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ORIGINAL ARTICLES AND REVIEWS

Rehabilitation strategies for low anterior resection syndrome. A systematic review

Giampiera Bulfone[1], Francesca Del Negro[2], Elena Del Medico[3], Lucia Cadorin[4], Valentina Bressan[5] and Simone Stevanin[6]

[1]*Dipartimento di Biomedicina e Prevenzione, Università degli Studi di Roma "Tor Vergata", Rome, Italy*
[2]*Uffield Orthopedic Centre, Oxford University Hospital, Headington, Oxford, United Kingdom*
[3]*Clinica Neurologica e di Riabilitazione, Azienda Ospedaliero-Universitaria Santa Maria della Misericordia, Udine, Italy*
[4]*Centro di Formazione Continua, Centro di Riferimento Oncologico, Aviano, Italy*
[5]*Dipartimento di Area Medica, Università degli Studi di Udine, Udine, Italy*
[6]*Policlinico Universitario, Padua, Italy*

Abstract

Objective. To summarize the evidence in the literature about rehabilitative treatments that reduce low anterior resection syndrome (LARS) symptoms in patients who underwent surgery for colorectal cancer.

Methods. We have search in PubMed, Cochrane Central Register of Controlled Trials, Cumulative Index of Nursing and Allied Health and Scopus databases. Studies selected were limited to those including only patient undergone low rectal resection with sphincter preservation and with pre-post assessment with a LARS score. Five articles fit the criteria.

Results. The percutaneous tibial nerve stimulation demonstrated moderate results and sacral nerve stimulation was found to be the best treatment with greater symptom improvement. Only one study considered sexual and urinary problems in the outcomes assessment.

Conclusions. In clinical practice patients should evaluate with the LARS and other score for evaluation of urinary and sexual problems. Future research must be implemented with higher quality studies to identify the least invasive and most effective treatment/s.

Key words

- low anterior resection syndrome
- rehabilitation
- therapy
- treatments
- quality of life

INTRODUCTION

Colorectal cancer is the third most common cancer worldwide [1]. Although surgical treatment has improved in recent years, patients who have a sphincter-preserving operation may experience symptoms that can affect their quality of life (QOL) [2-4]. Eighty percent of patients who undergo a low or very low anterior rectal resection will experience fecal or flatus urgency or incontinence, frequent bowel movements, bowel fragmentation, difficulties emptying, incomplete evacuation, and increased gas postoperatively [2]. This suite of symptoms is referred to as low anterior resection syndrome (LARS) [2, 3]. Anatomical, nervous/sensory, and muscular changes [2-4], the new sphincter's functional capacity [5], pelvic floor functionality [4], colon motility [6], post-prandial response [7], and the new rectum's compliance [8] are involved in LARS.

Although LARS has been recognized for years, a rigorous scientific definition of this syndrome never has been developed. Conventionally, it is defined as a bowel disorder following rectal resection that affects patient QOL [4]. After surgical treatment of a colorectal cancer, LARS appears immediately, becomes more evident in the first several months, and stabilizes after approximately one to two years [7].

The incidence of LARS in Europe is approximately 52% in patients with low rectal surgical treatment [9] and the approach to treat it is conservative, consisting of an appropriate diet, fiber intake, mass-forming agents [10] and enemas [11]. Nonetheless, LARS has adverse effects on patient satisfaction and QOL. The literature demonstrates the availability of different rehabilitation treatments [10, 12, 13-15], but currently there is no evidence of the best rehabilitative intervention to improve LARS patients' symptoms.

Therefore, the goal of this paper was to summarize the evidence available in the literature on different rehabilitative treatments to reduce LARS symptoms in patients who have undergone surgery for colorectal cancer.

Address for correspondence: Giampiera Bulfone, Dipartimento di Biomedicina e Prevenzione, Università degli Studi di Roma "Tor Vergata", Via Montpellier 1, 00133 Rome, Italy. E-mail: giampiera.bulfone@uniroma2.it.

METHODOLOGY

Study design

A systematic literature review was conducted according to Lefebvre *et al.* (2013) [16] and Liberati *et al.* (2009) [17] methodologies.

Literature search strategy

To identify relevant studies, we searched the following databases: Pubmed, Cochrane Central Register of Controlled Trials (CCTR), Cumulative Index of Nursing and Allied Health (CINAHL), and Scopus. The PICOS (Participants, Interventions, Comparisons, Outcomes, and Study Design), respectively: patients who underwent low or very low anterior rectal resection for rectal neoplasm (P), were treated with rehabilitation therapy (I) by comparison to standard care (C), and had fecal incontinence or bowel dysfunctions that compromise their quality of life (O). The study designs considered were randomized clinical trials and cohort studies. Search terms were "low anterior resection syndrome," "rectal neoplasms," "rectal cancer," "rehabilitation," "therapy," "treatments," "process assessment," "biofeedback," "electrical stimulation," "disability evaluation," "early intervention," "rehabilitation nursing," "fecal incontinence," "quality of life," "bowel dysfunction," and "outcome." The MESH terms were combined with free terms and Boolean operators (AND, OR) to include all possible combinations. Thereafter, a manual search was conducted using a snowball sampling technique [17].

The primary end-points of this systematic review were LARS score and QOL. Secondary end-points were anal pressure and urinary and sexual symptoms.

Inclusion and exclusion criteria

Studies included were those published through October 2018 that had abstracts available and included only adult patients (>18 years) who had undergone low rectal resection with sphincter preservation. As a large proportion of the elderly public, particularly in the 50 to 79 years age group, exhibits major LARS in the absence of any surgical procedure, only studies with pre-post treatment assessment with a LARS [18] score to identify patient with LARS were included.

Data extraction and risk of bias

Two researchers evaluated the studies independently. In the first phase, titles, abstracts, and full texts were analyzed to establish the studies' relevance to the research questions; the risk of bias was assessed using the Edward Score [19] for observational studies. The 11 items of the assessment tool are as follows: definition of aims; sample formation; description of inclusion and exclusion criteria; description of subject characteristics; power calculation; objectivity of outcome measures used; adequacy of follow-up; adequacy of analysis (intention to treat); adjustment for baseline differences between groups; appropriate unit of allocation to groups; randomization method. Each item is scored from 0 to 2 for adequacy and a high score indicates a study's high methodological quality. The total score possible ranges from 0 to 22 for experimental studies or from 0 to 16 for observational studies. In the second phase, the researchers combined the data and resolved any discrepancies by consensus.

RESULTS

Search results

We selected 439 articles, 186 of which were duplicates. Three researchers analyzed the remaining 254 studies independently and 5 articles that fit the criteria were selected *(Figure 1)*.

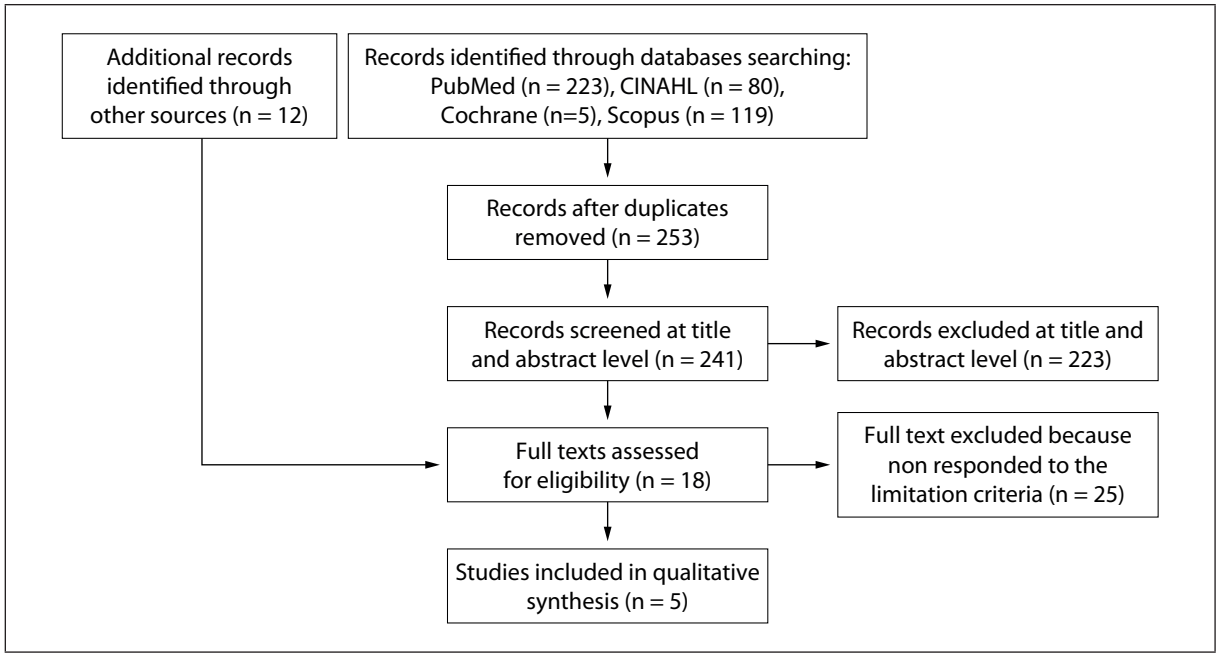

Figure 1
PRISMA Flow Diagram.

Table 1
Methodological quality of included studies

		Altomare *et al.* 2017 [23]	D'Hondt *et al.* 2017 [21]	Eftaiha *et al.* 2017 [20]	Mege *et al.* 2017 [22]	Vigorita *et al.* 2017 [24]
1. Aims/ outcomes	2: explicitly described in article	2	2	2	2	2
	1: implied in article					
	0: unclear					
2. Sample formation	2: random	1	1	0	1	1
	1: quasi-random, sequential series, or total available					
	0: selected, historical, other					
3. Inclusion/ exclusion	2: criteria clearly described	2	2	2	0	2
	1: implied by patient characteristics, setting					
	0: unclear					
4. Sample characteristics	2: three or four characteristics	2	2	2	2	2
	1: one or two characteristics					
	0: no characteristics					
5. Power of study calculated	2: yes, appropriate	0	0	0	0	0
	1: yes, inappropriate					
	0: no					
6. Outcome measures	2: objective or validated scale	2	2	2	2	2
	1: subjective/self-report					
	0: not explicit					
7. Follow-up	2: >90% of patients enrolled/approached	2	2	2	2	2
	1: 80%-90% of patients					
	0: <80% of patients/no information					
8. Analysis	2: intention to treat/including all available data	2	2	2	2	2
	1: excluding dropouts but evidence of bias adjusted or no bias evident					
	0: excluding dropouts and no attention to bias					
Total score (0-16) for observational studies		**13/16**	**13/16**	**12/16**	**11/16**	**13/16**
9. Baseline differences	2: none or adjusted					
	1: differences unadjusted					
	0: no information					
10. Unit of allocation	2: appropriate					
	1: nearly					
	0: inappropriate					
11. Randomization	2: random and concealed					
	1: random but not concealed					
	0: randomization before protocol exclusions, or no information					
Total score (0-22) for experimental studies						

Risk of bias in the studies

The description of the studies' quality assessment and risk of bias are provided in *Table 1*. The cohort studies included demonstrated a low quality in selection criteria [20-24], and no study included a statistical power analysis [20-24].

Interventions to reduce LARS symptoms

Table 2 provides a summary of the studies' characteristics. The rehabilitative treatments used in the studies included sacral nerve stimulation (SNS) [20-22] and percutaneous tibial nerve stimulation (PTNS) [23, 24].

Sacral nerve stimulation intervention

Three studies addressed SNS [20-22] with a total of 43 participants; one was [21] prospective and the others [20-22] retrospective. Patients included had undergone a surgical procedure for rectal cancer [20, 21] and

Table 2
Data extraction of included studies

Author, year of publication, country	Aim	Study design	Sample	Instrument	Intervention/ description	Results
Altomare et al. 2017 [23] **Italy and Spain**	To test effectiveness of PTNS in FI and UI in LARS.	Prospective Follow up: 6 months	Method: convenience N: 21 Age: average 66 ± 5.8 years Gender: M 47.6% (10/21), F 52.4% (11/21) Inclusion criteria: postoperative after rectal cancer free from anastomotic complications, age over 18 years, LARS score ≥ 20, LARS duration for at least 12 months, failure of conservative therapy (diet, medical treatments and BF) Surgical procedure: LAR in laparotomy 71.4% (15/21), 28.6% (6/21) laparoscopy Temporary stoma: 66.6% (14/21) Anastomosis type: 28.5% (6/21) EtE, 71.5% (15/21) StE Perioperative treatment: preoperative 47,6% (10/21), postoperative 61,9% (13/21) CT	LARS score (Emmertsen and Laurberg 2012) TAPE score (Altomare *et al.* 2017) FIQL (Rockwood *et al.* 2000) St Marks score (Vaizey *et al.* 1999) ODS score (Altomare *et al.* 2008). ICIQ-SF score (Tubaro *et al.* 2006). IUGA-Revised (PISQIR) (Rogers *et al.* 2013) for woman IIEF-5 Questionnaire (SHIM) (Rosen *et al.* 1999) and PEDT score (Symond *et al.* 2007) for man Baden-Walker score for genital prolapse (Baden and Walker 1972) Urinary retention Anorectal manometry	PTNS (12 sessions - 2 per week for the first 4 weeks, and 1 per week for the last 4 weeks - of 30 minutes. Stimulation parameters were set at 200 µs pulse width and 20 Hz frequency. Stimulation was gradually increased until sensory and/ or motor response were seen and set at a well-tolerated intensity)	The median LARS-score significantly decreased from 32 (IQ ranges 30-38) to 27 (IQ ranges 17- 37, p=0.009) The TAPE-score significantly improved from a median value of 55 (IQ ranges 49- 64.6) to 58 (IQ ranges 51-70, p=0.004). 43% (9/21) of patients reported a significant (>50%) improvement in the St Marks faecal incontinence score 50% (3/6) of patients showed an improvement in ICIQ-SF for the urinary incontinence score The ODS score only improved significantly (>50%) in 3 of the 21 cases and its median value was 9.5 (IQ ranges 7-14) before and 8.5 (IQ ranges 4.7-10.7) after PTNS (p= 0.05) Urinary retention was absent in all patients and no female patients complained of genital prolapse All the male patients except two and all the eleven women were not sexually active before and after treatment. Therefore, no changes were observed concerning sexual activity after PTNS The median FIQL score at 6 months follow-up however, did not show significant changes in any domain (lifestyle 2.7 *vs* 2.8, p=0.468, coping 1.6 *vs* 1.4 p=0.808, depression 1.7 *vs* 1.9 p=0.56, embarrassment 1 *vs* 1.3 p=0.27). The median resting and squeezing anal pressures did not change significantly before and after PTNS (33 (range 8-52) *vs* 35 (range 10-66) mmHg for resting pressure, and 49 (range 32-124) *vs* 46 (range 34-125) mmHg for squeeze pressure. Recto anal inhibitory reflex was present in 5 patients Drop out: none

Continues

other diseases, such as ulcerative recto-colitis [22].

Patients underwent low resection rectum (LAR) [20-22] with laparoscopic [20, 21] and laparotomic [22] approaches, and received different treatments, including chemotherapy [20, 21], and/or radiotherapy [22]. The authors included patients unresponsive to conservative therapy, such as diarrheal drugs [20-22], diet [20], biofeedback (BF) [20], pelvic floor muscle exercises (PFME) [21], or PFME and BF combined [22].

With respect to the outcome assessment [20-22], ev-

Table 2
Continued

Author, year of publication, country	Aim	Study design	Sample	Instrument	Intervention/ description	Results
D'Hondt et al. 2017 [21] **Belgium**	To investigate the impact of SNS on all symptoms of LARS	Prospective Follow up: 9 months (1-13)	Method: convenience N: 15 Age: average: 77.66 Gender: M 73.3% (11/15), F 26.7% (4/15) Inclusion criteria: surgical treatment for rectal cancer with LARS, unresponsive to conservative therapy (such as ant diarrheal drugs and pelvic floor physiotherapy). Surgical procedure: LAR 100% with TME 86.6% (13/15) and with PME 13.4% (2/15); in laparotomy 53.3% (8/15), in laparoscopy 46.7% (7/15) Temporary stoma: 26.7% (10/15) Anastomosis type: EtE 26,6% (4/15) StE 20% (3/15) and JP 53.4% (8/15) Perioperative treatment: preoperative 80% (12/15) and postoperative CT 86.6% (13/15)	LARS score (Emmertsen and Laurberg 2012). CCF-FI (Jorge and Wexner 1993). Manometry, colpo-cysto-defecography, ultrasound of the anal sphincter	SNS (First, the efficacy of the neurostimulation for the patient was verified through percutaneous nerve evaluation (PNE). The lead was introduced through the third sacral foramen and tested for 2 weeks)	The mean Wexner scores decreased from 17.7 to 4.6 (Z=2.93; p=0.003) The mean LARS score dropped from 36.9 to 11.4 (Z=2.93; p=0.003) Drop out: 4/15 Four patients, all with major LARS, had insufficient response to the PNE procedure
Eftaiha et al. 2017 [20] **Canada and USA**	To test the efficacy of SNS in LARS.	Retrospective Follow up:19.5 months (4-42)	Method: convenience N: 12 Age: average 67.8 ± 10.8 Gender: M 50% (6/12), F 50% (6/12) Inclusion criteria: surgical treatment of rectal cancer, with LARS, unresponsive to BF, fiber, anti-mobility agents for at least 12 months Surgical procedure: LAR in laparotomy 71.4% (15/21) and laparoscopy 28.6% (6/21) Temporary stoma: ND Anastomosis type: CA 58.3% (7/12) and CR 41.7% (5/12) Peri operative treatment: preparative CT 19% (4/21)	LARS score (Emmertsen and Laurberg 2012) CCF-FI (Jorge and Wexner 1993) Bowel diary Anal manometry, endo-anal ultrasound and defaecography	SNS (after failure of BF, fiber, anti-motility agents) 12 months)	At a median follow-up of 19.5 months, there were significant improvements in CCF-FI and in the LARS Scores (p=0.001) Drop out: none

Continues

ery study used the Cleveland Clinic Florida Fecal Incontinence (CCF-FI) [25], while diaries [20] for bowel habit assessment and the fecal incontinence quality of life score (FIQL) [26] were used for the QOL assessment [22].

The longest follow-up was 19 months (range 4-42) [20] and the shortest 9 (1-13) [21]. The outcomes demonstrated a statistically significant improvement in LARS syndrome [20-22], fecal incontinence (FI), and QOL [22].

Percutaneous tibial nerve stimulation

Two prospective studies [23, 24] that included 31 patients addressed PTNS to assess its efficacy in improving LARS, QOL, fecal and urinary incontinence, sexual dysfunction, and obstructed defecation. Patients underwent perioperative chemotherapy [23] or preoperative chemotherapy combined with postoperative radiotherapy [24]. In each study [23, 24], patients were included after conservative therapy failed (diet, drug, and BF).

Two studies [23, 34] used FIQL [26] to assess QOL;

Table 2
Continued

Author, year of publication, country	Aim	Study design	Sample	Instrument	Intervention/ description	Results
Mege et al. 2017 [22] **France**	To analyze the effectiveness of SNS on poor functional results and on the QOL, after different colorectal resections.	Retrospective Follow up: 18 (3.5-91) months	Method: convenience N: 16 Age: average 53 Gender: M 43.8% (7/11), F 56.2% (9/16) Inclusion criteria: surgical treatment for rectal cancer or other diseases, unresponsive to conservative therapy (i.e. medications influencing stool consistency, pelvic floor rehabilitation and biofeedback) Surgical procedure: TP 44% (7/16), LAR with TME 37% (6/16), LE 9% (3/16) Anastomosis type: IPAA 44% (7/16), CA 37% (6/16) CR 19% (3/16) Temporary stoma: 81.2% (13/16) Perioperative treatment: preoperative 25% (4/16) and postoperative CT 12.5% (2/16)	LARS score (Emmertsen and Laurberg 2012) CCF-FI (Jorge and Wexner 1993). FIQL score (Rockwood *et al.* 2000). Endo-anal ultrasonography or pelvic Magnetic Resonance	SNS (ND)	In PC patient fecal urgency had improvement from 5 to 0 (p=0.02) and bowel frequency from 11 to 5 (p=0.004); FI from 4 to 1.8 (p=0.03) In CA and CR anastomosis bowel frequency decreased from 10 to 2 (p=0.04), FI from 5 to 0.6 (p=0.02) while bowel urgency from 2 a 4.8 (p=0.86) FIQL significantly improved Drop out: 2/16
Vigorita et al. 2017 [24] **Spain**	To evaluate the effectiveness of treatment with PTNS in LARS and to identify predictors of the outcome	Prospective Follow up: 6 week	Method: convenience N: 10 Age: average 62 years Gender: M 60% (6/10), F 40% (4/10) Inclusion criteria: patients > 18 years old, surgical treatment for rectal cancer with LARS, unresponsive to conservative therapy (i.e. medications, fiber and biofeedback) Surgical procedure: LAR Anastomosis type: ND Perioperative treatment: CT 80% (8/10). Preoperative 50% (5/10) and postoperative RT	LARS score (Emmertsen and Laurberg 2012) CCF-FI (Jorge and Wexner 1993) FIQL score (Rockwood *et al.* 2000) Bowel diary Endo-anal ultrasound and anal manometry	PTNS (All patients had 2 PTNS sessions per week - 30 min for 6 weeks. Therefore patient with an improvement had second phase of PTNS)	LARS Score improvement has observed in 50% of patients with total resolution of LARS in 20% (2/10) FI decreased in 70% (7/10) of the patients. The median Wexner score decreased from 14 (IQR 10.75–18.5) to 10 (IQR 6.5–18) after treatment (p = 0.034) A significant improvement in FIQL score in lifestyle, depression, and daily defecation urgency (p=0.05). Drop out: 3/10 Only seven patients (70%) responded positively after the first phase and received the second phase of treatment. After the second phase, three patients with major LARS symptoms became classified as minor LARS and two patients with minor LARS had resolution of the syndrome. Two patients did not show improvement in LARSS; however, they demonstrated an improvement in defecation diary and FIQL Of the three patients who did not respond, two were from the major LARS group and one from the minor LARS group

Continues

Table 2
Continued

F = female; M = male; ND = non described; FI = fecal incontinence; UI = urinary incontinence; QOL = quality of life.
Surgical procedure: LAR = low anterior resection; LARS = low anterior resection syndrome; LE = left hemicolectomy; PEC = percutaneous endoscopic cecostomy; PME = partial mesorectal excision; TME = total mesorectal excision; TP = total proctolectomy.
Anastomosis type: CA = coloanal anastomosis; CR = colorectal anastomosis; EtE = end-to-end anastomosis; HS = hand-sewn anastomosis; IPAA = ileal pouch-anal anastomosis; JP = j-pouch anastomosis; StE = side-to-end anastomosis.
Treatments: AE = anterograde enema; BF = biofeedback; CT = chemotherapy; PNE = percutaneous nerve evaluation; PTNS = percutaneous tibial nerve stimulation; RT = radiotherapy; SNS = Sacral Nerve Stimulation.
Scales:
Baden-Walker score ((Baden and Walker 1972): for genital prolapse assessment.
Cleveland Clinic Florida Fecal Incontinence (CCF-FI) scoring system or Wexner Fecal Incontinence Score (Jorge JM and Wexner SD 1993): to assess fecal incontinence. The range score from 0-8 (midle incontinence), 9-14 (moderate incontinence), 15-20 (severe incontinence).
Fecal Incontinence Quality of Life score (FIQL) (Rockwood *et al.* 2000): to assess fecal incontinence quality of life: divided in 4 dimensions (Depression, Embarrassment, Life Style and Coping). The score range from 1 (low quality of life) to 4 (good quality of life).
Gastrointestinal Quality of Life Index (GIQLI) (Slimet *al.* 1999): to assess quality of life in physical status, emotions, social integration, and the effect of medical treatment. The score ranging from 0 to 144 (excellent).
International Index of Erectile Function (IIEF-5) (Rosen *et al.* 1999): diagnostic tool for erectile dysfunction.
International Consultation on Incontinence Questionnaires Short Form (ICIQ-SF) (Tubaro *et al.* 2006): for assessment of urinary incontinence.
Low Anterior Resection Syndrome score (LARS) (Emmertsen *et al.* 2012): to assess LARS syndrome. The range score was from 0 to 42: 0 to 20 (no LARS), 21 to 29 (minor LARS), and 30 to 42 (major LARS).
Obstructed Defecation Syndrome (ODS) (Altomare *et al.* 2008): to assess obstructed defecation.
Pelvic Organ Prolapse/Incontinence Sexual Questionnaire IUGA-Revised (PISQIR) (Rogers *et al.* 2013): questionnaire for sexual dysfunction.
Premature Ejaculation Diagnostic Tool (PEDT) (Symond *et al.* 2017): for assessment sexual disfunction in man.
St. Mark's score (Vaizey *et al.* 1999): to assess fecal incontinence. The score range from 0 (continence) to 24 (incontinence).
Three Axial Perineal Evaluation score (TAPE) (Atlomare *et al.* 2017): to assess pelvic floor function evaluation (urinary, fecal and sexual) normal value 100% of hexagonal area.
Urinary retention: was scored according to the volume of urine retention if present (score 0 when absent, 1 if >50 ml, 2 if between 50-100ml and 3 if > 100ml of urine).

one used the CCF-FI [25] and bowel diary to evaluate fecal incontinence and bowel movement; another [23] adopted the St Marks score [27] for fecal incontinence assessment, while the other studies adopted the three axial perineal evaluation (TAPE) score [28, 29] (comprehensive of the obstructed defecation syndrome (ODS) score [30], the International Consultation on Incontinence Questionnaire-Short Form (ICIQ-SF) score [31], the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQIR) (IUGA-Revised) [32], the International Index of Erectile Function (IIEF-5) Questionnaire (SHIM) [33], the Premature Ejaculation Diagnostic Tool (PEDT) score [34], and the Baden-Walker score [35] to measure obstructed defecation, urinary incontinence, sexual dysfunctions, and genital prolapse. Urinary retention was scored according to the volume of urine retention, if present (score 0 when absent, 1 if > 50 ml, 2 if between 50-100 ml, and 3 if > 100 ml of urine) and FI with the anal manometry for pressure assessment [23]. Follow up occurred from 6 weeks [24] to 6 months [23].

Patients reported a significant improvement in fecal and urinary incontinence; obstructive defecation improved in only three patients, and because the sample was not sexually active, sexual function was not assessed [23]. There were no significant changes in the FIQL and in anal pressure after PTNS [23]. In one study [24], all patients underwent PTNS in the first phase of the study; however, only those who experienced an improvement in incontinence (70%) were included in the second phase, and three patients showed no LARS improvements. In this study, QOL improved in lifestyle, depression, daily defecation, and urgency.

DISCUSSION

Eighty percent of patients who undergo a low or very low rectal anterior resection with sphincter preservation will experience LARS [2], a syndrome that has adverse effects on patients' QOL, in the postoperative period [2-4].

Currently, no indications of the best rehabilitative interventions are available, and thus, we conducted this review to identify the treatments that reduce LARS symptoms best in patients who have undergone surgery.

Methodological issues

The methodological quality of the studies selected differed significantly and all had a small sample size. Two used a retrospective design [20-22] that may have introduced a recall bias because patients must remember their symptoms. Moreover, the prospective studies used follow-up times that ranged from 6 weeks [24] to 91 months [22]. The literature underscored the fact that LARS appears immediately after surgery, becomes more evident during the first several months, and stabilizes after approximately one to two years [7]; with this assumption, follow-up times up to two years should be appropriate. At the same time, we should consider the results of studies with shorter follow-up times with caution, because patients likely will experience further improvements in outcomes. Moreover, the studies with long follow-ups may be associated with a high percentage of drop out and the possibility of confounding variables biases, such as age or changes in clinical conditions [36], and the author can attribute treatment efficacy or failure to the level of the anastomosis from the anal verge (lower anastomosis might have worst results) and preoperative radiotherapy [24]. Therefore, these factors' potential roles must be explored in future studies, which also should include larger samples to assess the differences in treatment results with respect to the surgical procedure and perioperative treatments.

The studies' inclusion criteria also differed greatly. One source of bias may be the inclusion of patient with a temporary stoma. The presence of a temporary

ileostomy is a risk factor for bowel dysfunction following surgery [37, 38] because prolonged inactivity of the pelvic floor and sphincter complex contributes to LARS [39-40].

The researchers used different instruments to assess LARS outcomes, QOL, and incontinence, and thus, the results of the studies are not comparable; moreover, a meta-analysis cannot be conducted. Therefore, we should consider the outcomes evaluations with caution. In addition, the LARS score simply is a screening instrument [21] and does not consider urinary and sexual dysfunction, which are included as symptoms in LARS syndrome [41, 42]. With this assumption, LARS [18] scores always should be accompanied by the TAPE score [28, 29].

Treatments to reduce LARS symptoms

We selected studies that included adult patients who underwent low rectum resection with sphincter preservation and with pre/post LARS evaluation. The treatments analyzed were the SNS [20-22] and PTNS [23, 24].

The patients recruited were treated first with conservative therapy, including constipating medications, physiotherapeutic pelvic floor exercises, and biofeedback, all of which have been demonstrated effective in improving FI, bowel movement [43-45], and QOL [43-45]. We need stronger evidence about conservative therapy's efficacy and which outcomes it improves most effectively; these findings should indicate whether to submit patients for conservative therapy initially, and then, in cases of inefficacy, for other treatments.

Two studies [23, 24] considered PTNS treatment. One [23] concluded that it offers a moderate improvement in LARS syndrome, but argued that it can be associated with the time or the level of the anastomosis and preoperative treatment, while the other study [24] included a sample of only 10 patients and considered only those who showed improvement after the first phase of PTNS in the outcome assessment. Among these, two demonstrated no improvement in the LARS score, but QOL and defecation habits did improve [24]. Future studies should investigate more thoroughly the roles the anastomosis level and type and preoperative treatment (chemotherapy and radiotherapy) play in the LARS rehabilitation process.

Three studies addressed SNS efficacy in improving LARS [20-22]. One found improvement in such FI and LARS symptoms as clustering and urgency. The second [21] demonstrated that SNS is effective for LARS and FI, fragmentation, and urgency, but four patients, all with major LARS, had insufficient responses to the treatment. The final study [22] was multi-centric, but retrospective, with a small sample, and found improvement in FI, LARS scores, stool frequency, and urgency in 86% of cases. In the outcome evaluation, these authors [20-22] also used manometry [20-22], colpocysto-defecography [20-22], ultrasound of the anal sphincter [20-22], anorectal dyssynergy [22], sphincter electromyogram [22], and magnetic resonance [22], and not simply self-reports or medical records alone. However, there were no post treatment data on these evaluations.

It is difficult to judge which treatment is the best, because only two studies considered PTNS [23, 24] and only one [23] evaluated patient outcomes thoroughly and extensively. Moreover, the authors argued about moderate improvement [23] or excluded patients who did not improve during the first phase of the study from the second phase of PTNS [24]. Among the three studies that evaluated SNS [20-22], two demonstrated improved outcomes, although they were retrospective [2,22]. Our conclusion seems to confirm Ramage *et al.* finding, in which the authors reported a significant improvement of LARS symptoms in 74% of patients after SNS. However, this technique's high cost also must be considered [46].

This review has several limitations. We consulted only certain databases and included only those studies with abstracts available. Therefore, despite the systematic approach we used to identify studies, these conditions may have excluded some publications. Lastly, by including only studies with pre and post treatment LARS score evaluations, we may have excluded from our review studies that reported potentially valid treatments.

Implications for practice and further research

Future studies must be multi-centric RCTs with larger samples of patients who have failed to respond to conservative therapy. Further, great attention should be given to the patient inclusion criteria. Because the LARS etiology is multifactorial [47, 48], we must consider patient groups that represent every surgical procedure and perioperative treatment.

Moreover, the follow up time should be approximately two years, because LARS symptoms have stabilized by that time [7].

In clinical practice patients should evaluate with the LARS [18] and TAPE scores [28, 29] in pre and post treatment, and the FIQL [26] should be considered in the QOL assessment. Only two studies [32, 33] consider the urinary and sexual dysfunction which are included as symptoms in LARS syndrome [41, 42]. Physician should take into consideration any patient problem and should include in their interventions also the caregivers. In addition, our findings highlight the importance to include in education programs the best rehabilitation strategies for the patient affected of LARS.

CONCLUSION

Most patients who undergo a low or very low rectal anterior resection experience LARS postoperatively, a syndrome that has significant adverse effects on their satisfaction and QOL. From our review, SNS seems to be the most effective treatment for LARS symptoms and is less expensive than is PTNS; however, PTNS is a minimally invasive procedure [23].

Future research must be implemented with higher quality studies and with pre-post treatment assessment with LARS scores. This will allow us to develop the most effective intervention protocol, with the goal of identifying the least invasive and most effective treatment for LARS.

Conflict of interest statement

There are no potential conflicts of interest or any financial or personal relationships with other people or organizations that could inappropriately bias conduct and findings of this study.

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