Surgical Oncology 30 (2019) 47–51

Contents lists available at ScienceDirect

Surgical Oncology

journal homepage: www.elsevier.com/locate/suronc

Does transanal total mesorectal excision of rectal cancer improve histopathology metrics and/or complication rates? A meta-analysis

Mahir Gachabayov[a], Inna Tulina[b], Roberto Bergamaschi[a,*], Petr Tsarkov[b]

[a] Section of Colorectal Surgery, Department of Surgery, New York Medical College, Westchester Medical Center, Valhalla, NY, USA
[b] Department of Surgery, Faculty of Preventive Medicine, Clinic of Colorectal and Minimally Invasive Surgery, Sechenov First Moscow State University, Moscow, Russia

ARTICLE INFO

Keywords:
Rectal cancer
Total mesorectal excision
Robotic surgery
Transanal surgery
Circumferential resection margin

ABSTRACT

Background: The aim of this meta-analysis was to determine whether transanal total mesorectal excision (taTME) improves histopathology metrics and/or complication rates when compared to robotic total mesorectal excision (R-TME) of resectable rectal cancer.
Methods: MEDLINE, Pubmed, Cochrane Library, and Scopus were systematically searched by two independent researchers. Six observational studies totaling 1,572 patients (811 taTME; 761 R-TME) were included after screening 14 potentially eligible records. Mantel-Haenszel method using odds ratios with 95% confidence intervals (OR (95%CI)) and inverse variance with mean difference with 95% confidence intervals (MD (95%CI)) as an effect measure for dichotomous and continuous variables, respectively, was employed for meta-analysis. Statistical heterogeneity among effect estimates was evaluated using I^2 and Tau^2.
Results: Circumferential resection margin (CRM) involvement rates (3.8% taTME; 5.3% R-TME) did not differ [OR (95%CI) = 0.86 (0.35, 2.15); p = 0.75] with low among-study heterogeneity (I^2 = 21%). Complication rates (35.4% taTME; 32.3% R-TME) did not differ [OR (95%CI) = 0.92 (0.64, 1.32); p = 0.65], although with moderate among-study heterogeneity (I^2 = 40%). CRM involvement [OR (95%CI) = 0.76 (0.40, 1.43); p = 0.40] and complication rates [OR (95%CI) = 0.84 (0.59, 1.21); p = 0.35] did not significantly differ in subgroup meta-analysis including mid- and low rectal cancer. Distal resection margin (mm) did not significantly differ between the interventions [MD (95%CI) = −0.41 (−1.29, 0.47); p = 0.37].
Conclusions: This meta-analysis found that taTME of rectal cancer does not improve histopathology metrics and complication rates when compared to R-TME.

1. Introduction

Total mesorectal excision (TME) has become the gold standard for resection of rectal cancer with curative intent. Circumferential resection margin (CRM) and quality of TME are the most critical histopathology metrics directly affecting local recurrence and cancer-specific survival rates [1]. There is a concern that obese males with low rectal cancer and bulky mesorectum [2,3] in a narrow pelvis [4] may currently be undergoing sphincter-sparing resection with involved CRM and poor quality of TME [5]. This reasonable concern prompted a search for different strategies among which transanal TME (taTME) seems to be promoted as an alternative to transabdominal TME. It seems appropriate to contribute to the ongoing debate as to whether taTME could lead to higher rates of uninvolved CRM and improved TME quality. In this regard, the question is what would be the most appropriate approach taTME should be compared to. Although the conclusions of the ACOSOG-Z6051 trial seem to favor open rather than laparoscopic surgery, a return to conventional surgery would seem unlikely at this time [6]. Hence, some form of minimally invasive surgery is here to stay and is likely to include robotic assistance [7,8]. This meta-analysis aimed at determining whether taTME improves histopathology metrics and/or complication rates when compared to robotic TME (R-TME).

2. Methods

Literature search was conducted according to recently published recommendations [9]. MEDLINE via Ovid, Pubmed, Cochrane Library, and Scopus were systematically searched by two researchers independently (GM, TI). The criterion for inclusion in quantitative data synthesis was any observational or experimental study comparing

* Corresponding author. Taylor Pavilion, Suite D-365, 100 Woods Road, Valhalla, NY, 10595, USA.
E-mail address: rcmbergamaschi@gmail.com (R. Bergamaschi).

https://doi.org/10.1016/j.suronc.2019.05.012
Received 17 February 2019; Received in revised form 1 May 2019; Accepted 18 May 2019

taTME to R-TME in patients with rectal cancer. Non-comparative studies and studies comparing either taTME or R-TME to an irrelevant intervention were included in qualitative data synthesis, however, excluded from the meta-analysis. Pathology and clinical outcomes were CRM involvement and postoperative complication rates, respectively. The quality of the included studies was assessed using Newcastle-Ottawa scale for cohort studies. RevMan (version 5.3; Nordic Cochrane Center, Cochrane Collaboration, Copenhagen, Denmark) was used for statistical analysis. Mantel-Haenszel method using odds ratios with 95% confidence intervals (OR (95%CI)) as an effect measure was employed to compare dichotomous variables. Continuous variables were compared using inverse variance method with mean difference and standard error (MD (95%CI)) as an effect measure. Hozo's formula was utilized to estimate mean and standard deviation for the outcomes reported in median with interquartile range [10]. Statistical heterogeneity among effect estimates was evaluated using I^2. Random-effects model for meta-analysis was utilized. Subgroup meta-analysis including patients with mid- and low rectal cancer only was performed. A p-value < 0.05 was considered statistically significant. Numbers needed to treat with 95% confidence intervals (NNT (95%CI)) was calculated for evaluation of clinical significance.

3. Results

Six out of 14 potentially eligible studies were included [11–16] totaling 1,572 patients (811 taTME and 761 R-TME). A description of the included studies as well as their quality assessment is shown in Table 1.

CRM involvement rates were reported in five studies (756 taTME vs. 701 R-TME) [11–14,16]. Pooled CRM involvement rates were 3.8% (29/756) in taTME and 5.3% (37/701) in R-TME. This difference was neither statistically nor clinically significant [OR (95%CI) = 0.86 (0.35, 2.15); p = 0.75; NNT (95%CI) = 70 (> 28 to harm, > 142 to benefit)] with low among-study heterogeneity ($I^2 = 21\%$) (Fig. 1A).

Complication rates were reported in all studies (808 taTME vs. 759 R-TME after excluding patients with missing data) [11–16]. Pooled postoperative complication rates were 35.4% (286/808) in taTME and 32.3% (245/759) in R-TME. This difference was neither statistically nor clinically significant [OR (95%CI) = 0.92 (0.64, 1.32); p = 0.65; NNT (95%CI) = 33 (> 13 to harm, > 64 to benefit)] with moderate among-study heterogeneity ($I^2 = 40\%$) (Fig. 1B).

Four out of the six studies included only patients with mid- and low rectal cancer [13–16]. A subgroup meta-analysis of the data extracted from those studies was conducted. A total of 917 patients were included (359 taTME vs. 558 R-TME). CRM involvement rates were reported in three studies (304 taTME vs. 498 R-TME) [13,14,16]. Pooled CRM involvement rates were 4.9% (15/304) in taTME and 6.2% (31/498) in R-TME. This difference was neither statistically nor clinically significant [OR (95%CI) = 0.76 (0.40, 1.43); p = 0.40; NNT (95%CI) = 78 (> 52 to harm, > 22 to benefit)] with low among-study heterogeneity ($I^2 = 0\%$) (Fig. 2A). Complication rates were reported in four studies (359 taTME vs. 558 R-TME) [13–16]. Pooled postoperative complication rates were 30.9% (111/359) in taTME and 33.5% (187/558) in R-TME. This difference was neither statistically nor clinically significant [OR (95%CI) = 0.84 (0.59, 1.21); p = 0.35; NNT (95%CI) = 39 (> 28 to harm, > 11 to benefit)] with low among-study heterogeneity ($I^2 = 11\%$) (Fig. 2B). Distal resection margin (mm) was reported in three studies (82 taTME vs. 105 R-TME) [13,15,16]. The mean distal resection margin was found to be 1.7 mm in taTME and 2.1 mm in R-TME. Statistical among study heterogeneity was high ($I^2 = 93\%$; $Tau^2 = 0.55$). This outcome did not significantly differ between the interventions [MD (95%CI) = −0.41 (−1.29, 0.47); p = 0.37] (Fig. 2C).

A subset analysis for patients with cancer of the distal 1/3 of the rectum only could not be done as none of the included studies stratified the outcomes by distance of the cancer from the anal verge. A

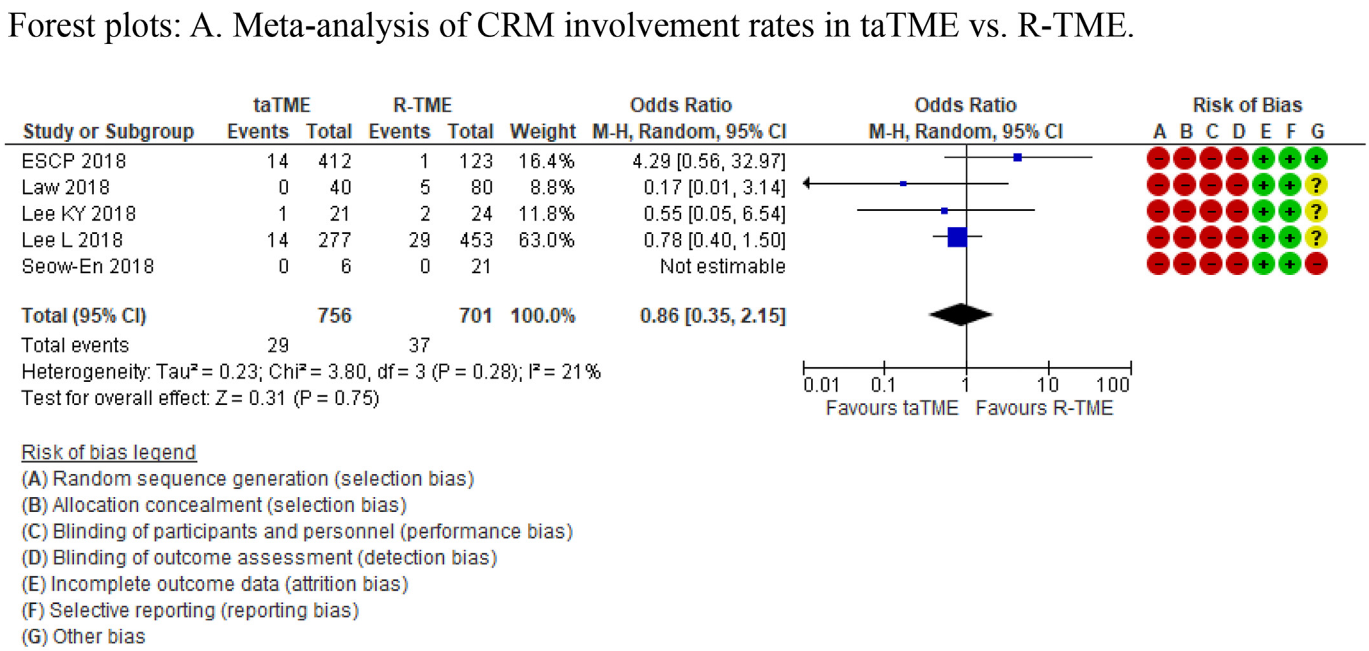
Table 1
Description of included studies.

Author	Publication	Study design	Sample size in taTME vs. R-TME (n)	Male: Female ratio	BMI (kg/m²)	Level of tumor (H/M/L)	Follow-up	NOS (S–C–O)
ESCP	Colorectal Dis 2018 [3]	PCS (2017)	412 vs. 123	280:132 vs. 84:39	NS	H + M + L	NS	3-2-1
Law	Surg Endosc 2018 [4]	RCS (2014–2017)	40 vs. 80	29:11 vs. 50:30	NR	H + M + L	30 days	4-2-1
Lee KY	Ann Coloproctol 2018 [5]	RCS (2013–2014)	21 vs. 24	16:5 vs. 13:11	24.4 vs. 23.6[b]	M + L	21.3 months[a]	4-2-3
Lee L	Ann Surg 2018 [6]	RCS (2011–2017)	277 vs. 453	175:102 vs. 284: 169	27.9 vs. 25.6[b]	M + L	30 days	4-2-1
Perez	Eur J Surg Oncol 2018 [7]	RCS (2013–2016)	55 vs. 60	40:15 vs. 44:16	24.9 vs. 25.8[a]	M + L	NS	4-2-1
Seow-En	Ann Acad Med Singapore 2018 [8]	PCS (2012–2015)	6 vs. 21	3:3 vs. 14:7	24 vs. 24[a]	M + L	30 days	3-2-1

ESCP, European Society of Coloproctology; PCS, prospective cohort study; RCS, retrospective cohort study; BMI, body mass index; NR, not reported; NS, not specified; H, high; M, mid; L, low; R, robotic; Ls, laparoscopic; NOS, Newcastle-Ottawa score; S–C–O, Selection-Comparability-Outcome.

[a] Median.

[b] Mean.



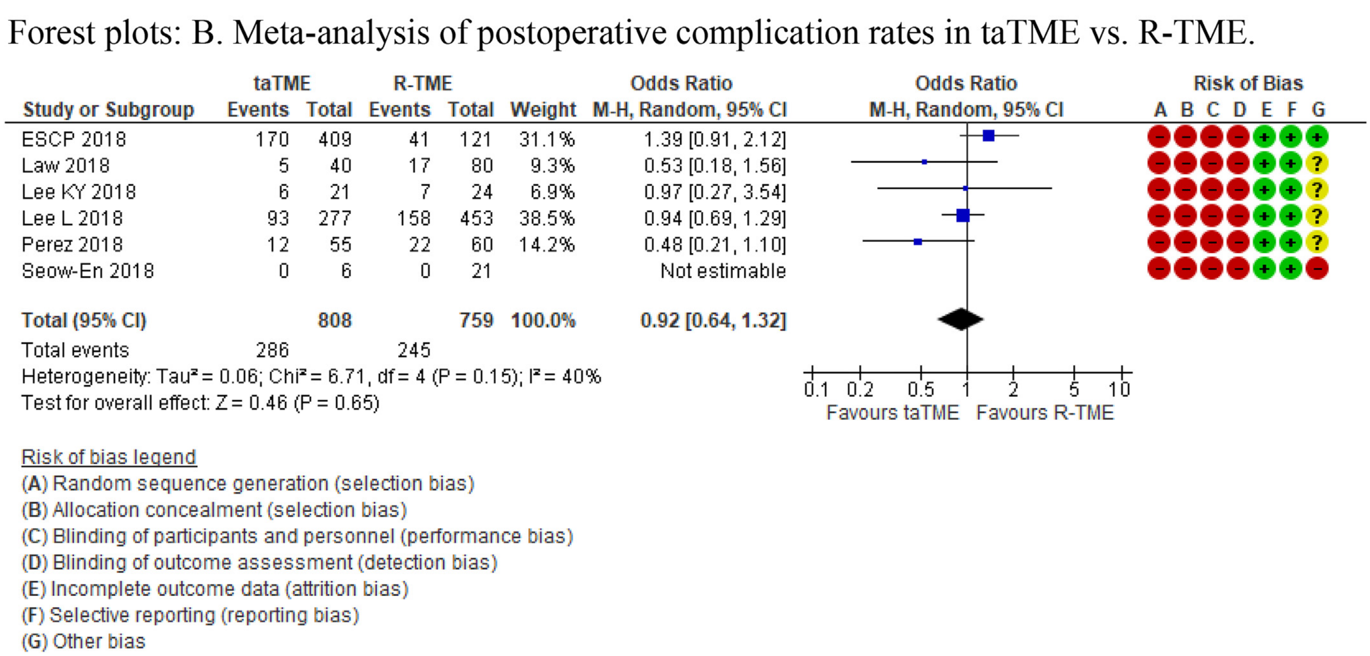


Fig. 1. Forest plots: A. Meta-analysis of CRM involvement rates in taTME vs. R-TME. B. Meta-analysis of postoperative complication rates in taTME vs. R-TME.

sequential exclusion of the studies with the highest risk of bias was performed for sensitivity analysis which did not affect the findings.

4. Discussion

The main finding of this meta-analysis was that taTME of rectal cancer did not lead to significant improvement of histopathology metrics and complication rates as compared to R-TME. The rationale behind taTME stems from a reasonable concern for involved CRM and incomplete quality of TME in obese males with low rectal cancer and bulky mesorectum in a narrow pelvis. In fact, the study by Targarona et al. [4] found that the promontory-subsacrum angle of an android pelvis can affect histopathology metrics when the resection is carried out laparoscopically. Two randomized control trials (RCT) (ACOSOG Z6051 and ALaCart) concluded that laparoscopic TME is not non-inferior to open TME [6,17]. ACOSOG Z6051 and ALaCart chose CRM and quality of TME as endpoints. Conversely, two other RCTs (COLOR 2 and COREAN) concluded that laparoscopic TME is not inferior to its open counterpart based on survival rates, which do not necessarily reflects the quality of surgery and can rather be impacted by gene mutations, chemoradiation, etc. [18,19]. It seems reasonable to speculate that the results of the abovementioned RCTs may turn the attention onto R-TME. In fact, a matched comparison of the first robotic cases by the same surgeon showed that the CRM was significantly improved when compared to open and lap TME despite the learning curve in robotic surgery [20]. Laparoscopic TME may decrease the CRM due to its

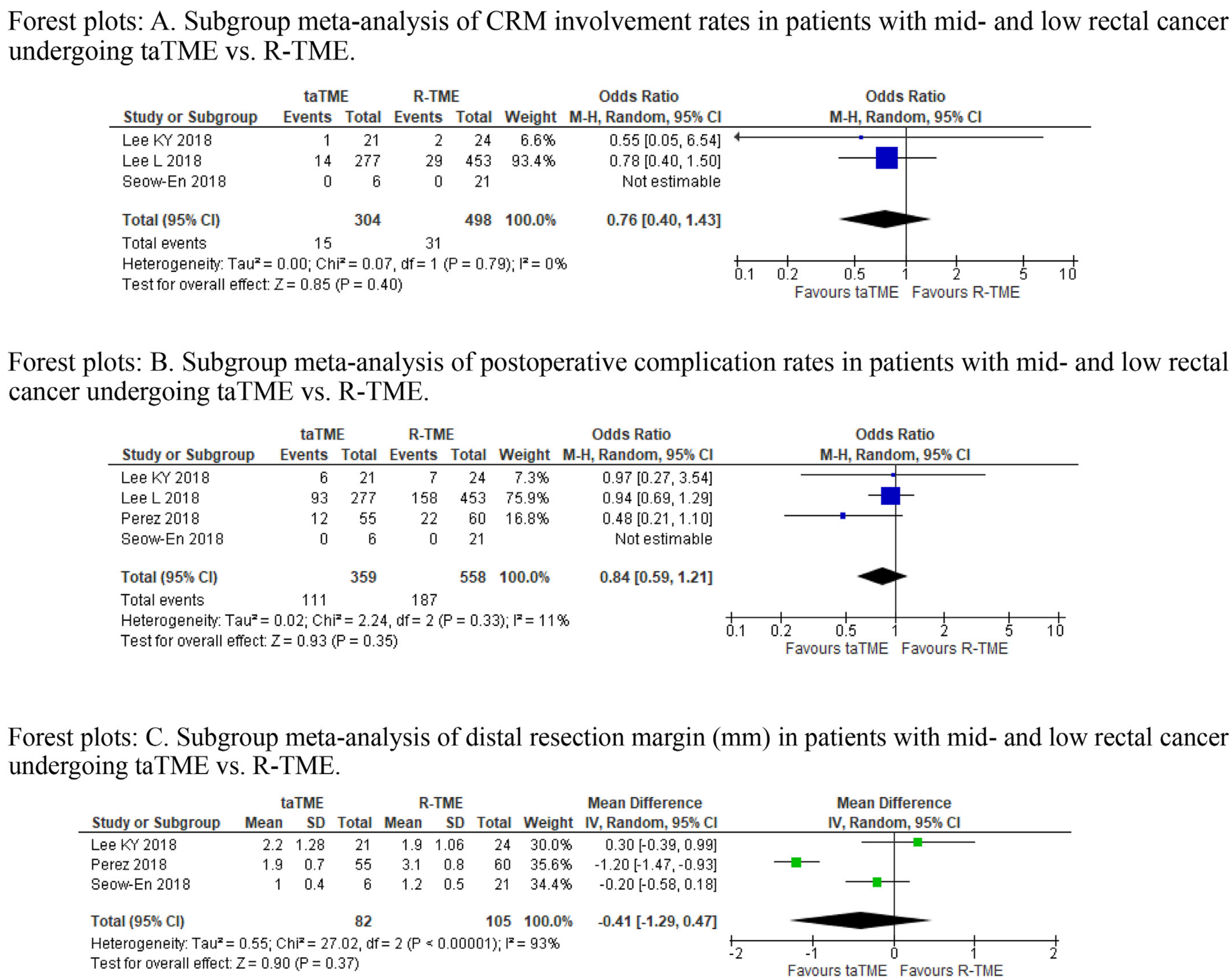


Fig. 2. Forest plots: A. Subgroup meta-analysis of CRM involvement rates in patients with mid- and low rectal cancer undergoing taTME vs. R-TME. B. Subgroup meta-analysis of postoperative complication rates in patients with mid- and low rectal cancer undergoing taTME vs. R-TME. C. Subgroup meta-analysis of distal resection margin (mm) in patients with mid- and low rectal cancer undergoing taTME vs. R-TME.

decreased degree of movements, a limitation overcome by the wristed instruments used in R-TME. The same study also concluded that the lack of tactile feedback did not adversely impact the quality of TME in the robotic cases [20]. A recent RCT comparing R-TME to laparoscopic TME concluded that R-TME, when performed by surgeons with varying experience in robotic surgery, does not confer an advantage in rectal cancer resection [21].

The fact that taTME would result in a very low anastomosis regardless of tumor location is particularly concerning when the International taTME Registry reports that 38% of the patients underwent taTME for tumors located up to 13 cm from the anal verge with a 5-cm distal resection margin [22]. In essence, taTME would have inflicted an unnecessary organ loss with the potential morbidity and functional disadvantages of a very low anastomosis [23].

In 2015 Warren & Solomon emphasized how taTME entails a rectal transection inside the pelvis, thereby mandating serious scrutiny due to the potentially increased risk of local recurrence [24]. In January 2019, the National Norwegian taTME data showed not only an increased rate but also a new pattern of local recurrence in terms of its multifocality as well as its early timing after taTME [25]. On the basis of such alarming data, a consensus was reached to cease performing taTME in Norway [25].

It has been claimed that transanal TME offers at least three oncological advantages: 1) A longer distal resection margin following taTME (2.8 ± 1.8 vs 1.7 ± 1.3 cm; $p < 0.01$) was likely obtained by performing an unnecessary low rectal transection on patients with cancer of the mid rectum [26]; 2) A decreased rate of involved CRM following taTME (2 vs 9 cases; $p = 0.025$) was reported in a randomized clinical trial despite no difference in mean CRM (7 vs 5 mm; $P = 0.833$) [27]; 3) Increased rates of complete TME quality following taTME (24 vs 18; $p < 0.05$) were claimed in a case series also including abdomino-perineal resection (APR) cases [28]. In fact, a comparison excluding APR cases would have resulted in a $p = 0.229$ (Fisher exact test).

Longer learning curve seems to be the disadvantage of taTME. In fact, a recent study utilizing CUSUM analysis found that 45 cases would be required to achieve acceptable quality of TME [29]. The length of the learning phase in robotic surgery varied from 15 to 29 in previously reported studies. Moreover, a recent meta-analysis found no detrimental impact of the learning curve in robotic surgery on histopathology metrics [30].

Although the International taTME Registry made a serious attempt to provide real world data on anastomotic leak rates [31], the focus has rather been on the intraoperative complications of taTME. In fact, unfamiliarity with the anatomy of a bottom up view and/or cavalier attempts to carry out the dissection entirely from below might be behind urethra perforations and/or laceration of the internal iliac vein we heard through the grapevine. A recent study by Shen et al. [32] provided a substantial contribution in terms of emphasizing the value of MRI-based preoperative pelvimetry in essence taking the work of Targarona et al. [4] one step farther. Probably, the authors' most useful contribution was identifying the landmarks between the trans-anal and the trans-abdominal phases of the operation [32] as a reminder that taTME is not meant to replace but rather complement its abdominal counterpart.

This meta-analysis has the following limitations: lack of standardization in reporting outcome metrics renders quantitative synthesis of the data difficult; all reports were observational studies with substantial risks of Berkman's, performance, and reporting biases; the learning curve was not taken into account in any of the six studies, thereby, introducing a risk of control group bias.

This meta-analysis found that taTME of rectal cancer did not lead to significant improvement of histopathology metrics and complication rates when compared to R-TME.

Disclaimers

No presentation; no conflict of interest; no copyrighted material used; no funding.

Compliance with ethical standards

Disclosure of potential conflicts of interest: The authors declare that they have no conflicts of interest.

Research involving human participants and/or animals: Not applicable as this is a summary design study.

Informed consent: Not applicable as this is a summary design study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.suronc.2019.05.012.

References

[1] K.F. Birbeck, C.P. Macklin, N.J. Tiffin, W. Parsons, M.F. Dixon, N.P. Mapstone, et al., Rates of circumferential resection margin involvement vary between surgeons and predict outcomes in rectal cancer surgery, Ann. Surg. 235 (4) (2002) 449–457.
[2] F. Kanso, L. Maggiori, C. Debove, A. Chau, M. Ferron, Y. Panis, Perineal or abdominal approach first during intersphincteric resection for low rectal cancer: which is the best strategy? Dis. Colon Rectum 58 (7) (2015) 637–644.
[3] E. Rullier, Transanal mesorectal excision: the new challenge in rectal cancer, Dis. Colon Rectum 58 (7) (2015) 621–622.
[4] E.M. Targarona, C. Balague, J.C. Pernas, et al., Can we predict immediate outcome after laparoscopic rectal surgery? Multivariate analysis of clinical, anatomic, and pathologic features after 3-dimensional reconstruction of the pelvic anatomy, Ann. Surg. 247 (4) (2008) 642–649.
[5] R. Bendl, R. Bergamaschi, Transanal TME: a bum rap? Colorectal Dis. 18 (1) (2016) 7–8.
[6] J. Fleshman, M. Branda, D.J. Sargent, et al., Effect of laparoscopic-assisted resection vs open resection of stage II or III rectal cancer on pathologic outcomes: the ACOSOG Z6051 randomized clinical trial, J. Am. Med. Assoc. 314 (13) (2015) 1346–1355.
[7] S. Tou, R. Bergamaschi, Laparoscopic rectal cancer resection: inferior to open or not? Colorectal Dis. 18 (3) (2016) 233.
[8] S.K. Abbas, S.B. Yelika, K. You, et al., Rectal cancer should not be resected laparoscopically: the rationale and the data, Tech. Coloproctol. 21 (3) (2017) 237–240.
[9] K. Goossen, S. Tenckhoff, P. Probst, et al., Optimal literature search for systematic reviews in surgery, Langenbeck's Arch. Surg. 403 (1) (2018) 119–129.
[10] S.P. Hozo, B. Djulbegovic, I. Hozo, Estimating the mean and variance from the median, range, and the size of a sample, BMC Med. Res. Methodol. 5 (2005) 13.
[11] 2017 European Society of Coloproctology (ESCP) collaborating group, An international multicentre prospective audit of elective rectal cancer surgery; operative approach versus outcome, including transanal total mesorectal excision (TaTME), Colorectal Dis. 20 (Suppl 6) (2018) 33–46.
[12] W.L. Law, D.C.C. Foo, Comparison of early experience of robotic and transanal total mesorectal excision using propensity score matching, Surg. Endosc. (2018 Jul 16), https://doi.org/10.1007/s00464-018-6340-8 [Epub ahead of print].
[13] K.Y. Lee, J.K. Shin, Y.A. Park, S.H. Yun, J.W. Huh, Y.B. Cho, et al., Transanal endoscopic and transabdominal robotic total mesorectal excision for mid-to-low rectal cancer: comparison of short-term postoperative and oncologic outcomes by using a case-matched analysis, Ann. Coloproctol. 34 (1) (2018) 29–35.
[14] L. Lee, B. de Lacy, M. Gomez Ruiz, A.S. Liberman, M.R. Albert, J.R.T. Monson, et al., A multicenter matched comparison of transanal and robotic total mesorectal excision for mid and low-rectal adenocarcinoma, Ann. Surg. (2018 Jun 18), https://doi.org/10.1097/SLA.0000000000002862 [Epub ahead of print].
[15] D. Perez, N. Melling, M. Biebl, M. Reeh, J.K. Baukloh, J. Miro, et al., Robotic low anterior resection versus transanal total mesorectal excision in rectal cancer: a comparison of 115 cases, Eur. J. Surg. Oncol. 44 (2) (2018) 237–242.
[16] I. Seow-En, F. Seow-Choen, An initial experience comparing robotic total mesorectal excision (RTME) and transanal total mesorectal excision (taTME) for low rectal tumours, Ann. Acad. Med. Singapore 47 (5) (2018) 188–190.
[17] A.R.L. Stevenson, M.J. Solomon, J.W. Lumley, et al., Effect of laparoscopic-assisted resection vs open resection on pathological outcomes in rectal cancer: the ALaCart randomized clinical trial, J. Am. Med. Assoc. 314 (13) (2015) 1356–1363.
[18] J.H. Bonjer, C.L. Deijen, G.A. Abis, et al., A randomized trial of laparoscopic versus open surgery for rectal cancer, N. Engl. J. Med. 372 (2015) 1324–1332.
[19] S.Y. Jeong, J.W. Park, B.H. Nam, et al., Open versus laparoscopic surgery for mid-rectal or lowrectal cancer after neoadjuvant chemoradiotherapy (COREAN trial): survival outcomes of an open-label, non-inferiority, randomized controlled trial, Lancet Oncol. 15 (7) (2014) 767–774.
[20] M. Barnajian, D. Pettet 3rd, E. Kazi, C. Foppa, R. Bergamaschi, Quality of total mesorectal excision and depth of circumferential resection margin in rectal cancer: a matched comparison of the first 20 robotic cases, Colorectal Dis. 16 (8) (2014) 603–609.
[21] D. Jayne, A. Pigazzi, H. Marshall, et al., Effect of robotic-assisted vs conventional laparoscopic surgery on risk of conversion to open laparotomy among patients undergoing resection for rectal cancer: the ROLARR randomized clinical trial, J. Am. Med. Assoc. 318 (16) (2017) 1569–1580.
[22] M. Penna, R. Hompes, S. Arnold, et al., Transanal total mesorectal excision: international registry results of the first 720 cases, Ann. Surg. 266 (1) (2017) 111–117.
[23] M. Gachabayov, A. Chudner, R. Bergamaschi, A succinct critical appraisal of indications to transanal total mesorectal excision, Ann. Surg. 268 (6) (2018) e94.
[24] O.J. Warren, M.J. Solomon, The drive toward transanal total mesorectal excision–science or rhetoric? Dis. Colon Rectum 58 (9) (2015) 909–910.
[25] M. Gachabayov, R. Bergamaschi, Is taTME delivering? Updat. Surg. (2019 Feb 22), https://doi.org/10.1007/s13304-019-00634-3 [Epub ahead of print].
[26] M. Fernandez-Hevia, S. Delgado, A. Castells, M. Tasende, D. Momblan, G. Díaz del Gobbo, et al., Transanal total mesorectal excision in rectal cancer: short-term outcomes in comparison with laparoscopic surgery, Ann. Surg. 261 (2015) 221–227.
[27] Q. Denost, J.P. Adam, A. Rullier, E. Buscail, C. Laurent, E. Rullier, Perineal transanal approach: a new standard for laparoscopic sphincter-saving resection in low rectal cancer, a randomized trial, Ann. Surg. 260 (2014) 993–999.
[28] S. Velthuis, D.H. Nieuwenhuis, T.E.G. Ruijter, M.A. Cuesta, H.J. Bonjer, C. Sietses, Transanal versus traditional laparoscopic total mesorectal excision for rectal carcinoma, Surg. Endosc. 28 (2014) 3494–3499.
[29] L. Lee, J. Kelly, G.J. Nassif, T.C. deBeche-Adams, M.R. Albert, J.R.T. Monson, Defining the learning curve for transanal total mesorectal excision for rectal adenocarcinoma, Surg. Endosc. (2018 Jul 11), https://doi.org/10.1007/s00464-018-6360-4 [Epub ahead of print].
[30] M. Gachabayov, K. You, S.H. Kim, et al., Meta-analysis of the impact of the learning curve in robotic rectal cancer surgery on histopathologic outcomes, Surg. Technol. Int. 34 (2019) 139–155.
[31] M. Penna, R. Hompes, S. Arnold, et al., Incidence and risk factors for anastomotic failure in 1594 patients treated by transanal total mesorectal excision: results from the international TaTME registry, Ann. Surg. (2018 Jan 5), https://doi.org/10.1097/SLA.0000000000002653 [Epub ahead of print].
[32] Z. Shen, J. Cheng, M. Yin, et al., Evaluation of anatomical landmarks for transanal total mesorectal excision based on MRI, Asian J. Surg. (18) (2018 Nov 9) 30050–30052, https://doi.org/10.1016/j.asjsur.2018.10.003 pii: S1015-9584 [Epub ahead of print].