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ORIGINAL ARTICLE

A novel bowel rehabilitation programme after total mesorectal excision for rectal cancer: the BOREAL pilot study

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Abstract

Aim: Low anterior resection syndrome (LARS) following sphincter-preserving surgery for rectal cancer has a high prevalence, with an impact on long-term bowel dysfunction and quality of life. We designed the bowel rehabilitation programme (BOREAL) as a proactive strategy to assess and treat patients with LARS. The BOREAL programme consists of a stepwise approach of escalating treatments: medical management (steps 0–1), pelvic floor physiotherapy, biofeedback and transanal irrigation (step 2), sacral nerve neuromodulation (step 3), percutaneous endoscopic caecostomy and anterograde enema (step 4) and definitive colostomy (step 5).

Methods: A pilot study was undertaken to assess the feasibility of collecting LARS data routinely with the parallel implementation of the BOREAL programme. All patients who underwent total mesorectal excision for rectal cancer between February 2017 and March 2019 were included. LARS was assessed using the LARS score and the Wexner Faecal Incontinence score at 30 days and 3, 6, 9 and 12 months postoperatively. A good functional result was considered to be a combined LARS score <20 and/or a Wexner score <4.

Results: In all, 137 patients were included. Overall compliance with the BOREAL programme was 72.9%. Major LARS decreased from 48% at 30 days postoperatively to 12% at 12 months, with a concomitant improvement in overall good function from 33% to 77%, $P < 0.001$. The majority of patients ($n = 106$, 77%) required medical management of their LARS.

Conclusion: The BOREAL programme demonstrates the acceptability, feasibility and effectiveness of implementing a responsive, stepwise programme for detecting and treating LARS.

KEYWORDS
functional outcomes, rectal cancer, rehabilitation program, TME

INTRODUCTION

Low anterior resection syndrome (LARS) following sphincter-preserving surgery for rectal cancer has a high prevalence, with long-term reported rates of 34%–49% [1–7]. LARS consists of a constellation of symptoms including faecal incontinence, frequency, urgency or evacuatory dysfunction, and was originally defined as 'disordered bowel function after rectal resection, leading to a

detriment in quality of life' [8]. This definition has recently been superseded by an international, expert consensus group, consisting of patients and surgeons, who have identified eight key symptoms and eight consequences of LARS of the highest priority to define LARS and enable its precise measurement [9].

LARS can contribute to long-term bowel dysfunction [2,10] and can have a profound impact on patients' quality of life (QoL) [10]. Consequently, there has been considerable focus over the last few years on the assessment and appropriate management of LARS in patients undergoing sphincter-preserving rectal cancer surgery. The management of LARS is usually reactive and symptom-based, consisting of a combination of lifestyle, pharmacological and interventional strategies, with varying efficacy. These treatment strategies are often implemented once patients self-report symptoms consistent with LARS. Consequently, current treatment algorithms are variable and reactive to symptom development. This is compounded by the lack of high quality evidence regarding preventative and rehabilitation strategies in patients following sphincter-preserving rectal cancer surgery [11]. We designed the bowel rehabilitation (BOREAL) programme to address the lack of a standardized approach for the management of LARS in patients undergoing sphincter-preserving rectal cancer surgery at our centre. The BOREAL programme consists of a series of stepwise, evidence-based and practice-based measures aimed at improving LARS symptoms [11–17] based on continuous postoperative assessment of LARS scores over a 12-month period. The BOREAL programme centres on high quality patient education and engagement, effective screening and timely and stepwise intervention. This pilot study reports on the implementation and early results of the BOREAL programme including its impact on functional and QoL outcomes.

What does this paper add to the literature?

The BOREAL programme highlights the acceptability, feasibility and effectiveness of timely assessment and treatment of low anterior resection syndrome.

MATERIALS AND METHODS

A pilot study was undertaken to assess the feasibility of collecting LARS data routinely with the parallel implementation of the BOREAL programme, and its efficacy over a 12-month period. All patients who underwent total mesorectal excision (TME) for rectal cancer in the colorectal surgical unit of Bordeaux University Hospital between February 2017 and March 2019 were included in this study.

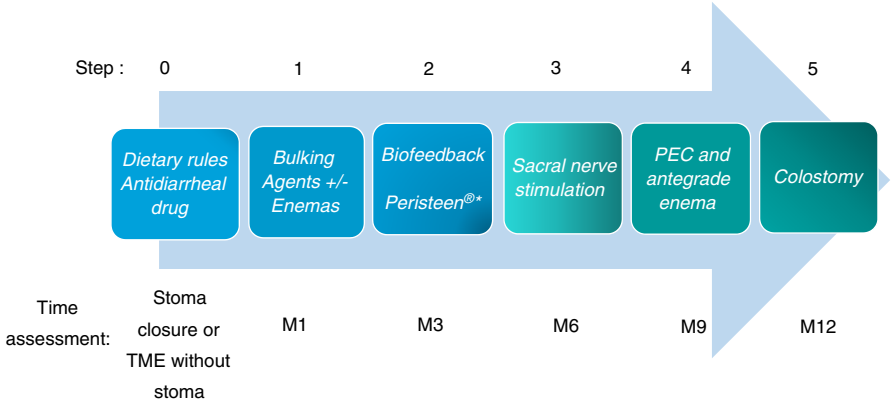
Eligibility criteria

All adult patients (>18 years old) undergoing a TME for rectal cancer with an anastomosis performed within 6 cm of the anal verge and a minimum follow-up of 12 months were eligible for inclusion. Patients with a temporary ileostomy were enrolled into the BOREAL programme following closure of the ileostomy and restoration of gastrointestinal continuity. Patients were excluded if an abdominoperineal resection or local excision was performed, if they had a permanent stoma, if they developed metastatic disease during follow-up or if they were unable to complete the study questionnaires due to cognitive impairment.

The BOREAL programme

The BOREAL programme assesses functional outcomes using the LARS and Wexner Faecal Incontinence scores at pre-specified time points postoperatively, with a parallel treatment strategy for minor and major LARS symptoms over a 12-month period. The BOREAL programme is delivered by the surgical team and supported appropriately by dedicated colorectal nursing staff. All LARS assessments are undertaken by the surgical team at all candidate time points in the outpatient setting. Patients complete the assessments at the time of their outpatient review jointly with the surgeon. On completion of the BOREAL programme patients' overall QoL is assessed using the EQ-5D. An overview of the BOREAL programme is provided in Figure 1. The BOREAL programme is underpinned by a patient education initiative, which starts preoperatively with in-depth discussion regarding the possible spectrum of postoperative functional outcomes and possible treatment options by the surgeon undertaking the operative procedure at the time of obtaining consent. The BOREAL programme consists of the following steps. Step 0 is the routine commencement of anti-diarrhoeal drugs (e.g., diosmectite, loperamide) and specific dietary advice on low residue diet for all patients at the time of hospital discharge. Initial assessment of LARS is carried out at 30 days, with the addition of bulking agents or enemas for patients with major LARS symptoms (step 1). Further assessment of LARS is carried out at 3, 6, 9 and 12 months. Patients with major LARS at 3 months are treated with a combination of pelvic floor physiotherapy, biofeedback and transanal irrigation (step 2). If symptoms of major LARS are present at the 6 monthly assessment sacral neuromodulation is offered to patients (step 3). Major LARS symptoms at 9 months are treated with percutaneous endoscopic caecostomy and anterograde enema (step 4) [18]. Finally, if LARS symptoms persist beyond 12 months a definitive colostomy is offered to patients (step 5). The principles of shared decision making are used at each stage of the BOREAL programme between the patient and the surgeon. Patients are informed of their LARS and Wexner scores followed by an informed discussion regarding treatment strategy including de-escalation or escalation of steps depending on patient priorities. Patients progress through each stage of the BOREAL programme in a stepwise fashion. The initiation of specific treatment steps, that is, pelvic floor physiotherapy, biofeedback and transanal irrigation, is supported by a colorectal nurse specialist.

FIGURE 1 Outline of the BOREAL programme



** Transanal irrigation system*

PEC : percutaneous endoscopic caecostomy

End-points

The primary end-point of our pilot study was overall compliance to the BOREAL programme, including completion of the questionnaires. Secondary end-points included the rate of LARS at each candidate time point as measured by the LARS and Wexner Faecal Incontinence scores, the proportion of patients considered to have good overall function at 12 months and overall QoL following completion of the BOREAL programme.

Outcome measures

LARS assessment was undertaken using the LARS score and the Wexner Faecal Incontinence score. The LARS score is a well validated scoring system consisting of five questions, which was developed specifically for use in patients undergoing restorative rectal cancer surgery [19]. The score has a range of 0–42 points and stratifies patients into three categories: no LARS (0–20), minor LARS (20–28) or major LARS (30–42). The Wexner score consists of five questions and assesses three types of faecal incontinence (solid, liquid and gas) and their consequences (pad wearing and lifestyle alteration) [20]. For each item, the five frequency options range from never (score 0) through to always (meaning at least once per day; score 4). The total score is the sum of the item scores that range from 0 (perfect continence) to 20 (complete incontinence). The LARS score and Wexner score were assessed at 30 days and at 3, 6, 9 and 12 months and coincided with dedicated clinic visits. A good functional result was considered to be a combination of LARS score <20 and Wexner score <4. These cut-off values represent the highest values associated with good functional outcomes; a value of <20 on the LARS score is considered to be associated with no LARS symptoms and a value of 4 on the Wexner score is associated with good continence function.

The EQ-5D was used to assess overall QoL on completion of the BOREAL programme at 12 months. The EQ-5D is a well-validated questionnaire used to assess generic QoL using five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression [21]. The EQ-5D VAS records the patient's self-rated health on a vertical visual analogue scale. The VAS is used as a quantitative measure of health outcome that reflects the patient's own judgement.

Statistical analysis

Compliance was assessed for LARS functional assessment by calculating the number of patients completing the LARS and Wexner scores at all candidate time points as a proportion of all patients undergoing rectal cancer surgery. Compliance for the BOREAL programme was assessed by calculating the number of patients completing the relevant step of the BOREAL programme at each candidate time point as a proportion of the total number of patients participating in the programme overall. Efficacy of the BOREAL programme was assessed by the proportion of patients having a LARS score <20 and Wexner score <4 at each step of the study.

Categorical variables were expressed as number and percentage. Continuous variables were expressed as mean and standard deviation. A chi-squared test was used to compare categorical variables and a non-parametric Mann–Whitney *U* test to compare continuous variables. All tests were two-sided, with type I error set at $\alpha = 0.05$. A multivariate analysis was undertaken to identify clinical factors associated with good function at 12 months. All analyses were conducted using IBM SPSS Statistics version 26.0.0.1 for Macintosh (IBM Corp.).

RESULTS

Between 2017 and 2019, 187 patients underwent TME for mid and low rectal cancer at our institution; a total of 137 patients were included in this study. Fifty patients were excluded from the study due to follow-up of less than 12 months ($n = 34$), disease progression ($n = 7$) and the presence of a definitive stoma ($n = 9$). Patient, disease and surgical characteristics are described in Table 1. The majority of patients underwent surgery for T3-4 disease ($n = 115$, 84%), with

TABLE 1 Patient and clinical characteristics

Variable	*n*	(%)
Male	88	(64)
Age (years)[a]	65 (35–85)	
BMI (kg/m²)[a]	25.1 (17.5–37.5)	
ASA score		
1	37	(27)
2	84	(61)
3	16	(12)
cT3-4	115	(84)
cN+	102	(75)
Metastases	18	(13)
Tumour size (cm)[a]	5 (1–12)	
Preoperative radiotherapy	93	(68)
RTCT	61	
CT-RTCT	29	
RT	3	
Surgical approach		
Mini-invasive	106	(77)
Open procedure	31	(23)
Height of anastomosis (cm)[a]	3.5 (0.5–6)	
Anastomosis		
Colorectal anastomosis	47	(34)
Coloanal anatomosis	60	(44)
Intersphincteric resection	21	(15)
Pelvectomy	9	(7)
Anatomosis		
Manual	72	(53)
Mechanical	65	(47)
Abdominal	46	
Trans-anal	19	
Protective stoma	110	(80)
Delayed anastomosis	16	(12)
No stoma	11	(8)
Delay of closure (days)[a]	72 (7–538)	
Pelvic sepsis at 12 months	23	(17)
Adjuvant chemotherapy	52	(38)
Pathological tumour stage		
pT0-1	28	(21)
pT2	44	(32)
pT3	60	(44)
pT4	5	(4)
Pathological nodal stage		
pN0	85	(62)
pN1-2	52	(38)
pT0N0	17	(12)
R1 resection	13	(10)
Vascular invasion	37	(27)
Neural invasion	15	(11)

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; CT-RTCT, chemotherapy followed by chemoradiotherapy; RT, radiotherapy; RTCT, chemoradiotherapy.

[a]Median (range).

preoperative radiotherapy used in 93 (68%) patients. The median height of anastomosis from the anal verge was 3.5 cm (range 0.5–6), with a handsewn anastomosis performed in 72 (53%) patients and a mechanical anastomosis in 65 (47%) patients. A defunctioning ileostomy was performed in 110 (80%) patients, with a median time to closure of 72 days (range 7–538).

Compliance

The response rates of all questionnaires (LARS score and Wexner) at all candidate time points were 100%. The compliance with the BOREAL programme was 93.4% ($n = 128$) at 3 months and gradually declined to 78.8% ($n = 108$) at 6 months and to 72.9% ($n = 100$) at 9 months. The overall compliance at 12 months with the BOREAL programme was 72.9%, with a total of 100 patients completing the programme. Thirty-seven (27.1%) patients did not complete the 12-month programme due to patients choosing not to participate ($n = 9$, 7%) or failure to appropriately progress through the component key steps in a timely fashion.

BOREAL programme outcomes

At 30 days the incidence of minor LARS was 14% ($n = 19$), major LARS was 48% ($n = 66$) and Wexner score >4 was 59% ($n = 46$) (Figure 2). Improvements were seen in all three categories at 12 months with an incidence of minor LARS of 6% ($n = 8$), major LARS of 12% ($n = 17$) and Wexner score >4 of 22% ($n = 30$). Overall, good functional results were observed in 33% of patients at 30 days compared to 77% at 12 months, $P < 0.001$. The median time to achieving good bowel function was 3.5 (interquartile range) months for patients compliant with the BOREAL programme compared to 11.7 months ($P < 0.001$) in patients who did not complete the programme.

There was little progression through the individual steps of the BOREAL programme throughout the 12-month time frame with the majority of patients ($n = 106$, 77%) remaining at baseline on step 0 (Figure 3). At 12 months, 19 (14%) patients progressed to step 2 requiring biofeedback ($n = 7$) ± transanal irrigations ($n = 12$), one (1%) patient progressed to step 3 (sacral neuromodulation), one (1%) patient progressed to step 4 (Malone antegrade continence enema) and one (1%) patient progressed to step 5 (permanent colostomy).

Predictive factors of good functional outcomes

On multivariate analysis, a body mass index of <25 kg/m² (relative risk [RR] = 2.62, 95% CI 1.05–6.53), no neoadjuvant radiotherapy (RR = 5.51, 95% CI 1.49–20.49) and mechanical anastomosis (RR = 7.03, 95% CI 2.40–20.61) were predictive of good functional outcomes at 12 months (Table 2).

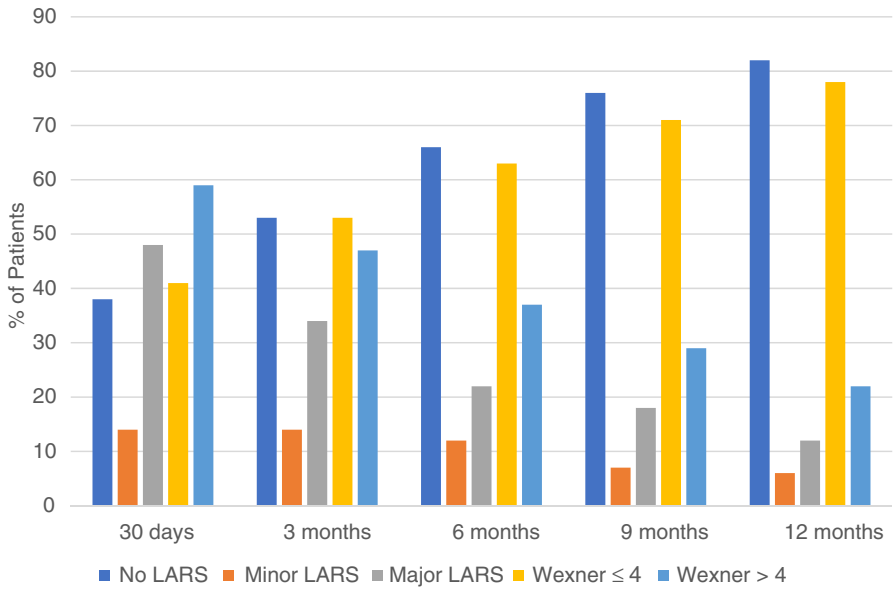


FIGURE 2 BOREAL programme functional outcomes

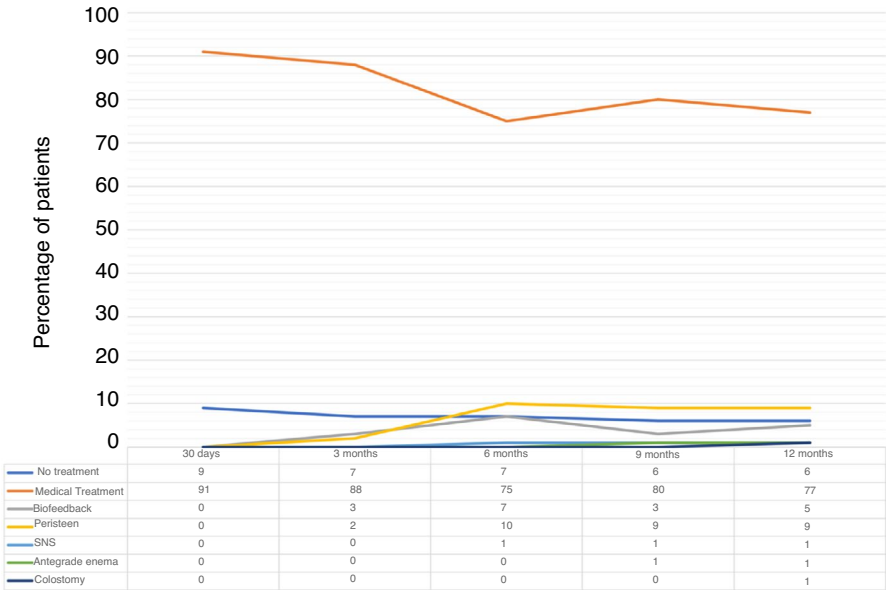


FIGURE 3 BOREAL programme treatment strategies. SNS, sacral neuromodulation

Quality of life

The EQ-5D demonstrated comparable QoL scores between patients with good and poor functional outcomes 12 months following surgery (Table 3). The presence of LARS did not have an impact on mobility, self-care, usual activity, pain/discomfort or anxiety/depression. There were no differences in patients' self-perceptions of their own QoL between the two groups.

DISCUSSION

Our study demonstrates the feasibility of integrating routine assessment of LARS in clinical practice, alongside the implementation of a standardized and structured programme to proactively manage its symptoms. We were able to demonstrate excellent compliance with completion of LARS scores at all clinical time points and good overall compliance to the BOREAL programme. Our study includes a high-risk

TABLE 2 Multivariate analysis of predictors of good functional results at 12 months

	Relative risk	95% confidence interval	*P* value
BMI ≤25.0 kg/m²	2.62	(1.05–6.53)	0.039
No neoadjuvant radiotherapy	5.51	(1.49–20.46)	0.011
Mechanical vs. manual anastomosis	7.03	(2.40–20.61)	<0.001

Abbreviation: BMI, body mass index.

TABLE 3 Relationship between functional outcomes and quality of life

	Good function[a]		Poor function		
	N	(%)	*N*	(%)	*P*
Mobility[b]	84	(93)	26	(93)	1.000
Self-care[b]	85	(94)	28	(100)	0.337
Usual activity[b]	73	(81)	26	(93)	0.237
Pain/discomfort[b]	53	(59)	15	(54)	0.619
Anxiety/depression[b]	67	(74)	20	(71)	0.751
EQ-VAS[c]	80 (68.75–90)		80 (70–90)		0.347
EQ-5D VAS ≥ 80	51	(57)	15	(54)	0.773

[a]LARS ≤20 and Wexner ≤4.

[b]No problem.

[c]Median (interquartile range).

cohort of patients with significant risk factors for the development of LARS including advanced tumours, preoperative radiotherapy and a low anastomosis. By using a stepwise, structured approach delivered through the BOREAL programme we were able to significantly improve functional outcomes in patients from 33% at 30 days postoperatively to 77% at 12 months, with an overall incidence of LARS of 18% and Wexner score >4 of 22% at 12-month follow-up.

Previous studies have demonstrated the importance of rehabilitation following sphincter-preserving surgery for rectal cancer [12]. The majority of these studies have focused on individual interventions using biofeedback with encouraging success [22–25]. There is some emerging evidence on the value of introducing structured, multimodal rehabilitation programmes for patients with LARS [26]. Pucciani et al. [27] reported encouraging, preliminary results with complete resolution of LARS symptoms in a quarter of patients using a rehabilitation programme consisting of pelviperineal kinesitherapy, biofeedback, volumetric rehabilitation and electrostimulation. Similarly, Fomenko et al. [28] demonstrated the efficacy of a two-staged approach to managing LARS, using a combination of medical management with biofeedback followed by tibial nerve neuromodulation in 29 patients. Employing this approach, they were able to reduce overall LARS symptoms by almost half. Our study builds on these works by employing a prospective, pre-emptive strategy for patients undergoing sphincter-preserving surgery, which starts at the time of discharge, thus changing the emphasis from reactive 'rehabilitation' to proactive management. There is now emerging interest in developing supportive, proactive management strategies for patients undergoing sphincter-preserving rectal cancer surgery, with Garfinkle et al. [29] publishing their trial protocol on the effectiveness of a LARS patient-centred programme consisting of an informational booklet, patient diaries and nursing support.

LARS symptoms are often underreported by patients and invariably assessed in routine clinical practice, thus leading to disclosure and treatment when significant symptoms manifest clinically [30]. Accurate LARS detection is essential to identify and treat its symptoms and consequences. Both the LARS score and the Wexner Incontinence score represent simple, effective and acceptable screening tools to detect and monitor the progress of patients [31], as demonstrated by the high response rates observed at all candidate time points in our study. Despite their relative ease of use, the measurement properties of the LARS score have been called into question, due to its differential sensitivity and responsiveness to specific LARS symptoms, its overestimation in measuring QoL and its high sensitivity and low specificity as an assessment tool [32]. Similarly, the Wexner score lacks specificity with regard to the overall assessment of LARS, focusing on symptoms of incontinence alone [33]. The LARS international collaborative group was established to address some of the issues around the measurement properties of the LARS score through engagement with all key stakeholders including patients [9]. This group redefined LARS as consisting of eight key symptoms and eight key consequences, with the aim of using this new definition to underpin the development of a more precise, robust and disease-specific outcome measure for LARS assessment. Precise definitions and robust measurement of LARS will facilitate improved treatment strategies in this cohort of patients. The BOREAL programme will continue to evolve in the future based on emerging research to ensure all symptoms and consequences of LARS are appropriately assessed and managed.

The BOREAL programme actively seeks to identify and treat patients with LARS symptoms within the first 12 months postoperatively as this is when symptoms are most pronounced [34]. Early identification and intervention are essential to improve long-term outcomes and reduce the effects of LARS. Bowel adaptation following surgery commonly occurs in the first postoperative year after which little improvement is thought to occur. Therefore, early initiation of pre-emptive, supportive interventions may improve bowel adaptation and patient outcomes. BOREAL demonstrates that early assessment and treatment intervention is associated with good postoperative function, with an overall incidence of LARS of 18% at 12 months. Our results represent a significantly lower incidence of LARS than in the current literature; this is largely due to our combined strategy of simultaneously detecting and treating LARS in a time-sensitive manner.

The BOREAL programme consists of a spectrum of interventions which escalate based on symptom severity at key clinical time points. Although the BOREAL programme predates the recently published manual guidelines on the management of LARS [35], our programme reflects the treatment recommendations outlined by this guidance.

The majority of available interventions for LARS are supported by very little high quality evidence [13,26]. The most common intervention in our pilot study was medical management with the majority of patients (n = 106, 77%) enrolled into BOREAL receiving this intervention at 12 months. The use of anti-diarrhoeal medication, bulking agents, dietary modifications and enemas are considered to be supported by a limited evidence base and have been largely adapted from treatment modalities used in the management of irritable bowel syndrome and ileoanal pouch dysfunction [26]. Mechanistically, the synergistic use of these agents can exert significant treatment effects when used pre-emptively, as demonstrated by our results, with a significant improvement in overall good function from 33% at 30 days postoperatively to 77% at 12 months. Furthermore, there was little progression through the programme to more invasive phases, with 17% of patients progressing beyond medical management.

Previous works have demonstrated a relationship between the presence of LARS and an adverse effect on overall QoL [34,36,37]. Our study did not demonstrate any significant QoL differences between patients with good and poor functional outcomes at 12 months, including patients' own perceptions of their own QoL. This may be a reflection on the measurement properties of the EQ-5D, as it may lack the specificity to detect disease-specific differences in this cohort of patients, which may be better assessed through the use of gastrointestinal specific questionnaires such as the European Organization of Research and Treatment of Cancer colorectal module EORTC CR29 or the Gastrointestinal Quality of Life Index. The comparable QoL outcomes seen between the two groups at the time of completion of the 12-month BOREAL programme may also be attributable to the fact that active participation in the programme itself may have led to improved QoL, thus ameliorating the adverse effect of LARS. Placebo effects of treatment participation on improved QoL outcomes have been noted previously in other areas of colorectal surgery [38,39] and warrant further investigation in patients with LARS.

The key strength of our work is the high response rate to the questionnaires, enabling us to accurately report functional outcomes in all eligible patients. This is coupled with the overall high compliance rate to the BOREAL programme. Demonstrating high fidelity and patient acceptance with an educational and treatment programme is essential to its success. However, we acknowledge the limitations of our work including the use of the LARS and Wexner scores to assess functional outcomes, given that the definition of LARS has recently been superseded and that not all LARS symptoms are adequately and equally assessed by these measures. Furthermore, our programme consists of a number of treatments delivered within a treatment bundle with a variable evidence base informing their use. Our programme does not demonstrate the clinical effectiveness of the combined treatment approach given that the majority of our patients remained on medical management throughout the 12-month programme. Furthermore, our pilot study demonstrates short-term results and requires longer-term data to assess the evolution of LARS symptoms and to demonstrate the longevity of the BOREAL programme. Further work on the BOREAL programme will include incorporating new robust measures of LARS as they are developed, incorporating new and emerging treatments into our algorithm over time, assessing longer time outcomes and establishing the cost-effectiveness of our programme.

CONCLUSION

The BOREAL programme provides a structured approach to patient assessment and treatment following sphincter-preserving surgery for rectal cancer, integrating clinical and oncological assessment with functional assessment, and creates a data-driven, patient-centred approach to managing the consequences of rectal cancer surgery. We demonstrate the acceptability, feasibility and effectiveness of implementing a responsive, stepwise programme for detecting and treating LARS.

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ETHICAL STATEMENT

All patients have signed informed consent and this study was approved by the local ethical committee of the Centre Hospitalier Universitaire of Bordeaux.

AUTHOR CONTRIBUTION

Conception and design: QD . Acquisition of data: BF,LB Statistical analysis : MC Interpretation of data: DH ,QD, ER, FZ, AB. Writing the manuscript: DM QD, Final approval of manuscript: all authors.

CONFLICT OF INTERESTS

FZ receives consulting fees from Coloplast.

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