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REVIEW ARTICLE

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Robotic rectal resection preserves anorectal function: Systematic review and meta-analysis

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Abstract

Background: Improving survival rates in rectal cancer patients has generated a growing interest in functional outcomes after total mesorectal excision (TME). The well-established low anterior resection syndrome (LARS) score assesses post-operative anorectal impairment after TME. Our meta-analysis is the first to compare bowel function after open, laparoscopic, transanal, and robotic TME.

Methods: All studies reporting functional outcomes after rectal cancer surgery (LARS score) were included, and were compared with a consecutive series of robotic TME ($n = 48$).

Results: Thirty-two publications were identified, including 5 565 patients. Anorectal function recovered significantly better within one year after robotic TME (3.8 [95% CI −9.709–17.309]) versus laparoscopic TME (26.4 [95%CI 19.524–33.286]), $p = 0.006$), open TME (26.0 [95%CI 24.338–29.702], $p = 0.002$) and transanal TME (27.9 [95%CI 22.127–33.669], $p = 0.003$).

Conclusions: Robotic TME enables better recovery of anorectal function compared to other techniques. Further prospective, high-quality studies are needed to confirm the benefits of robotic surgery.

KEYWORDS

anorectal function, laparoscopy, LARS, minimally-invasive surgery, rectal cancer, rectal resection, robotic surgery, total mesorectal excision

1 | INTRODUCTION

The ratio of sphincter-preserving rectal resections has increased over the past decades due to improved surgery and neoadjuvant radio-chemotherapy. Therefore, low anterior resection (LAR) with total mesorectal excision (TME) has become the favoured procedure for middle and low rectal cancer.[1] Meanwhile, different techniques for LAR have evolved, from conventional open TME (OTME) to minimally-invasive approaches such as laparoscopic TME (LaTME), robotic (RoTME) and transanal TME (TaTME). All techniques have been shown to deliver comparable oncological outcomes when conducted by experienced surgeons,[2–4] while the minimally-invasive techniques are able to reduce postoperative pain, morbidity and length of hospital stay.[5] Moreover, novel techniques, such as RoTME and TaTME, enable superior visualisation in the deep pelvis due to an immersive three-dimensional, magnifying and stable camera platform for RoTME[6] and a down-to-up approach for TaTME, which optimises the view on the most demanding part of the TME.[7] Therefore, both techniques are capable of facilitating minimally-invasive TME, even for demanding anatomy such as the narrow male pelvis, obesity and low, bulky tumours, resulting in lower conversion rates and comparable pathological and oncological outcomes.[8-10]

Advances in surgery and adjuvant therapy not only result in a higher ratio of sphincter preservation but also enable improved long-term survival[11,12]; therefore, quality of life (QoL) is an essential issue after rectal cancer surgery. Hence, anorectal function, in particular, attracts considerable attention. The term low anterior resection syndrome (LARS) summarises a wide range of functional impairments after low anterior resection (LAR), such as incontinence for faeces and flatus, urgency, stool fragmentation and evacuatory dysfunction.[13-15] Patients suffer from a pattern of obstructed defecation or urgency and incontinence, described in a growing number of publications with a prevalence ranging from 17.0%–59.4% for major LARS.[16,17] Current treatment options for LARS are non-specific and include pharmacological treatment (e.g., loperamide), physical methods such as anal plugs and rectal irrigation, and pelvic floor exercises, biofeedback, sacral neurostimulation or permanent colostomy.[14,18-21] Therefore, prevention of nerve damage is a priority.

Many scoring systems exist for anorectal function, with different acceptance in clinical practice and research and limited by a varying specificity for LARS and consideration of its impact on the QoL of patients.[15] Hence, the LARS score was established to facilitate the collection of comparable and relevant data, thus enabling comparison of postoperative anorectal function between different studies and techniques and making meta-analysis possible.[13] Although urogenital function has been examined before,[22] to date, no comparison of anorectal function for all major TME techniques exists. Thus, our study aimed to perform a systematic review and meta-analysis of the impact of the surgical technique on the prevalence and severity of LARS.

2 | MATERIALS AND METHODS

2.1 | Search strategy

A comprehensive database search was conducted using PubMed, Science Direct and Medline, according to the PRISMA guidelines, using the search terms '(rectal cancer) AND ([rectal resection] OR [total mesorectal excision] OR [low anterior resection]) AND ([LARS] OR [Low anterior resection syndrome] OR [anorectal function] OR [bowel function] OR [functional outcome])".[23] All articles were screened by title and abstract to determine their relevance for the study objective, which consists of bowel function after rectal resection for rectal cancer reported by disease-specific, multidimensional LARS score. All results on techniques, that is, conventional open, laparoscopic, transanal and robotic TME, were applicable. The bibliographies of included articles were cross-referenced and relevant articles were added.

2.2 | Eligibility criteria and data extraction

Two reviewers (JKG, MK) independently screened the identified articles for eligibility. Consensus or a third reviewer resolved disagreement. Inclusion criteria comprised original articles on rectal resection for cancer reporting continuous or categorical anorectal outcomes based on the LARS score. Exclusion was considered necessary if the inclusion criteria were not fully met, articles reported anorectal functioning scores other than the LARS score, in cases of redundant patient population, articles written in another language but English, only abstracts were available, or no original data were obtained. The data extraction was based on first author, year of publication, country, journal, study design, sample size for each technique sorted by gender and overall, tumour localisation and rate of perioperative irradiation. Moreover, LARS score as continuous and categorical results were categorised as no LARS, minor LARS and major LARS.

2.3 | Quality assessment and risk of bias

Methodical quality was independently assessed using the Newcastle-Ottawa Quality assessment scale,[24] as recommended by the Cochrane Collaboration. A total score of 5 points or above out of 9 were accepted for study inclusion.

2.4 | Bicentric series of robotic LAR

All patients operated between January 2014 and February 2018 for primary rectal cancer within 15 cm from the anal verge by sphincter-preserving RoTME were considered for inclusion in the unpublished, prospective bicentric case series. The ethics committee of the general medical council Hamburg (PV5591) approved the study. Reasons for exclusion were conversion of robotic surgery to open LAR, indication for abdominoperineal resection without sphincter preservation ($n = 7$), as well as death within the follow-up period. Of all patients initially screened ($n = 61$), 79% ($n = 48$) were eligible for inclusion in the analysis (the others were excluded due to refusal to participate or impossibility of contacting). Clinicopathological and demographic parameter and short-term outcome were analysed to ensure the comparability of both subgroups. Surgical procedures of RoTME were performed as previously published.[8] LARS score questionnaires were sent to the patients or administered by telephone calls four weeks before surgery and 12 m postoperatively.

2.5 | Statistical analysis

All statistical analyses were performed using SAS version 9.4 (SAS Inc.). The weighted average LARS score was computed using least-square means for each surgical technique, weighted by the number of patients in each study. The corresponding 95% confidence

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interval was computed using the weight standard deviation. An ANOVA test was conducted to test for overall differences in the average LARS score by surgical technique. Pairwise differences in the weighted average of the LARS score were computed using a Student's *t*-test. Categorical LARS scores were analysed using a continuity corrected Chi-squared test between surgical approaches. In all instances, a *p*-value <0.05 was considered statistically significant.

3 | RESULTS

3.1 | Literature search

The comprehensive database search yielded 38 papers in the qualitative synthesis, of which 32 studies could be included in the further quantitative analysis (Figure 1). Studies using the same patient cohorts as previous analysis were only employed for qualitative analysis.[25,26] The exclusion of specific subgroups of patients was performed to prevent overrepresentation of patients generated from sources used in multiple studies.[27] For studies reporting on the same techniques in different cohorts, overall values were extrapolated for LARS levels, if not provided.[28–30]

3.2 | Study characteristics

Overall, the studies included 5 565 patients. Most of the studies were consecutive case series (*n* = 23). Six studies report on LaTME, 23 on OTME, eight on TaTME, and only one study presenting anorectal outcomes based on LARS score with RoTME (Table 1). Most publications used the categorical classification, which provides for a three-level rating into no LARS, minor LARS, and major LARS (*n* = 28, Table 2). Absolute LARS score values were applied by 17 studies. Only a few studies compared the postoperative LARS score results to preoperative values (*n* = 6). Where listed, abdomino-perineal

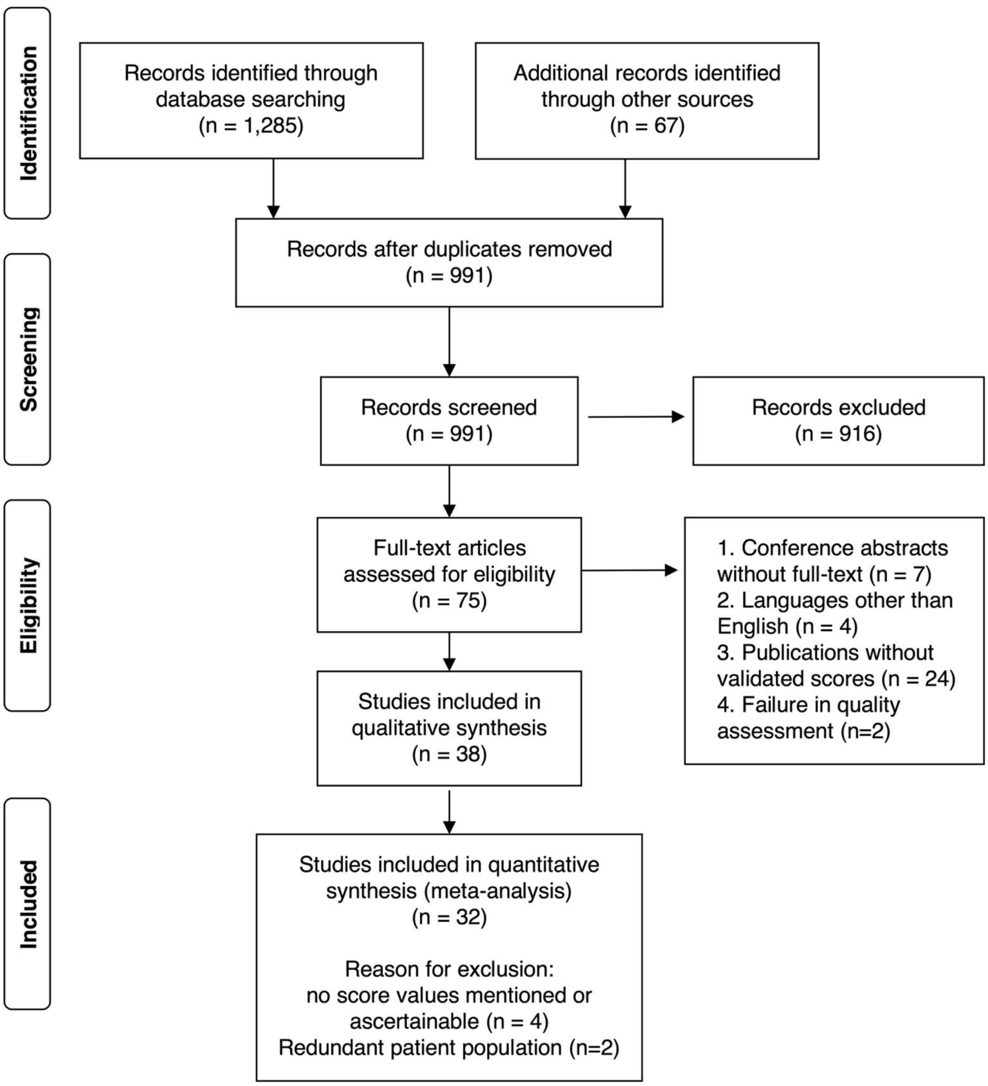


FIGURE 1 Prisma flow chart of the systematic literature search

TABLE 1 General information of the included studies

Author	NOS	Country	Study design	Follow-up	Technique	n	Subjects, n LaTME M	LaTME F	OTME M	OTME F	RoTME M	RoTME F	TaTME M	TaTME F
Ihnát (2018)[30]	7	Czech Republic	CS	12 m	L	65	41	24						
Akizuki (2018)[61]	6	Japan	CS	>12 m	O	149			94	55				
Battersby (2018)[27]	5	UK	CS	5.2 ± 2.4 y	O	463			279	184				
Beppu (2016)[39]	8	Japan	CS	2.4 – 13 y	O	87			63	24				
Bregendahl (2013)[47]	6	Denmark	CS	>12 m	O	938								
Chen (2015)[28]	7	Denmark	RT	14 y	O[a]	242			133	109				
Ekkarat (2016)[42]	5	Thailand	CS	>12 m	O	129			67	62				
Emmertsen (2013)[40]	5	Denmark	CS	12 m	O	183								
Gadan (2017)[62]	9	Sweden	RCT	12 y	O	87			49	38				
Hain (2017)[29]	8	France	MCC	46 ± 26 m	O	89			65	24				
Hughes (2017)[45]	5	UK	CS	>12 m	O	68			49	19				
Hupkens (2018)[17]	5	Netherlands	CS	4.9 (2.4–8.1) y	O	165			123	42				
Juul (2015)[41]	7	Denmark	CS	>12 m	O	451			272	179				
Juul (2014)[46]	6	Germany	CS	>14 m	O	801			442	359				
Kean (2019)[63]	7	New Zealand	CS	>12 m	O	82			48	34				
Kupsch (2018)[37]	6	Germany	CS	6.5 y	O	261			162	99				
Nuytens (2018)[31]	6	Belgium	CS	38 (5–45) m	O	100			68	32				
Qin (2017)[38]	6	China	CS[b]	>12 m	O	142			91	51				
Ribas (2017)[56]	6	Spain	CS	>12 m	O	70			47	23				
Samalavicius (2016)[44]	5	Lithuania	CS	35.2 ± 15.21 m	O	108			69	39				
Sun (2019)[36]	8	China	CS	40.2 (23.1–87.3) m	O	220			145	75				
Trenti (2018)[64]	5	Spain	CS	4.5 ± 2.2 y	O	152			105	47				
Sturiale (2017)[16]	5	Italy	CCS	13.7 y	O : L	93	26	15	32	20				
Rubinkiewicz (2018)[65]	7	Poland	CCS	6 m after stoma closure	O : T	39			12	2			19	6
Luca (2016)[50]	6	Italy	CS	12 m	R	23					8	15		
Keller (2019)[66]	5	USA	CS	>12 m	T	61							50	11
Kneist (2016)[33]	6	Germany	CS	6 m	T	10							9	1
Koedam (2017)[67]	6	Netherlands	CS	6 m	T	30							21	9
Bjoern (2019)[68]	7	Denmark	CCS	>12 m	T : L	85	16	20					37	12
Pontallier (2016)[69]	9	France	RCT	>12 m	T : L	72	21	13					26	12
Rubinkiewicz (2019)[70]	6	Poland	CCS	6 m after stoma closure	T : L	46	13	10					13	10
Veltcamp Helbach (2019)[71]	8	Netherlands	CCS	>6 m	T : L	54	18	9					20	17

Abbreviations: CS, case series; CCS, comparative case series; DST, double stapling technique; F, female; LaTME, L–laparoscopic TME; m, month; M, male; MCC, matched case series; *n*, number of patients; NOS, Newcastle Ottawa scale; OTME, open TME; RCT, randomised controlled trial; RoTME, robotic TME; RT, randomised trial; RTx, neoadjuvant radiochemotherapy; *T*, total number; TaTME, transanal TME; TME, total mesorectal excision; y, year.

[a]RTx versus Surgery alone.

[b]Cross-sectional study.

TABLE 2 LARS score data and risk factors for anorectal impairment of included studies

Author	Technique	Subjects, *n*	LARS score continuous		LARS score categorical		Tumour height		Perioperative chemoradiation
			Pre	Post	Pre	Post	<6cm (%)	Absolute (cm)	%
Ihnát (2018)[30]	LaTME	65	-	x	-	x		9.3 ± 1.8[a]	58.4
Akizuki (2018)[61]	OTME	149	-	-	-	x	41.0		
Battersby (2018)[27]	OTME	463	-	x	-	x		9.0 ± 3.3[a]	32.7
Beppu (2016)[39]	OTME	87	-	-	-	x		4.9 ± 2.5[a]	100.0
Bregendahl (2013)[47]	OTME	938	-	-	-	x	6.0		20.0
Chen (2015)[28]	OTME	242	-	-	-	x	7.0		51.2
Ekkarat (2016)[42]	OTME	129	-	x	-	x	28.4		38.0
Emmertsen (2013)[40]	OTME	183	-	-	-	x	6.5		19.6
Gadan (2017)[62]	OTME	87	-	-	-	x		5.0 (2.5–7.0)[b]	86
Hain (2017)[29]	OTME	89	-	x	-	x			71.1
Hughes (2017)[45]	OTME	68	-	x	-	x	42.6		35.3
Hupkens (2018)[17]	OTME	165	-	x	-	x		8.8 ± 3.4[a]	47.9
Juul (2015)[41]	OTME	451	-	-	-	x		9.0 ± 3.3[a]	31.3
Juul (2014)[46]	OTME	801	-	-	-	x			53.9
Kean (2019)[63]	OTME	82	-	x	-	x	47.6		25.6
Kupsch (2018)[37]	OTME	261	-	-	-	x		9.0[b]	55.4
Nuytens (2018)[31]	OTME	100	-	x	-	x			65.0
Qin (2017)[38]	OTME	142	-	-	-	x	33.1		61.9
Ribas (2017)[56]	OTME	70	-	-	-	x			75.5
Samalavicius (2016)[44]	OTME	108	-	x	-	x	25.9		49.1
Sun (2019)[36]	OTME	220	-	-	-	x	36.8		60.0
Trenti (2018)[64]	OTME	152	-	-	-	x			90.2
Sturiale (2017)[16]	OTME: LaTME	93	-	-	-	x	OTME: 30.0, LaTME: 30.0		OTME: 44.0, LaTME: 44.0
Rubinkiewicz (2018)[65]	OTME: TaTME	39	x	x	-	-	TaTME: 100.0, OTME: 100.0		TaTME: 96.0, OTME: 92.9
Luca (2016)[50]	RoTME	23	-	-	x	x	100.0		78.3
Keller (2019)[66]	TaTME	61	x	x	x	x		6.2 ± 2.1[a]	44
Kneist (2016)[33]	TaTME	10	x	x	-	-	100.0		70.0
Koedam (2017)[67]	TaTME	30	x	x	x	x		6.0 (4–8)[b]	73.0
Bjoern (2019)[68]	TaTME: LaTME	85	-	x	-	x	TaTME: 8.2, LaTME: 5.6		TaTME: 16.3, LaTME: 22.2
Pontallier (2016)[69]	TaTME: LaTME	72	-	x	-	-		TaTME: 4 (2–6)[b], LaTME: 4 (2–6)[b]	TaTME: 79.0, LaTME: 88.0
Rubinkiewicz (2019)[70]	TaTME: LaTME	46	x	x	-	x		TaTME: 3 (2–4)[b], LaTME: 4 (3–5)[b]	TaTME: 78.3, LaTME: 82.6
Veltcamp Helbach (2019)[71]	TaTME: LaTME	54	-	x	-	-	TaTME: 33.3, LaTME: 25.9		TaTME: 7.4, LaTME: 14.8

Abbreviations: CS, case series; CCS, comparative case series; LARS, low anterior resection syndrome; LaTME, laparoscopic TME; m, month; MCC, matched case series; *n*, patient number; OTME, open TME; Pre/Post, pre/postoperative; RCT, randomised controlled trial; RoTME, robotic TME; RT, randomised trial; TaTME, transanal TME; TME, total mesorectal excision; y, year.

[a]Numbers are presented as mean ± standard deviation.

[b]Numbers are presented as Median (interquartile range).

TABLE 3 Patient characteristics of the bicentric case series for robotic total mesorectal excision (RoTME)

	RoTME (n = 48)
Gender	
Male	33 (68.8)
Female	15 (31.3)
Age (y)	59.1 ± 11.5
Center	
Hamburg	34 (70.8)
Taiwan	14 (29.2)
BMI (kg/m^2)	26.7 ± 5.1
Previous abdominal surgery (yes)	5 (10.4)
Tumor localisation	
>6 cm ab ano	22 (45.8)
≤6 cm ab ano	26 (54.2)
Localisation ab ano (cm)	7.9 ± 6.9
Neoadjuvant radiation (yes)	14 (29.2)
Tumor stage	
ypT0	5 (10.4)
pT1	12 (25.0)
pT2	17 (32.7)
pT3	14 (29.2)
LN positive (n)	0.8 ± 1.3
LN harvested (n)	16.6 ± 7.8
Major complications (Clavien Dindo ≥3)	5 (10.4)
Anastomotic leakage	4 (8.3)
Resection margin	
Distal margin R0	48 (100.0)
CRM R0	47 (97.9)
Quality of mesorectal excision	
Grade 1	48 (100.0)
Grade 2	0 (0.0)
Grade 3	0 (0.0)
Length of hospital stay (d)	8.6 ± 4.6
Readmission (yes)	7 (14.6)

Note: Numbers indicated as absolute numbers and percentage or mean ± standard deviation.

Abbreviations: BMI, body mass index; CRM, circumferential resection margin; d, days; LN, lymph nodes; *n*, number; y, years.

resection (APR) was described in 5.7% (n = 6) TaTME, 0.0% (n = 0) RoTME, 0.0 (n = 0) LaTME cases and 26.7% (n = 268) OTME cases. All APR cases where not included by the respective study in functional outcome analysis.

3.3 | Patient characteristics in the bicentric RoTME group

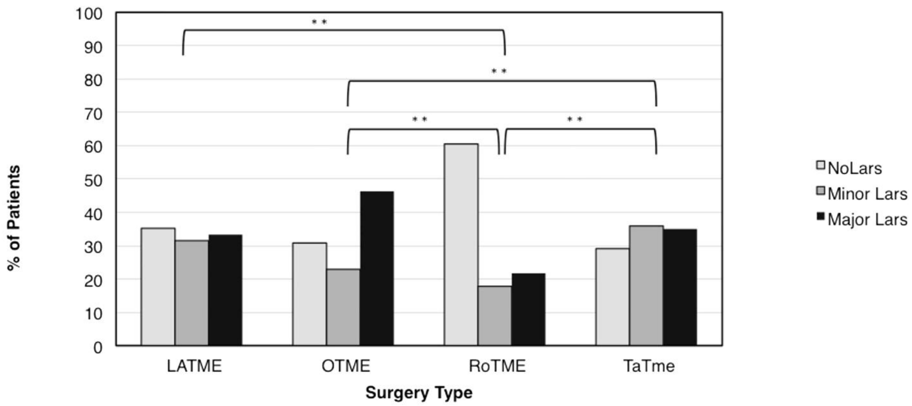
We analysed the published results together with a bicentric case series of 48 patients, operated at the participating institutions between January 2014 to February 2018 (33 male patients (68.8%), overall mean age 59.1 ± 11.5 years, mean body mass index in the overweight range (26.7 ± 5.1 kg/m^2) (Table 3). The response rate for functional outcome assessed at least 12 months after surgery was 79% (48 out of 60 eligible patients). The majority of tumours were in the lower third of the rectum (26/48 patients, 56.5%). In this group, 14 patients (29.2%) received neoadjuvant radiochemotherapy. In terms of short-term outcomes, five patients had major complications (10.4%). Four patients (8.3%) had an anastomotic leakage. The length of hospital stay was 8.6 ± 4.6 days. Surrogate parameters for oncological outcomes revealed negative resection margins in 47 patients (97.9%), and complete mesorectal excision all patients.

3.4 | Anorectal outcomes between groups

There was an approximately equal distribution between all three LARS score levels for LaTME, mainly major LARS cases (2 343 of 5 039 patients, 46.5 %) for OTME, and a majority of no LARS (43 of 71 patients, 60.5%) for RoTME (Figure 2). Overall, anorectal function was significantly better with RoTME compared to LaTME, OTME, and TaTME ($p < 0.001$, $p < 0.001$, and $p < 0.001$, respectively). Moreover, TaTME demonstrated significantly milder LARS compared to OTME ($p \leq 0.001$).

The distribution of studies per technique reporting on continuous LARS scores results was more balanced between LaTME, OTME and TaTME series with five, nine and eight studies, respectively. The bicentric RoTME series was the only one to report absolute LARS score values (Figure 3), and showed superior results compared to LaTME (p = 0.006), OTME (p = 0.002) and TaTME (p = 0.003). All other techniques could not reveal any significant differences in continuous LARS scores.

All available data concerning the LARS risk factors perioperative radiation and tumour height were collected (Table 4). Although some publications explicitly analysed the impact of perioperative radiation on LARS, the allocation of perioperative radiotherapy ranges only from 44.1%–52.5% (Table 4). The proportion of low tumours below 6 cm from the anal verge ranged between 20.2% and 43.2% for OTME, LaTME and TaTME, only the RoTME series demonstrated a high proportion (70.4%) of low tumours. Dissection was performed as TME in 74.8%–100.0% of cases., while the highest share of partial mesorectal excision (PME) was reported for OTME (24.3%). Reconstruction was predominately conducted by stapled (50.7%–97.8%) end-to-end (32.4%–74.6%) anastomosis. In contrast, the highest proportion of hand-sewn anastomosis was reported for RoTME (49.3%) side-to-end reconstruction (67.6%). Quality of mesorectal excision was rarely reported and ranged for Grad 1 from 78.0% for



Technique	No. studies	Total n	LARS classification, n (%)			p-value *			
			No	Minor	Major	LaTME	OTME	RoTME	Overall
LaTME	4	165	58 (35.2)	52 (31.5)	55 (33.3)				
OTME	22	5 039	1 544 (30.6)	1 152 (22.9)	2,343 (46.5)	0.083			
RoTME	2	71	43 (60.5)	13 (17.8)	15 (21.7)	**<0.001**	**<0.001**		**<0.001**
TaTME	4	163	47 (29.1)	59 (35.9)	57 (35.0)	0.712	**<0.001**	**<0.001**	

* p-values in bold indicate statistical significance between surgical techniques. LARS – low anterior resection syndrome; LaTME – laparoscopic TME; n – number of patients; OTME – open TME; RoTME – robotic TME; TaTME – transanal TME; TME, total mesorectal excision.

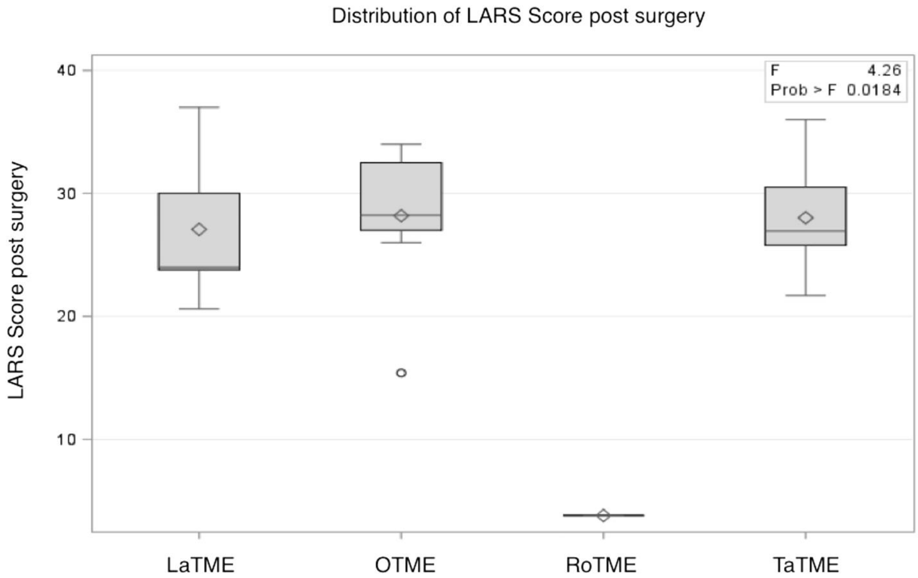
FIGURE 2 Categorical analysis of postoperative LARS scores. **p*-values in bold indicate statistical significance between surgical techniques. LARS, low anterior resection syndrome; LaTME, laparoscopic TME; *n*, number of patients; OTME, open TME; RoTME, robotic TME; TaTME, transanal TME; TME, total mesorectal excision

LaTME to 100% for RoTME. Anastomotic leakages were scarcest in LaTME cases and were most frequent in RoTME.

4 | DISCUSSION

The available data demonstrate the best preservation of anorectal function with RoTME. Conventional open TME serves as the gold standard for rectal cancer surgery. Yet, most publications reveal high rates of severe anorectal dysfunction after OTME, with a mean rate of major LARS of 46.5%. Our meta-analysis indicated that LaTME did not reduce the rate of severe bowel dysfunction compared to OTME, resulting in comparable anorectal outcomes. This is reflected in the literature, where LaTME and OTME led to similar anorectal function after adjusting for risk factors.[31] Same results were reported in a systematic review and meta-analysis for urogenital function.[32] Hampered by poor ergonomics with rigid laparoscopic instruments in the deep and curved space of the pelvis, and limited view of relevant anatomical structures such as the hypogastric nerve, these results are not surprising. Advanced techniques were developed to facilitate minimally-invasive rectal cancer surgery, even in demanding situations. TaTME offers various advantages for perioperative and oncological outcomes: it is known to enable sphincter preservation in 91.8% of cases, combined with a low conversion rate of 2.7%[7,33] and higher rates of negative circumferential resection margins compared to LaTME.[34] However, it is possible that prolonged dilatation of the anus could lead to intraoperative sphincter damage. Overall, TaTME had superior LARS score levels in our categorical analysis compared to OTME, but this could not be reproduced in the continuous analysis. TaTME might enhance outcomes of restorative surgery and preserve relevant nerval structures by improved exposition, but internal sphincter damage could compromise this effort.

RoTME allows safe oncological procedures with complete mesorectal excision in 95.8% and negative circumferential margins in 95.7%, even in demanding anatomical situations such as low and bulky tumours in the male pelvis.[9,35] Optimised visualisation and ambidextrous capability using instruments with multiple degrees of freedom facilitate TME and the identification and preservation of nerves, which is measurably reflected by the best TME quality of all compared techniques (quality of mesorectal excision Grad 1: RoTME 100.0%; OTME 93.0%; TaTME 88.3%; LaTME 78.0%). This is likely the reason that the evidence available demonstrates that RoTME outperforms all other TME techniques in terms of prevention of LARS. Remains to note though that meta-analysis was only possible for categorical LARS scores results since no other study reporting continuous LARS score levels could be identified.



Technique	No. studies	Total n	Subjects, n Av SD	Min	Max	LARS score WM	95% CI	p-value LaTME	OTME	RoTME	Overall
LaTME	5	185	10.1	20.6	37.0	26.4	19.524–33.286				
OTME	9	1 218	10.4	15.4	34.0	26.0	24.338–29.702	0.864			**0.018**
RoTME	1	48	1.9	3.8	3.8	3.8	-9.709–17.309	**0.006**	**0.002**		
TaTME	8	263	8.4	21.7	36.0	27.9	22.127–33.669	0.732	0.776	**0.003**	

* p-values in bold indicate statistical significance between surgical techniques. Av SD – average standard deviation; CI, confidence interval; LARS – low anterior resection syndrome; LaTME – laparoscopic TME; Max – maximum LARS score; Min – minimum LARS score; n – patient number; OTME – open TME; RoTME – robotic TME; TaTME – transanal TME; TME, total mesorectal excision; WM – weighted mean.

FIGURE 3 Continuous analysis of postoperative LARS scores. **p*-values in bold indicate statistical significance between surgical techniques. Av SD, average standard deviation; CI, confidence interval; LARS, low anterior resection syndrome; LaTME, laparoscopic TME; Max, maximum LARS score; Min, minimum LARS score; *n*, patient number; OTME, open TME; RoTME, robotic TME; TaTME, transanal TME; TME, total mesorectal excision; WM, weighted mean

During rectal cancer surgery, anorectal function can be impaired by several mechanisms. Damage to the internal anal sphincter, which consists of an involuntary innervated smooth muscle stimulated by parasympathetic pelvic splanchnic nerves, can be induced by endoanal instruments as well as denervation.[14] As a result, passive continence is affected, leading to unconscious leakage of rectal contents. The external anal sphincter mediates voluntary rectal control; faecal urgency and faecal urge incontinence occur if damaged. Most likely, this is caused by injury of the intramural nerve plexus, as structural damage has not been documented.[14]

Applying the LARS score, several risk factors for impairment of anorectal function following TME have been identified by various studies. The strongest impact on LARS is for location of anastomosis, with greatest adverse effects for tumours in the lower third of the rectum[16,17,25,36-42] and perioperative radiation.[16,17,25,27,30,31,36,38,40,42-47] In our analysis, the rates for perioperative radiation varied from 44.1% for OTME to 52.5% for TaTME. In particular, RoTME revealed significantly superior functional results in the continuous and categorical analysis and ranked midfield in terms of the proportion of irradiated patients. However, TaTME had the highest proportion of radiation and had significantly ($p < 0.001$) better categorical LARS score levels compared to OTME, which had the least radiated patients. The radiation regime provides equal impairment on anorectal outcomes, whether applied pre- or post-operatively[30,46] or as neoadjuvant short- or long-course therapy.[47-49] Conversely, other publications have revealed no impact of radiation on anorectal outcome in their cohorts.[39,50] Although irradiation supports local tumour control in locally advanced rectal cancer, in the TME age it has failed to improve overall survival, since survival seems to be more depended on distant metastasis.[51-53] However, there is evidence for the reduction of local recurrence and improved disease-free survival after complete pathological response to radiotherapy.[54,55] Therefore, optimised radiation regimes capable of reducing collateral tissue damage and precise patient selection are needed.[56]

TABLE 4 Risk factors for major LARS per technique provided in the studies

n (%)	TaTME	RoTME	LaTME	OTME
Perioperative (chemo-)radiation	138 (52.5)	32 (45.1)	117 (51.8)	2194 (44.1)
Tumor height ≤6 cm	48 (43.2)	50 (70.4)	21 (20.2)	441 (18.4)
Reconstruction				
Stapled	85 (70.9)	36 (50.7)	89 (97.8)	400 (81.6)
Hand-sewn	30 (24.9)	35 (49.3)	2 (2.2)	90 (18.4)
Side-to-end	36 (27.9)	48 (67.6)	38 (25.4)	560 (37.6)
End-to-end	89 (69.7)	23 (32.4)	111 (74.6)	741 (49.8)
Colonic pouch or coloplasty	2 (2.3)	0 (0.0)	0 (0.0)	326 (13.4)
Dissection level				
PME	0 (0.0)	4 (5.6)	0 (0.0)	1171 (24.3)
TME	86 (100.0)	67 (94.4)	57 (100.0)	3607 (74.8)
Quality of mesorectal excision Grad I	145 (88.3)	48 (100.0)	67 (78.0)	13 (93.0)
Anastomotic leakage	10 (5.9)	10 (14.1)	2 (3.5)	167 (6.6)

Note: Numbers indicated as absolute numbers and percentages of the total case number for which the respective risk factors was retrievable.

Abbreviations: LARS, low anterior resection syndrome; LaTME, laparoscopic TME; OTME, open TME; PME, partial mesorectal excision; RoTME, robotic TME; TaTME, transanal TME; TME, total mesorectal excision.

Tumour height and the consecutive level of anastomosis are independent risk factors for worse anorectal function.[16,17,25,36-42,57] Tumours located above 10 cm from the anal verge are at low risk of LARS[16]; a cut-off value for anastomosis of 5 cm correlates best with a high risk of major LARS, corresponding with tumour levels of 7 cm and below.[42] Among the included studies, the proportion of tumours in the lower third of the rectum showed little variation, from 20.2% for LaTME to 43.2% for TaTME. Noteworthy, RoTME provided the best anorectal outcomes, with 70.4% of low tumours. While OTME presents the highest proportion of partial mesorectal excision, major LARS was most frequent following this technique, whereas all other approaches performed TME in 94.4%–100.0%. Moreover, although RoTME was burdened with the highest share of risk factors, such as hand-sewn anastomosis (49.3%) and anastomotic leakage (14.1%), which might induce LARS by pelvic scarring,[40,47] anorectal function proved to be significantly better with this approach. Moreover, the role of ageing is discussed controversially: some data show severe LARS in elderly patients,[16,17] whereas other studies demonstrate worse anorectal function in the younger part of their cohorts.[27,37,47] This might be a result of subjective assessment, which may lead younger patients to rate the same symptoms more severely,[37] or elevated LARS score baselines in older patients.[37,58] Current treatment options for LARS are non-specific and include pharmacological treatment (e.g., loperamide), physical methods, such as anal plugs and rectal irrgitaion, pelvic floor exercises, biofeedback, sacral neurostimulation (SNS) or permanent colostomy.[14,18-21,59] Especially SNS has revealed promising results for urinary and fecal incontinence, although the exact mechanism is not yet fully understood.[21,60]

The unbalanced distribution of available data per technique and moderate evidence limits the significance of this study. In particular, we could only identify one relevant study for RoTME. Nevertheless, this is the first meta-analysis to compare all available data on LARS scores between the primary TME techniques. Further multicentre analyses are needed to consolidate the impact of surgical technique on anorectal outcome after restorative rectal cancer surgery, and further support the potential benefits of RoTME.

Oncologically safe procedures enabling minimal recurrence rates and optimal survival remain the main purpose of surgical oncology. Thus, the quality of life gains importance for rectal cancer survivors. Since specific therapies are lacking, the prevention of LARS is of vital importance, including adherence to nerve-sparing surgery, patient education and dose duration of pelvic radiation. In examining surgical techniques, our study reveals superior preservation of anorectal function for robotic rectal resection over the other primary TME techniques, whereas transanal TME provides benefit over conventional open TME. However, further analyses have to confirm these findings, and optimised radiation regimes are needed to lower long-time bowel dysfunction.

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CONFLICTS OF INTEREST

Daniel R. Perez is proctor for Intuitive Surgical and has received honoraria. All other authors declare no competing interests.

AUTHOR CONTRIBUTIONS

Julia K. Grass, Chien-Chih Chen, Marius Kemper, Jakob R. Izbicki and Daniel R. Perez conception and design, acquisition of data, analysis and interpretation of data, drafting of the article, and final approval of the version published. Bharathi Lingala analysis and interpretation of data, Nathaniel Melling, Roberto Persiani, Flavio Tirelli, Marco Caricato, Gabriella T. Capolupo interpretation of data, drafting of the article and critical revision for important intellectual content. All authors reviewed the manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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