



Restorative reconstruction after total mesorectal excision for rectal cancer is associated with significant bowel dysfunction from initial presentation[☆]

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ABSTRACT

Background: Patients often desire restorative reconstruction following total mesorectal excision. Reconstruction has become synonymous with providing high-quality rectal cancer care. However, the bowel functional outcomes of restoration from presentation are unknown. We aimed to evaluate the bowel functional effects of rectal cancer treatment from presentation through surveillance.

Methods: This was a retrospective cohort study from 2014 to 2019 using prospectively collected data. Patients underwent treatment for rectal adenocarcinoma including restorative reconstruction. Patients completed the validated Colorectal Functional Outcome questionnaire during clinic visits (1) at presentation, (2) after neoadjuvant therapy, (3) after restoration of continuity, and (4) at surveillance. Scores range from 0 to 100 with a higher score indicating worse bowel function.

Results: Sixty-eight patients (age: 62 ± 12 years, 40% female) were included. The mean tumor height was 7 ± 4 cm with 85% symptomatic. Bowel function did not worsen from presentation to after neoadjuvant therapy in Total Colorectal Functional Outcome and most domain scores; there was improvement in frequency and stool-related aspects. Bowel function worsened in all scores from after neoadjuvant to restoration of continuity (mean anastomotic height: 5 ± 2 cm); there were similar findings between presentation and restoration of continuity. At surveillance, there was improvement in most domains compared with restoration of continuity. There remained significant worsening of incontinence, social impact, and need for medication scores at surveillance compared with presentation.

Conclusion: Restorative reconstruction after total mesorectal excision is associated with significant bowel dysfunction. For some patients, restorative reconstruction may not be high-quality rectal cancer care.

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INTRODUCTION

A major criterion of high-quality rectal cancer care is high rates of restorative reconstruction after total mesorectal excision (TME) for rectal cancer [1]. Enthusiasm for restorative reconstruction originates from several sources. First, advances in surgical technique have expanded the potential for restorative reconstruction such as intersphincteric resection, transanal total mesorectal excision, and robotic assisted surgery [2–6].

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Secondarily, previous work has found increased mortality and morbidity in hospitals with higher rates of colostomy creation, centering mostly on low-volume centers [7]. Other work has also found that low-volume centers tend to only perform abdominoperineal resection and have associated poor outcomes [8–9]. Finally, there have been studies suggesting that a permanent colostomy has a negative impact on quality of life; however, it is unclear how this changes over time [10].

Even though restorative reconstruction has been associated with high-quality care, it is not a perfect solution for all patients. We know that many patients with restorative reconstruction experience bowel dysfunction called *low anterior resection syndrome* (LARS) that extends through survivorship [11–13]. LARS includes increased bowel movement frequency, incontinence, clustering, and significant social impact in severe cases. Many factors have been identified that contribute to LARS, such as lower anastomotic height, radiation therapy, and pelvic complications [11,17–20]. Several scoring systems have been validated

to assess the degree of LARS in the postreconstructive setting [14–16]. However, most studies of LARS do not compare postoperative bowel function to that experienced at time of presentation prior to any treatment. Additionally, little data exist on the natural history of patients' bowel function from presentation to after neoadjuvant therapy, restorative reconstruction, and first surveillance visit time points.

The aims of the study are to evaluate rectal cancer patients' bowel function at time of presentation and to define the natural history of bowel function changes from presentation to after completion of neoadjuvant therapy, after restoration of continuity, and at the first surveillance visit in those undergoing treatment for rectal cancer. Our hypothesis is that there would be no significant differences in bowel function scores that would be present at each paired time point.

METHODS

Study Design. This is a retrospective cohort analysis conducted from December 2014 to June 2019 using prospectively collected data. We collected patient-reported outcomes of bowel function from all patients seen in the Colon and Rectal Surgery clinic at our institution. This database was approved by our institutional committee for the Protection of Human Subjects and qualified for a waiver of consent for participants (CPHS 29129).

Inclusion Criteria. Our cohort included patients in the database, identified by *International Classification of Diseases, 9th and 10th Revision*, codes, who were evaluated for the diagnosis and treatment of *rectal cancer*, defined as adenocarcinoma of the rectum as determined by the surgeon on endoscopic or digital rectal examination. Patients were included in this study if they completed a questionnaire at presentation, questionnaire following neoadjuvant therapy, and/or a questionnaire following diverting loop ileostomy closure (restoration of continuity), regardless of treatment course. For the analysis at surveillance, we also included those who had undergone restoration of continuity and had completed a survey at a subsequent surveillance visit.

Exclusion Criteria. Patients were excluded if they were less than 18 years old, were incarcerated, or did not complete at least 1 of the required questionnaires. Those patients with ostomies are not administered the survey.

Bowel Function Patient Report Outcome Instrument (Colorectal Functional Outcome Questionnaire) [21] and Data Collection. The Colorectal Functional Outcome (COREFO) questionnaire is a validated bowel function survey that assesses bowel function in 5 domains and a global function score (Total COREFO score). The domains include incontinence, frequency, social impact (the impact of bowel habits/movements on social activities), need for medication (the use of food or medication to regulate bowel movements), and stool-related aspects (bleeding, pain, and/or skin irritation with bowel movements). Scores for each domain and global function range from 0 to 100 with a higher score indicating worse function. A score of 15 or higher is used by the authors to describe symptomatic patients based on data from the initial validation of the instrument, which compared scores of patients with and without bowel function complaints.

We used the COREFO questionnaire rather than the LARS score or Memorial Sloan Kettering Cancer Center (MSKCC) bowel function instrument because the latter instruments are validated in only a post-LAR population [16]. On the other hand, the COREFO questionnaire is validated in patients with multiple types of colorectal resection including patients who have undergone no resection, right hemicolectomy, coloanal anastomosis, and ileoanal anastomosis. We did not use other validated measures of incontinence because of their limited scope [16]. The COREFO provides a broad measure of bowel function, which we believe is necessary when assessing this population.

The COREFO questionnaire was administered via paper prior to April 2015 and by electronic tablet after April 2015. The questionnaire was administered during each visit for patients seen in the Colon and Rectal Surgery clinic prior to evaluation by a clinician. Responses were electronically integrated to each patient's medical record and, subsequently, integrated into our ongoing REDCap database for bowel function patient-reported outcomes. We collected demographic, clinical, operative, and postoperative data including rectal cancer-specific data such as distance from anal verge, stage, symptomatology (bothersomeness), and treatment course.

Data Analysis

Analysis 1: Unpaired Comparison With All COREFO Responses

We evaluated domain and Total COREFO scores for all respondents who completed a questionnaire in any of the 3 time points: at presentation (presentation), after neoadjuvant therapy (neoadjuvant), and after restoration of continuity (restoration). We conducted a univariate analysis using an unpaired *t* test of mean domain and Total COREFO scores at each time point grouping.

Analysis 2: Paired Analyses of Mean Domain and Total COREFO Scores

For all patients with more than 1 completed questionnaire, we conducted paired univariate analysis using a paired *t* test comparing mean domain and Total COREFO scores at each time point grouping: presentation to neoadjuvant, presentation to restoration of continuity, and neoadjuvant to restoration of continuity. For surveillance analysis, we conducted paired univariate analysis using a paired *t* test comparing mean scores between presentation to surveillance and restoration of continuity to surveillance.

All statistical analyses were performed with Stata 15 (Stata Corp, College Station, TX).

Primary Outcome and Null Hypothesis. The primary outcome was the change in domain and Total COREFO scores at each paired time point. Our null hypothesis was that there would be no differences in the mean domain and Total COREFO scores in both the unpaired and paired comparisons at each paired time point.

RESULTS

Cohort characteristics are described in Table 1. A total of 68 patients were included in the cohort, with a mean age of 62 ± 12 years, and 27 (40%) were women. Mean body mass index was 28.9 ± 8.2 kg/m². Fifty-nine (84%) were bothered by symptoms at time of presentation.

Mean distance of the lower edge of the tumor to the anal verge was 7 ± 4 cm measured endoscopically or by digital rectal examination. Stage at presentation included the following: I, 15 (23%); II, 18 (26%); III, 34 (50%); and IV, 1 (1%). Fifty-three (78%) underwent neoadjuvant therapy, with the majority undergoing long-course chemoradiotherapy. Forty-seven (69%) underwent systemic chemotherapy: 10 in the neoadjuvant setting and 37 in the adjuvant setting.

In total, 40 patients underwent low anterior resection. Mean anastomotic distance from the anal verge was 5 ± 2 cm, with the majority of anastomoses being stapled colorectal (Table 2). Thirty-nine patients (98%) received diverting loop ileostomy creation, and 35 (90%) underwent subsequent reversal. Four patients did not receive reversal because of anastomotic complication (2), development of metastatic disease (1), and patient preference (1). Thirty-one patients completed a questionnaire at restoration. Median time from ileostomy closure to restoration questionnaire completion was 5 weeks (interquartile range: 5 to 5). Four did not complete the questionnaire at restoration because of awaiting in-person follow-up (2) and loss to follow-up (2).

Table 3 shows the median time between questionnaire completion at each time point comparison.

Table 1
Cohort characteristics

Demographics	Total
Number of patients	68
Age, y, mean (SD)	62 (12)
Sex	
Male (%)	41 (60)
Female (%)	27 (40)
BMI, mean in kg/m ² (SD)	28.9 (8.2)
Local/regional staging modality (%)	
MRI	60 (88)
Endorectal ultrasound	6 (9)
Other	2 (3)
Preoperative stage (%)	
1	15 (23)
2	18 (26)
3	34 (50)
4	1 (1)
Neoadjuvant therapy (%)	
Long-course chemoradiotherapy	36 (50)
Short-course radiation therapy	7 (10)
Chemotherapy	3 (4)
Total neoadjuvant therapy	7 (10)
Adjuvant therapy (%)	
Chemotherapy	37 (54%)
Chemoradiotherapy	1 (1%)
Operation (%)	
Low anterior resection	40 (58)
Abdominoperineal resection	25 (37)
Colostomy only	2 (5)
Operative modality for TME (%)	
Robotic	37 (57)
Laparoscopic	17 (26)
Open	11 (17)

BMI, body mass index; MRI, magnetic resonance imaging.

Analysis 1. Table 4 demonstrates the unpaired comparisons of mean domain and Total COREFO scores at each time point from presentation to restoration. Sixty-one patients completed the questionnaire at the presentation time point, 39 completed at neoadjuvant, and 31 at restoration. Comparison of presentation to neoadjuvant scores demonstrates improvement in stool-related aspects, frequency, and Total COREFO scores, with no change in mean scores for the other domains. Comparison of presentation to restoration scores demonstrates significant worsening in mean Total COREFO score and all mean domain scores except for stool-related aspects at restoration. Comparison of neoadjuvant and restoration scores demonstrates significant worsening in all scores at restoration as well.

Analysis 2. The Figure, A–D demonstrates the paired comparison of domain and Total COREFO scores. Thirty-two patients had questionnaire completion at presentation and neoadjuvant. Comparison of scores demonstrates no differences except in the stool-related aspects and frequency where there is improvement at the neoadjuvant time point. Twenty-seven patients had questionnaire completion at presentation and restoration. Comparison of scores demonstrates significant worsening in all scores except for stool-related aspects at restoration.

Table 2
Anastomotic technique and location

Anastomotic characteristics	Total
Anastomotic height,* mean cm (SD)	5 (2)
Anastomotic type (%)	
Stapled end to end	25 (63)
Stapled side to end	9 (23)
Handsewn coloanal	6 (14)

* Anastomotic height from anal verge.

Table 3
Weeks between questionnaires

Median weeks between questionnaire completion (IQR)	
Presentation to neoadjuvant	15 (14–18)
Neoadjuvant to restoration	37 (30–47)
Presentation to restoration	49 (27–63)
Restoration to surveillance	25 (21–35)
Presentation to surveillance	77 (52–95)

IQR, interquartile range.

The Figure, C and D demonstrates the analysis at surveillance. From restoration to surveillance, there is significant improvement in all domains except need for medication. Additionally, there is improvement in the Total COREFO score. From presentation to surveillance, there is significant worsening of the Total COREFO score as well as the incontinence, social impact, and need for medication domains.

DISCUSSION

In this study, we found that there was significant variability in bowel function among patients that present with rectal cancer. We also found that there was improvement in bowel function between presentation and after neoadjuvant therapy driven by improvement in stool-related aspects such as bleeding with bowel movements, pain, and irritated skin around the anus and reported frequency of bowel movements. Furthermore, we noted that there was significant worsening of bowel function after reconstruction respect to bowel function both with at time of presentation and after neoadjuvant therapy. We did find that bowel function improved between ileostomy reversal and surveillance follow-up. However, bowel function at this follow-up was worse than bowel function at presentation, driven by higher scores in the incontinence, social impact, and need for medication domains.

Based on our results, bowel function is significantly worse after reconstruction and during surveillance than when most patients presented with a rectal cancer that was bothersome by symptoms. We found that bowel function at presentation varied in patients with newly diagnosed rectal cancer. Possible explanations include tumor size, location within the rectum, and stage.

Neoadjuvant therapy appeared to improve overall bowel function prior to TME in the short term. This suggests that reported bowel function effects of neoadjuvant therapy do not manifest in the early postneoadjuvant therapy period. Neoadjuvant chemotherapy alone or added to neoadjuvant chemoradiotherapy has also been shown to have no change in overall bowel function even after TME in prior studies [22].

Comparatively, restorative reconstruction and ileostomy reversal had a tremendous effect in diminishing most aspects of bowel function. Although a diverted colon may need time to regain function, bowel

Table 4
Analysis 1: unpaired comparison with mean (SD) COREFO domain and total scores from presentation to restoration

COREFO domains/total score	Presentation n = 61	Neoadjuvant n = 39	Restoration n = 31
Incontinence	17.8 (18.5)	12.2 (13.4)	38.7 (24.4) ^{†,‡}
Social impact	29.2 (26.9)	22.9 (20.0)	53.8 (24.0) ^{†,‡}
Frequency	26.0 (24.6)	18.4 (11.3) ^{*†}	46.3 (20.7) ^{†,‡}
Stool-related aspects	34.6 (23.2)	13.5 (16.0) [*]	35.7 (25.7) [†]
Need for medication	14.8 (19.9)	13.9 (19.6)	41.7 (28.2) ^{†,‡}
Total COREFO	24.0 (18.7)	16.7 (12.6) [*]	44.5 (20.2) ^{†,‡}

COREFO: range 0–100; higher score signifies worse function.

Legend for significant comparisons ($P < .05$):

* Presentation to neoadjuvant.

† Presentation to restoration.

‡ Neoadjuvant to restoration.

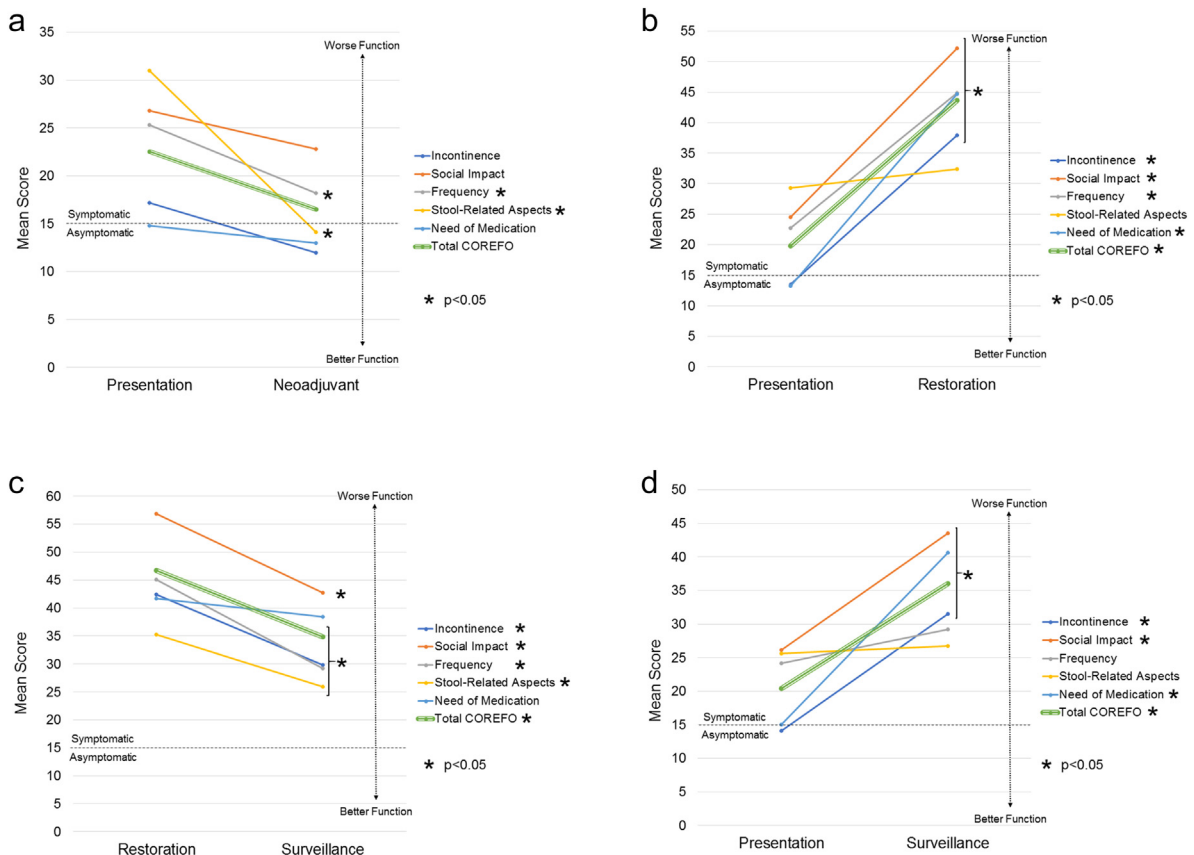


Figure. A–D, Paired analyses of mean domain and Total COREFO scores at time points. A, Presentation to neoadjuvant ($n = 32$). B, Presentation to restoration of continuity ($n = 27$). C, Restoration of continuity to surveillance ($n = 18$). D, Presentation to surveillance ($n = 15$).

function scores continue to be worse at surveillance as compared to presentation. These findings are consistent with the lower health-related quality of life scores in rectal cancer patients after restorative procedures in the Netherlands [23]. In essence, patients undergoing restorative procedures trade rectal cancer for poor bowel function.

Most patients prefer restorative reconstruction rather than permanent colostomy when facing the decision preoperatively [24], even though there are no differences in patient quality of life when comparing either restorative reconstruction or colostomy after TME [25]. Our findings suggest that one explanation for this discordance may be due to the severe bowel dysfunction that exists after ileostomy reversal and surveillance. Patients undergoing restorative reconstruction deal with poor bowel function, whereas those with colostomy deal with psychosocial issues related to the stoma and stoma care. It is clear that restorative reconstruction has a significant impact on patients' bowel function, but it is unclear how aware patients are about this effect preoperatively.

Given these findings, we advocate for optimal patient decisions on surgical management for rectal cancer based on their own preferences and goals. Shared decision making is the patient–clinician communication process that achieves this [26]. We believe that preoperative shared decision making is a vital element for high-quality rectal cancer care. We must take a thoughtful approach to offer eligible patients options for surgical treatment outlining benefits and tradeoffs for each surgical approach.

This study is constrained by important limitations. First, all patients did not receive the same treatment course; some underwent neoadjuvant therapy, whereas others did not, for example. However, we wanted to include all patient responses even if only for 1 visit. With this approach, we obtained a broader sense of bowel function at presentation by not limiting to treatment course. We attempted to mitigate this with the paired analysis with the same patient completing the same

questionnaire at different points in treatment. Second, restoration of continuity score query occurred at a median of 5 weeks after ileostomy reversal. We did follow these patients to surveillance and showed some domain improvement but overall worsening compared to baseline. Third, we were not able to perform a multiple-variable analysis without making potentially inaccurate estimation due to our current sample size. We hope to do so in the future as we accrue more patients. Next, we can only assess those patients that have completed the questionnaire appropriately. Our currently completion rate is >95% but has been as low as 87% in past years. Thus, we may have missed some patients who did not complete the questionnaire because of several reasons such as difficulty or noncompletion on the electronic tablet. Lastly, we did not measure parameters of anorectal physiology to elucidate further the cause of this phenomenon. We believe that patient-reported outcome measures are the true outcome to evaluate regardless of the outcomes of anorectal function measures.

In conclusion, restorative reconstruction after TME is associated with significant bowel dysfunction from initial presentation that persists during surveillance. For some patients, restorative reconstruction may not be high-quality rectal cancer surgery. High-quality rectal cancer care should include patient satisfaction with functional outcomes in addition to the oncologic outcomes for those undergoing restorative reconstruction. In high-quality/high-outcome centers, restorative reconstruction should not be the default position for every rectal cancer patient eligible for reconstruction. We believe that the next generation of metrics for the National Accreditation Program for Rectal Cancer [27] should include elements of decision satisfaction, decision quality, and decisional regret rather than programmatic rates of restorative reconstruction. With these data, we can better understand those factors that lead to a satisfied patient who has made a high-quality decision with minimal regret when facing rectal cancer. We can then align the structure and processes of rectal cancer care delivery to these factors

with the ultimate hope of raising the quality of life and decision satisfaction for all rectal cancer patients.

Author Contribution

All authors have substantial contributions to the conception or design of the work. Specifically, SJ contributed to the design. All authors were responsible for collection of data, the acquisition, analysis, and interpretation of data for the work. All authors drafted the work and revised it critically for important intellectual content including final approval of the version to be published. All authors are in agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of Interest

There are no conflicts of interest for any authors.

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