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Digestive and genitourinary sequelae in rectal cancer survivors and their impact on health-related quality of life: Outcome of a high-resolution population-based study

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ABSTRACT

Background: With the rising number of rectal cancer survivors, more patients with sphincter-preserving surgery are having to live with a potentially impaired quality of life. The survey aimed to assess bowel and genitourinary sequelae and their impact on quality of life in an unselected registry-based population of rectal cancer survivors.

Methods: This cross-sectional cohort survey (registered at ClinicalTrials.gov; ID: NCT03459235) included patients with rectal cancer who underwent curative surgery with sphincter-preserving surgery from January 1, 2007 to January 31, 2015. Patients with recurrent disease, intestinal stoma, or cognitive disorders were excluded. Validated scoring system included the Urinary Symptom Profile in women and the International Prostate Symptom Score in men for urinary function, International Index for Erectile Function 5 in men and Female Sexual Function Index in women for sexual function, and Core 30/ Colo Rectal 29 questionnaires for quality of life and Low Anterior Resection Syndrome score for bowel function. The impact of functional sequelae on global quality of life was evaluated by multiple linear regression.

Results: Responders (45.3%, 92/203 patients) and nonresponders were comparable according to sex, age, tumor stage, and neoadjuvant chemoradiation. With a mean follow-up of 6.5 years, 65.2% of the rectal cancer survivors had bowel dysfunction, of whom 41.3% experienced major Low Anterior Resection Syndrome and 80% of rectal cancer survivors experienced genitourinary dysfunction. In multiple linear regression, poor bowel function was a significant predictor of global quality of life in men ($P = .04$) and women ($P = .0003$).

Conclusion: This survey highlights the importance of sexual and bowel dysfunction in rectal cancer survivors and the strong correlation between high Low Anterior Resection Syndrome score and inferior quality of life. Further studies are needed to improve knowledge on how to predict bowel dysfunction and how to best support patients with bowel dysfunction.

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Introduction

In recent years, progress in the multimodal treatments of rectal cancer (RC) has improved local disease control and increased the survival rate (≤50% survival at 5 years).[1,2] At the same time, the evolution of surgical techniques and the achievement of a 1-cm distal margin below the tumor have pushed back the limits of sphincter-preserving surgery (SPS) without impairing oncologic prognosis.[3,4] Assessment of RC outcome has traditionally focused on morbidity rate, tumor recurrence, and survival, whereas functional sequelae (ie, bowel or genitourinary) have long been regarded as inherent to the nature of oncologic treatments.[5] However, with improved oncologic outcomes, we and others have observed a rising number of RC survivors who live with numerous potential side-effects and an eventually impaired quality of life (QoL).[6–9] Therefore, QoL has become an increasingly important focus of care.[10]

Most patients will experience significant side-effects of RC treatment.[6,7] After low anterior resection with SPS, it is widely accepted 50% to 90% of patients will experience a change in bowel habit[6,11,12] that is termed "low anterior resection syndrome" (LARS). LARS can severely affect QoL.[13] However, the ways in which bowel dysfunction is measured and reported vary considerably,[14] so estimates of adverse events may be unreliable. First used in Denmark in 2012, the "LARS score" is to date the best questionnaire for capturing postoperative bowel function among a number of instruments.[15,16] Furthermore, there may be considerable discrepancy between the clinician's judgement of patient perception and the patient's actual belief or experience.[17]

Furthermore, genitourinary problems are common, multifactorial, and inadequately explored.[7] De novo urinary sequelae (in ≈33% of patients) may occur after RC surgery, including de novo urinary incontinence in one-third of patients and voiding dysfunction in one-fourth.[7] Likewise, sexual sequelae occur in three-quarters of men (erectile and ejaculation dysfunction) and in two-thirds of women (dyspareunia or vaginal shrinkage), leading to de novo loss of sexual activity in 28% of men and 18% of women.[7] However, most studies are retrospective, have small samples, short-term follow-up, and use nonvalidated instruments.[7,18]

In addition, considerable variations in information provision regarding the pros and cons of treatments have been reported.[19] RC patients receive insufficient information regarding the potential side-effects of treatment,[19] yet they need precise details about the risk of developing such disturbances. Although recent studies have focused on various issues such as bowel and genitourinary function and health-related QoL,[8,20] very few studies to our knowledge have provided clinicians with a complete picture of overall functions.[21,22] Furthermore, there is little consensus regarding the use of specific instruments or validated scores.[6,7] This study therefore used well-validated instruments to assess functional outcomes in a holistic manner in an unselected general population of RC survivors. In addition, we investigated whether there is a strong relation between functional outcome and impaired QoL.

Methods

This study was carried out according to the terms of the Declaration of Helsinki, approved by the local ethics committee (ID-RCB: 2017-A02645-48), and registered at ClinicalTrials.gov (ID: NCT03459235).

Design and participants

In this cross-sectional population-based study, patients eligible for inclusion were identified by the digestive cancer registry of Calvados, which records all incident cases in Calvados, a French department located in Northwest of France. The population of Calvados was estimated at 694,660 people in 2016. Unlike a general cancer registry, a digestive cancer registry records high-resolution data on all diagnosed digestive cancers (updated follow-up, high-resolution data on treatment, detailed surgical data, adjuvant therapy, and ongoing monitoring). Data quality and completeness of the registry were assessed by the Registries Evaluation Committee and the International Agency for Research on Cancer (IARC). The database has been declared to the National Commission on Information Technology and Civil Liberties (CNIL, n°998018).

Data from all patients with a rectal adenocarcinoma diagnosed in Calvados between January 1, 2017, and January 31, 2015 (C20, 8140/3 in International Classification of Diseases for Oncology 3), were extracted ($N = 931$; Fig 1). Inclusion criteria were age >18 years and <80 years at inclusion, curative total or partial mesorectal excision (total mesorectal excision [TME] or partial mesorectal excision [PME]) for RC since 2007. Each RC was located between 0 and 15 cm from the anal verge. Low RC were defined as a tumor ≤6 cm from the anal verge. PME was performed on selected upper rectal tumors that mobilized sufficiently for the mesorectum to be transected at least 5 cm below the tumor.[4] The exclusion criteria were no resection or palliative cancer resection, the presence of known disseminated or recurrent disease, intestinal stoma, or patients whose bowel continuity had been restored for less than 24 months. Mental dementia, cognitive disorders, or the inability to read and understand the French language were also exclusion criteria.

Finally, 402 patients were eligible for crosschecking data with paper or computerized medical files (Fig 1). Medical data were updated and patients with exclusion criteria or who had died were excluded. Consequently, survivors were defined as follows: alive patients assessed for eligibility on February 1, 2018 ($n = 255$; Fig 1). Additional information regarding mental state, linguistic abilities, and postal addresses was obtained by checking medical records. Thus, 52 alive patients were excluded owing to local or distant recurrence and redo surgery for stoma. Consequently, 203 letters containing the questionnaires were sent and 150 dunning letters were resent (in the event of no response after 30 days). Patients who left their phone number on the questionnaire were reminded in the event of missing answers. Patients who had not responded to the questionnaires after 3 months were considered as nonresponders.

Questionnaires

Seven validated questionnaires were used. QoL was evaluated with the generic European Organization for Treatment and Research of Cancer (EORTC) Quality of Life Questionnaire Core 30 (QLQ-C30)[23] and the specific colorectal module (EORTC QLQ-CR29).[24] The scores were summed and converted to a 0 to 100 scale according to the EORTC scoring manual.[25]

Bowel function assessment included a translated French version of the LARS score to evaluate digestive sequelae.[26] The French version of the LARS score is currently being validated and supported by the French Research Group for Rectal Cancer Surgery. The LARS score is a patient-reported outcome measure to evaluate the severity of bowel dysfunction after rectal surgery by scoring the 5 major symptoms of LARS[15]: incontinence (flatus and liquid stool), frequent bowel movements, fragmentation and clustering of stools, and urge. The score ranges from 0 to 42 and defined no LARS (LARS score from 0 to 20), minor LARS (score from 21 to 29), and major LARS (score from 30 to 42).[15]

To evaluate urinary function in men, we used the International Prostate Symptom Score (IPSS), which is a structured and validated

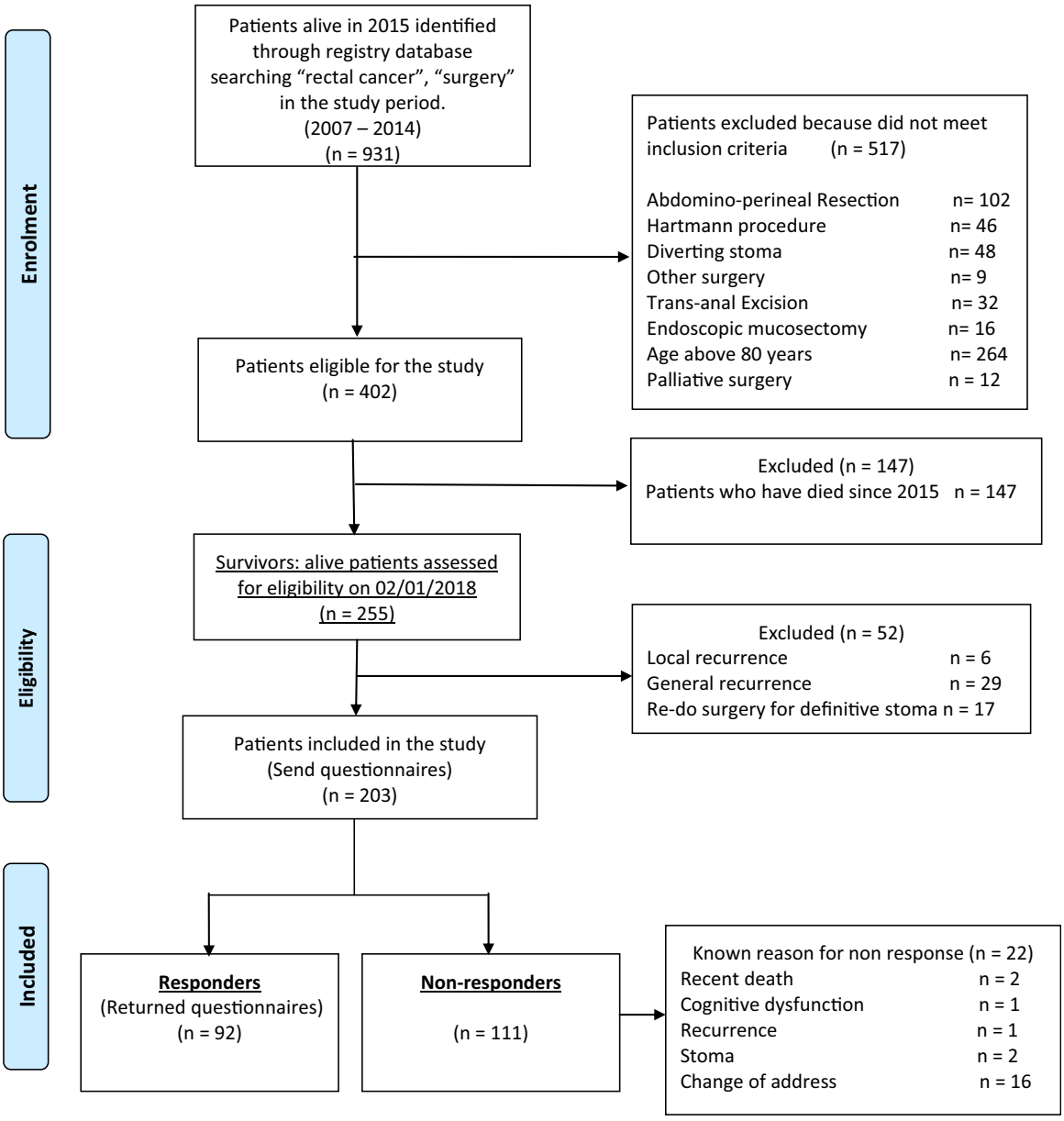

Fig 1. Flow diagram of the study population.

self-questionnaire evaluating lower urinary dysfunction.[7] The IPSS questionnaire includes a QoL assessment according to urinary symptoms from 0 (best) to 6 (worst). It is based on 7 items (incomplete bladder emptying, micturition frequency, intermittent micturition, urgency, strength of the stream, straining, and nocturia) during the preceding 4 weeks. Each item is scored from 0 (best) to 5 (worst). Urinary function was graded in 3 subgroups: normal function (0–7 points), moderate dysfunction (8–19 points), and severe dysfunction (20–35 points).

In women, we used the Urinary Symptom Profile (USP), which is a self-report instrument including a 13-item questionnaire developed and validated in French by Haab et al.[27] The instrument explores 3 dimensions: stress urinary incontinence, overactive bladder, and urinary obstruction symptoms. Dimensions 1 and 3 are scored from 0 to 9, and dimension 2 is scored from 0 to 21. A score of 0 represents absence of symptoms and 9 or 21 maximal severity symptoms. The USP has no cutoff score.

Male sexual function was assessed by the International Index of Erectile Function questionnaire (IIEF 5), which is composed of 5 questions divided into 5 domains: erection, orgasm, desire, satisfaction with sexual intercourse, and overall satisfaction.[7] The answers to each question indicate the experience of the patient during the preceding 4 weeks on a 5-point Likert scale. The IIEF-5 score was calculated by adding the score for each item and ranged from 5 to 25. Erectile function in patients with sexual inactivity (0–4 points) was not analyzed. A total score $\geq$21 was considered "normal."

In women, we used the Female Sexual Function Index (FSFI), which is the most widely used scale consisting in 19 items and evaluating female sexual dysfunction. The index consists of 6 individual domains: desire, excitation, lubrication, orgasm, satisfaction, and pain. Each title is scored between 0 or 1 and 5 points. The lowest score is 2 and the highest score is 36. A high score indicates better function. According to the authors, functional condition is

good if FSFI score is >30, moderate if between 23-29, and poor if <23. A score <26.55 was classified as Female Sexual Disorder (FSD).[28]

Statistical analysis

T tests were used to assess score differences between groups. Clinical significance of the score differences on each scale was determined using a validated minimal clinically important difference study of the EORTC questionnaire. The questionnaires EORTC QLQ-C30 and QLQ-CR29 were scored according to the methods recommended by the developers. Missing data were handled as instructed in the scoring manuals. For the other questionnaires, missing data were handled in complete case analysis. Data are presented in univariate analysis according to the predictive factors known to affect or impair functional outcomes (sex, age at surgery, neoadjuvant radiation therapy, extent of mesorectal excision PME or TME) and the kind of colorectal anastomosis (straight versus colonic reservoir). Linear regression and multiple linear regression (with backward selection) were performed in order to analyze the impact of the functional sequelae on global QoL. Statistical analyses were performed using SAS 9.4 software (SAS Institute, Cary, NC).

Results

Two hundred and three patients were included in the study (questionnaires sent). In summary, 92 patients (45.3% of included patients) returned the questionnaires and were considered as responders. The other 111 patients (54.7%) were considered as nonresponders (Fig 1). The average response time was 24.3 days (SD 17.3 days) ranging from 5 to 78 days. The completeness level of the various questionnaires was at least 94% except for the subscale "satisfaction" of the FSFI among women (28.6% missing answers).

Patient demographics

Both groups (responders and nonresponders) were comparable according to age, sex, tumor stage, neoadjuvant and adjuvant therapy, surgical approach, type of rectal resection, and type of intestinal reconstruction (ie, colon-J-pouch or side-to-end versus straight colorectal anastomosis).

The mean follow-up from the operation to the time of questionnaire completion for the responders was 6.5 years (range 3.01–10.86 years, Table I). The mean age of responders at the time of operation was 60.7 years (range 29.2–76.1 years) and 64 were men (69.6%). Most RC were located in the low- and mid-rectum (66.3%). Half of the responders underwent neoadjuvant radiotherapy and 59 (64.1%) did not have any adjuvant treatment. The most frequent surgical approach was the open approach (67.4%), followed by laparoscopy (23.9%), and by conversion to open surgery (7.6%). Colonic reservoir was the procedure in 66 responders (61.0%) and a temporary ostomy was performed in 53 patients (57.6%).

Health-related QoL and functional outcomes

Bowel function

Median LARS score in responders was 27 and the mean was 24.2 (SD 12.5) ranging from 0 to 39.

Almost two-thirds (65.2%) of the population had a LARS (score >20), including 41.3% with a major LARS. Data were missing for one of the 92 patients of the survey, as shown in Table II. Neoadjuvant radiation therapy ($P < .001$) and TME ($P = .006$) were significantly associated with the severity of LARS score.

Urinary function

In men, median IPSS score in responders was 5 and the mean was 6.0 (SD 5.4), ranging from 0 to 28. Most patients (98.4%) had mild or moderate dysfunction. Data were missing for 2 of the 64 male patients (Table III). In women, median USP score in responders was 4 and the mean was 5.0 (SD 4.6), ranging from 0 to 19. The 3 dimensions explored by the USP score are shown in Table IV. There was no missing data. For both men and women, IPSS category and USP scores were independent of neoadjuvant radiation therapy, extent of mesorectal excision, and type of colorectal anastomosis.

Sexual function

In men, median IIEF score was 7 and the mean was 8.75 (SD 7.8). Only 6 men (9.4%) did not have erectile dysfunction (Table V), and severe erectile dysfunction was observed in 59.3% of men. In women, median FSFI score was 5.7 and the mean was 12.4 (SD 12.0). Only 6 women (21.4%) did not have an Female Sexual Disorder (defined as a total FSFI score above 26.55). Data were missing for 4 women (14%) on the desire and arousal domains and for 8 women (29%) on the satisfaction domain (Table VI). For both men and women, IIEF5 categories and FSFI domains were independent of neoadjuvant radiation therapy, extent of mesorectal excision, and type of colorectal anastomosis.

Health-related quality of life

Results of the EORTC QLQ-C30 and CR29 are shown in Supplementary Tables 1 and 2 (supplementary material). The global QoL score was similar among men and women, as were role, emotional, cognitive, and social functions. In univariate analysis of the QLQ C-30, worse social functioning was significantly associated with TME (77.8 vs 92.2 $P = .008$) and use of neoadjuvant radiation therapy (77.4 vs 87.8 $P = .04$). Neoadjuvant radiation therapy was significantly associated with worse diarrhea (34.0 vs 18.8, $P = .01$). Otherwise, no significant differences were found. When CR29 was considered, patient's body image perception was significantly worse after neoadjuvant radiation therapy ($P = .003$) and TME ($P = .02$). Fecal incontinence was significantly worsened by TME ($P = .008$) and neoadjuvant radiation therapy ($P = .001$). Furthermore, neoadjuvant radiation therapy was significantly associated with increased stool frequency ($P < .001$), buttock pain ($P = .04$), flatulence ($P = .001$), sore skin ($P = .001$), and embarrassment ($P = .001$). Men seemed to have more blood and mucus in stools than women ($P = .05$).

Multiple linear regression

In univariate analysis, urinary function and bowel function were significantly associated to Qol for men, and the bowel function was the only predictor of QoL for women. In multiple linear regression using a backward selection, poor bowel function impaired global QoL significantly in men (coefficient estimate at −0.39 with $P = .04$) and in women (−1.22 with $P = .0003$), as shown in Table VII. In women, age was associated with QoL (coefficient estimate at 0.57 with $P = .03$).

Discussion

The results of this survey highlight the notable functional consequences reported by RC survivors after SPS. Based on validated instruments, 40% of RC survivors had a major LARS that significantly impaired their quality of life. More interestingly, bowel dysfunction was the only predictor of QoL for such patients after

Table I
Comparison between responders and nonresponders patients according to their characteristics

	Responders n = 92 [%]	Nonresponders n = 111 [%]	*P* value
Age at surgery (mean, [SD]), y	60.7 (11.3)	62.5 (8.2)	.23
Age at test (mean, [SD]), y	67.2 (10.2)	69.0 (7.8)	.16
Sex			
Male	64 [69.6]	70 [63.1]	.33
Female	28 [30.4]	41 [36.9]	
Tumor location			
High	31 [33.7]	35 [31.5]	.95
Mid	45 [49.0]	56 [50.5]	
Low	16 [17.3]	20 [18.0]	
Pathologic T-staging			
pT0 − pT2	54 [58.7]	67 [60.4]	.81
pT3 − pT4	38 [41.3]	44 [39.6]	
Pathologic N-staging			
pN0	63 [68.5]	86 [77.5]	.15
pN1-2	29 [31.5]	25 [22.5]	
Pathologic TNM staging			
Stage 1	43 [46.7]	58 [52.3]	.35
Stage 2	20 [21.7]	28 [25.2]	
Stage 3	29 [31.5]	25 [22.5]	
Stage 4	0	0	
Type of surgery			
TME	62 [67.4]	76 [68.5]	.87
PME	30 [32.6]	35 [31.5]	
Neoadjuvant therapy			
Chemoradiation	46 [50.0]	56 [50.5]	.95
Short-course radiotherapy	0	0	
None	46 [50.0]	55 [49.5]	
Surgical approach			
Open	62 [67.4]	57 [51.3]	.10
Laparoscopy	22 [23.9]	41 [36.9]	
Conversion in open surgery	7 [7.6]	12 [10.8]	
Robotic	1 [1.1]	1 [0.9]	
Intersphincteric resection	27 [29.3]	21 [18.9]	.08
Anastomosis construction			
Straight anastomosis (end-to-end)	36 [39.0]	61 [54.9]	.06
Colonic Reservoir:			
side-to-end anastomosis	44 [48.0]	36 [32.5]	
Colonic J-pouch	12 [13.0]	14 [12.6]	
Anastomosis type			
Handsewn CAA	22 [23.9]	22 [19.8]	.48
Stapled CRA	70 [76.1]	89 [80.2]	
Stoma type			
Temporary ostomy	53 [57.6]	72 [64.9]	.29
None	39 [42.4]	34 [35.1]	
Adjuvant treatment			
None	59 [64.1]	84 [75.7]	.20
Chemotherapy	31 [33.7]	25 [22.5]	
Chemoradiotherapy	2 [2.2]	2 [1.8]	
Time since surgery (mean, [SD]), y	6.5 (3.9)	6.5 (2.2)	.89

CAA, coloanal anastomosis; *CRA*, colorectal anastomosis.

Table II
Results of bowel function (LARS score) for responder patients who underwent curative rectal resection

Overall population	No LARS (0–20) [%]	Minor LARS (21–29) [%]	Major LARS (30–42) [%]	*P* value	Missing data [%]	Total [%]
Whole population	31 [33.7]	22 [23.9]	38 [41.3]	NA	1 [1.1]	92 [100]
Sex						
Male	22 [34.4]	14 [21.9]	28 [43.7]	.71	0 [0]	64 [69.6]
Female	9 [32.1]	8 [28.6]	10 [35.7]		1 [3.6]	28 [30.4]
Mesorectal excision						
TME	14 [22.6]	17 [27.4]	30 [48.4]	.006	1 [1.6]	62 [67.4]
PME	17 [27.4]	5 [16.7]	8 [26.6]		0 [0]	30 [32.6]
Chemoradiation						
Chemoradiation	10 [21.7]	8 [17.4]	28 [60.9]	<.001	0 [0]	46 [50.0]
No chemoradiation	21 [45.7]	14 [30.4]	10 [21.7]		1 [2.2]	46 [50.0]
Anastomosis construction						
Straight anastomosis	13 [36.1]	10 [27.8]	13 [36.1]	.65	0 [0]	36 [39.1]
Colonic reservoir	18 [32.2]	12 [21.4]	25 [44.6]		1 [1.8]	56 [60.9]

NA, not applicable.

Table III
Results of urinary function (IPSS score for men) for responder patients who underwent curative rectal resection

IPSS score	Mild (1–7) [%]	Moderate (21–29) [%]	Severe (30–42) [%]	*P* value	Missing data [%]	Total [%]
Male population	46 [71.8]	15 [23.4]	1 [1.6]	NA	2 [3.2]	64 [100]
Mesorectal excision						
TME	28 [68.3]	10 [24.5]	1 [2.4]	.68	2 [4.8]	41 [64]
PME	18 [78.3]	5 [21.7]	0 [0]		0 [0]	23 [36]
Chemoradiation						
Chemoradiation	25 [73.5]	7 [20.1]	1 [2.9]	.56	1 [1.6]	34 [53.1]
No chemoradiation	21 [70.0]	8 [26.7]	0 [0]		1 [1.6]	30 [46.9]
Anastomosis construction						
Straight anastomosis	23 [76.7]	6 [20.0]	0 [0]	.66	1 [3.3]	30 [46.9]
Colonic reservoir	23 [71.9]	9 [28.1]	1 [3.1]		1 [3.1]	34 [53.1]

NA, not applicable.

Table IV
Results of urinary function (USP score for women) for responder patients who underwent curative rectal resection

USP score	Stress urinary incontinence mean score (SD)	Overactive Bladder mean score (SD)	Low stream mean score (SD)	Total score mean score (SD)	Missing data [%]	Total [%]
Female population	0.86 (1.6)	4.2 (3.4)	0.3 (0.7)	5.0 (4.6)	0 [0]	28 [100]
Mesorectal excision						
TME	0.9 (1.8)	4.1 (3.7)	0.4 (0.8)	5 (5.1)	0 [0]	21 [75.0]
PME	0.7 (1.1)	4.4 (2.4)	0.1 (0.4)	5.1 (3.1)		7 [25.0]
P value	.79	.83	.46	.95		
Chemoradiation						
No Chemoradiation	0.9 (1.7)	5.0 (3.5)	0.3 (0.6)	5.6 (4.9)	0 [0]	16 [57.1]
	0.8 (1.6)	3.1 (3.2)	0.3 (0.9)	4.3 (4.3)		12 [42.9]
P value	.95	.15	.94	.49		
Anastomosis construction						
Straight anastomosis	0.2 (0.4)	3.7 (1.6)	0.2 (0.4)	3.8 (1.8)	0 [0]	6 [21.4]
Colonic reservoir	1 (1.8)	4.3 (2.6)	0.4 (0.8)	5.4 (5.1)		22 [78.6]
P value	.25	.69	.56	.48		

Table V
Results of sexual function (IIEF score for men) for responder patients who underwent curative rectal resection

IIEF score	Severe erectile dysfunction (5–10) [%]	Moderate erectile dysfunction (11–15) [%]	Mild erectile dysfunction (16–20) [%]	No erectile dysfunction (21–25) [%]	NA (1–4) [%]	*P* value	Missing data [%]	Total [%]
Male population	13 [20.3]	8 [12.5]	8 [12.5]	6 [9.4]	25 [39.0]	NA	4 [6.3]	64 [100]
Mesorectal excision								
TME	10 [24.3]	5 [12.2]	4 [9.7]	4 [9.7]	16 [39.0]	.80	2 [4.8]	41 [64.0]
PME	3 [13.0]	3 [13.0]	4 [17.4]	2 [8.7]	9 [39.2]		2 [8.7]	23 [36.0]
Chemoradiation								
No chemoradiation	5 [16.6]	4 [13.3]	2 [6.7]	3 [10.0]	14 [46.7]	.59	2 [6.7]	30 [46.9]
	8 [23.5]	4 [11.8]	6 [17.7]	3 [8.8]	11 [32.3]		2 [5.9]	34 [53.1]
Anastomosis construction								
Straight anastomosis	5 [16.6]	5 [16.6]	4 [13.3]	4 [13.3]	9 [30.2]	.52	3 [10.0]	30 [46.9]
Colonic reservoir	8 [23.5]	3 [8.8]	4 [11.8]	2 [5.9]	16 [47.1]		1 [2.9]	34 [53.1]

NA, not applicable.

adjustment on age and different parts of QoL (urinary and sexual function).

Although numerous studies have explored the impact of RC treatments on QoL,[10] they have often been limited by the duration of follow-up. However, a large proportion of the increasing number of RC survivors have to date been living >5 years after treatment. In contrast to many studies including RC survivors,[10] we used specific validated questionnaires for both bowel and genitourinary functions. In our study, 40% of RC survivors experienced major LARS. Three studies have previously used the LARS score to evaluate bowel function in RC survivors with a long-term follow-up. Bregendahl et al found that 41% of patients experienced major LARS after a median of 54 months.[29] Based on the outcome of a randomized multicenter trial, Chen et al reported that 46% of patients had major LARS at 14 years.[30] Consistent with previous studies, we found a strong relationship between neoadjuvant radiation therapy and major LARS, and between TME and major LARS.[6,29,30]

We also found a strong association in multivariable analysis between severe bowel dysfunction and QoL, especially regarding global health status. Our study is not the first to demonstrate an association between LARS score and QoL,[31] but it is the first to evaluate all functional sequelae (bowel and genito-urinary) and QoL (global and specific) at the same time and in a high-resolution, population-based study.[32] This strong association is even more important in that the prevalence of major LARS does not change over time.[33] QoL was significantly impaired by severe bowel dysfunction (LARS score $\geq$30) instead of sexual or urinary dysfunction, based on the 7 validated questionnaires used. Consequently, it will be relevant to predict early bowel dysfunction severity, based on predictive factors identified in the literature,

Table VI
Results of sexual function (FSFI score for women) for responder patients who underwent curative rectal resection

FSFI score	FSFI	Desire	Arousal	Lubrification	Orgasm	Satisfaction	Pain	Total [%]
Female population	12.4(12.0)	2.5(1.2)	2.0(2.0)	2.2(2.5)	2.3(2.5)	2.1(0.8)	2(2.5)	28 [100]
Missing data [%]	4 [14]	4 [14]	4 [14]	3 [11]	3 [11]	8 [29]	3 [11]	NA
Mesorectal excision								
TME	13.5 (13.1)	2.4 (1.3)	1.8 (2.2)	2.2 (2.7)	2.2 (2.7)	3.6 (2.3)	1.9 (2.6)	17 [70.8]
PME	16 (9.6)	2.8 (0.9)	2.3 (1.8)	2.3 (2.0)	2.5 (2.0)	3.7 (1.9)	2.3 (2.1)	7 [29.2]
P value	.65	.45	.60	.91	.81	.91	.67	
Chemoradiation								
Chemoradiation	13.5 (13.6)	2.6 (1.2)	1.9 (1.9)	2.3 (2.4)	2.3 (2.4)	3.9 (2.1)	2.2 (2.5)	9 [37.5]
No chemoradiation	14.7 (11.4)	2.5 (1.3)	2.0 (2.3)	2.1 (2.7)	2.1 (2.7)	3.3 (2.2)	1.7 (2.5)	15 [62.5]
P value	.82	.86	.90	.82	.86	.51	.61	
Anastomosis construction								
Straight anastomosis	13.9 (10.3)	2.6 (1.0)	1.3 (1.6)	2.6 (2.8)	2.3 (2.3)	3.5 (2.4)	2.0 (2.7)	5 [20.8]
Colonic reservoir	14.3 (12.7)	2.5 (1.3)	2.1 (2.1)	2.1 (2.5)	2.2 (2.6)	3.7 (2.1)	2.0 (2.5)	19 [79.2]
P value	.95	.97	.47	.72	.95	.89	1	

dysf., dysfunction; *NA*, not applicable.

Table VII
Results of simple and multiple linear regression (using backward selection) showing global quality of life score based on functional sequelae scores in men and women

	Men				Women			
	Simple linear regression		Multiple linear regression		Simple linear regression		Multiple linear regression	
	Coefficient estimate	*P* Value	Coefficient estimate	*P* Value	Coefficient estimate	*P* Value	Coefficient estimate	*P* Value
Age	0.14	.62	—	—	0.42	.18	0.57	.03
Bowel function	−0.39	.04	−0.39	.04	−1.09	.0006	−1.22	.0003
Urinary function	−0.84	.05	—	—	−0.51	.57	—	—
Sexual function	0.42	.17	—	—	0.44	.24	—	—

such as the POLARS score.[34] Furthermore, this individualized strategy may help us to guide our treatment decision, by avoiding neoadjuvant radiotherapy in high rectal lesions or in middle rectal lesions staged T3a/b[35] or by performing abdominoperineal excision with permanent stoma instead of sphincter-sparing surgery with intersphincteric resection in older patients who have ultralow rectal lesions. However, the POLARS score has not been validated in a French population, and there are several important factors that it does not control, such as socioeconomic status and comorbidities. We have recently reported that the prevalence of sphincter-sparing surgery might be influenced by socioeconomic deprivation.[36] In addition, better preoperative patient education and counselling might reduce symptoms and improve QoL.[37,38] A detailed algorithm has been suggested for managing anterior resection syndrome based on a review of the literature.[6]

An alternative strategy for high-risk patients is the "watch-and-wait" policy, which causes fewer functional problems than rectal resection. However, one-third of the patients included in this strategy still report major LARS symptoms.[39] Although there is to date insufficient evidence to draw firm conclusions about the oncologic safety of this approach, this "watch-and-wait" strategy will be part of the future management of patients with rectal cancer.

In addition, the strong correlation between major LARS and poor QoL may lead to a definitive stoma. According to several studies, a definitive stoma will be required in ≈1 patient out of 5 at 10 years owing to perianastomotic septic complications, fecal incontinence, and local recurrence.[40,41] The responders with major LARS are managed to date according to our decisional algorithm.[6] Thus, surgery and permanent stoma are indicated as a last resort, but only after ruling out a local recurrence. Most of our RC survivors experienced genitourinary sequelae, a finding in keeping with other studies using validated scoring systems.[7,18,32,42]

The major strength of this study is the consistency of the design. This was a high-resolution registry study based on a general population regardless of the medical center with an exhaustiveness close to 100%. To avoid any potential bias on QoL or dysfunctions, only patients treated with curative intention and free of cancer disease were included. Moreover, a minimum 2-year follow-up period after stoma reversal was used as an inclusion criterion in order for patients to experience the potential functional improvements that may be observed in this period, as described by several authors.[29,31] Another strength is that QoL, bowel, and genitourinary functions were studied with well-known and internationally validated questionnaires and scores. In a recent review, the EORTC questionnaires were shown to be the best health-related QoL tools for colorectal cancer patients.[43]

However, there are also some limitations. First, this survey was cross-sectional and not longitudinal. Nevertheless, cross-sectional mapping of sequelae and QoL is a necessary step before making a longitudinal assessment on a large scale. However, our results were based on a population-based cancer registry and may be generalizable to all patients undergoing rectal cancer surgery. On the other hand, the longitudinal prospective studies with both pre- and posttreatment scores were derived from a "convenience cohort" of surviving rectal cancer treated in a single dedicated center.[42,44,45] Recent findings highlight the difficulty of conducting these prospective studies, which were closed before reaching the target sample size.

Second, the high incidence of sexual dysfunction reported in our survey may be attributed not only to the use of validated instruments to assess dysfunction, but also to the inclusion of patients with probable preexisting sexual dysfunction before the rectal cancer treatment. However, we have recently reported that de novo urinary dysfunction was observed in nearly 33% of patients and sexually dysfunction resulted in de novo cessation of sexual activity in 28% of men and 18% of women.[7]

Third, the response rate was quite low, which might bias the results. This low response rate may be explained by both the strict inclusion criteria and the high number of validated questionnaires

used. Moreover, questionnaires on sexuality may be very intrusive for patients, especially for women. Even if the comparison between responders and nonresponders did not show any significant difference, we cannot definitively rule out that nonresponders were more satisfied than responders. This may limit the determination of the effect of the treatment on genitor-urinary functioning. Regarding our responders, more than two-thirds were male with a mean age of 61 years at surgery. According to statistics, 52% of elderly men may have varying degrees of sexual dysfunction.[46] This rate may partially explain our high incidence of sexual dysfunction. Moreover, rectal replacement with straight colorectal anastomosis was more frequent in the nonresponders. However, it seems to date that the formation of a neo-rectal pouch (ie, colonic J pouch or side-to-end anastomosis) provides advantages compared with a straight colorectal anastomosis only in the first year after surgery, as suggested by both a recent meta-analysis and a prospective randomized controlled trial.[47,48] In our survey, bowel continuity was restored in included patients for more than 24 months to avoid a bias. It was essential that responders and nonresponders were comparable in our survey according to predictive factors for a high LARS score (ie, age, sex, tumor location, preoperative radiotherapy and TME compared with PME).[34]

Finally, the QoL scores of RC patients were not compared with those of the general population in France. Unfortunately, our population-based study was not designed to evaluate the pretherapeutic QOL or LARS score. Theoretically, normative data from the general population may be useful and can serve as proxy baseline data. To our knowledge, very few normative data about QOL or LARS score are available in the literature. According to a recent study, $\leq$19% of females and 10% of males without a rectal cancer experienced a major LARS score.[49] In our population-based cancer registry, we reported LARS scores 2 to 4 times higher than those reported in the general population. In the future, it will be relevant to explore bowel function and QoL using validated instruments in the French population.

In summary, the results of this survey suggest that severe bowel dysfunction occurs in 40% of RC survivors. Despite a high prevalence of sexual dysfunction, poor QoL was mainly correlated with the severity of bowel dysfunction. Although these findings should be interpreted with caution because of several limitations, it is important to inform patients about the potential functional outcome of their surgery in terms of QoL and oncologic prognosis.

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Conflict of interest

The authors have indicated that they have no conflict of interest regarding the content of this article.

Supplementary materials

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