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The Role of Pelvic Floor Muscle Training on Low Anterior Resection Syndrome

A Multicenter Randomized Controlled Trial

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Background and Objective: Total mesorectal excision (TME) for rectal cancer (RC) often results in significant bowel symptoms, commonly known as low anterior resection syndrome (LARS). Although pelvic floor muscle training (PFMT) is recommended in noncancer populations for treating bowel symptoms, this has been scarcely investigated in RC patients. The objective was to investigate PFMT effectiveness on LARS in patients after TME for RC.

Methods: A multicenter, single-blind prospective randomized controlled trial comparing PFMT (intervention; n = 50) versus no PFMT (control; n = 54) 1 month following TME/stoma closure was performed. The primary endpoint was the proportion of participants with an improvement in the LARS category at 4 months. Secondary outcomes were: continuous LARS scores, ColoRectal Functioning Outcome scores, Numeric Rating Scale scores, stool diary items, and Short Form 12 scores; all assessed at 1, 4, 6, and 12 months.

Results: The proportion of participants with an improvement in LARS category was statistically higher after PFMT compared with controls at 4 months (38.3% vs 19.6%; $P = 0.0415$) and 6 months (47.8% vs 21.3%; $P = 0.0091$), but no longer at 12 months (40.0% vs 34.9%; $P = 0.3897$). Following secondary outcomes were significantly lower at 4 months: LARS scores (continuous, $P = 0.0496$), ColoRectal Functioning Outcome scores ($P = 0.0369$) and frequency of bowel movements ($P = 0.0277$), solid stool leakage (day, $P = 0.0241$; night, $P = 0.0496$) and the number of clusters ($P = 0.0369$), derived from the stool diary. No significant differences were found for the Numeric Rating Scale/quality of life scores.

Conclusions: PFMT for bowel symptoms after TME resulted in lower proportions and faster recovery of bowel symptoms up to 6 months after surgery/stoma closure, justifying PFMT as an early, first-line treatment option for bowel symptoms after RC.

Keywords: bowel symptoms, low anterior resection syndrome, pelvic floor muscle training, randomized controlled trial, rectal cancer

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Over the years, incorporating neoadjuvant treatment (chemotherapy and radiotherapy) has improved outcome with low local recurrence rates and improved survival.[1]

Most patients will undergo total mesorectal excision (TME) with a low colorectal or coloanal anastomosis. Despite the nerve-sparing and sphincter-sparing nature of the procedure, up to 60% to 90% of patients will experience cumbersome bowel symptoms, impacting quality of live.[2,3] These bowel symptoms can vary greatly and include, but are not limited to: increased frequency of bowel movements, urgency, clustering, and fecal incontinence. The combination of the symptoms and their impact on quality of life has been summarized in an international consensus definition and is referred to as the low anterior resection syndrome (LARS).[2,4] The LARS score (LARS questionnaire) was developed as a quick screening tool.[5] Other assessment tools, such as the ColoRectal Functioning Outcome (COREFO questionnaire)[6] and a stool diary, can provide a more comprehensive means to understand the clinical picture.

The current management of LARS after TME includes antidiarrheal medication, dietary instructions, enemas, or sacral nerve stimulation. However, most patients are instructed that spontaneous improvement will follow. Nevertheless, a pilot study regarding a novel bowel rehabilitation program (BOREAL) in LARS patients was recently published, using a stepwise approach to asses and treat LARS patients, starting with medical management as a first option, followed by pelvic floor physiotherapy, biofeedback, transanal irrigation, then sacral nerve stimulation, antegrade irrigation, and eventually a definitive colostomy.[7]

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Recent treatment guidelines on rectal cancer (RC) do not[8] or only briefly[9,10] mention pelvic floor muscle training (PFMT) as a conservative treatment option for LARS. However, in noncancer populations, PFMT is highly recommended as a treatment option for fecal incontinence.[11]

Previous reviews remained inconclusive, partly due to the limited number of studies and the rather low methodological quality (nonrandomized efficacy studies) of these studies.[12–14] Furthermore, 2 randomized controlled studies reported on the role of PFMT on fecal incontinence after RC surgery.[15,16] Notwithstanding the fact that these were randomized trials, the focus was specifically on PFMT effects for incontinence instead of bowel complaints as a whole complex of symptoms (LARS). Follow-up was only reported until maximally 9 months.[15,16] This randomized controlled trial (RCT) aims to evaluate the effects of a comprehensive PFMT program up to 1 year after TME for RC on the comprehensive set of bowel symptoms or LARS, in comparison to patients who received no training.

METHODS

Study Design

The study protocol has previously been published.[17] In short, this study was a multicenter, single-blind, prospective RCT. Patients treated for RC were recruited after TME in 3 Belgian hospitals: University Hospitals Leuven, Onze-Lieve-Vrouw (OLV) Hospital in Aalst or General Hospital Groeninge in Kortrijk. Ethics approval was granted by the coordinating Ethical Committee of the University Hospitals Leuven (s59761) and additionally a positive advice from the other local Ethical Committees was obtained. This study applies the principles established in the Declaration of Helsinki and was reported according to the CONSORT guidelines (Supplemental Digital Contents 1, 2, http://links.lww.com/SLA/E106, http://links.lww.com/SLA/E107). This trial was registered at Netherlands Trial Register (NTR6383).

Patients

Inclusion criteria were as follows: (1) patients who had a low anterior resection (LAR) with TME for RC, (2) patients with a minimal LARS score[5] of 21/42 (= at least minor LARS) at 1 month after surgery (no ileostomy) or after ileostomy closure, and (3) patients had to be able to come to the hospital once a week during the complete treatment period of 12 weeks. Exclusion criteria have previously been described.[17] A written consent form was signed by participants before data collection and obtained by the assessor before the first assessment. All data were deidentified and coded with a unique trial identification number.

Randomization and Blinding

One month after restoration of transit, patients were randomly assigned to the intervention group (receiving 12 weeks of PFMT) or to the control group (not receiving PFMT, standard care). The randomization was computer generated. Sequencing was determined by the date of rectal resection (in case of no ileostomy) or by the date of the ileostomy closing (in case the patient received a temporary ileostomy). The randomization was performed with 8 strata, using 6-size permuted blocks. The strata were a result from 3 binary stratification variables, which were: sex (male vs female), type of anastomosis (stapled vs handsewn), and type of reconstruction (colonic J-pouch/side-to-end coloanal anastomosis vs straight coloanal anastomosis). The assessor was blinded for the allocation of the participants to the 2 groups, and the participants were asked not to discuss the treatment of their bowel symptoms with the assessor. Blinding of the participants or of the therapist who performed the treatments was not possible given the nature of the intervention.

Procedures

The intervention group received 12 weeks of PFMT, consisting of 9 individual treatments: during the first 6 weeks once a week and 3 sessions over the last 6 weeks. Each session was provided by a specialized physiotherapist trained in pelvic re-education and with several years of experience in training these patients. The

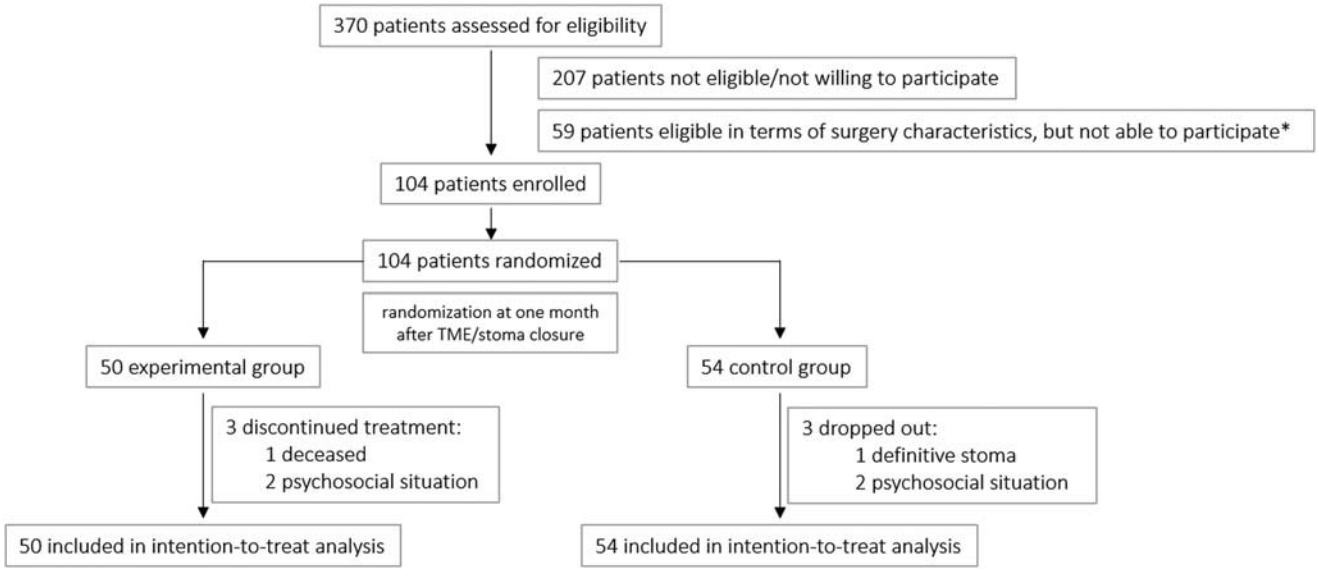

FIGURE 1. Trial recruitment. *Due to psychosocial circumstances, distance to the hospital or group preference.

sessions started with an assessment and evaluation of bowel symptoms with a stool diary, combined with patient education, pelvic floor muscle exercises (focused on strength, endurance, relaxation, proprioception, and coordination), electromyographic-biofeedback/electrical stimulation, and rectal balloon training (improvement of rectal sensation of filling and proper expelling). The content of the treatment has been described in detail in the published protocol.[17] The control group did not receive any PFMT. During follow-up, every participant was monitored by the department of abdominal surgery, and no adverse events were expected due to PFMT. If necessary, adverse events could be reported to members of the research team.

Outcomes

All outcome measures were assessed at 1, 4, 6, and 12 months after TME/stoma closure. The primary outcome was defined as the proportion of participants with an improvement in the LARS category at 4 months (from major LARS to minor LARS, from major LARS to no LARS, or from minor LARS to no LARS) compared with the LARS score measured at 1 month postoperatively. The primary outcome was the dichotomous classification of change in the LARS category (1: change in category, 0: no change in category). The LARS score itself (continuous variable) was recorded as a secondary outcome. Other secondary outcomes were bowel symptoms evaluated by (1) the COREFO questionnaire,[6] (2) a Numeric Rating Scale (NRS) regarding the subjective bother of bowel symptoms, and (3) a stool diary. A 7-day stool diary assessed: frequency of bowel movements, stool consistency (scored on the Bristol Stool Scale), urgency/incontinence/soiling episodes, fragmentation of stool (clustering). Quality of life was evaluated by the Short Form 12 (SF-12).[18]

Sample Size Calculation

The primary endpoint was defined as the proportion of patients with an improvement in the LARS category at 4 months (= minimal clinically important difference). The expected proportion of patients with success (improvement) in the control group was assumed to equal 10% after 12 weeks of PFMT, based on expert opinion. It was calculated that 49 subjects per group were needed to detect with at least 80% power a difference of 25% between groups (in the proportion of patients that improved in LARS category), based on expert opinion (thus 10% vs 35%). This calculation was based on a 2-sided Fisher exact test with α equal to 0.05. To anticipate for patient dropout and inclusion of strata (8 strata, resulting from 3 binary stratification variables) in the final analysis (a stratified exact test for proportions), 60 subjects per group were required.

Statistical Analysis

For the primary analysis, a 2-sided stratified exact Cochran-Mantel-Haenzel-test was used to compare the proportion of patients with a decrease in LARS category between both groups at 4, 6, and 12 months. Tipping point imputation was used for missing data on LARS category changes under MNAR (missing non-at-random) assuming no changes in the intervention group. Data were analyzed according to the intention-to-treat principle. For the secondary outcomes [LARS (continuous), COREFO, NRS, bowel diary frequencies, SF-12], linear mixed-effects models were used to assess changes over time (from 1 to 12 months). To assess different trajectories for patients in both groups, we included random effects (intercept and slope) and fixed effects (time, group, interaction of group, and time) into the model. For the primary and secondary outcomes, the α level was set at 0.05. Analyses were performed by Leuven Biostatistics and Statistical Bioinformatics Centre. The exact Cochran-Mantel-Haenzel test was performed in SAS 9.4, and linear mixed-effects models were fitted in R (v.4.0.3).

RESULTS

Between January 2017 and January 2021, 104 patients entered the study protocol. Initially, the inclusion of 120 patients was foreseen. As the accrual rate was hampered by the COVID-19 restrictions and based upon a lower-than-predicted dropout rate, inclusion was stopped at 49 months (104 patients). Figure 1 gives an overview of the trial. Baseline characteristics are shown in Table 1, and outcome values for the questionnaires in Table 2. At 4 months, after TME/stoma closure, there was a significant difference in the proportion of patients with an improvement in the LARS category ($P = 0.0415$). At 6 months, the difference remained

TABLE 1. Baseline Characteristics (N = 104)

Variables	Value	
	Intervention Group (n = 50) n (%)	Control Group (n = 54) n (%)
Age [mean (SD)/median (IQR)] (y)	58.8 (12.7)	57.1 (10.9)
≤ 49	11 (22.0)	14 (25.9)
50–69	29 (58.0)	35 (64.8)
≥ 70	10 (20.0)	5 (9.3)
Sex		
Male	36 (72.0)	35 (64.8)
Female	14 (28.0)	19 (35.2)
BMI [mean (SD)/median (IQR)] (kg/m^2)	24.6 (4.0)	24.1 (3.7)
< 25.0	28 (56.0)	30 (55.6)
25.1–30.0	19 (38.0)	16 (29.6)
> 30.0	3 (6.0)	8 (14.8)
Partner		
Yes	46 (92.0)	48 (88.9)
No	4 (8.0)	6 (11.1)
Employment status		
Retired	23 (46.0)	17 (31.5)
Employed/unemployed	27 (54.0)	27 (68.5)
Tumor height*		
Low (0–5 cm)	29 (58.0)	31 (59.3)
Mid (5.1–10 cm)	14 (28.0)	16 (29.6)
High (10.1–15 cm)	7 (14.0)	7 (11.1)
Type of reconstruction		
Straight coloanal anastomosis	36 (72.0)	31 (57.4)
Side-to-end coloanal anastomosis	5 (10.0)	16 (29.6)
Colon pouch-anal anastomosis/J-pouch	9 (18.0)	7 (13.0)
Anastomosis		
Handsewn	15 (30.0)	17 (31.5)
Stapled	35 (70.0)	37 (68.5)
Neoadjuvant therapy		
No	15 (30.0)	16 (29.6)
Chemotherapy and/or radiotherapy	35 (70.0)	38 (70.4)
Adjuvant therapy		
No	26 (52.0)	28 (51.9)
Chemotherapy	23 (46.0)	25 (46.2)
Chemoradiotherapy	1 (2.0)	1 (1.9)
Stoma		
Yes	43 (86.0)	47 (87.0)
No	7 (14.0)	7 (13.0)

*From the anal verge.
BMI indicates body mass index; IQR, interquartile range.

TABLE 2. Overview of Results

	1 mo		4 mo					6 mo					12 mo				
	E (N = 50)	C (N = 54)	E (N = 50)	C (N = 54)	Statistics			E (N = 50)	C (N = 54)	Statistics			E (N = 50)	C (N = 54)	Statistics		
Primary Outcome*	—		Proportion (%)		Adjusted Proportion Difference	Wald CI	*P*	Proportion (%)		Adjusted Proportion Difference	Wald CI	*P*	Proportion (%)		Adjusted Proportion Difference	Wald CI	*P*
LARS category improvement	—	—	38.30	19.61	−0.2040	−0.365; −0.042	**0.0415**	47.83	21.28	−0.2630	−0.042; −0.105	**0.0091**	40.00	34.88	−0.1000	−0.273; 0.074	0.3897
Secondary outcomes†	Mean (SD)		Mean (SD)		Value	Standard Error	*P*	Mean (SD)		Value	Standard Error	*P*	Mean (SD)		Value	Standard Error	*P*
LARS score	36.20 (5.70)	37.20 (4.42)	29.9 (8.09)	33.80 (7.70)	−3.1340	1.5888	**0.0496**	26.80 (10.30)	30.60 (8.89)	−3.3765	1.8174	0.0643	29.40 (9.69)	29.70 (9.09)	0.1836	1.9579	0.9254
COREFO score	45.10 (19.40)	45.30 (18.90)	31.1 (17.00)	36.30 (18.40)	−5.3905	2.5699	**0.0369**	28.40 (17.80)	29.00 (15.80)	−1.0715	2.5962	0.6801	27.10 (16.90)	28.20 (15.10)	−1.1730	2.7912	0.6746
NRS	5.50 (2.80)	6.06 (2.61)	4.21 (2.42)	4.96 (2.80)	−0.2449	0.4919	0.6190	4.00 (2.32)	3.96 (2.69)	0.5335	0.4928	0.2800	4.04 (2.70)	4.00 (2.29)	0.6364	0.6294	0.3129
BM/24 h‡	6.81 (3.85)	6.16 (3.33)	3.97 (2.39)	5.12 (4.10)	−1.6624	0.7503	**0.0277**	4.08 (2.37)	4.76 (3.98)	−1.0709	0.7256	0.1414	3.83 (2.20)	4.06 (3.02)	−0.9298	0.7699	0.2284
BM during day‡	6.01 (4.03)	5.04 (2.96)	3.51 (2.32)	4.11 (3.70)	−1.3622	0.7282	0.0627	3.64 (2.41)	3.93 (3.17)	−1.0811	0.7205	0.1349	2.95 (1.84)	3.28 (1.83)	−1.3320	0.6837	0.0526
BM during night‡	0.77 (0.93)	0.72 (0.66)	0.41 (0.68)	0.67 (0.86)	−0.3158	0.1909	0.0994	0.33 (0.43)	0.60 (1.10)	−0.2606	0.1971	0.1875	0.41 (0.62)	0.33 (0.46)	−0.0241	0.1998	0.9040
SL/24 h‡	2.02 (3.15)	1.55 (2.88)	0.36 (0.84)	0.83 (2.11)	−0.9447	0.5651	0.0959	0.54 (1.30)	0.35 (0.61)	−0.4342	0.5186	0.4034	0.24 (0.42)	0.27 (0.54)	−0.5676	0.5531	0.3059
Liquid SL during day‡	0.79 (1.82)	0.64 (1.67)	0.09 (0.22)	0.32 (1.28)	−0.3760	0.3710	0.3119	0.26 (1.00)	0.13 (0.33)	−0.0783	0.3488	0.8226	0.04 (0.11)	0.11 (0.27)	−0.2918	0.3386	0.3897
Solid SL during day‡	0.80 (1.53)	0.41 (0.83)	0.17 (0.54)	0.37 (0.80)	−0.5854	0.2579	**0.0241**	0.16 (0.49)	0.11 (0.36)	−0.3910	0.2592	0.1327	0.09 (0.23)	0.10 (0.27)	−0.4155	0.2472	0.0941
Liquid SL during night‡	0.17 (0.45)	0.11 (0.36)	0.02 (0.07)	0.02 (0.11)	−0.0559	0.0835	0.5037	0.03 (0.10)	0.05 (0.12)	−0.0638	0.0848	0.4522	0.03 (0.12)	0.01 (0.05)	−0.0565	0.0846	0.5051
Solid SL during night‡	0.21 (0.53)	0.06 (0.18)	0.06 (0.30)	0.10 (0.31)	−3.1340	1.5888	**0.0496**	0.08 (0.32)	0.02 (0.09)	−3.3765	1.8174	0.0643	0.08 (0.25)	0.01 (0.09)	0.1836	1.9579	0.9254
Clusters/day§	1.01 (1.4)	0.92 (1.13)	0.55 (0.90)	0.85 (1.26)	−5.3905	2.5699	**0.0369**	0.47 (0.71)	0.63 (0.76)	−1.0715	2.5962	0.6801	0.50 (0.70)	0.57 (0.65)	−1.1730	2.7912	0.6746
Urgency episodes/day§	3.08 (3.46)	2.85 (3.05)	0.86 (1.65)	1.45 (1.73)	−0.2449	0.4919	0.6190	0.91 (1.68)	1.13 (1.71)	0.5335	0.4928	0.2800	0.86 (1.76)	1.06 (1.46)	0.6364	0.6294	0.3129
SF-12, PCS	33.80 (4.32)	33.4 (3.63)	31.70 (3.88)	33.10 (3.76)	−1.7625	0.9471	0.0639	32.60 (3.50)	32.20 (3.44)	0.0776	0.8622	0.9284	32.50 (3.33)	33.50 (3.78)	−1.6075	0.9298	0.0850
SF-12, MCS	28.00 (4.55)	27.8 (4.48)	27.50 (4.60)	27.20 (3.96)	0.0346	1.0086	0.9727	27.10 (4.53)	26.60 (3.94)	0.3599	0.9893	0.7163	27.60 (4.32)	27.40 (4.34)	0.5113	1.0286	0.6195

Bold values indicate statistically significant $P < 0.005$.
*Cochran-Mantel-Haenzel.
†Linear mixed-effect models.
‡Average frequency.
§Average number.
C indicates control; E, experimental; BM, bowel movements; CI, confidence interval; MCS, Mental Component Score; PCS, Physical Component Score; SL, stool leakage.

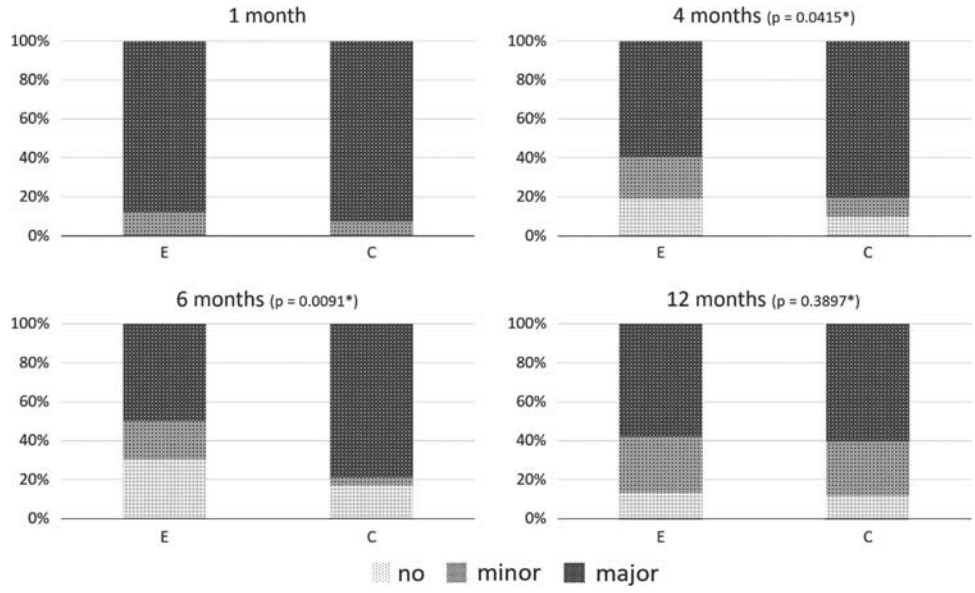

FIGURE 2. Representation of the LARS categories for the experimental and control group at each timepoint. *P-values correspond to the results of the exact proportion test of the proportion differences, based on the 1 month timepoint.

significant ($P = 0.0091$) but no longer at 12 months ($P = 0.3897$) (Table 2, Fig. 2). At 4 months, the continuous LARS score ($P = 0.0496$) and COREFO score ($P = 0.0369$) differed significantly between both groups (Table 2, Fig. 3). Furthermore, all the following items were significantly better in the intervention group at 4 months: the average frequency of bowel movements/24 hours ($P = 0.0277$), the average frequency of solid stool leakage (day: $P = 0.0241$; night: $P = 0.0496$) as well as the average number of clusters per day ($P = 0.0369$), assessed with the stool diary. Other secondary outcome variables (NRS scores, SF-12 scores, and the remaining stool diary items) were not found to be significantly different between the intervention and control group. An overview of the results is further presented in Table 2.

No serious adverse events related to PFMT were reported. No RC patients were withdrawn because of harm related to the intervention.

DISCUSSION

This is the first RCT justifying the use of PFMT to improve bowel symptoms in the early care pathway of RC patients. PFMT resulted in a significantly higher proportion of patients with an improvement in LARS at 4 and 6 months. At 4 months, the total LARS and COREFO scores were significantly decreased in the intervention group, and PFMT had a beneficial effect on stool frequency, incontinence, and clustering.

There is a natural tendency for functional improvement over time.[19] This study shows that PFMT can accelerate this process, as twice as many patients reached acceptable function at 4 months. The lack of improvement in the quality of life or the lack of differences between the groups regarding this aspect might be linked to the choice of a questionnaire rather than the intervention that is falling short. After all, the LARS questionnaire was developed as a short questionnaire for bowel dysfunction after LAR on the basis of symptoms and impact on quality of life. Seeing that PFMT was shown to have a significant influence on the LARS score, we can further perpetuate the foregoing reasoning regarding the choice in the quality of life questionnaires. We therefore propose that all patients with LARS symptoms at 1 month should receive PFMT for 12 weeks.

The pathophysiology of LARS is most likely multifactorial and results from a complicated interplay between anatomical, neurological, physiological, and psychological factors.[4,10] PFMT can only interact with some of these aspects, which explains that only 38% of patients benefited from this approach. To date, we

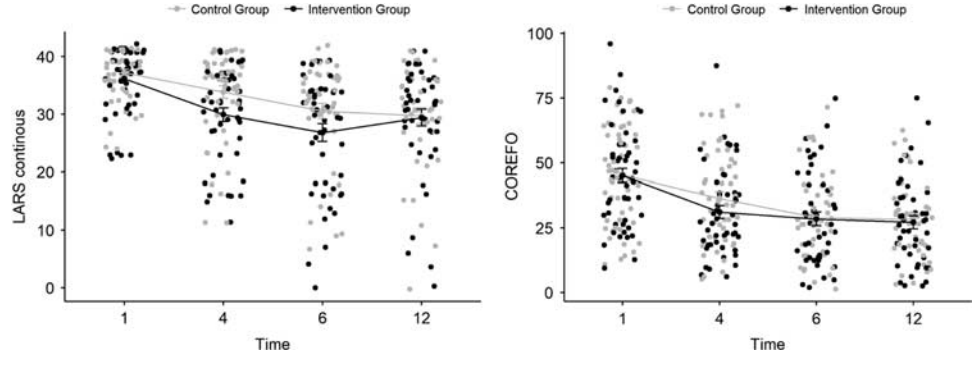

FIGURE 3. Representation of the trajectories of the LARS and COREFO scores over time.

do not know which factors influence the success or failure of PFMT. Therefore, we would advise to implement PFMT early on in the care pathway before exploring more invasive and often costly treatment options or waiting to see whether or not spontaneous recovery occurs. This is in line with the findings Harji et al[7] regarding their bowel rehabilitation program, in which they demonstrated that the median time to achieve good bowel function was significantly lower in patients following the program, which also included PFMT.

Previous reviews did not reach a consensus regarding the effectiveness of PFMT for bowel symptoms after RC due to several limitations of included trials, such as: retrospective design,[20,21] small or heterogeneous patient groups[20,22–24] and the fact that treatment was either too short or showed a lack of uniformity.[21–26] Furthermore, due to lack of evidence, PFMT was scarcely mentioned as a treatment option in current guidelines.[8–10]

Previously, 2 RCT's investigating the role of PFMT were published. Lin et al[15] showed a short-term effect of PFMT on fecal incontinence (as measured by the Wexner score) after LAR, which are partially in line with the results from the present study. The second RCT[16] could not demonstrate an effect of PFMT on Wexner incontinence scores in RC patients.[16] Analogous to the present study, a specialized physiotherapist provided PFMT, and the same treatment modalities were performed.[16] However, important differences should be noted. First of all, timing and duration of the interventions differed, that is, PFMT in the current study started 1 month after TME/stoma closure and lasted 9 sessions, compared with a start at 3 months after LAR/6 weeks after stoma closure and 12 sessions in the study by van der Heijden et al[16] Similar to the study of Lin et al,[15] the primary outcome focused on incontinence only. In addition, baseline Wexner incontinence scores differed significantly between groups sessions in the study by van der Heijden et al.[16] No differences after PFMT were found for the whole group; but subgroup analyses showed significant differences after PFMT for those patients who reported urgency or at least moderate incontinence at baseline.[16] These subgroup analyses are in line with our results, as incontinence-related items were also significantly better at the end of the treatment phase. However, the benefit for patients with urgency could not be confirmed.

Major strengths of this study were the randomized trial design and reporting the effect of PFMT on a range of bowel symptoms in the short (4 months), middle (6 months) as well as the long term (12 months). A broad range of bowel symptoms treated was investigated through reliable and valid questionnaires as well as a stool diary since LARS represents a myriad of bowel symptoms. In addition, a low dropout rate was observed, and all PFMT sessions were provided by experienced specialized physiotherapists using highly standardized procedures. Last, potential sources of bias were addressed by using a computer-generated and sequenced randomization process. A limitation of the present study was the fact that this study was stopped prematurely because of the COVID-19 pandemic. Also, a nonvalidated stool questionnaire was used to evaluate bowel symptoms.

Future research should determine whether PFMT should be started as soon as 1 month after TME/stoma closure and whether an extension of supervised PFMT sessions up to 6 months or even 12 months could enhance the outcomes.

To conclude, PFMT for bowel symptoms after TME for RC resulted in a lower proportion and faster recovery of bowel symptoms up to 6 months after surgery/stoma closure, justifying PFMT as a first-line option for the improvement of bowel symptoms after RC. Since there are no side effects or risks attached to PFMT, we advise that PFMT should be offered to all patients with bowel symptoms, starting ~1 month after surgery/stoma closure.

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DISCUSSANTS

Jean Jacques Tuech (Rouen, France)

Congratulations to Anne Asnong and her co-authors for this well-structured randomized controlled trial. The management of treatment sequelae, particularly in the field of rectal cancer, will become preponderant in the near future. Sequelae management is an integral part of personalized care. This is the first randomized trial on the management of LARS by perineal re-education; the authors are to be commended for conducting this trial, the results of which will change our practice. The authors have conducted a multicenter single-blind prospective randomized controlled trial, comparing pelvic floor muscle training to standard treatment following TME – stoma closure. The intervention group received 12 weeks of re-education, performed by multiple therapists specialized in pelvic re-education. This was strength for this study because authors chose a reproducible technique and a low cost one. The total cost of the reeducation process was around 264 euros, not taking into account the patient travel.

One hundred and twenty patients were initially planned, considering a forecast of 23% of patients lost to follow-up. Due to restrictions secondary to the COVID crisis, 104 were included. Fortunately, there were only 5.77% lost to FU. The numbers are, therefore, sufficient to highlight a difference of 25% improvement in LARS with a power of at least 80%. The proportion of participants with an improvement in the LARS-category was statistically higher after re-education at four (38.3% vs. 19.6%; p=0.0415) and six (47.8% vs. 21.3%; p=0.0091) months, but no longer at 12 months (40.0% vs. 34.9%; p=0.3897). Secondary outcomes, such as the LARS Score, solid stool leakage and the number of clusters were also significantly improved at four months. Sadly, no differences were found for QOL. These results allow the authors to conclude that re-education should be the first line treatment for bowel symptoms after rectal cancer surgery. We have 3 questions for the authors:

First, the design of the trial is clean and the study shows a significant improvement in the early phase of the follow-up. Can you explain why this effect disappears after a year? Second, do you have any suggestions for maintaining these results longer?

Third, this study shows that a significant effect on LARS was recognized in the early run, but, in contrast, the authors also mentioned that SF 12 has shown no difference between the groups. Does it mean that the shown difference in LARS is statistically significant, but not clinically relevant, for overall quality of life? Or, does it mean that the problem came from the choice of the questionnaire?

Response From Anne Asnong (Leuven, Belgium)

Thank you very much for your interesting questions. Regarding the disappearance of the results at 12 months, there is a natural improvement to be expected within the first few months after sphincter preservation, but we can speed up that recovery process with pelvic floor training. We also showed that there is significant improvement after 4 months. However, in view of the complete pathological and physiological nature of LARS, a substantial group of patients will also need a second line of treatment. Next to the spontaneous recovery process, we also think that long-term treatment adherence for pelvic floor muscle training is not as easy for patients as it might seem to be. So, maybe extending pelvic floor muscle training sessions for up to 6 months might also improve functional outcome.

Next, in our opinion, the lack of improvement in quality of life between the two groups is due, as you suggested, to the limited choice of questionnaire, rather than an intervention that is falling short. We would recommend a supplementary use of other questionnaires, specifically for this population. We would also like to create a digitalized stool diary, which could also include quality of life. In short, adapting the questionnaires would be a good option.

Frederic Ris (Geneva, Switzerland)

Thank you very much. I think that this is very important work for rectal patients. Do you think that the loss of effect could be attributed to the type of reconstruction after one year?

Response From Anne Asnong (Leuven, Belgium)

We did investigate the effect, but there was no difference.

Ronan P. O'Connell (Dublin, Ireland)

I have to say that I know how difficult these studies are, having done pelvic floor randomized trials. I have two questions. How did you standardize the intervention, and how do you account for the placebo effect of consultations during the postoperative period with an interested pelvic floor therapist?

Response From Anne Asnong (Leuven, Belgium)

Before treatments actually started, every therapist consulted with the PIs. The treatments were followed a standardized protocol. However, pelvic muscle training is always patient-oriented, rendering total standardization never fully possible. Regular follow-up meetings with the PIs were implemented. We also used standard techniques that are already described in the literature and in the published study protocol.

Regarding the placebo effect, the other group didn't receive any additional information or pelvic floor muscle training, and we asked them whether they consulted a specialised pelvic floor muscle therapist after their initial follow-up visits. They were instructed not to. Therefore, in the strict sense of "placebo-effect", the patients in the control group could not have experienced this, since no treatment was foreseen. Specifically, for the experimental group, of course, all patients met with an interested and compassionate therapist each week or bi-weekly. However, bowel symptoms were so severe that this interest and compassion on behalf of the therapist alone could not have accounted for the improvements. Furthermore, previously, several studies had already highlighted the added value of pelvic floor muscle training for the treatment of bowel symptoms. After

all, patients in the control group also received follow-up assessments, and thus, they also received attention, albeit not to the same extent.

Jeremie H. Lefevre (Paris, France)

We are performing a similar trial in France. Is there any interest in performing pelvic re-education before stoma closure?

Response From Anne Asnong (Leuven, Belgium)

Of course, being a therapist specialized in pelvic floor muscles, I'm always advocating for the start of pelvic floor therapy as soon as possible, even before the operation. Using your pelvic floor muscles and learning how to use them is easier to do when you don't have any complaints yet. So, implementing that in the care pathway, already prior to the operation, could be a valuable consideration. However, therapy is constantly evolving, and in the future, much will depend on the pre-operative trajectory of the patient.

Suzanne S. Gisbertz (Amsterdam, The Netherlands)

Thank you for this interesting presentation. This is exactly what I was wondering. Why didn't you choose to start the pelvic floor therapy before the operation, as this may be easier and more successful?

Response From Anne Asnong (Leuven, Belgium)

I refer to my previous answer. For this study, we started with symptomatic post-operative patients. However, I agree that using a pre-operative implementation could be a valuable consideration for future research.

Donato Altomare (Bari, Italy)

Did you look at the distance of the anastomosis from the dentate line because this is one of the key factors in LARS? For example, I expect that patients who had a stoma had a lower anastomosis than those who had a straight anastomosis.

Response From Anne Asnong (Leuven, Belgium)

We did register the height of the anastomosis, but we did not stratify for this factor in this study. However, 60% had a low rectal tumor, of whom 70% had major LARS at four months.