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RESEARCH

Impact on defecatory, urinary and sexual function after high-tie sigmoidectomy: a post-hoc analysis of a multicenter randomized controlled trial comparing extended versus standard complete mesocolon excision

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Abstract

Objective To assess the effect of high inferior mesenteric artery tie on defecatory, urinary, and sexual function after surgery for sigmoid colon cancer.

Summary background data Performing a sigmoidectomy poses a notable risk of causing injury to the preaortic sympathetic nerves during the high ligation of the inferior mesenteric artery, as well as to the superior hypogastric plexus during dissection at the level of the sacral promontory. Postoperative defecatory and genitourinary dysfunction after sigmoid colon resection are often underestimated and underreported.

Methods This study is a secondary research of a multicenter, single-blind, randomized clinical trial. The trial involved patients with sigmoid cancer who underwent either extended complete mesocolic excision (e-CME) or standard CME (s-CME). Patients completed questionnaires to assess defecatory, urinary, and sexual function before, 1 month after surgery, and 1 year after surgery. Multivariate analysis was conducted to identify factors associated with functional dysfunction.

Results Seventy-nine patients completed functional assessments before and 1 year after surgery. One year after sigmoidectomy with a high tie of the inferior mesenteric artery, 15.2% of patients had minor low anterior resection syndrome (LARS) and 12.7% had major LARS; 22.2% of males and 29.4% of females had urinary dysfunction; and 43.8% of males and 27.3% of females had sexual dysfunction. After multivariate analysis, no significant associations were found between clinical and surgical factors and gastrointestinal or urinary dysfunction after 1 year of surgery. Age was identified as the only factor linked to sexual dysfunction in both sexes (women, $\beta = -0.54$, $p = 0.002$; men $\beta = -0.38$, $p = 0.010$). Regarding recovery outcomes, diabetes mellitus was identified as a contributing factor to suboptimal gastrointestinal recovery ($p = 0.033$) and urinary recovery in women ($p = 0.039$). Furthermore, the treatment arm was found to be significantly associated with the recovery of erectile function after 1 year of surgery ($p = 0.046$).

Conclusions A high tie of the inferior mesenteric artery during sigmoidectomy is associated with a high incidence of defecatory and genitourinary dysfunction. Age was identified as a significant factor associated with sexual dysfunction 1 year after sigmoid colon resection in both sexes.

Trial registration Clinical trials NCT03083951

Highlights

- *One year after high-tie sigmoidectomy, 27.9% of patients had LARS; 22.2% of the men and 29.4% of the women had urinary dysfunction; and 43.8% of the men and 27.3% of the women had sexual dysfunction.*
- *e-CME is associated with a high rate of urinary dysfunction in men 1 year after surgery. However, after multivariate analysis, no association was found between e-CME and urinary dysfunction in men.*
- *Age was correlated with the recovery of sexual function in both sexes 1 year after surgery. Furthermore, diabetes mellitus was identified as the factor associated with poorer recovery of urinary function in females.*

Extended author information available on the last page of the article

Keywords Sigmoid cancer · Urinary dysfunction · Erectile dysfunction · Sexual dysfunction · Defecatory dysfunction; LARS

Introduction

Functional impairments after rectal cancer surgery have been extensively studied [1–3], but impairments after sigmoidectomy are still poorly documented, resulting in insufficient and imprecise information to candidates for surgery. Alterations in urinary, sexual, and defecatory function after sigmoid and rectal cancer surgery are interrelated, partly due to the common extramural autonomic innervation of the structures involved in these functions [4]. Sigmoidectomy entails a high risk of injury to the preaortic sympathetic nerves during high ligation of the inferior mesenteric artery (IMA) and to the superior hypogastric plexus during dissection at the level of the sacral promontory [5].

Accepted surgical techniques for the treatment of locally advanced cancer of the sigmoid colon are sigmoidectomy with high or low ligation of the IMA and left hemicolectomy with high ligation of the IMA including the territory of the left colic artery. Standard CME (s-CME) includes a central vascular ligation with removal of the lymphatic tissue surrounding the IMA. However, as the lymphatic system runs parallel to the venous system and a wide and variable part of the path of the inferior mesenteric vein (IMV) through the left mesocolon does not coincide with that of the IMA, s-CME does not include the mesocolon surrounding the IMV. We refer to CME that includes this portion as extended CME (e-CME).

The gold standard treatment for resectable sigmoid cancer is surgery with curative intention, followed by adjuvant chemotherapy in patients with locally advanced tumors [6]. Complete mesocolic excision (CME) and D3 lymphadenectomy aim to remove the mesentery and all lymphatic, vascular, and neural tissue in the tumor's drainage area to ensure the removal of any involved lymph nodes [7]. Although many publications have addressed the oncological outcomes of CME and D3 lymphadenectomy [7–9], little is known about the impact that these procedures may have on the patients' defecatory and genitourinary function. A multicenter, single-blind clinical trial (CMELL trial) was undertaken to evaluate whether the number of lymph nodes increases in an extended mesocolic excision [8].

The aim of this study was to depict defecatory, urinary, and sexual function after a high-tie sigmoid colon resection and identify risk factors associated with gastrointestinal and urogenital dysfunction in patients included in the CMELL trial.

Methods

Study design and patients

Data were collected within the single-blind multicenter randomized controlled trial comparing e-CME vs. s-CME for sigmoid colon cancer. The current study was nested within this population but designed to investigate patients' functionality and risk factors associated with gastrointestinal and urogenital dysfunction.

Between October 2017 and August 2019, all consecutive patients aged ≥ 18 years with histologically confirmed adenocarcinoma of the sigmoid colon, including endoscopically unresectable dysplasia adenomas expected to undergo R0 resection, were randomized to e-CME or s-CME. The trial methodology has been described in detail in the original trial publication [8].

In the s-CME group, only the lymphofatty tissue adjacent to the IMA was extracted, and in the e-CME group, in addition to the extraction of the lymphofatty tissue adjacent to the IMA, the lymphofatty tissue surrounding the IMV to the end of the left colic artery was dissected after high ligation of the IMV[8].

Randomization and masking

Patients were randomly assigned to undergo s-CME or e-CME in a 1:1 ratio using a random sequence generator, with block randomization by the center. Random allocations were sequentially numbered in sealed opaque envelopes, which were opened at the beginning of surgery. Patients were blinded to the assigned group until the end of the study.

Study procedures

Surgical procedures for sigmoid colon cancer resection allocated in the s-CME or e-CME group were described in detail previously [8].

Outcome measures

The primary endpoints were to describe defecatory, urinary, and sexual function after high-tie sigmoid colon resection. The secondary outcome was to identify risk factors associated with gastrointestinal and urogenital dysfunction in patients included in the CMELL trial.

Instruments to measure defecatory, urinary, and sexual function

Patients completed four questionnaires at three time points: before surgery (baseline), 1 month after surgery, and 12 months after surgery.

To assess defecatory function, we used two questionnaires: the COREFO (COloREctal Functional Outcome) questionnaire [10], which comprises 27 questions in five categories (defecation frequency, incontinence, social impact, stool-related aspects, and use of medication), and the Low Anterior Resection Syndrome (LARS) questionnaire [11], which comprises five questions (one about each of the following: gas incontinence, incontinence of liquid stool, frequency of bowel movements, clustering of stools, and urgency).

To evaluate the urinary function, we used the International Consultation on Incontinence Questionnaire-Short Form (ICIQ-SF) to assess the severity of urinary incontinence and its impact on the quality of life; possible scores range from 2 to 20 [12].

To evaluate the male erectile function, we used the International Index of Erectile Function (IIEF-5) [13], which evaluates five domains (erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction), classifying erectile dysfunction as severe (IIEF-5 = 5–7), moderate (IIEF-5 = 8–11), mild-to-moderate (IIEF-5 = 12–16), mild (IIEF-5 = 17–21), or absent (IIEF-5 = 22–25). Although erectile dysfunction is usually defined as IIEF-5 $\leq$ 21[14], because of the advanced age of our patients, we redefined erectile dysfunction as IIEF-5 $\leq$ 11 (moderate or severe erectile dysfunction).

To evaluate the female sexual function, we used the Female Sexual Functional Index (FSFI), which comprises 19 questions measuring 6 domains (desire, arousal, lubrication, orgasm, global satisfaction, and pain) [15]. We categorized female sexual function into four groups: severe sexual dysfunction (FSFI = 0–10), moderate sexual dysfunction (FSFI = 11–16), mild sexual dysfunction (FSFI = 17–25), and no sexual dysfunction (FSFI = 26–30); FSFI < 26.55 is commonly accepted as sexual dysfunction.

Predictive variables

We explored the following predictive variables: lymphadenectomy (e-CME or s-CME); age; body mass index (BMI); physical status according to the American Society of Anesthesiologists (ASA) score, dichotomized into I + II or III + IV; diabetes mellitus (no or yes); vein section (no or yes); pT; pN; and adjuvant therapy.

Sample size calculation

Formal power calculation was not undertaken as the original study was designed to investigate whether the number of lymph nodes increases in extended mesocolic excision. Despite functional results were provided as a secondary outcome in the main study, patient functionality was not evaluated in deep. Furthermore, factors associated with functionality at 1 year and surgical recovery were also not assessed previously.

Statistical analysis

We followed the intention-to-treat principle for all analyses. Continuous variables are expressed as medians and interquartile ranges or ranges, as appropriate. Categorical variables are expressed as frequencies and relative frequencies. To compare groups, we used Student's *t*-test or the Mann–Whitney *U* test for continuous variables and the chi-square or Fisher's exact test for categorical variables.

To identify risk factors associated with defecatory, urinary, and sexual dysfunction 1 year after surgery and with the recovery of defecatory, urogenital, and sexual function 1 year after surgery, we used multivariate linear regression.

Statistical significance was set at $p \leq 0.05$. All variables with $p \leq 0.100$ in the univariate analyses were included in the multivariate analyses. We used SPSS v. 20.0 (SPSS Inc, Chicago, IL, USA) for all analyses.

Ethical considerations

This study was conducted in accordance with the principles of the Declaration of Helsinki and "good clinical practice" guidelines. The study was registered as NCT03107650 at ClinicalTrials.gov, and the protocol was approved by each participating center's ethics committee. We followed the Consolidated Standards of Reporting Trials (CONSORT) Guidelines in reporting our findings. All patients provided written informed consent before surgery and before randomization. Patients retained the right to withdraw from the study at any time; patients could be excluded if an exclusion criterion appeared during follow-up.

Results

Patients and baseline characteristics

Seventy-nine patients [45 men and 34 women; 39 from the s-CME arm and 40 from the e-CME arm] were recruited into the original trial. Figure 1 is a flowchart detailing the inclusion of patients in the functional study. Table 1 summarizes the demographic, clinical, surgical, and postoperative

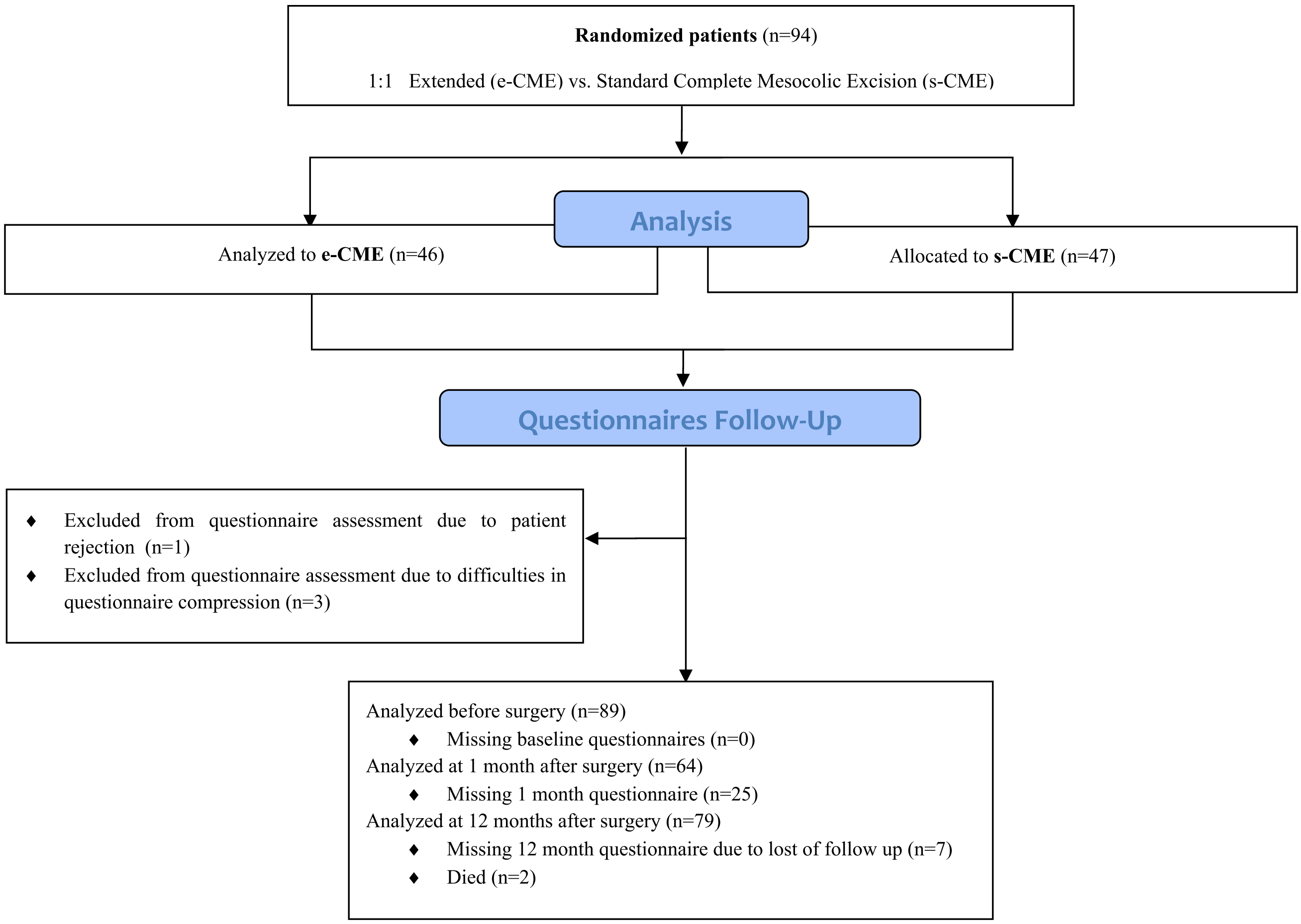

Fig. 1 Flow diagram of the study

characteristics of the patients who completed questionnaires at baseline and 12 months after surgery. There were no significant differences between the two treatment groups in patient characteristics, surgical variables, or pathological outcomes.

A total of 232 questionnaires were collected across the three points of time (baseline, 1 month after surgery, and 12 months after surgery).

Defecatory function

In the entire sample, the median COREFO score was 6.5 (IQR, 0.9−11.1) before surgery, 8.3 (IQR, 3.9−13.9) 1 month after surgery, and 5.5 (IQR, 2.8−10.2) 12 months after surgery.

The median LARS score was 5 (IQR, 0−20) before surgery, 15 (IQR, 3.3−27.8) 1 month after surgery, and 11 (IQR, 0−23) 12 months after surgery (Table 2).

The defecatory function was similar between the two treatment groups at baseline, at 1 month, and at 12 months. The median difference between baseline and 12-month scores was similar for the two groups. One month after surgery, 25.0% of patients had minor LARS and 17.2% had major LARS; the rates of LARS were similar between treatment arms ($p = 0.529$). Twelve months after surgery, 15.2% of patients had minor LARS and 12.7% had major LARS; the rates of LARS were similar between treatment arms (23.1% in s-CME vs. 32.5% in e-CME, $p = 0.548$) (Table 2).

In the univariate regression analysis to identify factors associated with bowel function 1 year after surgery, only positive nodal stage was significant with COREFO scores ($\beta = 0.24$, $p = 0.032$), although there was a trend toward significance for adjuvant chemotherapy ($\beta = 0.20$, $p = 0.084$). However, in the multivariate regression analysis, none of the variables remained significant. No significant associations were observed between any factors and LARS scores (Table 3).

In the univariate regression analysis to identify factors associated with the recovery of defecatory function 1 year after surgery, only diabetes was significantly associated with the difference in COREFO scores ($\beta = 0.24$, $p = 0.032$); this factor remained significant in the multivariate analysis

Table 1 Patient demographics, clinical, surgical, and morbidity variables

	Extended lymphadenectomy ($N=40$)	Standard lymphadenectomy ($N=39$)	Total ($N=79$)	P value
Sex				0.581
Men	24 (60.0%)	21 (53.8%)	45 (57.0%)	
Women	16 (40.0%)	18 (46.2%)	34 (43.0%)	
BMI, kg/m^2*	27.8 (25.7–29.9)	26.7 (23.9–29.1)	27.3 (24.7–29.4)	0.187
Age, years*	69 (58.3–71)	67 (61–72)	67 (59–71)	0.841
ASA score				0.205
ASA I + II	29 (72.5%)	23 (59.0%)	52 (65.8%)	
ASA III + IV	11 (27.5%)	16 (41.0%)	27 (34.2%)	
Tumor location, cm *	20 (18–25)	20 (16–28)	20 (17–25)	0.890
Pre-CEA, ng/mL*	2 (1.3–4)	2.5 (1.6–4.4)	2.2 (1.3–4.2)	0.387
Pre-hemoglobin, g/dL*	14.1 (13.1–15.1)	13.6 (12.3–15.1)	13.8 (12.5–15.1)	0.270
Pre-protein, g/dL *	7 (6.2–7.4)	6.9 (6.5–7.3)	6.9 (6.2–7.3)	0.630
Synchronic metastases				1.000
No	39 (97.5%)	38 (97.4%)	77 (97.5%)	
Yes	1 (2.5%)	1 (2.6%)	2 (2.5%)	
Neoadjuvant treatment				1.000
No	39 (97.5%)	39 (100%)	78 (98.7%)	
Yes	1 (2.5%)	0 (0%)	1 (1.3%)	
Surgical approach				0.337
Laparoscopic	35 (87.5%)	31 (79.5%)	66 (83.5%)	
Robotic	5 (12.5%)	8 (20.5%)	13 (16.5%)	
Conversion to open surgery				0.712
No	37 (92.5%)	35 (89.7%)	72 (91.1%)	
Yes	3 (7.5%)	4 (10.3%)	7 (8.9%)	
Initial approach				0.288
Artery	22 (55.0%)	26 (66.7%)	48 (60.8%)	
Vein	18 (45.0%)	13 (33.3%)	31 (39.2%)	
Anastomosis				0.300
End-to-end	29 (72.5%)	24 (61.5%)	53 (67.1%)	
Side-to-end	11 (27.5%)	15 (38.5%)	26 (32.9%)	
Vein length, cm*	5.5 (4–6)			
Estimate bleeding, mL*	50 (50–100)	50 (50–100)	50 (50–100)	0.210
Operative time, min*	195 (150–241)	180 (160–215)	185 (155–234)	0.224
Dindo Clavien classification				0.773
No	34 (85.0%)	36 (92.3%)	70 (88.6%)	
I	1 (2.5%)	1 (2.6%)	2 (2.5%)	
II	4 (10.0%)	2 (5.1%)	6 (7.6%)	
IIIa	0 (0%)	0 (0%)	0 (0%)	
IIIb	1 (2.5%)	0 (0%)	1 (1.3%)	
Anastomotic leakage				1.000
No	39 (97.5%)	39 (100%)	78 (98.7%)	
Yes	1 (2.5%)	0 (0%)	1 (1.3%)	
Length of stay, days*	5 (4–6)	4 (3–5)	4 (3–6)	0.054
Re-hospitalization				1.000
No	40 (100%)	38 (97.4%)	90 (96.8%)	
Yes	0 (0%)	1 (2.6%)	3 (3.2%)	
T stage				0.339
pTis	4 (10.0%)	3 (7.7%)	7 (8.9%)	
pT1	10 (25.0%)	5 (12.8%)	15 (19.0%)	
pT2	4 (10.0%)	10 (25.6%)	14 (17.7%)	
pT3	14 (35.0%)	15 (38.5%)	29 (36.7%)	
pT4	8 (20.0%)	6 (15.4%)	14 (17.7%)	
N stage				0.935
N0	25 (62.5%)	26 (66.7%)	51 (64.6%)	
N1	12 (30.0%)	10 (25.6%)	22 (27.8%)	
N2	3 (7.5%)	3 (7.7%)	6 (7.6%)	
Adjuvant treatment				0.746
No	24 (60.0%)	22 (56.4%)	46 (58.2%)	
Yes	16 (40.0%)	17 (43.6%)	33 (41.8%)	

Values in parentheses are percentages unless indicated otherwise

*Values are median (interquartile range)

CME, complete mesocolic excision; *BMI*, body mass index; *ASA*, American Society of Anesthesiologists Physical Status Classification System; *CEA*, carcinoembryonic antigen

($\beta = 0.24$, $p = 0.033$). The regression analyses found no significant associations between any factor and the difference in LARS scores (Table 4).

Urinary function

In the entire sample, urinary function was similar at all time points. The median ICIQ-SF score was 2 (IQR, 2−5) before surgery, 2 (IQR, 2−3) 1 month after surgery, and 2 (IQR, 2−3) 1 year after surgery; the median difference between scores on baseline and 12-month assessments was 0 (IQR, 0−0) (Table 2).

Postsurgical urinary function in men

One year after surgery, the ICIQ-SF identified urinary dysfunction in 10 (22.2%) men. Median ICIQ-SF scores 1 month after surgery were similar in the two treatment arms [2 (IQR, 2−2.5) in s-CME and 2 (IQR, 2−3) in e-CME, $p = 0.596$]; however, scores 12 months after surgery were significantly different between arms [2 (IQR, 2−2) in s-CME and 2 (IQR, 2−6.8) in e-CME, $p = 0.026$].

In the univariate regression analysis, only e-CME was significantly associated with ICIQ-SF scores 12 months after surgery ($\beta = 0.33$, $p = 0.026$); we found no significant associations between ICIQ-SF scores at this time point and age, BMI ≥ 30 kg/m^2, diabetes mellitus, IMV section, tumor or nodal pathology stage, or adjuvant treatment (Table 3).

In the univariate regression analysis to identify factors associated with the recovery of male urinary function 1 year after surgery, only e-CME was significantly associated ($\beta = 0.31$, $p = 0.039$); however, after adjustment in the multivariate analysis, this factor did not remain significant (Table 4).

Postsurgical urinary function in women

One year after surgery, the ICIQ-SF identified urinary dysfunction in 10 (29.4%).

The regression analyses found no significant associations between demographic, clinical, or surgical variables and women's ICIQ-SF scores 12 months after surgery (Table 3).

In the univariate regression analysis to identify factors associated with the recovery of female urinary function 1 year after surgery, only diabetes mellitus was significant in the univariate analysis ($\beta = -0.43$, $p = 0.011$); this factor remained significant in the multivariate analysis ($\beta = -0.37$, $p = 0.039$) (Table 4).

Sexual function

Erectile function in men

Median IIEF-5 scores were 18.5 (IQR, 15.8−21.3) at baseline, 15 (IQR, 8.5−19.5) 1 month after surgery, and 13 (IQR, 5.3−18.8) 1 year after surgery (Table 2). One month after surgery, 7 of 21 (33.3%) men had erectile dysfunction; no differences were observed between treatment arms. One year after surgery, 14 of 32 (43.8%) men had moderate-to-severe erectile dysfunction; this proportion was greater in s-CME (60.0%) than in e-CME (29.4%), although differences in median IIEF-5 scores did not reach statistical.

The only risk factor associated with an IIEF score 1 year after surgery was age (β: −0.38, $p = 0.010$, in both the univariate and multivariate analyses). Men with erectile dysfunction 1 year after surgery were older than those without erectile dysfunction at this time point [72 (IQR, 67−74) years vs. 62.5 (IQR, 59.5−69) years, respectively, $p = 0.010$] (Table 3).

The difference between median IIEF scores at baseline and 1 year after surgery was greater in the s-CME group [−7 (IQR, −15.5−0.5) vs. −3 (IQR, −6−0) in the e-CME group, $p = 0.046$]. In the regression analyses to identify factors associated with the recovery of erectile function 1 year after surgery, only the treatment arm was associated with erectile function recovery ($\beta = 0.38$, $p = 0.046$, on both the univariate and multivariate analyses) (Table 4).

Sexual function in women

Median FSFI scores were 27.1 (IQR, 23−30) at baseline, 5.8 (IQR, 2−30.2) 1 month after surgery, and 28.3 (IQR, 23.9−31.2) 1 year after surgery (Table 2). The median difference in scores between baseline and 12 months after surgery was 0.9 (IQR, −2.9−3.1).

Median baseline sexual function was similar in the two treatment arms. Of the 11 women who were sexually active before surgery, 8 (73%) were sexually active 1 year after surgery.

In the regression analyses to identify factors associated with sexual function 1 year after surgery, only age was significant (in the univariate analysis β: −0.59, $p = 0.001$; in the multivariate analysis β: −0.54, $p = 0.002$) (Table 3).

The regression analyses found no significant associations between any factor and the difference in FSFI scores at baseline and 1 year after surgery (Table 4).

Table 2 Questionnaire assessments of defecatory, urinary, and sexual function at different time points

	Baseline				1 month				12 months			
	s-CME	e-CME	Total		s-CME	e-CME	Total		s-CME	e-CME	Total	
	n = 45	*n* = 44	*N* = 89	*p*-value	*n* = 31	*n* = 33	*N* = 64	*p*-value	*n* = 39	*n* = 40	*N* = 79	*p*-value
COREFO*	8.3 (1.4–12.9)	5.6 (0.9–10.2)	6.5 (0.9–11.1)	0.118	8.3 (3.7–14.8)	8.3 (4.6–12.0)	8.3 (3.9–13.9)	0.657	5.6 (1.8–11.1)	6.0 (2.8–9.9)	5.5 (2.810.2)	0.662
LARS questionnaire*	5 (0–19)	8 (1–23.8)	5 (0–20)	0.381	9 (0–27)	20 (4.5–29)	15 (3.3–27.8)	0.261	9 (0–20)	13 (5–23.8)	11 (0–23)	0.249
LARS												
0–20 (no LARS)	37 (82.2%)	31 (70.5%)	68 (76.4%)	0.294	20 (64.5%)	17 (51.5%)	37 (57.8%)	0.513	30 (76.9%)	27 (67.5%)	57 (72.2%)	0.548
21–29 (minor LARS)	6 (13.3%)	7 (15.9%)	13 (14.6%)		6 (19.4%)	10 (30.3%)	16 (25.0%)		4 (10.3%)	8 (20.0%)	12 (15.2%)	
30–42 (major LARS)	2 (4.4%)	6 (13.6%)	8 (9.0%)		5 (16.1%)	6 (18.2%)	11 (17.2%)		5 (12.8%)	5 (12.5%)	10 (12.7%)	
ICIQ-SF*	2 (2–5)	2 (2–4.3)	2 (2–5)	0.543	2 (2–3)	2 (2–4.5)	2 (2–3)	0.434	2 (2–2)	2 (2–4.8)	2 (2–3)	0.119
FSFI*	27.1 (23–30.6)	26.9 (22.9–30)	27.1 (23–30)	0.931	14.9 (2–31.3)	5.8 (3.9–28)	5.8 (2–30.2)	0.905	28.3 (24.7–30.6)	28.9 (22.8–32.9)	28.3 (23.9–31.2)	0.792
IIEF-5*	19.5 (17–23.8)	17.5 (14.8–20.3)	18.5 (15.8–21.3)	0.164	13 (6–21.5)	17 (11.8–19.5)	15 (8.5–19.5)	0.476	9 (5–15)	12 (7–18)	13 (5.3–18.8)	0.220

*Numeric variables are expressed as median (IQR)

COREFO, COloREctal Functional Outcome questionnaire; *LARS*, low anterior resection syndrome; *ICIQ-SF*, International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form; *FSFI*, Female Sexual Function Index; *IIEF-5*, International Index of Erectile Function

Table 3 Factors associated with defecatory, urinary, and sexual function 12 months after surgery

	COREFO		LARS		Male ICIQ-SF		Women ICIQ-SF		IIEF-5		FSFI	
	β	p-value	β	p-value	β	p-value	β	p-value	β	p-value	β	p-value
Univariate linear regression												
Lymphadenectomy (e-CME vs. s-CME)	0.08	0.662	0.12	0.249	0.33	**0.026**	−0.06	0.735	0.18	0.220	0.01	0.996
Age	−0.14	0.211	0.01	0.899	0.07	0.667	−0.27	0.124	−0.38	**0.010**	−0.59	**0.001**
BMI, kg/m^2 (≥ 30 vs. < 30)	0.10	0.378	−0.14	0.210	−0.16	0.294	−0.12	0.512	−0.15	0.348	0.02	0.924
ASA (III + IV vs. I + II)	−0.14	0.211	−0.10	0.384	−0.13	0.386	0.12	0.478	−0.19	0.222	0.18	0.308
DM (yes vs. no)	0.17	0.136	0.08	0.502	0.07	0.663	−0.17	0.334	0.03	0.836	−0.08	0.669
Vein section (yes vs. no)	0.11	0.322	0.18	0.105	0.25	0.100	0.14	0.430	−0.04	0.820	0.18	0.292
T stage (T3-T4 vs. Tis-T2)	0.10	0.337	0.08	0.500	0.25	0.109	0.11	0.524	−0.16	0.314	−0.34	0.051
N stage (N + vs. N0)	0.24	**0.032**	0.07	0.550	−0.18	0.250	−0.05	0.783	0.03	0.834	−0.23	0.195
Adjuvant treatment (yes vs. no)	0.20	0.084	0.08	0.493	−0.13	0.386	−0.06	0.735	0.11	0.467	−0.30	0.082
Multivariate linear regression												
Lymphadenectomy (e-CME vs. s-CME)	0.07	0.554	0.05	0.717	0.27	0.104	−0.05	0.779	0.18	0.216	−0.06	0.720
Age							0.12	0.500	−0.38	**0.010**	−0.54	**0.002**
BMI, kg/m^2 (≥ 30 vs. < 30)												
ASA (III + IV vs. I + II)												
DM (yes vs. no)	0.17	0.123										
Vein section (yes vs. no)			0.16	0.191	0.12	0.462						
T stage (T3-T4 vs. Tis-T2)					0.23	0.117					−0.12	0.287
N stage (N + vs. N0)	0.21	0.222									0.02	0.920
Adjuvant treatment (yes vs. no)											−0.03	0.912

BMI, body mass index; *ASA*, American Society of Anesthesiologists Physical Status Classification System; *e-CME*, extended complete mesocolic excision; *s-CME*, standard complete mesocolic excision; *DM*, diabetes mellitus; *COREFO*, COloREctal Functional Outcome questionnaire; *LARS*, Low Anterior Resection Syndrome questionnaire; *ICIQ-SF*, International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form; *IIEF-5*, International Index of Erectile Function; *FSFI*, Female Sexual Function Index (FSFI)

Table 4 Differences between total scores on questionnaires assessing defecatory, urinary, and sexual function administered before and 12 months after surgery for sigmoid cancer

	COREFO		LARS		Male ICIQ-SF		Women ICIQ-SF		IIEF-5		FSFI	
	β	*p*-value	β	*p*-value	β	*p*-value	β	*p*-value	β	*p*-value	β	*p*-value
Univariate linear regression												
Lymphadenectomy (e-CME vs. s-CME)	0.18	0.117	0.01	0.933	0.31	**0.039**	−0.09	0.634	0.38	**0.046**	0.03	0.930
Age	−0.13	0.245	−0.08	0.514	0.14	0.375	−0.08	0.658	0.03	0.851	0.01	0.984
BMI, kg/m^2 ($\geq$30 vs. <30)	0.09	0.431	−0.04	0.746	0.02	0.907	−0.32	0.065	−0.08	0.655	−0.08	0.827
ASA (III+IV vs. I+II)	−0.04	0.722	−0.14	0.225	−0.07	0.663	−0.16	0.355	0.01	0.961	−0.10	0.767
DM (yes vs. no)	0.24	**0.032**	0.06	0.573	0.12	0.441	−0.43	**0.011**	0.17	0.320		
Vein section (yes vs. no)	−0.03	0.793	0.14	0.204	0.22	0.158	0.20	0.244	0.11	0.554		
T stage (T3-T4 vs. Tis-T2)	−0.02	0.842	0.20	0.076	0.15	0.337	0.19	0.276	−0.12	0.503	−0.47	0.148
N stage (N+vs. N0)	0.11	0.392	−0.03	0.793	−0.16	0.291	−0.24	0.174	0.09	0.596	0.23	0.496
Adjuvant treatment (yes vs. no)	0.04	0.703	−0.03	0.763	−0.03	0.861	−0.67	0.704	0.10	0.585	−0.11	0.756
Multivariate linear regression												
Lymphadenectomy (e-CME vs. s-CME)	0.17	0.121	0.01	0.948	0.27	0.116	−0.15	0.362	0.38	**0.046**	−0.22	0.529
Age												
BMI, kg/m^2 ($\geq$30 vs. <30)							−0.20	0.238				
ASA (III+IV vs. I+II)												
DM (yes vs. no)	0.24	**0.033**					−0.365	**0.039**				
Vein section (yes vs. no)					0.10	0.549						
T stage (T3-T4 vs. Tis-T2)			0.20	0.078							−0.57	0.135
N stage (N+vs. N0)							−0.22	0.184				
Adjuvant treatment (yes vs. no)												

BMI, body mass index; *ASA*, American Society of Anesthesiologists Physical Status Classification System; *e-CME*, extended complete mesocolic excision; *s-CME*, standard complete mesocolic excision; *DM*, diabetes mellitus; *COREFO*, COloREctal Functional Outcome questionnaire; *LARS*, Low Anterior Resection Syndrome questionnaire; *ICIQ-SF*, International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form; *IIEF-5*, International Index of Erectile Function; *FSFI*, Female Sexual Function Index (FSFI)

Discussion

The current study explored the impact of high-tie sigmoidectomy with s-CME and e-CME for sigmoid colon cancer on defecatory and genitourinary function. Regardless of the extent of lymphadenectomy, sigmoid resection with high ligation had an impact on defecatory and genitourinary function. One year after surgery, 15.2% of patients had minor LARS and 12.7% had major LARS; 22.2% of the men and 29.4% of the women had urinary dysfunction; and 43.8% of the men and 27.3% of the women had sexual dysfunction. Changes in defecatory, urinary, and sexual function after colon cancer surgery are often underestimated and underreported [16]. Our findings underline the importance of taking into account the changes that sigmoid resection has on many patients' defecatory and genitourinary functions.

In men, extending lymphadenectomy to include the IMV territory (e-CME) resulted in higher rates of urinary dysfunction 1 year after surgery. However, after adjustment in the multivariate analysis, this factor did not remain significant. In women, e-CME was not associated with urinary dysfunction or worse recovery of urinary function at 1 year of surgery.

Remarkably, 1 year after surgery, 43.8% of men had moderate-to-severe erectile dysfunction and 27.3% of the women who were sexually active before surgery had not resumed sexual activity. In both sexes, age was the only risk factor associated with sexual dysfunction 1 year after surgery, and e-CME was not associated with worse recovery of sexual function. However, given the high median age of our sample (71 years in men and 56 years in women), in interpreting our findings, it is important to consider that declines in sexual interest correlate with age and that age-related health problems have a negative impact on sexual desire [17]. Moreover, genitourinary dysfunction manifests as mostly subjective symptoms that are susceptible to evaluation bias when measured with questionnaire-based interviews. Despite strong evidence for deteriorated sexual function in colon cancer survivors of both sexes [8, 18, 19], it is important to remember that multiple factors can influence sexual dysfunction [20]. Finally, a lack of data from women, possibly related to a reluctance to respond to questions about their sexuality, makes it difficult to reach firm conclusions [18, 20].

The main cause of genitourinary dysfunction after colorectal surgery seems to be injuries to the hypogastric nerves and/or to the sacral splanchnic nerve [21–23]. Damage to the hypogastric plexus during para-aortic dissection and high ligation of the IMA can result in defecatory and/or genitourinary dysfunction. However, current recommendations regarding CME for cancer of the sigmoid colon reflect the relative lack of information about its effects on defecatory, urinary, and sexual function.

Defecatory function after colon surgery depends on preoperative function, possible nerve damage during surgery, and mechanical changes in the rectum. Up to 41% of patients have minor or major LARS after sigmoid resection for cancer [16, 24]. In our study, only 23.1% of the patients in the s-CME group and 32.5% of those in the e-CME group developed LARS; there were no significant differences between groups at any time point.

The high rates of defecatory and genitourinary dysfunction in both treatment arms of our trial are probably due, at least, in part, to using a high tie in all patients. The oncological benefits of the high tie are controversial. In a randomized study of 331 patients in 2018, Fujii et al. [25] found no differences between high tie and low tie in the rate of anastomotic dehiscence, survival, or local recurrence. Moreover, an observational study including 999 patients found that increasing the number of lymph nodes dissected had no benefit in overall survival or recurrence [26].

Limitations

This was an exploratory study with a small number of patients and with no formal power calculation. Additionally, due to the logistics of questionnaire collection, there were some missing data, mostly in the 1-month postoperative time point, highlighting the difficulty of collecting questionnaires for research. However, there was good-quality data collection at the different study time points.

We did not collect information about whether the surgeon damaged the hypogastric plexus during lymphadenectomy; collecting this information would have allowed us to stratify analyses about functional outcomes and would probably have improved our interpretation of the results. Moreover, we did not use questionnaires to assess ejaculatory function, the International Prostate Symptom Score to assess male urinary function, or other measures that might also have provided useful information.

Nevertheless, the data are useful exploratory results that justify and guide further larger studies to investigate the trend, which were identified in this study.

Conclusions

High tie of the IMA during sigmoidectomy is associated with a high rate of defecatory and genitourinary dysfunction. In both sexes, the sexual function at 1 year after surgery was associated with age. Further studies are needed to investigate the impact of lymphadenectomy and its effects on urinary and sexual function in patients with sigmoid cancer.

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Author's contributions **Pere Planellas** participated in study conception and design, literature review, acquisition of data, analysis and interpretation of data, drafting of the manuscript, and critical revision and final approval of the manuscript. **Franco Marinello** participated in study conception and design, acquisition of data, analysis and interpretation of data, and critical revision and final approval of the manuscript. **Garazi Elorza** participated in the acquisition of data and critical revision and final approval of the manuscript. **Thomas Golda** participated in the study conception and design, acquisition of data, analysis and interpretation of data, and critical revision and final approval of the manuscript. **Ramon Farrés** participated in the acquisition of data, analysis and interpretation of data, and critical revision and final approval of the manuscript. **Eloy Espín-Basany** participated in the study conception and design, acquisition of data and critical revision and final approval of the manuscript. **José María Enríquez-Navascués** participated in the study conception and design, acquisition of data, analysis and interpretation of data, and critical revision and final approval of the manuscript. **Esther Kreisler** participated in the acquisition of data and critical revision and final approval of the manuscript. **Lídia Cornejo** participated in the study conception and design, literature review, acquisition of data, analysis and interpretation of data, drafting of the manuscript, and critical revision and final approval of the manuscript. **Antoni Codina-Cazador** participated in the study conception and design, literature review, analysis and interpretation of data, critical revision and final approval of the manuscript. All authors agree to be held accountable for all aspects of the work.

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Data availability The data used to support the findings of this study are not publicly available due to the center-patient nature.

Declarations

Competing interests The authors declare no competing interests.

Ethical approval This randomized clinical trial was approved by the 4 hospital's ethics committees and was carried out in accordance with the 1964 Helsinki Declaration and its later amendments.

Consent to participate All patients provided written informed consent before inclusion. Patients retained the right to withdraw from the study at any time throughout the study and were excluded if any exclusion criterion appeared during the follow-up. The study was registered at Clinicaltrials.org (NCT03083951) on March 20, 2017.

Conflict of interest The authors declare no competing interests.

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