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ORIGINAL ARTICLE

Optimal interventions for low anterior resection syndrome: Bayesian network meta-analysis of randomized controlled trials

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Abstract

Background The optimal intervention for managing low anterior resection syndrome (LARS) remains uncertain. This Bayesian network meta-analysis was conducted to compare and rank the effectiveness of various interventions on LARS.

Methods Randomized controlled trials (RCTs) addressing interventions for LARS were extracted from six electronic databases until September 2023. A network meta-analysis was performed using a Bayesian random-effects and consistency model. The results were presented as mean differences (MDs) with credible interval (CrI) or standardized mean differences (SMDs) with CrI.

Results A total of 11 RCTs were included. In the short term (≤ 6 months), transanal irrigation (TAI) had significant positive impacts on overall LARS symptoms (MD (95% CrI) −14.13 (−20.11, −7.83)) and the severity of bowel incontinence (SMD (95% CrI) −1.34 (−1.97, −0.71)) compared with the control group. Pelvic floor rehabilitation (PFR) also exhibited significant improvements in bowel incontinence as compared with the control group (SMD (95% CrI) −0.56 (−0.88, −0.23)). TAI was ranked highest for reducing LARS symptoms, followed by PFR, and percutaneous tibial nerve stimulation (PTNS). In the long term (> 6 months), the results indicated that TAI was most likely to rank first, followed by PTNS, and PFR; however, no significant differences were observed.

Conclusions In the short term, TAI was identified as the most effective treatment for managing LARS, followed by PFR. Both TAI and PTNS demonstrated promising potential in enhancing bowel function over the long term. Further trials are needed to confirm these findings.

Keywords Low anterior resection syndrome · Bayesian network meta-analysis · Transanal irrigation · Pelvic floor rehabilitation · Percutaneous tibial nerve stimulation

Introduction

With the advancement of surgical techniques and neoadjuvant chemoradiotherapy, sphincter-preserving surgery has become the preferred method for treating low-lying rectal cancer [1, 2]. Patients undergoing sphincter-preserving surgery exhibit

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recurrence probabilities and survival rates comparable with those who underwent abdominoperineal resection [3, 4]. In total, overall, 70% of patients with rectal cancer have opted for sphincter-preserving surgery [5, 6], and in the future, this number will increase owing to concerns over body image. However, the risk of injury to the anal sphincter muscle or nerves can lead to lower anterior resection syndrome (LARS), a frustrating and persistent gastrointestinal sequela characterized by impaired bowel function, including fecal incontinence, urgency, emptying difficulties, increased stool frequency, and so on [7]. Typically, between 41% and 69% of patients experience major LARS within the first year after surgery or the closure of a diverting stoma [8, 9]. Among these, symptoms persist from 7 years to 16 years in nearly half of the patients [10]. The unpredictable loss of control over bowel function significantly degrades quality of life (QoL), eliciting negative emotions, daily activities disruption, and social restriction [11, 12]. Despite the profound impact of LARS on QoL, standardized evidence-based protocols are currently lacking [13]. Most patients with LARS only receive supportive care, including antidiarrheal medication, dietary modification, and small-volume enemas [14], which prove ineffective for one out of five patients [14]. Recently, advanced interventions such as pelvic floor muscle exercise, biofeedback training, rectal balloon training, transanal irrigation (TAI), and neuromodulation have become popular [15]. Several randomized controlled trials (RCTs) [16–27] have assessed the efficacy of these therapies in managing LARS symptoms. However, most RCTs used usual care as the control group, with only a few directly comparing different interventions [21, 23]. One traditional meta-analysis pooled results from the original RCT studies [28], yet the most effective and optimal therapies for LARS management remain unclear. Hence, it remains unclear which therapies are the most effective and optimal for LARS management.

Network meta-analysis (NMA) represents a robust statistical method that enables the comparison of more than two interventions by integrating both direct and indirect evidence when head-to-head treatment comparisons are absent [29]. Unlike conventional meta-analysis, Bayesian NMA provides estimates of each intervention relative to all others, simultaneously ranking various interventions [29]. Consequently, we conducted the first Bayesian network meta-analysis of RCTs to compare the efficacy of different interventions for LARS, thereby offering evidence-based guidance for healthcare professionals in clinical practice.

Materials and methods

Protocol and registration

This study was performed according to the guidance of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) extension statement for network meta-analysis of healthcare interventions [30]. The PRISMA checklist is shown in Supplementary Table S1. The NMA was preregistered in PROSPERO (CRD42022371398) and did not deviate from the protocol when conducting and reporting this study.

Search strategy

We searched the PubMed, EMBASE, the Cochrane Central Register of Controlled Trials, MEDLINE, Chinese National Knowledge Infrastructure (CNKI), and Wanfang databases (a Chinese database) from inception to September 2023. Assisted by a librarian, the search strategy encompassed three blocks of terms: rectal cancer, LARS, and intervention, using a combination of Medical Subject Headings and text words (Supplementary Table S2). Additionally, we examined the reference lists of existing meta-analysis [28, 31–35] and related studies to identify original RCTs to supplement database searches.

Eligibility criteria

According to the objective of our study, we designed population, intervention, comparison, outcomes, and study (PICOS) criteria to select relevant literature.

Population (P): Patients with rectal cancer who experienced sphincter-preserving surgery, and are currently without stoma. There were no restrictions based on the symptom's duration and severity of LARS. Patients over 18 years old, presenting with any stages of preoperative rectal tumors, were included.

Interventions (I): At least one of the treatments was utilized for LARS, including pelvic floor muscle exercise, biofeedback training, rectal balloon training, transanal irrigation (TAI), sacral nerve stimulation, and percutaneous tibial nerve stimulation (PTNS). The description of each type of intervention is presented in Supplementary Table S3. There were no restrictions in terms of initiation time, frequency, and duration of interventions.

Comparisons (C): Control group applied nonintervention, usual care, sham rehabilitation therapies, or any other types of rehabilitation therapies. Usual care was defined as a control that received basic dietary advice, bulk-forming agents, loperamide, and/or was just given muscle exercise leaflets without tracking compliance.

Outcomes (O): The study evaluated one of the LARS and its subsymptoms—fecal incontinence and constipation—as well as quality of life, with available data. The measurement instruments for outcomes were required to have undergone reliability and validity testing in their development. The instruments were as follows: (1) severity of overall symptoms of LARS; LARS score; (2) severity of fecal incontinence; Cleveland Clinic Florida Fecal Incontinence (CCF-FI) scale, Vaizey incontinence score, Fecal Incontinence Severity Index (FISI), St. Mark's incontinence score, Colorectal Functional Outcome (COREFO) questionnaire, and Memorial Sloan Kettering Bowel Function Instrument (MSK-BFI); (3) overall quality of life; European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30), 36-Item Short-Form health survey (SF-36), 12-Item Short-Form health survey (SF-12), and EuroQol-Five Dimensions (EQ-5D), (4) incontinence related quality of life; Fecal Incontinence Quality of Life (FIQL) scale, (5) severity of constipation; Altomare Obstructive Defecation Syndrome scores, and Obstructed Defecation Syndrome (ODS) score, and (6) constipation- related quality of life; Constipation-Related Quality of Life scale.

Study design (S): The studies were required to be RCTs and written in either English or Chinese. Any studies without a control group were excluded. In cases of duplicate publication, we included the trial that provided the most detailed data.

Study selection and data extraction

All the searched records were imported into Endnote X9. After deleting duplications, two authors (M.Y. and Y.L.) independently screened titles and abstracts in accordance with the eligible criteria. In this step, any article with disagreement was included for full-text review. Then, the remaining studies underwent further full manuscript reviews by two independent authors. Any disagreements were resolved through consultation with a third author.

Two authors independently extracted data from each literature using an electronic standardized data extraction sheet and performed a preliminary pilot-test extraction. The formal form included variables such as study characteristics (author, year of publication, and country), characteristics of the participants in each intervention and control arm (sample size, gender, age, preoperative tumor stage, tumor size and location, neoadjuvant therapy, type of surgical approach, and postoperative duration), details of interventions (types, frequency, duration per session, length of intervention, and comparator), and outcomes (measurement tools, the statistics at each available time-point, and estimating effect sizes). When relevant statistics were incompletely reported, we estimated the mean and standard deviation on the basis of the sample size, median, range, and *P* value, in accordance with previously published methods [36, 37]. The data were cross-checked, and any differences were resolved by referring to the original article or team discussion.

Quality appraisal

The risk of bias in the included RCTs was evaluated by two independent authors using the Cochrane Collaboration's Risk of Bias 2.0 (ROB2) tool (https://training.cochrane.org/handbook/current/chapter-08). Discrepancies in study quality were resolved through team discussions.

Statistical analysis

A Bayesian network meta-analysis was conducted using R 4.1.2 (number of chains, four; number of adaptation iterations, 20,000; simulation iterations, 50,000; and a thinning interval of 1) employing a random effects model. Unlike frequentist NMA, the Bayesian method considers all of the sources of variation, reflects these changes in the combined results, provides accurate estimates for small sample sizes, and allows the calculation of prediction distributions.

Network plots were generated to explore the direct comparative relationships among rehabilitation and control groups. Each node represents a rehabilitation, and the thickness of the lines between nodes represents the number of studies. All outcomes of interest were continuous and measured on a uniform scale, reported as mean difference (MD) with their 95% credible intervals (CrI) estimated. If continuous variables were measured on different scales, effects estimated are presented as standardized mean differences (SMDs). When it comes to ordinal variables, the odds ratio (OR) was used with corresponding 95% CrI.

To assess the consistency between direct and indirect comparisons within the network, we used a node-splitting method to analyze the local inconsistency. *P*-value greater than 0.05 indicated statistically significant consistency. The deviation information criterion was compared between the consistent model and the inconsistent model to assess the global inconsistency. Lesser divergence between these values suggests greater alignment with the consistency hypothesis. Subgroup analyses were conducted according to the severity of LARS among participants to further investigate heterogeneity. Forest plots were used to display relative estimates between rehabilitation and control groups. League tables provided data on relative effects across all possible intervention comparisons. The ranking of interventions was determined using surface under the cumulative ranking curve (SUCRA) method, and the probability of an intervention being the most effective was ranked. A higher

SUCRA indicates a greater likelihood of the intervention being among the most effective. If 10 or more studies were analyzed regarding specific outcomes, Egger's test was applied to analyze publication bias in network meta-analysis.

Results

Study selection and characteristics of included studies

We identified 10,983 studies, of which 11 RCTs [16–26] met the eligibility criteria after reading full text, and they were finally included in network meta-analysis. The detailed literature selection procedure is presented in Fig. 1. A total

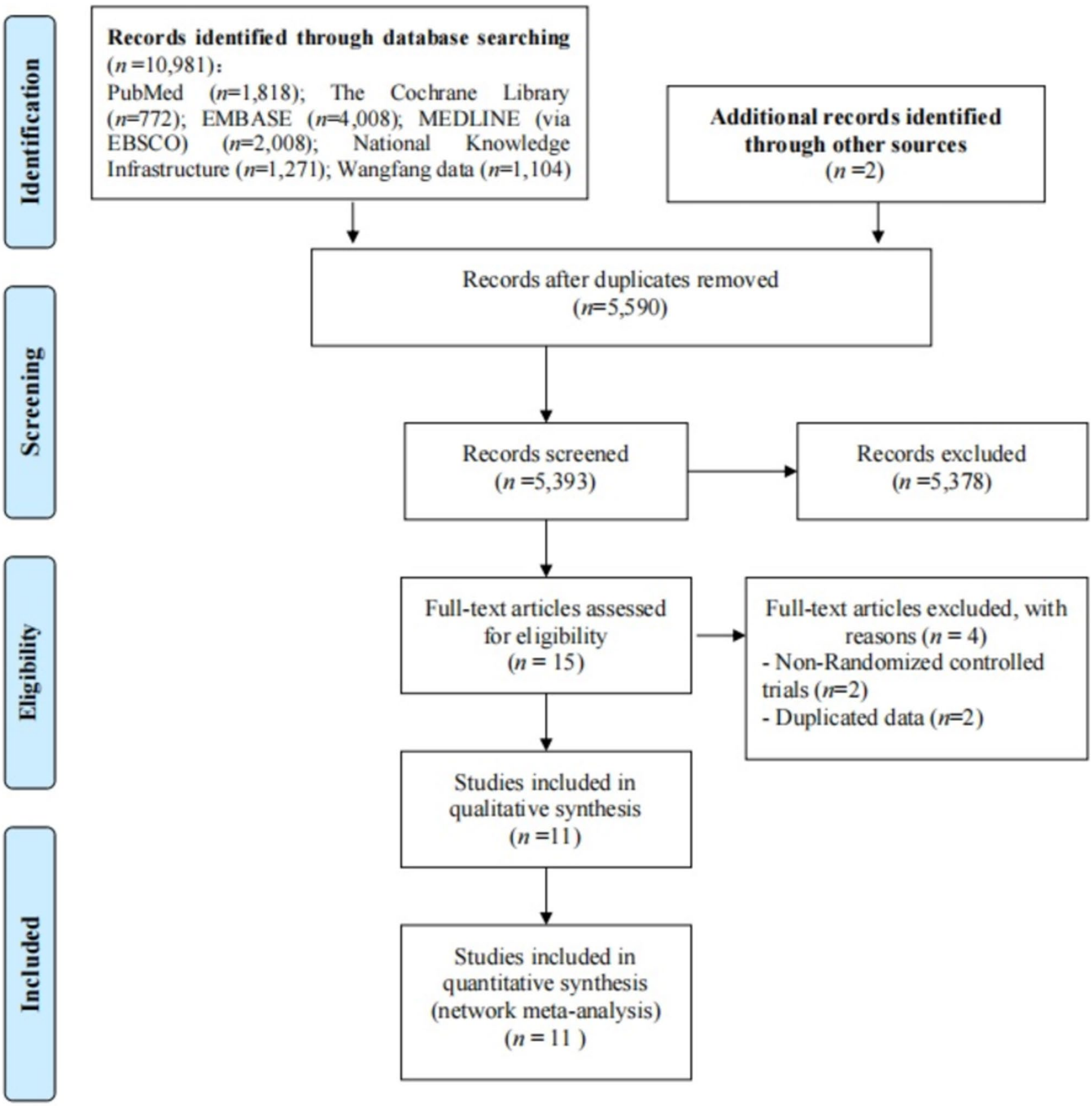


Fig. 1 PRISMA flow diagram for study selection

of 614 participants (317 in the intervention group and 297 in the control group) were included in the analysis. Characteristics of patients and studies are shown in Table 1. Further detailed information on patient characteristics, tumor stage, tumor size, type of operation, neoadjuvant therapy, duration of symptoms, and rehabilitation treatment is provided in Supplementary Table S4.

Of 11 RCTs, three kinds of interventions were applied: TAI, PTNS, and pelvic floor rehabilitation (PFR). The control groups received usual care which included basic dietary advice, bulk-forming agents, and loperamide. The duration and frequency of interventions varied, with the average length of intervention and follow-up ranging from 2 weeks to 12 months. Therefore, a 6-month postintervention cutoff was established for this study, in line with previous meta-analyses [28]. The “short term” refers to the period within 6 months after the interventions, and the “long term” extended beyond 6 months after the interventions. Owing to limited data, it was not feasible to include fecal and defecation quality of life in the NMA (Table 1). The NMA focused on the severity of LARS, fecal incontinence severity, and overall quality of life.

Quality assessment of included studies

A summary of the risk of bias for the included studies is shown in Fig. 2. Overall, the majority of studies demonstrated a low risk of bias in the randomization process ($n = 9$, 81.8%), and measurement of outcomes ($n = 11$, 100%). Approximately half of the studies had a low risk of bias owing to deviations from intended ($n = 5$, 45.4%), missing outcome data ($n = 6$, 54.5%), and selection of the reported bias ($n = 7$, 63.6%). Details of the quality of each included study are reported in Fig. S1.

Severity of overall LARS symptoms

On analysis of overall LARS symptoms at short term (≤ 6 months) , seven RCT studies were included in network meta-analysis (Fig. 3a). Compared with the control group, TAI demonstrated significant improvements in LARS scores (MD (95% CrI) −14.13 (−20.11, −7.83)). TAI improved statistically significant LARS symptoms on analysis versus PTNS (MD (95% CrI) −10.42 (−18.27, −2.56)). The main findings of the network meta-analysis are presented in Table 2. TAI ranked the best for improving LARS at short term with the highest cumulative ranking probabilities (SUCRA%: 98.5%), followed by PFR (SUCRA%: 47.8%) (Fig. 4).

In the subgroup analysis, data were not available for major LARS at short term following PFR (Fig. S2). For patients with major LARS, TAI demonstrated significant improvement effects in comparison with the control group (MD (95% CrI) −12.52 (−21.49, −3.45)) and PTNS (MD (95% CrI) −9.31 (−20.12, −1.21)). There were no significant differences between other comparisons (Table S6). The SUCRA results indicated that TAI had the highest probability (97.8%) of ranking as the most effective treatment (Table S5). Four studies reported severity of LARS in binary variable (Fig. S3). No significant differences were found between any of the comparisons (Table S7).

Regarding long-term (> 6 months) overall symptoms of LARS, three RCT studies were included in the analysis (Fig. 3b). No statistically significant associations were observed between any comparisons (Table 2). SUCRA results indicated that TAI was most likely to rank first (82.9%), followed by PTNS (54.6%), and PFR (33.9%). Similar findings were noted on the analysis of patients with major LARS in the long term compared with PTNS (Tables S5 and S6).

Severity of fecal incontinence

A total of six RCTs and three interventions were analyzed for fecal incontinence at short term (≤ 6 months). Network map is shown in Fig. 3c. Compared with control, TAI (SMD (95% CrI) −1.34 (−1.97, −0.71)) and PFR (SMD (95% CrI) −0.56 (−0.88, −0.23)) had significant positive effects on bowel incontinence. TAI also showed a superior improvement when compared with PTNS (SMD (95%CrI): −0.96 (−1.87, −0.05)) and PFR (SMD (95% CrI) −0.78 (−1.32, −0.24)) (Table 3). TAI was the most effective rehabilitation for fecal incontinence at short term (SUCRA%: 99.4%), followed by PFR (SUCRA%: 56.2%) (Fig. 4).

Seven RCTs reported long-term effect (> 6 months) on fecal incontinence (Fig. 3d). We did not find any evidence of significant differences between comparisons (Table 3). TAI had the highest probability to rank first out of all interventions (SUCRA%: 87.0%), followed by PTNS (SUCRA%: 56.1%).

Quality of life

Six RCTs assessed the short-term effect (≤ 6 months) on overall quality of life using generic measurements (Fig. 3e). In this network meta-analysis, no significant improvements were observed between comparisons (Table 4).

The network meta-analyses examining the long-term effect (> 6 months) on overall quality of life, as assessed by generic measures, included four RCT studies (Fig. 3f). Among these, one study on TAI and another report on PTNS showed that there were significant differences in the global health status of EORTC-QLQ-C30. However, the significant differences were not observed in the network meta-analysis (Table 4).

Table 1 Characteristics of included RCTs

ID	First author, year of publication	Country	Sample size (n, IG/CG)	Age (year, IG/CG)	Height of anastomosis above dentate line (cm, IG/CG)	Intervention methods	Duration of intervention	Duration of follow-up	Outcomes reported
1	Pieniowski, 2023	Swenden	22/23	Mean (SD): 65 (10)/64 (13)	No information provided	IG: TAI plus usual care CG: Usual care	2 weeks	12 months	①⑧
2	Rosen, 2019	Multicenter (Germany and Austria)	18/19	Median (range): 58.5 (52–70)/58 (42–80)	Median (range): 3 (2–5)/3.5 (2–5)	IG: TAI CG: standard of care	12 months	No additional follow-up	①②⑨
3	Meurette, 2023	Multicenter (Switzerland, Denmark, and France)	15/15	Mean (SD): 63.3 (12.9)/62.9 (10.1)	No information provided	IG: TAI plus standard of care CG: Standard of care	3 months	No additional follow-up	①②⑪⑫
4	Enriquez-Navascues, 2020	Spain	13/14	Mean (range): 68 (48–71)/68 (56–76)	Median (range): 4 (1.5–7)/4.5 (2–7)	IG: TAI CG: PTNS	Up to 6 months	No additional follow-up	①③⑧⑬
5	Cuicchi, 2020	Italy	6/6	Median (range): 62.5 (50–75)/71.5 (56–79)	Mean (SD): 4.2 (1.5)/3.2(1.0)	IG: PTNS plus Medical therapy CG: Medical therapy	15 sessions with top-up sessions	One year after the treatment	①④⑧⑭⑮
6	Van der Heijden, 2022	the Netherlands	44/51	Median (IQR): 63 (12)/63 (17)	Mean (SD): 5.7 (2.5)/5.4 (2.3)	IG: PFR CG: usual care	3 months	12 months	①②⑧
7	Marinello, 2021	Spain	23/23	Mean (SD): 62.7 (7.2)/61.7 (7.2)	No information provided	IG: PTNS CG: sham stimulation	16 sessions	12 months	①⑤⑧
8	Asnong, 2022	Belgium	50/54	Mean (SD)/median (IQR): 58.8 (12.7)/57.1 (10.9)	- Low (0–5 cm, n): 29/31 - Mid (5.1–10 cm, n): 14/16 - High (10.1–15 cm, n):7 /7	IG: PFR CG: no PFR	12 weeks	12 months	①⑥⑩
9	Cho, 2021	Korea	28/28	$\geq$65 years (n): 15/12	3.71 (1.48)/3.96 (1.46)	IG: biofeedback plus Kegel exercise CG: Kegel exercise	12 months after sphincter-preserving surgery with temporary stoma	No additional follow-up	⑦
10	Wu, 2019	China	35/36/38	Mean (SD): 54.3 (9.9)/53.5 (10.4)/51.2 (12.3)	Mean (SD): 5.0 (1.6)/5.1 (1.9)/5.1 (1.9)	IG1: biofeedback plus pelvic floor muscle training IG2: pelvic floor muscle training CG: usual care	About 16 months	9 months after stoma closure	①⑦

Table 1 (continued)

ID	First author, year of publication	Country	Sample size (n, IG/CG)	Age (year, IG/CG)	Height of anastomosis above dentate line (cm, IG/CG)	Intervention methods	Duration of intervention	Duration of follow-up	Outcomes reported
11	Lin, 2016	China	27/26	≥ 65 years (n): 16/13	(> 5 cm, n): 16/13	IG: pelvic floor muscle training CG: Usual care	9 months	No additional follow-up	②

Severity of overall symptoms of LARS: ①LARS score

Severity of fecal incontinence: ②Cleveland Clinic Florida Fecal Incontinence (CCF-FI) scale, ③Vaizey Incontinence score, ④Fecal Incontinence Severity Index (FISI), ⑤St. Mark's Incontinence score, ⑥Colorectal Functional Outcome (COREFO) questionnaire, and ⑦Memorial Sloan Kettering Bowel Function Instrument (MSK-BFI)

Overall quality of life: ⑧European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30), ⑨36-Item Short-Form health survey (SF-36), ⑩12-Item Short-Form health survey (SF-12), and ⑪EuroQol-Five Dimensions (EQ-5D);

Incontinence related quality of life: ⑫Fecal Incontinence Quality of Life (FIQL) scale

Severity of constipation: ⑬Altomare Obstructive Defecation Syndrome scores, and ⑭Obstructed Defecation Syndrome (ODS) score

Constipation-related quality of life: ⑮Constipation-Related Quality of Life scale

IG intervention group, *CG* control group, *RCT* randomized controlled trial, *SD* standard deviation, *PFR* pelvic floor rehabilitation, *TAI* transanal irrigation, *PTNS* percutaneous tibial nerve stimulation

Heterogeneity and inconsistency

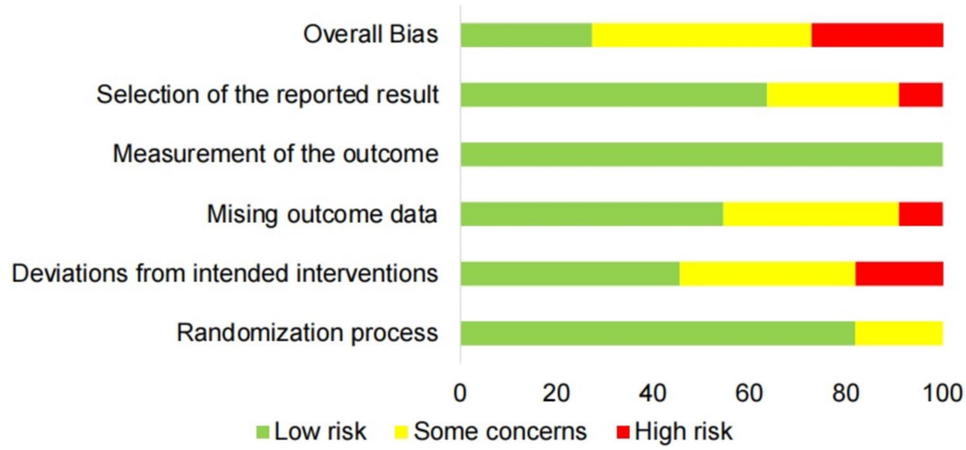
The deviance information criterion was comparable between the consistency and inconsistency models, illustrating that the consistency model was suitable for this Bayesian network meta-analysis (Table S8). The results demonstrated reliability. Node-splitting analysis revealed local inconsistency between direct and indirect comparisons in PTNS versus TAI, and TAI versus control, in terms of long-term fecal incontinence (Table S9). High *I*-squared values (40% ~ 100%) were observed in the analysis of effects on LARS score, fecal incontinence, and quality of life at long term, attributable to a lack of direct comparisons (Fig. S4 and Table S10). The trace and density plots showed good mixing (Fig. S5), validating the interpretation of our results. Convergence diagnostics plots are presented in Fig. S6.

Discussion

To our knowledge, this is the inaugural systematic review and network meta-analysis that comprehensively examines the RCTs pertaining to various interventions for LARS up to the year 2023. We synthesized data from 11 RCTs of acceptable quality and discovered that TAI was the most effective intervention for reducing the severity of LARS and fecal incontinence in the short term (≤ 6 months), with PFR as the second most effective. In the long term (> 6 months), both TAI and PTNS showed potential in improving LARS, although no statistical differences were observed.

TAI introduces water into the colon and rectum via anus, aiding in fecal evacuations. Rank analysis indicated that TAI was the most effective intervention for alleviating bowel function in the short term (≤ 6 months), compared with a control group, PTNS, and PFR. Consistent with our findings, previous studies have shown that TAI significantly reduces the frequency of daily bowel movements and lowers the LARS score within 6 months [38]. The efficacy of TAI may be attributed to its mechanical stimulation of the colon, which speeds up fecal emptying and enables patients to select the timing and location of defecation [39]. However, no significant differences were found in the severity of LARS symptoms between patients using TAI and those in other groups over the long term, potentially owing to a high dropout rate (about 30%) in the TAI group. Many patients found TAI time-consuming and lacked motivation to continue the procedure after experiencing improved bowel function. Thus, introducing TAI earlier in the LARS treatment could be beneficial, particularly for patients with severe short-term symptoms. Nevertheless, additional strategies are necessary to enhance patient compliance with this treatment, such as the development of automated and intelligent

Fig. 2 Summary of risk of bias. Green, yellow, and red area represent low, unclear, and high risk of bias, respectively



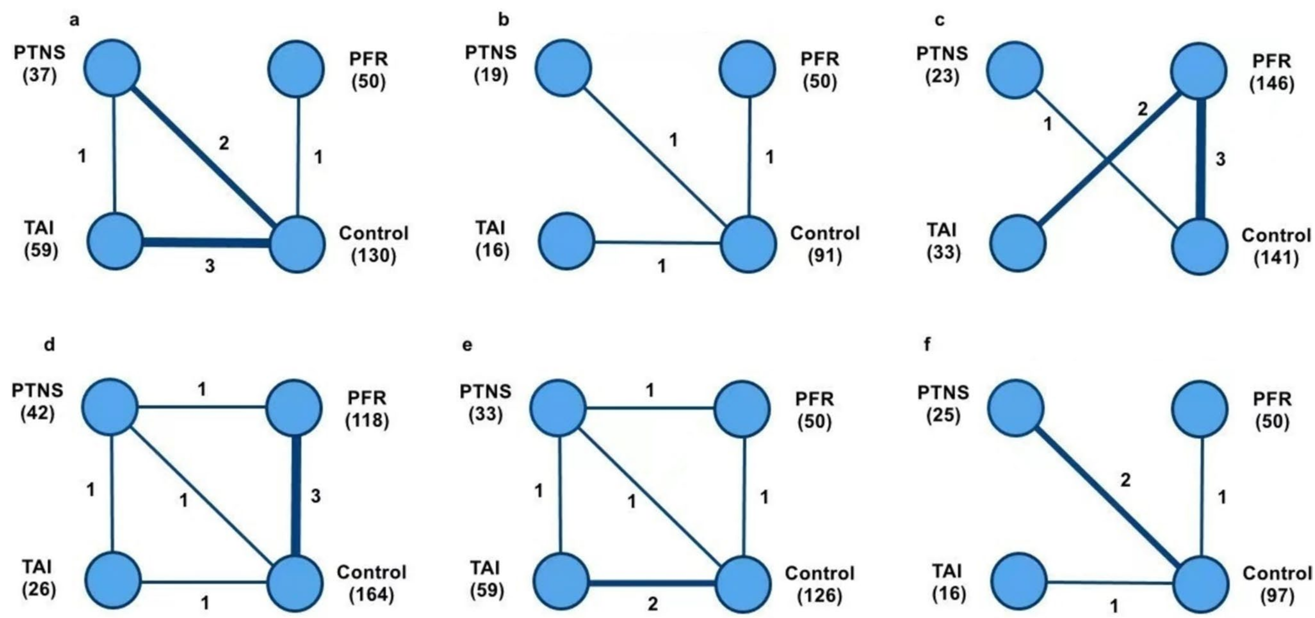


Fig. 3 Network maps of the studies examining the effect of intervention on **a** LARS score at short term, **b** LARS score at long term, **c** fecal incontinence at short term, **d** fecal incontinence at long term, **e** quality of life at short term, and **f** quality of life at long term. The thickness of lines between the interventions relates to the number of studies for that comparison. *LARS* low anterior resection score, *PFR* pelvic floor rehabilitation, *PTNS* percutaneous tibial nerve stimulation, *TAI* transanal irrigation

TAI devices or the exploration of other, more convenient methods equivalent to TAI.

PFR encompasses pelvic floor muscle training, biofeedback, and rectal balloon training. The most utilized aspects within these programs are muscle contraction and relaxation, coupled with biofeedback [40]. A systematic review that incorporated nonRCTs suggested that pelvic floor training could enhance functional outcomes following low anterior resection [40]. Consistent with previous findings, our research also indicates that PFR can effectively ameliorate the severity of fecal incontinence in patients who do not respond to standard care in the short term (≤ 6 months), with efficacy second only to TAI. The positive effects observed may be attributed to enhancements in sphincter and pelvic floor muscle strength, rectal sensation, and anorectal coordination [41]. Similar to TAI, the substantial benefits of PFR on fecal incontinence do not persist in the long term. This may be due to diminishing patient compliance as the treatment duration extends. Further investigation into the long-term effects of PFR and the establishment of sustained exercise routines for patients with low anterior resection syndrome (LARS) is essential.

PTNS is a novel and minimally invasive form of percutaneous neuromodulation targeting the tibial nerve (L4–S3). This stimulation can enhance rectal sensitivity, colonic motility, sphincter function, and the perception of afferent

Table 2 Relative effectiveness on low anterior resection syndrome score

Short-term effect (≤ 6 months)	TAI			
	−10.42 (−18.27, −2.56)	PTNS		
	−10.28 (−21.25, 1.22)	0.17 (−11.29, 12.08)	PFR	
	−14.13 (−20.11, −7.83)	−3.71 (−10.48, 3.47)	−3.91 (−13.40, 5.69)	Control
Long-term effect (> 6 months)	TAI			
	−6.35 (−26.73, 14.34)	PTNS		
	−9.24 (−29.12, 10.74)	−2.88 (−21.10, 15.13)	PFR	
	−9.51 (−25.24, 6.40)	−3.20 (−16.43, 9.94)	−0.30 (−12.60, 12.01)	Control

Significant results are presented in bold

An estimate less than 0 indicates that treatment reported in column is more effective than corresponding treatment reported in row (mean difference (95% CrI))

CrI credible interval, *PFR* pelvic floor rehabilitation, *TAI* transanal irrigation, *PTNS* percutaneous tibial nerve stimulation

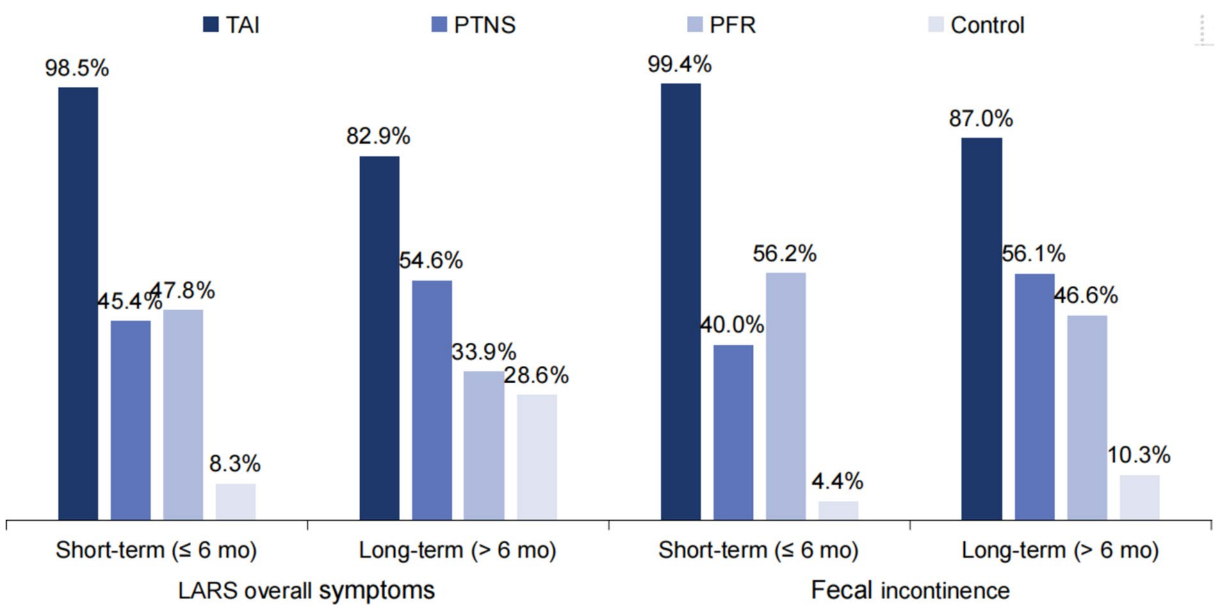


Fig. 4 Ranking of the effect of interventions on LARS score and fecal incontinence. The number in bracket is the percentage of surface under the cumulative ranking curves (SCURA). The higher the SUCRA percentage, the more likely that therapy is one of the most effective

information [42]. However, our study's evaluation did not reveal a significant improvement in the targeted outcomes between any comparisons, aligning with results from conventional head-to-head meta-analyses. Previous literature suggests that PTNS is more effective in the early stages of LARS [28]; however, in our analysis, all LARS patients treated with PTNS were enrolled at least 1 year post-rectal surgery, potentially explaining the minimal improvement in intestinal symptoms observed. Early application of PTNS following rectal reconstruction may provide greater benefits. Additionally, despite no significant differences, the results of SUCRA suggested that PTNS might be superior to PFR in terms of long-term effects, improving from third to second rank. These findings indicate that PTNS holds promise for long-term management in the follow-up period, and further investigation into the effects of its early implementation and multiple courses for LARS patients is warranted.

Patients with LARS consistently report impaired quality of life, particularly in physical and social functions [11]. No interventions have been found to positively affect the overall

Table 3 Relative effectiveness on fecal incontinence

Short-term effect (≤ 6 months)	TAI			
	−0.96 (−1.87, −0.05)	PTNS		
	−0.78 (−1.32, −0.24)	0.18 (−0.55, 0.91)	PFR	
	−1.34 (−1.97, −0.71)	−0.38 (−1.03, 0.27)	−0.56 (−0.88, −0.23)	Control
Long-term effect (> 6 months)	TAI			
	−0.41 (−1.37, 0.54)	PTNS		
	−0.55 (−1.62, 0.51)	−0.14 (−1.05, 0.77)	PFR	
	−0.87 (−1.79, 0.05)	−0.46 (−1.26, 0.35)	−0.32 (−0.88, 0.25)	Control

Significant results are presented in bold

An estimate less than 0 indicates that treatment reported in column is more effective than corresponding treatment reported in row (standardized mean difference (95% CrI))

CrI credible interval, *PFR* pelvic floor rehabilitation, *TAI* transanal irrigation, *PTNS* percutaneous tibial nerve stimulation

Table 4 Relative effectiveness on quality of life

Short-term effect (≤ 6 months)	TAI			
	0.16 (−0.40, 0.73)	PTNS		
	−0.02 (−0.55, 0.50)	−0.19 (−0.85, 0.48)	PFR	
	0.07 (−0.29, 0.43)	−0.09 (−0.63, 0.45)	0.09 (−0.29, 0.48)	Control
Long-term effect (> 6 months)	TAI			
	−0.45 (−3.88, 2.97)	PTNS		
	0.48 (−3.35, 4.32)	0.94 (−2.45, 4.32)	PFR	
	0.40 (−2.33, 3.14)	0.86 (−1.21, 2.92)	−0.08 (−2.77, 2.60)	Control

Significant results are presented in bold

An estimate more than 0 indicates that treatment reported in column is more effective than corresponding treatment reported in row (standardized mean difference (95% CrI))

CrI credible interval, *PFR* pelvic floor rehabilitation, *TAI* transanal irrigation, *PTNS* percutaneous tibial nerve stimulation

quality of life, in either the short term or the long term. This may be attributed to the multifaceted impact of LARS on various dimensions of QoL, including emotional, physical, role, and sexual function. These aspects seem resistant to change through a single procedure. For future studies, it is recommended to use symptom-specific quality-of-life scales to evaluate improvements in patients' quality of life.

In recent years, sacral nerve stimulation was considered as an effective therapy by permanently implanting a subcutaneous low-current releaser [43]. However, high-quality RCTs are limited. Subsequent to the submission of our study, only one RCT on sacral nerve stimulation was published in 2024 [27]. The Sacral Neuromodulation in Patients with Low Anterior Resection Syndrome (SANLARS) trial demonstrated that patients with severe LARS who underwent sacral neuromodulation with a 3-week test phase followed by a 4-week formal trial exhibited significant improvements in bowel function and QoL [27]. Future research should compare sacral nerve stimulation with other interventions. Additionally, there is a scarcity of high-quality research on the combined effects of different interventions, such as PTNS with TAI and PTNS with PFR. Further RCTs focusing on sacral nerve stimulation and these combined interventions are needed.

To our knowledge, this is the first comprehensive network meta-analysis assessing the efficacy of interventions for patients with LARS, including only RCTs to ensure rigorous study design and high-quality evidence. The findings from this analysis could potentially guide healthcare providers in making optimal decisions for LARS management. However, several limitations of this meta-analysis must be acknowledged. Firstly, fewer than 10 RCTs were assessed for all outcomes, precluding an evaluation of publication bias, which necessitates a cautious interpretation of the results. Secondly, our search for relevant nonpharmacological interventions was restricted to English and Chinese, potentially overlooking pertinent studies published in other languages, and excluded grey literature. Thirdly, limitations inherent in the original studies were identified, such as the use of the LARS Score, which has poor sensitivity to change in trials targeting LARS treatment and the limited use of the LARS-specific quality of life scale.

Conclusions

On the basis of the acceptable quality of RCTs, this initial network meta-analysis assessed the effectiveness of various interventions for LARS management. In the short term, TAI emerged as the most effective therapy to alleviate LARS symptoms, with PFR as the next effective treatment. Both TAI and PTNS showed promising potential to enhance bowel function over the long term, though no significant differences were noted. Future large-scale RCTs are necessary to corroborate these findings.

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Declarations

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Ethical approval All analyses were based on previous published studies, thus no ethical approval are required.

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