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META-ANALYSIS

Meta-analysis of transanal *vs* laparoscopic total mesorectal excision of low rectal cancer: Importance of appropriate patient selection

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Abstract

BACKGROUND

Achieving a clear resection margins for low rectal cancer is technically challenging. Transanal approach to total mesorectal excision (TME) was introduced in order to address the challenges associated with the laparoscopic approach in treating low rectal cancers. However, previous meta-analyses have included mixed population with mid and low rectal tumours when comparing both approaches which has made the interpretation of the real differences between two approaches in treating low rectal cancer difficult.

AIM

To investigate the outcomes of transanal TME (TaTME) and laparoscopic TME (LaTME) in patients with low rectal cancer.

METHODS

A comprehensive systematic review of comparative studies was performed in line with Preferred Reporting Items for Systematic Reviews and Meta-Analyses standards. Intraoperative and postoperative complications, anastomotic leak, R0 resection, completeness of mesorectal excision, circumferential resection margin (CRM), distal resection margin (DRM), harvested lymph nodes, and operation time were the investigated outcome measures.

RESULTS

We included twelve comparative studies enrolling 969 patients comparing TaTME (n = 969) and LaTME (n = 476) in patients with low rectal tumours. TaTME was associated with significantly lower risk of postoperative complications (OR: 0.74, P = 0.04), anastomotic leak (OR: 0.59, P = 0.02), and conversion to an open procedure (OR: 0.29, P = 0.002) in comparison with LaTME. Moreover, the rate of R0 resection was significantly higher in the TaTME group (OR: 1.96, P = 0.03). Nevertheless, TaTME and LaTME were comparable in terms of rate of intraoperative complications (OR: 1.87; P = 0.23), completeness of mesoractal excision (OR: 1.57, P = 0.15), harvested lymph nodes (MD: -0.05, P = 0.96), DRM (MD: -0.94; P = 0.17), CRM (MD: 1.08, P = 0.17), positive CRM (OR: 0.64, P = 0.11) and procedure time (MD: -6.99 min, P = 0.45).

CONCLUSION

Our findings indicated that for low rectal tumours, TaTME is associated with better clinical and short term oncological outcomes compared to LaTME. More randomised controlled trials are required to confirm these findings and to evaluate long term oncological and functional outcomes.

Key Words: Total mesorectal excision; Laparoscopic; Transanal; Rectal cancer

Core Tip: The meta-analysis of best available evidence demonstrated that for low rectal tumours, Transanal total mesorectal excision (TaTME) is associated with better clinical and short term oncological outcomes compared to Laparoscopic TME. More randomised controlled trials with adequate power and high quality are required to not only confirm these findings, but also to evaluate long term oncological and functional outcomes.

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INTRODUCTION

The incidence of rectal cancer is increasing making it one of the most common cancers worldwide[1]. Rapidly evolving use of total mesorectal excision (TME) and neoadjuvant chemotherapy have led to considerable improvements in the outcomes of rectal cancer surgery[2]. A clear resection margin associated with a high quality TME is important for an ideal oncological resection, reducing the incidence of local or regional recurrence, and increasing survival from cancer[3,4].

Achieving a negative resection margins during resection of low rectal tumours can be challenging due to existence of diminishing gap between the wall of the rectum and mesorectal fascia towards the anal canal[5]. This has resulted in worse oncological outcomes associated with resection of lower rectal tumours, in comparison with resection of middle or high rectal tumours, because of greater incidence of local recurrence and positive resection margin[6]. Transanal approach to TME was introduced in order to address the challenges associated with the laparoscopic and even open TME in surgical management of low rectal cancers[7].

In 2020, in a comprehensive meta-analysis of comparative studies, we reported that Transanal TME (TaTME) led to higher R0 resection rate and number of harvested lymph nodes while decreasing rates of positive circumferential resection margin (CRM) and conversion to open procedure when compared to laparoscopic TME (LaTME)[8]. Moreover, our findings indicated that TaTME and LaTME may have similar risk of perioperative morbidity[8]. Nevertheless, most of the evaluated studies in the aforementioned meta-analysis compared TaTME and LaTME in patients with middle and low rectal tumours subjecting the findings to bias. Considering the existence of new studies focusing on the clinical outcomes of TaTME and LaTME in management of low rectal cancer, conduction of another meta-analysis is worthwhile in order to help defining more appropriate patient selection.

This study aimed to systematically evaluate the best available comparative evidence surrounding TaTME and LaTME in surgical management of low rectal cancer only and compare the outcome so both approaches using meta-analytical model.

MATERIALS AND METHODS

Study design and selection of eligible studies

In our review protocol, we highlighted the inclusion and exclusion criteria, our methodology, and evaluated outcome measures. This study was carried out in line with standards of Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement[9].

All comparative studies investigating the outcomes of transanal and laparoscopic TME in patients with low cancer were considered for inclusion. A rectal tumour within 6 cm of anal verge was considered as a low rectal tumour. We considered all adult (aged > 18 years) patients undergoing TaTME or LaTME for low rectal cancer. TaTME was the intervention of interest and LaTME was the comparison of interest.

The primary outcome measures were intraoperative and postoperative complications, and anastomotic leak. The investigated primary oncological outcome measures were R0 resection, CRM, positive CRM, distal resection margin (DRM), completeness of mesorectal excision, and number of harvested lymph nodes. Moreover, conversion to open and operative time were defined as secondary outcome measures.

Literature search strategy

Following sources: MEDLINE, Web of Science, and CENTRAL were searched by two independent authors. Appendix 1 outlines the used search strategy (Supplementary Table 1). The most recent literature search was carried out on 08 July, 2022. Moreover, we screened the reference lists of the included studies and previous review articles in order to identify more relevant articles.

Study selection

Two independent review authors screened the title and abstract of the identified studies. This was followed by retrieval of the full-texts of the related studies and their assessment in line with our inclusion and exclusion criteria. Discrepancies in this stage were addressed by discussion among the reviewers.

Extraction and management of data

We created a data extraction tool and extracted details of study-related data, data regarding demographic characteristics of the included patients in each study and outcome data. Two independent reviewers were involved in this process. Disagreements between the authors were resolved following discussion. In case of no resolution, an additional reviewer was consulted.

Assessment of risk of bias

The methodological quality of the included studies was assessed by 2 review authors who determined their associated risk of bias using the Newcastle-Ottawa scale[10] for observational studies and Cochrane's tool[11] for randomized controlled trials (RCTs). We resolved disagreements in methodological quality assessment by discussion between the reviewers. However, if disagreement remained unresolved, a third reviewer was consulted as an adjudicator.

Summary measures and synthesis

For dichotomous outcome measures the odds ratio (OR) was calculated as the summary measures. For continuous outcome parameters, the mean difference (MD) between the two groups was calculated. If mean values were not reported, we extracted data on median and interquartile range and converted those to mean and standard deviation using Hozo *et al*[12]'s equation.

The unit of analysis for all of the analyzed outcome measures in this study was an individual participant. We did not require contacting the authors of the included studies to ask for any potential missing information.

Data analysis was carried out *via* Review Manager 5.4 software[11]. One author extracted and entered the data into the software and another author cross-checked the data. Random-effects modelling were used for analysis of all outcomes. We reported outcome of analyses in Forest plots with 95% confidence intervals (CIs).

The Cochran Q test (χ^2) was used to assess between-study heterogeneity. We calculated I^2 and used the following guide for interpreting the degree of heterogeneity: 0% to 50% might not be important; 50% to 75%: May represent moderate heterogeneity; 75% to 100% may represent substantial heterogeneity. Moreover, we constructed funnel plots for any outcome synthesis involving more than 10 studies.

We performed sensitivity analyses to assess for potential sources of heterogeneity and evaluate the robustness of our findings. Finally, we conducted leave-one-out sensitivity analysis to assess the effect of each study on the overall effect size and heterogeneity.

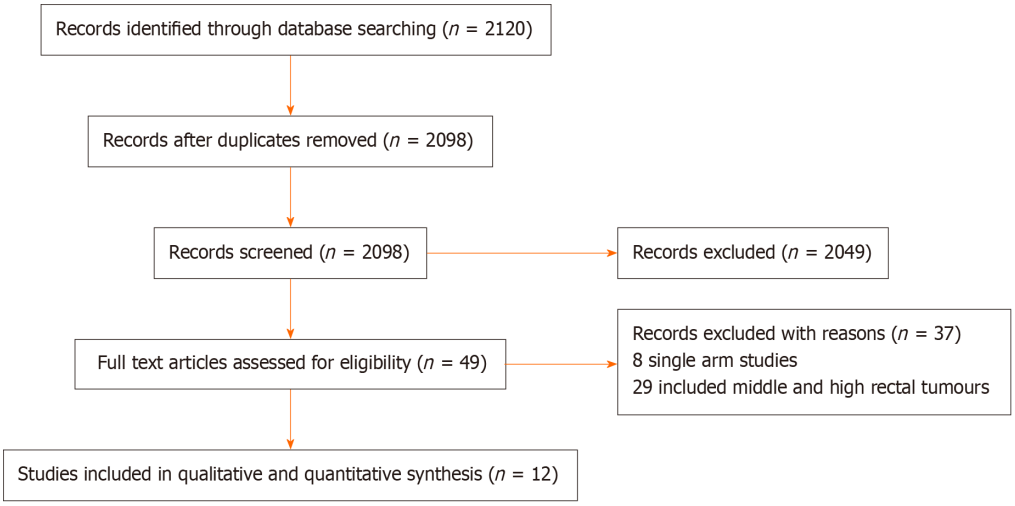

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Figure 1 Study flow diagram.

RESULTS

The literature search resulted in 2120 articles. Following further assessment of the aforementioned articles, 12 comparative studies (2 randomised and 10 observational studies)[13-24] met the inclusion criteria (Figure 1). The included studies enrolled 969 patients of whom 493 underwent TaTME and the remaining 476 patients had LaTME for rectal cancer.

Table 1 presents the included studies related data. Table 2 presents baseline demographic and clinical characteristics of the included patients. The patients in the transanal and laparoscopic groups were of similar age (P = 0.53), gender (P = 0.19), and BMI (P = 0.68). No significant difference was found between the TaTME and LaTME groups in rectal cancer stages I (P = 0.29), II (P = 0.30) and III (P = 0.95). Furthermore, the mean distance of the tumour to the anal verge in the TaTME and LaTME groups were 3.4 cm ± 1.4 cm and 3.6 cm ± 1.5 cm, respectively, which was not significantly different (P = 0.07). Neoadjuvant chemotherapy was carried our similarly between two groups (P = 0.22).

Methodological appraisal

The methodological assessment of 10 observational studies is presented in Table 3. In 7 studies, the risk of bias was low and in 3 studies it was moderate. Moreover, the outcome of methodological assessment of the included randomized controlled trials is demonstrated by Figure 2.

Data synthesis

Outcomes are summarised in Figures 3 and 4.

Intraoperative complications: Six studies (382 patients) reported intraoperative complications as an outcome. The rate of intraoperative complications in the TaTME and LaTME were 7.3% and 4.2%, respectively. There was no significant difference in intraoperative complications between TaTME and LaTME (OR: 1.87; 95%CI: 0.68-5.18, P = 0.23). There was low between-study heterogeneity (I^2 = 6%, P = 0.36).

Postoperative complications: Eleven studies (923 patients) reported postoperative complications as an outcome. The rate of overall postoperative complications in the TaTME and LaTME were 30.0% and 35.9%, respectively. TaTME significantly reduced postoperative complications when compared to LaTME (OR: 0.74; 95%CI: 0.56-0.99, P = 0.04). There was moderate heterogeneity among the included studies (I^2 = 2%, P = 0.42).

Anastomotic leak: This outcome was reported by eleven studies (896 patients). Anastomotic leak occurred in 10.1% and 15.5% of patients in the TaTME and LaTME groups, respectively. TaTME was associated with a significantly lower rate of anastomotic leak compared with LaTME (OR: 0.59; 95%CI: 0.38-0.91, P = 0.02). Heterogeneity among the included studies was low (I^2 = 0%, P = 0.49).

R0 resection: Nine studies (609 patients) reported R0 resection as an outcome. An R0 resection was achieved in 93.5% and 87.8% of patients in the TaTME and LaTME groups, respectively. The rate of R0 resection was significantly higher in the TaTME group (OR: 1.96; 95%CI: 1.07-3.58, P = 0.03). Low between-study heterogeneity was detected (I^2 = 0%, P = 0.51).

Table 1 Included studies related data

Ref.	Publication year	Journal	Country	Study design	TaTME	LaTME
de'Angelis *et al*[13]	2015	*Langenbecks Arch Surg*	France	Retrospective observational study	32	32
Kanso *et al*[14]	2015	*Dis Colon Rectum*	France	Retrospective observational study	51	34
Pontallier *et al*[15]	2016	*Surg Endosc*	France	RCT	38	34
Marks *et al*[16]	2016	*Tech. Coloproctol*	United States	Retrospective observational study	17	17
Lelong *et al*[17]	2017	*J Am Coll Surg*	France	Retrospective observational study	34	38
Denost *et al*[18]	2018	*Surg Endosc*	France	RCT	50	50
Mege *et al*[19]	2018	*Colorectal Dis*	France	Retrospective observational study	34	34
Rubinkiewicz *et al*[20]	2018	*Cancer Manag Res*	Poland	Retrospective observational study	35	35
Roodbeen *et al*[21]	2019	*Surg Endosc*	Netherlands	Retrospective observational study	41	41
Rubinkiewicz *et al*[22]	2019	*BMC Surg*	Poland	Prospective observational study	23	23
Ren *et al*[23]	2021	*Asian J Surg*	China	Prospective observational study	32	32
Li *et al*[24]	2022	*Gastroenterol Res Pract*	China	Prospective observational study	106	106

TaTME: Transanal total mesorectal excision, LaTME: Laparoscopic total mesorectal excision; RCT: Randomised controlled trial.

Completeness of mesorectal excision: This outcome was reported by nine studies (766 patients). The rate of completeness of mesorectal excision in the TaTME and LaTME groups were 81.4% and 74.0%, respectively. The pooled analysis did not demonstrated similar rate of completeness of mesorectal excision between two groups (OR: 1.57; 95%CI: 0.85-2.90, $P = 0.15$). There was moderate between-study heterogeneity ($I^2 = 60\%$, $P = 0.01$).

Number of harvested lymph nodes: Eight studies (747 patients) reported the number of harvested lymph nodes in the TaTME and LaTME groups. The mean number of harvested lymph nodes in the TaTME was 16.1 ± 2.1, while it was 16.3 ± 3.2 in the LaTME group. The pooled analysis demonstrated no significant difference in the number of harvested lymph nodes between two groups (MD: -0.05; 95%CI: -1.98-1.89, $P = 0.96$). The between-study heterogeneity was moderate ($I^2 = 71\%$, $P = 0.001$).

DRM: Eight studies (745 patients) reported DRM in their study groups. The mean DRM in the TaTME group was 15.8 mm ± 3.9 mm whereas it was 17.6 mm ± 3.8 mm in the LaTME group. The pooled analysis found no significant difference in DRM between two groups (MD: -0.94; 95%CI: -2.26-0.39, $P = 0.17$). There was low heterogeneity among the included studies ($I^2 = 0\%$, $P = 0.53$).

CRM: Six studies (465 patients) reported CRM in their study groups. The mean CRM in the TaTME group was 8.5 mm ± 1.2 mm and it was 8.1 mm ± 2.9 mm in the LaTME group. The pooled analysis did not identify any significant difference in CRM between two groups (MD: 1.08; 95%CI: -0.46-2.61, $P = 0.17$). There was moderate between-study heterogeneity ($I^2 = 71\%$, $P = 0.004$).

Positive CRM: Eight studies (717 patients) reported the rate of positive CRM in their study groups. The rate of positive CRM in the TaTME group was 9.0% and it was 13.3% in the LaTME group. There was no significant difference in the rate of positive CRM between two groups (OR: 0.64; 95%CI: 0.37-1.10, $P = 0.11$). Between-study heterogeneity was low ($I^2 = 0\%$, $P = 0.59$).

Procedure time: Ten studies (889 patients) reported the procedure time as an outcome. The mean procedure time in the TaTME and LaTME groups were 274.1 min ± 91.8 min and 282.4 min ± 103.0 min, respectively. There was no significant difference in procedure time between two groups (MD: -6.99 min; 95%CI: -25.28-11.30, $P = 0.45$). Heterogeneity among the studies was significant ($I^2 = 86\%$, $P < 0.00001$).

Conversion to open: This outcome was reported by eleven studies (923 patients). The rate of conversion to an open procedure in the TaTME group was 1.5% and it was 7.5% in the LaTME group. The conversion rate was significantly lower in the TaTME group compared to the LaTME group (OR: 0.29; 95%CI: 0.13-0.64, $P = 0.002$). There was low between-study heterogeneity ($I^2 = 0\%$, $P = 0.54$).

Considering that the included study inadequately reported length of hospital stay as an outcome, we were unable to conduct an analysis on this outcome.

Sensitivity analysis

There was no change in the direction of pooled effect size when the risk ratio, or risk difference was

Table 2 Included studies related data

Ref.	Publication year	Age	Gender	BMI	Neoadjuvant therapy	Tumour stage	Tumour location	Distance of tumour to anal verge
de'Angelis[13]	2015	64.91 ± 10.05 *vs* 67.16 ± 9.61	66% *vs* 66%	25.19 ± 3.52 *vs* 24.53 ± 3.19	100% *vs* 100%	I: 65.6% *vs* 56.3%; II: 31.3% *vs* 40.6%; III: 3.1% *vs* 3.1%	Low rectum	4 (2.5-5.0) *vs* 3.7 (2.5-5.0)
Kanso *et al*[14]	2015	59 ± 11 (32-79) *vs* 59 ± 11 (33-82)	71% *vs* 77%	24 ± 4 (17-32) *vs* 24 ± 4 (15-34)	80% *vs* 79%	NR	Lower rectum	1.6 ± 0.8 (0-3.5) *vs* 1.8 ± 0.9 (0-3.5)
Pontallier *et al*[15]	2016	62 (39-81) *vs* 62 (35-82)	68% *vs* 62%	25.5 *vs* 24.8	79% *vs* 88%	I: 21% *vs* 21%; II: 19% *vs* 14%; III: 60% *vs* 65%	Low rectum	4 (2-6) *vs* 4 (2-6)
Marks *et al*[16]	2016	60 *vs* 59	NR	25.9 *vs* 26.4	NR	I: 29.4% *vs* 23.5%; II: 70.6% *vs* 76.5%	Low rectum	< 4 *vs* < 4
Lelong *et al*[17]	2017	NR	68% *vs* 58%	24 (18.6-45.0) *vs* 24.2(17.7-32.7)	88.2% *vs* 92.1%	I: 17.6% *vs* 23.7%; II: 70.6% *vs* 71.0%; III: 11.8% *vs* 5.3%	Low rectum	NR
Denost *et al*[18]	2018	64 (39-82) *vs* 63 (31-90)	74% *vs* 64%	25.1 (17.3-33.2) *vs* 25.6 (18.3-38.3)	78% *vs* 84%	NR	Low rectum	4 (2-6) *vs* 4 (2-6)
Mege *et al*[19]	2018	58 ± 14 *vs* 59 ± 13	68% *vs* 68%	25 ± 4 *vs* 25 ± 3	85% *vs* 85%	I: 29.4% *vs* 11.8%; II: 67.6% *vs* 82.3%; III: 43.5% *vs* 47.8%; IV: 2.9% *vs* 5.9%	Low rectum	NR
Rubinkiewicz *et al*[20]	2018	64.3 ± 10.1 *vs* 60.3 ± 10.2	69% *vs* 69%	26.10 ± 4.09 *vs* 27.10 ± 4.71	88.6% *vs* 88.6%	I: 42.9% *vs* 45.7%; II: 57.1% *vs* 54.3%	Low rectum	2.90 ± 1.17 *vs* 3.19 ± 1.47
Roodbeen *et al*[21]	2019	62.5 ± 10.7 *vs* 66.0 ± 9.2	82.9% *vs* 78%	26.7 ± 1.9 *vs* 26.1 ± 4.0	43.9% *vs* 43.9%	I: 22.0% *vs* 19.5%; II: 36.6% *vs* 39%; III: 31.7% *vs* 31.7%; IV: 9.8% *vs* 9.8%	Low rectum	2.0 (0.0-4.0) *vs* 1.5 (0.0-3.0)
Rubinkiewicz *et al*[22]	2019	60 (51-67) *vs* 64 (58-67)	69% *vs* 69%	26 (22.8-29.7) *vs* 26.5 (23.8-30.6)	78.2% *vs* 82.6%	NR	Low rectum	3(2-4) *vs* 4 (3-5)
Ren *et al*[23]	2021	65.78 ± 12.37 *vs* 67.16 ± 10.03	59.3% *vs* 56.2%	22.87 ± 2.66 *vs* 23.05 ± 2.70	71.8% *vs* 65.6%	I: 34.3% *vs* 37.5%; II: 28.1% *vs* 31.2%; III: 31.2% *vs* 21.8%	Low rectum	5.53 ± 0.98 *vs* 5.78 ± 0.94
Li *et al*[24]	2022	55 ± 12 (23-78) *vs* 56 ± 12 (26-79)	100% *vs* 100%	23:0 ± 2.9 *vs* 22:9 ± 3.2	100% *vs* 100%	NR	Low rectum	3.6 ± 0.9 (2.0-5.0) *vs* 3.8 ± 0.9 (1.4-5.0)

Transanal total mesorectal excision *vs* Laparoscopic total mesorectal excision. BMI: Body mass index; NR: Not reported.

calculated or during leave-one-out sensitivity analysis.

DISCUSSION

In view of ongoing debates regarding the best surgical approach for resection of low rectal cancer, we conducted a comprehensive systematic review and meta-analysis to evaluate comparative outcomes of transanal *vs* laparoscopic TME in management of low rectal cancer. We identified two RCTs and 10 observational studies[13-24] enrolling 969 patients of whom 493 had TaTME and 476 patients had LaTME for low rectal tumour. The subsequent outcome synthesis showed that TaTME significantly reduced rate of postoperative complications, anastomotic leak, and conversion to open in comparison to LaTME. Moreover, TaTME resulted in significantly higher rate of R0 resection. However, no significant difference was found in intraoperative complications, completeness of mesoractal excision, harvested lymph nodes, DRM, CRM, positive CRM and procedure time between TaTME and LaTME

The between-study heterogeneity in the analyses of intraoperative and postoperative complications, anastomotic leak, R0 resection, DRM, positive CRM, and conversion to open were low suggesting that the reported findings with respect to these outcomes can be considered robust. Moderate heterogeneity

Table 3 Methodological quality of the observational studies assessed with the Newcastle-Ottawa scale

Author	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts	Total score
de'Angelis[13], 2015	*	*	*	*	**	*	*	*	9
Kanso *et al*[14], 2015	*	*	*	*	**	*	*	*	9
Marks *et al*[16], 2016	*	*	*	*	-	*	*	*	7
Lelong *et al*[17], 2017	*	*	*	*	*	*	*	*	8
Mege *et al*[19], 2018	*	*	*	*	**	*	*	*	9
Rubinkiewicz *et al*[20], 2018	*	*	*	*	**	*	*	*	9
Roodbeen *et al* [21], 2019	*	*	*	*	**	*	*	*	9
Rubinkiewicz *et al*[22], 2019	*	*	*	*	*	*	*	*	8
Ren *et al*[23], 2021	*	*	*	*	**	*	*	*	9
Li *et al*[24], 2022	*	*	*	*	**	*	*	*	9

among the included studies in the analyses of completeness of mesorectal excision, and number of harvested lymph nodes may suggest variation of reporting in the included studies on these outcomes. There was high between-study heterogeneity regarding procedure time suggesting that our findings about procedure time may be less robust.

The findings of our meta-analysis are not consistent with some of the findings of our previous meta-analysis on this topic published in 2020[8]. The simple explanation for such disagreement is the difference in the inclusion criteria of the two studies with regards to the location of the rectal cancer. We only included low rectal cancer patients in this meta-analysis while previously we included both middle and low rectal cancer patients. In fact, as a direction for future research, in our previous meta-analysis we encouraged future studies to consider patients with low rectal cancer only when comparing TaTME and LaTME to evaluate a more realistic comparison between these two management approaches[8]. This is indeed reassuring to observe growing evidence in the context of comparative outcomes of TaTME and LaTME in management of low rectal cancer. The appropriate patient selection in this context is of great importance as inappropriate patient selection for TaTME has been demonstrated to result in

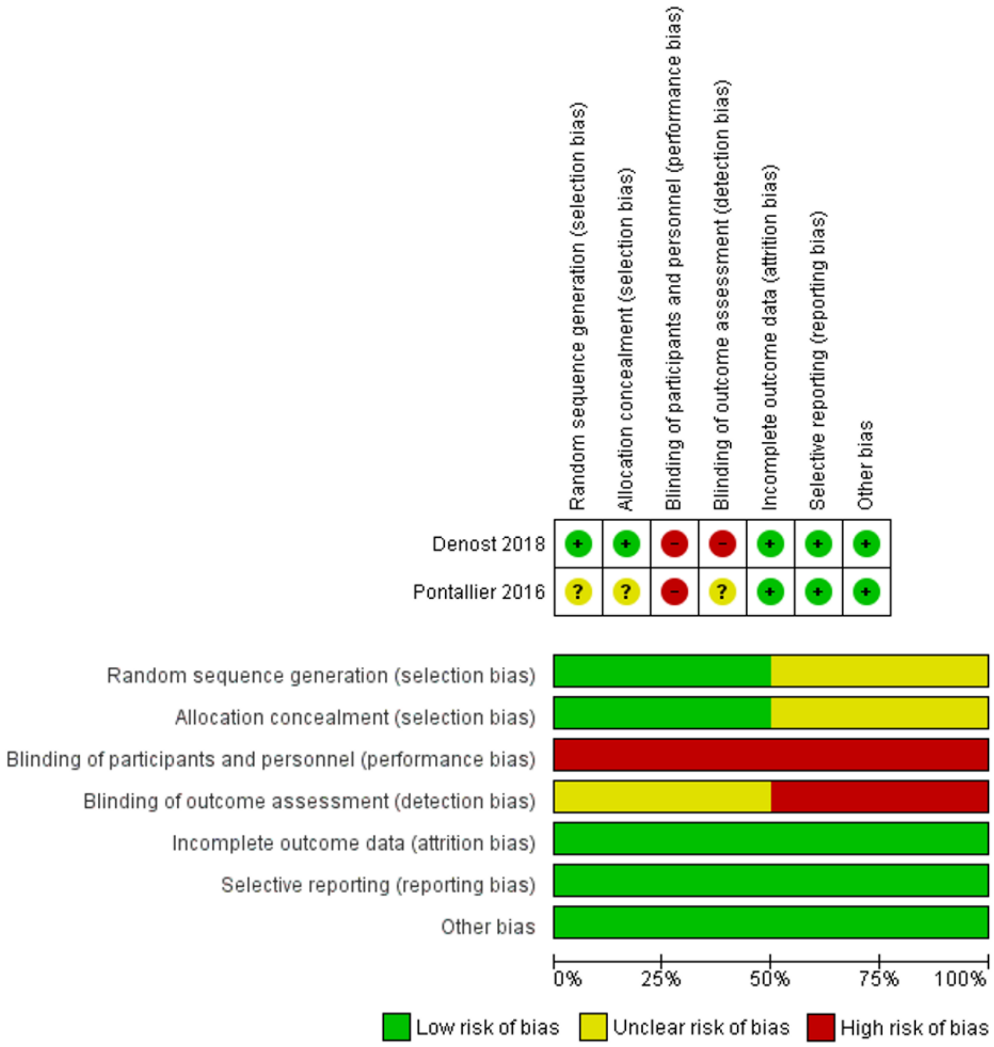

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Figure 2 Risk of bias summary and graph showing authors' judgments about each risk of bias item.

unfavourable outcomes of TaTME leading to suspension of TaTME in some countries. Wasmuth *et al*[25] reported high rate of anastomotic leak and local recurrence associated with TaTME, the findings that led to suspicion of TaTME in Norway. However, only 5% of their included patients had low rectal tumours with the remaining patients having middle or high rectal cancers. Moreover, the study lacked a control group, hence low level of evidence.

In the current meta-analysis, we independently evaluated the baseline characteristics of the study population to assess if the patients in the TaTME and LaTME groups were comparable. We found no significant difference in age, gender, BMI, rate of neoadjuvant chemotherapy, and stage of cancer between two groups. Moreover, we demonstrated similar distance between the distal tumour and anal verge between the TaTME and LaTME patients. This is of a cardinal importance as TaTME has been introduced to address the challenges associated with open and laparoscopic approaches in resecting very low rectal cancers, particularly in male patients with narrow pelvis[8]. Therefore, comparability of our included populations in both groups makes our findings more robust.

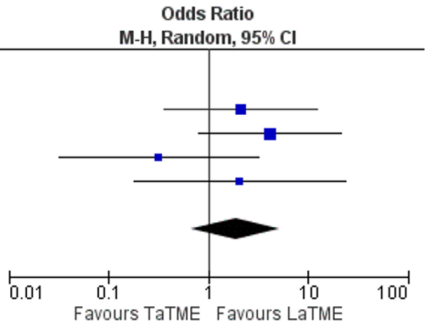
We were not able to conduct any analyses on comparative functional outcomes of TaTME and LaTME considering that only two of the included studies reported such outcomes. Lelong *et al*[17] compared functional outcomes of TaTME and LaTME and demonstrated no significant difference in urinary complications and faecal incontinence between two groups. Rubinkiewicz *et al*[22] also investigated functional outcomes in patients undergoing TaTME and LaTME for low rectal tumours and reported no significant differences in risk of low anterior resection syndrome between two groups and its severity. The authors found comparable median Wexner score in both groups[22]. Considering the current limited evidence in the context of functional outcomes of TaTME compared with LaTME, no definitive conclusions can be made.

Although we were not able to analyse long term oncological outcomes including disease recurrence, the findings of one of our included RCTs in this context is important. After 5 years follow-up, Denost *et al*[18] reported no significant differences in long-term outcomes between TaTME and LaTME. Although

A

Study or Subgroup	TaTME Events	TaTME Total	LaTME Events	LaTME Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
de'Angelis 2015	0	32	0	32		Not estimable	2015
Marks 2016	0	17	0	17		Not estimable	2016
Rubinkiewicz 2018	4	35	2	35	30.5%	2.13 [0.36, 12.46]	2018
Mege 2018	7	34	2	34	34.5%	4.15 [0.79, 21.66]	2018
Roodbeen 2019	1	41	3	41	18.5%	0.32 [0.03, 3.18]	2019
Ren 2020	2	32	1	32	16.5%	2.07 [0.18, 24.01]	2020
Total (95% CI)		**191**		**191**	**100.0%**	**1.87 [0.68, 5.18]**	
Total events	14		8				

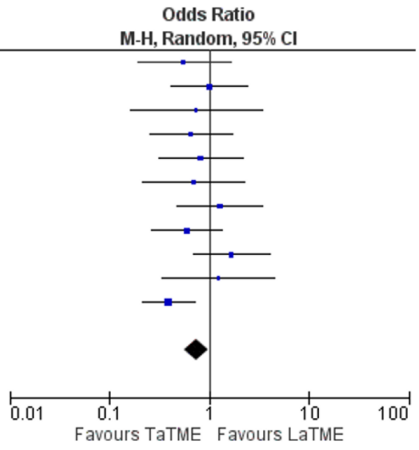
Heterogeneity: Tau² = 0.07; Chi² = 3.20, df = 3 (*P* = 0.36); I² = 6%
Test for overall effect: Z = 1.21 (*P* = 0.23)



B

Study or Subgroup	TaTME Events	TaTME Total	LaTME Events	LaTME Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
de'Angelis 2015	8	32	12	32	7.0%	0.56 [0.19, 1.63]	2015
Kanso 2015	24	51	16	34	10.6%	1.00 [0.42, 2.39]	2015
Marks 2016	4	17	5	17	3.5%	0.74 [0.16, 3.41]	2016
Pontallier 2016	12	38	14	34	8.6%	0.66 [0.25, 1.73]	2016
Lelong 2017	11	34	14	38	8.5%	0.82 [0.31, 2.17]	2017
Rubinkiewicz 2018	6	35	8	35	5.8%	0.70 [0.21, 2.28]	2018
Mege 2018	14	34	12	34	8.4%	1.28 [0.48, 3.42]	2018
Denost 2018	16	50	22	50	12.0%	0.60 [0.27, 1.35]	2018
Roodbeen 2019	19	41	14	41	10.1%	1.67 [0.68, 4.06]	2019
Ren 2020	6	32	5	32	4.8%	1.25 [0.34, 4.59]	2020
Li 2022	21	106	41	106	20.6%	0.39 [0.21, 0.73]	2022
Total (95% CI)		**470**		**453**	**100.0%**	**0.74 [0.56, 0.99]**	
Total events	141		163				

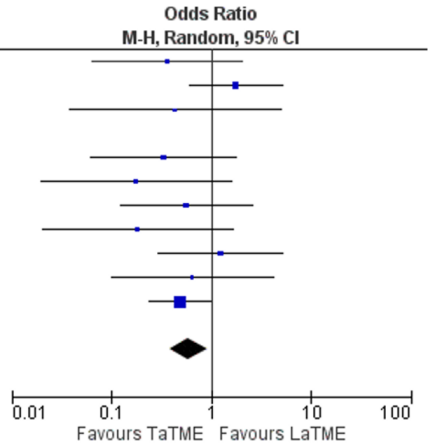
Heterogeneity: Tau² = 0.00; Chi² = 10.19, df = 10 (*P* = 0.42); I² = 2%
Test for overall effect: Z = 2.03 (*P* = 0.04)



C

Study or Subgroup	TaTME Events	TaTME Total	LaTME Events	LaTME Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
de'Angelis 2015	2	32	5	32	6.3%	0.36 [0.06, 2.01]	2015
Kanso 2015	14	51	6	34	16.0%	1.77 [0.60, 5.17]	2015
Pontallier 2016	1	38	2	34	3.1%	0.43 [0.04, 4.99]	2016
Marks 2016	0	17	0	17		Not estimable	2016
Lelong 2017	2	34	6	38	6.6%	0.33 [0.06, 1.78]	2017
Mege 2018	1	34	5	34	3.8%	0.18 [0.02, 1.59]	2018
Rubinkiewicz 2018	3	35	5	35	8.1%	0.56 [0.12, 2.56]	2018
Denost 2018	1	50	5	50	3.9%	0.18 [0.02, 1.63]	2018
Roodbeen 2019	5	28	4	27	9.0%	1.25 [0.30, 5.26]	2019
Ren 2020	2	32	3	32	5.4%	0.64 [0.10, 4.14]	2020
Li 2022	15	106	27	106	37.9%	0.48 [0.24, 0.97]	2022
Total (95% CI)		**457**		**439**	**100.0%**	**0.59 [0.38, 0.91]**	
Total events	46		68				

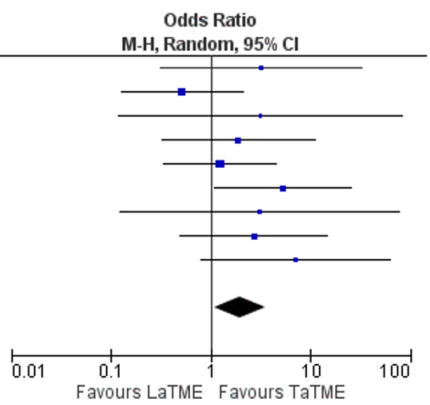
Heterogeneity: Tau² = 0.00; Chi² = 8.47, df = 9 (*P* = 0.49); I² = 0%
Test for overall effect: Z = 2.41 (*P* = 0.02)



D

Study or Subgroup	TaTME Events	TaTME Total	LaTME Events	LaTME Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
de'Angelis 2015	31	32	29	32	6.8%	3.21 [0.32, 32.60]	2015
Kanso 2015	43	51	31	34	18.4%	0.52 [0.13, 2.12]	2015
Marks 2016	17	17	16	17	3.4%	3.18 [0.12, 83.76]	2016
Lelong 2017	32	34	34	38	11.7%	1.88 [0.32, 10.99]	2017
Mege 2018	29	34	28	34	21.7%	1.24 [0.34, 4.54]	2018
Denost 2018	48	50	41	50	14.4%	5.27 [1.08, 25.78]	2018
Rubinkiewicz 2018	35	35	34	35	3.5%	3.09 [0.12, 78.41]	2018
Roodbeen 2019	39	41	36	41	12.6%	2.71 [0.49, 14.84]	2019
Ren 2020	31	32	26	32	7.6%	7.15 [0.81, 63.30]	2020
Total (95% CI)		**326**		**313**	**100.0%**	**1.96 [1.07, 3.58]**	
Total events	305		275				

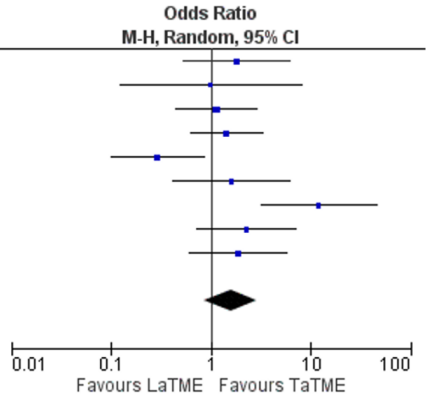
Heterogeneity: Tau² = 0.00; Chi² = 7.24, df = 8 (*P* = 0.51); I² = 0%
Test for overall effect: Z = 2.19 (*P* = 0.03)



E

Study or Subgroup	TaTME Events	TaTME Total	LaTME Events	LaTME Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
de'Angelis 2015	27	32	24	32	10.8%	1.80 [0.52, 6.25]	2015
Marks 2016	15	17	15	17	6.0%	1.00 [0.12, 8.06]	2016
Lelong 2017	19	34	20	38	13.4%	1.14 [0.45, 2.89]	2017
Denost 2018	35	50	31	50	14.3%	1.43 [0.62, 3.29]	2018
Mege 2018	18	34	27	34	12.2%	0.29 [0.10, 0.85]	2018
Rubinkiewicz 2018	31	35	29	35	9.9%	1.60 [0.41, 6.26]	2018
Roodbeen 2019	38	41	21	41	10.2%	12.06 [3.21, 45.40]	2019
Ren 2020	26	32	21	32	11.5%	2.27 [0.72, 7.16]	2020
Li 2022	101	106	97	106	11.7%	1.87 [0.61, 5.79]	2022
Total (95% CI)		**381**		**385**	**100.0%**	**1.57 [0.85, 2.90]**	
Total events	310		285				

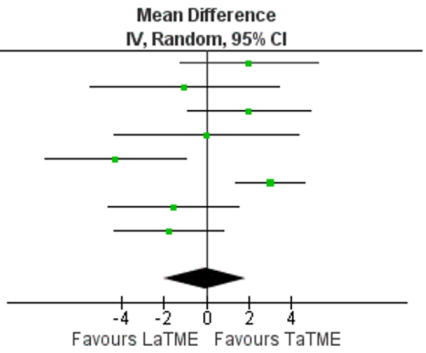
Heterogeneity: Tau² = 0.50; Chi² = 19.79, df = 8 (*P* = 0.01); I² = 60%
Test for overall effect: Z = 1.44 (*P* = 0.15)



F

Study or Subgroup	TaTME Mean	TaTME SD	TaTME Total	LaTME Mean	LaTME SD	LaTME Total	Weight	Mean Difference IV, Random, 95% CI	Year
Kanso 2015	15	8	51	13	7	34	12.3%	2.00 [-1.22, 5.22]	2015
de'Angelis 2015	17.6	7.14	32	18.63	10.7	32	9.4%	-1.03 [-5.49, 3.43]	2015
Lelong 2017	14	7	34	12	5.25	38	13.2%	2.00 [-0.88, 4.88]	2017
Mege 2018	14	10	34	14	8	34	9.7%	0.00 [-4.30, 4.30]	2018
Denost 2018	16.5	8	50	20.75	8.9	50	12.1%	-4.25 [-7.57, -0.93]	2018
Roodbeen 2019	18.75	3.75	41	15.75	3.76	41	16.5%	3.00 [1.37, 4.63]	2019
Ren 2020	19.5	6.54	32	21.06	5.94	32	12.7%	-1.56 [-4.62, 1.50]	2020
Li 2022	13.75	7.8	106	15.5	10.9	106	14.1%	-1.75 [-4.30, 0.80]	2022
Total (95% CI)			**380**			**367**	**100.0%**	**-0.05 [-1.98, 1.89]**	

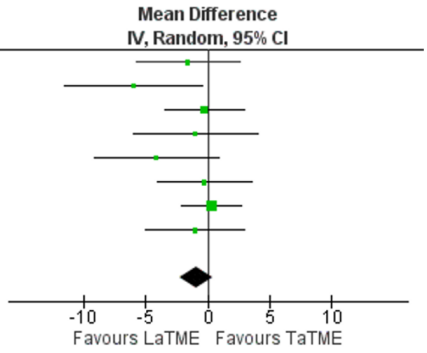
Heterogeneity: Tau² = 5.22; Chi² = 23.96, df = 7 (*P* = 0.001); I² = 71%
Test for overall effect: Z = 0.05 (*P* = 0.96)



G

Study or Subgroup	TaTME Mean	TaTME SD	TaTME Total	LaTME Mean	LaTME SD	LaTME Total	Weight	Mean Difference IV, Random, 95% CI	Year
de'Angelis 2015	21.32	8.59	32	22.92	8.44	32	10.1%	-1.60 [-5.77, 2.57]	2015
Kanso 2015	12	9	51	18	15	34	5.6%	-6.00 [-11.61, -0.39]	2015
Denost 2018	12.5	8	50	12.75	8.38	50	17.0%	-0.25 [-3.46, 2.96]	2018
Mege 2018	13	9	34	14	12	34	6.9%	-1.00 [-6.04, 4.04]	2018
Rubinkiewicz 2018	15.7	9.2	35	19.8	12.2	35	6.8%	-4.10 [-9.16, 0.96]	2018
Roodbeen 2019	22.5	8.66	41	22.77	9.1	41	11.9%	-0.27 [-4.12, 3.58]	2019
Ren 2020	17.7	3.4	32	17.4	6	32	30.7%	0.30 [-2.09, 2.69]	2020
Li 2022	12	9	106	13	19	106	11.0%	-1.00 [-5.00, 3.00]	2022
Total (95% CI)			**381**			**364**	**100.0%**	**-0.94 [-2.26, 0.39]**	

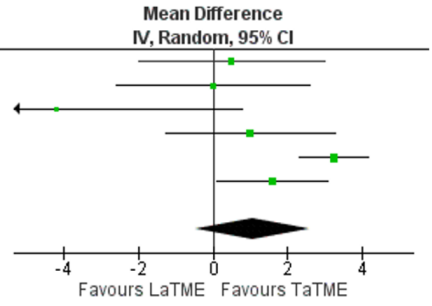
Heterogeneity: Tau² = 0.00; Chi² = 6.04, df = 7 (*P* = 0.53); I² = 0%
Test for overall effect: Z = 1.39 (*P* = 0.17)



H

Study or Subgroup	TaTME Mean	TaTME SD	TaTME Total	LaTME Mean	LaTME SD	LaTME Total	Weight	Mean Difference IV, Random, 95% CI	Year
de'Angelis 2015	9.68	4.57	32	9.19	5.55	32	15.6%	0.49 [-2.00, 2.98]	2015
Kanso 2015	7	6	51	7	6	34	15.1%	0.00 [-2.60, 2.60]	2015
Rubinkiewicz 2018	9.9	7.8	35	14.1	12.9	35	7.0%	-4.20 [-9.19, 0.79]	2018
Denost 2018	8.5	5.8	50	7.5	5.8	50	16.8%	1.00 [-1.27, 3.27]	2018
Roodbeen 2019	9	2.29	41	5.75	2.02	41	24.2%	3.25 [2.32, 4.18]	2019
Ren 2020	6.81	2.99	32	5.22	3.05	32	21.3%	1.59 [0.11, 3.07]	2020
Total (95% CI)			**241**			**224**	**100.0%**	**1.08 [-0.46, 2.61]**	

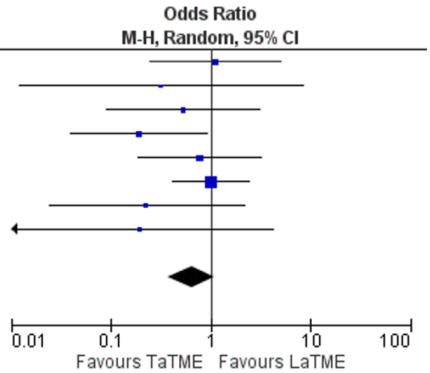
Heterogeneity: Tau² = 2.31; Chi² = 17.38, df = 5 (*P* = 0.004); I² = 71%
Test for overall effect: Z = 1.37 (*P* = 0.17)



I

Study or Subgroup	TaTME Events	TaTME Total	LaTME Events	LaTME Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Kanso 2015	5	51	3	34	13.1%	1.12 [0.25, 5.04]	2015
Marks 2016	0	17	1	17	2.8%	0.31 [0.01, 8.27]	2016
Lelong 2017	2	34	4	38	9.5%	0.53 [0.09, 3.10]	2017
Denost 2018	2	50	9	50	11.7%	0.19 [0.04, 0.93]	2018
Mege 2018	4	34	5	34	14.8%	0.77 [0.19, 3.17]	2018
Roodbeen 2019	19	41	19	41	39.2%	1.00 [0.42, 2.38]	2019
Ren 2020	1	32	4	32	5.8%	0.23 [0.02, 2.14]	2020
Li 2022	0	106	2	106	3.2%	0.20 [0.01, 4.14]	2022
Total (95% CI)		**365**		**352**	**100.0%**	**0.64 [0.37, 1.10]**	
Total events	33		47				

Heterogeneity: Tau² = 0.00; Chi² = 5.56, df = 7 (*P* = 0.59); I² = 0%
Test for overall effect: Z = 1.62 (*P* = 0.11)



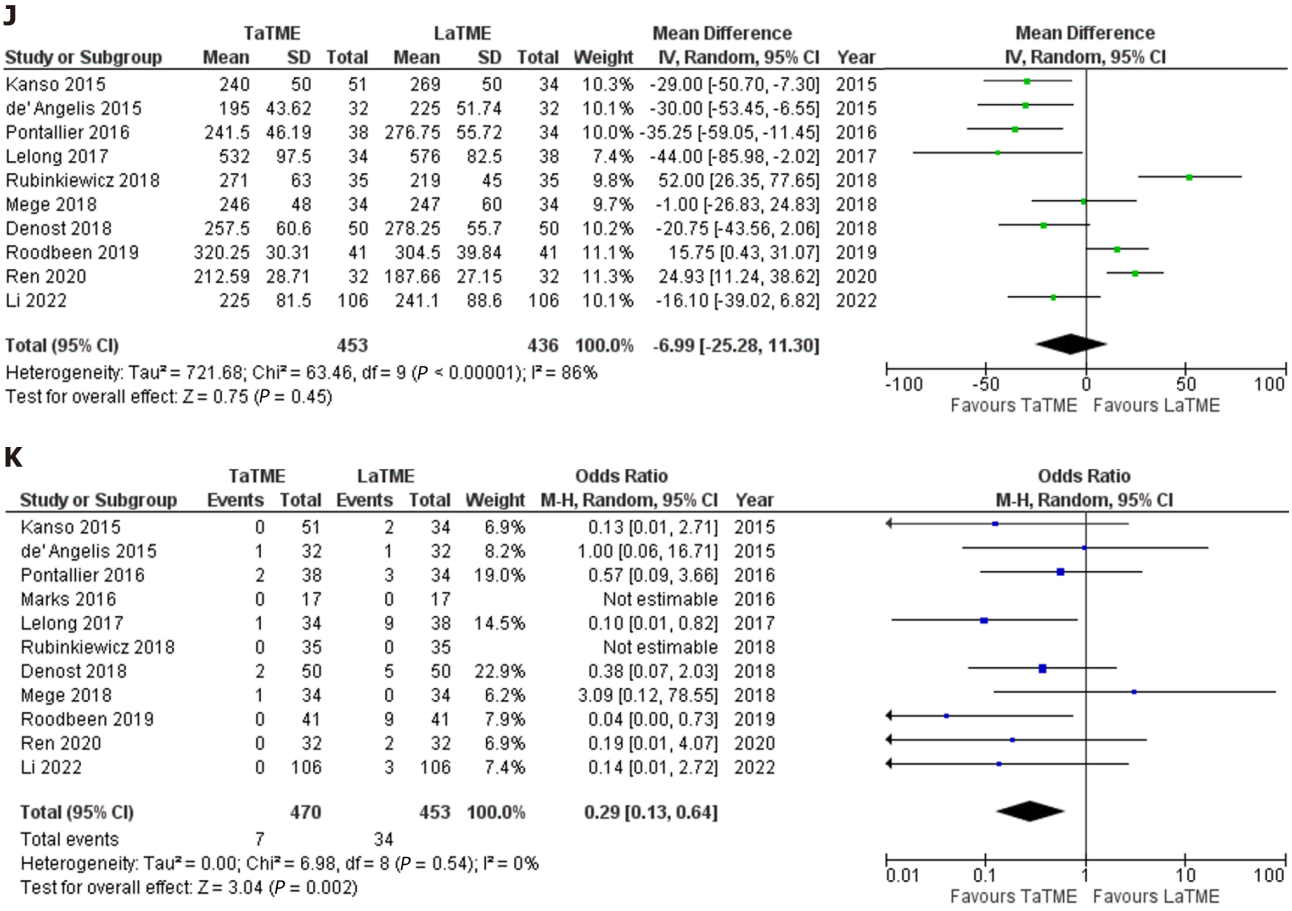


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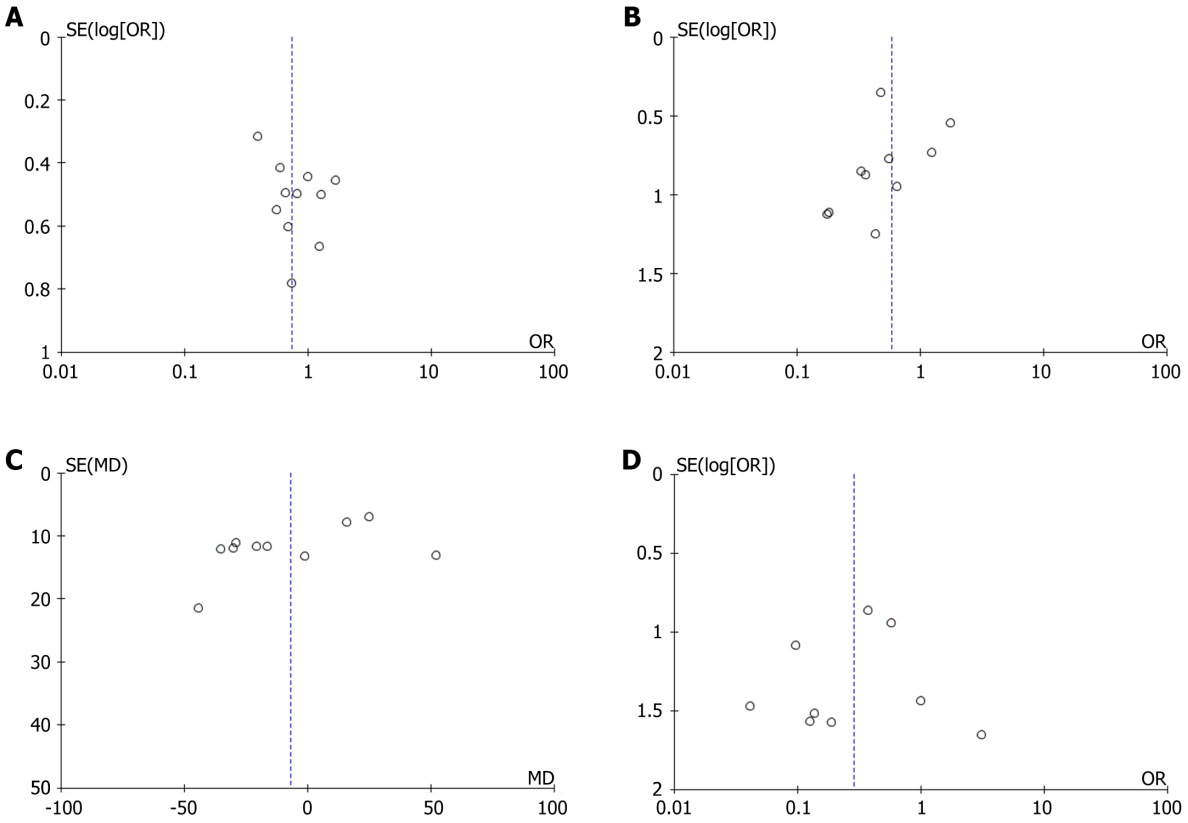
Figure 3 Forest plots of comparison. A: Intraoperative complications; B: Postoperative complications; C: Anastomotic leak; D: R0 resection; E: Completeness of mesorectal excision; F: Number of harvested lymph nodes; G: Distal resection margin; H: Circumferential resection margin; I: Positive circumferential resection margin; J: Procedure time; K: Conversion to an open procedure. The solid squares denote the odds ratios or mean difference. The horizontal lines represent the 95% confidence intervals, and the diamond denotes the pooled effect size. M-H: Mantel Haenszel test.

the authors found a significant association between CRM involvement and local recurrence (P = 0.011), the 5-year local recurrence rate was similar between two groups (3% *vs* 5%, P = 0.30). Moreover, the authors reported similar 5-year disease-free survival between two groups (72% *vs* 74%, P = 0.351). The rate of local recurrence in the aforementioned RCT is comparable with the recurrence rate of 4% reported in a review by Deijen *et al*[26]. Undoubtedly, futures high quality randomized studies with adequate follow-up periods are required to investigate long term oncological outcomes of transanal and laparoscopic approaches to TME.

This study has a number of limitations. Only two of the considered studies were RCTs. Most of the included studies were observational studies with their inherited selection bias. Some of the included studies had small sample sizes which might have introduced Type 2 error to our findings. We were unable to conduct independent analyses on length of hospital stay, functional outcomes or long term oncological outcomes as the data provided by the included studies on such outcomes was inadequate. Finally, there was moderate risk of bias in 3 of our included studies.

CONCLUSION

Our meta-analysis demonstrated that for low rectal tumours, TaTME is associated with better clinical and short term oncological outcomes compared to LaTME. More randomised controlled trials with adequate power and high quality are required to not only confirm these findings, but also to evaluate long term oncological and functional outcomes.



DOI: 10.4240/wjgs.v14.i12.1397

Figure 4 Funnel plots of comparison. A: Postoperative complications; B: Anastomotic leak; C: Procedure time; D: Conversion to open procedure.

ARTICLE HIGHLIGHTS

Research background

Achieving a clear resection margins for low rectal cancer is technically challenging. Transanal TME (TaTME) has been introduced in order to address the chalenges associated with the open and laparoscopic TME (LaTME) in resecting low rectal tumours.

Research motivation

Previous meta-analyses have included mixed patients with mid and low rectal tumours when comparing TaTME and LaTME which has made the interpretation of the real differences between two approaches in treating low rectal cancer difficult.

Research objectives

To investigate the outcomes of transanal TaTME and LaTME in patients with low rectal cancer.

Research methods

A comprehensive systematic review of comparative studies were conducted according to the standards of Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement. Intraoperative and postoperative complications, anastomotic leak, completeness of mesorectal excision, R0 resection, distal (DRM) and circumferential resection margin (CRM), number of harvested lymph nodes, and procedure time were the evaluated outcome parameters.

Research results

We identified twelve comparative studies enrolling a total of 969 patients comparing the outcomes of TaTME (n = 969) and LaTME (n = 476) in patients with low rectal cancer. The meta-analysis demonstrated that TaTME was associated with significantly lower rate of postoperative complications (OR: 0.74, P = 0.04), anastomotic leak (OR: 0.59, P = 0.02), and conversion to an open procedure (OR: 0.29, P = 0.002) compared with LaTME. Moreover, it was associated with significantly higher rate of R0 resection (OR: 1.96, P = 0.03). However, there was no significant difference in intraoperative complications (OR: 1.87; P = 0.23), completeness of mesoractal excision (OR: 1.57, P = 0.15), harvested lymph nodes (MD: -0.05, P = 0.96), DRM (MD: -0.94; P = 0.17), CRM (MD: 1.08, P = 0.17), positive CRM (OR:

0.64, P = 0.11) and procedure time (MD: -6.99 minutes, P = 0.45) between TaTME and LaTME.

Research conclusions

Our findings indicated that for low rectal tumours, TaTME is associated with better clinical and short term oncological outcomes compared to LaTME.

Research perspectives

The available evidence does not allow evaluation of long term oncological and functional outcomes. More randomized controlled trials are required to confirm the findings of this meta-analysis regarding clinical and short term oncological outcomes and to evaluate long term oncological and functional outcomes.

FOOTNOTES

Author contributions: Shahi H designed the research study; Patel I, Bhattacharya P, and Fazili N collected the data for the meta-analysis; Hajibandeh S and Hajibandeh S analysed and interpreted the data, did the statistical analysis, and wrote the article; all authors critically revised the article and provided final approval for the article.

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