



Short- and long-term outcomes of transanal versus laparoscopic total mesorectal excision for mid-to-low rectal cancer: a meta-analysis

Xuan Zhang¹ · Yi Gao¹ · XingLong Dai² · HongTao Zhang¹ · ZhongJun Shang³ · XinYi Cai¹ · Tao Shen¹ · XianShuo Cheng¹ · Kun Yu¹ · YunFeng Li¹

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Abstract

Background and objectives Transanal total mesorectal excision (TaTME) is positioned at the cutting edge of minimally invasive approach to mid- and low rectal cancer. This meta-analysis was to compare the short- and long-term outcomes of TaTME versus laparoscopic total mesorectal excision (LTME) and to evaluate the safety, efficacy, and possible superiority of TaTME.

Methods A comprehensive search was conducted for randomized controlled trials (RCTs) and non-RCTs (NRCTs) comparing TaTME with LTME. Inter-group differences were evaluated via standardized mean differences and relative risks (RRs). All outcomes were analyzed using fixed effects or random effects models according to the heterogeneity. Statistical analysis was performed using Stata/SE 12.0 software.

Results Eleven studies (1 RCT and 10 NRCTs) with involving 757 patients were included. Among which, 361 patients underwent TaTME and 396 patients underwent LTME. Comparing the surgical and oncological quality of resection of TaTME with that of LTME, reports of TaTME indicated favorable outcomes considering mesorectal resection quality, circumferential resection margin involvement, intraoperative blood loss, conversions, and postoperative complications, while the differences between the two groups had no statistical significance in terms of distal resection margin, harvested lymph node, operation time, hospital stay, recurrence, 2-year overall survival (OS), and 2-year disease-free survival.

Conclusion TaTME is a promising surgical technique and is fully a safe, efficacious, and diffusible alternative to LTME in managing mid- and distal rectal cancer. Larger scale, national, multicentric RCTs are warranted to further verify these results and the possible superiority of TaTME.

Keywords Rectal cancer · Transanal · Laparoscopy · Total mesorectal excision · Meta-analysis

Worldwide, rectal carcinoma ranks as one of the most common malignancies [1]. Total mesorectal excision (TME) was initially described by Heald [2] in 1982 and since then it has

been established as the leading surgical principle for rectal cancer surgery because it can decrease local recurrence (LR) and improve survival. Laparoscopic surgery has been widely considered as the second revolution of surgery and has frequently used in rectal surgery due to better visibility of the workplace. Several studies elucidated that laparoscopic total mesorectal excision (LTME) can achieve non-inferior oncological results with equivalent long-term survival compared with open TME [3–6]. However, LTME is difficult to perform in the subset of patients with visceral obesity, narrow pelvis, voluminous prostate or individuals after neoadjuvant chemoradiation therapy (NCRT). Furthermore, the lowest part of the rectum is especially at risk regarding incomplete TME specimens, involved circumferential resection margin (CRM), nerve and sphincter injury, and conversion, mainly due to “up-to-down” technical barriers associated with

✉ YunFeng Li
13330445776@qq.com

¹ Department of Colorectal Cancer Surgery, Clinical Research Center of Colorectal Cancer, Tumor Hospital of Yun Nan Province, The Third Affiliated Hospital of Kunming Medical University, Kunming, People's Republic of China

² Department of Gastrointestinal Surgery, The First Affiliated Hospital of Chongqing Medical University, Chongqing, People's Republic of China

³ Department of Hospital Affairs Management, Tumor Hospital of Yun Nan Province, The Third Affiliated Hospital of Kunming Medical University, Kunming, People's Republic of China

confined pelvic exposure and distortion of “holy plane” [5–7].

To address the aforementioned constraints, the original “bottom-to-up” transanal TME (TaTME) procedure for mid- and low rectal cancer have been developed, which was first introduced by Sylla et al. [8]. TaTME is not a completely novel concept and it could be interpreted as a combination of previous surgical concepts: the definition of TME [2], the approach of transabdominal-transanal (TATA) [9], the platform of transanal endoscopic microsurgery (TEM) and transanal minimally invasive surgery (TAMIS) [10], and the introduction of natural orifice transluminal endoscopic surgery (NOTES) [11]. TaTME-inspired technique is an emerging option to accomplish oncological rectal resection using a variety of flexible and moderate-cost transanal platforms, which has potential advantage of better nerve and sphincter preservation of the distal third of the rectum and clearer visibility of hard-to-access anatomical areas and more accurate identification of the resection plane and excellent anastomotic techniques, especially in male patients with a bulky mesorectum and advanced distal rectal cancer [12]. Potentially, TaTME achieves the possibility of making a purse-string suture on the rectal stump and obviating the need for a distal staple line. Additionally, TaTME shows theoretical advantages such as excellent specimen quality with superior radicality, less postoperative pain, improved cosmetic results, reduced morbidity, as well as lower conversion rates [2, 11, 13].

Several studies demonstrate a relative merit of TaTME over LTME. However, more direct evidence of the obvious superiority of TaTME remains under scrutiny, as the published studies performed were relatively small sample size. Therefore, we conducted a meta-analysis of the current data from the latest researches comparing the safety and the short- and long-term outcomes of TaTME with those of LTME for mid- and low rectal surgery.

Materials and methods

Literature search strategy

Two investigators independently searched the PubMed, MEDLINE, Ovid, Embase, and Cochrane Library from January 2014 to February 2018 using the following search strategy: (transanal OR transanal endoscopic microsurgery OR TEM OR transanal minimally invasive surgery OR TAMIS OR natural orifice transluminal endoscopic surgery OR NOTES OR peritoneal) AND (laparoscopy OR laparoscopic) AND (total mesorectal excision OR TME) AND (rectal cancer OR rectal carcinoma). The “related articles” option in PubMed was used to broaden the search, and all retrieved abstracts, studies, and citations were reviewed.

Additionally, we attempted to identify other studies by manual search of the reference lists of the identified reports.

Inclusion and exclusion criteria

The inclusion criteria were as follows: (a) population: patients were diagnosed with rectal cancer; (b) intervention: surgical treatment; (c) comparison: TaTME versus LTME; (d) outcomes: perioperative details, oncological parameters, recurrence, and survival data; and (e) study design: RCT, NRCTs, or observational (cohort and case-control) trials with sample size more than 15. The exclusion criteria were as follows: (a) lack of the sufficient data or outcomes of interest; (b) duplicate publication; and (c) non-comparative studies, conference abstracts, expert opinions, editorials, letters, and commentaries.

Data extraction

The qualified data were extracted independently by two reviewers (ZJS and XYZ) using standard data extraction forms, and cross-checked to arrive at a consensus. Disagreements were confirmed by another co-author. For each study, the following information was collected: (a) study characteristics: first author, country, year of publication, number of patients, and study type; (b) patient baseline: TNM stage, Tumor distance from anal verge, gender, age, body mass index (BMI), and NCRT; (c) study outcomes: perioperative parameters [operation time, hospital stay, intraoperative blood loss (IBL), conversion, and postoperative complications], oncological details [mesorectal resection quality, harvested lymph nodes (HLN), distal resection margin (DRM), and positive circumferential resection margin (CRM)]; and (d) follow-up results [recurrence, 2-year overall survival (OS), and 2-year disease-free survival (DFS)].

Quality assessment

RCT was evaluated by the modified Jadad Rating Scale [14] which included four metrics: method of randomization, concealment of allocation, number of patients lost to follow-up and corresponding reasons, and blinding. The modified Jadad Rating Scale is a seven-score scale, in which $1 \leq \text{scores} \leq 3$, $4 \leq \text{scores} \leq 7$ indicates low, and high-quality evidence, respectively. NRCT was assessed by the modified Newcastle Ottawa Scale (NOS) [15] including three metrics: selection criteria for case and controls, comparability between groups, and ascertainment of outcome (case-control studies) or exposure (cohort studies). The modified NOS is a nine-star scale, in which $1 < \text{stars} \leq 3$, $4 \leq \text{stars} \leq 6$, and $7 \leq \text{stars} \leq 9$ were defined as low, moderate, and high quality, respectively.

Statistical analysis

Stata/SE 12.0 software (Stata Corp LP, College Station, TX, USA) was used for statistical analysis. Relative risks (RRs) with 95% confidence intervals (95% CIs) were calculated for dichotomous variables. Standard mean differences (SMDs) with 95% CIs were calculated for continuous variables. I^2 statistic ≤ 30 , $30 < I^2 < 50$, and $\geq 50\%$ was considered indicative of low, moderate, and high heterogeneity, respectively [16]. Fixed effects model were chosen for $I^2 \leq 30\%$, and random effects model were chosen for $30 < I^2 < 50$ and $I^2 \geq 50\%$. Funnel plots and Egger's test were used to evaluate publication bias. $P < 0.05$ was considered statistically significant.

Results

Characteristics of included studies

The study selection process is illustrated in Fig. 1. A total of 1478 relevant publications were identified on initial literature search. Of these, 1 RCT [17] and 10 NRCTs [18–28] (4 prospective plus 6 retrospective) with high quality involving 757 patients met the inclusion criteria. Among these, 361 (47.69%) patients underwent TaTME and 396 (52.31%)

were subjected to LTME. The RCTs with a score of 6 were considered to be of high quality. All NRCTs ranged from 7 to 8 stars were indicative of high quality.

The study characteristics, patient baseline, study outcomes, and quality assessment scores of studies included are displayed in Table 1.

Meta-analysis results

Operation time

Ten studies [17, 19–27] reported the data. No significant difference was discovered between the two groups with respect to operation time (SMD = -0.25 , 95% CI -0.54 to 0.04 , $P = 0.090$). Nonetheless, heterogeneity was high significant ($P = 0.000$, $I^2 = 70.3\%$) and the random effects model was used (Fig. 2).

Hospital stay

Ten studies [17, 19–27] described the LHS. We observed no significant difference when comparing TaTME group with LTME group in LHS (SMD = -0.12 , 95% CI -0.32 to 0.08 , $P = 0.252$). However, there was evidence of moderate heterogeneity ($P = 0.007$, $I^2 = 41.7\%$) (Fig. 3).

Fig. 1 Schematic illustration of criteria for literature search and inclusion of studies in the meta-analysis

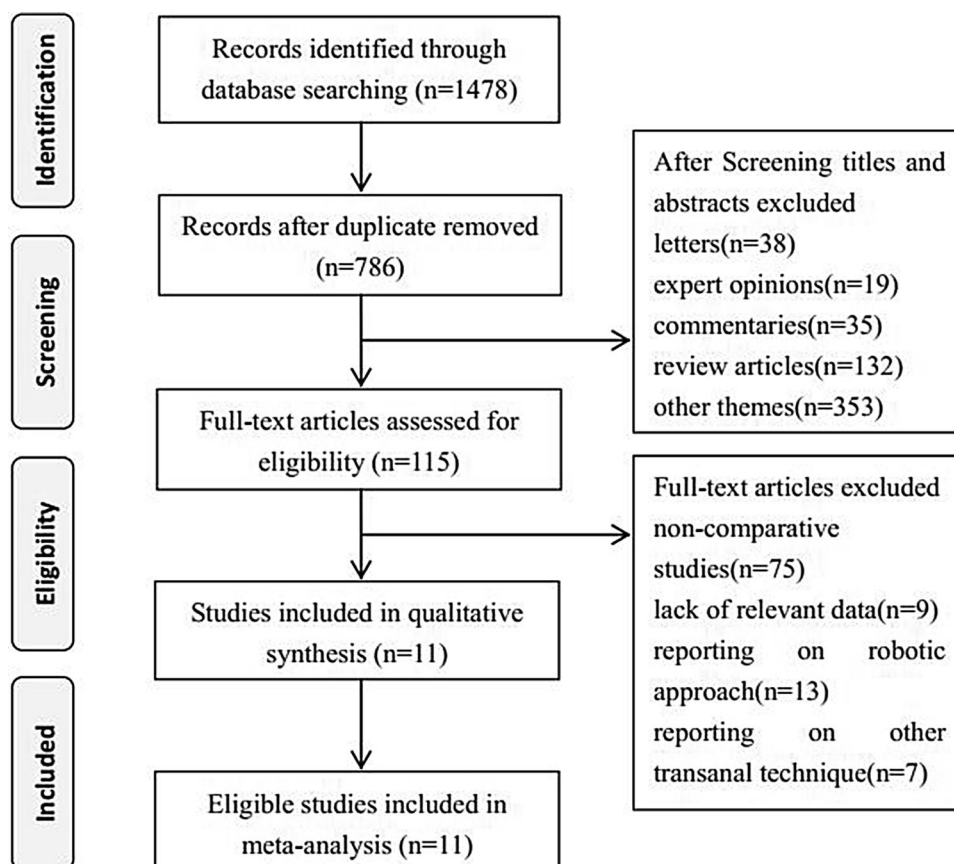


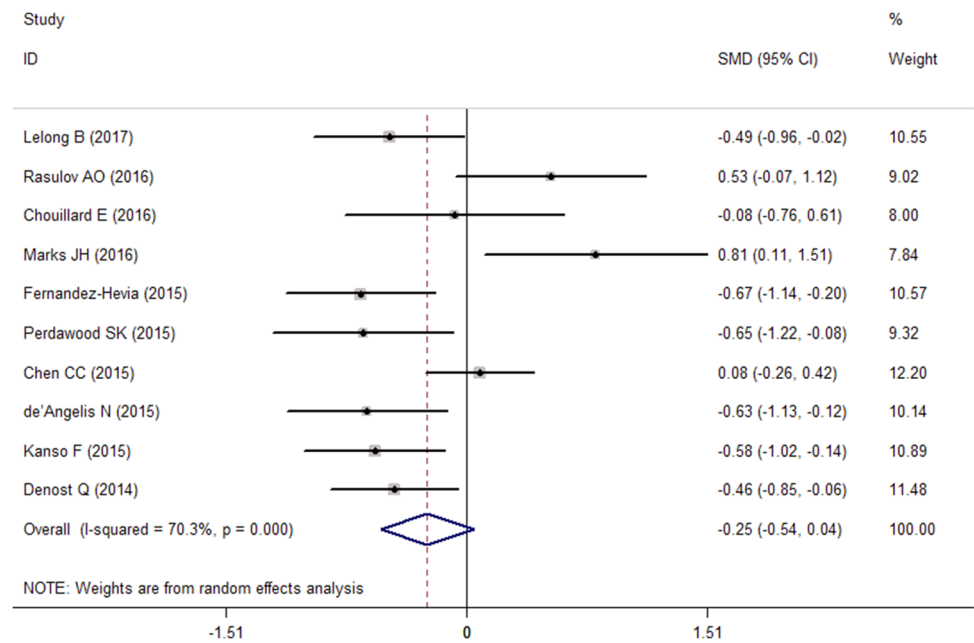
Table 1 Clinical and demographic characteristics of included studies in the meta-analysis

Study	Country	Year	TNM Stage	Tumor distance from anal verge (cm)		Patients (n)		Gender (M/F)		NCRT (n)		Age (median or mean ± sd)		BMI (median or mean ± sd)	
				TaTME	LTME	TaTME	LTME	TaTME	LTME	TaTME	LTME	TaTME	LTME	TaTME	LTME
Lelong [27]	France	2017	I–III	≤5	≤5	34	38	23/11	22/16	30	35	NS		24 ± 6.6	24 ± 3.75
Rasulov [26]	Russia	2016	I–III	6.5	7	22	23	11/11	14/9	19	11	52.8 ± 9.8	53.3 ± 15.8	26.0 ± 3.2	26.9 ± 4.7
Chouillard [25]	France	2016	I–III	≤9	≤9	18	15	6/12	7/8	14	12	55.4 ± 11.9	57.8 ± 7.4	27.1 ± 4.5	29.0 ± 4.2
Marks [24]	America	2016	I–III	6.9	6.8	17	17	NS		17	17	61.5 ± 10.0	62.0 ± 9.5	26.3 ± 3.1	26.1 ± 3.2
Fernandez-H [23]	Spain	2015	I–IV	8.2 ± 1.5 3.9 ± 1.2	8.1 ± 1.7 3.5 ± 1.2	37	37	24/13	22/15	27	21	64.5 ± 11.8	69.5 ± 10.5	23.7 ± 3.6	25.1 ± 4.0
Perdawood [22]	Denmark	2015	I–IV	7.5 ± 1.5	7.6 ± 1.3	25	25	19/6	19/6	7	4	67.5 ± 5.5	68.3 ± 8.8	30.0 ± 7.0	27.3 ± 4.8
Chen CC [21]	Taiwan, China	2015	II–III	5.8 ± 2.1	6.7 ± 2.0	50	100	38/12	76/24	50	100	57.3 ± 11.9	58.3 ± 11.3	24.2 ± 3.7	24.6 ± 3.1
de'Angelis [20]	France	2015	I–III	4.0 ± 0.6	3.7 ± 0.6	32	32	21/11	21/11	27	23	64.9 ± 10.1	67.2 ± 9.6	25.2 ± 3.5	24.5 ± 3.2
Kanso F [19]	France	2015	I–III	4.1 ± 0.8	4.3 ± 0.9	51	34	36/15	26/8	41	27	59.0 ± 11.0	59.0 ± 11.0	24.0 ± 4.0	24.0 ± 4.0
Velthuis S [18]	Netherlands	2014	I–III	8.0 ± 4.0	7.3 ± 3.8	25	25	18/7	18/7	25	25	NS		26.5 ± 4.0	27.8 ± 3.3
Denost [17]	France	2014	I–III	4.0 ± 1.0	4.0 ± 1.0	50	50	37/13	32/18	40	44	64.0 ± 10.8	63.0 ± 14.8	25.1 ± 4.0	25.6 ± 5.0
Study	Country	Year	Study type	ASA I+ II/III+IV		Outcomes		Quality assessment score (☆)							
				TaTME	LTME										
Lelong [20]	France	2017	RCCS	30/4	36/2	(0) (2) (4) (6) (7) (8) (9) (10) (12)		☆☆☆☆☆☆☆☆							
Rasulov [19]	Russia	2016	PCCS	NS		(0) (2) (3) (4) (6) (7) (8) (9)		☆☆☆☆☆☆☆☆							
Chouillard [18]	France	2016	RCCS	14/4	11/4	(0) (2) (4) (5) (6) (7) (8) (9)		☆☆☆☆☆☆☆☆							
Marks [17]	America	2016	PCCS	NS		(0) (2) (3) (4) (6) (7) (8) (9) (10)		☆☆☆☆☆☆☆☆							
Fernandez-H [16]	Spain	2015	PCCS	30/7	25/12	(0) (2) (4) (5) (6) (7) (8) (9)		☆☆☆☆☆☆☆☆							
Perdawood [15]	Denmark	2015	PCCS	19/6	22/3	(0) (2) (3) (4) (5) (6) (7) (8) (9)		☆☆☆☆☆☆☆☆							
Chen CC [14]	Taiwan, China	2015	RCCS	33/17	69/31	(0) (2) (3) (4) (5) (6) (7) (8) (9)		☆☆☆☆☆☆☆☆							
de'Angelis [13]	France	2015	RCCS	31/1	31/1	(0) (2) (4) (5) (6) (7) (8) (9) (10) (12)		☆☆☆☆☆☆☆☆							
Kanso [12]	France	2015	RCCS	47/4	31/3	(0) (2) (4) (5) (7) (8) (9)		☆☆☆☆☆☆☆☆							
Velthuis [10]	Netherlands	2014	RCCS	NS		(4) (5) (6) (7)		☆☆☆☆☆☆☆☆							
Denost [11]	France	2014	RCT	49/1	49/1	(0) (2) (4) (5) (6) (7) (8) (9)		☆☆☆☆☆☆☆☆	6 scores						

TaTME transanal total mesorectal excision, LTME laparoscopic total mesorectal excision, NCRT neoadjuvant chemoradiotherapy, BMI body mass index, ASA American Society of Anesthesiologists, RCCS retrospective case–control study, PCCS prospective case–control study, RCT randomized controlled trial, NS not stated

(1) operation time; (2) hospital stay; (3) intraoperative estimated blood loss (IBL); (4) harvested lymph nodes (HLN); (5) distal resection margin (DRM); (6) mesorectal resection quality; (7) involved circumferential resection margin (CRM); (8) conversion; (9) postoperative complications; (10) overall recurrence; (11) 2-year overall survival(OS); (12) 2-year disease-free survival (DFS)

Fig. 2 Forest plot of data on operation time by study group (TaTME vs. LTME). *TaTME* transanal total mesorectal excision, *LTME* laparoscopic total mesorectal excision, *SMD* standard mean difference



Intraoperative blood loss (IBL)

Four studies [21, 22, 24, 26] revealed the IBL. The IBL were significantly lower in TaTME group as compared to those for LTME group (SMD = -0.40, 95% CI -0.64 to -0.15, $P=0.001$). And heterogeneity among the studies was not significant ($P=0.357$, $I^2=7.2\%$) (Fig. 4).

Harvested lymph nodes (HLN)

All of the studies [17–27] mentioned the HLN. No significant difference was found with respect to HLN between the two groups (SMD = -0.05, 95% CI -0.19 to 0.10, $P=0.535$). Meanwhile, no heterogeneity was observed in this respect ($P=0.616$, $I^2=0.0\%$) (Fig. 5).

Fig. 3 Forest plot of data on hospital stay by study group (TaTME vs. LTME). *TaTME* transanal total mesorectal excision, *LTME* laparoscopic total mesorectal excision, *SMD* standard mean difference

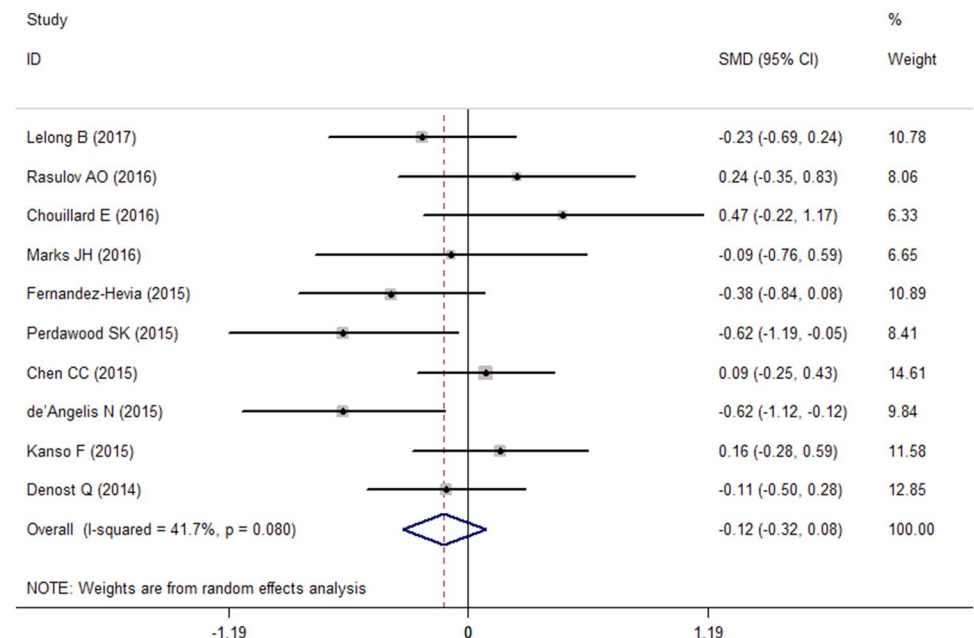


Fig. 4 Forest plot of data on intraoperative blood loss (IBL) by study group (TaTME vs. LTME). *TaTME* transanal total mesorectal excision, *LTME* laparoscopic total mesorectal excision, *SMD* standard mean difference

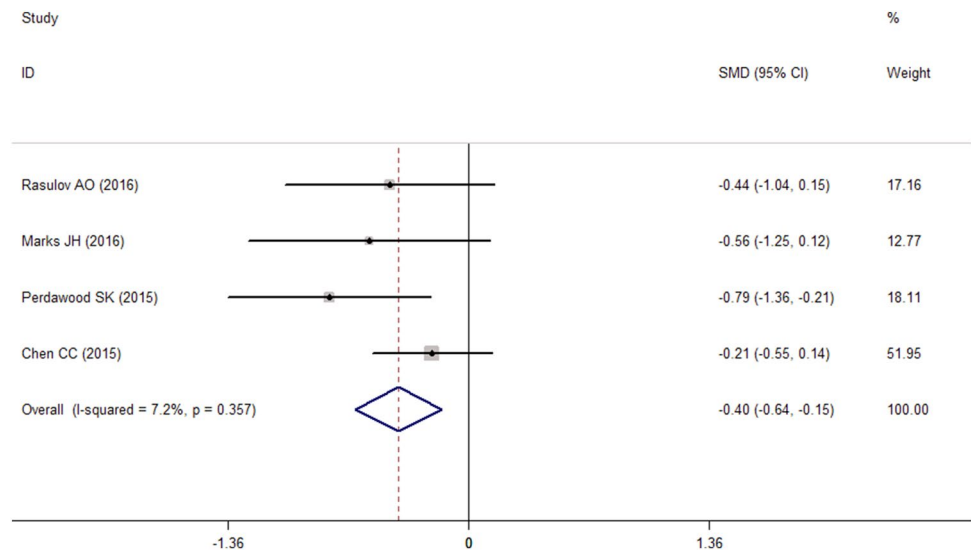
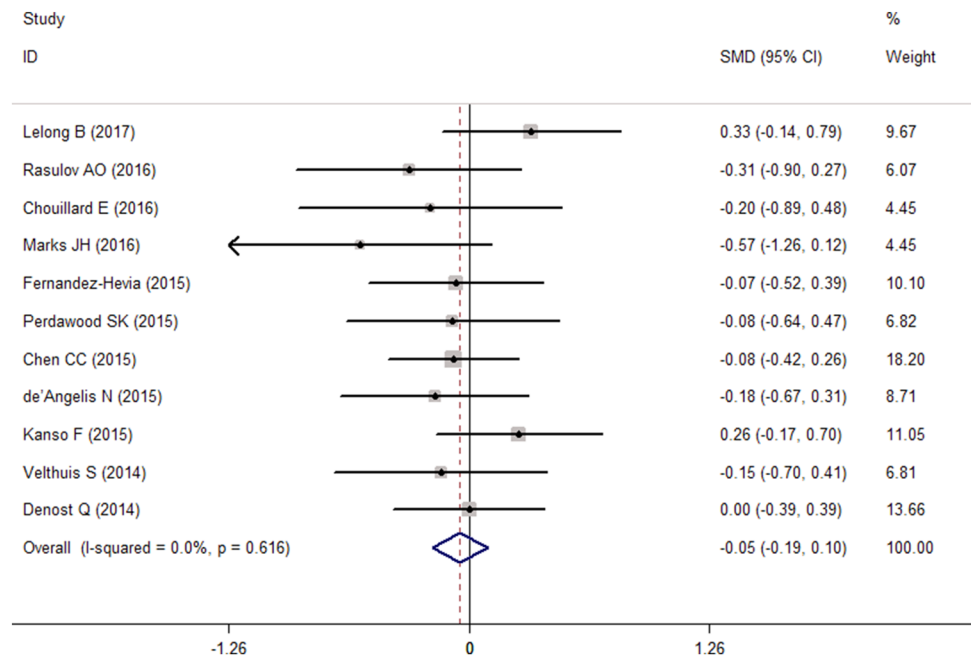


Fig. 5 Forest plot of data on harvested lymph nodes (HLN) by study group (TaTME vs. LTME). *TaTME* transanal total mesorectal excision, *LTME* laparoscopic total mesorectal excision, *SMD* standard mean difference



Distal resection margin (DRM)

Eight studies [17–23, 25] described the DRM. Pooled analysis indicated that the inter-group difference in terms of DRM was not significant (SMD = 0.16, 95% CI -0.22 to 0.53, $P = 0.409$). Nevertheless, a significant heterogeneity was observed ($P = 0.000$, $I^2 = 79.7\%$) (Fig. 6).

Incompleteness of mesorectum

Nine studies [17, 18, 20, 22–27] revealed the rates of incompleteness of mesorectum, whose inter-group difference was statistically significant (RR = 0.53, 95% CI = 0.31–0.93,

$P = 0.026$). Again, heterogeneity across the studies was not significant ($P = 0.566$, $I^2 = 0\%$) and the fixed effects model was used (Fig. 7).

Circumferential resection margin (CRM) involvement

Ten studies [17–24, 26, 27] reported the data. On pooled analysis, the rates of CRM involvement were significantly lower in TaTME group as compared to those for LTME group (RR = 0.46, 95% CI 0.26–0.83, $P = 0.010$). No significant heterogeneity across these studies ($P = 0.811$, $I^2 = 0\%$) (Fig. 8).

Fig. 6 Forest plot of data on distal resection margin (DRM) by study group (TaTME vs. LTME). *TaTME* transanal total mesorectal excision, *LTME* laparoscopic total mesorectal excision, *SMD* standard mean difference

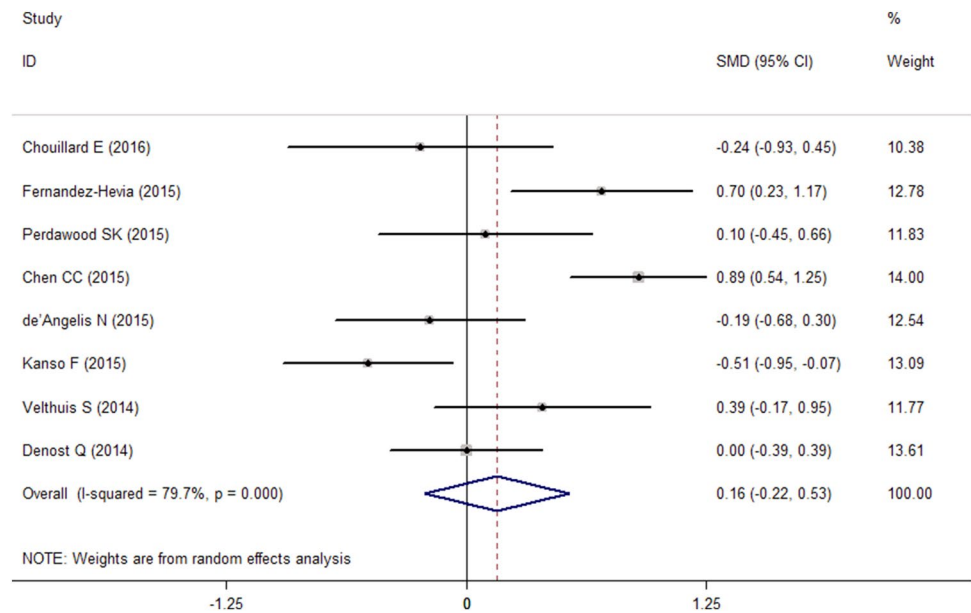
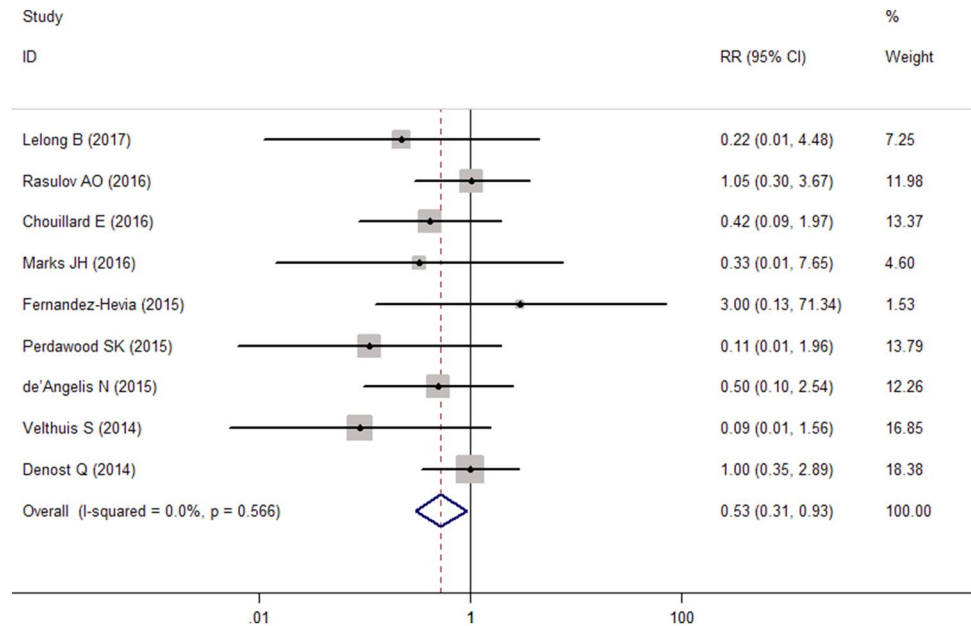


Fig. 7 Forest plot of data on incompleteness of mesorectum by study group (TaTME vs. LTME). *TaTME* transanal total mesorectal excision, *LTME* laparoscopic total mesorectal excision, *RR* risk ratio



Conversion rates

Ten studies [17, 19–27] reported the data. TaTME group was associated with lower rates of conversion ($RR = 0.48$, $95\% \text{ CI} = 0.26–0.86$, $P = 0.014$) as compared to that in the LTME group. The heterogeneity was moderate significant ($P = 0.174$, $I^2 = 31.9\%$) (Fig. 9).

Postoperative complications

Ten studies [17, 19–27] described the data. Pooled analysis manifested that the rates of postoperative complications

were significantly lower in TaTME group as compared to that in the LTME group ($RR = 0.80$, $95\% \text{ CI} = 0.66–0.98$, $P = 0.032$), again with no heterogeneity ($P = 0.836$, $I^2 = 0.0\%$) (Fig. 10).

Overall recurrences

Only 3 eligible studies [20, 24, 27] reported the data. Pooled analysis demonstrated no significant difference with respect to the rates of overall recurrence ($RR = 0.88$, $95\% \text{ CI} = 0.29–2.62$, $P = 0.816$). No heterogeneity was found among the studies ($P = 0.573$, $I^2 = 0.0\%$) (Fig. 11).

Fig. 8 Forest plot of data on circumferential resection margin (CRM) involvement by study group (TaTME vs. LTME). *TaTME* transanal total mesorectal excision, *LTME* laparoscopic total mesorectal excision, *RR* risk ratio

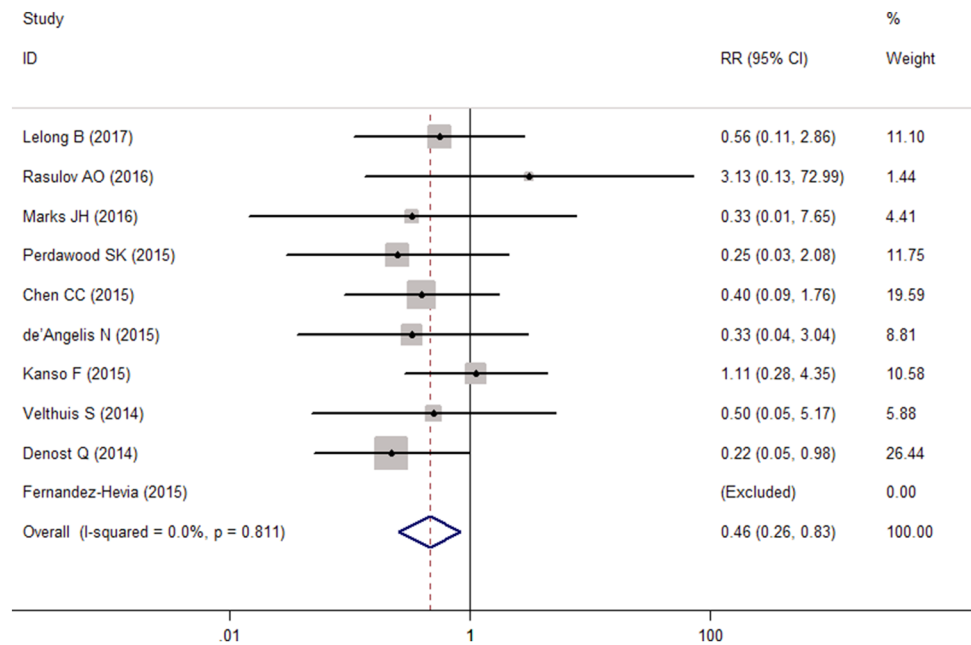
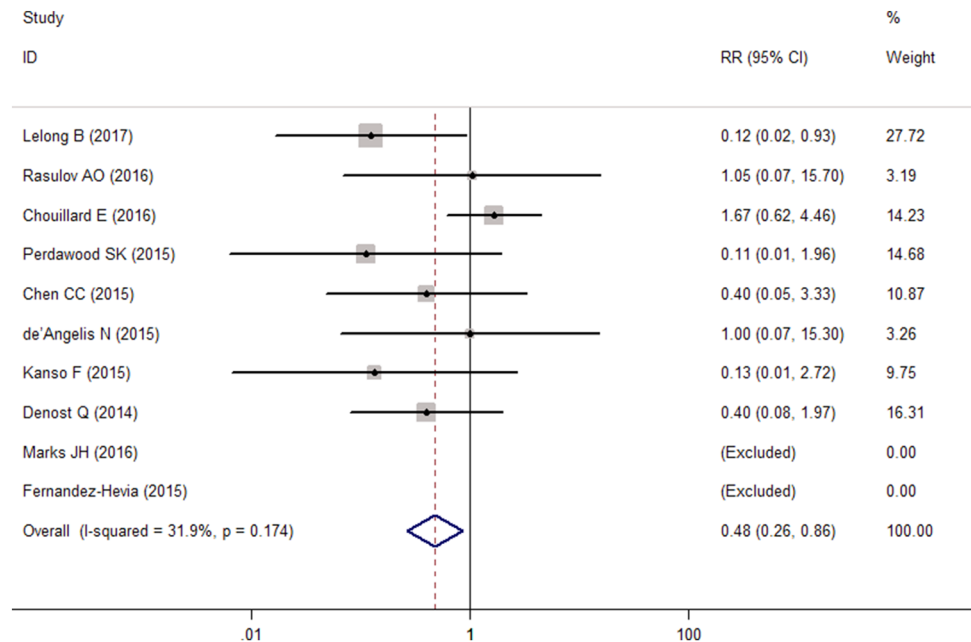


Fig. 9 Forest plot of data on conversion rates by study group (TaTME vs. LTME). *TaTME* transanal total mesorectal excision, *LTME* laparoscopic total mesorectal excision, *RR* risk ratio



Two-year overall survival (OS)

Two eligible studies [20, 27] mentioned the rates of 2-year OS, which were similar between the two groups (RR = 1.01, 95% CI 0.94–1.09, $P = 0.723$). The heterogeneity was not significant ($P = 0.241$, $I^2 = 27.3\%$) (Fig. 12).

Two-year disease-free survival (DFS)

Only 2 studies [20, 27] revealed the rates of 2-year DFS, which were comparable between the two approaches

(RR = 1.02, 95% CI 0.90–1.17, $P = 0.715$). Meanwhile, heterogeneity in this regard was not significant ($P = 0.505$, $I^2 = 0.0\%$) (Fig. 13).

Publication bias

Funnel plot analysis (Fig. 14) and Egger's test (Fig. 15) based on the involved CRM did not indicate significant publication bias. The shape of funnel plot was no obvious asymmetry, and all of the studies were within the 95% CI.

Fig. 10 Forest plot of data on postoperative complications by study group (TaTME vs. LTME). *TaTME* transanal total mesorectal excision, *LTME* laparoscopic total mesorectal excision, *RR* risk ratio

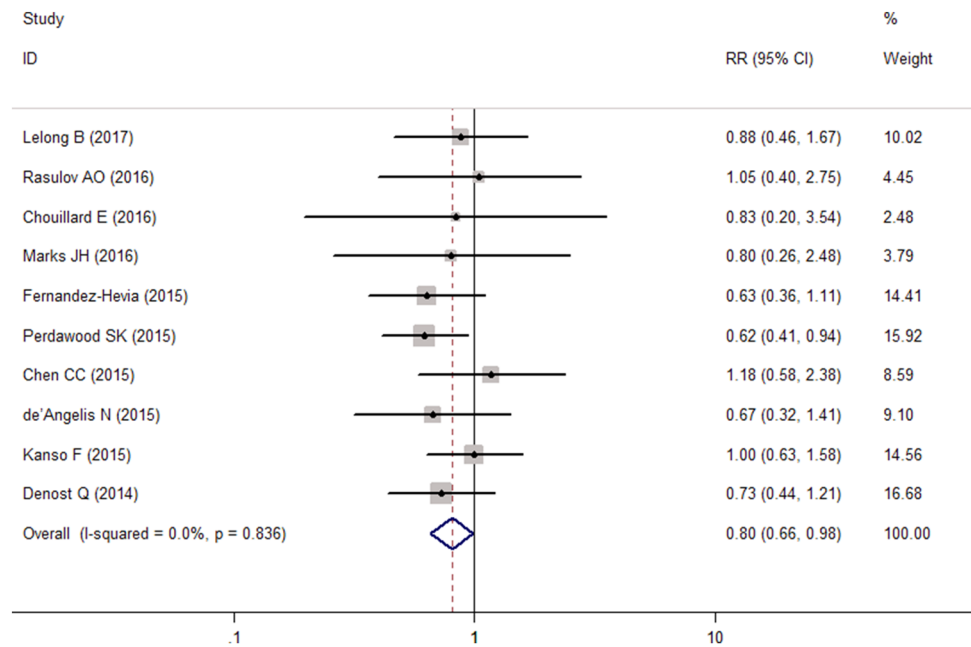
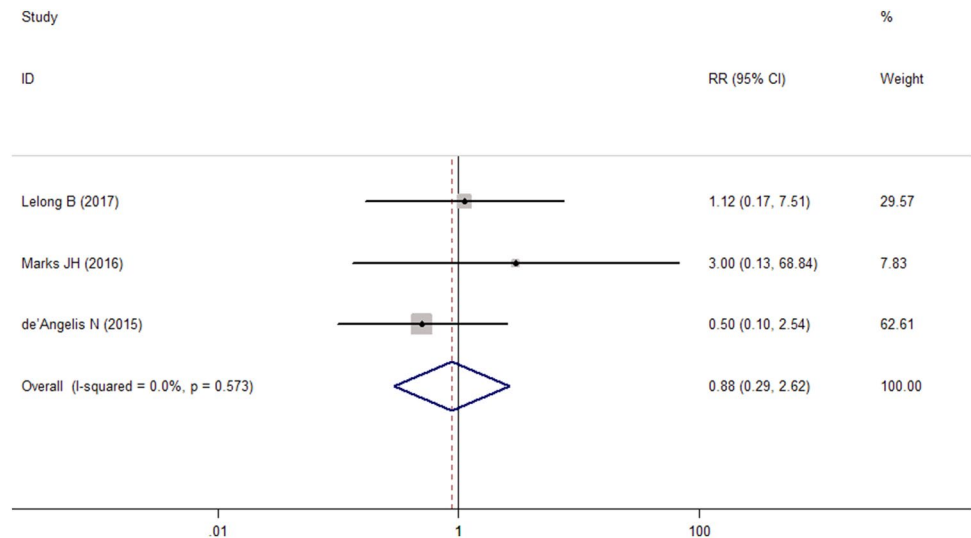


Fig. 11 Forest plot of data on overall recurrences by study group (TaTME vs. LTME). *TaTME* transanal total mesorectal excision, *LTME* laparoscopic total mesorectal excision, *RR* risk ratio



Discussion

The gold standard curative treatment for mid- and distal rectal carcinomas is TME, which has been elucidated to optimize locoregional clearance [2], and decreasing LR rates from 20 to 45% to around 10% [28]. LTME represents a clear leap forward in the treatment of rectal neoplasms, providing improved short-term outcomes and analogous long-term outcomes [6]. However, radical resection of mid- and low rectal lesions with definitive CRM with LTME is technically challenging due to the tapering of the distal mesorectum and inadequate identification of the neurovascular bundle, and mainly because of the limited operative field and unclear

visualization and difficult placement of endoscopic staplers and mobilization in the deep pelvis. Aforementioned factors in combination with poor anastomotic techniques with LTME evoke insufficiency of DRM, incompleteness of mesorectum and involvement of CRM, with consequent LR, and high rates of complications, with consequent conversions. Most importantly, previous RCTs [6, 29] found a high involved CRM rate of 7–12.1% and a high conversion rate of 16% for LTME. Under above-mentioned conditions, the “bottom-to-up” TaTME procedure to pelvic dissection was pioneered to minimize the inherent defects of “up-to-down” LTME approach.

Fig. 12 Forest plot of data on 2-year overall survival (OS) by study group (TaTME vs. LTME). *TaTME* transanal total mesorectal excision, *LTME* laparoscopic total mesorectal excision, *RR* risk ratio

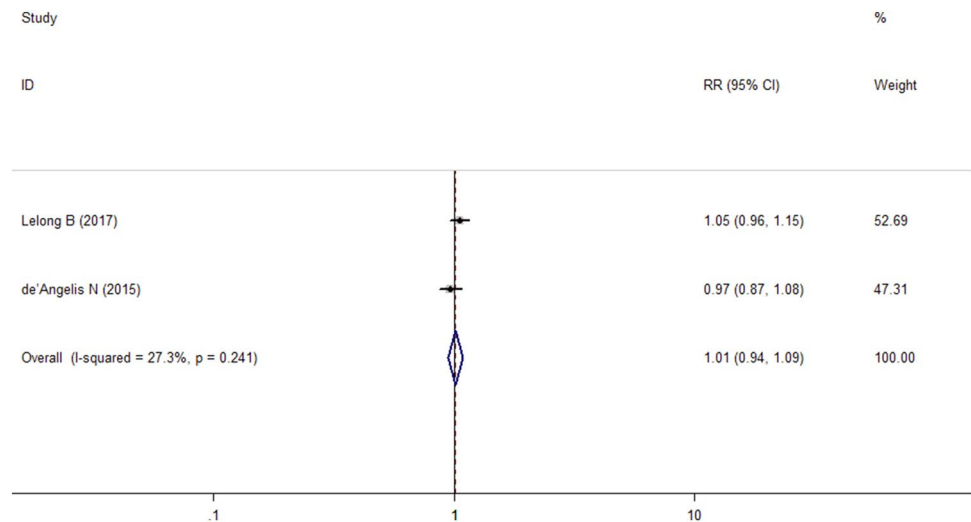


Fig. 13 Forest plot of data on 2-year disease-free survival (DFS) by study group (TaTME vs. LTME). *TaTME* transanal total mesorectal excision, *LTME* laparoscopic total mesorectal excision, *RR* risk ratio

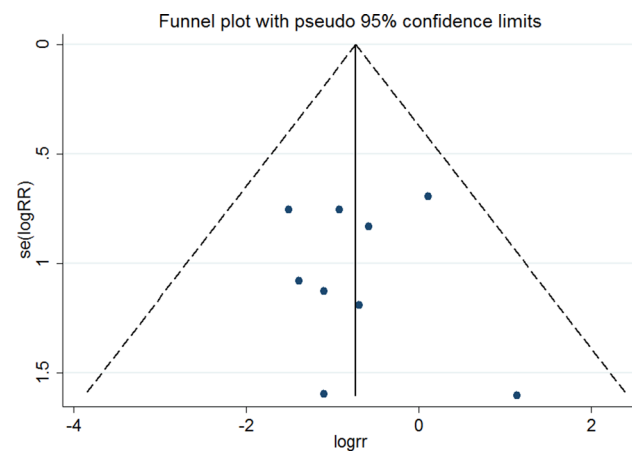
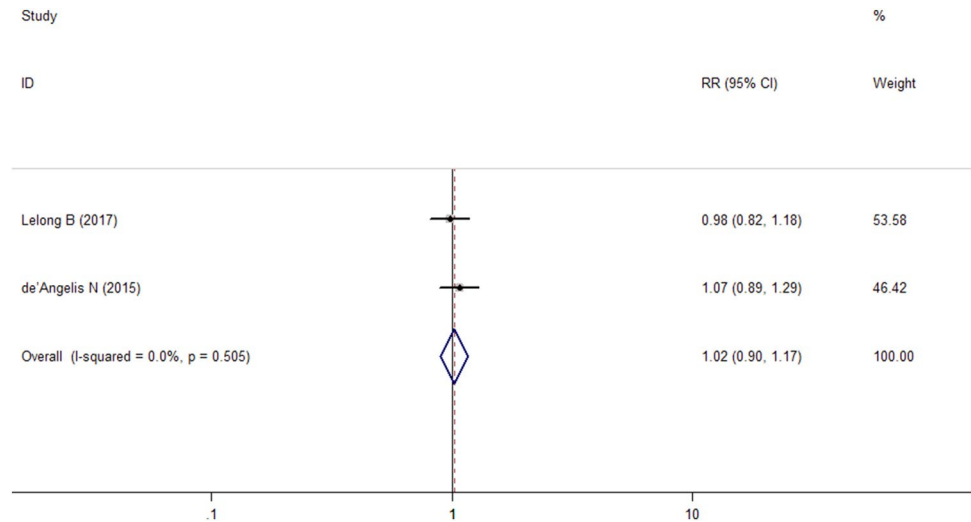


Fig. 14 Funnel plot of data on involved circumferential resection margin (CRM) by study group (TaTME vs. LTME). *TaTME* transanal total mesorectal excision, *LTME* laparoscopic total mesorectal excision, *RR* risk ratio

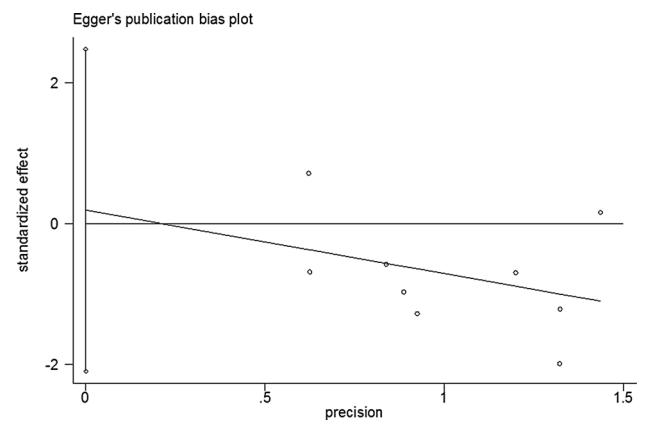


Fig. 15 Egger's test of data on involved circumferential resection margin (CRM) by study group (TaTME vs. LTME). *TaTME* transanal total mesorectal excision, *LTME* laparoscopic total mesorectal excision

TaTME is an innovative technical advancement in the field of minimally invasive surgery, which helps to expose the anatomical plane more clearly and accurately determine the margin of the resection in a narrow pelvis, as well as a more direct approach to the most problematic aspect of the distal rectal dissection, thus in turn producing preferable perioperative results, enhanced oncological quality, as well as superior nerve-sparing [30, 31].

Accordingly, we conducted this meta-analysis to critically contrast the short-term outcomes on perioperative variables and oncological details, and the long-term outcomes on recurrence and survival data of TaTME versus LTME. As described, our RCT was of great quality and all NRCTs included were of moderate to high quality. To our knowledge, this is the first comprehensive overview with relatively large sample size to compare outcomes of interest between the two groups for mid-to-low rectal cancer using latest data, thus providing more dependable analysis and drawing a clearer conclusion about the safety and efficacy of TaTME.

TME is the pivotal oncological principle in the management of rectal carcinomas [2]. Admittedly, the intactness of the mesorectum, DRM, and CRM are recognized as the measure of the TME specimen quality and are deemed as the major predictive factors for rectal resection [13, 32, 33], affecting the risk of local control as well as survival [34]. CRM is considered as the strongest independent parameter for tumor local recurrence [13]. It was found that the rates of involved CRM to TaTME were significantly lower than those of LTME via our meta-analysis. Mesorectal resection quality was scored using three grades—complete, nearly complete, or incomplete, as defined by Quirke et al. [35]. The quality of TME surgery can be reflected in the integrity of the mesorectal envelope, and the latter may serve as a prognostic factor of local and overall recurrences [13]. Rates of incompleteness of mesorectum were lower in TaTME as compared to those in LTME, with no evidence of heterogeneity across these studies. These findings are in accordance with those reported elsewhere and therefore confirm that a more adapted dissection plane in mid- and distal rectum can potentially enhance oncological results. A positive CRM of 2 mm or less is associated with LR rates of 16% compared with 5.8% in patients without involved CRM, and incomplete mesorectum is associated with overall recurrence rates of 28.6% compared with 14.9% in patients with a nearly complete or complete mesorectum [13].

Considering the above conditions, we speculate that TaTME can reduce the likelihood of recurrences. Nevertheless, regarding rates of overall recurrence, there were no significant differences between TaTME and LTME in our meta-analysis. Similarly, the difference did not reach statistical significance between the two groups in terms of rates of 2-year OS and DFS. However, it is not hard to find out that the main reason is that only three of the included studies had

reported recurrence and survival data, which underpowered the statistical analyses and the significance of conclusions [36]. Hence, these results of prognosis should be interpreted discreetly because of insufficient data.

DRM plays a significant part in the oncological outcomes of patients with TME for low and middle rectal cancer. It is undeniable that the core value of TaTME technique lies in achieving safe adequate distal margin length and further improving the quality of dissection of distal mesorectum. Nonetheless, the differences between the two approaches had no statistical significance in terms of DRM. Still, considerable heterogeneity existed in this respect, and potential explanations may be the unlike tumor locations, diverse tumor sizes, and different TNM stages in the studies included. For example, seven studies enrolled patients with mid- and distal rectal cancer [18, 21–27], while the rest of four studies enrolled patients with only distal rectal cancer [17, 19, 20, 27]. Hence, this result pertaining to DRM should be interpreted cautiously. The adequate lymph nodes removal is a vital index of long-term oncological results. With regard to HLN, no significant difference was seen. To sum up, the obvious advantages of lower rates of CRM and incompleteness of mesorectum and the lack of difference in DRM and HLN are key to the more widespread application of TaTME. Notwithstanding, a long-term follow-up is vital for accurate assessment of oncological details associated with TaTME [37].

One of the major concerns in TaTME is operation time. The operation time was shorter, however, in TaTME group, although the difference did not reach the level of significance. This might be explained by the fact that some vital steps of the surgery are simplified by this technique, which facilitates an outstanding exposure and a direct visual control, particularly in the case of previous irradiation, bulky or advanced tumors, confined pelvis, prostatic hypertrophy [38]. Another reason for the shorter operative duration of TaTME were mainly that two teams (abdominal transanal collaboration) were operating simultaneously [39, 40]. Nevertheless, the heterogeneity among the studies was considerable mainly due to the variability in the skill-mix of surgeons who are likely to be at different points on the learning curve [41]. Meanwhile, the flexible platform used (TEM or SILS or GelPOINT), the TaTME type performed (fully or hybrid), and the specimen extracted (transanal or transabdominal) in TaTME group, are other determinants of the operating duration.

It is well known that achieving a lower conversion rate is of paramount importance for surgical resection. Rates of conversion were significantly lower in TaTME as compared to those for LTME. This finding is consistent with published analyses but using a comparatively small sample sizes [3, 42]. Main reasons for conversion included visceral obesity with heavy mesentery, poorly accessible pelvis, bulky or

distally located tumor, vascular injury, difficult dissection, and technical barriers that included inadequate view and stapler misfiring. Therefore, the lower conversion rates in TaTME may be mainly due to clear visualization and direct exposure in the deep workplace, as well as exact determination of the resection margin.

With respect to other perioperative parameters, rates of postoperative complications were lower, and IBL were fewer in TaTME as compared to those in LTME, respectively, which are another advantage of TaTME, whereas the hospital stay was demonstrated to have no statistically significant difference between the two approaches. These results are in line with the previous research that affirmed the merits of TaTME [18, 23]. It is especially noteworthy to highlight that these well results might be attributed to the technical advantages conferred by TaTME mentioned above.

Moreover, another certain novelty of TaTME is that it allows transanal specimen extraction without abdominal wound and associated complications such as wound infection, tumor implantation, and hernia formation [43, 44]. Transanal specimen extraction and the anal stretch during TaTME will theoretically result in partial sacrifice of the anal sphincter. However, a study of satisfactory results with a median follow-up period of more than 30 months in both the TaTME and LTME groups reported that the evaluation of anal sphincter function demonstrated no differences in the two approaches (Kirwan score 1/2, 73.5% vs 73.7%) [27]. And recently, a comprehensive study of assessing the anorectal sphincter function after TaTME by using the low anterior resection syndrome (LARS, which was categorized into no LARS (0–20 scores), minor LARS (21–29 scores), and major LARS (> 30 scores) [45]) questionnaire suggested that preoperative score, the score at 1 and 6 months after surgery were 15.4, 35.7, and 21.7, respectively; this similarly indicated that compared to LTME, TaTME does not substantially impair anal sphincter function [46]. And long-term functional outcomes are awaited.

Additionally, it is economical due to lessened use of linear staplers. The significance of this novel technique was stressed in the editorial ‘a new solution to some old problems’ by Heald et al. [30], who also mentioned that the simultaneous approach promotes reciprocal feedback during dissection, thereby raising surgical efficiency and security.

Although promising, the results of our meta-analysis need to be interpreted with caution because of several limitations. First, perhaps several data of NRCTs included were biased, either exaggerating or underestimating the magnitude of measured effects. Second, the confounding factors inherent in the individual studies might bias the results of studies. Third, the potential limitations and heterogeneities exist in the two groups, as it was impractical to compare certain variables such as the patients’ characteristics, the location and staging of tumor, and the incidence of NCRT. Fourth, the

inclusion of different transanal platforms and TaTME surgery types, to some extent, produces some heterogeneities. Fifth, a potential publication bias and lack of analysis of the subgroup of postoperative complications are other prominent limitations. Lastly, little is known regarding the long-term follow-up data investigating the quality of life and the risk of anorectal functional impairment related to TaTME.

Conclusions

In aggregate, our meta-analysis of short- and long-term outcomes indicates that TaTME, though still evolving, is a promising, absolutely safe, efficacious, and reproducible technique for mid- and low rectal cancer. The present meta-analysis not only validates the ability of TaTME to reduce postoperative complications, IBL, and conversions to open surgery, but also confirms it is superior to LTME in achieving complete mesorectum and adequate CRM after mid- and distal restorative rectal cancer surgery. Regarding the operation time, hospital stay, DRM, overall recurrences, 2-year DFS and OS, there were no significant differences between the two techniques. Based on above findings, TaTME definitely has the potential to become a valid alternative fashion for the treatment of mid- and low rectal cancer, but well-designed, larger scale, national, multicenter RCTs like the ongoing trials of the COLOR III [47] and the French ETAP-GRECCAR 11 [48] are still needed to further confirm these findings and elucidate the merits of TaTME, as determined by clinical and long-term functional and oncological results as well as quality of life.

Author contributions XZ and YG conceived and designed the study. ZJS and XYC researched literature and extracted the data. XZ, XLD, HTZ, KY, and TS participated in analysis, manuscript drafting, and editing. XSC and YFL revised the study.

Compliance with ethical standards

Disclosures Xuan Zhang, Yi Gao, XingLong Dai, HongTao Zhang, ZhongJun Shang, XinYi Cai, Tao Shen, XianShuo Cheng, Kun Yu, and YunFeng Li have declared that no conflicts of interest or financial ties to disclose.

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