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Robotic, laparoscopic, open, and transanal total mesorectal excision for rectal cancer: an updated systematic review and network meta- analysis of randomized controlled trials

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Robotic, laparoscopic, open, and transanal total mesorectal excision for rectal cancer: an updated systematic review and network meta-analysis of randomized controlled trials

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Abstract

Background: Open, laparoscopic, robotic, and transanal total mesorectal excision (TME) are used for rectal cancer, but randomized trials compare only two approaches. We performed a systematic review and network meta-analysis of randomized controlled trials (RCTs) to compare surgical and oncological outcomes.

Methods: PubMed, Web of Science, and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched through November 7, 2026. Eligible RCTs compared two TME approaches in adults undergoing curative rectal cancer surgery. The primary outcome was circumferential resection margin (CRM) positivity. Frequentist random-effects network meta-analysis and Bayesian treatment ranking were conducted.

Results: Of 409 records, 15 reports covering 11 RCTs were included; nine RCTs contributed to the primary CRM analysis. Compared with laparoscopy, open TME was associated with lower CRM positivity odds (odds ratio [OR] 0.50, 95% confidence interval [CI] 0.27–0.94), whereas robotic (OR 0.67, 95% CI 0.40–1.13) and transanal TME (OR 1.17, 95% CI 0.30–4.53) showed no statistically significant difference. Transanal TME lowered conversion odds (OR 0.07, 95% CI 0.02–0.28). Thirty-day complication rates did not differ significantly. Robotic TME showed the most favorable point estimate for disease-free survival (hazard ratio 0.74, 95% CI 0.40–1.37), although uncertainty remained.

Conclusions: Open TME had the lowest CRM positivity estimate, while robotic TME showed favorable long-term point estimates. Findings support individualized technique selection and warrant cautious interpretation of indirect comparisons.

Keywords: rectal cancer; total mesorectal excision; robotic surgery; transanal total mesorectal excision; laparoscopic surgery; network meta-analysis

1. Introduction

Rectal cancer accounts for approximately one-third of colorectal cancers, and total mesorectal excision (TME), introduced by Heald [1,2], remains the cornerstone of curative surgery. Over three decades, the operative approach has evolved from open surgery to laparoscopy, then to robotic platforms and, most recently, the transanal "bottom-up" technique (taTME). Each transition promised better visualization of the deep pelvis and higher-quality specimens.

The supporting evidence matured unevenly. For laparoscopic versus open TME, the international COLOR II trial established non-inferior long-term outcomes [3], the earlier MRC CLASICC trial reported comparable short-term oncological outcomes [22], whereas the contemporaneous ACOSOG Z6051 [5] and ALaCaRT [7] trials failed to demonstrate non-inferiority for short-term pathological composite outcomes; the large Chinese LASRE trial subsequently confirmed comparable pathological outcomes for low rectal cancer [22]. For robotic TME, ROLARR found no advantage in conversion [8], but the larger REAL trial (n=1171) demonstrated significantly lower CRM positivity (3.8% vs 6.7%) and improved 3-year local control (1.6% vs 4.0%) [9,10]. For taTME, despite early international-registry experience [22] and a Norwegian safety moratorium [22], the TaLaR trial (n=1089) established non-inferiority of transanal versus laparoscopic TME for 3-year DFS (82.1% vs 79.4%) [14].

Because every trial compares only two approaches, the relative standing of all four techniques has never been tested within a single randomized design. Three network meta-analyses have compared all four approaches [27-29], but all predated the pivotal contemporary trials: the most recent, by Seow et al. [22], searched only to September 2020, excluded REAL, LASRE, TaLaR, and Ta-LaTME, and concluded that the four techniques did not differ in circumferential margin clearance. We therefore performed an updated systematic review and NMA restricted to RCTs, incorporating the large trials published since 2020, to determine whether this conclusion still holds.

2. Materials and Methods

2.1 Protocol and registration

This review followed a prespecified protocol registered with PROSPERO (CRD420261560684). Protocol amendments before completion: EMBASE was removed from the registered list of sources, and full-text retrievability was added as an eligibility requirement. Reporting follows PRISMA 2020 and its NMA extension [17,18].

2.2Eligibility criteria

Population: adults (≥18 years) undergoing curative resection for non-metastatic rectal adenocarcinoma. **Interventions:** open, laparoscopic, robotic, or transanal TME. **Outcomes:** primary—CRM positivity (tumor ≤1 mm from the mesorectal fascia); secondary—conversion to open surgery, 30-day complications (Clavien-Dindo), anastomotic leak, completeness of TME, and long-term disease-free survival (DFS), overall survival (OS), and local recurrence. **Study design:** RCTs only. **Retrievability:** full texts had to be obtainable; studies without retrievable full texts were excluded at full-text screening with reasons recorded.

2.3 Search strategy

We searched PubMed, Web of Science, and the Cochrane Central Register of Controlled Trials (CENTRAL) from inception to November 7, 2026, without language restriction, combining controlled vocabulary and free-text terms for rectal cancer, TME, and the four surgical approaches with a randomized-trial filter. Complete search strings are provided in Supplementary Material S1.

2.4 Study selection

Records were deduplicated in Zotero and screened by title/abstract and then full text by one reviewer. CENTRAL records, which could not be exported because of institutional subscription limits, were screened on-screen; candidate trials underwent full-text retrieval. Exclusion decisions were documented with reasons (Fig. 1).

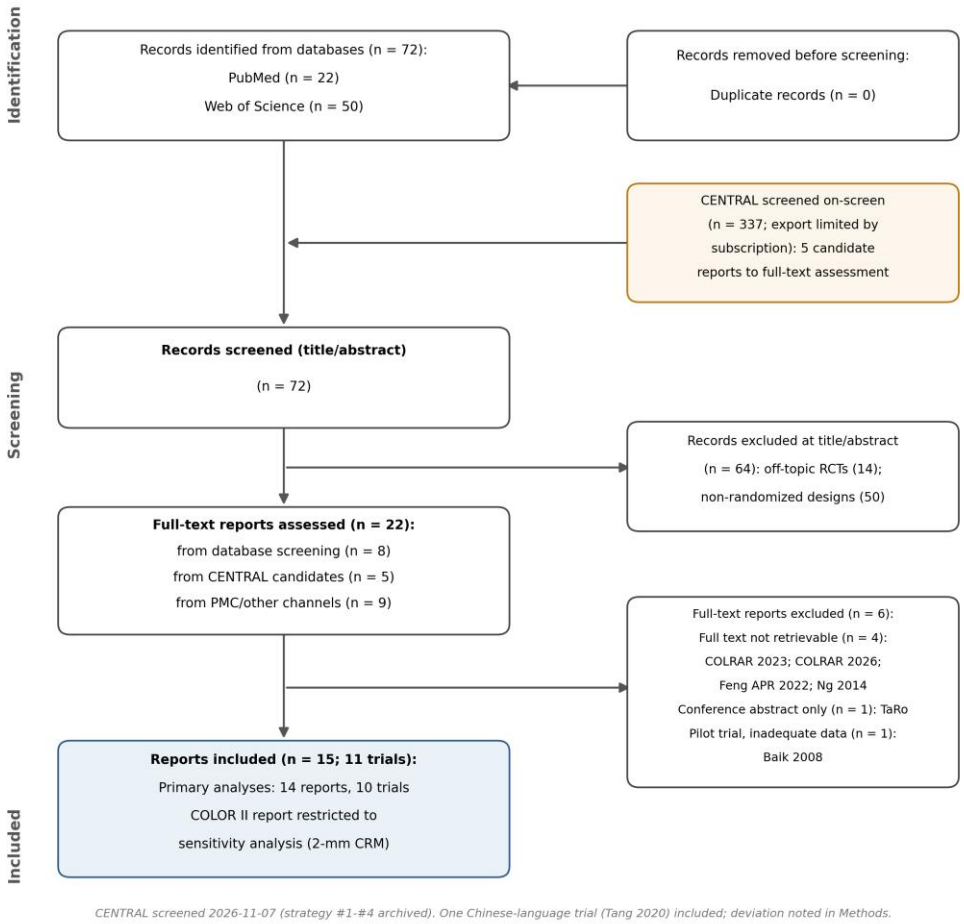

Fig. 1. PRISMA 2020 flow diagram of study selection (409 records identified; 15 reports of 11 trials included).

2.5 Data extraction and risk of bias

A standardized extraction table captured arm-level event counts and hazard ratios with 95% confidence intervals. Risk of bias was assessed at the outcome level with the Cochrane RoB 2 tool [20] across five domains.

2.6 Statistical analysis

Pairwise meta-analysis used Mantel-Haenszel odds ratios with random-effects (REML) pooling and Hartung-Knapp confidence intervals. Frequentist random-effects NMA used a contrast-based weighted least-squares estimator with DerSimonian-Laird between-study variance [37,38]; 95% CIs used t-distribution quantiles (df = studies − treatments + 1). Heterogeneity was quantified with I^2 and τ^2 [19]. A Bayesian consistency model (binomial likelihood, logit link; 3 chains; 20,000 adaptation plus 50,000 iterations; gemtc/JAGS) [22] estimated rank probabilities (lower CRM preferred). The network was star-shaped with laparoscopic surgery as the common comparator; no closed loops existed, so loop-specific inconsistency assessment was not applicable. Sensitivity analyses excluded COLOR II (CRM defined at 2 mm) and COLOR III-era abstract-only reports. Two-sided $P<0.05$ was significant. Analyses used R (meta) [21], Python (numpy/scipy), and JAGS (gemtc) [22].

3. Results

3.1 Study selection and characteristics

The search identified 409 records; 15 reports of 11 RCTs met eligibility and were included (Fig. 1): REAL (n=1171) [9,10], ROLARR (n=471) [8], Tang 2020 (n=129) [22], Kim 2018 (n=139) [22], Z6051 (n=486) [5,6], ALaCaRT (n=475) [7], LASRE (n=1070) [22], TaLaR (n=1115) [14,15], Ta-LaTME (n=116) [16], COLOR III (n=1061) [22], and COREAN (n=340) [11-13]. Four reports were excluded for unretrievable full texts (COLRAR 2023, COLRAR 2026 5-year, Feng APR 2022, Ng 2014), one for conference-abstract-only reporting (TaRo), and one pilot trial for inadequate data (Baik 2008); COLOR II (n=1044) [3,4] was retained for sensitivity analyses only; the remaining exclusions with reasons are listed in Supplementary Table S1 (Table 1).

Table 1. Characteristics of included randomized controlled trials.

Trial (acronym)	Reports	Country; centers	Randomized (analyzed), n	Arms (n)	Tumor/Stage	Neoadjuvant therapy	Primary outcome; follow-up
REAL	Feng 2022 Lancet G&H; Feng 2025 JAMA	China; 11	1,240 (1,171)	R 586 / L 585	Mid/low rectum, cT1-3N0-1	Mixed (stratified)	3-y LRR; 3 y
ROLARR	Jayne 2017 JAMA	International (10 countries); 29	471 (471)	R 236 / L 235	Rectal cancer (resection)	Per local standard	Conversion; 30 d (LARS sub-study)
Tang 2020	Tang 2020 Chin J Gastrointe	China; 1	130 (129)	R 65 / L 64	≤12 cm, cT1-3N0-1	Rare (1.5%)	Short- and mid-term; median 24

	st Surg						mo
Kim 2018	Kim 2018 Ann Surg	Korea; 1	163 (139)	R 66 / L 73	≤9 cm, cT1-3Nx	CRT ~78%	TME quality; 30 d (QoL 12 mo)
Z6051	Fleshman 2015 JAMA; 2019 Ann Surg	USA/Canada; 35	486 (462)	L 240 / O 222	≤12 cm, stage II-III	All (protocol)	Composite pathologic; 2-y DFS
ALaCaRT	Stevenson 2015 JAMA	Australia/NZ; 24	475 (473)	L 238 / O 235	Rectal cancer (resection)	~50%	Composite successful resection; 30 d
LASRE	Jiang 2022 JAMA Oncol	China; 22	1,070 (1,039)	L 685 / O 354	Low rectum	>95% of II/III (CRT)	3-y DFS (reported separately)
TaLaR	Liu 2023 Ann Surg; Zeng 2025 JAMA	China; 16	1,115 (1,089)	Ta 544 / L 545	Below peritoneal reflection, cT1-3	~35%	3-y DFS; ≥3 y
COLOR III	Tuynman 2026 Lancet G&H	International (13 countries); 28	1,103 (1,061)	Ta 711 / L 350	(y)cT1-3N0-2, ≤10 cm	~50%	3-y LRR (ongoing); short-term reported
Ta-LaTME	Serra-Aracil 2023 Br J Surg	Spain; 4	116 (105)	Ta 55 / L 50	≤10 cm, cT1-3N0-1 (no APR)	62.5%	Composite conversion; median 39 mo
COLOR II*	Bonjer 2015 NEJM	International (8 countries); 30	1,103 (1,044)	L 699 / O 345	≤15 cm, T1-3 (no T4)	59%	3-y LRR; 3 y

3.2 Risk of bias

No trial was rated high risk overall. TaLaR remained the only trial at low risk across all domains [14,15]. LASRE featured central blinded review of TME specimen photography [22]. Concerns predominantly reflected open-label design; Z6051 modified its composite primary outcome during the trial [5], and COLOR II lacked centralized pathology and used a 2-mm CRM definition [3] (Table 2).

Table 2. Risk of bias summary (RoB 2) at the outcome level.

Trial	Pathological outcomes (CRM, TME)	Long-term outcomes (DFS, OS, LRR)	Short-term complications	Key concerns
REAL	Some concerns	Some concerns	Some concerns	Open-label
ROLARR	Some concerns	—	Some concerns	Open-label; partial pathology blinding
Tang 2020	Some concerns	Some concerns	Some concerns	Small single-center; open-label
Kim 2018	Some concerns	—	Some concerns	Open-label; phase II
Z6051	—	—	Some concerns	Composite primary modified during trial; 14.2% robot-assisted in lap arm
ALaCaRT	—	—	Some concerns	Open-label; 9% conversion incl. hybrid
LASRE	Low	Low	Some concerns	Open-label; crossover 50 open→lap, 17 lap→open
COLOR II	Some concerns	—	Some concerns	No centralized pathology; 2-mm CRM definition
COREAN	Some concerns	—	Some concerns	Open-label; 2022 erratum
TaLaR	Low	Low	Low	Low risk overall (blinded central pathology review)
Ta-LaTME	—	—	Some concerns	Small; non-independent randomization
COLOR III	Some concerns	Low	Some concerns	Central MRI review + video QA; no central pathology

3.3 Pairwise meta-analysis (laparoscopic vs open)

Under the 1-mm CRM definition (Z6051, ALaCaRT, LASRE), open surgery was associated with lower CRM positivity (fixed-effect OR 1.84, 95% CI 1.02–3.31 for laparoscopic vs open; I^2=0%); the network estimate below supersedes the pairwise pooling (Supplementary Fig. S1). No difference was observed for 30-day complications. Conversion to laparotomy in the laparoscopic arm occurred in 11.3% (Z6051), 8.8% (ALaCaRT), 2.5% (LASRE), and 16% (COLOR II, percentage only).

3.4 Network meta-analysis

The geometry of the evidence network, with laparoscopic TME as the common comparator, is shown in Fig. 2.

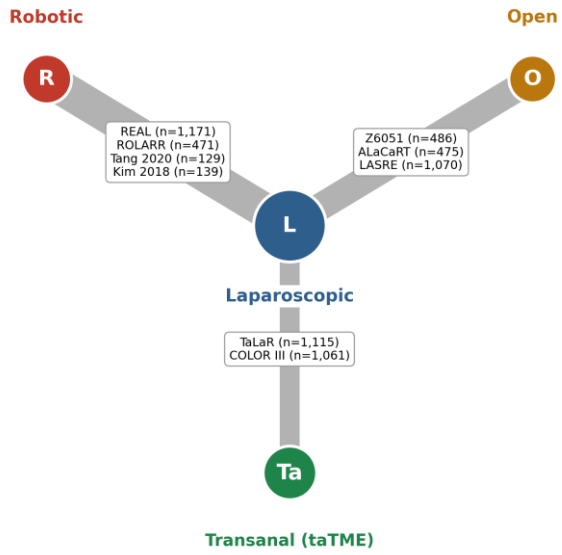

Fig. 2. Network geometry of the four surgical approaches (node size proportional to number of patients; edge width proportional to number of RCTs). Laparoscopic TME was the common comparator.

CRM positivity (primary; 9 RCTs; I^2=0%, τ^2=0). Open surgery showed a significantly lower odds of CRM positivity than laparoscopic surgery (OR 0.50 (0.27–0.94)); robotic surgery showed an intermediate point estimate (OR 0.67 (0.40–1.13)) and transanal TME neutral (OR 1.17 (0.30–4.53)) (Fig. 3, Table 3). In the Bayesian framework (all PSRF=1.00; residual deviance ratio 0.967), posterior medians were 0.44 (95% CrI 0.17–0.88) for open, 0.73 (95% CrI 0.38–1.80) for robotic, and 1.25 (95% CrI 0.35–4.89) for transanal versus laparoscopic surgery. The probability of ranking best for CRM clearance was 81.1% for open, 12.3% for robotic, 6.3% for transanal, and 0.3% for laparoscopic surgery (Fig. 4).

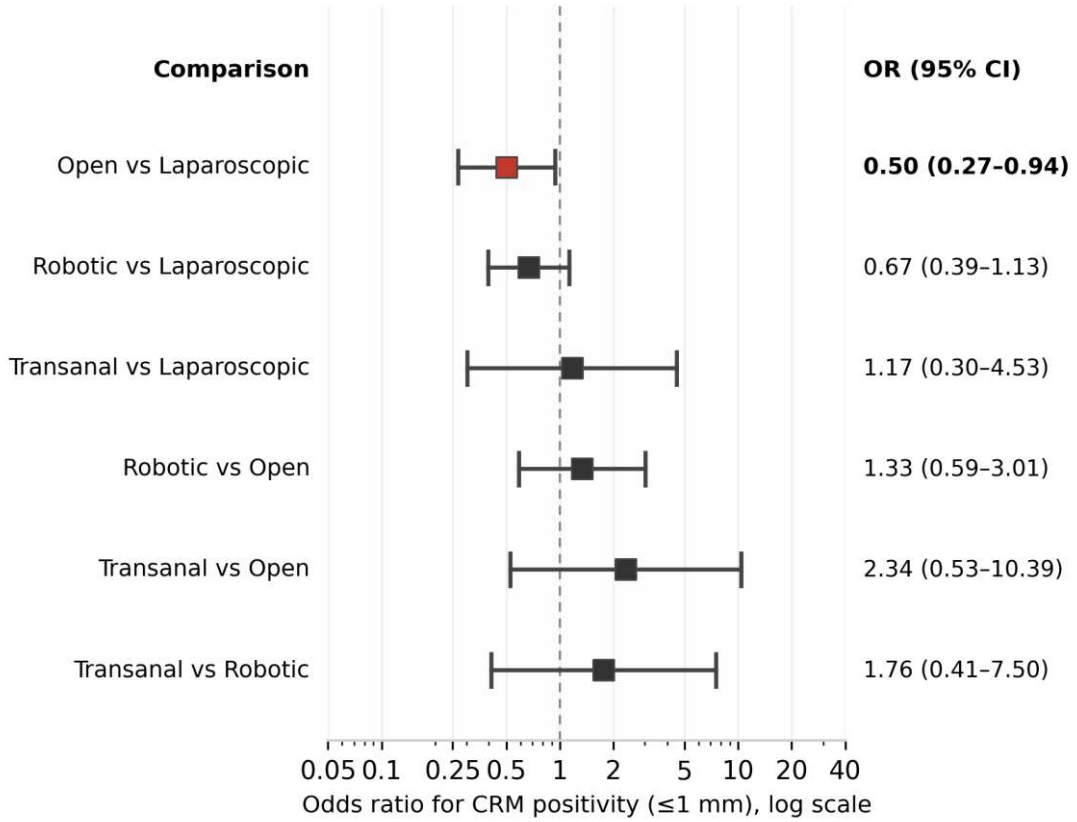

Fig. 3. Network meta-analysis of CRM positivity (≤1 mm; k=9 RCTs, I^2=0%): all pairwise odds ratios with 95% CIs. The open-versus-laparoscopic comparison is statistically significant.

Table 3. League table of the CRM positivity network meta-analysis (odds ratios, 95% CIs).

	Laparoscopic	**Robotic**	**Open**	**Transanal**
Laparoscopic	—	0.67 (0.39–1.13)	0.50 (0.27–0.94)	1.17 (0.30–4.53)
Robotic	1.50 (0.89–2.53)	—	0.75 (0.33–1.70)	1.76 (0.41–7.50)
Open	2.00 (1.07–3.73)	1.33 (0.59–3.01)	—	2.34 (0.53–10.39)
Transanal	0.85 (0.22–3.30)	0.57 (0.13–2.43)	0.43 (0.10–1.90)	—

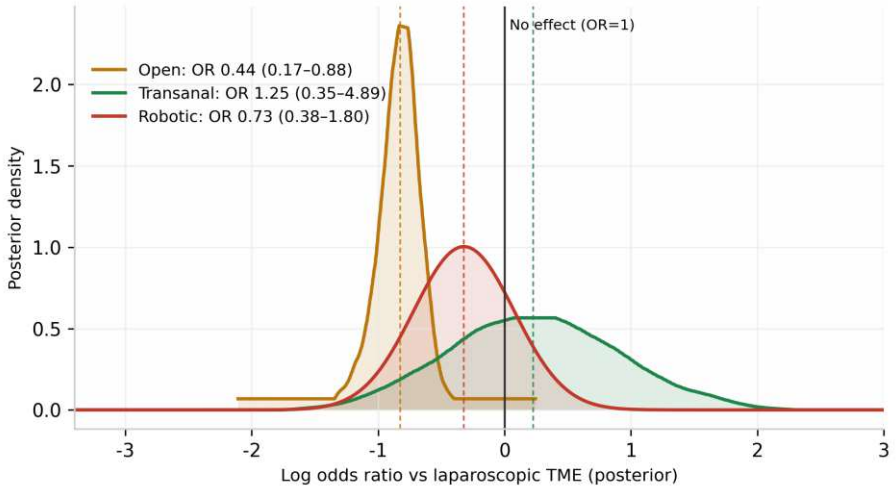

Fig. 4a. Bayesian posterior densities of relative effects versus laparoscopic TME (gemtc, k=9; PSRF=1.00).

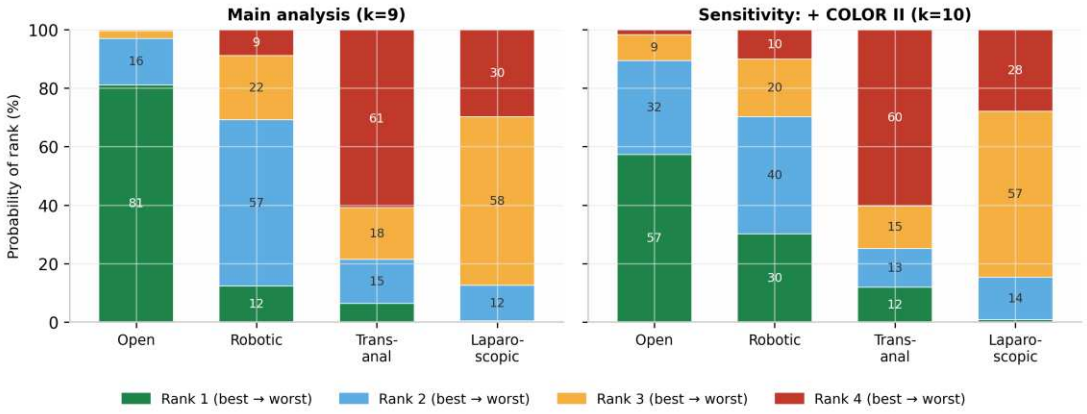

Fig. 4b. Bayesian rank probabilities (left: main analysis k=9; right: sensitivity analysis including COLOR II, k=10).

Anastomotic leak (9 RCTs; I^2=0%). Open surgery showed the highest point estimate of odds versus laparoscopic (OR 1.72, 95% CI 0.85–3.46); robotic (OR 1.40, 95% CI 0.71–2.77) and transanal (OR 1.22, 95% CI 0.81–1.84) estimates were directionally similar. Denominators varied across trials (all operated patients vs sphincter-preserving patients); results are presented per trial-defined denominators (pairwise estimates in Supplementary Fig. S2; network estimates in Supplementary Fig. S3).

Conversion to open surgery (9 RCTs; I^2=31%). Transanal TME showed markedly lower odds of conversion than laparoscopic TME (OR 0.07, 95% CI 0.02–0.28), driven by the large contrast in COLOR III (1% vs 17%); robotic TME was intermediate (OR 0.53, 95% CI 0.21–1.32), and open surgery had the lowest by definition.

30-day complications. The any-complication NMA (8 RCTs; I^2=48.9%) showed no differences reaching significance: versus laparoscopic surgery, ORs were 1.21 (0.76–1.94) for open, 0.90 (0.60–1.34) for robotic, and 1.07 (0.61–1.90) for transanal surgery (all 95%

CIs crossing unity); heterogeneity reflected variable complication ascertainment across eras and definitions.

Completeness of TME. Pooling remained inappropriate (I^2=57.8%); results are reported descriptively in Supplementary Table S2.

Long-term outcomes. For DFS, robotic TME showed the largest point-estimate benefit versus laparoscopic (HR 0.74 (0.40–1.37)), followed by transanal (HR 0.86 (0.43–1.71)); open surgery was neutral (HR 0.99 (0.65–1.51)). The LASRE estimate derives from the prespecified primary analysis of the 3-year follow-up report [22]; point-estimate orderings for OS and local recurrence were similar, with wide intervals because single trials inform each edge.

3.5 Sensitivity analysis

Adding COLOR II (2-mm CRM definition) attenuated the open-versus-laparoscopic contrast (OR 0.69 (0.40–1.18); network I^2=27.8%) while leaving the robotic estimate essentially unchanged (OR 0.70 (0.37–1.33)), supporting the 1-mm evidence base as primary. Bayesian sensitivity estimates were 0.61 (95% CrI 0.25–1.13) for open and 0.74 (0.35–1.88) for robotic surgery, with open retaining the highest probability of ranking best (57.2%).

4. Discussion

4.1 Principal findings

Across nine RCTs, open and robotic TME showed the lowest point estimates of CRM positivity (the open-versus-laparoscopic contrast reaching statistical significance), while transanal and laparoscopic TME showed the highest. Robotic TME showed the most favorable long-term local control and DFS, whereas open surgery showed the highest anastomotic leak odds. Frequentist and Bayesian estimates agreed closely.

4.2 Interpretation

The open surgery paradox—cleanest margins but highest leak rates and (in earlier-era trials) the highest local-recurrence rates—largely reflects era and case-mix effects, alongside the prognostic weight of circumferential margin involvement established by the MRC CR07 trial [22] and standardized specimen reporting [22]: open-arm data derive from trials conducted in 2006–2018, whereas the robotic advantage is anchored in the contemporary, centrally quality-controlled REAL trial [9,10]. The leak gradient favoring laparoscopic over open surgery in LASRE (2.5% vs 6.1%) [22] is consistent with the network point estimate. The conversion advantage of transanal TME observed in COLOR III (1% vs 17%) [22] is now quantified within the network.

4.3 Comparison with existing evidence

Three network meta-analyses have compared all four approaches [27-29]. The most recent RCT-restricted analysis, by Seow et al. [22], included 32 trials but searched only to September 2020; its network therefore lacked REAL, LASRE, TaLaR, and Ta-LaTME, and it concluded that the four techniques did not differ in CRM clearance. Our updated network detects a significant open-versus-laparoscopic contrast and a consistent Open < Robotic <

Laparoscopic = Transanal gradient, demonstrating that incorporating the pivotal contemporary randomized trials materially changes the conclusions of this literature. An observational meta-analysis [22] suggested lower leak rates with laparoscopic than transanal TME; our randomized evidence does not confirm this contrast, underscoring the value of restricting synthesis to randomized trials.

4.4 Limitations

First, the transanal CRM estimate rests on two trials (TaLaR and COLOR III) with few CRM events in the transanal arm. Second, COLOR II used a 2-mm CRM definition and lacked central pathology review. Third, 14.2% of laparoscopic-arm cases in Z6051 were robot-assisted [5]. Fourth, all trials were open-label; selection and RoB assessment were performed by a single reviewer. Fifth, leak denominators varied across trials. Finally, certainty of evidence was not formally graded [22].

4.5 Conclusions

Among contemporary randomized evidence, open TME achieved the lowest point estimate of CRM positivity, robotic TME showed the most favorable point estimates for long-term local control and margin quality approaching that of open surgery, and transanal TME matched laparoscopic TME across outcomes; conversion could not be compared within the included randomized evidence. These hypothesis-generating findings may inform individualized technique selection according to pelvic anatomy, surgeon expertise, and resource context.

Declarations

Ethics approval and consent to participate

Not applicable. This study is a systematic review and network meta-analysis of previously published, de-identified aggregate data; no new data involving human participants or animals were collected.

Consent for publication

Not applicable.

Data availability

The datasets generated and analysed during the current study are available from the corresponding author on reasonable request. The data extraction table and complete analysis outputs accompany the submission as supplementary materials.

Code availability

The analysis code (R meta pipeline, Python network meta-analysis implementation, and gemtc/JAGS scripts) is available from the corresponding author on reasonable request and will be deposited in a public repository upon acceptance.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Xiaolu Jiang: Conceptualization, Methodology, Investigation, Writing—original draft, Writing—review and editing.Renlu Xu: Methodology, Data curation, Formal analysis, Validation. Qiang Wang: Investigation, Data curation, Resources. Sheng Xie: Software, Formal analysis, Visualization. Jun Zhang: Methodology, Validation, Writing—review and editing. Weidong Li: Conceptualization, Supervision, Project administration, Funding acquisition, Writing—review and editing. All authors read and approved the final manuscript.

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References

[1] Heald RJ, Ryall RD. Recurrence and survival after total mesorectal excision for rectal cancer. Lancet. 1986;1(8496):1479-1482. https://doi.org/10.1016/S0140-6736(86)91510-2

[2] MacFarlane JK, Ryall RD, Heald RJ. Mesorectal excision for rectal cancer. Lancet. 1993;341(8843):457-460. https://doi.org/10.1016/0140-6736(93)90207-W

[3] Bonjer HJ, Deijen CL, Abis GA, et al. A randomized trial of laparoscopic versus open surgery for rectal cancer. N Engl J Med. 2015;372(14):1324-1332. https://doi.org/10.1056/NEJMoa1414882

[4] van der Pas MH, Haglind E, Cuesta MA, et al. Laparoscopic versus open surgery for rectal cancer (COLOR II): short-term outcomes of a randomised, phase 3 trial. Lancet Oncol. 2013;14(3):210-218. https://doi.org/10.1016/S1470-2045(13)70016-0

[5] Fleshman J, Branda M, Sargent DJ, et al. Effect of laparoscopic-assisted resection vs open resection of stage II or III rectal cancer on pathologic outcomes: the ACOSOG Z6051 randomized clinical trial. JAMA. 2015;314(13):1346-1355. https://doi.org/10.1001/jama.2015.10529

[6] Fleshman J, Branda ME, Sargent DJ, et al. Disease-free survival and local recurrence for laparoscopic resection compared with open resection of stage II to III rectal cancer: follow-up results of the ACOSOG Z6051 randomized controlled trial. Ann Surg. 2019;269(4):589-595. https://doi.org/10.1097/SLA.0000000000003002

[7] Stevenson ARL, Solomon MJ, Brown CSL, et al. Effect of laparoscopic-assisted resection vs open resection on pathological outcomes in rectal cancer: the ALaCaRT randomized clinical trial. JAMA. 2015;314(13):1356-1363. https://doi.org/10.1001/jama.2015.12009

[8] Jayne D, Pigazzi A, Marshall H, et al. Effect of robotic-assisted vs conventional laparoscopic surgery on risk of conversion to open laparotomy among patients undergoing resection for rectal cancer: the ROLARR randomized clinical trial. JAMA. 2017;318(16):1569-1580. https://doi.org/10.1001/jama.2017.7219

[9] Feng Q, Yuan W, Li T, et al. Robotic versus laparoscopic surgery for middle and low rectal cancer (REAL): short-term outcomes of a multicentre randomised controlled trial. Lancet Gastroenterol Hepatol. 2022;7(11):991-1004. https://doi.org/10.1016/S2468-1253(22)00248-5

[10] Feng Q, Yuan W, Li T, et al. Robotic vs laparoscopic surgery for middle and low rectal cancer: the REAL randomized clinical trial. JAMA. 2025;334(2):136-148. https://doi.org/10.1001/jama.2025.8123

[11] Kang SB, Park JW, Jeong SY, et al. Open versus laparoscopic surgery for mid or low rectal cancer after neoadjuvant chemoradiotherapy (COREAN trial): short-term outcomes of an open-label randomised controlled trial. Lancet Oncol. 2010;11(7):637-645. https://doi.org/10.1016/S1470-2045(10)70131-5

[12] Jeong SY, Park JW, Nam BH, et al. Open versus laparoscopic surgery for mid-rectal or low-rectal cancer after neoadjuvant chemoradiotherapy (COREAN trial): survival outcomes of an open-label, non-inferiority, randomised controlled trial. Lancet Oncol. 2014;15(7):767-774. https://doi.org/10.1016/S1470-2045(14)70205-0

[13] Park JW, Kang SB, Hao J, et al. Open versus laparoscopic surgery for mid or low rectal cancer after neoadjuvant chemoradiotherapy (COREAN trial): 10-year follow-up of an open-label, non-inferiority, randomised controlled trial. Lancet Gastroenterol Hepatol. 2021;6(7):569-577. https://doi.org/10.1016/S2468-1253(21)00094-7

[14] Zeng Z, Luo S, Zhang H, et al. Transanal vs laparoscopic total mesorectal excision and 3-year disease-free survival in rectal cancer: the TaLaR randomized clinical trial. JAMA. 2025;333(9):774-783. https://doi.org/10.1001/jama.2024.24276

[15] Liu H, Zeng Z, Zhang H, et al. Morbidity, mortality, and pathologic outcomes of transanal versus laparoscopic total mesorectal excision for rectal cancer: short-term outcomes from a multicenter randomized controlled trial. Ann Surg. 2023;277(1):1-6. https://doi.org/10.1097/SLA.0000000000005523

[16] Serra-Aracil X, Zarate A, Bargallo J, et al. Transanal versus laparoscopic total mesorectal excision for mid and low rectal cancer (Ta-LaTME study): multicentre, randomized, open-label trial. Br J Surg. 2023;110(2):150-158. https://doi.org/10.1093/bjs/znac324

[17] Tang B, Gao G, Zou Z, et al. Efficacy comparison between robot-assisted and laparoscopic surgery for mid-low rectal cancer: a prospective randomized controlled trial. Chin J Gastrointest Surg. 2020;23(4):377-383. https://doi.org/10.3760/cma.j.cn.441530-20190401-00135

[18] Kim MJ, Park SC, Park JW, et al. Robot-assisted versus laparoscopic surgery for rectal cancer: a phase II open label prospective randomized controlled trial. Ann Surg. 2018;267(2):243-251. https://doi.org/10.1097/SLA.0000000000002321

[19] Jiang WZ, Xu JM, Xing JD, et al. Short-term outcomes of laparoscopy-assisted vs open surgery for patients with low rectal cancer: the LASRE randomized clinical trial. JAMA Oncol. 2022;8(11):1607-1615. https://doi.org/10.1001/jamaoncol.2022.4079

[20] Jiang W, Xu J, Cui M, et al. Laparoscopy-assisted versus open surgery for low rectal cancer (LASRE): 3-year survival outcomes of a multicentre, randomised, controlled, non-inferiority trial. Lancet Gastroenterol Hepatol. 2025;10(1):34-43. https://doi.org/10.1016/S2468-1253(24)00273-5

[21] Tuynman JB, Yao H, Moolenaar LR, et al. Transanal total mesorectal excision versus laparoscopic total mesorectal excision for mid and low rectal cancer (COLOR III): short-term outcomes of an international, multicentre, phase 3, randomised, controlled, non-inferiority trial. Lancet Gastroenterol Hepatol. 2026;11(5):355-366. https://doi.org/10.1016/S2468-1253(26)00022-1

[22] Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. https://doi.org/10.1136/bmj.n71

[23] Hutton B, Salanti G, Caldwell DM, et al. The PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions: checklist and explanations. Ann Intern Med. 2015;162(11):777-784. https://doi.org/10.7326/M14-2385

[24] Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ. 2003;327(7414):557-560. https://doi.org/10.1136/bmj.327.7414.557

[25] Sterne JAC, Savovic J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898. https://doi.org/10.1136/bmj.l4898

[26] Balduzzi S, Rucker G, Schwarzer G. How to perform a meta-analysis with R: a practical tutorial. Evid Based Ment Health. 2019;22(4):153-160. https://doi.org/10.1136/ebmental-2019-300117

[27] van Valkenhoef G, Lu G, de Brock B, Hillege H, Ades AE, Welton NJ. Automating network meta-analysis. Res Synth Methods. 2012;3(4):285-299. https://doi.org/10.1002/jrsm.1054

[28] Simillis C, Lal N, Thoukididou SN, et al. Open versus laparoscopic versus robotic versus transanal mesorectal excision for rectal cancer: a systematic review and network meta-analysis. Ann Surg. 2019;270(1):59-68. https://doi.org/10.1097/SLA.0000000000003227

[29] Ryan OK, Ryan EJ, Creavin B, et al. Surgical approach for rectal cancer: a network meta-analysis comparing open, laparoscopic, robotic and transanal TME approaches. Eur J Surg Oncol. 2021;47(2):285-295. https://doi.org/10.1016/j.ejso.2020.06.037

[30] Seow W, Dudi-Venkata NN, Bedrikovetski S, Kroon HM, Sammour T. Outcomes of open vs laparoscopic vs robotic vs transanal total mesorectal excision (TME) for rectal cancer: a network meta-analysis. Tech Coloproctol. 2023;27(5):345-360. https://doi.org/10.1007/s10151-022-02739-1

[31] Yi Chi Z, Gang O, Xiao Li F, et al. Laparoscopic total mesorectal excision versus transanal total mesorectal excision for mid and low rectal cancer: a systematic review and meta-analysis. Medicine (Baltimore). 2024;103(4):e36859. https://doi.org/10.1097/MD.0000000000036859

[32] Guillou PJ, Quirke P, Thorpe H, et al. Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomised controlled trial. Lancet. 2005;365(9472):1718-1726. https://doi.org/10.1016/S0140-6736(05)66545-2

[33] Quirke P, Steele R, Monson J, et al. Effect of the plane of surgery achieved on local recurrence in patients with operable rectal cancer: a prospective study using data from the MRC CR07 and NCIC-CTG CO16 randomised clinical trial. Lancet. 2009;373(9666):821-828. https://doi.org/10.1016/S0140-6736(09)60485-2

[34] Nagtegaal ID, van de Velde CJ, van der Worp E, Kapiteijn E, Quirke P, van Krieken JH. Macroscopic evaluation of rectal cancer resection specimen: clinical significance of the pathologist in quality control. J Clin Oncol. 2002;20(7):1729-1734. https://doi.org/10.1200/JCO.2002.20.7.1729

[35] Penna M, Hompes R, Arnold S, et al. Transanal total mesorectal excision: international registry results of the first 720 cases. Ann Surg. 2017;266(1):111-117. https://doi.org/10.1097/SLA.0000000000001948

[36] Wasmuth HH, Faerden AE, Myklebust TA, et al. Transanal total mesorectal excision for rectal cancer has been suspended in Norway. Br J Surg. 2020;107(1):121-130. https://doi.org/10.1002/bjs.11459

[37] Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008;336(7650):924-926. https://doi.org/10.1136/bmj.39489.470347.AD

[38] Salanti G, Higgins JPT, Ades AE, Ioannidis JPA. Evaluation of networks of randomized trials. Stat Methods Med Res. 2008;17(3):279-301. https://doi.org/10.1177/0962280207080643

[39] Chaimani A, Higgins JPT, Mavridis D, Spyridonos P, Salanti G. Graphical tools for network meta-analysis in Stata. PLoS One. 2013;8(10):e76654. https://doi.org/10.1371/journal.pone.0076654

Supplementary Material

Supplementary figures are cited in the text at: Supplementary Fig. S1 (Results 3.3, pairwise CRM meta-analysis); Supplementary Figs. S2 and S3 (Results 3.4, anastomotic leak outcomes).

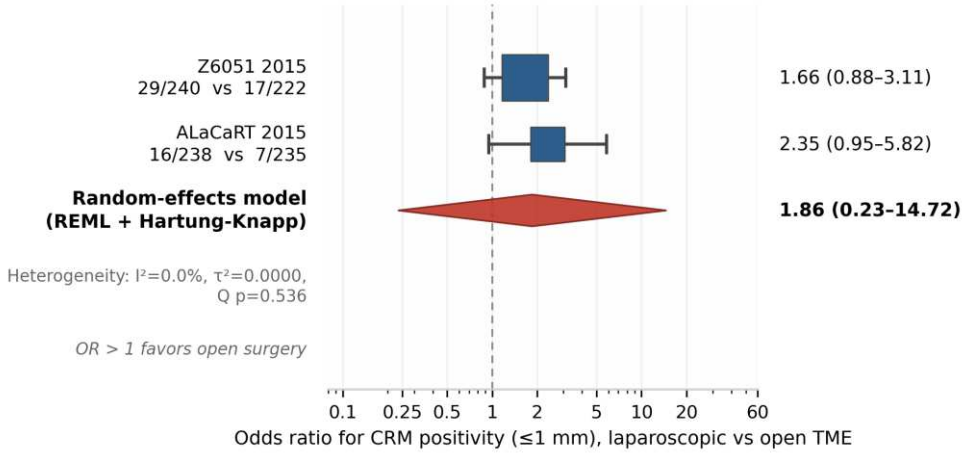

Fig. S1. Pairwise meta-analysis of CRM positivity (≤1 mm), laparoscopic versus open TME (Z6051, ALaCaRT; random-effects, Hartung-Knapp).

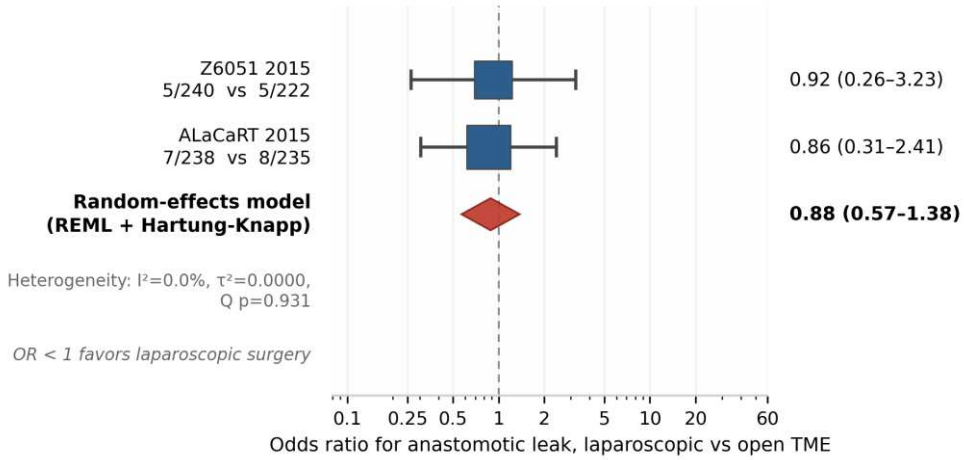

Fig. S2. Pairwise meta-analysis of anastomotic leak, laparoscopic versus open TME (Z6051, ALaCaRT).

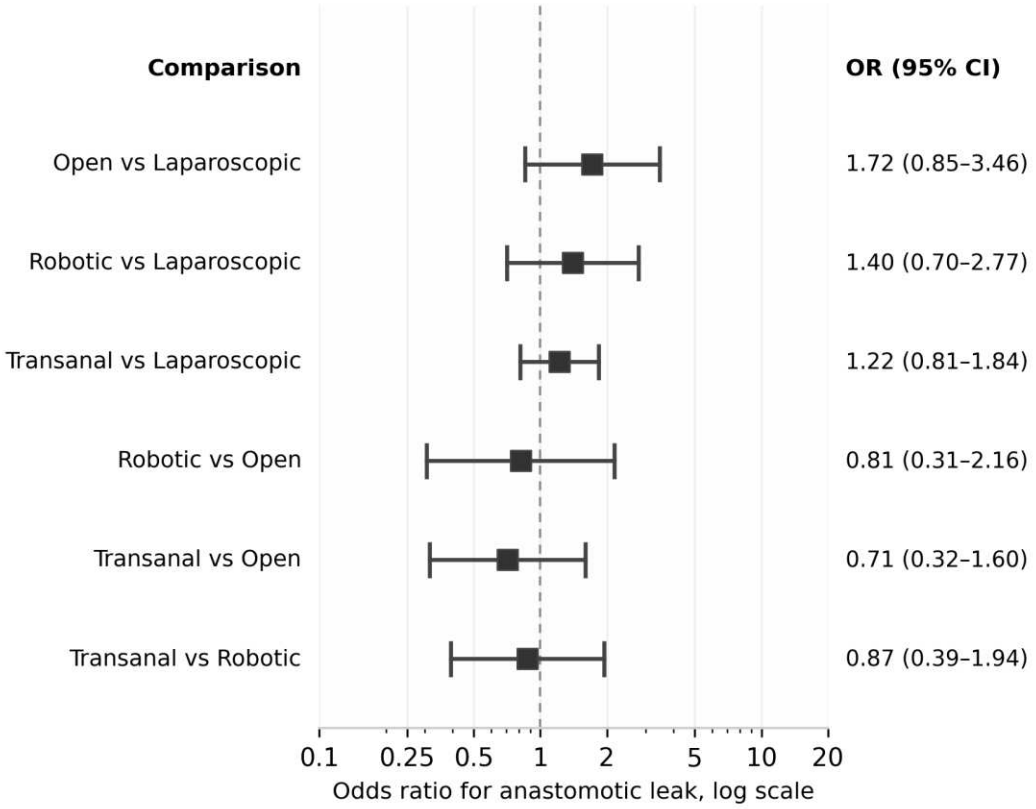

Fig. S3. Network meta-analysis of anastomotic leak (9 RCTs, I^2=0%): all pairwise comparisons.