Functional outcomes of patients undergoing successful redo surgery after failed primary colorectal or coloanal anastomosis for rectal cancer

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Abstract

Q1 ***Background*:** After a failure of a colorectal or coloanal anastomosis, redo anastomotic surgery aims to avoid the risk of permanent stoma but, overall, to provide a satisfactory functional result and quality of life. Very limited data exist regarding the long-term results after a successful redo anastomosis. The present study aimed to report the long-term functional outcomes and quality of life in patients after a successful redo colorectal anastomosis or coloanal anastomosis.

***Methods*:** Between 2007 and 2018, all patients who had a successful restoration of bowel continuity after a failed primary anastomosis performed for a rectal cancer were included. Functional outcomes and quality of life were assessed using the low anterior rectal syndrome score and the Gastrointestinal Quality of Life Index.

***Results*:** One hundred and twenty-seven patients were eligible for inclusion in this study, with long-term functional outcomes assessed in 73 patients (57%). After a median follow-up of 69 months, 31 patients presented no or minor low anterior rectal syndrome (42%), whereas 31 patients reported a major low anterior rectal syndrome (42%). A definitive stoma was confectioned in 11 patients (15%), despite the technical success of redo anastomosis due to poor functional results. Only operative interval <36 months was associated with a poor functional outcome (P = .001), whereas all other factors such as pelvic radiotherapy were not (P = .848). An absence of major low anterior rectal syndrome was the only factor associated with improved quality of life (P = .001).

***Conclusion*:** After successful redo colorectal anastomosis or coloanal anastomosis, good functional outcomes can be achieved in almost half of patients with a well-preserved quality of life but requires a prolonged postoperative period of rehabilitation.

Introduction

Q2 Avoidance of a permanent stoma is one of the main outcomes in colorectal surgery, with improved surgical techniques, including intersphincteric resections for low rectal cancers, being developed to reduce stoma rates.[1,2] However, when an anastomotic complication occurs, the preservation of long-term bowel continuity is threatened. For patients

undergoing rectal cancer resection with a colorectal (CRA) or coloanal anastomosis (CAA), 5% to 22% will ultimately require a permanent stoma due to anastomotic failure or poor functional outcomes.[3,4] Numerous surgical procedures including delayed CAA or rectal sleeve advancement (derived from the Soave's procedure) have been employed to restore bowel continuity to patients with unfavorable local conditions following failed primary anastomosis. Restoration of bowel continuity with redo CRA or CAA requires skilled surgeons as it is a challenging operation; however, successful restoration has been reported in up to 79% of patients.[5]

Ultimately the goal of redo anastomotic surgery is to provide bowel continuity with superior quality of life compared to a permanent stoma. While the benefit of bowel continuity over permanent stoma in rectal cancer is well documented,[6] redo anastomosis constitutes a specific and different situation with limited data to date.[5,7–10]

Therefore, the objective of this study was to report the long-term functional outcomes and quality of life in patients after a successful redo CRA or CAA in the context of rectal cancer surgery.

Methods

Population

Between October 2007 and March 2018, all consecutive patients undergoing a redo anastomosis after a failed primary CRA or CAA performed for a rectal cancer in our institution were recorded. Patients initially operated for another disease than a rectal cancer were excluded. A failed CRA or CAA was defined as being unable to preserve bowel continuity due to an anastomotic leakage, a necrotic anastomosis, or a symptomatic anastomotic stricture. At the time of redo surgery, the initial anastomosis was either in situ associated with a diverting stoma or previously resected by a Hartmann's procedure. Data regarding the index surgery and redo surgery was collected retrospectively from patient records.

Because the objective of the current study was to evaluate the long-term results of successful redo surgery, only living patients were included. Patients with a definitive stoma following poor functional outcomes post redo surgery were also included in the study. Patients who observed an initial failure of the redo surgery defined by the absence of restoration of bowel continuity, patients requiring a stoma formation due to local tumor recurrence, and deceased patients were excluded.

Surgical technique

All surgical procedures were always performed by a specialized colorectal surgeon in our tertiary reference center. A full mid-line laparotomy and adhesionolysis was performed in the lithotomy position. The redo surgery consisted of the formation of a tension-free CRA or CAA. To do so, the colon was mobilized as much as necessary, with additional maneuvers such as a transmesenteric passage of the colon (Toupet procedure[11]) or a Deloyers procedure[12] used. When redo surgery was performed for stenosis, the colon was usually transected 2 cm below the stenosis. A local tumor recurrence was always ruled out before performing a redo anastomosis.

Primary anastomosis with the rectum or anus was performed at the end of the procedure. If necessary, a delayed CAA was performed where the colonic stump was externalized during the first procedure and anastomosed with the anus in a second procedure usually within 22 days to allow local healing.

In cases with unfavorable local conditions, rectal sleeve advancement was performed as described in the Soave procedure. This technique consists of preserving the distal rectal muscular layer by performing a mucosectomy of the rectal stump and bringing the colon through the rectal sleeve to anastomose with the anus.[7]

The pelvis was systematically drained. A diversion ileostomy or colostomy was performed at the surgeon's discretion, which was reversed 6 to 8 weeks later after favorable clinical and radiological assessment of the anastomosis.

Standardized scoring of long-term results

To assess long-term outcomes, all patients were prospectively contacted between September and December 2019 by phone, mail, or during a consultation in clinics and, after obtaining consent, they were asked to answer questionnaires corresponding to different standardized scores. All patients received the questions from both the low anterior rectal syndrome (LARS) score and Gastrointestinal Quality of Life Index (GIQLI). In addition, the female sexual function

index (FSFI) was submitted to women, whereas the international prostate symptom score (IPSS) and the international index of erectile function (IIEF5) was submitted to men. The delay between the redo surgery and the questionnaire was at least 12 months.

The LARS score allows a standardized assessment of functional outcomes after rectal surgery.[13] It contains 5 questions, each with 3 to 4 possible answers rated from 0 to 16 points. The total of the score defines the value of the LARS score, from 0 to 42. There are 3 scoring levels: no LARS (score between 0 and 20), minor LARS (score between 21 and 29), and major LARS (score between 30 and 42). In the present study, a poor, long-term functional outcome was defined by patients with a major LARS or by the formation of a definitive stoma for poor functional outcomes after a failed restoration of bowel function.

The GIQLI evaluates the global quality of life for digestive diseases.[14] This score is composed of 36 items ranging from 0 to 4; the higher the score the better the quality of life. This correlation is progressive with no threshold value identified.

The FSFI is a validated questionnaire for the evaluation of sexual function of women.[15] It consists of 19 items scored from 0 to 5. The total of the scores determines the value of the FSFI score ranging from 4 to 95. A FSFI score <26 is the cutoff defining the presence of a sexual dysfunction.[16]

The IPSS score assesses the urinary functional results in men.[17] It contains 7 items, each item ranging from 0 to 5. The sum of the scores determines the value of the IPSS score, which varies from 0 to 35. There are 3 degrees of severity: absence or mild urinary dysfunction (score between 0 and 7), moderate urinary dysfunction (score between 8 and 19), and severe urinary dysfunction (score between 20 and 35).

The IIEF5 score evaluates erectile function in men with 5 items, each score between 0 and 5.[18] The total determines the value of the IIEF5 score from 1 to 25. There are 5 degrees of erectile dysfunction: noninterpretable score (score between 1 and 4), severe erectile dysfunction (score between 5 and 10), moderate erectile dysfunction (score between 11 and 15), mild erectile dysfunction (score between 16 and 20), and normal erectile function (score between 21 and 25).

Statistical analysis

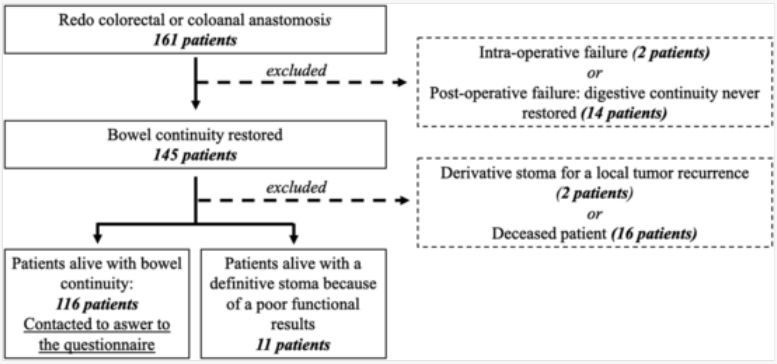
Quantitative data following a normal distribution was expressed as mean ± standard deviation (range) and compared using the *t* test, whereas quantitative data not normally distributed was expressed as medians and interquartile range (IQR) and compared using the Mann-Whitney *U* test. Qualitative data was reported as frequencies and percentages and compared using the χ^2 test or the Fisher exact test, as appropriate. All tests were 2-sided. A P value of $< .05$ was considered statistically significant. All analyses were performed using SPSS software, version 26 (IBM Corp, Armonk, NY).

Results

Population

From October 2007 to March 2018, 161 patients underwent an attempted redo anastomosis after a failed primary CRA or CAA performed for a rectal cancer. Bowel continuity was restored in 145 patients (90%). After exclusion of deceased patients (n = 16) and patients with a stoma formed for a local recurrence (n = 2), 127 patients (79%) were eligible for evaluation of long-term functional outcomes. Among these, 116 patients were alive with bowel continuity, and 11 patients were alive with a definitive stoma performed due to poor functional outcomes after a median interval of 15 months (IQR 10–27) from the redo surgery (Fig 1). From the 116 patients alive with bowel continuity, 62 patients (53%) were successfully contacted and agreed to complete the LARS questionnaire. The median interval time between the redo surgery and the LARS questionnaire was 69 months (IQR 39–102). Demographics and details concerning the initial and redo surgery are reported in Table I.

Fig 1



Flow chart of patients undergoing redo CRA or CAA.

Table I

The table layout displayed in this section is not how it will appear in the final version. The representation below is solely purposed for providing corrections to the table. To preview the actual presentation of the table, please view the Proof.

Demographics and characteristics of initial and redo surgeries among analyzed patients (responder to LARS questionnaire or definitive stoma because of poor functional results after redo surgery)

	Population *N* = 73
Population	
Sex (female versus male)	36 (49)*/37 (51)
Age (y)	62 ± 10 (36–80)†
BMI (kg/m^2)	24 ± 4 (16–35)
BMI ≥30 kg/m^2	10 (14)
ASA ≥3	5 (7)
Diabetes	11 (15)
Active smoking	11 (15)
Pelvic radiotherapy	48 (66)
Initial surgery	
Distance from the tumor low margin to the anal sphincter (cm)	3.0 (IQR 1.9–4.9)‡
Distance from the anastomosis to the anal sphincter (cm)	1.0 (IQR 0–1.0)
Initial anastomosis (colorectal versus coloanal)	5 (7)/68 (92)
Redo surgery	
Date of redo surgery	
Period 1: 2007–2012	20 (27)
Period 2: 2013–2018	53 (73)
Initial anastomosis preserved versus Hartmann procedure prior to redo surgery	69 (95)/4 (5)
Causes	
Anastomotic leakage	59 (81)
Stricture of the anastomosis	13 (18)
Necrosis of the anastomosis	1 (1)

Distance from the anastomosis to the anal sphincter (cm)	0 (IQR 0–0)
Redo anastomosis (colorectal versus coloanal)	1 (1)/72 (99)
Coloanal anastomosis	
Immediate versus delayed	54 (75)/18 (25)
Rectal sleeve advancement	21 (29)
Surgical anastomotic reconstruction	
Straight	68 (93)
Side-to-end	5 (7)
Associated procedure	
Toupet procedure	18 (25)
Deloyers procedure	9 (12)
Defunctioning stoma	70 (96)
Postoperative morbidity	31 (43)
Postoperative severe morbidity[§]	16 (22)
Intra-abdominal septic morbidity	25 (34)
Anastomotic leakage	18 (25)
Intra-abdominal abscess	7 (10)

ASA, American Society of Anesthesiologists; *BMI,* body mass index;

Table Footnotes

Q7

* Number of cases (percentage of cases).

† Mean ± standard deviation (minimum-maximum) for quantitative variables following normal distribution.

‡ Median (IQR) for quantitative variables following non-normal distribution.

§ Defined by Dindo-Clavien ≥3.

Finally, long-term functional outcomes were assessed in 73 of the 127 eligible patients (57%) including the 62 patients with a bowel continuity who completed the LARS questionnaire and the 11 patients with a definitive stoma performed due to poor functional outcomes of the redo anastomosis.

Long-term outcomes

After a median follow-up of 69 months (IQR 39–102) from redo surgery, the median value of the LARS score was 30 (IQR 18–35). Details of intestinal function and LARS scores are reported in Table II. A good, long-term functional outcome (no stoma for poor functional outcome and no major LARS) was observed in 43% of patients after a technical success of restorative surgery (31 of 73). More broadly, among patients who underwent an attempted redo anastomosis after a failed primary CRA or CAA, including patients without restoration of bowel continuity because of intraoperative (n = 2) or postoperative failure (n = 14) and patients secondarily developing tumor local recurrence requiring a derivative stoma (n = 2), a good, long-term functional outcome was achieved in only 35% (31 of 94).

Table II

The table layout displayed in this section is not how it will appear in the final version. The representation below is solely purposed for providing corrections to the table. To preview the actual presentation of the table, please view the Proof.

Long-term digestive, sexual, urinary, and erectile function

	Population
Digestive outcome and LARS score	N = 62

Daytime fecal frequency	
<1 per d: 4 points	9 (15) *
Between 1 and 3 per d: 2 points	23 (37)
Between 4 and 7 per d: 0 point	26 (42)
>7 per d: 5 points	4 (6)
Leakage of liquid stool	
No, never: 0 point	10 (16)
Yes, less or at least once a week: 3 points	52 (84)
Flatus incontinence	
No, never: 0 point	25 (40)
Yes, less than once per week: 4 points	10 (16)
Yes, at least once per week: 7 points	27 (44)
Fecal fragmentation	
No, never: 0 point	10 (16)
Yes, less than once per week: 9 points	14 (23)
Yes, at least once per week: 11 points	38 (61)
Urgencies	
No, never: 0 point	19 (31)
Yes, less than once per week: 11 points	18 (29)
Yes, at least once per week: 16 points	25 (40)
No LARS (0–20 points)	17 (27)
Minor LARS (21–29 points)	14 (23)
Major LARS (30–42 points)	31 (50)
Sexual function in women (FSFI score)	$n = 25$
No sexual function disorder (26–95 points)	9 (36)
Sexual function disorder (4–25 points)	16 (64)
Urinary function in men (IPSS score)	$n = 25$
Absence or mild urinary dysfunction (0–7 points)	16 (64)
Moderate urinary dysfunction (8–19 points)	8 (32)
Severe urinary dysfunction (20–35 points)	1 (4)
Erectile function in men (IIEF5 score)	$n = 24$
Normal erectile function (21–25 points)	3 (13)
Mild erectile dysfunction (16–20 points)	2 (8)
Moderate erectile dysfunction (11–15 points)	1 (4)
Severe erectile dysfunction (5–10 points)	18 (75)
Noninterpretable (1–4 points)	0 (0)

Table Footnotes

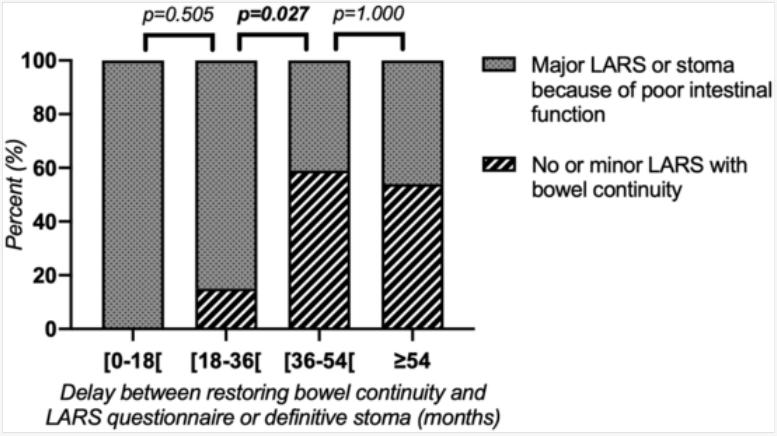
* Number of cases (percentage of cases).

A total of 62 patients with restorative bowel continuity responded to the LARS questionnaire, of whom 33 patients were female. Twenty-five women (76%) agreed to respond to the FSFI score after a median delay from the redo surgery of 70 months (IQR 43–104). Among the 29 men, 25 consented to respond to the IPSS score (86%), with 24 responding to the IIEF5 score (83%). The median delay between the redo surgery and the patient surveys was 70 months (IQR 43–104) for the IPSS score and 81 months (IQR 49–108) for the IIEF5 score. Sixty-four percent of women had sexual dysfunction (16 of 25). Seventy-nine percent of men had moderate to severe erectile dysfunction (19 of 24), with 36% having moderate to severe urinary dysfunction (9 of 25) (Table II).

Predictive factors of long-term outcomes

The median interval between redo surgery and functional evaluation was significantly longer for patients with good functional result (73 months [IQR 48–108]) compared to patients with major LARS (37 months [IQR 26–74]; P = .004). The proportion of patients with good functional outcomes increased progressively with longer follow-up, with a cutoff of 36 months being the time for improved outcomes (Fig 2). The analysis of the risk factors potentially responsible for poor functional outcomes is presented in Table III. A postoperative interval of <36 months was the only risk factor significantly associated with poor functional outcomes (P = .001). Interestingly, pelvic radiotherapy did not have an impact on functional outcomes (bad outcomes 67% vs good outcomes 65%; P = .848).

Fig 2



Evolution of functional outcomes over time following redo surgery.

Table III

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Analysis of factors associated with poor functional outcomes

	No or minor LARS with bowel continuity n = 31	Major LARS or stoma because of poor intestinal function n = 42	P value
Population			
Sex (female versus male)	15 (48)*/16 (52)	21 (50)/21 (50)	.982
Age (y)	64 ± 9 (47–79)†	60 ± 11 (36–80)	.796
BMI (kg/m^2)	25 ± 5 (17–35)	24 ± 4 (16–32)	.131
BMI ≥30 kg/m^2	3 (10)	7 (17)	.391
ASA ≥3	2 (7)	3 (7)	1.000
Diabetes	3 (10)	8 (19)	.335
Active smoking	5 (16)	6 (14)	1.000

Pelvic radiotherapy	20 (65)	28 (67)	.848
Initial surgery			
Distance from the tumor low margin to the anal sphincter (cm)	4.5 (IQR 2.5–6.6)‡	2.8 (IQR 1.6–3.8)	.121
Distance from the anastomosis to the anal sphincter (cm)	1.0 (IQR 0.75–1.0)	1.0 (IQR 0–1.0)	.161
Initial anastomosis (colorectal versus coloanal)	3 (10)/28 (90)	2 (5)/40 (95)	.645
Redo surgery			
Date of the redo surgery			.183
Period 1: 2007–2012	11 (35)	9 (21)	
Period 2: 2013–2018	20 (65)	33 (79)	
Initial anastomosis preserved versus Hartmann procedure before redo surgery	29 (94)/2 (7)	40 (95)/2 (5)	1.000
Causes			
Anastomotic leakage	24 (77)	35 (83)	.526
Stricture of the anastomosis	7 (23)	6 (14)	.360
Necrosis of the anastomosis	0 (0)	1 (2)	1.000
Distance from the anastomosis to the anal sphincter (cm)	0 (IQR 0–0)	0 (IQR 0–0)	.390
Redo anastomosis (colorectal versus coloanal)	0 (0)/31 (100)	1 (2)/41(92)	1.000
Coloanal anastomosis			
Immediate versus delayed	24 (77)/7 (23)	30 (73)/11 (27)	.680
Rectal sleeve advancement	10 (32)	11 (27)	.616
Surgical anastomotic reconstruction (straight versus side-to-end)	28 (90)/3 (10)	40 (95)/2 (5)	.645
Associated procedure			
Toupet procedure	9 (29)	9 (21)	.456
Deloyers procedure	4 (13)	5 (12)	1.000
Defunctioning stoma	29 (94)	41 (98)	.571
Postoperative morbidity	14 (45)	17 (41)	.811
Postoperative severe morbidity§	7 (23)	9 (21)	.906
Intra-abdominal septic morbidity	12 (39)	13 (31)	.490
Anastomotic leakage	8 (26)	10 (24)	.845
Intra-abdominal abscess	4 (13)	3 (7)	.448
Interval between redo surgery and LARS questionnaire or definitive stoma <36 mon	2 (7)	19 (45)	**.001**

Q8 Bolded value xxxx.

ASA, American Society of Anesthesiologists; *BMI, b*ody mass index.

Table Footnotes

* Number of cases (percentage of cases).

† Mean ± standard deviation (minimum-maximum).

‡ Median (IQR) for quantitative variables following non-normal distribution.

§ Defined by Dindo-Clavien ≥3.

A postoperative interval of <36 months was not associated with sexual dysfunction in women (P = .602) and moderate to severe erectile (P =1.000) or urinary dysfunction (P =1.000) in men.

Quality of life

Among the 62 patients who responded to the LARS questionnaire, 60 completed the GIQLI score (97%), with a median delay from the redo surgery of 69 months (IQR 38–100). The median value of the GIQLI score was 110 (IQR 100–120). As no cutoff for good or poor quality of life has been defined in the literature, the median value observed in this study was arbitrary and chosen to separate patients with good quality of life (GIQLI ≥110) from patients with poor quality of life (GIQLI <110). In univariate analysis conducted to find pre, peri, and postoperative factors impacting long-term quality of life, only the absence of major LARS was significantly associated with a good quality of life (P = .001) (Table IV). A poor quality of life (GIQLI <110) was not associated with sexual dysfunction in women (P = 1.000) or moderate to severe erectile dysfunction (P = .317) or moderate to severe urinary dysfunction in men (P = 1.000).

Table IV

The table layout displayed in this section is not how it will appear in the final version. The representation below is solely purposed for providing corrections to the table. To preview the actual presentation of the table, please view the Proof.

Pre, peri, and postoperative factors associated with good quality of life

	Patients with good quality of life (GIQLI ≥110) n = 30	Patients with poor quality of life (GIQLI <110) n = 30	P value
Population			
Sex (female versus male)	16 (53)*/14 (47)	15 (50) /15 (50)	.796
Age (y)	63 ± 11 (38–79)†	60 ± 10 (36–80)	.284
BMI (kg/m^2)	24 ± 4 (17–33)	24 ± 5 (16–35)	.734
BMI ≥30 kg/m^2	3 (10)	4 (13)	1.000
ASA ≥3	2 (7)	1 (3)	1.000
Diabetes	3 (10)	5 (17)	.706
Active smoking	5 (17)	5 (17)	1.000
Pelvic radiotherapy	18 (60)	20 (67)	.592
Initial surgery			
Distance from the tumor low margin to the anal sphincter (cm)	3.0 (IQR 1.0–5.5)‡	2.4 (IQR 1.6–4.4)	.602
Distance from the anastomosis to the anal sphincter (cm)	1.0 (IQR 0–1.0)	1.0 (IQR 0–1.0)	.341
Initial anastomosis (colorectal versus coloanal)	3 (10)/27 (90)	1 (3)/29 (97)	.612
Redo surgery			
Date of redo surgery			.774
Period 1: 2007–2012	9 (30)	8 (27)	
Period 2: 2013–2018	21 (70)	22 (73)	
Initial anastomosis preserved versus Hartmann procedure prior to redo surgery	28 (93)/2 (7)	28 (93)/2 (7)	1.000
Causes			
Anastomotic leakage	25 (83)	25 (83)	1.000

Stricture of the anastomosis	5 (17)	4 (13)	1.000
Necrosis of the anastomosis	0 (0)	1 (4)	1.000
Distance from the anastomosis to the anal sphincter (cm)	0 (IQR 0–0)	0 (IQR 0–0)	1.000
Redo anastomosis (colorectal versus coloanal)	0 (0)/100 (100)	0 (0)/100 (100)	1.000
Coloanal anastomosis			
Immediate versus delayed	22 (73)/8 (27)	21 (70)/9 (30)	.774
Rectal sleeve advancement	10 (33)	7 (23)	.390
Surgical anastomotic reconstruction (straight versus side-to-end)	2 (7)/28 (93)	0 (0)/30 (100)	.492
Associated procedure			
Toupet procedure	8 (27)	7 (23)	.766
Deloyers procedure	4 (13)	4 (13)	1.000
Defunctioning stoma	28 (93)	29 (96)	1.000
Postoperative morbidity	9 (30)	12 (40)	.417
Postoperative severe morbidity[§]	4 (13)	5 (17)	1.000
Intra-abdominal septic morbidity	8 (24)	9 (30)	.607
Anastomotic leakage	5 (16)	7 (23)	.519
Intra-abdominal abscess	3 (10)	27 (90)	1.000
Long-term functional outcomes			
LARS score ≤29 (no major LARS)	7/30 (23)	24/30 (80)	**.001**
FSFI ≥26 in women (no sexual dysfunction)	4/11 (36)	5/13 (39)	1.000
IPSS score ≤ 7 in men (no moderate or severe urinary dysfunction)	7/11 (64)	9/14 (64)	1.000
IIEF5 ≥ 16 in men (no moderate or severe erectile dysfunction)	1/11 (9)	4/12 (33)	.317

Q9 Bolded values xxxx.

ASA, American Society of Anesthesiologists; *BMI,* body mass index.

Table Footnotes

* Number of cases (percentage of cases).

† Mean ± standard deviation (minimum-maximum) for quantitative variables following normal distribution.

‡ Median (IQR) for quantitative variables following non-normal distribution.

§ Defined by Dindo-Clavien ≥3.

Discussion

Failure of a redo CRA or CAA is a feared outcome for both surgeons and patients. In the present study, bowel continuity was restored in 145 patients corresponding to a success rate of 90%. More than half of the patients reported poor functional outcomes; however, functional outcomes improved significantly over time. Furthermore, sexual dysfunction in women and erectile dysfunction in men were frequently reported and did not improve with time. Overall, patient quality of life was directly correlated to the postoperative functional outcomes.

Because redo anastomotic surgery is rare, previous studies have only included up to 66 patients.[7] With 145 patients who initially underwent technically successful redo anastomosis, this study provided the potential for a very high number of patients for survey and analysis. Unfortunately, only 57% of eligible patients participated; however, this still

represents the largest number of similar patients in the literature, which provides useful information on assessment of long-term outcomes.

Poor functional outcomes were reported by 57% of the 73 patients after a successful redo anastomosis (including 42% of major LARS and 15% of definitive stoma performed because of a poor functional result). These results are similar to reports in the literature comparing LARS post anterior resection. Indeed, in a recent meta-analysis, the mean rate of major LARS after primary CRA or CAA was 41% (95% confidence interval [CI] [34–48]).[19] Trenti et al reported on 358 patients undergoing rectal cancer resection, with major LARS seen in 57% of patients after CRA vs 83% after CAA.[20] In addition, a recent study estimated the prevalence of major LARS in a Danish population, with major LARS encountered in 4% to 20% of people depending on sex and age.[21] In this study between the ages of 50 and 79, 19% of women and 10% of men reported major LARS. These findings are similar to the present study and support the role of redo anastomotic surgery in the management algorithm for patients with failed primary anastomosis.

As the LARS score was introduced in 2012 and has taken time to be validated in different languages, its use in previous studies on redo anastomosis has been limited and, therefore, has not allowed a direct comparison with the present study.[7–10,13,22] However, in previous reports, incontinence ranged from 11% to 17%,[8–10] with a stool fragmentation rate of 63%,[7] which may suggest the presence of low anterior rectal syndrome. Three recent studies investigating LARS focused on specific subgroups including redo anastomosis after a Hartmann procedure[23] and delayed CAA.[24,25] Caille et al[23] encountered major LARS in 33% of patients after redo anastomosis because of an initial failed anastomosis treated with a Hartmann procedure. These results are consistent with the rate of major LARS found in the present study, as a previous Hartmann procedure did not significantly influence the risk of poor functional outcomes. With regards to published data of redo anastomosis treated with delayed CAA, the rate of major LARS was between 18% and 46%.[24,25] Although fluctuation in LARS scores in previous studies may be due to small sample sizes, the present study reported a higher rate of major LARS scores of 59% in patients after delayed CAA.

Although there has been considerable interest in the literature in defining risk factors for major LARS in the context of initial proctectomy with CRA or CAA, there have been no studies focusing on risk factors for LARS post redo anastomosis.[7–10,23–25] LARS post initial CRA or CAA was assessed by Croese et al,[19] who showed that pelvic radiation, type of anastomosis (CRA versus CAA), age, sex, and anastomotic leakage to be significantly associated with LARS. However, these factors were not reproducible in the present study. Interestingly, in 184 rectal cancer patients, Jimenez-Gomez et al found, in multivariate analysis, 3 criteria associated with major LARS: total mesorectal excision and preoperative and postoperative radiotherapy.[26] In the present study, 68 of 73 patients (92%) had initial CAA with total mesorectal excision, which was not associated with poor functional outcomes. In addition, neither the level of the first or redo surgery nor the level of the primary tumor influenced the functional results after redo surgery in our cohort. Similarly, 48/73 patients (66%) underwent pelvic radiotherapy without increasing the risk of poor functional outcomes. These results suggest that the risk factors involved in poor functional outcomes after redo anastomosis differ from the factors associated with poor functional outcomes after primary anastomosis. Local lesions related to anastomotic failure as well as lesions caused by redo surgery may cause these differences.

Interestingly, we found that the bowel function can improve until 3 years after bowel continuity restoration in the setting of redo surgery. Here again, this result about the redo surgery significantly differs from the data published about functional outcomes after primary anastomosis.[27,28] Emmertsen et al[27] reported a considerable reduction of major LARS incidence until 1 year after proctectomy, but 1 year after rectal surgery, the bowel function intestinal function seems to stabilize.[28] This discordance between primary and redo anastomosis is essential for the surgeon to propose an appropriate postoperative monitoring of bowel function, well-adjusted to the specific context of redo surgery.

After anterior resection for low rectal cancer with CAA, urinary function preservation has been reported in 68% to 77% of men.[29] In the present study, 64% of patients observed an absence or only mild urinary dysfunction suggesting a good preservation of urine function after redo anastomosis. In contrast, sexual function was extremely impacted as 79% of men reported moderate or severe erectile dysfunction. Previous reports on erectile dysfunction post anterior resection vary between 32% to 93%, making it difficult to accurately assess the impact redo anastomosis has on erectile function.[29–31] In addition, we do not know the erectile function (as the other functions) prior to the redo surgery in our cohort, so we cannot discriminate between alterations related to the first surgery and those related to the redo surgery. In women, sexual dysfunction was observed in 64%. Again, this rate is difficult to compare with previous reports due to the wide variation in results.[29–31] Interestingly, Hendren et al[31] observed almost 50% of women and 35% of men had

altered sexual function after the diagnosis of a rectal cancer and prior to treatment. In addition, after rectal surgery, abdominoperineal resection was associated with greater impairment of sexual function in both male and female patients compared with restorative rectal resection. Therefore, the authors hypothesize that restoring the bowel continuity may reduce alterations in sexual outcomes compared to patients with permanent stomas; although, this was not fully examined in that study. Interestingly, in our series, the impact on sexual function did not seem to improve with time as opposed to the improvement seen in functional outcomes over time. This highlights the importance of an appropriate and detailed preoperative counselling with patients to ensure all functional outcomes are clearly explained to them.

With regards to quality of life, the median GIQLI value in the present series was 110 of 144. By comparison, a mean value of 107 of 140 has been reported 10 days after laparoscopic cholecystectomy[32] and 112 of 140 3 months after laparoscopic ileocecal resection for Crohn's disease.[33] This suggests that a good median quality of life after redo anastomosis is encountered. Analysis in the present study identified a major LARS or definitive stoma as risk factors for poor quality of life. This result raises the importance of optimizing treatments for LARS, including medication, pelvic floor exercises,[34] or more invasive treatments such as sacral neurostimulation[35] or anterograde enema.[36]

There are a number of limitations in the present study. Urinary, sexual, and digestive functions and quality of life before redo surgery were unknown, so the direct impact of the redo surgery could not be reported, and our results supported only the consequences of both the primary and the redo surgery. The response rate was only 57%, which had a significant impact on the sample size affecting the statistical power. In addition, this response rate could have possibly induced a selection bias. Finally, including patients over an 11-year period constitutes a limitation, although, no difference in functional outcomes or quality of life was seen in patients pre- and post-2013.

In conclusion, this study analyzed the long-term functional outcomes of a large series of patients who underwent redo anastomosis after an initial failed CRA or CAA. After a technical success of the redo anastomosis, a major LARS score was observed in 42% of patients, with an additional 15% of patients preferring a permanent stoma for poor functional outcomes. Among all patients who underwent an attempted redo anastomosis, including the patients observing a surgical failure of bowel continuity restoration, a good long-term functional outcome concerned only 35% of them. No modifiable factors that may influence functional outcomes were identified. Thus, the surgeon, and, most of all, the patient, must be aware of the high technical success rate of restorative surgery but the relatively poor functional outcomes it carries. Q11

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The corrections made in this section will be reviewed and approved by a journal production editor. The newly added/removed references and its citations will be reordered and rearranged by the production team.

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Queries and Answers

Q1

Query: Per journal style, abbreviations should not be used in the abstract. I replaced all the abbreviations appearing in the abstract with their expansions. Please review and confirm okay as revised.

Answer: ok

Q2

Query: Please verify changes to the first sentence of the introduction.

Answer: OK

Q3

Query: In the sentence beginning « In addition, the female…, » I revised « females » to « women » and « males » to « men. » Per journal style, « male » and « female » should not be used as nouns only as adjectives. In « the female sexual function index », female is used as an adjective.

Answer: OK

Q4

Query: Please verify the correct acronym for internation prostate symptom score is IPSS and not IPPS.

Answer: OK, thank you for this.

Q5

Query: In the sentence beginning « In univariate analysis…, » please confirm the revision of « per » to « peri , » as in « perioperative. »

Answer: ok

Q6

Query: Please provide an access date for ref 26 or updated print publication information.

Answer: Acess date 1/9/2020. On pubmed today, the reference is : Colorectal Dis. 2017 Sep 29. doi: 10.1111/codi.13901. Online ahead of print.Factors associated with low anterior resection syndrome after surgical treatment of rectal cancerLuis Miguel Jimenez-Gomez [1 2], Eloy Espin-Basany [1], Loris Trenti [3], Marc Martí-Gallostra [1], José Luis Sánchez-García [1], Francesc Vallribera-Valls [1], Esther Kreisler [3], Sebastiano Biondo [3], Manuel Armengol-Carrasco [1]

Q7

Query: Table I, I revised the footnote symbols to match journal style. Please review and confirm okay as revised. IQR does not need to be expanded in the notes beneath the table as it has already been expanded and used in the text.

Answer: OK

Q8

Query: Table III, please provide a note beneath the table to explain the bolded value.

Answer: bold value was added to significant p value. It can be change to normal font.

Q9

Query: Table IV, please provide a note beneath the table to explain the bolded value.

Answer: Same for the previous table. All value can be in normal font.

Q10

Query: Please provide the corresponding author's Twitter handle, if any.

Answer: @jeremielefevre

Q11

Query: Correctly acknowledging the primary funders and grant IDs of your research is important to ensure compliance with funder policies. We could not find any acknowledgement of funding sources in your text. Is this correct?

Answer: No funding to report.

No grant to report.

Q12

Query: Please confirm that given names and surnames have been identified correctly and are presented in the desired order and please carefully verify the spelling of all authors' names.

Answer: Yes I have corrected one name.