

Systematic review of oncological outcomes following laparoscopic vs open total mesorectal excision

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Abstract

AIM: To systematically analyze the randomized trials comparing the oncological and clinical effectiveness of laparoscopic total mesorectal excision (LTME) vs open total mesorectal excision (OTME) in the management of rectal cancer.

METHODS: Published randomized, controlled trials comparing the oncological and clinical effectiveness of LTME vs OTME in the management of rectal cancer were retrieved from the standard electronic medical databases. The data of included randomized, controlled trials was extracted and then analyzed according to the principles of meta-analysis using RevMan[®] statistical software. The combined outcome of the binary variables was expressed as odds ratio (OR) and the combined outcome of the continuous variables was

presented in the form of standardized mean difference (SMD).

RESULTS: Data from eleven randomized, controlled trials on 2143 patients were retrieved from the electronic databases. There was a trend towards the higher risk of surgical site infection (OR = 0.66; 95%CI: 0.44-1.00; $z = 1.94$; $P < 0.05$), higher risk of incomplete total mesorectal resection (OR = 0.62; 95%CI: 0.43-0.91; $z = 2.49$; $P < 0.01$) and prolonged length of hospital stay (SMD, -1.59; 95%CI: -0.86--0.25; $z = 4.22$; $P < 0.00001$) following OTME. However, the oncological outcomes like number of harvested lymph nodes, tumour recurrence and risk of positive resection margins were statistically similar in both groups. In addition, the clinical outcomes such as operative complications, anastomotic leak and all-cause mortality were comparable between both approaches of mesorectal excision.

CONCLUSION: LTME appears to have clinically and oncologically measurable advantages over OTME in patients with primary rectal cancer in both short term and long term follow ups.

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Key words: Total mesorectal excision; Anterior resection; Abdominoperineal resection; Rectal cancer; Oncological outcomes

Core tip: Based upon the findings of this systematic review of eleven randomized trial on 2143 patients of rectal cancer, there is a higher risk of surgical site infection, higher risk of incomplete total mesorectal resection and prolonged length of hospital stay following open total mesorectal excision (OTME) compared to laparoscopic total mesorectal excision (LTME). The number of harvested lymph nodes, tumour recurrence and risk of positive resection margins were statistically similar in both groups. In addition, the operative complications, anastomotic leak and mortality were comparable between both approaches of mesorectal excision.

parable between LTME and OTME. LTME appears to have clinically and oncologically measurable advantages over OTME in patients with primary resectable rectal cancer.

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INTRODUCTION

Colorectal cancer is one of the major causes of mortality among western population^[1,2]. Radical resection of the rectum in the form of anterior resection and abdominoperineal resection has been advocated for many decades to achieve highest level of oncological clearance and overall survival^[3-8]. The introduction of total mesorectal excision in the management of rectal cancer has also enhanced survival and reduced the risk of local recurrence^[9-14] because it achieves complete excision of the rectum together with its lymphatics and lymph nodes. Therefore, total mesorectal excision has become gold standard surgical strategy to treat rectal malignancies^[10,11]. Laparoscopic total mesorectal excision (LTME) offers several advantages over conventional and orthodox open total mesorectal excision (OTME) such as reduced blood loss, faster recovery, reduced postoperative pain score, early feeding, early return to normal activities and a reduced risk of postoperative complications^[12-16]. However, these advantages of LTME can only be availed optimally by colorectal surgeons when its oncological viability is proven on scientific grounds. One would assume that LTME for rectal cancer should offer survival and recurrence similar to OTME^[17-19]. In addition, several studies have also reported the concerns towards LTME requiring longer duration of operation, needing extensive learning curve for colorectal surgeons, particularly junior colorectal trainees and cost implications of the procedure^[20,21]. Aforementioned three limitations of LTME can be offset if its oncological and clinical adequacy matches the OTME. The objective of this article is to explore the oncological safety and clinical effectiveness of the LTME comparing to OTME based upon the principles of meta-analysis.

MATERIALS AND METHODS

Electronic data sources and their search planning

In order to obtain pertinent studies, a search of common medical electronic databases such as MEDLINE, EMBASE, and the Cochrane library for randomized, controlled trials was conducted and screened according to PRIMSA flow chart (Figure 1). The MeSH terms published in the Medline library relevant to the oncological and clinical outcomes following LTME or OTME

were used to hit upon the relevant trials. No limits for language, gender, sample size and place of study origin were entered for the search in the database search engine. Boolean operators (AND, OR = NOT) were additionally used to narrow and widen the results of potentially usable studies. The titles of the published articles from the search results were examined closely and determined to be suitable for potential inclusion into this review article. The reference list from selected articles was also examined as a further search tool to discover additional trials.

Selection criteria for included trials

For inclusion in this meta-analysis, a study had to fulfill the following criteria: (1) randomized, controlled trial; (2) comparison between LTME and OTME; (3) evaluation of a well-defined primary outcome; (4) main outcome measures reported preferably as an intention-to-treat (ITT) analysis; and (5) trials on surgical patients those have endoscopically and histologically proven rectal cancer.

Data abstraction from included trials

Two independent reviewers using a predefined meta-analysis form abstracted relevant data of oncological and clinical outcomes following LTME and OTME from each study which resulted in high and satisfactory interobserver agreement. The extracted data contained name of the publishing authors, title of the published study, journal in which the study was published, country and year of the study, intervention protocol in the both limbs of the trial, method by which LTME and OTME was performed, testing sample size (with sex differentiation if applicable), the number of patients receiving each regimen and within the group the number of patients who succeeded and the number of patients who failed the allocated treatment, the patient compliance rate in each group, the number of patients reporting complications and the number of patients with absence of complications in each arm of the trial. After completing the data abstraction the two independent reviewers discussed the data related results and, if discrepancies were present, a consensus was reached.

Statistical analysis

The software package RevMan 5.2^[22,23], provided by the Cochrane Collaboration, was used for the statistical analysis. The odds ratio (OR) with a 95%CI was calculated for binary data, and the standardized mean difference (SMD) with a 95%CI was calculated for continuous variables. The random-effects model^[24,25] was used to calculate the combined outcomes of both binary and continuous variables. Heterogeneity was explored using the χ^2 test, with significance set at $P < 0.05$, and was quantified^[26] using I^2 , with a maximum value of 30 percent identifying low heterogeneity^[26]. The Mantel-Haenszel method was used for the calculation of OR under the random effect models^[27]. In a sensitivity analysis, 0.5 was added to each cell frequency for trials in which no event occurred in either

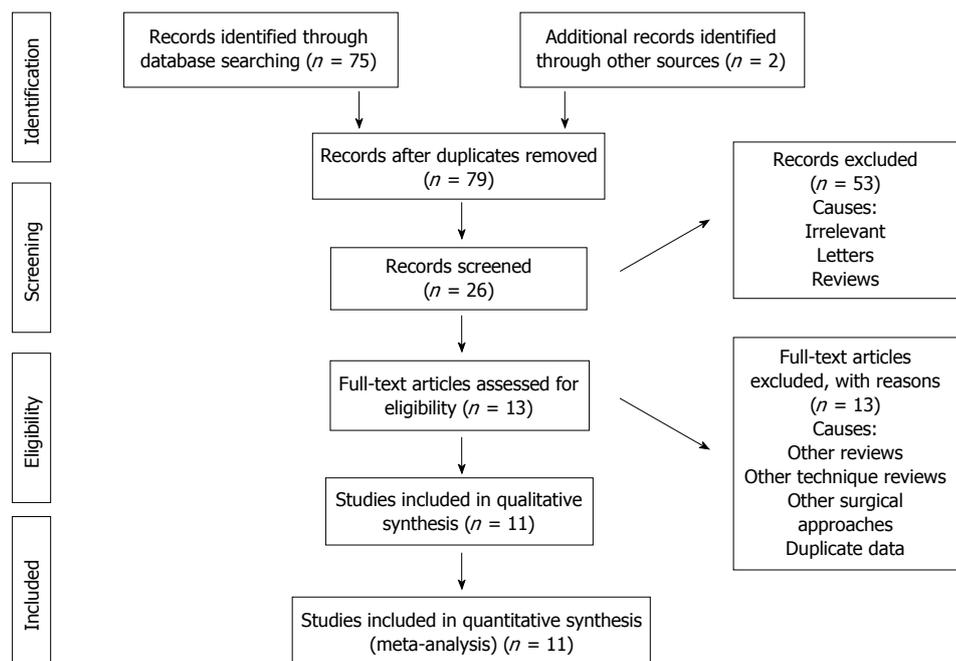


Figure 1 PRISMA flow diagram.

the treatment or control group, according to the method recommended by Deeks *et al.*^[28]. If the standard deviation was not available, then it was calculated according to the guidelines of the Cochrane Collaboration^[22]. This process involved assumptions that both groups had the same variance, which may not have been true, and variance was either estimated from the range or from the *P*-value. The estimate of the difference between both techniques was pooled, depending upon the effect weights in results determined by each trial estimate variance. A forest plot was used for the graphical display of the results. The square around the estimate stood for the accuracy of the estimation (sample size), and the horizontal line represented the 95%CI. The methodological quality of the randomized, controlled trials was assessed using the published guidelines of Jaddad *et al.*^[29] and Chalmers *et al.*^[30]. Based on the quality of the included randomized, controlled trials, the strength and summary of the evidence was further evaluated by GradePro[®]^[31], a tool provided by the Cochrane Collaboration.

Outcomes

Incidence of complete TME was analysed as primary endpoint in this study. Secondary endpoints included circumferential resection margin (CRM) positivity, number of harvested lymph nodes, mortality, morbidity, anastomotic leak, surgical site infection and length of hospital stay.

RESULTS

Eleven randomized, controlled trials encompassing 2143 patients^[32-42] were retrieved from the electronic databases. There were 1189 patients in the LTME group and 954

patients in the OTME group. The characteristics of the included trials are given in Table 1. The salient features and treatment protocols adopted in the included trials are given in Table 2. We used the data from one publication only from two published articles^[35,36] of same randomized, controlled trial in order to avoid the duplication of data.

Methodological quality of included studies

Based upon the published guidelines of Jaddad *et al.*^[29] and Chalmers *et al.*^[30] the quality of majority of included randomized, controlled trials^[33,35-41] was considered good. Only three^[32,34,42] included trials were scored of low quality due to the absence of adequate randomisation technique, power calculations, blinding, adequate concealment process and lack of intention-to-treat analysis. Based on the quality of included trials, the strength and summary of the evidence analyzed on GradePro[®]^[31] is given in Figure 2. The reported quality variables of included trials are given in Table 3.

Risk of incomplete total mesorectal excision

There was no heterogeneity [$\text{Tau}^2 = 0.00$, $\chi^2 = 2.41$, $\gamma = 3$, ($P = 0.49$); $I^2 = 0\%$] among included studies. In the random effects model (OR = 0.62; 95%CI: 0.43-0.91; $z = 2.49$; $P < 0.01$; Figure 3A), the risk of incomplete total mesorectal excision was higher following OTME compared to LTME.

Risk of positive circumferential resection margins

There was no heterogeneity [$\text{Tau}^2 = 0.0$, $\chi^2 = 1.80$, $\gamma = 7$, ($P = 0.97$); $I^2 = 0\%$] among included studies. In the random effects model (OR = 0.98; 95%CI: 0.63, 1.51; $z = 0.10$; $P = 0.71$; Figure 3B), the risk of positive circum-

Table 1 Characteristics of included trials

Ref.	Year	Country	Age (yr)	Gender (M:F)	Follow up (mo)	Rectal cancer details	Procedure
Araujo <i>et al</i> ^[32]	2003	Brazil				Lower rectal cancer with neoadjuvant chemoradiotherapy	Abdominoperineal resection
LTME			59.1	9:4	47.2		
OTME			56.4	10:5	47.2		
Baraga <i>et al</i> ^[33]	2007	Italy				Adenocarcinoma of the rectum suitable for resection with neoadjuvant chemoradiotherapy	Anterior resection and Abdominoperineal resection
LTME			62.8 ± 12.6	55:28	53.6		
OTME			65.3 ± 10.3	64:21			
Gong <i>et al</i> ^[34]	2012	China				Lower and mid rectal adenocarcinoma without neoadjuvant chemoradiotherapy	Anterior resection and Abdominoperineal resection
LTME			58.4 ± 13.6	1.3:1	21 (9-56)		
OTME			59.6 ± 9.4	1.29:1			
Guillou <i>et al</i> ^[35]	2005	United Kingdom				Adenocarcinoma of left colon and rectum	Anterior resection and Abdominoperineal resection
LTME			69 ± 11	44% female	3		
OTME			69 ± 12	46% female	3		
Jayne <i>et al</i> ^[36]	2007	United Kingdom				Adenocarcinoma of left colon and rectum	Anterior resection and Abdominoperineal resection
LTME			69 ± 11	44% female	36.5		
OTME			69 ± 12	46% female	36.5		
Kang <i>et al</i> ^[37]	2010	South Korea				Lower and mid rectal adenocarcinoma with neoadjuvant chemoradiotherapy	Anterior resection and Abdominoperineal resection
LTME			57.8 ± 11.1	110:60	3		
OTME			59.1 ± 9.9	110:60	3		
Lujan <i>et al</i> ^[38]	2009	Spain				Upper rectal adenocarcinoma Mid or low rectal adenocarcinoma cT3N0-2 stage Preoperative chemoradiotherapy	Anterior resection and Abdominoperineal resection
LTME			67.8 ± 12.9	62:39	32.8		
OTME			66 ± 9.9	64:39	34.1		
Ng <i>et al</i> ^[39]	2008	Hong Kong				Lower rectal cancer within 5 cm of the anal verge	Abdominoperineal resection
LTME			63.7 ± 11.8	31:20	90.1		
OTME			63.5 ± 12.6	30:18	87.2		
Ng <i>et al</i> ^[40]	2009	Hong Kong				Upper rectal adenocarcinoma Preoperative chemoradiotherapy	Anterior resection
LTME			66.5 ± 11.9	37:39	112.5		
OTME			65.7 ± 12	48:29	108.8		
Ng <i>et al</i> ^[41]	2013	Hong Kong				Rectal adenocarcinoma located between 5 and 12 cm from the anal verge. None of the included patient had neoadjuvant treatment	Sphincter sparing total mesorectal excision
LTME			60.2 ± 11.3	24:16	84.6		
OTME			62.1 ± 12.6	22:18	92.7		
Zhou <i>et al</i> ^[42]	2004	China				Low rectal adenocarcinoma Intraperitoneal and 1.5 to 8 cm from the dentate line Dukes D with local infiltration Anal sphincter sparing	Anterior resection
LTME			26-85(44)	43:46			
OTME			30-81(45)	46:36	1-16		

LTME: Laparoscopic total mesorectal excision; OTME: Open total mesorectal excision; M: Male; F: Female.

ferential resection margins was similar following both approaches.

Number of harvested lymph nodes

There was significant heterogeneity [$\tau^2 = 0.12$, $\chi^2 = 48.61$, $\gamma = 8$, ($P > 0.00001$); $I^2 = 84\%$] among included studies. In the random effects model (SMD, -0.14; 95%CI: -0.40-0.12; $z = 1.08$; $P < 0.28$; Figure 3C), the number of harvested lymph nodes following both procedures was statistically similar.

Recurrence

There was no heterogeneity [$\tau^2 = 0.00$, $\chi^2 = 4.57$, $\gamma = 7$, ($P = 0.71$); $I^2 = 0\%$] among included studies. In the random effects model (OR = 0.82; 95%CI: 0.59-1.15; $z = 1.16$; $P = 0.24$; Figure 3D), the risk of rectal cancer recurrence was similar between both types of excisions.

Duration of hospital stay

There was significant heterogeneity [$\tau^2 = 0.21$, $\chi^2 = 82.18$, $\gamma = 9$, ($P < 0.00001$); $I^2 = 89\%$] among included studies. In the random effects model (SMD, -1.59;

95%CI: -0.86--0.25; $z = 4.22$; $P < 0.00001$; Figure 3E), the length of hospital stay was shorter following LTME compared to OTME.

Short term and long term operative complications

There was significant heterogeneity [$\tau^2 = 0.30$, $\chi^2 = 28.55$, $\gamma = 9$, ($P < 0.0008$); $I^2 = 68\%$] among included studies. In the random effects model (OR = 0.69; 95%CI: 0.43, 1.08; $z = 1.62$; $P = 0.11$; Figure 3F), the incidence of complications was similar following both approaches of rectal cancer resection.

Overall mortality

There was no heterogeneity [$\tau^2 = 0.00$, $\chi^2 = 0.45$, $\gamma = 3$, ($P = 0.93$); $I^2 = 0\%$] among included studies. In the random effects model (OR = 0.70; 95%CI: 0.41-1.18; $z = 1.33$; $P = 0.18$; Figure 3G), the incidence of overall mortality was similar following LTME and OTME.

Anastomosis leak

There was no heterogeneity [$\tau^2 = 0.00$, $\chi^2 = 6.18$, $\gamma = 7$, ($P = 0.52$); $I^2 = 0\%$] among included studies. In the

Table 2 Treatment protocol adopted in included trials

Ref.	LTME group	OTME group
Araujo <i>et al</i> ^[32]	4 × 10/11 mm ports were used with some variations Trendelenburg position Harmonic scalpel for dissection Lateral to medial dissection Endoscopic stapler for inferior mesenteric pedicle division Colonic division by endostapler Standard technique of colostomy construction Standard perineal phase, dissection and closure	Procedure protocol was not reported
Baraga <i>et al</i> ^[33]	Intracorporeal vascular pedicle division, rectal mobilization and division, and anastomosis Anastomosis by Knight-Griffen technique Selective defunctioning stoma placement	Procedure protocol was not reported Selective defunctioning stoma placement
Gong <i>et al</i> ^[34]	4 ports were used with some variations Medial to lateral dissection Clips to secure inferior mesenteric pedicle Rectal division by endostapler Standard technique of colostomy construction Standard perineal phase, dissection and closure	Standard open TME Sphincter preserving surgery in both groups in selective patients No defunctioning stoma in both groups
Guillou <i>et al</i> ^[35]	Detailed procedure protocol was not reported	Detailed procedure protocol was not reported
Jayne <i>et al</i> ^[36]	3 yr results of Guillou <i>et al</i> ^[35] Detailed procedure protocol was not reported	3 yr results of Guillou <i>et al</i> ^[35] Detailed procedure protocol was not reported
Kang <i>et al</i> ^[37]	Six weeks after completion of chemoradiotherapy 5 ports were used Clips to secure inferior mesenteric pedicle Splenic flexure was mobilized in all patients Harmonic scalpel or diathermy for dissection Rectal division by endostapler Colorectal anastomosis by double staple technique or by trans-anal suture All patients had defunctioning stoma	Detailed procedure protocol was not reported Detailed procedure protocol was not reported Sphincter preservation in selective patients in both groups
Lujan <i>et al</i> ^[38]	4 ports were used Stapled side to end colorectal or colo-anal hand sewn anastomosis Selective defunctioning stoma placement	Lloyd-Davis position and midline laparotomy Stapled side to end colorectal or colo-anal hand sewn anastomosis Sphincter preservation in selective patients in both groups Selective defunctioning stoma placement
Ng <i>et al</i> ^[39]	4 or 5 ports were used Staplers for vascular pedicle and bowel transection Standard perineal resection	Standard open abdominoperineal resection
Ng <i>et al</i> ^[40]	Protocol of the laparoscopic resection technique was not reported	Protocol of the open resection technique was not reported
Ng <i>et al</i> ^[41]	Lateral to medial mobilization Endostapler for rectal and vascular pedicle transection Electrocautry was used to dissect through "Holy plane" for total mesorectal resection Splenic flexure mobilization in selective patients Anastomosis by double stapling technique Defunctioning stoma in selective patients	Protocol of the open resection technique was not reported
Zhou <i>et al</i> ^[42]	Lithotomy position with head down tilt Laparoscopy technique was not reported Intracorporeal anastomosis Endostapler for vascular and rectal transactions Harmonic scalpel was used for dissection No defunctioning stoma	Standard open total mesorectal excision previously published by Heald <i>et al</i> ^[10,11] Electrocautry was used for hemostasis No defunctioning stoma

TME: Total mesorectal excision; LTME: Laparoscopic total mesorectal excision; OTME: Open total mesorectal excision.

random effects model (OR = 0.92; 95%CI: 0.56-1.50; $z = 0.33$; $P = 0.74$; Figure 3H), the risk of colorectal anastomotic dehiscence was similar following both approaches.

Surgical site infection

There was significant no heterogeneity [$\tau^2 = 0.07$, $\chi^2 = 10.61$, $\gamma = 9$, ($P = 0.30$); $I^2 = 15\%$] among included studies. In the random effects model (OR = 0.66; 95%CI:

0.44-1.00; $z = 1.94$; $P < 0.05$; Figure 3I), the risk of surgical site infection was higher following OTME compared to LTME.

DISCUSSION

Based upon the findings of this largest ever systematic review of eleven randomized, controlled trial on 2143

All variables in LTME <i>vs</i> OTME for [health problem]						
Patient or population: patients with [health problem]						
Settings:						
Intervention: All variables in LTME <i>vs</i> OTME						
Outcomes	Illustrative comparative risks ¹ (95%CI)		Relative effect (95%CI)	No of participants (students)	Quality of the evidence (GRADE)	Comments
	Assumed risk Control	Corresponding risk All variables in LTME <i>vs</i> OTME				
Incidence of incomplete TME OR Follow-up: 3-12 mo	Study population 85 per 1000 Moderate 0 per 1000 (0 to 0)	54 per 1000 (38 to 78) 0 per 1000 (0 to 0)	OR = 0.62 (0.43 to 0.91)	1762 (10 studies)	Moderate	
Incidence of CRM positivity OR Follow-up: 3-112 mo	Study population 55 per 1000 Moderate 35 per 1000	54 per 1000 (36 to 81) 34 per 1000 (22 to 52)	OR = 0.98 (0.63 to 1.51)	1563 (8 studies)	Moderate	
Number of harvested lymph nodes Standardized mean difference Follow-up: 3-112 mo		The mean number of harvested lymph nodes in the intervention groups was 0.14 standard deviations lower (0.4 lower to 0.12 higher)		1633 (9 studies)	Moderate	SMD -0.14 (-0.4 to 0.12)
Recurrence OR Follow-up: 3-112 mo	Study population 131 per 1000 Moderate 133 per 1000	110 per 1000 (82 to 148) 112 per 1000 (83 to 150)	OR = 0.82 (0.59 to 1.15)	1422 (9 studies)	Moderate	
Length of stay Standardized mean difference Follow-up: 3-112 mo		The mean length of stay in the intervention groups was 0.55 standard deviation lower (0.86 to 0.25 lower)		1762 (10 studies)	Moderate	SMD -0.55 (-0.86 to -0.25)
Short and long term complications OR Follow-up: 3-112 mo	Study population 430 per 1000 Moderate 503 per 1000	342 per 1000 (245 to 449) 411 per 1000 (303 to 522)	OR = 0.69 (0.43 to 1.08)	1762 (10 studies)	Moderate	
All cause mortality OR Follow-up: 3-112 mo	Study population 41 per 1000 Moderate 430 per 1000	29 per 1000 (17 to 48) 430 per 1000 (0 to 0)	OR = 0.7 (0.41 to 1.18)	1762 (10 studies)	Moderate	
Anastomosis leak rate OR Follow-up: 3-112 mo	Study population 46 per 1000 Moderate 34 per 1000	42 per 1000 (26 to 67) 31 per 1000 (19 to 50)	OR = 0.92 (0.56 to 1.5)	1732 (9 studies)	Moderate	
Surgical site infection OR Follow-up: 3-112 mo	Study population 99 per 1000 Moderate 117 per 1000	68 per 1000 (46 to 99) 80 per 1000 (55 to 117)	OR = 0.66 (0.44 to 1)	1762 (10 studies)	Moderate ²	

¹The basis for the assumed risk (*e.g.*, the median control group risk across studies) is provided in footnotes.

The corresponding risk (and its 95%CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95%CI) GRADE Working Group grades of evidence.

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

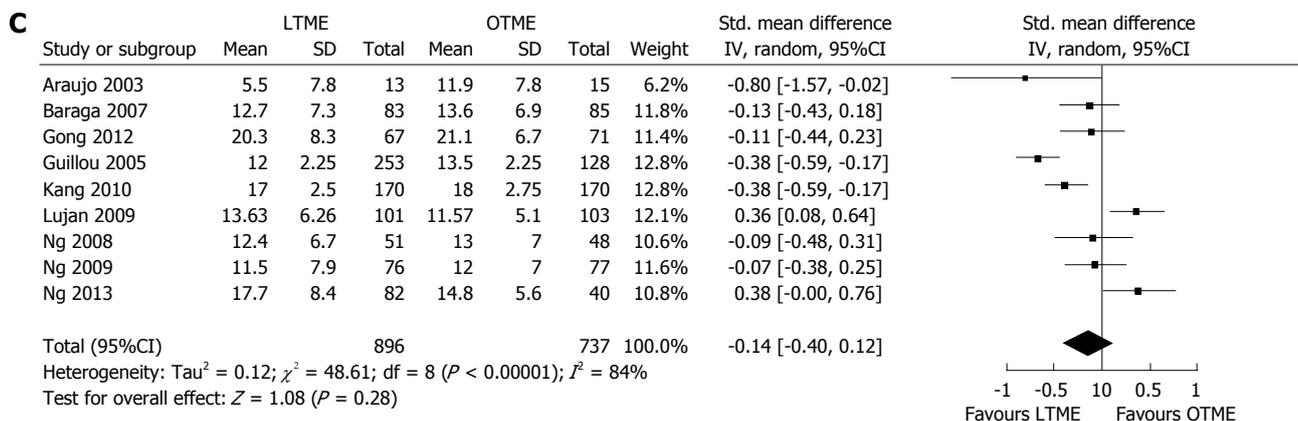
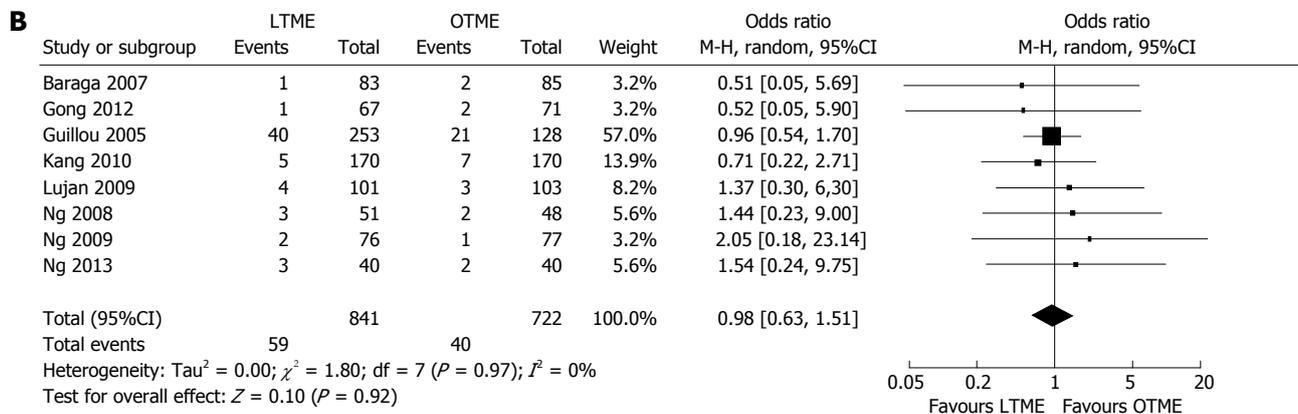
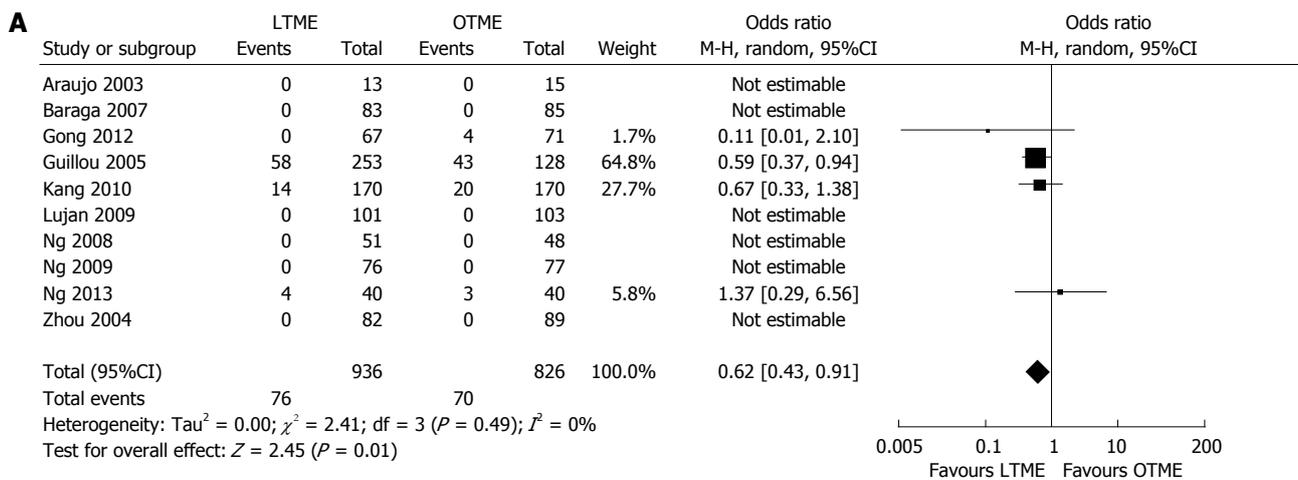
²No explanation was provided.

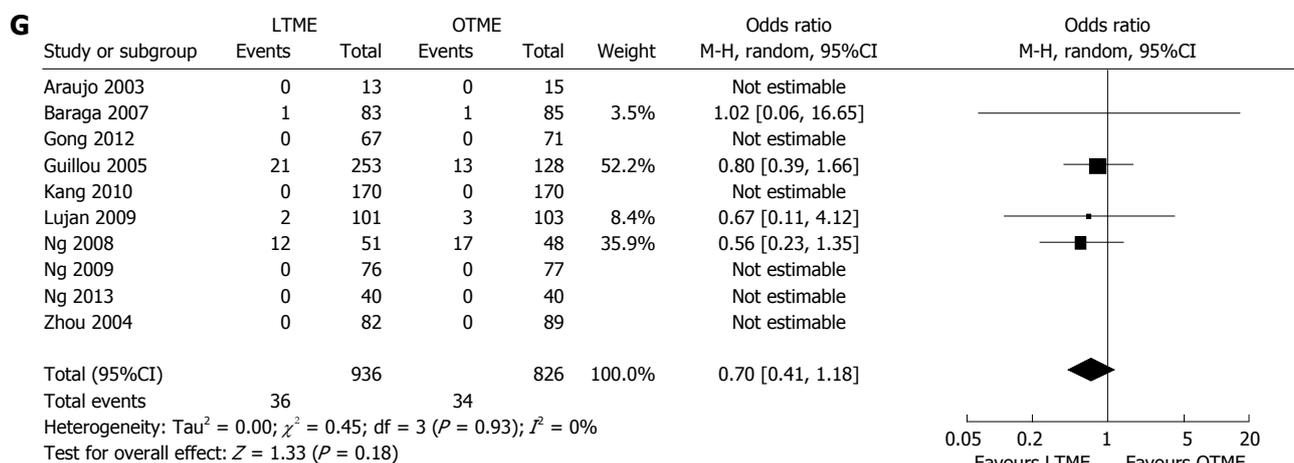
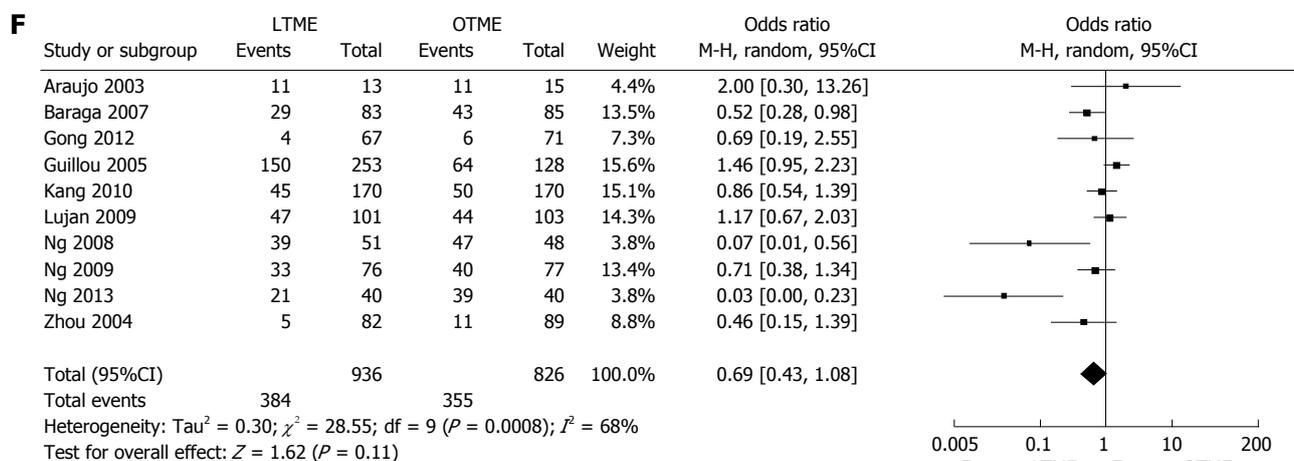
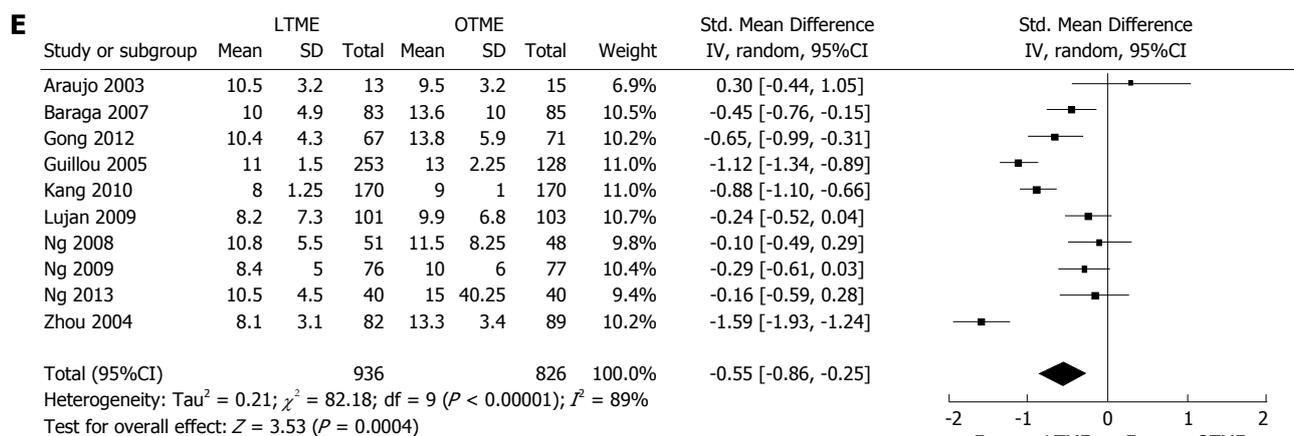
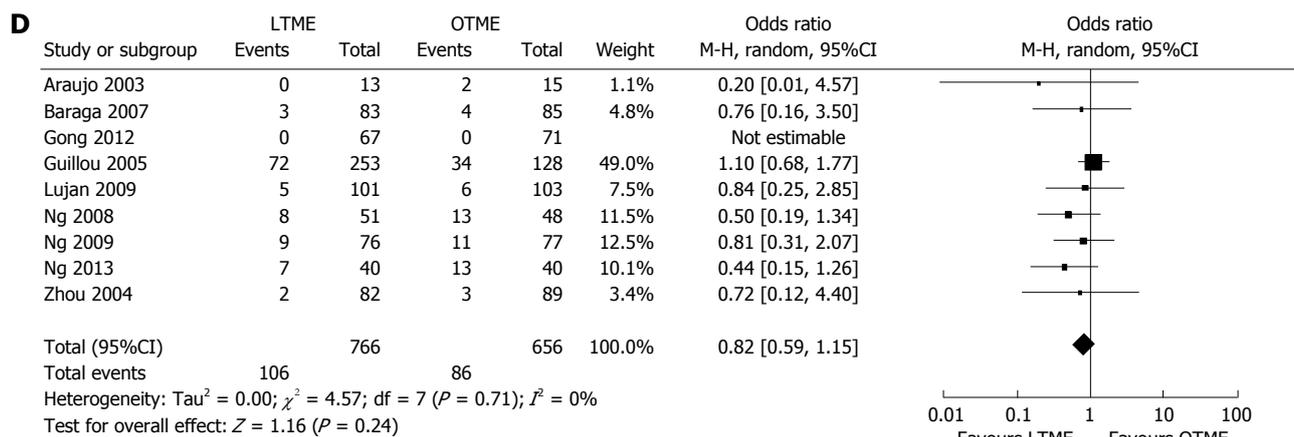
Figure 2 Strength and summary of the evidence analysed on GradePro®.

Table 3 Quality variables reported in the included trials

Ref.	Randomization	Power calculations	ITT	Blinding	Concealment
Araujo <i>et al</i> ^[32]	Not reported	Not reported	Not reported	Not reported	Not reported
Baraga <i>et al</i> ^[33]	Computer generated	Yes	Yes	Yes	Sealed blinded envelopes
Gong <i>et al</i> ^[34]	Not reported	Not reported	Not reported	Not reported	Not reported
Guillou <i>et al</i> ^[35]	Random allocation with 2 to 1 ratio	Yes	Yes	Not reported	Allocation communicated by telephone
Jayne <i>et al</i> ^[36]	Random allocation with 2 to 1 ratio	Yes	Yes	Not reported	Allocation communicated by telephone
Kang <i>et al</i> ^[37]	Computer generated with block permutation	Yes	Yes	Yes	Allocation communicated by telephone
Lujan <i>et al</i> ^[38]	Computer generated	Yes	Yes	Yes	Sealed blinded envelopes
Ng <i>et al</i> ^[39]	Computer generated random sequence	Yes	Yes	Yes	Concealed by theatre coordinator
Ng <i>et al</i> ^[40]	Computer generated	Yes	Yes	Not reported	Not reported
Ng <i>et al</i> ^[41]	Computer generated random sequence	Yes	Yes	Yes	Concealed by theatre coordinator
Zhou <i>et al</i> ^[42]	Not reported	Not reported	Not reported	Not reported	Not reported

ITT: Intention-to-treat.





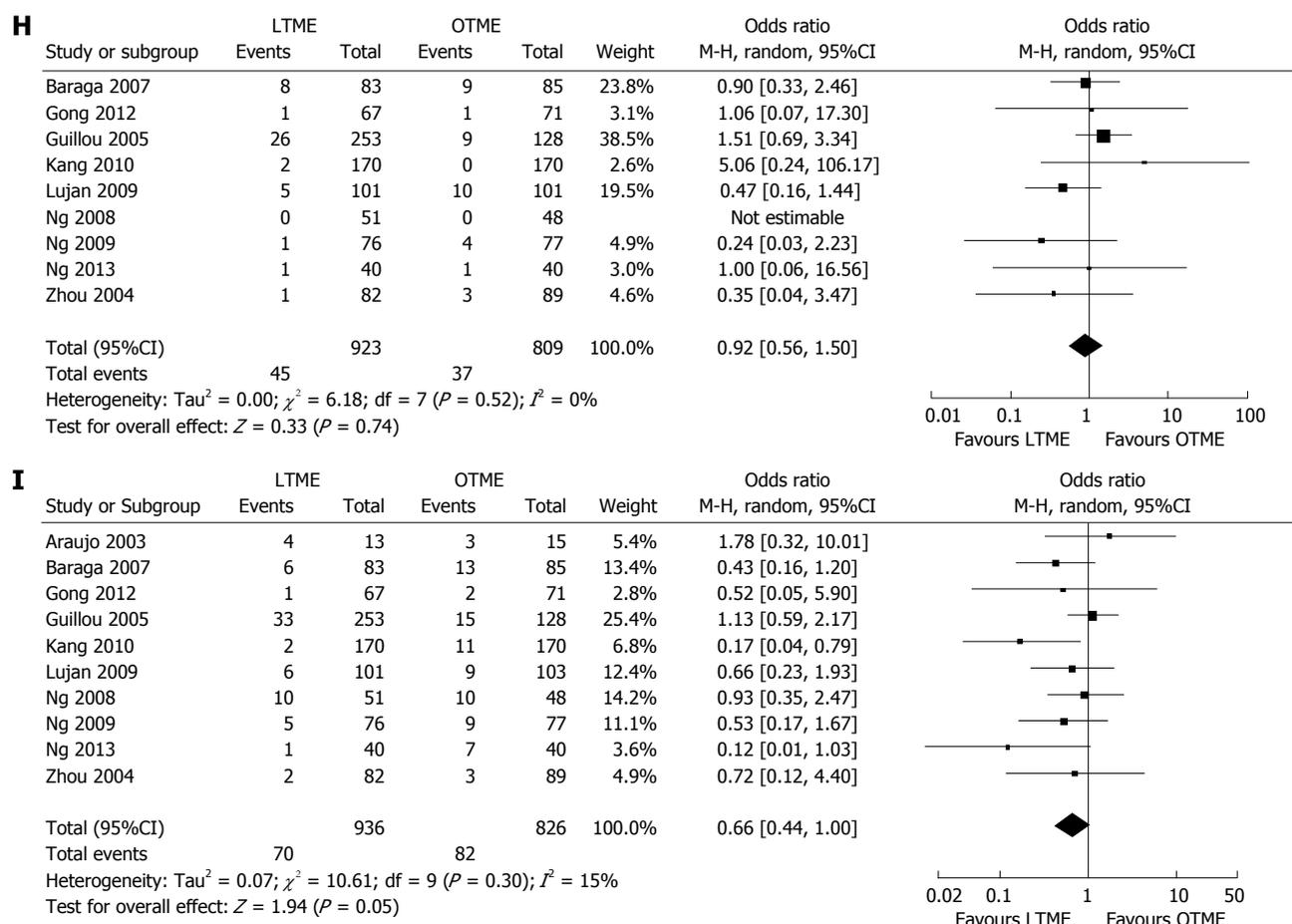


Figure 3 Forest plot. A: Of risk of incomplete total mesorectal excision following laparoscopic total mesorectal excision (LTME) vs open total mesorectal excision (OTME) for rectal cancer. Odds ratios are shown with 95% CIs; B: Of risk of risk of circumferential resection margin positivity following LTME vs OTME for rectal cancer. Odds ratios are shown with 95% CIs; C: Of number of harvested lymph nodes following LTME vs OTME for rectal cancer. Standardized mean differences are shown with 95% CIs; D: Of recurrence following LTME vs OTME for rectal cancer. Odds ratios are shown with 95% CIs; E: Of length of stay following LTME vs OTME for rectal cancer. Standardized mean differences are shown with 95% CIs; F: Of complications following LTME vs OTME for rectal cancer. Odds ratios are shown with 95% CIs; G: Of all-cause mortality following LTME vs OTME for rectal cancer. Odds ratios are shown with 95% CIs; H: Of anastomosis leak following LTME vs OTME for rectal cancer. Odds ratios are shown with 95% CIs; I: Of surgical site infection following LTME vs OTME for rectal cancer. Odds ratios are shown with 95% CIs.

patients of rectal cancer, there is a higher risk of surgical site infection, higher risk of incomplete total mesorectal resection and prolonged length of hospital stay following OTME compared to LTME. The oncological outcomes like the number of harvested lymph nodes, incidence of tumour recurrence and risk of positive resection margins were statistically similar in both groups. In addition, the clinical outcomes such as operative complications, anastomotic leak and all-cause mortality were comparable between both approaches of the mesorectal excision. LTME appears to have clinically and oncologically measurable advantages over OTME in patients with primary resectable rectal cancer in both short term and long term follow ups.

The findings of this article are consistent with previously published Cochrane review and a meta-analysis^[43,44]. Majority of the studies in the Cochrane review^[44] were non-randomized, trials and therefore the conclusion was considered weaker and biased. Similarly a recently published meta-analysis^[43] failed to demonstrate the oncological safety and advantages of LTME over OTME.

This review article presents a comprehensive assessment on the oncological safety of the LTME in addition to the proven clinical advantages of laparoscopy in the curative resections of rectal cancer. Proven clinical advantages of LTME have also been reported in many published studies^[32,33,35,42] which include the lesser blood loss, shorter length of hospital stay and lower postoperative pain score. In addition, the oncological adequacy of LTME has been confirmed in many recent publications^[34,37,38,40].

Authors are fully aware of the fact that there are several limitations to this study. There is significant heterogeneity among included studies. Causes of heterogeneity are both clinical as well as methodological in terms of trial recruitment process. Included studies recruited patients with different stages of the rectal cancer and therefore one would expect their oncological outcome different. Combined analysis of studies on rectal cancer patients with and without neoadjuvant treatment can potentially influence the oncological outcomes which would result in biased conclusions. Variable grade and stage of the disease in recruited patients can also manipulate overall

survival and risk of recurrence. Preoperative nodal disease staging by MRI scan is a standard approach and all included studies did report the use of this imaging prior to surgery. Preoperative diagnostic and staging modalities across the included trials were significantly heterogeneous and therefore can potentially be a strong source of study sample contamination leading to biased outcomes. Colorectal follow up protocol among various centres conducting these trials was significantly diverse and inconsistent. Future trials should be directed towards the involvement of major colorectal units recruiting patients of similar stage and grade of the disease with different arms evaluating outcomes with and without neoadjuvant chemoradiotherapy. In addition, an agreed preoperative staging as well follow up protocol will also help to curtail the clinical and methodological flaws reported in previous trials.

COMMENTS

Background

Total mesorectal excision (TME) has been the gold standard treatment for the management of rectal cancer. Laparoscopic approach for TME has been reported with several advantages such as quicker recovery, reduced postoperative pain and shorter hospital stay. But the limitations compared to open approach include higher cost, longer learning curve and longer operating time.

Research frontiers

Due to clinically measurable advantages, the laparoscopic approach may be a preferred way forward as long as oncological safety of both approaches is at least similar. Several non-randomized and randomized studies have reported the inconsistent oncological findings following laparoscopic TME and precise guidelines are still scarce. Since the introduction of new generation of laparoscopic instruments and stapling devices, the recently published studies have reported encouraging results in favour of laparoscopic TME.

Innovations and breakthroughs

This article highlights the role of laparoscopic approach for TME in current situations. This article reports the oncological safety of laparoscopic TME in terms of clear circumferential resection margins, number of harvested lymph nodes, recurrence and mortality following both open and laparoscopic TME. This article compared to other peer review publications on the same subject provides the latest and strongest evidence and may assist the colorectal surgeons in decision making.

Peer review

It is an important topic, clear presentation, good readability, appropriate methods, precise results, interesting discussion, coherent tables, unambiguous conclusion. This is a very good paper.

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