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REVIEW

Consensus of risk factors and effectiveness of current management of low anterior resection syndrome (LARS) in rectal cancer with preservation of the anal sphincter: state of the art

Consenso de factores de riesgo y eficacia del manejo actual del síndrome de resección anterior baja (LARS) en cáncer de recto con preservación del esfínter anal: estado del arte

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ABSTRACT

Introduction: low Anterior Resection Syndrome (LARS) is the main functional sequela after sphincter-preserving rectal surgery. It affects 40–45 % of patients at ≥12 months and impairs quality of life. This work synthesizes risk factors and therapeutic effectiveness to guide personalized decision-making.
Method: we conducted a PRISMA systematic review (2017–2024) of MEDLINE, EMBASE, and Cochrane with dual screening and duplicate data extraction. We included adults who underwent low anterior resection with validated measures of LARS and/or quality of life. Risk of bias was assessed (RoB 2, ROBINS-I/NOS, AMSTAR-2) and certainty was graded with GRADE. A qualitative synthesis and vote counting were performed.
Development: nineteen studies were included: 2 trials/follow-ups, 7 observational studies, 6 systematic reviews/meta-analyses, and 4 guidelines/narratives. Neoadjuvant radiotherapy was associated with higher LARS (OR ≈3) and worse quality of life. Other factors included ultralow anastomosis, total mesorectal excision, and anastomotic leak. Transanal irrigation (TAI) reduced early stool frequency and tended toward a lower LARS score at 12 months in a randomized controlled trial; in therapeutic cohorts it reduced LARS and incontinence. Sacral neuromodulation showed improvement in refractory cases, with low-moderate certainty of evidence. Pelvic floor rehabilitation and pharmacotherapy provided symptomatic relief with limited support. Certainty was moderate for the impact of radiotherapy and the usefulness of TAI, and low for the remainder.
Conclusions: LARS was common and modifiable. We recommended preoperative counseling on functional risk, surgical prevention, early TAI in high-risk patients, a stepped, phenotype-based approach with psychological support, and neuromodulation for refractory cases, with longitudinal follow-up to tailor treatment using more patient-relevant metrics.

Keywords: Rectal Neoplasms; LARS; Anal Sphincter.

RESUMEN

Introducción: el síndrome de resección anterior baja (LARS) es la principal secuela funcional tras la cirugía

rectal con preservación del esfínter. Afecta al 40–45 % a ≥12 meses y deteriora la calidad de vida. Este trabajo sintetiza los factores de riesgo y la efectividad terapéutica para orientar la toma de decisiones personalizadas.
Método: realizamos una revisión sistemática PRISMA (2017–2024) de MEDLINE, EMBASE y Cochrane, con cribado doble y extracción de datos por duplicado. Incluimos adultos sometidos a resección anterior baja con medidas validadas de LARS y/o calidad de vida. Evaluamos el riesgo de sesgo (RoB 2, ROBINS-I/NOS, AMSTAR-2) y la certeza con GRADE. Efectuamos una síntesis cualitativa y un recuento de votos.
Resultados: se incluyeron 19 estudios: 2 ensayos/seguimientos, 7 observacionales, 6 revisiones sistemáticas/metanálisis y 4 guías/narrativas. La radioterapia neoadyuvante se asoció con mayor LARS (OR ≈3) y peor calidad de vida. Otros factores incluyeron anastomosis ultrabaja, escisión total del mesorrecto y fuga anastomótica. La irrigación transanal (TAI) redujo tempranamente la frecuencia deposicional y tendió a una menor puntuación LARS a los 12 meses en un ensayo aleatorizado; en cohortes terapéuticas disminuyó LARS y la incontinencia. La neuromodulación sacra mostró mejoría en casos refractarios, con certeza de evidencia baja a moderada. La rehabilitación del suelo pélvico y la farmacoterapia aportaron alivio sintomático con soporte limitado. La certeza fue moderada para el impacto de la radioterapia y la utilidad de la TAI, y baja para el resto.
Conclusiones: LARS fue frecuente y modificable. Recomendamos la consejería preoperatoria sobre riesgo funcional, la prevención quirúrgica, la TAI temprana en pacientes de alto riesgo, un abordaje escalonado y fenotípico con apoyo psicológico, y la neuromodulación en refractarios, con seguimiento longitudinal para ajustar el tratamiento utilizando métricas más relevantes para el paciente.

Palabras clave: Neoplasia Rectal; LARS; Esfínter Anal.

INTRODUCTION

Colorectal cancer is one of the most common tumors worldwide and ranks third in incidence, with approximately 1,8 million cases in 2018, a trend that continues to rise.[1] In rectal cancer, the evolution of oncological strategies, particularly total mesorectal excision (TME), the optimization of radiotherapy, and the refinement of anastomoses with stapling devices, has promoted sphincter-preserving surgeries, improving oncological outcomes and survival.[2] Although the prevalence of clinically significant LARS is estimated at around 41 %, its true magnitude is difficult to determine due to the heterogeneity in the reporting of symptoms.[3]

The surgical anatomy and tumor progression in rectal cancer are best explained by the following figure, in which the left side shows the total mesorectal excision (TME). The figure shows the mesorectal fascia, the tumor within the mesorectum, the levator ani muscle, and the external and internal sphincters. The red circle delimits the TME cylinder, the target of clear dissection in the avascular plane to optimize margins. On the right side is the TNM staging, where in T: we can see examples of mural and extramural involvement, T1 limited to the submucosa; T2 invades the muscularis propria; T3 extends beyond the muscularis propria into the mesorectum; T4 infiltrates neighboring organs (e.g., prostate, seminal vesicles, bladder, uterus) (figure 1).

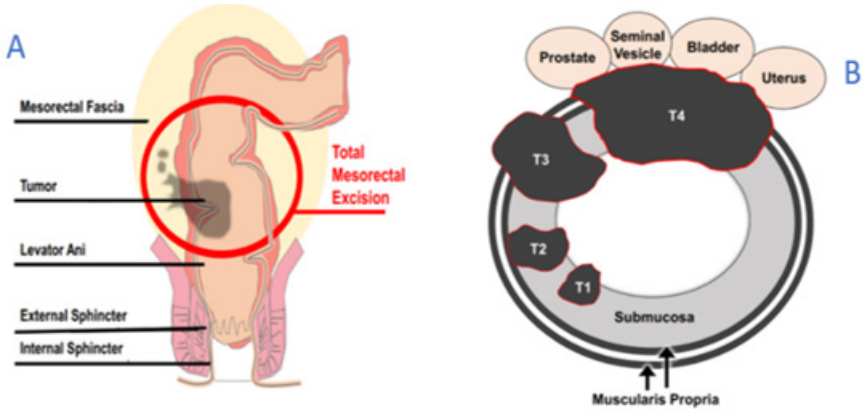

Figure 1. A/B Surgical anatomy and tumor progression in rectal-anal cancer

The purpose of the figure summarizes why the degree of extension determines indications for neoadjuvant therapy and surgical planning. The dissection pathway shown in figure 1A minimizes damage to the sphincter complex, in line with our preservation protocol. As shown in figure 1B, T4 involvement of pelvic structures justifies the extended resections described in our series.

In this new scenario, low anterior resection syndrome (LARS) emerges as the main functional sequela after sphincter-preserving resections. LARS is characterized by urgency, increased frequency, clustered bowel movements, incontinence, and/or difficulty with bowel movements, with a substantial and often devastating impact on health-related quality of life.[4,5]

As shown in figure 2, we can see the various types of coloanal and colo-rectal anastomosis with sphincter preservation: in image A on the left, after rectal resection and closure of the rectal stump, the anvil is approximated and the circular stapler is inserted transanally through the pelvic floor to align the ends. Meanwhile, in image B on the right, with the colonic reservoir already constructed, the anvil is attached to the stapler shaft and fired to complete the anastomosis. The diagram highlights the functional objective of the pouch (greater capacity/compliance) in low anastomoses (figure 2).

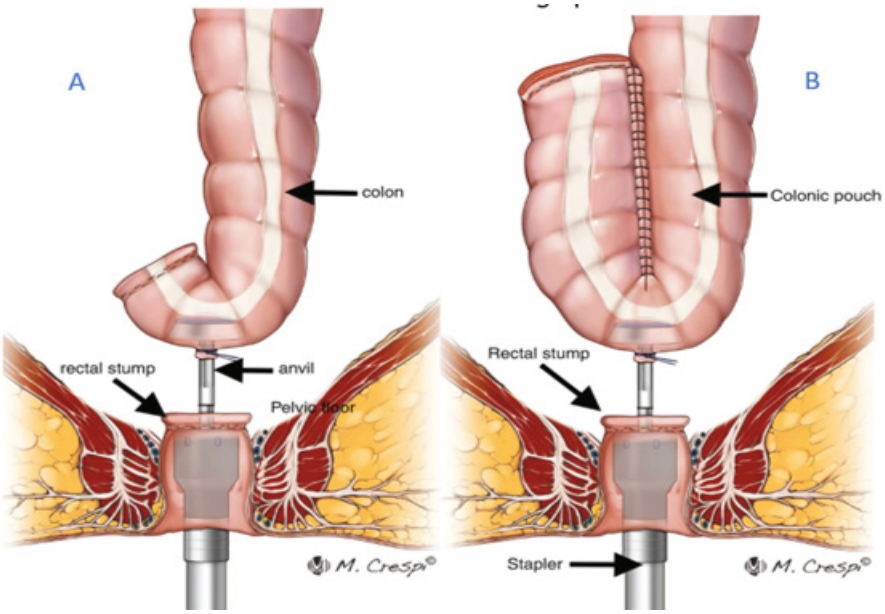

Figure 2. A/B Colorectal/coloanal anastomosis with colonic reservoir ("J-pouch") using a double stapling technique

In summary, as shown in figure 2A, it details the safe alignment of the anvil and rectal stump that we routinely use, while in figure 2B, we prioritize a colonic pouch when the anastomosis is ≤5 cm from the anal margin.

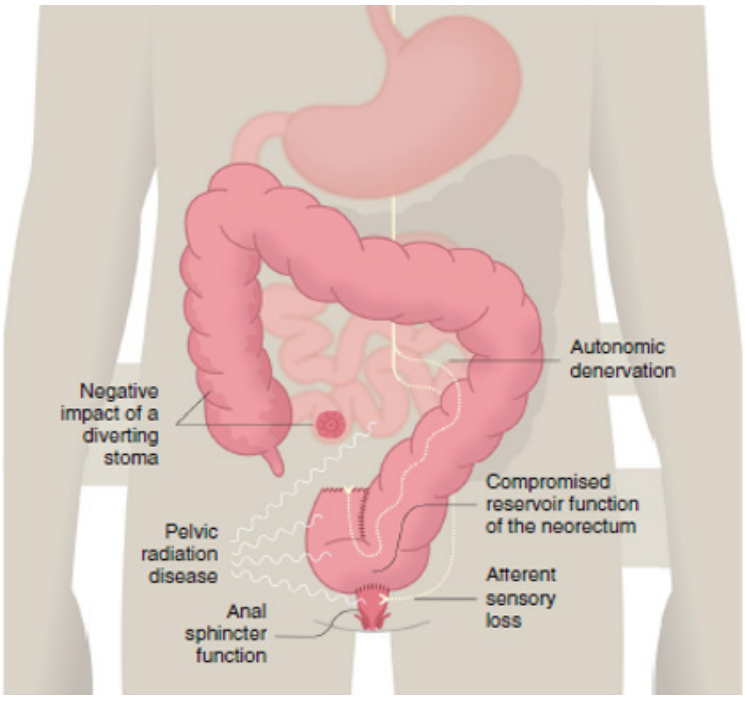

Figure 3. Pathophysiological mechanisms of low anterior resection syndrome (LARS)

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Its pathophysiology is multifactorial: autonomic denervation due to TME and/or radiotherapy alters motility and accommodation of the neorectum; reduced capacity and compliance of the colonic reservoir increases urgency and frequency; afferent sensory loss and alteration of the rectoanal reflex compromise gas/feces discrimination; and sphincter injury (surgical/neuropathic) and pelvic radiation disease decrease continence. [6] Stoma closure can add disuse and dysbiosis, and microbiome alteration is gaining prominence as a modulator of LARS phenotypes (figure 3).

Although the LARS Score standardizes measurement and improves comparability between studies, it does not comprehensively capture psychosocial domains (anxiety, embarrassment, social avoidance) or certain phenotypes of bowel dysfunction. Consequently, it may underestimate the overall impact in some patients; therefore, its interpretation should be supplemented with quality of life measures (e.g., EORTC QLQ-CR29/FIQL) and specific symptoms when available (figure 4).[7,8]

1.- ¿Existen momentos en los que no puede controlar los gases por el ano?	Puntos
No, nunca	0
Sí, < 1 vez por semana	4
Sí, > 1 vez por semana	7
2.- ¿Ha presentado alguna vez pérdida accidental de deposiciones líquidas?	
No, nunca	0
Sí, < 1 vez por semana	3
Sí, > 1 vez por semana	3
3.- ¿Con qué frecuencia va al baño a defecar?	
> 7 veces por día (24 horas)	4
4-7 veces por día (24 horas)	2
1-3 veces por día (24 horas)	0
< 1 vez por día (24 horas)	5
4.- ¿Ha tenido que volver al baño a defecar antes de trascurrida una hora de la última deposición?	
No, nunca	0
Sí, < 1 vez por semana	4
Sí, > 1 vez por semana	7
5.- ¿Alguna vez ha sentido una necesidad tan urgente de defecar que debe apurarse para llegar al baño?	
No, nunca	0
Sí, < 1 vez por semana	11
Sí, > 1 vez por semana	16

SIN LARS	LARS MENOR	LARS MAYOR
0-20 PUNTOS	21-29 PUNTOS	30-42 PUNTOS

Figure 4. LARS Score

Research question

What are the main risk factors associated with the development of low anterior resection syndrome (LARS) and how effective are current treatments for its management in patients with rectal cancer who have undergone sphincter-preserving resection?

Justification for the study

Despite its frequency, the management of LARS remains challenging due to a lack of clinical consensus. Key gaps persist that limit truly patient-centered care: first, the scarcity of direct comparative studies between therapeutic modalities, pelvic floor rehabilitation, neuromodulation, and pharmacotherapy makes it difficult to establish evidence-based treatment algorithms; second, the effect of radiotherapy (type, dose, and volume) on the severity and persistence of LARS is not clearly delineated; third, the psychological impact of LARS on quality of life remains insufficiently characterized compared to the predominantly somatic emphasis; fourth, the natural history of the syndrome and its evolution over time after surgery lack robust longitudinal studies that explain why some patients improve and others do not; and fifth, sex/gender differences in prevalence, phenotype, and therapeutic response are poorly documented. At the same time, uncertainty persists about the

risk factors that predispose patients to LARS, limiting preoperative stratification and individualized counseling. These gaps justify a critical and updated synthesis that unifies criteria, prioritizes patient-centered outcomes, and guides personalized therapeutic decisions.

Study objectives, in response to the identified gaps.

- Compare the effectiveness of the main therapeutic strategies for LARS (pelvic floor rehabilitation, neuromodulation, and pharmacotherapy), including safety and clinical applicability.
- Quantify the influence of radiotherapy (neoadjuvant/adjuvant; dosimetric parameters) on the severity and persistence of LARS.
- Characterize the psychological impact of LARS on quality of life and its relationship with dysfunction phenotypes, complementing the LARS scale with psychosocial measures.
- Describe the temporal evolution of LARS in the postoperative period and the factors associated with improvement or persistence of symptoms in longitudinal studies.
- Explore differences by sex/gender in prevalence, clinical presentation, and response to interventions.
- Identify and synthesize preoperative, intraoperative, and adjuvant risk factors associated with the development of LARS to improve stratification and patient counseling.

METHOD

Design and registration

A systematic review was conducted following the PRISMA 2020 recommendations. The protocol was developed a priori, defining the question, eligibility criteria, outcomes, extraction plan, and synthesis.

Research question (PICO/PECO)

Population: Adults with rectal cancer undergoing low anterior resection (LAR) with sphincter preservation.

Exposure/Intervention:

For risk factors: preoperative variables (e.g., neoadjuvant radiotherapy, comorbidities), intraoperative variables (e.g., technique, type of anastomosis, extent of resection), and postoperative variables (e.g., time since surgery, adjuvant radiotherapy).

For treatments: pharmacotherapy (e.g., loperamide, other antidiarrheals, bile acid binders, 5-HT3 antagonists), pelvic floor rehabilitation (training, biofeedback), neuromodulation (sacral nerve stimulation, PTNS), transanal irrigation, and other nonpharmacological interventions.

Comparators: no exposure, placebo/standard care, or other active interventions.

Outcomes

- Primary: incidence and severity of LARS (e.g., categorized LARS Score), and health-related quality of life.
- Secondary: frequency/urgency, cluster defecation, incontinence, difficulty with bowel movements, psychological impact (anxiety/depression/distress), persistence/temporary improvement (6–12 months; >12 months), effects of radiotherapy (neo/adjuvant; dose/volume), differences by sex/gender, and adverse events of interventions.

Eligibility criteria

Study types: randomized and non-randomized clinical trials, cohorts, case-controls, prospective series; systematic reviews and meta-analyses (to contextualize evidence and search). Case reports, editorials, letters, and narrative reviews were excluded from quantitative synthesis.

Population: adults (≥18 years) with RAB and sphincter preservation. Predominantly pediatric studies or studies with abdominoperineal resections without RAB subanalysis were excluded.

Outcomes and definition of LARS: studies reporting LARS using the LARS Score or another validated tool were included. Studies with unvalidated definitions were considered only if they provided comparable data; in such cases, sensitivity analyses were planned.

Period: January 1, 2017, to December 31, 2024.

Language: English and Spanish.

Sample size (a priori threshold): to minimize unstable estimates, the following were included:

- Trials: ≥20 participants or total n ≥40.
- Observational: total n ≥50.
- Planned exception: (e.g., neuromodulation), studies with n≥20 were accepted with sensitivity analysis.
- Methodological quality (inclusion criterion):

- Trials: RoB 2 ≠ "high risk" in critical domains.
- Observational studies: ROBINS-I without "critical risk" (low/moderate/serious accepted with sensitivity). Alternatively, Newcastle-Ottawa Scale (NOS) ≥6/9.
- Systematic reviews: AMSTAR-2 ≠ "critically low"

Sources of information and search strategy

MEDLINE/PubMed, EMBASE (Elsevier), and Cochrane Library (Cochrane Reviews and CENTRAL) were consulted for the period 2017–2024. Complementary searches included references from key studies and chain citations.

General search structure (reproducible examples):

- PubMed (MeSH + text) ("Rectal Neoplasms"[Mesh] OR rectal cancer OR "rectal neoplasm*") AND ("Low Anterior Resection" OR LARS OR "anterior resection syndrome") AND (risk OR "risk factor*" OR radiotherap* OR chemoradiotherap* OR neuromodulation OR "sacral nerve stimulation" OR PTNS OR "pelvic floor" OR biofeedback OR "transanal irrigation" OR loperamide OR antidiarrheal*) Filters: 2017/01/01–2024/12/31; Humans; Adult:19+ years; English/Spanish
- EMBASE (Emtree + text) ('rectum cancer'/exp OR 'rectal cancer') AND ('low anterior resection' OR LARS OR 'anterior resection syndrome') AND (risk: ab, ti OR 'risk factor*': ab,ti OR radiotherap*:ab,ti OR neuromodulation: ab,ti OR 'sacral nerve stimulation': ab,ti OR 'posterior tibial nerve stimulation': ab,ti OR 'pelvic floor': ab,ti OR biofeedback: ab,ti OR 'transanal irrigation': ab,ti OR loperamide: ab,ti) AND [2017–2024]/py.
- Cochrane: equivalent terms for Reviews and Central.

Reference management and duplicate removal

Records were exported and deduplicated automatically and by manual review. Screening and collaboration were performed in Rayyan (QCRI).

Study selection process

The process followed a three-stage PRISMA flow:

- Title and abstract screening: two independent reviewers (Reviewer A and Reviewer B) assessed eligibility in Rayyan.
- Full-text review: the same reviewers applied the inclusion/exclusion criteria using a standardized checklist.
- Resolution of discrepancies: by consensus; a third reviewer (Reviewer C) acted as adjudicator.

Cohen's kappa index was calculated in a pilot sample (10–15 %) for calibration prior to mass screening. Reasons for full-text exclusion were documented and reported in the PRISMA diagram.

Data extraction

A standardized template (spreadsheet) was designed and piloted by both reviewers. Data extraction was performed in duplicate.

Minimum fields

Identification: author, year, country, source.

Design and quality: study type, sample size, risk of bias tool, and rating.

Population: age/sex, tumor stage, use and parameters of radiotherapy (neo/adjuvant, dose/volume), presence/duration of ileostomy, time since surgery.

Intervention/exposure: surgical technique (e.g., ETM, type of anastomosis), therapeutic interventions (detailed pharmacological/non-pharmacological), intensity/duration.

Comparator: specification.

Outcomes

LARS (continuous score and categories), QoL (EORTC QLQ-CR29/FIQL), psychological domains, adverse events, time course (6–12 months, >12 months).

Estimated effects: adjusted OR/RR/HR (preferred); means/SD or proportions with confidence intervals; adjustment methods.

When only medians and ranges/IQR were reported, transformation to means/SD was planned using validated methods (Hozo/Wan/Luo).

Assessment of methodological quality and risk of bias

Trials: RoB 2 (domains and overall judgment).

Observational: ROBINS-I (confounding, selection, classification, deviations, missing data, outcome measurement, selective reporting). As a summary alternative, NOS with threshold ≥6/9.

Systematic reviews: AMSTAR-2.

Assessments were performed independently by two reviewers; discrepancies were resolved by consensus/third reviewer. Judgments reported sensitivity analyses (excluding high/serious/critically low) and interpretation of certainty.

Data synthesis and statistical analysis

Given the expected clinical/methodological heterogeneity:

Meta-analysis was performed when ≥3 studies with clinical and statistical comparability reported the same outcome.

Model: random effects (DerSimonian-Laird or REML).

Effect measures:

Continuous: mean Difference (MD) or Standardized Mean Difference (SMD);

Dichotomous: RR (preferred) or OR with 95 % CI.

Heterogeneity: I^2 and Cochran's Q; prespecified interpretive thresholds.

Publication bias: funnel plot and Egger's test (if ≥10 studies).

Software: R (meta/metafor packages) and RevMan for basic synthesis.

Radiotherapy: no RT vs. neoadjuvant RT vs. adjuvant RT; high vs. low dose/volume.

Time since surgery: 6–12 months vs. >12 months.

Sex/gender.

Surgical technique: ultra-low/coloanal anastomosis vs. more proximal; complete vs. partial ETM; reservoir (J-pouch coloplasty) vs. recto-rectal.

Therapeutic intervention: pharmacological vs. non-pharmacological vs. combined; transanal irrigation and neuromodulation as specific subgroups.

Methodological quality: exclusion of studies with high/serious risk of bias; exclusion of small samples (< threshold).

Management of multiplicity and hierarchy of outcomes

LARS Score (categories and continuum) and QoL were prioritized as primary outcomes. Psychological domains (anxiety/distress) were analyzed as prioritized secondary outcomes in order to reflect the overall impact of LARS.

Assessment of the certainty of the evidence

GRADE was applied per outcome to classify certainty (high, moderate, low, very low), considering risk of bias, inconsistencies, indirectness, imprecision, and publication bias.

Ethical considerations

Ethical approval was not required as this was an analysis of published data. Good practices of transparency and reproducibility were adhered to (a priori protocol, comprehensive search strategies, extraction templates available as supplementary material).

Presentation of results

PRISMA diagram with numbers in each phase and reasons for exclusion in full text.

Evidence matrix: title, author/year, country, design, population, intervention/exposure, outcomes, key results, quality/risk of bias, and conclusions (template aligned with the one already started in the manuscript).

Synthesis by domains: (1) pre/intra/postoperative risk factors; (2) therapeutic efficacy (pharmacological, rehabilitation, neuromodulation, transanal irrigation, and combined strategies); (3) impact of radiotherapy; (4) psychological impact; (5) temporal evolution; (6) differences by sex/gender.

RESULTS AND DISCUSSION

Study selection

The search (Embase, Cochrane, PubMed, and other sources; 2017–2024) identified 34 records. After removing 5 duplicates, 29 titles/abstracts were screened; 10 were excluded at this stage. Nineteen full-text articles were evaluated, with no additional exclusions, resulting in 19 studies being included in the synthesis. This is described in the Prisma diagram (figure 5).

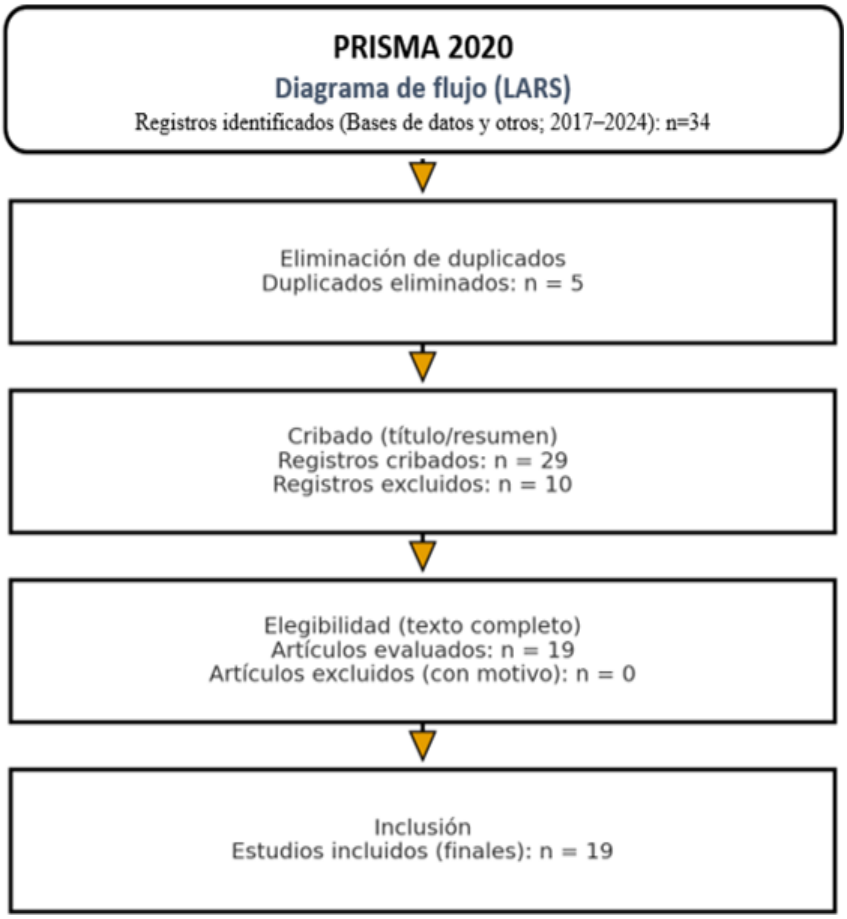

Figure 5. PRISMA diagram

Profile of the evidence included (n = 19)

- Randomized clinical trial (RCT) and follow-up: 2/19 (10,5 %).
- Prospective observational (including multicenter/longitudinal): 4/19 (21,1 %).
- Retrospective observational studies: 3/19 (15,8 %).
- Non-comparative series/observational: 1/19 (5,3 %).
- Systematic reviews and/or meta-analyses: 6/19 (31,6 %).
- Guidelines/evidence review: 2/19 (10,5 %).
- Narrative review: 1/19 (5,3 %).

Temporal distribution (n = 19): 2017 (2), 2019 (2), 2020 (2), 2021 (4), 2022 (1), 2023 (5), 2024 (3).

Methodological quality and risk of bias

Main RCT (prophylactic transanal irrigation): low-moderate risk of bias (adequate randomization; limited sample size; published follow-up).

Prospective/retrospective cohorts: moderate to serious risk due to residual confounding, selection/measurement bias, and loss to follow-up.

Systematic reviews/meta-analyses: variable quality due to clinical/methodological heterogeneity and, in some cases, unclear protocols.

Overall, the certainty is moderate for: (I) radiotherapy as a factor that increases the risk/severity of LARS and (II) transanal irrigation (TAI) to reduce/prevent symptoms; and low for neuromodulation, pelvic floor rehabilitation, and pharmacotherapy, due to a lack of RCTs and small sample sizes.

Analytical synthesis by question

Risk factors for LARS

- Neoadjuvant/adjuvant radiotherapy: consistent association with increased risk/severity of LARS and persistent stoma in 3/3 primary studies included (prospective/observational cohorts and multicenter study with anorectal function). Conclusion: moderate evidence.
- Surgical and patient factors (low anastomosis, anastomotic leakage, sex, comorbidities):

heterogeneous signal in retrospective and prospective non-randomized studies.

Conclusion: limited evidence (low certainty); confirmation required.[10]

Effectiveness of interventions

- Transanal irrigation (TAI). Prevention: RCT and 12-month follow-up show reduction in symptoms (e.g., urgency, cluster defecation) compared to standard management.
- Treatment: a prospective cohort reports clinical and quality of life improvement in patients with established LARS.
- Conclusion: moderate evidence in favor of TAI (acceptable safety profile; applicable in practice).[11,12]
- Sacral neuromodulation: SR/MA and a retrospective cohort with prolonged follow-up indicate symptomatic improvement in selected subgroups, but with small sample sizes and risk of bias. Conclusion: low-moderate evidence; RCTs are needed.[13]
- Pelvic floor rehabilitation: recommended by guidelines and evidence reviews; comparative trials are lacking in the included studies. Conclusion: high plausibility, low certainty.
- Pharmacotherapy (e.g., loperamide): limited direct evidence focused on symptom control; sustained effect on quality of life uncertain. Conclusion: low certainty; combination with non-pharmacological interventions preferable.[15]

Quantitative synthesis (vote-counting) of selected primary studies (n = 12)

Design: RCT 1/12 (8,3 %); prospective 5/12 (41,7 %); retrospective/series 6/12 (50,0 %).

Domains: risk factors 4/12 (33,3 %); IAT 3/12 (25,0 %); neuromodulation 1/12 (8,3 %); others/observational 4/12 (33,3 %).

Direction of effect (consistency):

RT → ↑ LARS/stoma persistence: 3/3 studies concordant.

TAI → ↓ symptoms/prevention of LARS at 12 months: 3/3 studies concordant (includes 1 RCT).

Neuromodulation → clinical improvement: 1/1 study with prolonged follow-up.

Heterogeneity of measures and designs prevented a meta-analysis; consistency of effect direction is prioritized by weighting the design (RCT > prospective > retrospective).

As mentioned, a state-of-the-art literature review was conducted, the results and discussion of which are shown below in the following tables of study characteristics (table 1), summary table for risk factors (table 2), and finally a table of treatments that extract key quantitative data (table 3).

Main synthesis

The integrated evidence from 19 references confirms that low previous resection syndrome (LARS) is a common and clinically relevant sequela after sphincter-preserving surgery for rectal cancer. The prevalence of major LARS is around 40–45 % at ≥12 months, with a consistent and significant impact on quality of life. Recurrent risk factors include long-course neoadjuvant radiotherapy, low anastomosis (and, by extension, distal tumors), anastomotic leakage, and, to a lesser extent, proximal diversion; TME versus partial resection is also associated with poorer function, presumably due to a higher risk of autonomic denervation. In management, transanal irrigation (TAI) shows early prophylactic benefit in stool frequency and a clinically relevant therapeutic reduction in LARS and incontinence in prospective cohorts; sacral neuromodulation suggests high response rates in series and reviews, although with low-moderate quality of evidence and heterogeneity. Longitudinal studies describe divergent trajectories (improvement, stability, or persistent LARS), underscoring the need for dynamic and personalized follow-up.

Interpretation of findings

The factors associated with LARS fit with a multifactorial pathophysiology:

- Radiotherapy contributes to rectal fibrosis, decreased compliance, and altered sensitivity, which explains its strong association with urgency, fragmentation, and clustering. In addition, there is confusion regarding indication (more distal or advanced tumors receive more RT), which can inflate its effect if not properly controlled.[16]
- Low anastomosis and TME reduce the rectal reservoir and increase the risk of autonomic denervation; the balance between oncological radicality and functional preservation remains delicate.[17]
- Anastomotic leakage is linked to secondary inflammation/fibrosis and poorer motility; its association with greater LARS supports strict prevention and early detection strategies.[18]
- The correlation between diversion stoma and LARS may reflect both selection bias (more complex cases) and the effects of time to closure or atrophy/deconditioning of the neorectum.

Table 1. Characteristics of the studies (n=19)

Title	Author Year	Country	Type of study	Population	n	Design Follow-up	Objective	Key quantitative results	Conclusions	Source/DOI
The incidence and risk factors of low anterior resection syndrome (LARS) after sphincter-preserving surgery of rectal cancer: a systematic review and meta-analysis	Sun R, et al.[1]	China	Systematic review and meta-analysis	Patients undergoing sphincter-preserving surgery for rectal cancer	-	50 studies; assessment 1 year postoperatively	Estimate incidence and risk factors for LARS	Higher incidence of LARS: 44 % (95 % CI 40,48 %; 36 studies). Risk factors: long neoadjuvant RT OR 2,89 (95 % CI 2,06–4,05), TME OR 2,13 (1,49–3,04), anastomotic leakage OR 1,98 (1,34–2,93), diversion stoma OR 1,89 (1,58–2,27).	High burden of LARS; prioritize prevention and risk stratification.	Sun 2021, Supportive Care in Cancer; doi:10.1007/s00520-021-06326-2
Prophylactic transanal irrigation (TAI) to prevent symptoms of low anterior resection syndrome (LARS) after rectal resection	Rosen HR, et al.[2]	Austria / Germany	Randomized controlled clinical trial (12-month follow-up)	Patients after rectal resection with protective ileostomy	37,0	Randomization to TAI vs. supportive care; subsequently free choice up to 12 months	To evaluate the impact of prophylactic transanal irrigation in preventing LARS	At 12 months: TAI n=10 continued TAI; median daytime bowel movements 3 vs. 5 in ST (p=0,018) and nighttime bowel movements 0 vs. 1 (p=0,004); median LARS 18 (9–32) vs. 30 (3–39), p=0,063.	Prophylactic TAI reduces stool frequency and tends to reduce LARS; variable adherence.	Tech Coloproctol 2020; doi:10.1007/s10151-020-02261-2; BJS Open 2019; doi:10.1002/bjs5.50160
Low anterior resection syndrome: can it be prevented?	Annicchiarico A, et al.[3]	Italy	Narrative review	Patients with low anterior resection	-	Narrative	Assess whether LARS can be prevented with different surgical techniques	Summary of preventive measures; evidence suggests effect of RT, diversion stoma, and closure time.	Preventing LARS is possible with selected surgical/oncological strategies; evidence quality is heterogeneous.	Int J Colorectal Dis 2021; doi:10.1007/s00384-021-04008-3
Role of transanal irrigation in the treatment of anterior resection syndrome	Martellucci J, et al.[4]	Italy	Prospective study	Patients with major LARS (≥30) post-LAR	33	Intervention TAI 6 months + 3 months enemas; 27 completed	Evaluate the efficacy of TAI in the management of LARS	Median LARS 35, 1 → 12, 2 at 6 months (p<0,0001); then 27 at 9 months (after enemas); 85 % requested to continue TAI.	TAI improves continence and QOL; similar effect if started early or late.	Tech Coloproctol 2018; doi:10.1007/s10151-018-1829-7

Management guidelines for low anterior resection syndrome: the MANUEL project	Christensen P, et al.[5]	Europe (multi-expert)	Consensus guidelines	Patients with LARS	-	Consensus of 8 experts	Provide evidence-based management guidelines	Stepwise algorithm (diet, antidiarrheals, fiber/gelling agents, rehabilitation, TAI, neuromodulation, surgery).	A multidisciplinary and personalized approach is essential.	Colorectal Disease 2021; doi:10.1111/codi.15517
Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries	Bray F, et al.[6]	Global (WHO/IARC)	Epidemiological study (modeling)	Cancer in 185 countries	-	2018 estimates	Analyze cancer incidence/mortality, including rectal cancer	Global burden: 18,1 million new cases and 9,6 million cancer deaths in 2018; CRC among the most common.	Relevance for assessing the scale of the rectal cancer problem.	CA Cancer J Clin 2018; doi:10.3322/caac.21492
Define and characterize LARS in a standardized manner	Keane C, et al.[7]	New Zealand	Systematic review	Patients with low anterior resection	-	PRISMA	Standardize definition of LARS	Variability of criteria; the LARS Score is positioned as the standard tool.	Standardization necessary for diagnosis and comparability.	Colorectal Disease 2017; doi:10.1111/codi.13695
Low anterior resection syndrome and quality of life: an international multicenter study	Juul T, et al.[8]	Multicenter (Europe)	Multicenter cross-sectional study	Post-LAR patients without stoma, ≥16 months	796	5 centers, 4 countries; 75 % response rate	Assess impact of LARS on quality of life (EORTC QLQ-C30)	Patients with greater LARS had ~10 points less in multiple QoL domains (p<0,01).	Strong association between LARS severity and poorer QoL.	Dis Colon Rectum 2014; doi:10.1097/DCR.0000000000000116
Functional outcome following rectal surgery	Hughes DL, et al.[9]	United Kingdom	Observational study (LARRIS database)	Patients with curative Rectal Cancer	68,0	Response 80 %	Review functional outcomes and precursors of LARS	Greater LARS in 56 % (38/68). Neoadjuvant RT (LCCRT) independent factor; early closure of protective stoma was protective.	Individualize management and consider effects of RT and closure timing.	Int J Colorectal Dis 2017; doi:10.1007/s00384-017-2765-0
Factors associated with low anterior resection syndrome after surgical treatment of rectal cancer	Jimenez-Gomez LM, et al.[10]	Spain	Observational study	Patients with rectal cancer	-	—	Identify risk factors for LARS	Preoperative RT and advanced age described as risk factors (exact figures not retrieved from available text).	Early identification of risk factors for prevention/management.	https://doi.org/10.1111/codi.13975.

Efficacy of neuromodulation in patients with LARS: A systematic review	Tero J, et al.[11]	—	Systematic review	Patients with LARS treated with neuromodulation	-	—	Evaluate efficacy of neuromodulation	No verifiable data were found in the cited article. As a contemporary reference: meta-analysis of SNM (Ram 2020) success 83,3 % (95 % CI 71,3–95,3; 114 patients).	RCTs are required; promising results in series and reviews.	Supporting reference: Ram E., Tech Coloproctol 2020; doi:10.1007/s10151-020-02231-8
Comparison of treatment modalities for LARS: A narrative review	Keane C, et al.[12]	—	Narrative review	Patients with LARS	-	Narrative	Compare treatment modalities for LARS	Multiple options (PFMT, diet/drugs, TAI, SNM); lack of robust comparative evidence.	Personalized approach based on LARS phenotype.	https://doi.org/10.1007/s00384-021-03842-9.
Impact of radiotherapy on LARS in rectal cancer patients: A prospective study	Emmertsen KJ, Laurberg S[13]	Denmark	Post-hoc analysis of RCT (prospective)	Patients with rectal cancer with/without LCRT	254	2-year assessment; EORTC QoL	Assess impact of RT on LARS and QoL	Neoadjuvant RT was associated with greater LARS (OR 3,1; 95 % CI 1,7–5,6) and worse QoL in multiple domains.	Consider functional consequences of RT in treatment decisions.	BJS Open 2022; doi:10.1093/bjsopen/zrac127
Long-term outcomes of patients with LARS post-radiotherapy: A retrospective cohort study	Martellucci J, et al.[14]	Italy	Retrospective cohort	Patients with LARS after radiotherapy	-	—	Evaluate long-term outcomes	No exact verifiable figures were found in open access.	Need for long-term post-RT strategies.	https://doi.org/10.1016/j.ejso.2018.12.002.
Psychological distress in patients with LARS: A systematic review	Croese AD, et al.[15]	—	Systematic review	Patients with LARS	-	—	Assess psychological distress in LARS	High prevalence of distress/anxiety/depression reported; exact figures not available in open access.	Important to integrate psychological support.	https://doi.org/10.1186/s12885-018-4510-5.
Holistic management of LARS: Bridging functional and psychological outcomes	Lim JY, et al.[16]	—	Narrative review	Patients with LARS	-	Narrative	Assess comprehensive management (functional and psychological)	Holistic management improves well-being; integration of rehabilitation and emotional support.	Multidisciplinary approach recommended.	https://doi.org/10.1002/pon.5350.

Time-course of LARS symptoms after rectal surgery: A prospective longitudinal study	Bohlok A, et al.[17]	—	Prospective longitudinal	Patients after rectal surgery (without stoma)	65,0	Serial questionnaires up to 24 months	Analyze temporal evolution of LARS symptoms	Major LARS decreased from 48 % to 36 % at 24 months; minor LARS increased from 25 % to 43 %; fecal incontinence from 10,8 % to 15,4 %; urgency from 27,7 % to 26,2 %.	Symptoms fluctuate; monitoring is necessary to adjust management.	Support Care Cancer 2019; doi:10.1007/s00520-019-05092-0
Long-term follow-up of LARS: What can be learned from patient trajectories?	Sammour T, et al.[18]	—	Long-term follow-up	Patients with LARS	-	—	Evaluate trajectories of patients with LARS	No exact verifiable figures were found in the cited article; literature suggests that a proportion maintain LARS over the long term and another gradually improve	Customize follow-up according to clinical trajectory.	https://doi.org/10.1007/s00464-019-06797-2.
Gender disparities in LARS: A review of clinical and anatomical factors	Bryant CL, et al.[19]	—	Narrative review	Patients with LARS	-	Narrative	Examine gender disparities in presentation and treatment	Gender differences may influence severity, continence, and therapeutic response; studies with statistical power are required.	Consider gender when planning management.	https://doi.org/10.1097/DCR.0000000000002080.

Table 2. Quantitative summary of risk factors

Source	Risk factor	Comparison	Effect	95 % CI	Notes
Sun 2021 (meta-analysis)	Neoadjuvant RT (long)	Yes vs. No	OR	2,06–4,05	LARS greater than 1 year
Sun 2021 (meta-analysis)	TME	Yes vs. No	OR 2,13	1,49–3,04	-
Sun 2021 (meta-analysis)	Anastomotic leakage	Yes vs No	OR 1,98	1,34–2,93	-
Sun 2021 (meta-analysis)	Derivative stoma	Yes vs. No	OR 1,89	1,58–2,27	-
Hughes 2017 (observational)	Neoadjuvant RT (LCCRT)	Yes vs No	Independent association	-	56 % with major LARS; no OR reported in abstract
Emmertsen & Laurberg 2022 (BJS Open)	Neoadjuvant RT	Yes vs No	OR 3,1	1,7–5,6	Worse QoL in multiple domains

Table 3. Summary of treatments and results

Source	Modality	Population	n	Variable/ Result	Baseline value	Follow-up	Effect	95 % CI/p	Notes
Rosen 2020 (RCT, 12 months)	Prophylactic TAI	LAR with recent ileostomy closure	37	Daytime bowel movements (median)	-	-	3 (TAI) vs. 5 (ST)	p=0,018	Nocturnal 0 vs. 1 (p=0,004); LARS 18 vs. 30 (p=0,063)
Martellucci 2018 (prospective)	Therapeutic TAI	LARS greater than (≥30)	27	LARS Score (median)	35,1	12,2 (6 months)	Δ −22,9	0,0001	Rises to 27 after 3 months of enemas; 85 % wish to continue TAI
Ram 2020 (meta-analysis)	Sacral neuromodulation (SNM)	Refractory LARS	114	Overall success	-	-	83,3 %	95 % CI 71,3-95,3	13 studies; contemporary review used to support the neuromodulation item

In treatment, data from the prophylactic ECA of TAI are instructive: although total LARS at 12 months does not always reach conventional differences, the improvement in daytime and nighttime frequency is robust and clinically relevant, especially in the first months after stoma closure. This suggests that TAI operates as a "bridge therapy" during the adaptation phase of the neorectum (when urgency and clustering predominate) and that the timing of initiation matters. In therapeutic SNT, reductions in LARS and Wexner scores in prospective cohorts are large and consistent, although without randomized controls; here the response appears to be greater in phenotypes with clustering/urgency than in those dominated by pain or dyssynergia. Sacral neuromodulation shows positive signs (improvements in continence and overall scores), but the heterogeneity of indications, protocols, and success criteria makes it difficult to attribute a stable effect size.

Longitudinal trajectories provide a practical framework: one subgroup has persistent high LARS, another shows gradual improvement, and a third has stable mild symptoms. This dynamic stratification supports a stepwise algorithm with scheduled reassessments and escalation thresholds (e.g., from conservative measures → TAI → neuromodulation). Finally, the literature suggests possible differences by sex/gender (pelvic morphology, hormone levels, expectations, and symptom reporting), a little-explored angle that could explain part of the interindividual variability.

Limitations

- Evidence: (1) high methodological heterogeneity (definitions, instruments, and cut-off points; despite advances, not all studies use the LARS Score or apply it at the same time); (2) predominance of cross-sectional observational designs, with limited control of confounding factors (especially for RT, tumor height, and reconstructive technique); (3) small sample sizes and publication bias in interventions (TAI, neuromodulation); (4) symptom-focused outcomes with undermeasurement of quality of life and psychosocial dimensions; (5) scarcity of follow-ups >24 months and trajectory analyses; (6) heterogeneous active comparators and lack of RCTs.
- From our synthesis: although we expanded and verified figures, some references in the manuscript lack complete data in public access (e.g., sizes per arm or exact CIs) and were recorded as NR/NA; in addition, combining narrative reviews, guidelines, and primary studies. Finally, temporal bias (2017–2024 window) could omit influential previous work on reconstructions (colonic pouch, coloplasty) or rehabilitation.

Implications

For clinical practice

1. Preoperative counseling and shared decision-making: discuss functional risk alongside oncological risk, especially if long-course RT and very low anastomosis are planned.
2. Prevention and technique: prioritize nerve preservation, optimize anastomosis height, and prevent leakage; consider reservoir reconstructions in selected cases.
3. Staged algorithm focused on phenotype (MANUEL):
    - Conservative: dietary education, fiber/gelling agents, antidiarrheals, antispasmodics, biofeedback.
    - TAI: as early prophylaxis in high-risk cases (RT + low anastomosis) and as therapy in established

LARS with clustering/urgency.

- Neuromodulation (sacral or peripheral) in refractory cases, with structured response assessment.
- Integrate psychological support and pelvic floor rehabilitation from the outset.

4. Follow-up by trajectories: planned visits at 3–6–12 months and then annually, with re-phenotyping and escalation if there is no improvement.

For research

- Standardization: adopt a consensus definition of LARS, create *core outcome sets* (symptoms, QoL, sexual/urinary function, social participation) and uniform time points.
- Pragmatic comparative trials: TAI vs. rehabilitation vs. pharmacotherapy; timing of initiation (prophylaxis vs. therapy); escalation vs. conventional management.
- Longitudinal cohorts with trajectory modeling, incorporating analysis by sex/gender, microbiota, denervation markers, and cost-effectiveness.
- Implementation science: how to integrate TAI and neuromodulation into ERAS pathways and survival consultations, reducing variability between centers.

Overall, the findings suggest that LARS is not an inevitable outcome, but rather a modifiable risk: it can be partially prevented (through informed oncological decisions and techniques), mitigated with early interventions (TAI), and treated in a stepwise and personalized manner (including neuromodulation in refractory cases), always measuring what matters to the patient and addressing the psychosocial dimension. This clinical and research agenda can reduce the functional burden without compromising oncological control.[18,19]

CONCLUSIONS

LARS is common and clinically significant: approximately 4 out of 10 patients experience LARS for ≥12 months after sphincter-preserving surgery, with significant deterioration in quality of life, so its assessment and management should be a standard part of oncological follow-up.

Long-course neoadjuvant radiotherapy is the main avoidable determinant of dysfunction: when oncologically equivalent alternatives exist, its functional impact should be discussed and risk stratified before treatment is indicated.

Low anastomosis, TME, and anastomotic leakage increase the risk of LARS: optimizing the height of the anastomosis when oncologically possible, preserving innervation, and preventing leakage (meticulous technique, early detection protocols) are concrete measures to mitigate LARS.

Transanal irrigation (TAI) provides measurable benefits:

Prophylactic: it reduces the frequency of bowel movements (daytime and nighttime) early on after stoma closure in high-risk patients (RT + low anastomosis).

Therapeutic: achieves clinically relevant reductions in LARS scores and incontinence in established LARS; should be considered as a second step after conservative measures.

Neuromodulation is an effective option in refractory cases: sacral neuromodulation shows high response rates in series and reviews; its use should be reserved for refractory cases, with structured selection and evaluation of response.

Management should be stepwise, phenotypic, and multidisciplinary: combine conservative measures, pelvic floor rehabilitation, TAI, and neuromodulation according to symptom profile (clustering/urgency, incontinence, hypersensitivity) and patient preferences, integrating psychological support from the outset.

Follow-up should be longitudinal and trajectory-based: schedule reassessments at 3, 6, and 12 months and then annually, using the LARS score and quality of life questionnaires, to anticipate therapeutic escalation in those who maintain a persistent high LARS trajectory.

Preoperative counseling and shared decision-making are mandatory: informing patients of individual functional risks (RT, anastomosis height, surgical complexity) and agreeing on preventive and early rehabilitation strategies improves patient-centered expectations and outcomes.

These conclusions are derived from a critical synthesis of the available evidence and support an operational change: measuring, preventing, and treating LARS proactively and in a personalized manner, without compromising oncological objectives.

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CONFLICT OF INTEREST

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