently reported bowel function outcome measures including the 95% confidence intervals [21]. Between-study heterogeneity was calculated using the I² measure of inconsistency, where values $\geq 75\%$ were interpreted as considerable [22]. If means and standard deviations of the primary outcome measures were not reported, the transformation techniques of Hozo and colleagues and Wan and colleagues were used [23,24]. By serially excluding studies, sensitivity analysis was performed to analyze if the pooled outcomes were significantly influenced by any study specifically. If the included intervention studies only reported the bowel function outcome measure or measures for the intervention and the control arm of the study separately, each study arm was considered as a study population in the meta-analysis. For longitudinal studies, the outcomes at the longest time to follow-up were included in the meta-analysis. The bowel function scores were only shown if the scores were described in more than one study. If meta-analysis was not possible descriptive synthesis was provided to summarize the results. Figures were generated using GraphPad Prism, version 8.4.2 (GraphPad Software, California USA). All statistical analyses were performed using R, version 3.6.3 (R Foundation of Statistical Computing, Vienna, Austria).

Results

Study characteristics

A total of 3027 unique records were screened based on titles and abstracts and review of the full texts of 99 studies was performed, resulting in 26 studies that met the eligibility criteria [25–50]. Both descriptive and meta-analysis of all studies were performed. The PRISMA flow diagram is shown in Fig. 1. The characteristics of all included studies are reported in Table 1. These 26 studies represented a total of 8620 patients. A right hemicolectomy was performed in 4207 patients, a left hemicolectomy or sigmoid colon resection in 4211 patients, and a subtotal/total colectomy in 161 patients. In 41 patients the type of colectomy was not reported. The postoperative time to follow-up ranged from three to 178 months. The pooled age of all included patients was 69.3 years (95% CI,

67.8–70.7), with high heterogeneity (I 2 = 96.4%, P < 0.001, Supplementary Fig. S1). Both the included randomized studies had a Jadad score of 3. The mean NOS score of the 24 non-randomized studies was 6.0 \pm 1.3. The separate Jadad and NOS score components for all 26 individual studies are shown in Supplementary Table S2.

Bowel function according to scores

Fourteen studies (53.8%) reported the outcomes of one bowel function score and two studies (7.7%) reported the outcomes of two scores. The most frequently used score for bowel function was the Wexner score (n = 6, 23.1%, Supplementary Table S3). Meta-analysis of the Wexner scores showed a pooled mean of 1.42 (95% CI, 0.77–2.07), with considerable heterogeneity ($I^2 = 74.4\%$, P < 0.001, Fig. 2A). Two studies could not be included in this meta-analysis as the Wexner scores were not reported adequately. Sensitivity analysis showed that the pooled result was highly

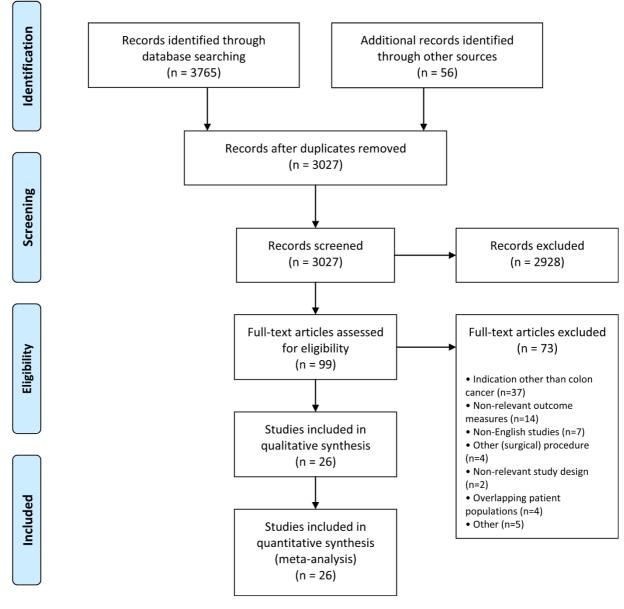


Fig. 1. PRISMA flow diagram of the study selection process.

 Table 1

 Characteristics of the studies included in the systematic review and meta-analysis.

Study details		Single or multi-					Time to follow-up ^b	Risk of bias	
Study	Study design	center	patients ^a	according to type of colectomy				Jadad or Newcastle Ottawa score ^c	Level of evidence
				Right	Left	STC			
Adachi (2000) [25]	Cross-sectional	Single	38	N/A	38	N/	NR	6/9	2B
Böhm (2008) [26]	Retrospective cohort	Single	11	8	2	A N/ A	36 (14-55) months	6/9	2B
Brigic (2017) [27]	Prospective cohort	Multi	91	47	44	N/ A	6 and 12 months	5/9	2B
	Cross-sectional	Multi	85	48	37		2–4 years		
Buchli (2018) [28]	Prospective cohort	NR	517	287	230		1 year	5/9	2B
Dobrowolski (2009) [29]	Prospective cohort	Single	43	N/A	43	N/ A	6 and 12 months	8/9	2B
Elfeki (2019) [30]	Cross-sectional	Multi	3061	N/A	3061		66 (11–178) months	7/9	2B
Graf (1996) [31]	Cross-sectional	Single	40	NR	NR	NR	60 (36-83) months	7/9	2B
Ho (1996) [32]	Cross-sectional	Single	172	63	109	N/ A	27.2 (0.8) months	6/9	2B
Но (1999) [33]	Randomized controlled trial	NR	43	N/A	43	N/ A	Transanal stapling group: 11.7 (1) months	5/5	1B
Ho (2000) [34]	Randomized controlled trial	Single	35	N/A	35	N/ A	BAR group: 11.4 (1.1) months 6 months	5/5	1B
Keane (2020) [35]	Prospective cohort	Multi	123	N/A	123		45 (IQR, 24-80) months	7/9	2B
Khan (2018) [36]	Retrospective cohort	Single	25	N/A	N/A		49 months	5/9	3B
Larsen (2020) [37]	Cross-sectional	Multi	3306	3306	N/A	N/ A	4.6 (0.8–14.7) years	7/9	2B
Lim (2001) [38]	Cross-sectional	Single	20				41 (11-125) months	4/9	3B
Matsuoka (2010) [39]	Prospective cohort	NR	45	N/A	45	N/ A	6 months	7/9	2B
Min (2016) [40]	Prospective cohort	Single	24	N/A	N/A		3-6 months	5/9	3B
Nehmeh (2019) [41]	Retrospective cohort	0	92	N/A	N/A	92	3 and 12 months	3/9	4
Ng (2020) [42]	Prospective cohort	Single	150	150	N/A	N/ A	5.4 (2.8) years	6/9	2B
Ohigashi (2011) [43]	Cross-sectional	Single	82	38	44	N/ A	Right group: 892 (417) days Left group: 885 (430) days	6/9	2B
Sarli (2006) [44]	Cross-sectional	Single	57	N/A	57	N/ A	12–18 months	6/9	2B
Sato (2003) [45]	Cross-sectional	Single	22	N/A	22	N/ A	NR	5/9	4
Scheele (2015) [46]	Cross-sectional	Single	105	105	N/A	N/ A	5.0 (3.0–8.3) years	6/9	2B
Su (2020) [47]	Retrospective cohort	Single	57	57	N/A		3, 6, and 12 months	5/9	2B
Thorsen (2016) [48]	Prospective cohort	Multi	98	98	N/A		Experimental group: 31 (6–74) months Control group: 14 (6–30) months	7/9	2B
Van der Heijden (2019) [49]	Cross-sectional	Single	29	N/A	29	N/ A	After protocol: 9.0 (4.4) months	7/9	2B
Van Heinsbergen (2018) [50]	Cross-sectional	Multi	249	N/A	249	N/ A	5.2 (2.3–8.3) years	7/9	2B

Abbreviations: BAR, biofragmentable anastomotic ring; CME, complete mesocolic excision; IQR, interquartile range; NR, not reported; N/A, not applicable; STC, subtotal/total colectomy.

influenced by one study arm (Dobrowolski study arm IMA ligation). Meta-analysis of the Wexner scores without this study arm resulted in a pooled mean of 0.98 (95% CI, 0.67–2.78), with no heterogeneity ($I^2 = 0.0\%$, P = 0.69).

The Low Anterior Resection Syndrome (LARS) score and the McDonald & Heald Continence Grades were reported in five (19.2%) and four (15.4%) studies, respectively (Supplementary Table S3). Pooled prevalence of major LARS was 21.5% (95% CI, 19.3–23.9)

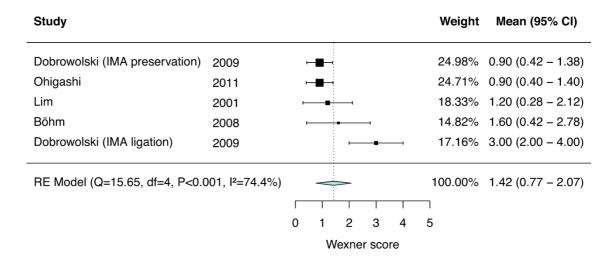
with moderate heterogeneity between studies ($I^2=31.3\%$, P=0.201). Pooling of the McDonald & Heald Continence Grades ≥ 3 (continence problems affecting lifestyle) resulted in a prevalence of 20.3% (95% CI, 12.2–31.9) with considerable heterogeneity between studies ($I^2=77.5\%$, P<0.001). Three studies used an adapted version of the McDonald & Heald Continence Grades, which was converted into the original grading system based on the description of the different grades.

^a Only the patients who met our inclusion criteria are shown, in some studies this was not the whole study population.

b Time to follow-up is reported in mean (SD), median (range) or IQR if indicated, follow-up was only for the included patients.

^c The Jadad score applied to randomized studies (scores range from 0 to 5) and the Newcastle Ottawa Scale applied to all non-randomized studies (scores range from 0 to 9).

A.



B.

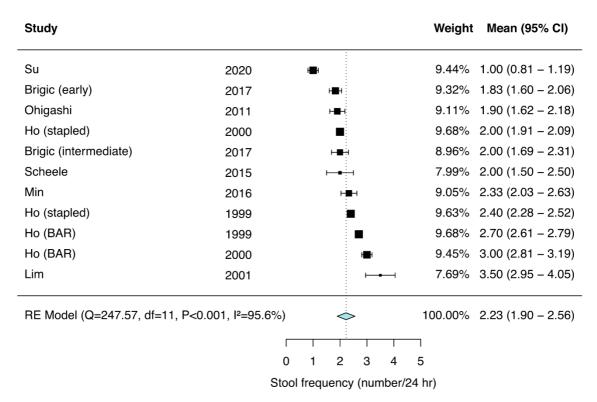


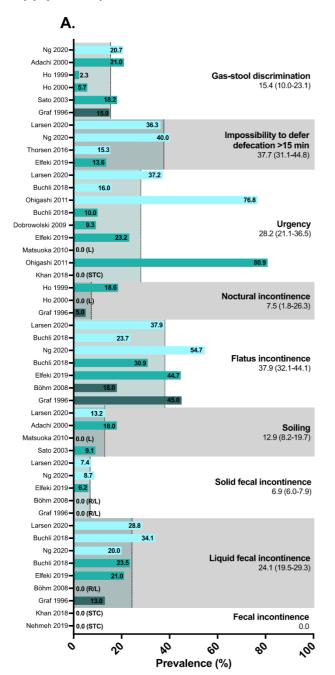
Fig. 2. Random-effects meta-analysis of the studies that reported the Wexner score (A) or the stool frequency per 24 h (B) following surgery for colon cancer.

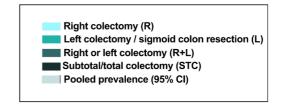
Bowel function according to the prevalence of bowel symptoms

The most frequently reported bowel symptom in the included studies was stool frequency per 24 h (n = 20, 76.9%). Meta-analysis of stool frequency showed a pooled mean of 2.23 (95% CI, 1.90–2.56) per 24 h, with high heterogeneity ($I^2 = 95.6\%$, P < 0.001, Fig. 2B). Sensitivity analysis showed that the pooled result was significantly influenced by one study (Su) and meta-analysis of stool frequency without this study resulted in a pooled mean of 2.35 (95% CI, 2.08–2.62), with high heterogeneity ($I^2 = 95.7\%$,

P < 0.001). In this meta-analysis we could not include twelve out of the twenty studies reporting stool frequency per 24 h because it was inadequately described. The pooled prevalence of all other reported bowel symptoms associated with fecal incontinence or constipation is shown in Fig. 3. The symptoms 'incontinence for flatus' (37.9%, 95% CI, 32.1–44.1), 'impossibility to defer defecation for more than 15 min' (37.7%, 95% CI, 31.1–44.8), and 'incomplete defecation' (33.3%, 95% CI, 20.5–49.2) had the highest pooled prevalence.

The use of laxatives was reported in three studies with a pooled





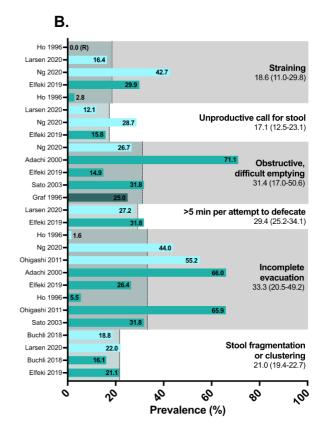


Fig. 3. Prevalence of all reported bowel symptoms according to type of colectomy. Showing bowel symptoms associated with fecal incontinence (A) or constipation (B) that were reported in multiple studies.

prevalence of 9.0% (95% CI, 5.0—15.9). Antidiarrheals were used by 10.5% (95% CI, 5.2—20.3) of the pooled patients in nine studies. Six studies described pad wearing, resulting in a pooled prevalence of 13.8% (95% CI, 10.7—17.6).

Bowel function according to length of postoperative follow-up

The outcomes of the Wexner score, LARS score, and McDonald & Heald Continence Grades did not show differences depending on the duration of postoperative follow-up, ranging from 6 to 41, 9 to 66, and 6–27 months, respectively (Fig. 4). Additionally, stool frequency was analyzed showing a comparable number of stools per 24 h, independent of the duration of postoperative follow-up that

ranged from 5 to 60 months (Fig. 5). Unfortunately, it was impossible to make a subgroup meta-analysis of the effect of time to follow-up on bowel function, because of the limited number of studies for each length of follow-up.

Bowel function according to type of colectomy

The outcomes of the Wexner score, LARS score, and McDonald & Heald Continence Grades according to the type of colectomy (right, left, or subtotal/total) were comparable (Fig. 4). Stool frequency per 24 h was also comparable for the three different types of colectomy (Fig. 5). In addition, there were no differences in the prevalence of fecal incontinence or constipation-related symptoms according to

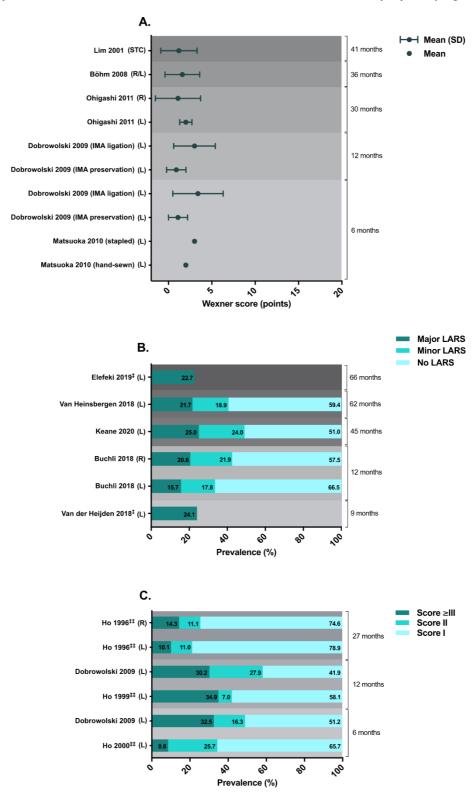


Fig. 4. Bowel function scores according to length of postoperative follow-up and the type of colectomy. The three bowel function scores that were reported in more than one study are shown: the Wexner score (A), the Low Anterior Resection Syndrome score (B), and the McDonald & Heald Continence Grades (C). The type of colectomy is indicated on the left-hand side of the figure in letters. The length of postoperative follow-up is shown on the right-hand side of the figure. A darker background color indicates a longer follow-up. Abbreviations: LARS, Low Anterior Resection Syndrome; L, left hemicolectomy/sigmoid colon resection; R, right hemicolectomy; STC, subtotal/total colectomy. ‡ Three studies lacked data on no and minor LARS. ^{‡†} These studies used an adapted version of the McDonald & Heald Continence Grades, which was converted into the original grading system based on the description of the different grades.

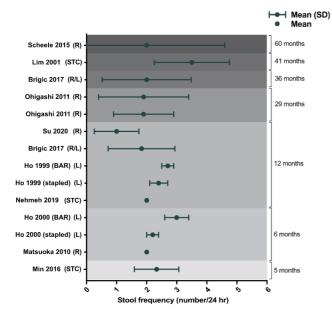


Fig. 5. Stool frequency according to length of postoperative follow-up and the type of colectomy. The type of colectomy is indicated on the left-hand side of the figure in letters. The length of postoperative follow-up is shown on the right-hand side of the figure. A darker background indicates a longer follow-up.; Abbreviations: L, left hemicolectomy/sigmoid colon resection; R, right hemicolectomy; STC, subtotal/total colectomy.

type of colectomy (Fig. 3). Subgroup meta-analysis of the effect of type of colectomy on bowel function was impossible because of the limited number of studies including patients with right, or subtotal/total colectomies.

Discussion

This systematic review and meta-analysis shows that bowel function problems occur frequently following surgery for colon cancer. Even though studies with a long-term follow-up were included, no improvement of bowel function over time was observed. Moreover, the type of colectomy did not seem to influence functional outcomes.

To the best of our knowledge, this is the first systematic review and meta-analysis of bowel function following surgery for colon cancer. With regard to fecal incontinence, the prevalence of incontinence for liquid (24.1%) and solid stool (6.9%) found following surgery for colon cancer were more than four times the prevalence of both liquid and/or solid fecal incontinence in the general population with comparable age (6.9%) [51]. The extent of constipation was not reported in any of the included studies. Nevertheless, the pooled prevalence of the constipation-associated symptoms 'incomplete evacuation' (33.3%) and 'obstructive, difficult emptying' (31.4%) was around twice that of chronic idiopathic constipation in the general population with comparable age, which in a previous meta-analysis had been pooled as 17.0% [52]. Moreover, the prevalence of major LARS following surgery for colon cancer, which incorporates symptoms of both fecal incontinence and constipation [53], was one and a half times that reported in the community with comparable age (21.1% versus 14.0%) [54].

Even though bowel function following surgery for colon cancer was impaired, these patients still had favorable outcomes compared to patients who had undergone surgery for rectal cancer, for which a prevalence of 41% major LARS has been pooled [13]. However, the LARS score was built to capture the major symptoms following rectal resections and was not validated for use following

colon cancer [53]. Additionally, the majority of studies regarding surgery for rectal cancer concentrated on patients with very low rectal resections [11] and neoadjuvant radiotherapy, both of which are known to severely impair bowel function [8,13,55].

Our findings indicate that impaired bowel function still occurred following colon cancer, despite not having to enter the pelvis which has vulnerable neural structures, as is necessary in surgery for rectal cancer. Given the diversity of the postoperative bowel symptoms, the causes of bowel function problems following surgery for colon cancer are probably multifactorial. One factor that has been postulated to reduce sensory and motor functions of the colon is traction and iatrogenic injury to the colonic vascularization and/or innervation that may occur during mobilization of the colon [42,56]. This might be supported by the high number of constipation-associated symptoms that were shown in this systematic review. Furthermore, different animal studies showed increased colonic migrating motility following partial resection or denervation of the colon, probably due to fewer inhibitory signals after autonomic denervation [57-59]. This has, however, not yet been fully established following surgery for colon cancer in humans. Finally, surgical removal of a part of the colon may lead to reduced stool storage capacity and therefore more liquid stool, causing increased stool frequency, urgency, and incontinence for liquid stool.

Although the majority of the studies focused solely on aspects of fecal incontinence following surgery for colon cancer, we found that patients suffered equally from constipation-associated symptoms. In general, clinicians have the tendency to overestimate the impact of fecal incontinence and underestimate the discomfort of constipation-associated symptoms such as clustering of stools [60,61]. As we found a pooled Wexner score of 1.4, which indicates minimal fecal incontinence [62], it would seem that the combination of different defecation problems, rather than fecal incontinence alone, is what afflicts colon cancer patients following surgery. Therefore, we conclude that bowel function problems following surgery for colon cancer cannot be captured by measuring fecal incontinence only.

In contrast to general opinion, we found no clear indication that bowel function following surgery for colon cancer improves over time. This observation is solely based on descriptive findings, because the data were too heterogeneous for conducting a meta-analysis. The finding that bowel dysfunction does not improve over time was also observed in a systematic review of patients with rectal cancer [9]. Improving the quality of evidence regarding bowel function over time warrants longitudinal studies with a follow-up of more than one year. Prior to such studies, it would be advisable to starting targeted treatment early, because post-operative bowel function problems are unlikely to disappear spontaneously over time.

Regarding the types of colectomy, either right, left, or subtotal/total, no clear differences in functional outcome were observed. Once again, this analysis could only be performed descriptively because of the heterogeneity of the data. Some of the included studies suggested more bowel dysfunction following right-sided colon resections compared to left-sided resections, reportedly related to the loss of the ileocecal valve [28,43]. To answer this question conclusively, large longitudinal studies are required that focus primarily on the differences between different oncological colectomies.

Limitations

The pooled functional outcomes were of considerable heterogeneity, which implies that they should be interpreted with caution. The diversity of the studies precluded sub-analyses

according to the time to follow-up and differences between the types of colectomy. Apart from the heterogeneity in the metaanalyses, it was difficult to assemble a uniform picture of postoperative functional outcomes, because of the variety in bowel function scores and symptoms that were reported. This issue was raised previously in systematic reviews regarding surgery for rectal cancer [7–11]. We did not pool overall postoperative incontinence and/or constipation, because the resulting estimate would be unreliable. Furthermore, less than two-thirds of the included studies used a validated bowel function score, which restricts the value of the available evidence. Because there is no currently validated bowel function score for use after surgery for colon cancer, we included not only all bowel function scores, but also the individual bowel symptoms to strengthen the validity of our outcomes. Finally, some interesting studies had to be excluded due to the inclusion of patients with and without a pouch, which was an exclusion criterion in the current meta-analysis because previously pouches have been described as influencing postoperative bowel function [63,64].

Clinical implications

The number of bowel function problems following surgery for colon cancer underscores the necessity of paying more attention to bowel dysfunction during preoperative counseling and post-operative follow-up, although oncological outcomes still need to be prioritized. The fact that only 9.0% of the patients used laxatives and that 10.5% were on antidiarrheals despite the high incidence of bowel function problems, suggests that bowel dysfunction goes practically untreated following surgery for colon cancer. Clinicians should address both fecal incontinence and constipation-associated complaints regularly during the long-term follow-up of colon cancer patients so as to promptly commence targeted treatment of the bowel function problems.

Future research

More large, longitudinal studies are required that use validated bowel function scores following surgery for colon cancer. Furthermore, multiple validated bowel function scores should be included in future trials investigating new ways of treating colon cancer. In addition, broad risk analyses of surgical details could lead to identifying surgical innovations that would benefit functional outcomes. Lastly, more attention needs to be paid to the physiological and pathophysiological sensory and motor functions of the colon and to colonic innervation. This knowledge could point to new ways of avoiding colonic denervation during surgery for colon cancer.

Conclusions

This systematic review and meta-analysis shows that bowel function problems following surgery for colon cancer are common and seem to persist over time. Regarding the type of colectomy no clear difference in functional outcome was observed. Both fecal incontinence and constipation-associated symptoms were prevalent, indicating that postoperative bowel function problems cannot be captured by only measuring fecal incontinence. During preoperative counseling more attention should be paid to possible bowel dysfunction and to long-term follow-up of these patients and targeted treatment should commence promptly. Future studies will be valuable in determining the pathophysiological mechanisms of bowel dysfunction following surgery for colon cancer and in identifying areas for surgical innovations that benefit patients' postoperative bowel function.

Declarations of interest

None.

Acknowledgments

The authors would like to thank T. van Wulfften Palthe, PhD, for correcting the English manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejso.2020.11.136.

References

- Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394

 –424.
- [2] Labianca R, Nordlinger B, Beretta GD, Brouquet A, Cervantes A, ESMO Guidelines Working Group. Primary colon cancer: ESMO Clinical Practice Guidelines for diagnosis, adjuvant treatment and follow-up. Ann Oncol 2010;21(Suppl 5): 70.
- [3] National Comprehensive Cancer Network. Colon cancer NCCN clinical practice guidelines in oncology V4, vol. 2020; 2020. p. 2020.
- [4] Siegel RL, Miller KD, Jemal A. Cancer statistics. CA Cancer J Clin 2020;70:7–30.
- [5] van der Sijp MP, Bastiaannet E, Mesker WE, van der Geest LG, Breugom AJ, Steup WH, et al. Differences between colon and rectal cancer in complications, short-term survival and recurrences. Int J Colorectal Dis 2016;31:1683—91.
- [6] Tamas K, Walenkamp AM, de Vries EC, van Vugt MA, Beets-Tan RG, van Etten B, et al. Rectal and colon cancer: not just a different anatomic site. Cancer Treat Rev 2015;41:671–9.
- [7] Scheer AS, Boushey RP, Liang S, Doucette S, O'Connor AM, Moher D. The long-term gastrointestinal functional outcomes following curative anterior resection in adults with rectal cancer: a systematic review and meta-analysis. Dis Colon Rectum 2011;54:1589–97.
- [8] Loos M, Quentmeier P, Schuster T, Nitsche U, Gertler R, Keerl A, et al. Effect of preoperative radio(chemo)therapy on long-term functional outcome in rectal cancer patients: a systematic review and meta-analysis. Ann Surg Oncol 2013;20:1816—28.
- [9] Lai X, Wong FK, Ching SS. Review of bowel dysfunction of rectal cancer patients during the first five years after sphincter-preserving surgery: a population in need of nursing attention. Eur J Oncol Nurs 2013;17:681–92.
- [10] Chapman SJ, Bolton WS, Corrigan N, Young N, Jayne DG. A cross-sectional review of reporting variation in postoperative bowel dysfunction after rectal cancer surgery. Dis Colon Rectum 2017;60:240–7.
- [11] Keane C, Wells C, O'Grady G, Bissett IP. Defining low anterior resection syndrome: a systematic review of the literature. Colorectal Dis 2017;19:713–22.
- [12] Dulskas A, Miliauskas P, Tikuisis R, Escalante R, Samalavicius NE. The functional results of radical rectal cancer surgery: review of the literature. Acta Chir Belg 2016;116:1–10.
- [13] Croese AD, Lonie JM, Trollope AF, Vangaveti VN, Ho YH. A meta-analysis of the prevalence of Low Anterior Resection Syndrome and systematic review of risk factors. Int J Surg 2018;56:234–41.
- [14] O'Connor G, Coates V, O'Neill S. Randomised controlled trial of a tailored information pack for patients undergoing surgery and treatment for rectal cancer. Eur | Oncol Nurs 2014;18:183—91.
- [15] Herrinton LJ, Altschuler A, McMullen CK, Bulkley JE, Hornbrook MC, Sun V, et al. Conversations for providers caring for patients with rectal cancer: comparison of long-term patient-centered outcomes for patients with low rectal cancer facing ostomy or sphincter-sparing surgery. CA Cancer J Clin 2016;66:387–97.
- [16] Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ 2009;339:b2535.
- [17] Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials 1996;17:1–12.
- [18] Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. 2020. p. 2020.
- [19] OCEBM Levels of Evidence Working Group. The Oxford 2011 Levels of evidence. Oxford Center for Evidence-Based Medicine; 2020. p. 2020.
- [20] Kwaan MR. Bowel function after rectal cancer surgery: a review of the evidence. Semin Colon Rectal Surg 2011;22:235–42.
- [21] DerSimonian R, Laird N. Meta-analysis in clinical trials revisited. Contemp Clin Trials 2015;45:139–45.
- [22] Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ 2003;327:557–60.

- [23] Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. BMC Med Res Methodol 2005;5:13.
- [24] Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. BMC Med Res Methodol 2014;14:135.
- [25] Adachi Y, Kakisako K, Sato K, Shiraishi N, Miyahara M, Kitano S. Factors influencing bowel function after low anterior resection and sigmoid colectomy. Hepato-Gastroenterology 2000;47:155–8.
- [26] Böhm G, Kirschner-Hermanns R, Decius A, Heussen N, Schumpelick V, Willis S. Anorectal, bladder, and sexual function in females following colorectal surgery for carcinoma. Int J Colorectal Dis 2008;23:893–900.
- [27] Brigic A, Sakuma S, Lovegrove RE, Bassett P, Faiz O, Clark SK, et al. A prospective case control study of functional outcomes and related quality of life after colectomy for neoplasia. Int J Colorectal Dis 2017;32:777–87.
- [28] Buchli C, Martling A, Sjövall A. Low anterior resection syndrome after rightand left-sided resections for colonic cancer. BJS Open 2018;3:387–94.
- [29] Dobrowolski S, Hać S, Kobiela J, Sledziński Z. Should we preserve the inferior mesenteric artery during sigmoid colectomy? Neuro Gastroenterol Motil 2009:21 1288-e123
- [30] Elfeki H, Larsen HM, Emmertsen KJ, Christensen P, Youssef M, Khafagy W, et al. Bowel dysfunction after sigmoid resection for cancer and its impact on quality of life. Br J Surg 2019;106:142–51.
- [31] Graf W, Ekström K, Glimelius B, Påhlman L. A pilot study of factors influencing bowel function after colorectal anastomosis. Dis Colon Rectum 1996;39: 744–9.
- [32] Ho YH, Low D, Goh HS. Bowel function survey after segmental colorectal resections. Dis Colon Rectum 1996;39:307–10.
- [33] Ho YH, Tan M, Leong A, Eu KW, Nyam D, Seow-Choen F. Anal pressures impaired by stapler insertion during colorectal anastomosis: a randomized, controlled trial. Dis Colon Rectum 1999;42:89–95.
- [34] Ho YH, Tsang C, Tang CL, Nyam D, Eu KW, Seow-Choen F. Anal sphincter injuries from stapling instruments introduced transanally: randomized, controlled study with endoanal ultrasound and anorectal manometry. Dis Colon Rectum 2000;43:169—73.
- [35] Keane C, O'Grady G, Bissett I, Woodfield J. Comparison of bowel dysfunction between colorectal cancer survivors and a non-operative non-cancer control group. Colorectal Dis 2020;22:806–13.
- [36] Khan M, Jayne D, Saunders R. Comparison of defecatory function after laparoscopic total colectomy and ileorectal anastomosis versus a traditional open approach. Ann R Coll Surg Engl 2018;100:235–9.
- [37] Larsen HM, Elfeki H, Emmertsen KJ, Laurberg S. Long-term bowel dysfunction after right-sided hemicolectomy for cancer. Acta Oncol 2020:1–6.
- [38] Lim JF, Ho YH. Total colectomy with ileorectal anastomosis leads to appreciable loss in quality of life irrespective of primary diagnosis. Tech Coloproctol 2001;5:79–83.
- [39] Matsuoka H, Masaki T, Kobayashi T, Sato K, Mori T, Sugiyama M, et al. Neurophysiologic investigation of anal function following double stapling anastomosis. Dig Surg 2010;27:320–3.
- [40] Min CK, Kim HO, Lee D, Jung KU, Lee SR, Kim H, et al. Obstructive left colon cancer should Be managed by using a subtotal colectomy instead of colonic stenting. Ann Coloproctol 2016;32:215–20.
- [41] Nehmeh WA, Gabriel M, Tarhini A, Chaktoura G, Sarkis R, Abboud B, et al. Total or subtotal colectomy with primary anastomosis for occlusive left colon cancer: a safe, acceptable and applicable procedure. Gulf J Oncolog 2019;1: 57–60
- [42] Ng KS, Gladman MA. Patient-reported and physician-recorded bowel dysfunction following colorectal resection and radical cystectomy: a prospective, comparative study. Colorectal Dis 2020;22:1336—47.
- [43] Ohigashi S, Hoshino Y, Ohde S, Onodera H. Functional outcome, quality of life, and efficacy of probiotics in postoperative patients with colorectal cancer. Surg Today 2011;41:1200–6.
- [44] Sarli L, Cinieri FG, Pavlidis C, Regina G, Sansebastiano G, Veronesi L, et al. Anorectal function problems after left hemicolectomy. J Laparoendosc Adv Surg Tech 2006;16:565–71.

- [45] Sato K, Inomata M, Kakisako K, Shiraishi N, Adachi Y, Kitano S. Surgical technique influences bowel function after low anterior resection and sigmoid colectomy. Hepato-Gastroenterology 2003;50:1381–4.
- [46] Scheele J, Lemke J, Meier M, Sander S, Henne-Bruns D, Kornmann M. Quality of life after sphincter-preserving rectal cancer resection. Clin Colorectal Cancer 2015;14:33.
- [47] Su H, Wu H, Mu B, Bao M, Luo S, Zhao C, et al. The feasibility and safety of complete laparoscopic extended right hemicolectomy with preservation of the ileocecal junction in right-transverse colon cancer. World J Surg Oncol 2020;18. 159-8.
- [48] Thorsen Y, Stimec B, Andersen SN, Lindstrom JC, Pfeffer F, Oresland T, et al. Bowel function and quality of life after superior mesenteric nerve plexus transection in right colectomy with D3 extended mesenterectomy. Tech Coloproctol 2016;20:445–53.
- [49] van der Heijden JAG, van Heinsbergen M, Thomas G, Caers F, Slooter GD, Maaskant-Braat AJG. Implementation of a postoperative screening and treatment guidance for the low anterior resection syndrome: preliminary results, Dis Colon Rectum 2019;62:1033—42.
- [50] van Heinsbergen M, Janssen-Heijnen ML, Leijtens JW, Slooter GD, Konsten JL. Bowel dysfunction after sigmoid resection underestimated: multicentre study on quality of life after surgery for carcinoma of the rectum and sigmoid. Eur J Surg Oncol 2018;44:1261–7.
- [51] Quander CR, Morris MC, Melson J, Bienias JL, Evans DA. Prevalence of and factors associated with fecal incontinence in a large community study of older individuals. Am J Gastroenterol 2005;100:905–9.
- [52] Suares NC, Ford AC. Prevalence of, and risk factors for, chronic idiopathic constipation in the community: systematic review and meta-analysis. Am J Gastroenterol 2011;106:1582. 91; quiz 1581, 1592.
- [53] Emmertsen KJ, Laurberg S. 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 2012;255:922–8.
- [54] Juul T, Elfeki H, Christensen P, Laurberg S, Emmertsen KJ, Bager P. Normative data for the low anterior resection syndrome score (LARS score). Ann Surg 2019:269:1124–8.
- [55] Abraha I, Aristei C, Palumbo I, Lupattelli M, Trastulli S, Cirocchi R, et al. Preoperative radiotherapy and curative surgery for the management of localised rectal carcinoma. Cochrane Database Syst Rev 2018;10:CD002102.
- [56] Thorsen Y, Stimec BV, Lindstrom JC, Nesgaard JM, Oresland T, Ignjatovic D. Bowel motility after injury to the superior mesenteric plexus during D3 extended mesenterectomy. J Surg Res 2019;239:115–24.
- [57] Morita H, Mochiki E, Ogawa A, Yanai M, Toyomasu Y, Tabe Y, et al. Effects of denervation at ileocecal junction and ileocecal resection in dogs. Neuro Gastroenterol Motil 2012;24:86–93. e14.
- [58] Tanabe Y, Hotokezaka M, Mibu R, Tanaka M. Effects of extrinsic autonomic denervation and myenteric plexus transection on colonic motility in conscious dogs. Surgery 2002;132:471–9.
- [59] Lee WY, Takahashi T, Pappas T, Mantyh CR, Ludwig KA. Surgical autonomic denervation results in altered colonic motility: an explanation for low anterior resection syndrome? Surgery 2008;143:778–83.
- [60] Chen TY, Emmertsen KJ, Laurberg S. Bowel dysfunction after rectal cancer treatment: a study comparing the specialist's versus patient's perspective. BMJ Open 2014;4. e003374-003374.
- [61] Thomas G, van Heinsbergen M, van der Heijden J, Slooter G, Konsten J, Maaskant S. Awareness and management of low anterior resection syndrome: a Dutch national survey among colorectal surgeons and specialized nurses. Eur J Surg Oncol 2019;45:174—9.
- [62] Jorge JM, Wexner SD. Etiology and management of fecal incontinence. Dis Colon Rectum 1993;36:77–97.
- [63] Heriot AG, Tekkis PP, Constantinides V, Paraskevas P, Nicholls RJ, Darzi A, et al. Meta-analysis of colonic reservoirs versus straight coloanal anastomosis after anterior resection. Br J Surg 2006;93:19–32.
- [64] Brown CJ, Fenech DS, McLeod RS. Reconstructive techniques after rectal resection for rectal cancer. Cochrane Database Syst Rev 2008;2. CD006040. doi:CD006040.