

BMJ Open Randomised controlled trial to assess efficacy of pelvic floor muscle training on bowel symptoms after low anterior resection for rectal cancer: study protocol

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ABSTRACT

Introduction Radical surgery after a total mesorectal excision (TME) for rectal cancer often results in a significant decrease in the patient's quality of life, due to functional problems such as bowel, urinary and sexual dysfunction. The effect of pelvic floor muscle training (PFMT) on these symptoms has been scarcely investigated. We hypothesise that the proportion of successful patients will be significantly higher in the intervention group, receiving 12 weeks of PFMT, compared with the control group without treatment. The primary outcome of this trial is the severity of bowel symptoms, measured through the Low Anterior Resection Syndrome questionnaire, 4 months after TME or stoma closure. Secondary outcomes are related to other bowel and urinary symptoms, sexual function, physical activity and quality of life.

Methods and analysis This research protocol describes a multicentre single blind prospective, randomised controlled trial. Since January 2017, patients treated for rectal cancer (n=120) are recruited after TME in three Belgian centres. One month following surgery or, in case of a temporary ileostomy, 1 month after stoma closure, patients are randomly assigned to the intervention group (n=60) or to the control group (n=60). The assessments concern the preoperative period and 1, 4, 6, 12 and 24 months postoperatively.

Ethics and dissemination The study will be conducted in accordance with the Declaration of Helsinki. Ethics approval was granted by the local Ethical Committee of the University Hospitals Leuven (s59761) and positive advice from the others centres has been obtained. Dissemination of the results will be accomplished via guidelines and (non-)scientific literature for professionals as well as organisation of patient symposia.

Trial registration number NTR6383.

INTRODUCTION

Colorectal cancer is the second most common cancer in women and the third most common cancer in men and corresponds to 10.2% of

Strengths and limitations of this study

- This study comprehends a well-powered clinical trial, investigating the effect of pelvic floor muscle training on bowel symptoms after a total mesorectal excision (TME) for rectal cancer.
- Besides bowel symptoms, also urinary symptoms, sexual function, physical activity and quality of life after TME for rectal cancer will be assessed and followed up until 24 months after surgery (TME) or, in case of a temporary ileostomy, after stoma closure.
- An essential strength of this study is the applicability in daily clinical practice, as well as the pragmatic nature of study.
- A limitation is the lack of data on pre-existing bowel symptoms (before the tumour occurred); this can only be assessed retrospectively.
- A golden standard measurement to assess physical activity (such as the DynaPort MoveMonitor) could provide more detailed information than a questionnaire alone.

all new cancer diagnoses. Nearly 40% of these tumours are located in the rectum.¹

Standard of surgical care is a nerve and sphincter sparing total mesorectal excision (TME).²⁻⁵ This technique consists of excising the rectum, together with the total mesorectal envelope. By performing a TME, the anal sphincter as well as the surrounding autonomic nerves are spared.⁶ However, the rectal reservoir as such is lost after excision. Different techniques have been described to allow reconstruction, such as a straight coloanal anastomosis or a type of rectal neoreservoir reconstruction: colonic J-pouch, side-to-end coloanal anastomosis, transverse coloplasty.^{7,8} A rectal neoreservoir could lead to a better functional outcome than a straight

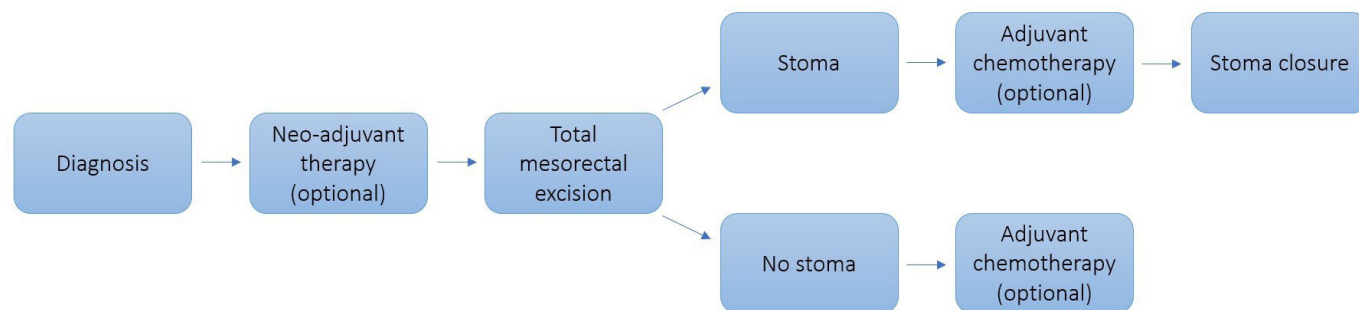


Figure 1 Possible treatment options for rectal cancer.

coloanal anastomosis, especially during the first postoperative year.⁸ Depending on the distal margin, a stapled or handsewn anastomosis is performed. A sleeve resection with a manual coloanal anastomosis could further compromise postoperative function.⁹ After a TME, a temporary ileostomy can be performed to reduce the risk for and the septic consequences of an anastomotic leakage.^{10–12}

To optimise local tumour control neoadjuvant therapy (using radiotherapy and/or chemotherapy) has significantly improved outcome. MRI now plays a pivotal role for staging and indicating neoadjuvant therapy. Moreover, downsizing and downstaging of the tumour could lead to more conservative surgery and more sphincter preservation.^{2 3 13 14} **Figure 1** provides a basic overview of possible treatment options for rectal cancer, starting from diagnosis.

However, radical surgery (although nervesparing)—and especially after neoadjuvant radiotherapy—often results in a significant decrease in the patient’s quality of life, due to functional problems such as bowel, urinary and sexual dysfunction.^{7 15–17}

About 60%–90% of patients experience a wide range of bowel symptoms after Low Anterior Resection (LAR): incontinence for flatus or faeces, frequent bowel movements, urgency and clustering of defecation. The combination of these specific bowel symptoms is often referred to as the Low Anterior Resection Syndrome (LARS).^{18–23} Moreover, LARS symptoms are more common and more pronounced after neoadjuvant radiotherapy.^{22 24–29} A validated LARS score has been introduced to facilitate screening for and assessing functional outcome after surgery for rectal cancer. This 5-item questionnaire reflects functional outcome after LAR for rectal cancer and total scores are divided into three categories: ‘no LARS’, ‘minor LARS’ and ‘major LARS’.³⁰ The current management of bowel symptoms after LAR for rectal cancer (ie, usual care) includes antidiarrheal medication, dietary instructions or a rather negligible advice to wait for improvement.²

According to a review by Norton and Cody,³¹ pelvic floor muscle training (PFMT) is highly recommended in the treatment of bowel symptoms in non-cancer populations. Recent reviews by Lin *et al*,³² Visser *et al*²² and Maris *et al*³³ included 10 non-randomised efficacy studies

and summarised the effect of PFMT for bowel dysfunction following colorectal cancer surgery. However, no consensus has been reached regarding the effectiveness of PFMT for bowel symptoms after rectal cancer due to several limitations of the trials included. Mentioned limitations were: a retrospective design,^{34 35} small or heterogeneous patient groups^{34 36–38} and the fact that treatment was either too short or showed a lack of uniformity.^{24 35–39}

There is only one randomised controlled trial (RCT) on a large sample size.⁴⁰ Lin *et al* showed a short-term effect of PFMT on faecal incontinence after LAR. Unfortunately, this study exclusively focused on faecal incontinence, while LARS includes several other bowel symptoms than incontinence, such as incontinence for flatus, frequency of bowel movements, urgency and clustering. There is no RCT to evaluate the effect of PFMT in patients suffering from LARS.

Also, urinary and sexual dysfunction is not seldom after rectal cancer treatments.^{41–43} Although urinary and sexual dysfunction occur frequently after TME, the effect of PFMT on these symptoms after TME has never been thoroughly investigated, even though pelvic floor muscles play an important role in urinary continence and sexual function.⁴⁴

Physical activity after the diagnosis and treatment of different cancers is frequently investigated and results reveal that physical activity is associated with a lower risk of mortality in breast, prostate and colorectal cancer survivors.^{45 46} Physical activity consists of many different aspects, more specifically: occupational, sports, household and total physical activity. These different aspects have already been investigated in breast and prostate cancer survivors.^{47 48} The majority of the studies about physical activity after colorectal cancer focused only on one of the many aspects of physical activity and their interest was mainly targeting the effect of several exercise interventions on physical activity.^{49–52} Until now, there are no studies describing the evolution of the different levels of physical activity (sports, household, work and leisure time) during the first year after LAR.

Objectives

The main objective of this trial is to investigate the additional effect of PFMT on bowel symptoms in patients who undergo radical surgery for rectal cancer. We hypothesise

that the proportion of successful patients, defined as an improvement in LARS category, will be significantly higher in the intervention group receiving 12 weeks of PFMT compared with the control group without additional treatment. As secondary endpoint, the effect of PFMT on urinary as well as sexual symptoms will be assessed. Physical activity levels and risk factors for reduced physical activity after surgery will be documented.

METHODS AND ANALYSIS

This RCT protocol has been developed in accordance to the recommended Standard Protocol Items: Recommendations for Interventional Trials 2013 statement to report on the following items (<https://www.spirit-statement.org>).⁵³

Trial design and study setting

This research protocol describes a multicentre single blind prospective, RCT. Since January 2017, patients treated for rectal cancer (n=120) are recruited after TME from either the University Hospitals Leuven, Onze-Lieve-Vrouw (OLV) Hospital in Aalst or General Hospital Groeninge in Kortrijk. All centres are located in Belgium. An overview of the study design is demonstrated in [table 1](#).

Patient and public involvement

All authors involved in treatment/assessment (AA, MVK, KS, HL and IG) have years of clinical experience in pelvic floor re-education and the treatment of bowel complaints after rectal cancer. The leading colorectal surgeons (AD, AW, YVM and BVG) contributed, based on current knowledge of bowel dysfunction after rectal cancer surgery, to develop the research questions.

Patients were questioned extensively about their complaints in an explorative study in our own institution. This allowed us to develop the Patient-Reported Outcome Measures (PROMs). This study was performed in 37 patients who underwent a TME with/without temporary ileostomy for primary rectal cancer.⁵⁴ Results indicated that PFMT had a positive effect on urgency, soiling, faecal incontinence and well-being, providing a proof of concept on this matter. The burden of the intervention was not assessed by patients themselves, but the low drop-out rates so far and satisfaction expressed to the therapists and assessors, indicate that the current intervention is well perceived by patients.

Study results will be disseminated to study participants through patient symposia and associations (without lucrative purpose) or organisations for patients with colorectal cancer.

Eligibility criteria

Inclusion criteria are as follows: (1) patients who had a LAR, with TME for rectal cancer, (2) patients with a minimal LARS-score of 21/42 (at 1 month after closure of the ileostomy or after TME, in case no ileostomy was performed), which is defined as the cut-off score for at

least minor LARS-symptoms³⁰ and (3) patients who are able to come to the hospital once a week during the complete treatment period of 12 weeks. Patients are excluded if they: (1) had another type of surgery of colorectal cancer: a Hartmann procedure, abdominoperineal excision, transanal endoscopic microsurgical resection, or sigmoid resection, (2) were incontinent for faeces before surgery, (3) have neurological diseases, (4) are not able to perform PFMT because of cognitive problems, or (5) already had previous pelvic surgery, previous pelvic radiation or LAR for non-cancer reasons.

Participants

For each participating centre (University Hospitals Leuven, OLV Hospital in Aalst, General Hospital Groeninge in Kortrijk), the operation lists are screened for patients who are scheduled to undergo a TME for rectal cancer. This screening is done by the same research assistant (HL), different from the one who performs randomisation (AA and MW). If the inclusion criteria are met after the initial screening process, potentially eligible patients are approached postoperatively by a member of the research team (AA, HL and MW), within 2–7 days. Written and oral information about the trial, as well as the consent form are provided and explained. Before and during their stay at the abdominal ward, patients also receive several information brochures (surgery details, dietary information, ...).

When patients are approached, postoperative bowel complaints are still largely unknown. Therefore, the second inclusion criterion ‘LARS-score ≥ 21 ’ is not considered at this point in time. Potentially eligible patients are already signing the informed consent form, because they are asked to fill out retrospective questionnaires about the period before surgery, immediately after surgery. Randomisation, however, only takes place after all inclusion criteria are fulfilled (cfr. *infra*).

Allocation and randomisation

One month following surgery or, in case of a temporary ileostomy, 1 month after stoma closure, patients are randomly assigned to the intervention group (n=60)—receiving 12 weeks of PFMT—or to the control group (n=60)—not receiving PFMT—in a 1:1 ratio. The randomisation is carried out by the therapist performing the treatments of the intervention group (AA and MW; who do not perform assessments) and is computer generated. Sequencing is determined by date of rectal resection (in case of no temporary ileostomy) or by date of ileostomy closing (in case the patient received a temporary ileostomy). This way, the sequencing of patients cannot be tampered with. In this trial, randomisation is performed with eight strata, using 6-size permuted blocks. The strata are a result from three binary stratification variables, which are: sex (male vs female), type of anastomosis (stapled vs hand-sewn) and type of reconstruction (J-pouch/side to end vs straight).

Table 1 Time points of enrolment, intervention and assessment of outcome measures

Timepoint	Study period																	
	Enrolment					Allocation					Postallocation							
	t ₋₂	t ₋₁	t ₀	t ₁	t ₂	t ₃	t ₄	t ₀	t ₁	t ₂	t ₃	t ₄	t ₀	t ₁	t ₂	t ₃	t ₄	
Enrolment																		
Eligibility screen	X																	
Informed consent		X																
Randomisation			X															
Allocation			X															
Intervention																		
Intervention group (n=60)				X														
Control group (n=60)				/														
Outcome measures																		
Bowel symptoms																		
LARS		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
COREFO		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
NRS		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Stool diary			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Urinary symptoms																		
Bladder diary			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
ICIQ-FLUTS/MLUTS			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
No of pads			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
1-hour pad test			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Sexual function																		
FSFI/IIEF		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Physical activity																		
FPACQ		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Quality of life																		
SF-12		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Pelvic floor muscles																		
Pelvic floor muscle function			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

COREFO, ColoRectal Functional Outcome questionnaire; FPACQ, Flemish Physical Activity Computerised Questionnaire; FSFI, Female Sexual Function Index; ICIQ-FLUTS/MLUTS, International Consultation on Incontinence Modular Questionnaire-Female/Male Lower Urinary Tract Symptoms; IIIEF, International Index of Erectile Function; LARS, Low Anterior Resection Syndrome; NRS, Numeric Rating Scale; SF-12, Short Form 12.

Blinding

The assessor (KS and MJ) is blinded for the allocation of the participants to the two groups. To ensure blinding of the assessor, the participants are asked not to discuss the treatment of their bowel symptoms with the assessor. Blinding of the participants or of the therapist who performs the treatments in the intervention group is not possible.

Interventions

Treatment

The treatment is based on efficacy studies.^{22 32 33} The intervention group receives 12 weeks of PFMT, consisting of nine individual treatments: during the first 6 weeks once a week, in the following 6 weeks once every fortnight. The aim of the intervention is (1) to give the patients a better insight in improvement possibilities and a better understanding of the pathology and (2) to perform a variety of techniques to improve the force, endurance, proprioception and coordination of the pelvic floor muscles.

Referring to the first aim of the intervention, the first treatment session starts with explaining continence-related anatomy to the participant, in order to clarify the impact of surgery and for the participant to be able to better understand and apply the correct technique of contracting the pelvic floor muscles (without breath holding or contraction of other muscles).

As for the second aim of the intervention, proper contractions are taught and checked by means of anal palpation. This will be performed during the first and every following session. Participants are asked to perform 60 pelvic floor muscle contractions per day at home, spread over two to three exercise series and in different positions (lying down, sitting, standing up). Exercises that are taught during the sessions, are variations of short (training of the fast twitch muscle fibres, force) and long contractions (training of the slow twitch muscle fibres, endurance) and relaxation. During the entire treatment period, participants are asked to fill out a stool diary, to be able to objectify bowel movements, stool consistency, urgency and incontinence. Starting from the second session, the stool diary is discussed during treatment and personal advice is formulated. Using anal palpation, the pelvic floor muscle contraction is controlled again. If a correct contraction can be achieved, biofeedback can be used (using an anal electromyography probe) if necessary, to provide immediate biofeedback regarding the contraction. If muscle contraction against gravity is not achievable, electrical stimulation may be used to facilitate muscle contraction. Furthermore, bowel training is explained: positioning on the toilet, evacuation technique and controlling urgency.

Every subsequent session is tailored to the participant's specific needs. According to the patient's abilities the difficulty level is gradually increased and functional exercises (PFMT in varying positions and during activities of daily living) are implemented. From the sixth session onwards,

rectal balloon training is started, to improve rectal sensation of filling and proper expelling.⁵⁵

The control group does not receive the aforementioned therapy, nor any extra information.

Every participant is monitored by the department of abdominal surgery. No adverse events are expected due to treatment, but any (serious) adverse event can be reported to members of the research team. All serious adverse events are reported to the Ethical Committee.

Treatment adherence

Since the success of PFMT mainly depends on the motivation and self-discipline of the participants to do the exercises at home,⁵⁶ patients are encouraged to perform their exercises (60 contractions/day) daily at home. Every therapy session, a notelet with short instructions of the home-exercises is provided and the physiotherapist checks the execution of the instructed exercises during the following therapy session. The importance of performing the exercises at home is emphasised during every session.

Therapist

A therapist specialised in pelvic reeducation performs the treatments (AA and MW in UH Leuven, LDW in Kortrijk, LV in Aalst). Every therapist has at least 4 years of former experience in the management of pelvic floor dysfunction. The therapist is able and has experience in performing a correct digital anal examination, in assessing pelvic floor muscle function, in using the biofeedback equipment, performing electrostimulation of the pelvic floor and using a rectal balloon.

Concomitant care

Following additional treatments is allowed in our protocol, but not encouraged. Some patients have so much bowel complaints, that it would be unethical to withdraw the use of medication or colon irrigation.

When patients experience faecal incontinence and urgency due to diarrhoea following LAR, they often use medication such as diarrhoea inhibitors (often Loperamide derivatives). The treating physiotherapist collects information about medication intake during every session through an interview, to be able to incorporate this information throughout statistical analyses.

Retrograde colon irrigation is designed to assist the evacuation of faeces from the bowel by introducing water into these compartments via the anus and is considered to be a cointervention, since it might be effective for certain cases of severe faecal incontinence.

To make sure the participant does not follow PFMT elsewhere, the participant has to communicate whether he or she consulted a physiotherapist for any reason during the follow-up period, to make sure that outcomes are not influenced. Consulting a physiotherapist outside the scope of the study is not allowed until 4 months post-surgery or stoma closure (primary endpoint of trial).

After this period, it is not encouraged but when patients do consult a physiotherapist, it is registered.

Outcomes

Assessor

A physical therapist blinded for allocation to the treatment groups and specialised in pelvic reeducation (KS and MJ) performs the assessments. This person is experienced in the management of pelvic floor muscle dysfunction and especially anal incontinence. This person is able and experienced in performing a correct digital anal examination and in evaluating the pelvic floor muscle function.

Assessments

The assessments are carried out at 1, 4, 6, 12 and 24 months postoperatively. Table 2 gives an overview of the primary and secondary outcome measures as well as a more detailed description. Table 1 provides an overview of time points used for the different assessments.

The primary outcome of this trial is the severity of bowel symptoms, 4 months after TME or stoma-closure. At this point in time, participants in the intervention group received 12 weeks of PFMT. The primary outcome is measured through the LARS questionnaire.^{30 57} The primary endpoint is defined as the proportion of participants with an improvement in LARS category (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 dichotomous classification of change in LARS category (1: change in category, 0: no change in category) is the primary outcome, the LARS-score itself (continuous variable) is recorded as a secondary outcome. Other secondary outcomes are: (1) bowel symptoms, evaluated by the LARS questionnaire (LARS questionnaire),^{30 57} by the ColoRectal Functional Outcome questionnaire (COREFO),⁵⁸ by a Numeric Rating Scale (NRS)^{59–61} and by a stool diary⁶² (2) urinary symptoms, evaluated by the International Consultation on Incontinence Modular Questionnaire-Female/Male Lower Urinary Tract Symptoms (ICIQ-FLUTS/MLUTS),^{63–65} a bladder diary,⁶⁶ the number of pads⁶⁶ and the 1-hour pad test⁶⁷ (3) sexual function, evaluated by the Female Sexual Function Index (FSFI)^{68 69} for women or the International Index of Erectile Function (IIEF) for men⁷⁰ (4) physical activity, evaluated by the Flemish Physical Activity Computerised Questionnaire⁷¹ (5) quality of life, evaluated by the Short Form 12 (SF-12)^{72 73} and (6) functionality of the pelvic floor muscles (not at 24 months), that is, muscle tone, strength and endurance through digital palpation.^{74 75}

Sample size

The primary endpoint has been defined as the proportion of patients with an improvement in LARS category (from major LARS to minor LARS, from major LARS to no LARS or from minor LARS to no LARS). The expected

percentage of success (improvement) in the control group is assumed to equal 10%, based on expert opinion. To detect with at least 80% power an improvement of 25%, that is, the minimally clinically important difference of the LARS-score based on expert opinion (thus 10% vs 35%), based on a two-sided Fisher's exact test with alpha equal to 0.05, 49 subjects per group are needed. To anticipate patient drop-out and inclusion of strata (eight strata, resulting from three binary stratification variables) in the final analysis (a stratified exact test for proportions), 60 subjects per group will be included.

Data collection, management and analysis

Data collection

Researchers will enable the proper conduct of the study by documenting all information accurately and verifying study data subsequently. Alternative ways to achieve all outcome data, such as sending questionnaires by post or email and calling the patient on the phone as a reminder, are applied to improve response rate. The incentive given to participants to maintain their participation to the study, includes the perception that their problems after surgery will be followed up closely.

Data management and monitoring

All participant data will be stored in the secured network of University Hospitals Leuven, according to the General Data Protection Regulations (2018). A backup of the database will be made regularly. Only members of the research team have access to the database with a personal login and password. The data monitoring committee (objective physiotherapist, biostatistician and board member of a patient association) does not participate in data collection or randomisation in any way, but oversees the study design, execution and data analysis at least once every year.

Data analysis

The strategy for statistical analysis is developed under supervision of a biostatistician of the Leuven Biostatistics and Statistical Bioinformatics Centre (L-Biostat).

Descriptive statistics will be used to present baseline characteristics of both groups.

For the primary outcome, the proportion of success (for which improvement is based on categorised LARS-score) a two-sided (stratified) test for proportions will be applied. Data will be analysed according to the intention-to-treat principle. To handle the dropouts (at 4 months)—in an additional analysis—a multiple imputation approach will be used. In this approach, LARS scores at 4 months will be imputed based on LARS information at 1 month, baseline characteristics, COREFO and stool diary (such as frequency of stool, frequency of incontinence...).

Concerning the secondary outcomes, for the continuous variables (LARS-score, COREFO, NRS, bladder diary volumes, ICIQ-F/MLUTS, pad test, FSFI/IIEF, Flemish Physical Activity Computerised Questionnaire, SF-12, pelvic floor muscle force and endurance) a multivariate

Table 2 Overview of outcome measures

	Tool	Evaluation of	Description	Score
Primary outcome				
Bowel symptoms	LARS-questionnaire ³⁰ ⁵⁷	Low Anterior Resection Syndrome symptoms	Five questions: incontinence for flatus (score 0–7), incontinence for faeces (score 0–3), frequency of bowel movements (score 0–5), fragmentation of stools (clustering) (score 0–11), urgency (score 0–16), 4-week period	LARS-categories: ▶ ‘no LARS’ (0–20 points) ▶ ‘minor LARS’ (21–29 points) ▶ ‘major LARS’ (30–42 points)
Secondary outcomes				
Bowel symptoms	LARS-questionnaire ³⁰ ⁵⁷	See above	See above	Between 0 and 42, with a higher score representing more (severe) LARS
	ColoRectal Functional Outcome ⁵⁸	Functional outcome after colorectal surgery	27 questions, score 0–4 on each question (exclusion of question 19; question about medication to make stools thinner), 2-week period <i>domains:</i> ▶ incontinence (nine questions) ▶ social impact (nine questions) ▶ frequency (two questions) ▶ stool-related aspects (three questions) ▶ need for medication (four questions)	Between 0 and 100, with a higher score representing more symptoms
	Numeric Rating Scale (NRS) ^{59–61}	The subjective bother from bowel symptoms	Score from “none at all” (=0) to “the worst imaginable” (=10), mean score of the last 4 weeks	Between 0 and 10
	Stool diary ⁶²	Information about the frequency of bowel movements, stool consistency and faecal incontinence	7-day diary, describing the following items during the week before the assessment in the hospital: ▶ frequency of bowel movements (during day + night) ▶ stool consistency (Bristol Stool Form Scale type 1–7) ▶ urgency episodes ▶ (urgency-)incontinence episodes ▶ episodes of passive incontinence ▶ soiling ▶ fragmentation of stool (clustering)	Frequency of each variable
Urinary symptoms	Bladder diary ⁶⁶	Information about voiding and urinary incontinence	3-day diary, describing the following items during the days before the assessment in the hospital: ▶ volumes of fluid intake ▶ voided volumes ▶ urinary frequency (number during day and night) ▶ incontinence episodes ▶ urgency episodes	Volume in millilitres and frequency of each variable
	NRS ^{59–61}	The subjective bother from urinary symptoms	Score from ‘none at all’ (=0) to ‘the worst imaginable’ (=10), mean score of the last 4 weeks	Between 0 and 10
	International Consultation on Incontinence Questionnaire Female/Male Lower Urinary Tract Symptoms ^{63–65}	Lower urinary tract symptoms and their impact on quality of life	♀: 12 questions score 0–4 on each question, 4-week period <i>domains:</i> ▶ filling symptoms (four questions) ▶ voiding symptoms (three questions) ▶ incontinence symptoms (five questions) ♂: 13 questions, score 0–4 on each question, 4-week period <i>domains:</i> ▶ voiding symptoms (five questions) ▶ incontinence symptoms (six questions) ▶ individual items evaluating frequency and nocturia (two questions)	♀: ▶ 0–16 filling symptoms subscale ▶ 0–12 voiding symptoms subscale ▶ 0–20 incontinence symptoms subscale ♂: ▶ 0–20 voiding symptoms subscale ▶ 0–24 incontinence symptoms subscale ▶ 0–4 frequency ▶ 0–4 nocturia
	No of pads ⁶⁶	Incontinence material usage	4-week period, description of the amount of incontinence material a patient uses per day and the reason why incontinence material is used	No of incontinence materials used per day
	1-hour pad test ⁶⁷	Stress incontinence	1-hour period, the amount of urine loss while performing a series of activities during 1 hour (drinking 500 mL of water, walking, climbing one flight of stairs, standing up from sitting, coughing vigorously, running in place, picking up small objects from the floor and washing hands under running water)	Urine loss (pad weighing) in millilitres

Continued



Table 2 Continued

	Tool	Evaluation of	Description	Score
Sexual function	Female Sexual Function Index/ International Index of Erectile Function ⁶⁸⁻⁷⁰	Female/male sexual function	<p>♀: 19 questions, 4-week period <i>domains:</i></p> <ul style="list-style-type: none"> ▶ desire (two questions, score range 1-5) ▶ arousal (four questions, score range 0-5) ▶ lubrication (four questions, score range 0-5) ▶ orgasm (three questions, score range 0-5) ▶ satisfaction (three questions, score range 0/1-5) ▶ pain (three questions, score range 0-5) <p>♂: 15 questions, score range 0-5, 4-week period <i>domains:</i></p> <ul style="list-style-type: none"> ▶ erectile function (six questions) ▶ orgasmic function (two questions) ▶ sexual desire (two questions) ▶ intercourse satisfaction (three questions) ▶ overall satisfaction (two questions) 	<p>♀: ▶ desire: 2-10 ▶ arousal: 0-20 ▶ lubrication: 0-20 ▶ orgasm: 0-15 ▶ satisfaction: 2-15 ▶ pain: 0-15</p> <p>♂: ▶ erectile function: 0-30 ▶ orgasmic function: 0-10 ▶ sexual desire: 0-10 ▶ intercourse satisfaction: 0-15 ▶ overall satisfaction: 0-10</p>
Physical activity (PA)	Flemish Physical Activity Computerised Questionnaire ⁷¹	PA and sedentary behaviour during a usual week	<p>57-90 questions (employed/unemployed), 56-70 (retired), 1-week period <i>domains:</i></p> <ul style="list-style-type: none"> ▶ demographic factors (11 items) ▶ occupation (1-20 items) (not included in questionnaire for retired people) ▶ transportation in leisure time (six items) ▶ watching television or video and playing computer games (two items) ▶ home and garden activities (three items) ▶ eating (one item) ▶ sleeping (one item) ▶ moderate and vigorous PA in leisure time (two items) ▶ sports participation (1-15 items) ▶ determinants of PA (29 items) 	Total PA is calculated by adding up occupational, sport and household activities and activity variables are calculated with the Metabolic Equivalent Task values
Quality of life	Short Form-12 ^{72 73}	Health-related quality of life	<p>12 questions, 4-week period <i>domains - physical health:</i></p> <ul style="list-style-type: none"> ▶ physical functioning (two questions) ▶ role-physical (two questions) ▶ bodily pain (one question) ▶ general health (one question) <p><i>domains - mental health:</i></p> <ul style="list-style-type: none"> ▶ energy/fatigue (one question) ▶ social functioning (one question) ▶ role-emotional (two questions) ▶ mental health (two questions) 	Range from 0 (=the lowest level of health) to 100 (=highest level of health)
Pelvic floor muscles	Pelvic floor muscle function ⁷⁴⁻⁷⁶	Pelvic floor muscles	Assessment of pelvic floor muscle tone, force, endurance and coordination, using digital palpation	<ul style="list-style-type: none"> ▶ Tone: hypotone, normotone or hypertone ▶ Force: Maximum Voluntary Contraction (MVC) (without cocontraction), rated on the Modified Oxford Grading Scale; 0=no contraction, 1=flicker, 2=weak, 3=moderate, 4=good, 5=strong ▶ Endurance: a maximal voluntary contraction is asked and the result is expressed in the number of seconds the contraction could be sufficiently maintained, with a cut-off time of 10 s ▶ Coordination: presence of pelvic floor muscle contraction during cough (1=yes/0=no)

linear model for longitudinal measurements will be used to compare the evolution between both groups (1, 4, 6, 12 and 24 months). For the dichotomous variables and count variables (stool/bladder diary, pad use, pelvic floor muscle tone and coordination) a logistic regression and a negative binomial model will be considered. In both models, generalised estimating equations will be used to handle the correlations over time.

For the primary outcome, the alpha level is set at 0.05. For the secondary outcomes, the same level will be used and therefore a single significant p-value should be interpreted with caution.

ETHICS AND DISSEMINATION

Ethics approval was granted by the local Ethical Committee of the University Hospitals Leuven (s59761) and additionally a positive advice from the Ethical Committees of the OLV Hospital in Aalst and the General Hospital Groeninge in Kortrijk has been obtained.

This study applies the principles established in the Declaration of Helsinki. A written consent form is signed by participants before data collection and obtained by the assessor before the first assessment. All data are deidentified and coded with a unique trial identification number.

The latest version of the protocol is V.3.4. Any future modifications demand approval by the principal researcher and a formal amendment approved by all Ethical Committees.

Contact details of the investigator are provided to the patient for queries and concerns. No adverse events are expected as all treatments are low risk. Patients are free to withdraw from the study at any time without any consequences regarding their treatments in the hospital.

Dissemination of the results

Dissemination of the results is based on two pillars: (1) all involved practitioners have to be informed through implementation of the project results in the guidelines, (non-)scientific literature, the training of medical doctors and specialised physiotherapists and (2) all patients have to be informed by means of implementation of the treatment in the hospitals and in the primary care and by the organisation of patient symposia.

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