

Transanal versus laparoscopic total mesorectal excision for mid and low rectal cancer: a meta-analysis of short-term outcomes

Dezheng Lin^{1,2}, Zhaoliang Yu^{2,3}, Wenpei Chen⁴, Jiancong Hu^{1,2}, Xuming Huang^{1,2}, Zhen He^{2,3}, Yi-feng Zou^{2,3}, Xiangan Yu^{2,3}, Xuefeng Guo^{1,2}, Xiao-jian Wu^{2,3}

¹Ambulatory Surgery Center, The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, Guangdong, China

²Department of Colorectal Surgery, The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, Guangdong, China

³Guangdong Provincial Key Laboratory of Colorectal and Pelvic Floor Diseases, The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, Guangdong, China

⁴Department of Anesthesia and Surgery, The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, Guangdong, China

Videosurgery Miniinv 2019; 14 (3): 353–365
DOI: <https://doi.org/10.5114/wiitm.2019.82798>

Abstract

Introduction: The benefit of transanal total mesorectal excision (TaTME) for mid and low rectal cancer is conflicting.

Aim: To assess and compare the short-term outcomes of TaTME with conventional laparoscopic total mesorectal excision (LaTME) for middle and low rectal cancer.

Material and methods: We searched PubMed, Embase and Cochrane Library databases for studies addressing TaTME versus conventional LaTME for rectal cancer between 2008 and December 2018. Randomized controlled trials (RCTs) and retrospective studies which compared TaTME with LaTME were included.

Results: Twelve retrospective case-control studies were identified, including a total of 899 patients. We did not find significant differences in overall intraoperative complications, blood loss, conversion rate, operative time, overall postoperative complication, anastomotic leakage, ileus, or urinary morbidity. Also no significant differences in oncological outcomes including circumferential resection margin (CRM), positive CRM, distal margin distance (DRM), positive DRM, quality of mesorectum, number of harvested lymph nodes, temporary stoma or local recurrence were found. Although the TaTME group had better postoperative outcomes (readmission, reoperation, length of hospital stay) on average, the difference did not reach statistical significance.

Conclusions: Transanal total mesorectal excision offers a safe and feasible alternative to LaTME although the clinicopathological features were not superior to LaTME in this study. Currently, with the lack of evidence on benefits of TaTME, further evaluation of TaTME requires large randomized control trials to be conducted.

Key words: rectal cancer, transanal total mesorectal excision, laparoscopic total mesorectal excision, meta-analysis.

Introduction

Colorectal cancer is one of the most common cancers worldwide [1]. Since laparoscopic surgery was first applied in colorectal cancer in 1991, the technique has spread worldwide [2]. Compared to open surgery, laparoscopic surgery for rectal cancer

is safe and feasible with comparable short-term outcomes and long-term outcomes [3–6].

Since the principles of total mesorectal excision (TME) were first described by Heald *et al.* in 1982 [7], it has become a standard procedure for rectal cancer, and reduced the local recurrence to less than 5% [8–10]. However, there remained some difficulties in

Address for correspondence

Xuefeng Guo MD, PhD, Xiao-jian Wu MD, PhD, The Sixth Affiliated Hospital, Sun Yat-sen University, 26 Yuancun Erheng Road, Guangzhou, 510655 Guangdong, China, phone: 011-86-020-38254009, fax: 011-86-20-38254166, e-mail: guoxf@126.com; wuxjian@mail.sysu.edu.cn

middle or low rectal cancer, especially in a low location, obese patients, or males with a deep, narrow pelvis. In 2010, the down-to-up approach, transanal total mesorectal excision (TaTME), was introduced to solve these problems [11–13]. And then, there were several randomized controlled trials focusing on middle and low rectal cancer compared TaTME with laparoscopic TME (LaTME) [14, 15].

Previous meta-analyses had demonstrated a relative merit of TaTME over LaTME [16–20]. However, these studies had a relatively small sample size. What is more, some previous meta-analyses included data from abdominoperineal resections, which may generate bias, affecting outcomes [18]. Hence, we conducted this meta-analysis to assess and compare the short-term outcomes of TaTME with LaTME for middle and low rectal cancer. Intraoperative outcomes, postoperative outcomes, oncological outcomes and local recurrence were measured with meta-analytical methods.

Aim

The aim of the study was to assess and compare the short-term outcomes of TaTME with conventional LaTME for middle and low rectal cancer.

Material and methods

This meta-analysis adheres to the Preferred Reporting Items for Systematic Reviews and Meta-analysis and Meta-analysis guidelines [21, 22].

Literature-search strategy

Literature searches of PubMed, Embase and Cochrane Library databases for studies addressing TaTME versus conventional LaTME for rectal cancer between 2008 and December 2018 were performed. Only English-language publications were involved. The search terms were “Transanal or transanal total mesorectal excision or TaTME or transanal minimally invasive surgery or TAMIS or transanal endoscopic microsurgery or TEM or natural orifice transluminal endoscopic surgery or NOTES or natural orifice specimen extraction or NOSE or transanal specimen extraction” and “rectal cancer or proctectomy”.

Inclusion and exclusion criteria

Randomized controlled trials (RCTs) and retrospective studies that comparing TaTME with LaTME

were included. All the included studies had to have at least one of the relevant outcomes mentioned below. The exclusion criteria were as follows: (a) lack of the sufficient data or outcomes of interest; (b) duplicate publication; (c) non-comparative studies, editorials, letters, conference abstracts, review articles, case reports and animal experimental studies; (d) studies included high rectal cancer (tumor distance from anal verge more than 10 cm) and abdomino-perineal resection (APR).

Data extraction and outcomes of interest

Two independent authors extracted and summarized the data from the included studies independently.

The intraoperative outcomes were estimated blood loss, operative time, conversion rate, and intraoperative complications. The postoperative outcomes were overall postoperative complications, anastomotic leakage, ileus, urinary morbidity, reoperation, readmission rate, and length of hospital stay. The oncological outcomes were quality of mesorectum, circumferential resection margin (CRM), positive CRM, distal margin distance (DRM), positive DRM, harvested lymph nodes and local recurrence.

Quality assessment

For continuous variables weighted mean differences (WMDs) were calculated. For dichotomous variables odds ratios (ORs) were calculated. For continuous data as median and range values, the means and standard deviations were calculated by the formula described by Liberati *et al.* [22].

Statistical analysis

Statistical heterogeneity between studies was assessed using the χ^2 test with significance set at $p < 0.10$ [23]. A random effects model was used and funnel plots were used to evaluate publication bias. The Newcastle-Ottawa scale was used to evaluate the methodological quality of all the retrospective studies.

Statistical analyses were done using RevMan 5.3 software (Cochrane Collaboration, Oxford, UK).

Results

One thousand two hundred and forty-seven citations were retrieved from the search strategy. Finally,

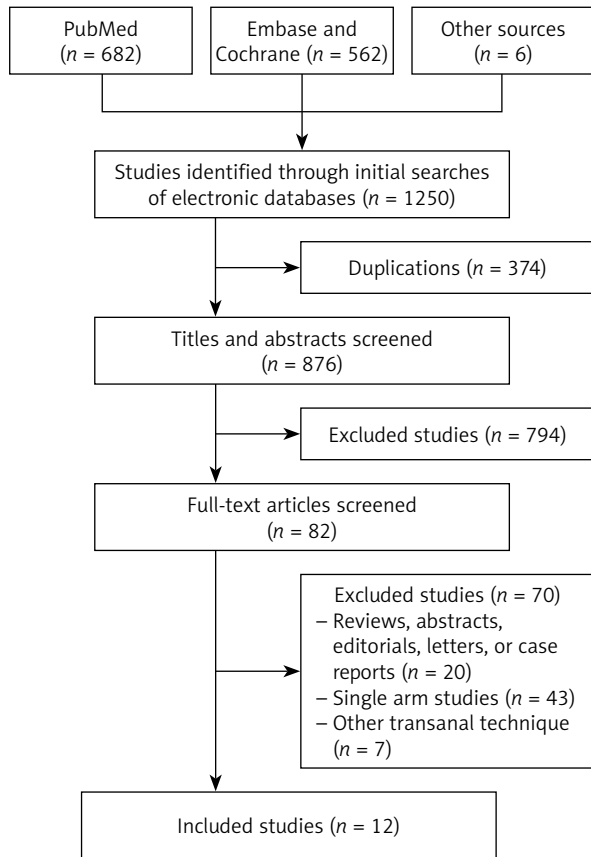


Figure 1. Flow diagram of trial identification, screening, inclusion and exclusion

twelve studies [24–35] were included in the analysis, with a total of 899 patients (411 patients in TaTME group, 488 patients in LaTME group) (Figure 1). The characteristics of eligible studies are shown in Table I.

Meta-analysis revealed no statistically significant difference in intraoperative outcomes: There were no statistically significant differences in blood loss ($p = 0.85$), operative time ($p = 0.79$), conversion rate ($p = 0.69$) or intraoperative complications ($p = 0.70$) between the two groups (Figure 2). There was no heterogeneity among studies, $I^2 = 0\%$.

Ten studies [24–26, 28, 30–35] that assessed 821 patients reported on overall postoperative complication rate. Meta-analysis showed no statistically significant differences in overall postoperative complication ($p = 0.39$), anastomotic leakage ($p = 0.60$), ileus ($p = 0.38$) or urinary morbidity ($p = 0.79$) between the two groups (Figure 3). The TaTME group had non-significantly better postoperative outcomes in readmission ($p = 0.08$), reoperation ($p = 0.34$) and length of hospital stay ($p = 0.09$) (Figure 4).

Table I. Characteristics of studies included in this meta-analysis

Study	Design	Country	Patients TaTME/LaTME	BMI		T stage	Tumor location	Neoadjuvant therapy TaTME/LaTME	Quality score
				TaTME	LaTME				
Fernandez-Hevia 2014 [24]	MCC	Spain	37/37	23.7 ±3.6	25.1 ±4.0	T2–T4	L + M	28/23	7
De'Angelis 2015 [25]	MCC	France	32/32	25.2 ±3.5	24.5 ±3.2	T2–T4	L	27/23	8
Chen 2016 [26]	MCC	Taiwan, China	50/100	24.2 ±3.7	24.6 ±3.1	T2–T3	L + M	50/100	7
Chouillard 2016 [27]	Prospective cohort study	France	18/15	27.1 ±4.5	29.0 ±4.2	T1–T3	L + M	14/12	7
Lelong 2016 [28]	MCC	France	34/38	24 (18.6–45.0)	24.2 (17.7–32.7)	T1–T4	L	30/35	8
Rasulov 2016 [29]	Prospective cohort study	Russia	22/23	26.0 (19.7–32.3)	26.0 (18.3–37.2)	T1–T4	L + M	19/11	8
Chang 2017 [30]	MCC	Taiwan, China	23/23	25.8 ±4.3	25.0 ±3.0	T1–T3	L	8/14	7
Mege 2018 [31]	MCC	France	34/34	25 ±4	25 ±3	T1–T4	L	29/29	8
Persiani 2018 [32]	MCC	Italy	46/46	25 (19.1–32.8)	25.6 (18.8–33.4)	T1–T3	L + M	26/32	7
Chen YT 2018 [33]	MCC	Taiwan, China	39/64	25.4 ±4.0	24.6 ±3.3	T1–T3	L + M	115/31	8
Roodbeen 2018 [34]	MCC	Netherlands	41/41	26.7 ±1.9	26.1 ±4.0	T1–T4	L	18/18	7
Rubinkiewicz 2018 [35]	MCC	Poland	35/35	26.1 ±4.09	27.1 ±4.71	T1–T3	L	31/31	7

TaTME – transanal total mesorectal excision, LaTME – laparoscopic total mesorectal excision, BMI – body mass index, MCC – matched case control, Tumor location: L – low, M – middle.

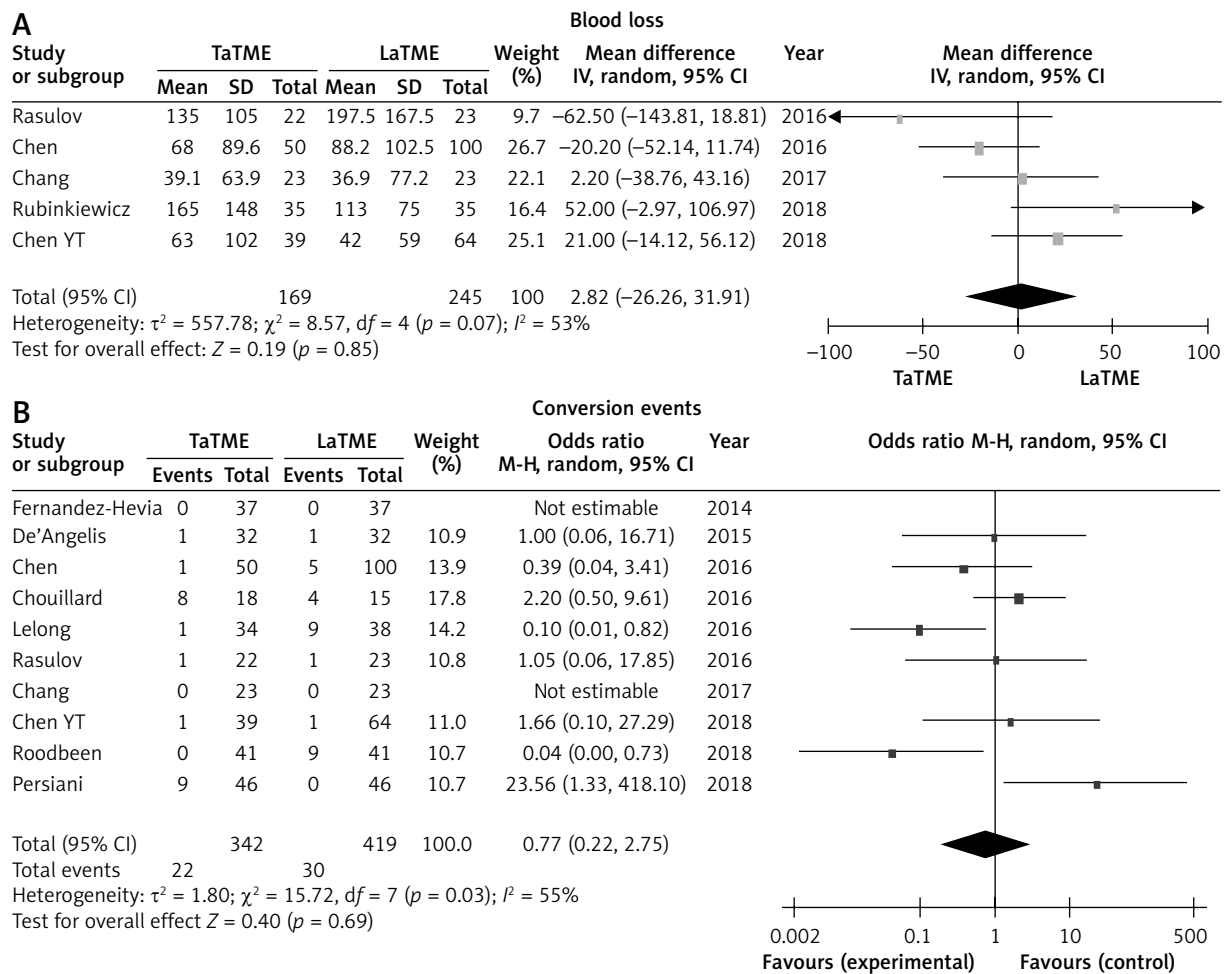


Figure 2. Forest plots describing estimated blood loss (A), conversion events (B), operative time (C) and intraoperative complications (D) between TaTME and LaTME

There were six studies [24–27, 31, 34] that reported CRM, eleven studies [24–26, 28–35] that reported positive CRM, eight studies [24–27, 30, 32–34] that reported DRM and five studies [25, 28, 31, 34, 35] that reported positive DRM. No differences were found in these pathological outcomes (Figure 5). Meanwhile, we did not find statistically significant differences in quality of mesorectum ($p = 0.39$), harvested lymph nodes ($p = 0.62$) or temporary stoma ($p = 0.27$) (Figure 6).

Four studies [25, 28, 31, 33] reported local recurrence; no difference was found in this outcome (Figure 7).

Publication bias

The funnel plot based on overall complication rate indicated no obvious publication bias (Figure 8).

Discussion

This study was the largest meta-analysis including 899 patients (411 patients in TaTME group, 488 patients in LaTME group). Our results showed no significant difference between TaTME and LaTME in overall intraoperative complications, postoperative outcomes, oncological outcomes or local recurrence. We hope that our findings can illustrate the safety and feasibility of TaTME, and promote its application in middle and low rectal cancer.

The TaTME is a novel technique which is expected to have better oncological outcomes. Lots of previous studies had shown that TaTME is superior to LaTME and may benefit in some surgical and pathological outcomes, but no RCT results prove these findings. There have been many meta-analyses [16–20] about TaTME in the last 3 years, but

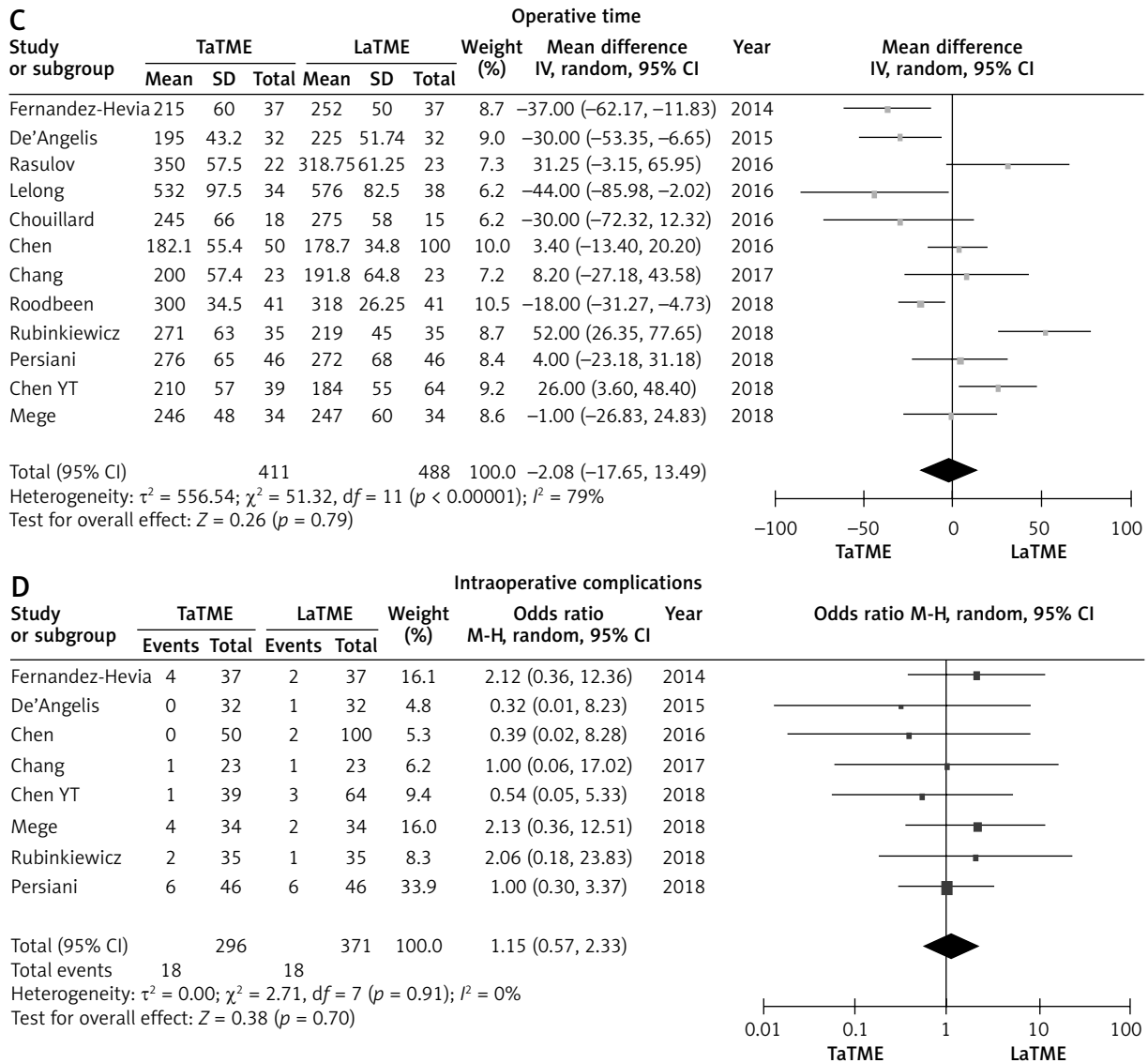


Figure 2. Cont.

most of them contained substantial bias, and the results of Rubinkiewicz *et al.* [18] showed no significant differences in clinical outcomes between TaTME and LaTME recently. But we found this negative result based on overall complications and some surgical outcomes without systematically analyzing intraoperative outcomes, postoperative outcomes, oncological outcomes. What is more, TaTME is more suitable for middle and low rectal cancer, and it is inappropriate to include high rectal cancer, which was included in Rubinkiewicz's study [35].

In this study, we included several of the most recent papers which were not included in previous

analyses, and systematically analyzed surgical outcomes aiming to find out new proof of differences of clinical outcomes between TaTME and LaTME. Previous meta-analyses [16, 17] had conflicting results in conversion rate and postoperative complications. In this meta-analysis which included 899 patients, we were able to show evidence of decrease of the overall postoperative complication rate, urinary morbidity and readmission rate in the TaTME group. However, we found no significant difference in conversion rate in our result. As previous reports, temporary stoma may affect recovery after surgery [36–38], but there was no difference in the rate of temporary stoma between two groups.

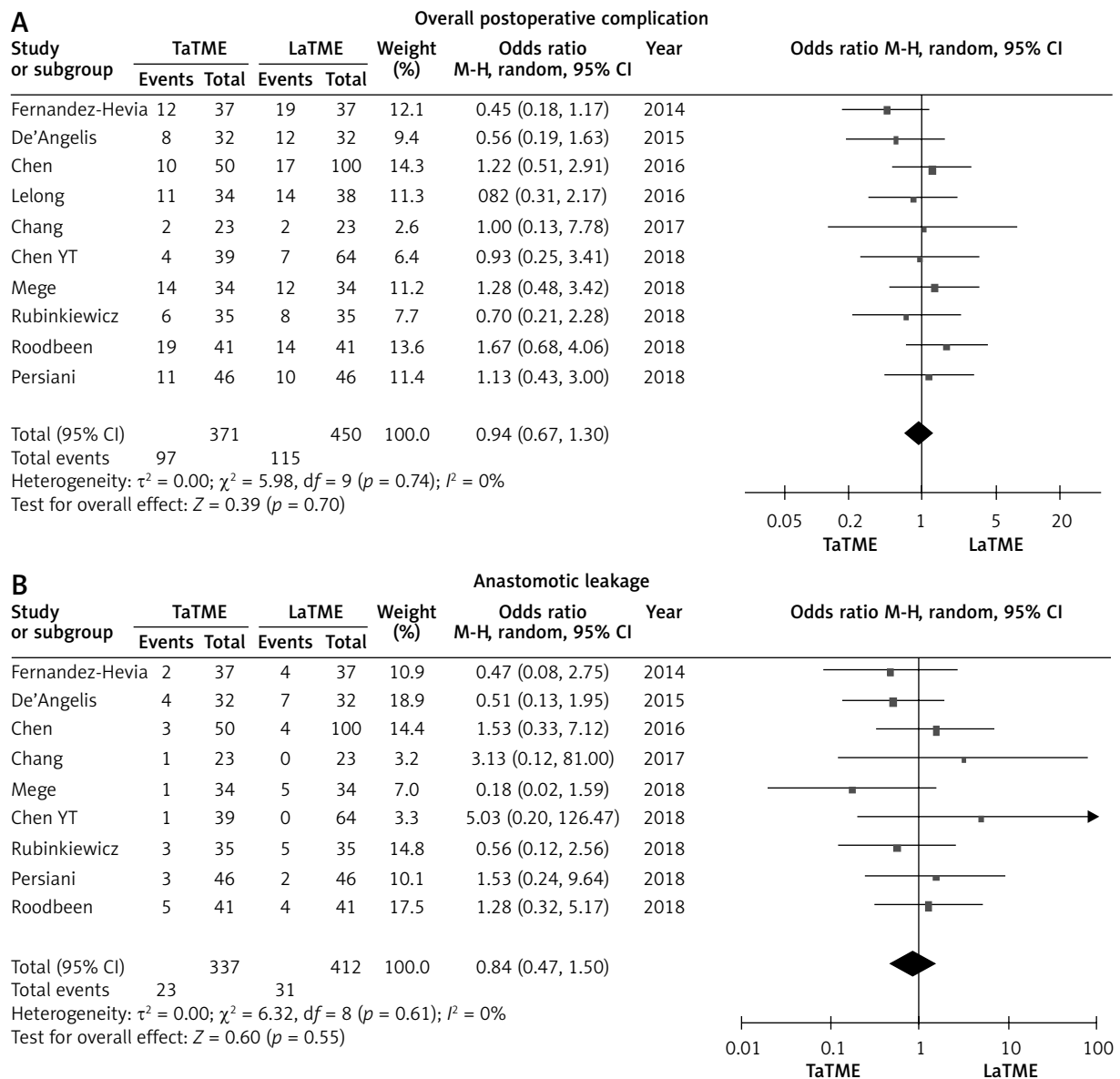


Figure 3. Forest plots describing postoperative outcomes: overall postoperative complication (A), anastomotic leakage (B), ileus (C), urinary morbidity (D) between TaTME and LaTME

In our study, the quality of mesorectum did not reach statistical significance between the two groups. A previous meta-analysis [16] including six studies found a significant difference in the complete rate of complete mesorectum. But after adding more studies in this study, no significant result was found in the complete rate of complete mesorectum. Interestingly, the TaTME group had better postoperative outcomes (readmission, reoperation, length of hospital stay) on average, although the difference did not reach statistical significance. The heterogeneities in these parameters were 10%, 15%, 76%

respectively, which may be an important factor affecting these results.

Fewer studies have assessed long-term observation. Only Zhang's meta-analysis [19] reported 2-year survival and 2-years disease-free survival between TaTME and LaTME, which included only two studies, and found no significant result. It is impossible to prove the superiority of any technique due to lack of new data. One of the most different procedures between TaTME and LaTME is separating the rectum during the small pelvis. Therefore, we think the rate of local recurrence is an important long-term outcome. In

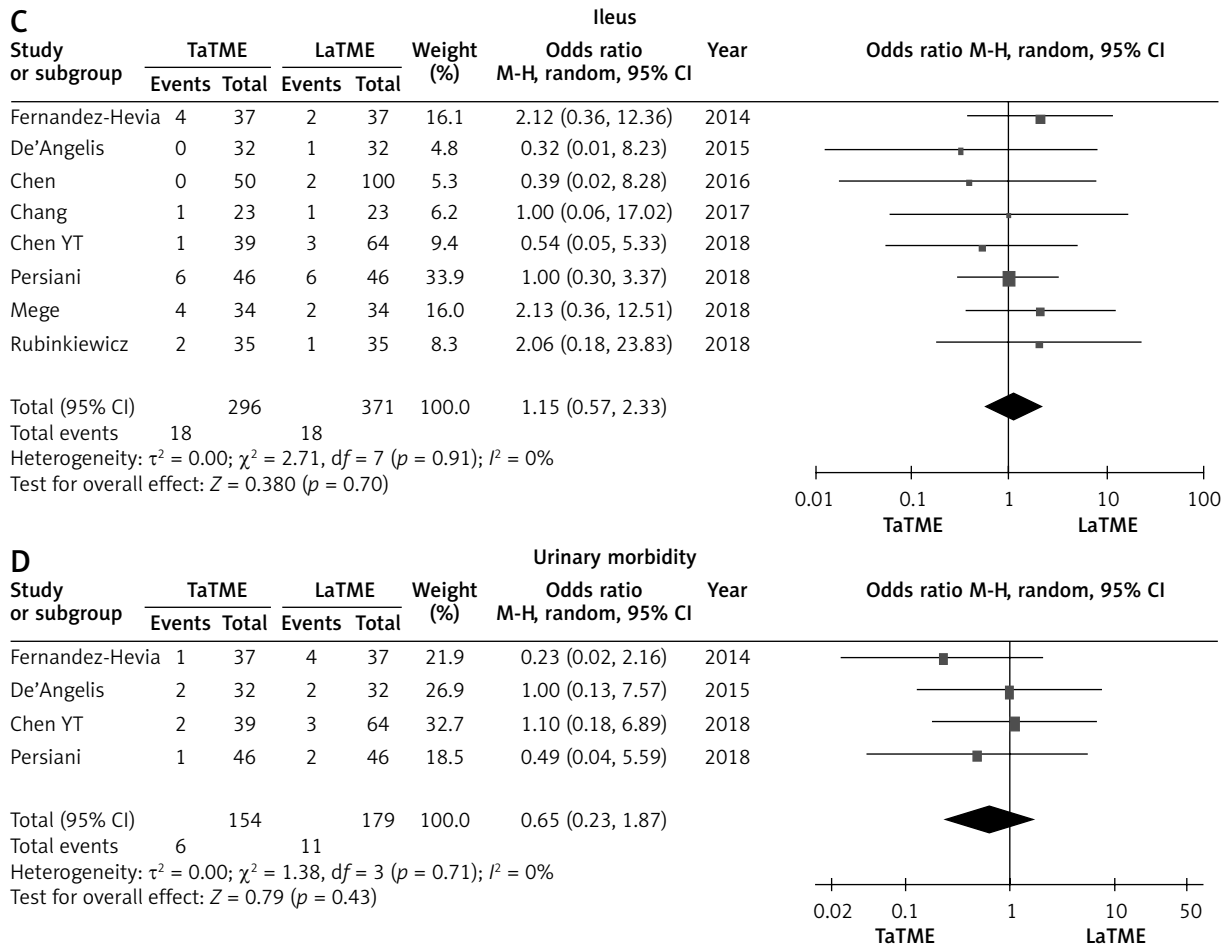


Figure 3. Cont.

this study we first compared local recurrence between TaTME and LaTME; the result showed no difference between TaTME and LaTME. It means that changing this key operative approach may not affect the surgical outcome of TME. It still requires more time for long-term follow-up in RCT studies, or more any other long-term outcome data from non-RCT results.

This meta-analysis has several limitations that must be taken into account. Firstly, all the included studies were observational studies but without RCTs. Without adequate random sequence generation and blinding, the risk of bias might increase. Therefore, the quality of the evidence pooled from these retrospective trials must be judged as low. Secondly, there may be publication bias due to all the included studies being in English, and these data were not from a high-volume center, which may also affect the results. Finally, no long-term outcome, such as overall survival and disease free survival, was measured in the analysis.

Conclusions

TaTME offers a safe and feasible alternative to LaTME although the clinicopathological features were not superior to LaTME in this study. Currently, in view of the lack of evidence on benefits of TaTME, further evaluation of TaTME necessitates large randomized control trials.

Acknowledgments

Dezheng Lin, Zhaoliang Yu and Wenpei Chen contributed equally to this study and should be considered as co-first authors.

Conflict of interest

The authors declare no conflict of interest.

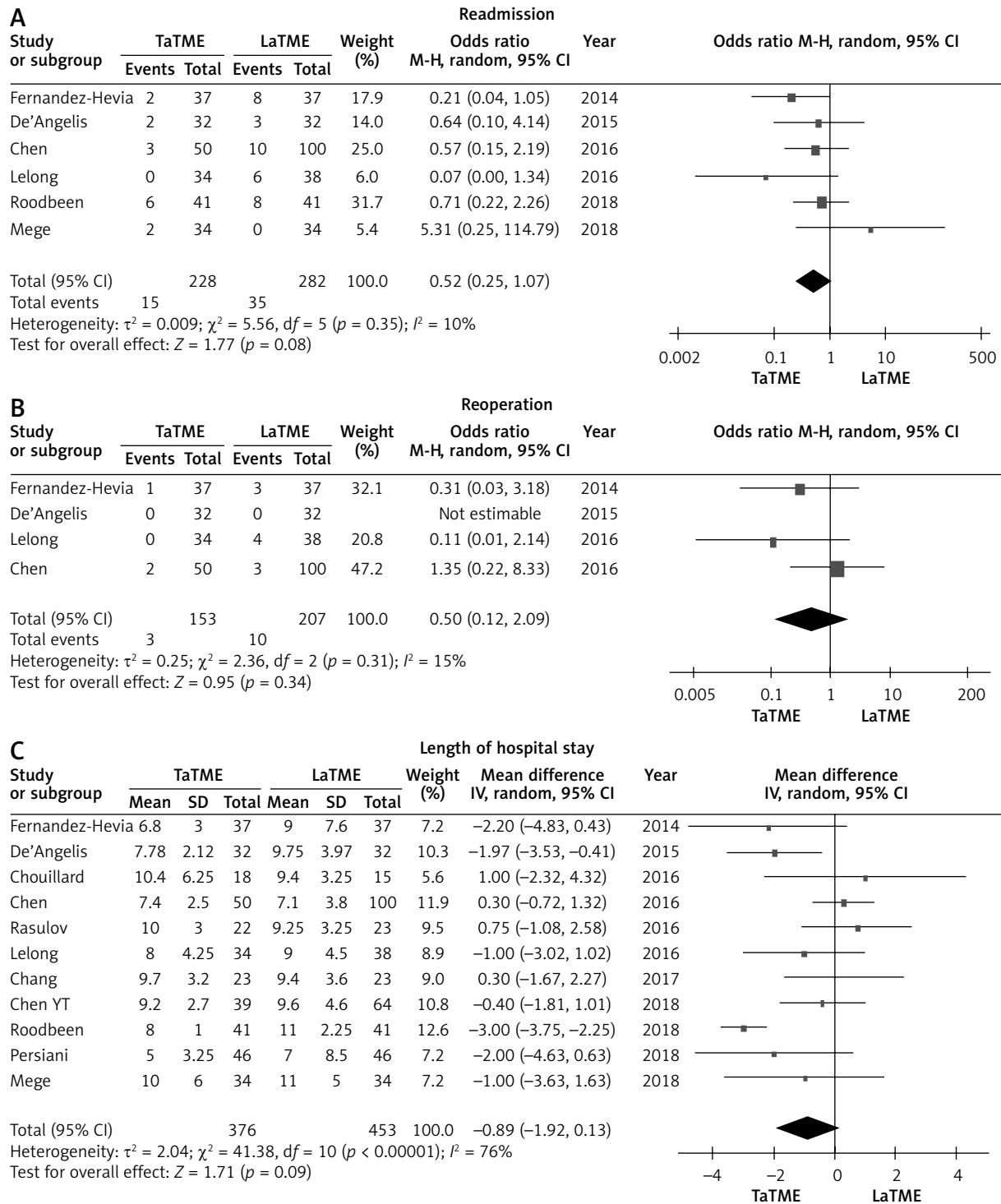


Figure 4. Forest plots describing postoperative outcomes: readmission (A), reoperation (B), length of hospital stay (C) between TaTME and LaTME

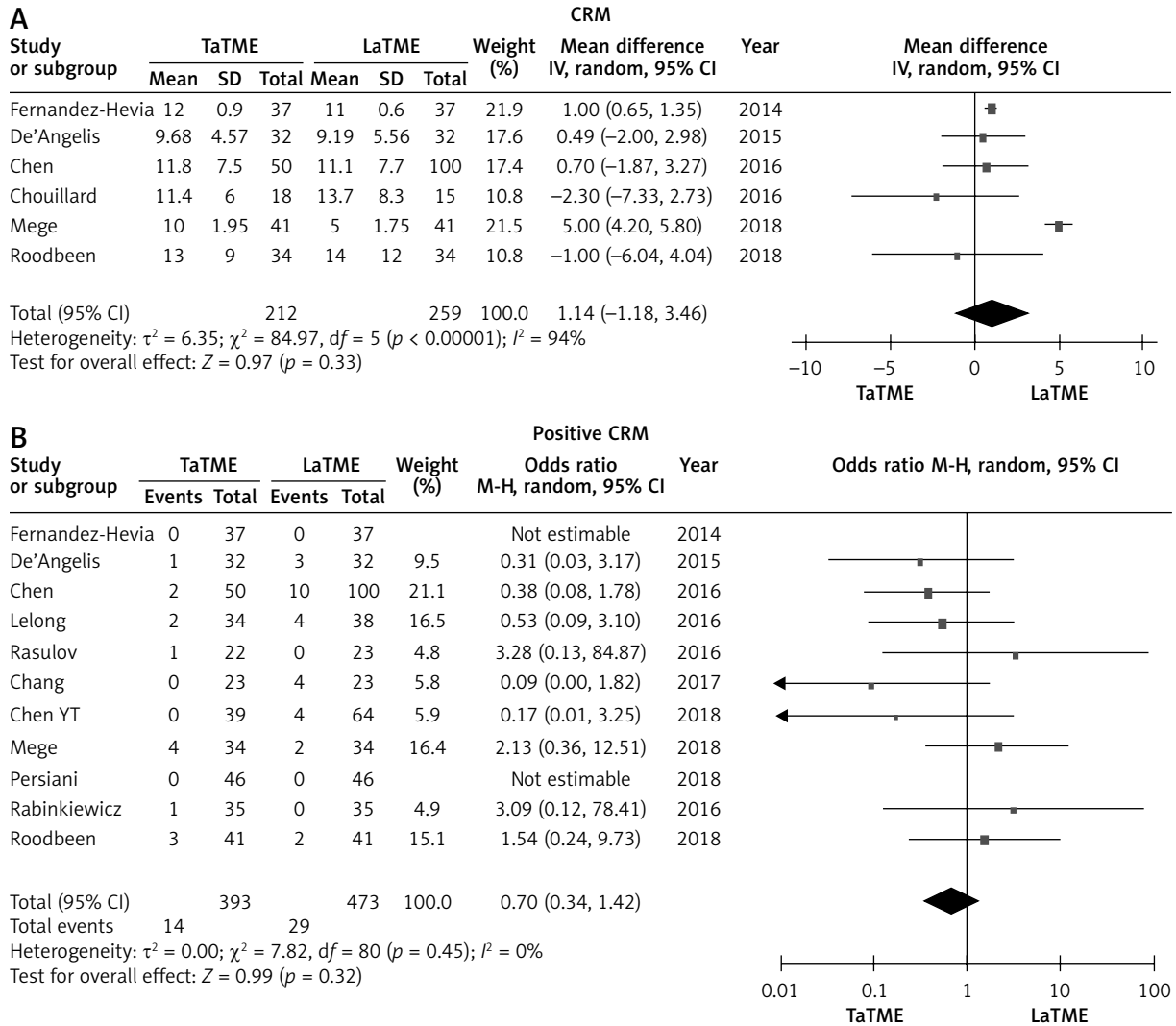


Figure 5. Forest plots describing oncological outcomes: CRM (A), positive CRM (B), DRM (C), positive DRM (D) between TaTME and LaTME

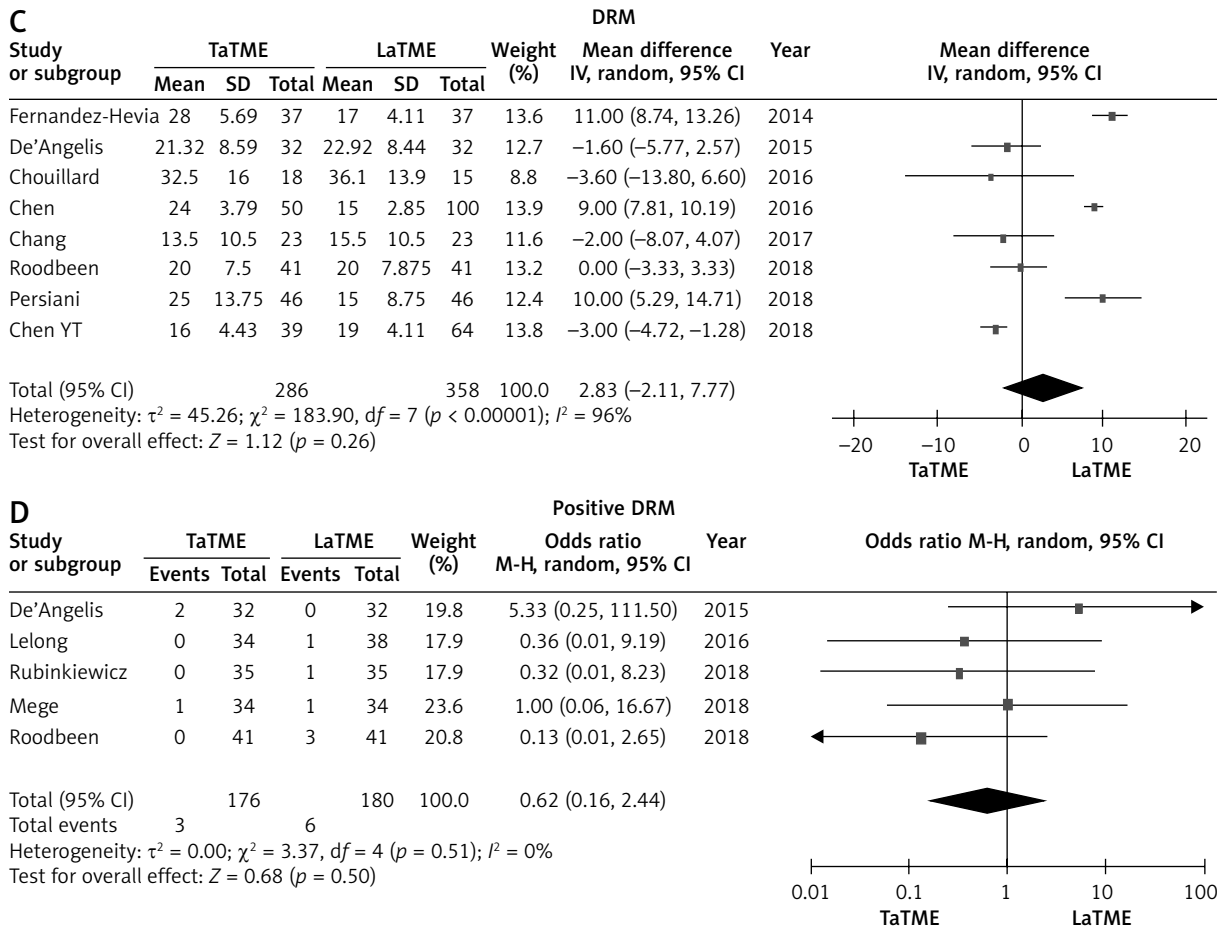


Figure 5. Cont.

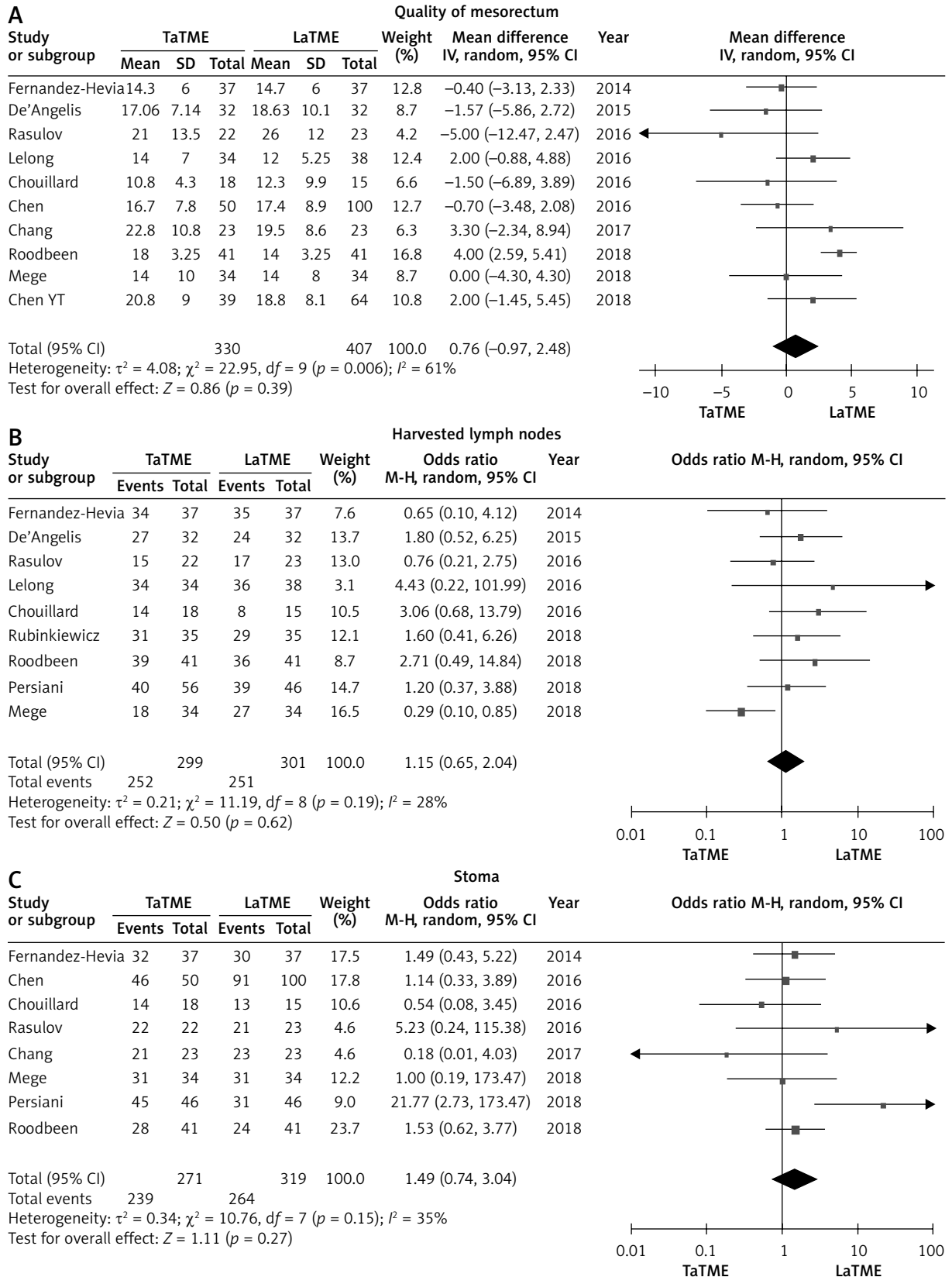


Figure 6. Forest plots describing oncological outcomes: quality of mesorectum (A), number of harvested lymph nodes (B) and temporary stoma (C) between TaTME and LaTME

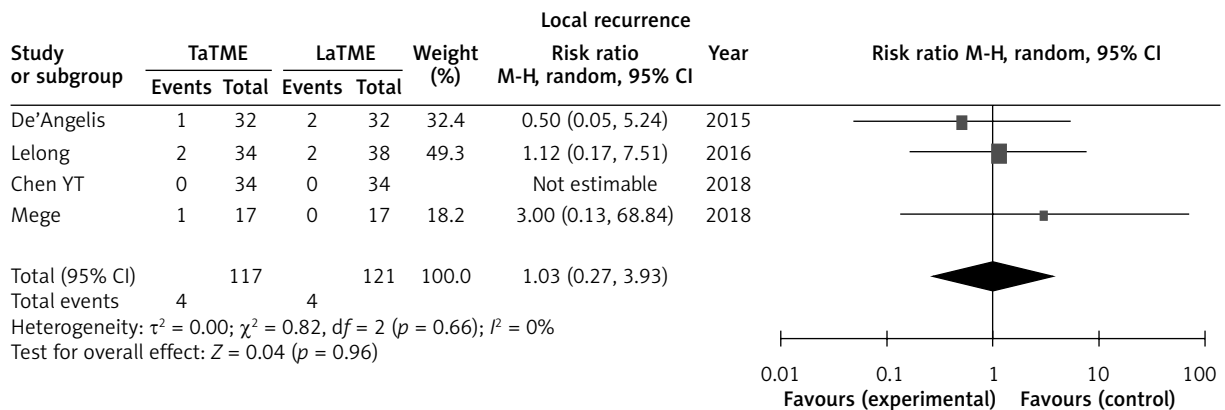


Figure 7. Forest plot describing oncological outcome of local recurrence

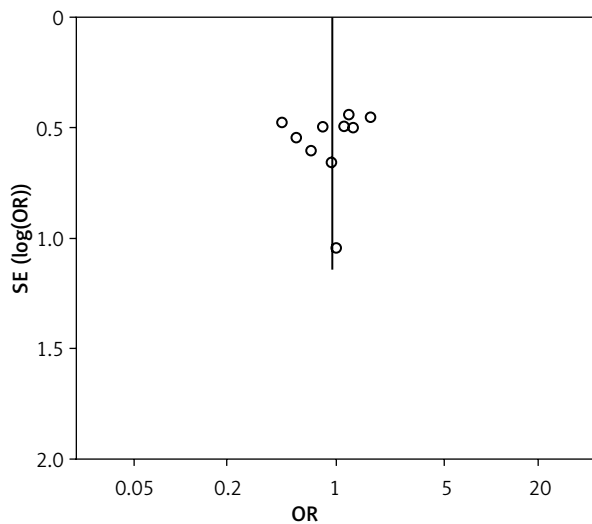


Figure 8. Funnel plot showing publication bias based on overall complication rate

References

- Ries LA, Wingo PA, Miller DS, et al. The annual report to the nation on the status of cancer, 1973-1997, with a special section on colorectal cancer. *Cancer* 2000; 88: 2398-424.
- Jacobs M, Verdeja JC, Goldstein HS. Minimally invasive colon resection (laparoscopic colectomy). *Surg Laparosc Endosc* 1991; 1: 144-50.
- Kearney DE, Coffey JC. A Randomized trial of laparoscopic versus open surgery for rectal cancer. *N Engl J Med* 2015; 373: 194.
- Jeong SY, Park JW, Nam BH, et al. Open versus laparoscopic surgery for mid-rectal or low-rectal cancer after neoadjuvant chemoradiotherapy (COREAN trial): survival outcomes of an open-label, non-inferiority, randomised controlled trial. *Lancet Oncol* 2014; 15: 767-74.
- Pedziwiatr M, Malczak P, Mizera M, et al. There is no difference in outcome between laparoscopic and open surgery for rectal cancer: a systematic review and meta-analysis on short- and long-term oncologic outcomes. *Tech Coloproctol* 2017; 21: 595-604.
- Malczak P, Mizera M, Torbic G, et al. Is the laparoscopic approach for rectal cancer superior to open surgery? A systemat-

ic review and meta-analysis on short-term surgical outcomes. *Videosurgery Miniinv* 2018; 13: 129-40.

- Heald RJ, Husband EM, Ryall RD. The mesorectum in rectal cancer surgery: the clue to pelvic recurrence? *Br J Surg* 1982; 69: 613-6.
- Enker WE, Thaler HT, Cranor ML, Polyak T. Total mesorectal excision in the operative treatment of carcinoma of the rectum. *J Am Coll Surg* 1995; 181: 335-46.
- Bach SP, Hill J, Monson JR, et al. A predictive model for local recurrence after transanal endoscopic microsurgery for rectal cancer. *Br J Surg* 2009; 96: 280-90.
- Enker WE. Potency, cure, and local control in the operative treatment of rectal cancer. *Arch Surg* 1992; 127: 1396-401; discussion 1402.
- Sylla P, Rattner DW, Delgado S, Lacy AM. NOTES transanal rectal cancer resection using transanal endoscopic microsurgery and laparoscopic assistance. *Surg Endosc* 2010; 24: 1205-10.
- Zhang H, Zhang YS, Jin XW, et al. Transanal single-port laparoscopic total mesorectal excision in the treatment of rectal cancer. *Tech Coloproctol* 2013; 17: 117-23.
- Heald RJ. A new solution to some old problems: transanal TME. *Tech Coloproctol* 2013; 17: 257-8.
- Deijen CL, Velthuis S, Tsai A, et al. COLOR III: a multicentre randomised clinical trial comparing transanal TME versus laparoscopic TME for mid and low rectal cancer. *Surg Endosc* 2016; 30: 3210-5.
- Lelong B, de Chaisemartin C, Meillat H, et al. A multicentre randomised controlled trial to evaluate the efficacy, morbidity and functional outcome of endoscopic transanal proctectomy versus laparoscopic proctectomy for low-lying rectal cancer (ETAP-GRECCAR 11 TRIAL): rationale and design. *BMC Cancer* 2017; 17: 253.
- Xu W, Xu Z, Cheng H, et al. Comparison of short-term clinical outcomes between transanal and laparoscopic total mesorectal excision for the treatment of mid and low rectal cancer: a meta-analysis. *Eur J Surg Oncol* 2016; 42: 1841-50.
- Ma B, Gao P, Song Y, et al. Transanal total mesorectal excision (taTME) for rectal cancer: a systematic review and meta-analysis of oncological and perioperative outcomes compared with laparoscopic total mesorectal excision. *BMC Cancer* 2016; 16: 380.

18. Rubinkiewicz M, Czerwinska A, Zarzycki P, et al. Comparison of short-term clinical and pathological outcomes after transanal versus laparoscopic total mesorectal excision for low anterior rectal resection due to rectal cancer: a systematic review with meta-analysis. *J Clin Med* 2018; 7: 448.
19. Zhang X, Gao Y, Dai X, et al. Short- and long-term outcomes of transanal versus laparoscopic total mesorectal excision for mid-to-low rectal cancer: a meta-analysis. *Surg Endosc* 2018; doi: 10.1007/s00464-018-6527-z.
20. Jiang HP, Li YS, Wang B, et al. Pathological outcomes of transanal versus laparoscopic total mesorectal excision for rectal cancer: a systematic review with meta-analysis. *Surg Endosc* 2018; 32: 2632-42.
21. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 2000; 283: 2008-12.
22. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ* 2009; 339: b2700.
23. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003; 327: 557-60.
24. Fernandez-Hevia M, Delgado S, Castells A, et al. Transanal total mesorectal excision in rectal cancer: short-term outcomes in comparison with laparoscopic surgery. *Ann Surg* 2015; 261: 221-7.
25. De'Angelis N, Portigliotti L, Azoulay D, Brunetti F. Transanal total mesorectal excision for rectal cancer: a single center experience and systematic review of the literature. *Langenbecks Arch Surg* 2015; 400: 945-59.
26. Chen CC, Lai YL, Jiang JK, et al. Transanal total mesorectal excision versus laparoscopic surgery for rectal cancer receiving neoadjuvant chemoradiation: a matched case-control study. *Ann Surg Oncol* 2016; 23: 1169-76.
27. Chouillard E, Regnier A, Vitte RL, et al. Transanal NOTES total mesorectal excision (TME) in patients with rectal cancer: is anatomy better preserved? *Tech Coloproctol* 2016; 20: 537-44.
28. Lelong B, Meillat H, Zemmour C, et al. Short- and mid-term outcomes after endoscopic transanal or laparoscopic transabdominal total mesorectal excision for low rectal cancer: a single institutional case-control study. *J Am Coll Surg* 2017; 224: 917-25.
29. Rasulov AO, Mamedli ZZ, Gordeyev SS, et al. Short-term outcomes after transanal and laparoscopic total mesorectal excision for rectal cancer. *Tech Coloproctol* 2016; 20: 227-34.
30. Chang TC, Kiu KT. Transanal total mesorectal excision in lower rectal cancer: comparison of short-term outcomes with conventional laparoscopic total mesorectal excision. *J Laparoendosc Adv Surg Tech A* 2018; 28: 365-9.
31. Mege D, Hain E, Lakkis Z, et al. Is trans-anal total mesorectal excision really safe and better than laparoscopic total mesorectal excision with a perineal approach first in patients with low rectal cancer? A learning curve with case-matched study in 68 patients. *Colorectal Dis* 2018; 20: O143-51.
32. Persiani R, Biondi A, Pennestri F, et al. Transanal total mesorectal excision vs laparoscopic total mesorectal excision in the treatment of low and middle rectal cancer: a propensity score matching analysis. *Dis Colon Rectum* 2018; 61: 809-16.
33. Chen YT, Kiu KT, Yen MH, Chang TC. Comparison of the short-term outcomes in lower rectal cancer using three different surgical techniques: transanal total mesorectal excision (TME), laparoscopic TME, and open TME. *Asian J Surg* 2018; doi: 10.1016/j.asjsur.2018.09.008.
34. Roodbeen SX, Penna M, Mackenzie H, et al. Transanal total mesorectal excision (TaTME) versus laparoscopic TME for MRI-defined low rectal cancer: a propensity score-matched analysis of oncological outcomes. *Surg Endosc* 2018; doi: 10.1007/s00464-018-6530-4.
35. Rubinkiewicz M, Nowakowski M, Wierdak M, et al. Transanal total mesorectal excision for low rectal cancer: a case-matched study comparing TaTME versus standard laparoscopic TME. *Cancer Manag Res* 2018; 10: 5239-45.
36. Veltcamp HM, Koedam T, Knol JJ, et al. Quality of life after rectal cancer surgery: differences between laparoscopic and transanal total mesorectal excision. *Surg Endosc* 2019; 33: 79-87.
37. Klek S, Pisarska M, Milian-Ciesielska K, et al. Early closure of the protective ileostomy after rectal resection should become part of the Enhanced Recovery After Surgery (ERAS) protocol: a randomized, prospective, two-center clinical trial. *Videosurgery Miniinv* 2018; 13: 435-41.
38. Nowakowski MM, Rubinkiewicz M, Gajewska N, et al. Defunctioning ileostomy and mechanical bowel preparation may contribute to development of low anterior resection syndrome. *Videosurgery Miniinv* 2018; 13: 306-14.

Received: 4.12.2018, **accepted:** 12.01.2019.