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ORIGINAL ARTICLE

Systematic review of the management options available for low anterior resection syndrome (LARS)

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Abstract

Background Rectal cancer incidence is increasing. Low anterior resection is currently the gold standard surgical management. Postoperatively, patients may present with symptoms indicative of low anterior resection syndrome (LARS). LARS can be debilitating and is difficult to treat with low efficacy of treatment modalities. This systematic review aims to highlight the current evidence regarding LARS management.

Methods Systematic review of Medline, Cochrane and Embase used the following terms: "low anterior resection syndrome" AND "management", "low anterior resection syndrome" AND "treatment". Articles that focus solely of low anterior resection syndrome management in patients > 18 years were included. Bias risk was assessed via the Newcastle-Ottawa quality assessment scale for cohort studies and the JBI critical appraisal tool for randomized controlled trials. Due to heterogeneity of methodology, no statistical analysis was performed.

Results Thirty-eight articles with a total of 1914 patients were included in this review. Ninety-five per cent underwent surgery for malignancy. Treatment options included pharmacology, pelvic floor rehabilitation (PFR), transanal irrigation (TAI), sacral nerve modulation (SNM), percutaneous tibial nerve stimulation (PTNS) and "treatment programs" starting from the least invasive procedures escalating to more invasive treatments upon failure. The most common published medical therapies report Ramoestron use; however, studies are low impact. PFR showed significant improvement in LARS mostly in those with symptoms of faecal incontinence. However, long-term outcomes are inconsistent. TAI supplies pseudo-continence with its greatest benefit reported in those with incomplete evacuation. TAI has significant short-term effects on LARS but little long-term effect. TAI is also associated with a significant drop-out rate. SNM's hypothesised benefit is extrapolated from non-LARS associated FI. Results show improvements in FI but a high rate of explantation. PTNS evidence suggests little if any significant LARS improvement. A single "stepwise programme" study reported that 77 per cent did not progress further than diet and medication. Little evidence suggests benefit regarding diet or acupuncture.

Discussion There is no consensus as to the optimal treatment strategy for LARS. LARS is multifactorial and requires sensitive discussion between patient and surgeon to address the most prominent symptom. It requires physical and psychological input. No single treatment option provides superior results. Treatment is based on symptom control and patient acceptance.

Keywords Low anterior resection syndrome · LARS · Management · Treatment

Introduction

Colorectal cancer is the most common gastrointestinal (GI) malignancy [1] and the third most common cancer worldwide [2], presenting a substantial burden of morbidity and mortality [1]. Rectal cancer is increasing [3] and survival improving [3–8]. Surgery remains the cornerstone of rectal cancer treatment [6] to achieve the best oncological outcome [9, 10]. Sphincter-preserving surgery in the form of low anterior resection (LAR) is recognised as the gold standard for localised rectal cancer [11, 12]. LAR accounts

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for up to 80% of rectal cancer procedures [6], and improvements in technique and sub-specialisation have seen more sphincter preserving procedures performed [13]. An important adverse outcome after LAR is the development of low anterior resection syndrome (LARS). LARS is defined as "a patient who has had an anterior resection (sphincter preserving rectal resection) and have at least one symptom that results in at least one consequence" (Table 1) [14]. Coupled with "symptoms" are potentially devastating psychosocial influences culminating in deleterious effects on quality of life (QoL) (Table 1).

LARS is a combination of symptoms which may include one or all of the following: urgency, faecal incontinence (FI), frequency, fragmentation or constipation post LAR [15–18]. With a greater ability to surgically resect lower rectal tumours, avoidance of a permanent stoma is achievable in up to 80% [19]. However, the lack of a stoma does not necessarily mean a better QoL [6], and as more LARs are undertaken, the prevalence of LARS increases [20, 21]. LARS symptoms are underreported and often underassessed [22, 23]. Recognition and treatment are important because LARS is associated with poor QoL [20]. Symptoms arise immediately after surgery or stoma reversal [24, 25], and whilst previously thought to be transient [26], it is now recognised to be a longer-term phenomenon [11].

The pathophysiology of LARS is multifactorial [27] and poorly understood [2]. It is hypothesised to arise because of the anatomical and physiological sequelae of surgery [6] and includes, but is not limited to, alterations in the rectoanal inhibitory reflex (RAIR), decreased resting internal anal sphincter pressures, decreased anal sensation due to pudendal nerve damage, poor rectal compliance due to chemoradiation, low (< 5 cm) anastomoses [6, 7, 18], neorectum formation with reduced capacity and left colon mobilisation [17, 28]. The reported incidence varies greatly but can be up to 80% [17, 19, 27, 29].

Some authors have suggested scoring systems that measure FI principally do not account for the impact on QoL associated with LARS [16]. As such a validated LARS scoring system was created [16], consisting of three subgroups with a score ranging from 0 to 42. A score of 0–20 equates to "no LARS", 21–29 "minor LARS" and 30–42 "major LARS" [16]. This enables categorisation of LARS for the development of treatment algorithms and research [16].

There are multiple risk factors for LARS (Table 2) with the most consistently reported as neo-adjuvant radiotherapy [26] and low anastomotic height [2]. Pre-treatment counselling regarding LARS is important, especially in those patients with known preoperative risk factors. The use of the short on-line questionnaire "Pre-Operative LARS (POLARS) score" can aid in this consent process by alerting the patient to their risk of LARS severity [20, 30].

LARS poses a huge psychological burden on the patient (Table 3). Despite such morbidity, patients are often reluctant to verbalise negative outcomes to clinicians due to fear of "complaining" [31]. Currently, there is no consensus on LARS treatment [9], no gold standard [5] and no cure [32]. LARS is notoriously difficult to treat [33] with inconsistent results [34] coupled with it being underreported by patients

Table 1 Low anterior resection syndrome definition [14]

Symptoms	Consequences
Variable, unpredictable bowel function	Toilet dependency
Emptying difficulties	Preoccupation with bowel function
Altered stool consistency	Dissatisfaction with bowels
Urgency	Strategies and compromises
Increased stool frequency	Impact on:
Incontinence	• Mental and emotional wellbeing
Repeated painful stools	• Social and daily activities
Soiling	• Relationships and intimacy
	• Roles, commitments and responsibilities

Table 2 Factors affecting LARS incidence

Risk factor
Nerve damage [9]
TME results in worse LARS when compared to partial mesorectal excision [19]
Intersphincteric resections [3]
Diverting ileostomy [3, 19, 20, 27]
Anastomotic leak [3]
Protective factors
BMI < 25 [22]
Mechanical anastomoses [22]
No significance suggested
Age [20]
Gender [20]

TME total mesorectal excision, *LARS* low anterior resection syndrome, *BMI* body mass index

Table 3 Psychosocial outcome of LARS

Lower QoL [2, 3, 15, 16, 20, 26, 27, 33, 34, 37, 38]
Social isolation [15, 20, 21]
Depression [15, 21]
Loss of independence [15]
Lack of sleep, broken sleep [31]
Become housebound due to the severity of urgency and frequency [31]
Affects employment [31]
Many patients are too embarrassed to seek help for their lower GI symptoms [3]

QoL quality of life, *LARS* low anterior resection syndrome

and under-diagnosed by clinicians [35]. LARS treatment is symptom based [36] with evidence extrapolated from FI treatment [9] or expert opinion [3]. The literature acknowledges a lack of robust evidence [35] whilst also acknowledging early recognition of LARS is essential to optimise outcomes [22]. Several authors suggest a step-wise progression of LARS management commencing with conservative measures, pelvic floor rehabilitation (PFR), trans-anal irrigation (TAI) and then sacral nerve modulation (SNM) [17] or percutaneous tibial nerve stimulation (PTNS) [27, 37]. Finally, permanent colostomy is offered to those with ongoing untreatable issues [15, 27]. The aim of this systematic review is to highlight the current evidence in the management of LARS to enable prompt treatment of affected individuals.

Methods

Information sources

A systematic computerised literature search was performed of Medline, EMBASE and the Cochrane database from inception to June 2024.

Search strategy

These searches used the following terms: "low anterior resection syndrome" AND "management", "low anterior resection syndrome" AND "treatment". The results were combined and duplicates removed.

Eligibility criteria

Inclusion criteria were English articles, adult population, those with a continuous gastrointestinal tract and patients with a diagnosis of LARS. Exclusion criteria included non-humans, non-English articles, paediatric population, conference abstracts, letters, case studies, operative dilemmas/techniques, ileostomy vs closure, anastomotic leak (as defined by the individual study), articles focussing solely on neoadjuvant therapy effects on LARS, review articles and those concentrating on the psychosocial impact of LARS and not management.

Selection process

The Medline search yielded n-173 articles, Embase n-691 and Cochrane database n-0. A total of 864 articles were reviewed by two authors (GS and NF). Titles and abstracts were initially reviewed and then, if inclusion criteria were met, full articles were collected. This resulted in n-59 articles remaining (see Fig. 1). These full articles (n-59) were reviewed by two separate researchers (GS and NF). Those that did not focus on postoperative management of LARS or were review articles (n-26) were removed. The included articles' (n-33) references were then reviewed by GS and NF, which yielded a further five articles (n-38). Data extraction was undertaken independently by two authors (GS and NF) and any disagreement was adjudicated by JH.

Bias assessment and reporting

Observational studies (n-23) were critically appraised using the validated Newcastle-Ottawa quality assessment scale for cohort studies by two authors (GS and NF) and no discrepancies were found (Table 4). This allocates "stars" to each category within the assessment tool with a maximum of nine stars for each study. Those with a score with fewer than five stars are at high risk of bias. Randomized controlled trials (RCT) were critically appraised via the revised JBI critical appraisal tool for the assessment of risk of bias for RCTs [39] (Table 5). Two authors (GS and NF) reviewed these articles independently, and any disagreements were adjudicated by the senior author JH.

Statistical analysis

Due to substantial heterogeneity of the included articles, only descriptive statistics were used.

The publication date of the included articles ranged from 2009 to 2024, the majority being published between 2020 and 2022 (n-17, 44.7%). Thirty-four studies recorded their data collection period, which ranged from 4 weeks to 11 years. Most data stemmed from European institutions with Spain (n-6) and Italy (n-3) contributing the most. The most common interventions were TAI (n-10), SNM (n-8), pelvic floor rehabilitation (n-6), drug therapy (n-4), rehabilitation "programmes" (n-3) and acupuncture (n-1).

Study designs included 14 RCTs, 13 prospective and 10 retrospective studies, and one development of a scoring system. Sample sizes ranged from 9 to 517, with a mean of 50 patients. One study collected data from 17 institutions, whilst 25 studies collected data from a sole institution, and 10 collected data from two or three institutions. Only 9 studies (23%) had > 60 patients and only 3 studies had > 100 patients [20, 22, 40]. In total, 1914 patients were included, 672 females and 1242 males; two studies included males only [12, 38] whilst two studies did not specify sex [41, 42]. Malignancy accounted for 95% of the sample (n-1815), four studies failed to supply data, and the remaining were benign n-24 (4%). Six articles failed to record administration of neoadjuvant therapy; the remainder received treatment, most receiving chemoradiotherapy.

Protective ileostomy was utilised to some extent in 31 studies and ranged from 28.6 to 100%. In total, 1130

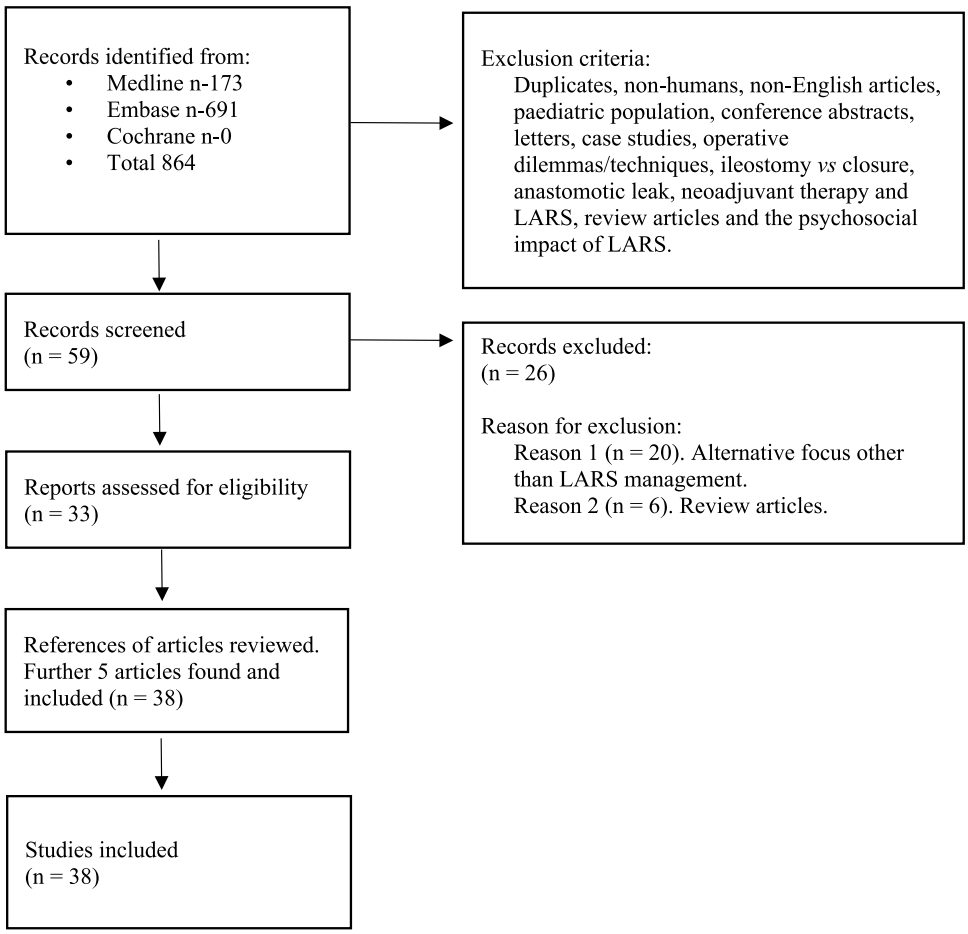

Fig. 1 PRISMA flow diagram of systematic search

diverting ileostomies were performed, representing 59% of the samples. Ten studies (26.3%) documented colonic "J pouch" use, which ranged from 0 to 36%. The total number of patients that received a J pouch was n-46 (2.4% of total sample).

Only 11 studies clearly reported anastomotic leak rate. The number of leaks ranged from 0 to 5 patients (0–20%) [17]. One study reported "pelvic sepsis" in 17% of the sample but did not specify cause [22]. Surgical reintervention was poorly documented with only six studies reporting data (range 0–16%). The majority defined LARS via the LARS score (76%) either alone or in conjunction with another assessment tool, most commonly the Cleveland Clinic Fecal Incontinence Severity Score (CCFIS) (Table 6).

Nutritional supplement

Nutritional supplements to manage LARS were addressed in one study [43]. This pilot study RCT investigating the probiotic *Lactobacillus plantarum* versus a placebo found no significant difference between cohorts [43].

Acupuncture

Dulskas et al. 2022 [37] investigated the use of acupuncture on nine patients with severe LARS over a 10-week period [37]. Their cohort included those patients with an anastomosis < 5 cm from the anal verge who were > two years post-surgery and had failed conservative management [37]. Results showed a significant reduction in reported symptoms [37].

Anti-motility agents

The most common published medical therapy used was serotonin antagonists. Using a specific serotonin antagonist called ramoestron was investigated because of a suggested greater efficacy [12]. Two studies reported data following ramoestron use. Itagaki et al. [38] administered ramosetron 25 mcg once daily and found statistically significant reductions in incontinence, urgency and number of daily bowel movements at 1 month. Results were more pronounced in those with lower anastomoses and those who started treatment within 6 months of their procedure [38]. Follow-up ceased at 1 month with no longer term data available.

Table 4 Newcastle-Ottawa quality assessment scale for cohort studies

	Author and year	Number of stars			
		Selection (X/4)	Comparability (X/2)	Outcome (X/3)	Total (X/9)
1	Altomare 2017	1	0	2	3
2	Croese 2018	2	0	2	4
3	Dalsgaard 2021	3	0	2	5
4	De Meyere 2020	2	0	2	4
5	De Miguel 2010	2	0	2	4
6	Dulskas 2022	2	0	2	4
7	Eftaiha 2017	1	0	2	3
8	Embleton and Henderson 2021	1	0	1	2
9	Enomoto 2021	2	0	2	4
10	Harji 2021	2	0	2	4
11	Itagaki 2014	1	0	2	3
12	Kim 2011	2	0	2	4
13	Koch 2009	2	0	2	4
14	Lee 2019	3	1	2	6
15	Liang 2016	2	0	2	4
16	Martellucci 2018	1	0	2	3
17	McKenna 2022	1	0	1	2
18	McCutchan 2017	3	0	2	5
19	Rodrigues 2022	1	0	2	3
20	Rosen 2011	1	0	2	3
21	Rubio-Perez 2020	1	0	2	3
22	Schwander 2013	1	0	2	3
23	Vigorita 2017	1	0	1	2

Ryoo et al.'s [12] RCT in male rectal cancer patients using ramosteron once daily versus a conservative treatment group showed significantly fewer major LARS after 4 weeks, significant increases in QoL and reduced bowel frequency [12].

One study reviewed ondansetron use. Ondansetron is a serotonin receptor antagonist, most commonly used for nausea; however, it also reduced colonic motility in this multicentric, double-blinded, placebo-controlled, crossover RCT [44]. Patients with LARS were randomised to receive either 4 weeks or ondansetron 4 mg PO BD OR 4 weeks of placebo; these groups were then crossed over to receive the alternative treatment [44]. Questionnaires were completed prior to commencement and at each treatment point/cross-over [44]. Thirty-eight patients were included in the analysis, and ondanstron, when used, showed a reduction in LARS score by an average of 25% [44].

Pelvic floor rehabilitation

Six studies focussed on PFR. Kim et al. reported significant improvements in FI, number of daily bowel movements, use of antidiarrhoeal medication and increased satisfaction [45]. Subset analysis showed that those who commenced biofeedback > 18 months post-surgery had significantly greater improvements in FI [45]. Liang et al. used external sphincter strength training and intra-anal balloon therapy training, which exhibited significant improvements in FI [13]. Lee et al. showed an immediate reduction in symptoms in the biofeedback cohort [46]; however, significant symptomatic improvement was only found at long-term follow-up. Van der Haijen et al.'s RCT described no improvements in incontinence scores, QoL, urgency or LARS score after PFR [36]. Asnong et al.'s programme of PFR vs standard care reported significant LARS score improvements at 4 and 6 months, which were not maintained at 12 months [40]. Significant reductions in average daily frequency, frequency of solid stool leakage and clustering were also reported [40]. Yuanyun et al.'s non-blinded RCT of 60 patients was undertaken at a single institution over a 4-week period. Patients were randomly placed into either Group A (loperamide and pelvic floor training) or Group B (loperamide only) [47]. Results documented anal sphincter function and strength showed significant increases in resting and squeeze pressures, significantly lower Wexner scores and mental health improvements in Group A [47]. LARS scores post-intervention were not reported.

Transanal irrigation

Ten articles reported the use of TAI. Koch et al. reported significant improvement in FI [48]. Five patients discontinued because of time constraints, impracticality or pain [48]. Rosen et al. reported significant reductions in daily bowel movements, FI and QoL improvements [11]. Another study by Rosen et al. reported significant reductions in daily bowel movements and LARS scores at 1 and 3 months but no effect on QoL [49]. Five patients (27.7%) ceased TAI because of complications. Subsequently, Rosen et al. also reported significant reductions in daily bowel movements with TAI [42]. However, 69% ceased because of pain and time constraints [42]. Martellucci et al. found no sustained reduction in LARS score or QoL with TAI [50]. FI scores did show significant improvement [50]. McCutchen et al. reviewed TAI patient acceptability [31]. Two males withdrew because of psychological impact [31], whilst others found TAI positively "life changing" [31]. Enriquez-Navascues et al.'s RCT (TAI vs PTNS) reported a 50% reduction in LARS score in both groups and improved QoL scores in both arms [34]. Twenty-three per cent from the TAI group withdrew [34]. Pieniowski et al.'s RCT (TAI vs conservative measures)

Table 5 JBI critical appraisal tool for randomized controlled trials

		Domain	Internal validity									Statistical conlusion validity		
			Selection and allocation			Administration of intervention			Assessment, detection and measurement of primary outcome			Participant retention	Statistical conclusion validity		
	Study/year	Question	1	2	3	4	5	6	7	8	9	10	11	12	13
1	Asnong et al. 2022		Y	N	Y	N	N	N	Y	Y	Y	Y	Y	Y	Y
2	Cuicchi et al. 2020		Y	N	Y	N	N	N	N	Y	Y	Y	Y	Y	Y
3	Enriquez-Navascues et al. 2019		U	N	Y	N	N	N	N	Y	Y	N	Y	Y	Y
4	Marinello et al. 2021		Y	Y	Y	Y	N	N	Y	Y	Y	N	Y	Y	Y
5	Marinello et al. 2024		Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y
6	Meurette et al. 2023		U	N	U	N	N	U	N	Y	Y	Y	Y	Y	Y
7	Pieniowski et al. 2023		Y	N	Y	N	U	N	N	Y	Y	N	Y	Y	Y
8	Popeskou et al. 2024		Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
9	Rosen et al. 2019		Y	N	Y	U	U	U	N	Y	Y	Y	Y	Y	Y
10	Rosen et al. 2020		Y	N	Y	U	U	U	N	Y	Y	Y	Y	Y	Y
11	Ryoo et al. 2021		Y	Y	Y	U	U	U	U	Y	Y	Y	Y	Y	Y
12	Van der Heijden et al. 2022		Y	Y	Y	N	N	Y	Y	Y	Y	U	Y	Y	Y
13	Yoon et al. 2020		Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
14	Yuanyuan et al. 2023		Y	U	Y	N	N	Y	N	Y	Y	Y	Y	Y	Y

Y YES, *N* no, *U* unclear

showed a significant reduction in major LARS score at 6 and 12 months plus significant reductions in medical therapies required within the TAI cohort [32]. Six TAI patients withdrew [32]. Rodrigues et al. reported 1-year follow-up of no major LARS and 95% reduction in incontinence, clustering and urgency, and 90% reported QoL improvement following TAI [1]. Thirty-seven per cent of TAI patients withdrew [1].

Meurette et al.'s multicentre RCT compared standard of care (conservative measures, diet, pelvic floor exercises and medications) vs TAI [51]. Although both groups mean LARS score improved, this was significantly greater in the TAI group [51]. All TAI patients requested to continue TAI usage post study follow-up [51].

Sacral nerve modulation

Eight articles reported SNM. De Miguel et al. reported a significant reduction in FI in the seven patients (46.7% of initial enrolled cohort) converted to a permanent SNM [52]. Schwander et al. converted 100% of their sample (n-9) to permanent SNM with significant improvement in symptoms and QoL [53]. Eftaiha et al. reported significant LARS score reduction in those with permanent SNM implants [33]. De Meyere et al. showed significantly better LARS scores with SNM [15]. Rubio-Perez et al. reported better LARS scores at follow-up and a negative relationship between radiotherapy and SNM satisfaction [18]. Enomoto et al. showed an overall significant improvement in bowel frequency, FI and LARS score in 40% [17]. Four devices required explantation, whilst two patients had non-significant results [17]. Croese et al. found median improvements in FI and QOL of 90% and 80%, respectively, following SNM [54]. Marinello et al.'s RCT assessed SNM's effect on LARS symptoms [55]. Seventy-six per cent converted to an implantable device [55]. Once the SNM device had been inserted, the patient was entered into the blind phase of the study, either having the SNM turned "on" or sham stimulation with the SNM turned "off" for 4 weeks [55]. The mode was then switched to the opposite, i.e., off to on, on to off, for another 4 weeks. Following this, every patient's SNM was switched to "on" (the cross-over phase) [55]. Results showed that when the SNM was activated, LARS scores were significantly reduced [55]. Long-term follow-up at 12 months showed that LARS improvement was not maintained [55].

Table 6 Study characteristics

Author	Year	Country	n	Female	Malignant	Ileostomy	AL	Intervention	Methodology
Altomare	2017	Italy	21	11	21 (100%)	14 (66%)	NR	PTNS	Prospective
Asnong	2022	Belgium	104	33	104 (100%)	90 (86.5%)	NR	PFR	RCT
Croese	2018	Australia	12	8	12 (100%)	12 (100%)	NR	SNM	Prospective
Cuicchi	2020	Italy	12	5	12 (100%)	12 (100%)	0 (0%)	PTNS	RCT
Dalsgaard	2021	Denmark	86	34	86 (100%)	76 (88.4%)	1 (1.2%)	Rehab "programme"	Retrospective
De Meyere	2020	Belgium	25	9	23 (92%)	19 (76%)	2 (8%)	SNM	Retrospective
de Miguel	2010	Spain	15	3	15 (100%)	15 (100%)	NR	SNM	Prospective
Dulskas	2022	Lithunia	9	5	9 (100%)	NR	NR	Acupuncture	Prospective
Eftaiha	2017	USA	12	6	9 (75%)	6 (50%)	NR	SNM	Retrospective
Embleton	2021	UK	12	NR	NR	NR	NR	TAI	Retrospective
Emmertson	2012	Denmark	NR	NR	NR	NR	NR	N/A	Development of LARS score
Enomoto	2021	Japan	10	3	10 (100%)	10 (100%)	2 (20%)	SNM	Retrospective
Enriquez-Navascues	2019	Spain	27	10	23 (85%)	24 (88.9%)	0 (0%)	TAI V's PTNS	RCT
Harji	2021	France	137	49	137 (100%)	110 (80%)	NR	Rehab "programme"	Prospective
Itagaki	2014	Japan	25	0	23 (92%)	18 (72%)	0 (0%)	Ramosetron	Prospective
Kim	2011	Korea	70	21	70 (100%)	21 (30%)	NR	PFR	Retrospective
Koch	2009	Netherlnds	26	5	26 (100%)	NR	NR	TAI	Retrospective
Lee	2019	Korea	31	12	31 (100%)	12 (38.7%)	NR	PFR	Prospective
Liang	2016	China	61	21	61 (100%)	33 (54.1%)	NR	PFR	Prospective
Marinello	2021	Spain	46	19	46 (100%)	36 (78.3%)	NR	PTNS	RCT
Marinello	2024	Spain	46	14	100%	36 (78.2%)	5 (10.8%)	SNM	RCT
Martellucci	2018	Italy	27	10	24 (89%)	21 (77.8%)	NR	TAI	Prospective
Mc Kenna	2022	US	517	214	517 (100%)	253 (48.9%)	NR	Rehab "programme"	Retrospective
McCutchan	2017	UK	21	3	21 (100%)	6 (28.6%)	NR	TAI	Retrospective
Meurette	2023	France	32	10	-	-	-	TAI	RCT
Pieniowski	2022	Sweden	45	20	45 (100%)	45 (100%)	2 (9%)	TAI	RCT
Popeskou	2024	Switzerland	48	21	100%	35 (72.9%)	4 (8.3%)	Ondansetron	RCT
Rodrigues	2022	Brazil	22	16	22 (100%)	15 (68.2%)	NR	TAI	Prospective
Rosen	2020	Switzerland	31	NR	NR	NR	NR	NR	RCT
Rosen	2011	Switzerland	14	3	12 (86%)	12 (85.7%)	NR	TAI	Prospective
Rosen	2019	Germany and Austria	37	20	37 (100%)	37 (100%)	NR	TAI	RCT
Rubio-Perez	2020	Spain	25	11	18 (72%)	13 (52%)	NR	SNM	Retrospective
Ryoo	2021	South Korea	98	0	98 (100%)	60 (61.2%)	NR	Ramosteron	RCT
Schwander	2013	Germany	9	3	9 (100%)	9 (100%)	NR	SNM	Prospective
van der Heijden	2022	Netherlands	95	36	95 (100%)	44 (46.3%)	4 (4.2%)	PFR	RCT
Vigorita	2017	Spain	10	4	9 (90%)	NR	NR	PTNS	Prospective
Yoon	2020	South Korea	36	13	36 (100%)	36 (100%)	0 (0%)	Probiotics	RCT
Yuanyuan	2023	China	60	22	100%	-	-	PFR	RCT

AL anastomotic leak, *NR* not reported, *PTNS* percutaneous tibial nerve stimulation, *PFR* pelvic floor rehab, *SNM* sacral nerve modulation, *RCT* randomised controlled trial, *TAI* transanal irrigation

Percutaneous tibial nerve stimulation

PTNS was reported in four studies. Altomare et al. described significantly reduced LARS scores; however, QoL scores did not improve [24]. Vigorita et al. reported a 50% positive response rate with PTNS and a statistically significant increase in QoL questionnaire scores [10]. Enriquez-Navascues et al.'s RCT (TAI vs PTNS) showed a 50% reduction in both groups' LARS scores; QoL scores also improved in both [34]. Marinello et al.'s RCT, PTNS vs sham stimulation (insertion of electrode needles without current being passed through them), reported at 1 month that both groups had reductions in LARS score, but only the PTNS group had lasting improvement at 1 year, albeit this

result was not significant [7]. FI also improved at 12 months in the PTNS group, but no significant change in QoL was found [7].

One study reported results from a "pilot stepwise programme" [22]. Steps consisted of diet and medical therapy, PFR, biofeedback, TAI, cecostomy and antegrade enemas, SNM and finally colostomy. Seventy-seven per cent did not progress further than diet and medication over 12 months. Results showed a reduction in LARS score in those enrolled [22].

Discussion

LARS is an under-reported, heterogeneous condition, and differing efficacies of the various treatment strategies have hampered the development of standardised management algorithms.

Outlined here are the most common management strategies from the least to most invasive treatment options.

Nutritonal supplements were only addressed in one study which showed no evidence to endorse using the probiotic *Lactobacillus plantarum* [43]. The Newcastle-Ottawa score was also 4, highlighting a high risk of bias.

The single study regarding the use of acupuncture did show significant benefit [37]. However, these were self-reported results in nine patients at a single institution after a 10-week acupuncture treatment regime. Follow-up was at 6 months post-intervention, 14 weeks after the last acupuncture session. The question remains whether acupuncture effects can remain significant enough to actually affect LARS.

Medical therapy is guided by the predominant symptom [4, 23]. However, no benefit has been reported with the following medical treatments: topical anal phenylephrine [23], NSAIDs, steroids or probiotics [19]. No evidence was found for using anticholinergics within our literature search. Interestingly, more than a third of patients with major LARS used no medication [20]. This highlights potential flaws in LARS management by medical specialists. The most common published medical therapy used was serotonin antagonists. The rationale for their use is the hypermotility hypothesis. After sphincter-preserving surgery, the neorectum and colon may become hypermobile [38]. Serotonin, released from intestinal enterochromaffin cells, causes acetylcholine release, culminating in greater mucosal secretion, visceral sensitivity and increased gut motility [12]. Ramoestron, a serotonin antagonist, has been investigated because of greater efficacy [12].

Ramoestron significantly reduced FI, urgency and frequency with better results if started within 6 months of LAR [38]. Follow-up was only until 1 month post-initiation of treatment. Similar findings by Ryoo et al.'s [12] RCT were reported; however, this study included males only and focused on patients diagnosed with LARS at 1 month post-operatively with no long-term follow-up. It is reasonable to suggest that a LARS diagnosis at 1 month may be a colonic adjustment period. Effects seem to be most pronounced, as one may expect, on urgency and frequency; as such, if this is not a predominant symptom, efficacy may be reduced. Evidence highlights a lack of medication-based therapy, which is easily administered with minimal morbidity. Therefore, clinicians should remember its potential benefits as a starting point for LARS management.

If symptoms persist, most clinicians refer patients to a physiotherapist for assessment and PFR. There is no standard PFR regime; as such, a vast array of possible techniques and intensities is available. Evidence for the beneficial use of PFR is currently not consistent, which may be due to poor patient selection by clinicians. Results show that those with near-complete FI are unlikely to benefit from PFR [36], whilst those with lesser FI may benefit. Any beneficial results obviously require an ongoing commitment from the patient to maintain gains. Otherwise, the LARS score will decrease [40].

PFR/biofeedback seems beneficial for some; however, it is invasive, potentially uncomfortable, timely and requires commitment and continued practice. There is also a paucity of qualified physiotherapists in this field, leading to long wait times for appointments. The main benefit of PFR/biofeedback is its lack of complications [36].

If physiotherapy is unsuccessful, many recommend TAI [56]. The aim of TAI is to flush the bowel of residual matter to reduce urge, frequency or FI [23, 31, 41] and increase colonic motility [34], resulting in pseudo-continence [56]. Patients are taught how to insert a rectal tube and instil a volume of fluid into the rectum, retain the fluid for a period of time and then evacuate the contents. Significant improvements in FI [1, 11, 48], bowel movements per day [11, 42, 49], LARS score [1, 32, 34, 49, 51] and QoL [1, 11, 34] have been reported. However, all TAI studies are consistently associated with significantly high drop-out rates ranging from 19 [48] to 69% [42]. Significant adverse side effects are also experienced [48].

One study focused on the psychological acceptability of TAI [31]. Results showed mixed views with some withdrawing because of the negative psychological impact [31]. Unfortunately, findings in this article are limited by its retrospective, qualitative and unpowered methodology. TAI appears to have advantageous outcomes in those with incomplete evacuation or soiling [4] and who complete treatment and continue TAI. Those who continue with TAI remain pseudo-continent but upon cessation symptoms return, as highlighted by Martellucci et al. [50], whose impressive improvements of LARS score and QoL measures at6 months were not sustained upon TAI cessation.

It is relatively inexpensive and can be carried out at home [50], but long-term follow-up is lacking, coupled with time constraints [41] and consistent withdrawal from intervention. Risks in general appear to be minor but do include six colonic perforations globally [50], minor abdominal pain [11] and minor rectal bleeding [11]. Lastly, TAI affords "pseudo-continence" [23]; it does not treat the pathophysiology. Regardless, it does allow patient-led timing of evacuation, thereby reducing the risk of incontinent episodes [31].

SNM has been used in the management of FI since 1995 [23] and is considered in LARS after failure of other conservative measures/interventions to treat FI [18]. Rather than treating the "syndrome" associated with LAR, it focusses on treating FI in those who have undergone a LAR. Most published research suggests that LARS scores significantly improve post-SNM implantation [15, 17, 18, 33, 55], as does FI [17, 52]. However, there is some disparity within the published data regarding conversion from temporary to permanent SNM implantation in this cohort. De Miguel et al. [52] reported only 46.7% of their sample were converted to permanent SNM, whilst Schwander et al. [53] reported a 100% conversion rate to permanent SNM with significant improvement in symptoms and QoL [53]. However, only nine patients were enrolled in this study with a limited follow-up. Within the eight included studies, the largest sample was n-46 with a mean of 19 patients. SNM for FI without a preceding LAR is a common treatment modality but the limited evidence in the LAR syndrome population requires further larger scale research as recognised by acknowledged power flaws in current literature [33]. Others found a negative relationship between radiotherapy and SNM satisfaction [18]. Although results may seem promising, several studies report SNM removal due to infection [15, 17, 18, 28], mechanical failure [15], pain [18] or treatment failure [17]. In one study, 50% of devices were explanted because of pain or device failure [33]. SNM does not necessarily treat LARS, but rather FI, which can be a symptom of LARS, and such psychosocial and QoL issues must also be seperately addressed.

PTNS has been effectively used in FI [7] and constipation [34]; nonetheless, little evidence exists regarding its use in LARS [34]. The four included articles all arose from European institutes between 2017 and 2021, making this a relatively new LARS management strategy with minimal evidence. Ultimately, PTNS may help some with major LARS, although authors argue its limited clinical significance [7, 24]. As a relatively new treatment modality in the management of LARS with limited available data, further clinical trials are required.

Lastly, a single study focussed on a "stepwise programme". Harji et al. performed a pilot study consisting of progression through "steps", progressing to the next step upon failure of the current management/step. Steps consisted of diet and medical therapy, PFR, biofeedback, TAI, cecostomy and antegrade enemas, SNM and finally colostomy. Seventy-seven per cent did not progress further than diet and medication over 12 months. The breakdown of those that did progress required: PFR/biofeedback 7 (5.1%), TAI 12 (8.7%), SNM 1 (0.7%), cecostomy 1 (0.7%) and colostomy 1 (0.7%). This stepwise progression showed a reduction in LARS score [22]. This highlights the need to trial medical therapy in the symptomatic patients promptly.

No studies focussed on permanent end colostomy as the sole intervention. Rather, authors have noted it as an option when intractable FI is present and all else has failed [19] or if treatment persists for > 2 years [9].

Ultimately large-scale, long-term follow-up randomised studies are required to provide an evidence-based management strategy for those with LARS. In the rapidly progressing era of total neoadjuvant therapy and "watch and wait" management of rectal cancer, it will be interesting to follow these patients and their functional outcomes compared to LAR patients.

Conclusion

The aim of this systematic review was to highlight the current evidence in the management of LARS. The evidence presented here is generally of low quality, with a wide range of scoring systems used in retrospective studies with small sample sizes and limited follow-up. LARS is a multifaceted physical and psychological syndrome that may manifest in many signs and symptoms. Evidence suggests there is no "magic bullet"; rather, clinicians must assess symptoms and then base treatment around those. Both pre-emptive assessment and reactive symptom-based management must be addressed to ensure a positive outcome through the aforementioned treatment modalities.

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Declarations

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