Original Article

Transanal total mesorectal excision compared to laparoscopic TME for mid and low rectal cancer—current evidence

Stefan E. van Oostendorp[1], Thomas W. A. Koedam[1], Colin Sietses[2], H. Jaap Bonjer[1], Jurriaan B. Tuynman[1]

[1]Department of Surgery, VU University Medical Centre, Amsterdam, The Netherlands; [2]Department of Surgery, Gelderse Vallei Hospital, Ede, The Netherlands

Contributions: (I) Conception and design: JB Tuynman; (II) Administrative support: None; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: SE van Oostendorp; (V) Data analysis and interpretation: SE van Oostendorp, JB Tuynman; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Stefan E. van Oostendorp. Department of Surgery, VU University Medical Centre, De Boelelaan 1117, Postbus 7057, 1007 MB, Amsterdam, The Netherlands. Email: s.vanoostendorp@vumc.nl.

Background: Transanal total mesorectal excision (TaTME) is potentially the answer to refractory challenges in rectal cancer surgery. The surgical dissection in the deep pelvis is facilitated by a down to up approach with modern laparoscopic techniques. Potential benefits are decrease in short-term morbidity including anastomotic leakages, in conversion and colostomy rate, and better quality of specimens including less R1 rates. Long-term oncological outcome data is lacking and needs to be reviewed thoroughly. Initial (comparative) series show promising results, however there is a lack of audited data and comparative data between laparoscopic TME (LaTME) and TaTME. This review compares available data of LaTME and TaTME.

Methods: A systematic review was performed in PubMed to identify papers reporting TaTME series with minimal 15 patients. A comparative set of recent large RCT data on LaTME was constructed. Weighted averages were derived from the extracted data. Primary endpoints were short-term morbidity, anastomotic leakage, conversion, pathological outcomes and local recurrences (LR).

Results: The search yielded 1,093 papers, of which after the selection process resulted in the inclusion of 23 series on TaTME. To make a comparison, the four latest RCT's on LaTME were identified as a referential group. The international TaTME registry paper was presented separately to make a third comparative group. Average morbidity 31.5% and 39.6% and anastomotic leakage 6.9% *vs.* 8.0% both in favor of TaTME. Conversion rate was 2.0% *vs.* 15.7% for TaTME and LaTME respectively. Complete mesorectal integrity 86.2% *vs.* 81.5% and CRM+ 4.6% *vs.* 7.9%. Five urethral injuries (0.7%) were reported. Long-term outcomes of LRs were reported in a minority of studies with heterogeneous follow-up intervals.

Conclusions: This review summarizes the data and potential benefits of TaTME. Compared to LaTME, TaTME decreases short-term morbidity, conversion, suboptimal quality of the specimen and involved CRM rate. Due to concerns about underreporting of poor outcomes, a well-designed randomized controlled trial with quality assurance and report on oncological safety is needed before widespread implementation can be justified.

Keywords: Transanal total mesorectal excision (TaTME); NOTES TME; review

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Background

Transanal total mesorectal excision (TaTME) is the potential answer to refractory challenges in the surgical resection of mid and low rectal cancer. Since the first reports of this approach by its pioneers in 2010, the technique has gained wide attention in the surgical community (1,2). The technique facilitates dissection of the very distal rectum and mesorectum providing excellent view of the anatomy in the deep pelvis. Especially difficult cases (e.g., obese, male patients with bulky distal tumors) seem to benefit from the transanal approach. Nevertheless, no randomized evidence is present to support any benefits. Also, in systematic reviews as well as reported in registries the benefits of TaTME compared to LaTME seem modest and long-term oncological outcome is awaited (3-5). Current problems in TME surgery are short-term morbidity including anastomotic leakage, conversions to open surgery in 10–25%, unintended end colostomies, poor specimen quality, circumferential resection margin (CRM) involvement, distal margins rates and local recurrences (LR).

Laparoscopic TME (LaTME) surgery is associated with substantial short-term morbidity of 30–40%. This includes anastomotic leakage rates around 8% (6,7). The conversion rate in LaTME is still above 10% as reported in recent trials and even with robotic surgery this percentage remains between 10% and 20%, especially in obese patients (8-11). Conversion to open surgery occurs due to difficult dissection and is associated with higher morbidity and worse oncological outcome (12-15).

Currently an increase focus is seen towards sphincter preserving therapy (16,17). The open intersphincteric resection and transanal dissection creates the possibility of saving the sphincter avoiding end colostomies, but LaTME still results in a relatively high rate of APR, which has negative impact on quality of life. Transanal minimal invasive access with high-quality images creates the potential to achieve a higher rate of sphincter saving procedures. Nevertheless, data regarding unintended AP resections are scarce and only within a randomized comparison it will be possible to evaluate this aspect. High-quality surgery with respect to the embryological avascular planes aims to achieve an intact mesorectal envelope and offers good local control, especially with neoadjuvant radiotherapy if indicated (18,19). An involved CRM remains a concern since this is a substantial risk factor for LRs. Laparoscopic surgery with an intent for TME result in an involved CRM of 17% as is shown in national registries (20). Potentially the mesorectum is not totally removed in TME surgery as shown by the presence of residual mesorectum in 40% upon evaluation by MRI 6 months after surgery in 46.9% (21).

The TaTME technique could improve outcomes for patients with mid and low rectal cancer overcoming the limitations of dissection the angulated rectum deep within the pelvis (1,12). Especially the known difficult LaTME resection will probably benefit from the TaTME approach such as male sex, low tumor, high body mass index (BMI) and bulky or anteriorly situated tumours (22). In these situations, deep mesorectal dissection, safe resection margins (both distal and circumferential) and safe stapled transection, without the need for multiple firings, may not be achieved requiring conversion to open surgery (12,20). Furthermore, in (ultra)low anterior resections for tumours situated close to but not grown into the pelvic floor, the rate of end-colostomy (APR) for technical considerations outstands the rate in which it is an oncological necessity (16). TaTME may overcome these challenges by improved visualization and ergonomics. By enabling a more precise distal dissection in the embryological planes, theoretically the autonomic nerves can be preserved possibly leading to improved functional outcomes (23,24).

In this review we focus to current evidence of laparoscopic rectal surgery and TaTME with respect to morbidity including anastomotic leakage, conversion, colostomy, involved resection margins and LRs.

Methods

We performed a PubMed search with a similar syntax as recently published to identify studies, published since January 2005, reporting on outcomes of TaTME (4). The final search was performed at 25 January 2018 with the following syntax:

((((excision*[tiab] OR resection*[tiab] OR TME[tiab] OR TaTME[tiab] OR TAMIS[tiab] OR NOTES[tiab] OR proctectom*[tiab]) AND (transanal*[tiab] OR trans-anal*[tiab])) OR ((excision*[ot] OR resection*[ot] OR TME[ot] OR TaTME[ot] OR TAMIS[ot] OR NOTES[ot] OR proctectom*[ot]) AND (transanal*[ot] OR trans-anal*[ot]))) AND (((("Neoplasms"[Mesh] OR neoplas*[tw] OR tumor*[tw] OR tumour*[tw] OR cancer*[tw] OR malignan*[tw] OR oncolog*[tw] OR carcinom*[tw] OR adenocarcinom*[tw]) AND ("Rectum"[Mesh] OR rectum[tiab] OR rectal[tiab] OR colorect*[tiab] OR mesorect*[tiab])) AND ("surgery"[Subheading] OR surgery[tiab] OR surgical[tiab] OR operati*[tiab])) OR (“Rectal Neoplasms/surgery”[Mesh:noexp]))).

For this paper, case-series, cohorts and comparative studies, with a minimum of 15 patients that underwent Transanal TME for rectal cancer were included. The transanal approach had to be an endoscopic technique, therefore papers on open transanal approach (TaTa) were excluded. Moreover, animal and cadaver studies were not included. Language in which the cohorts were reported was restricted languages with the Latin alphabet.

The international registry of TaTME was isolated from the other retrieved series on TaTME, because of its different design and the rather large proportion of indications other that rectal cancer such as IBD, completion proctectomy and Hartmann reversal (25).

In addition, to provide the most recent evidence from randomized clinical trials regarding LaTME, data from the laparoscopic arms of large, n≥200, multi-center RCT’s published after 01-01-2015 were isolated and recorded.

Primary endpoints were type of surgery, morbidity, anastomotic leakage, defined as (partial) dehiscence, intraoperative complication as urethral injury, intraoperative bleeding, stoma-rate, conversion, clinicopathological parameters as quality of the mesorectum, CRM and distal margin involvement and long-term oncological outcome as LRs.

Statistical analysis

Because a minority reported comparative data on TaTME and LaTME, no direct comparative meta-analysis could be performed. Instead, for the retrieved laparoscopic and TaTME studies, a separate weighted average was provided for the retrieved baseline characteristics and outcomes. The calculated weighted percentages and crude data (events and adjusted total population per outcome) of the LaTME and retrieved TaTME series, as well as the TaTME registry are presented in tables.

For the primary endpoints, if possible, a separate weighted average of the proportions was determined by means of the generic inverse-variance method. This is a method for aggregating multiple effect sizes to minimize the variance of the weighted average, giving more weight to the effect of large studies than to small ones. Analyses were performed with the inverse-variance method, using a random-effects model. Heterogeneity was assessed by use of the I^2 statistic. The software used for statistical analysis was R version 3.2.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

The PubMed search on TaTME resulted in 1,093 papers. Selection by title/abstract excluded 1,058 studies which resulted in 35 papers for full text analysis. Of those, nine papers were excluded for N≤15 (26-34). Other reasons of exclusion were the use of another technique or non-availability of full-text for two other articles (35,36). Eventually, 24 papers on TaTME were included in this paper, of which overlap existed by 2 papers from the same clinic (37,38). Since the latter paper focused on pathological outcomes, from this paper only the pathological data were extracted; quality of mesorectum, CRM and DRM positivity (38). Because of its unique design the TaTME registry was not pooled with the other series in the meta-analysis (25). See *Figure 1* flowchart and *Table S1* search results.

The selection of the open/robotic versus LaTME multicenter RCT’s with an arm of N≥200 resulted in the ROLARR, COLOR II, ALaCaRT and ACOSOG Z6051 (8,9,39-41).

TaTME series and registry

The 23 included TaTME cohorts varied in design and inclusion criteria and reported clinical and pathological outcomes of 1,107 patients, online: http://ales.amegroups.com/public/system/ales/supp-ales.2018.04.02-2.pdf TaTME (37,38,42-62). Fourteen single center series (37, 43-47,51,53-55,57-60), of which one published 2 papers (37,38), 7 dual or multicenter (42,48,50,53,56,61,62) and one paper of an implementation pathway (49) were included. One of the single center papers included solely advanced or recurrent low rectal cancers (59). Furthermore, for the pathological data of the largest single center experience, Hospital Clinic, we extracted the data of their latest paper on pathological endpoints (38). The indication for TaTME was merely rectal cancer varying from <5 to 15 centimeter from the anal verge, however some included a few benign cases. Due to heterogeneous inclusion criteria regarding intent for continuity; pooling for APR or LAR rate could not be performed (*Table 1*). Baseline characteristics, Surgical and postoperative outcomes of the TaTME series can be found in online: http://ales.amegroups.com/public/system/ales/supp-ales.2018.04.02-2.pdf TaTME.

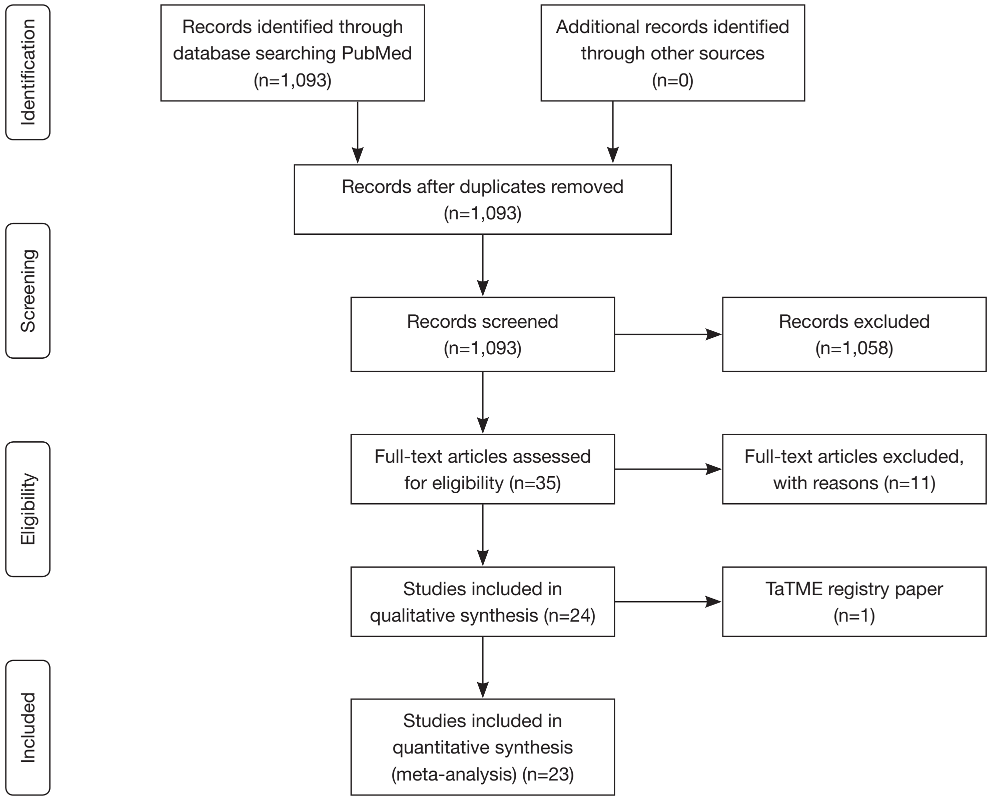

Figure 1 Flow-chart of TaTME search. Meta-analysis of the single proportions by inverse variance with a random effects model. Proportions are shown with 95% CI. From: Moher D, Liberati A, Tetzlaff J, *et al.* Preferred reporting items for systematic reviews and meta-analyses: The PRISMA Statement. *PLoS Med* 2009;6:e10000097. TaTME, transanal total mesorectal excision.

The TaTME registry encompasses 1,594 patients who received an anastomosis after TaTME, of which 1,540 procedures were for rectal cancer, and in the appendix an additional 161 abdominoperineal resections (APR) were reported (25).

LaTME

The LaTME arms of the before mentioned RCT's covered short-term and pathological outcomes of 1,411 patients (8,9,39-41). Only the COLOR II trial reported the long-term outcomes: 5% LRs after 3 years (39). Patient demographics were comparable, but Fleshman *et al.* reported an neo-adjuvant therapy rate of 98% which was rather high compared with the 46–59% rate reported by the other trials, see *Table S2* LaTME (41).

The 4 studies reported an APR percentage of 11–29%, and had a weighted colostomy rate of 27% (*Table 1*). Conversion to open surgery was done in 13.7% and LaTME resulted in 8% anastomotic leakage. The retrieved crude data can be found in *Table S2* LaTME.

Short-term morbidity and anastomotic leakage

The reported short-term morbidity (30-day) of the retrieved TaTME series varies between 8.7% and 52% with a weighted average of 31.5% versus an average of 39.6% short-term morbidity in laparoscopy (*Table 1*). In the meta-analysis of short-term morbidity, an average rate of 0.32 (95% CI, 0.28–0.36, I^2=25.8%) of TaTME versus 0.39 (95% CI, 0.33–0.46, I^2=80.6%) laparoscopy was calculated, but with serious risk at heterogeneity for LaTME. See *Figure 2A,B*.

The incidence of anastomotic leakage, defined as (partial dehiscence) was more or less equal for weighted average of laparoscopic (8.0%), TaTME (6.9%) and the Registry (7.8%) (*Table 1*). Interestingly, anastomotic failure, including pelvic abscess, fistula and sinus reached 15.8% if the 30-day

Table 1 Weighted averages

Outcome	TaTME	LaTME	Registry
Baseline			
Population (N)	1,107	1,411	1,594
Male (sex)	65.3% (710/1,088)	65% (923/1,411)	68% (1,080/1,594)
Age (years, RoM)	63.7 (55.0–70.0)	64.7 (57.7–66.8)	63.7
BMI (RoM)	26.2 (24.2–29.5)	26.3 (26.1–27.0)	26.3
Neoadj treatment	65.3% (680/1,041)	61.9% (874/1,411)	56% (895/1,594)
Surgery			
Colostomy (definite)	7.4% (75/1,007)	27.0% (378/1,398)	12% (211/1,755)*
Conversion	2.0% (22/1,083)	13.7% (192/1,403)	5.6% (90/1,594)
Duration of surgery (min, RoM)	249.1 (166–368.6)	242.9 (210.0–266.0)	252 (30.0–733.0)
Intraoperative complications	4.2% (36/865)	12.1% (141/1,164)	30.6% (487/1,594)
Intraoperative bleeding	1.7% (10/585)	3.5% (41/1,164)	4.2% (67/1,594)
Urethral injury	0.7% (5/694)	NR	0.8% (12/1,594)
Pathology			
Mesorectal integrity			
Complete	86.2% (871/1,010)	81.5% (1,139/1,398)	85.5% (1,193/1,540)**
Partial	12.6% (111/1,010)	11.9% (166/1,398)	10.8% (150/1,540)**
Incomplete	2.8% (25/1,010)	4.1% (58/1,398)	3.4% (47/1,540)**
CRM positive	4.6% (51/1,118)	7.9% (102/1,290)	4.1% (60/1,451)
DRM positive	0.7% (7/1,013)	1.0% (7/702)	0.7% (10/1,445)
Postoperative outcomes			
Short-term morbidity (30 days)	31.7% (317/1,000)	39.6% (462/1,167)	34.8% (555/1,594)
Anastomotic leakage (30 days) ***	6.9% (67/975)	8.0% (88/1,104)	7.8% (124/1,594)
Length of stay (days, RoM)	7.5 (4.0–4.0)	7.9 (7.3–8.2)	8 (2.0–94.0)
Mortality (30 days)	0.6% (7/110)	0.9% (13/1,407)	0.6% (9/1,594)

*, included 161 APR; **, minus 54 benign; ***, defined as dehiscence. RoM, range of reported means or medians; DRM, distal resection margin; CRM, circumferential resection margin; BMI, body mass index; TaTME, transanal total mesorectal excision; LaTME, laparoscopic TME.

was extended to 3 months (25). The meta-analysis of the weighted average of the proportions can be found in *Figure 3A,B*.

For TaTME specific intraoperative complications such as pelvic (sidewall or prescaral) bleeding and urethral injury, 10 (1.7%) and 5 (0.7%) cases were reported. The international TaTME registry report 4.2% intraoperative bleeding and 0.8% (n=12) urethral injuries (*Table 1*). The 30.6% intraoperative complication rate included technical aspects, such as difficulties with the transanal platform (25).

Conversion

Conversion to open surgery is encountered less frequently in TaTME, 2.0% versus 13.7%. The registry reports an intermediate conversion rate of 5.6% (*Table 1*). Meta-analysis by inverse variance with a random effects model resulted in a 0.03 (95% CI, 0.02–0.05) rate of conversion

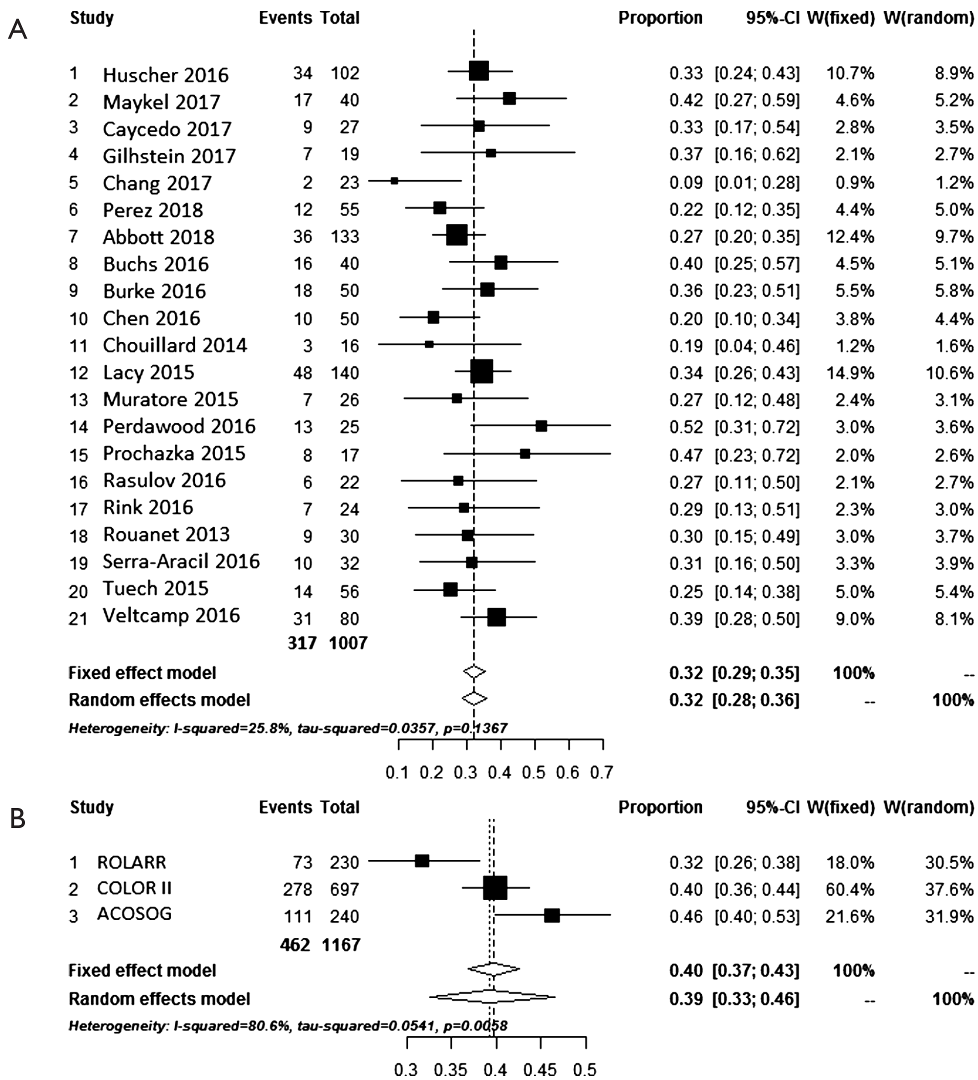

Figure 2 Meta-analysis of the single proportions by inverse variance with a random effects model. Proportions are shown with 95% CI. (A) TaTME morbidity; (B) LaTME morbidity. TaTME, transanal total mesorectal excision; LaTME, laparoscopic TME.

in TaTME with low risk of heterogeneity (I^2=0%), see *Figure 4A*. In LaTME this was 0.13 (95% CI, 0.09–0.16, I^2=69.6%) with risk of heterogeneity, see *Figure 4B*.

Colostomy

The four RCT's of LaTME encompassed an average of 20% APR for TME surgery, with a definitive stoma rate of 27% (*Tables 1,S2*). The retrieved TME series varied in inclusion criteria for APR's, intersphincteric TME and low anterior resections. Therefore, an average APR-rate could not be calculated, but the reported definitive stoma rate was 7.6%. The registry paper focused on anastomotic leakage and excluded APR's. However, the supplement stated 161 registered APR's leading to a 12% definitive stoma rate in which also total proctocolectomies or completion proctectomies for benign indications were included (25).

Irradicality

The integrity of the mesorectum, defined by Quirke, was complete in 81.5% in laparoscopy and 86.2% in TaTME (*Table 1*). Distal resection margin positivity was 1.0% and 0.7% for LaTME and TaTME respectively. The weighted

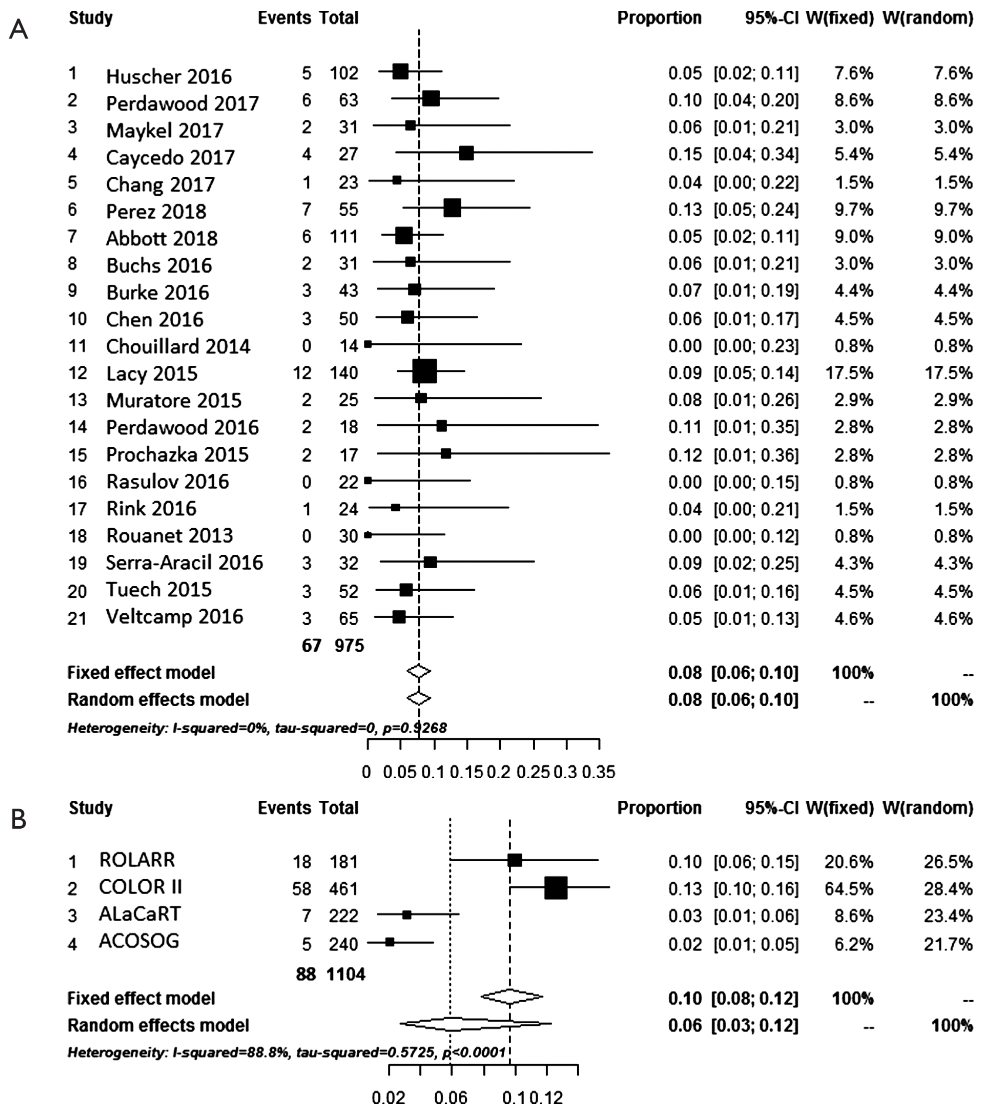

Figure 3 Meta-analysis of the single proportions by inverse variance with a random effects model. Proportions are shown with 95% CI. (A) TaTME leakage; (B) LaTME leakage. TaTME, transanal total mesorectal excision; LaTME, laparoscopic TME.

rate of a positive CRM, was 7.9% versus 4.6% in the LaTME and TaTME groups respectively (*Table 1*). For the pathological outcomes of the latest paper from the group of Lacy *et al.* was used (38).

Meta-analysis of complete mesorectum and CRM+ for both approaches are shown in *Figures 5A,B* and *6A,B*. The percentage of complete is 86% *vs.* 80% in the transanal versus pure laparoscopic approach, but with a high I^2 of 90.8% in LaTME. The weighted average of the proportions shows a positive CRM of 0.08 (95% CI, of laparoscopic 0.06–0.11, I^2=58%) in laparoscopy compared to 0.06 in TaTME (95% CI, 0.04–0.07, I^2=0).

LR

LR rate was reported 5% the 3-year follow-up paper in COLOR II-trial (39). None of the other LaTME trials reported 3-year follow-up yet. Neither the TaTME papers reported 3 years follow-up with LR percentages. However, an incidence of 17 LRs was reported, but (37,46,51,59,61,62). Of these 17 LRs, 5 were reported by Rouanet *et al.* who included locally advanced rectal cancer

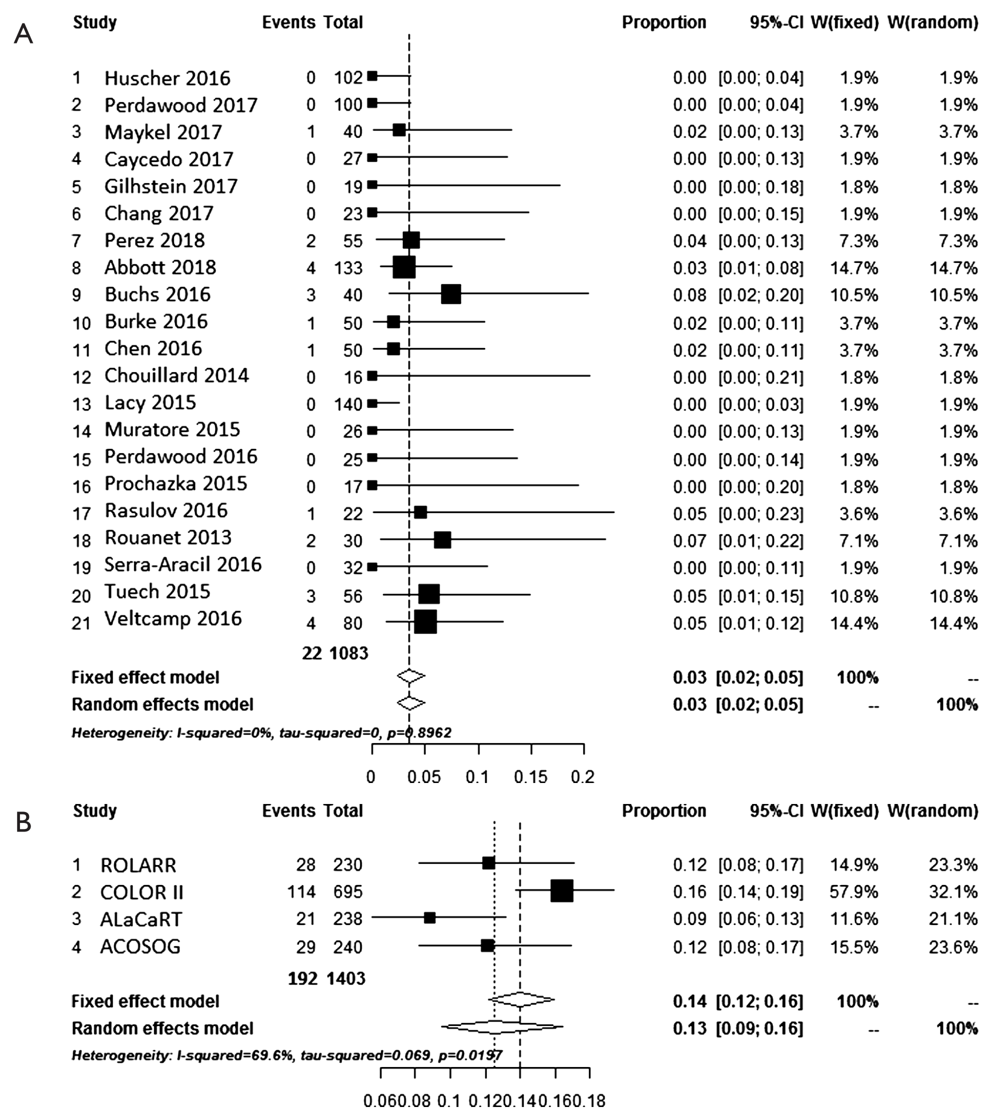

Figure 4 Meta-analysis of the single proportions by inverse variance with a random effects model. Proportions are shown with 95% CI. (A) TaTME conversion; (B) LaTME conversion. TaTME, transanal total mesorectal excision; LaTME, laparoscopic TME.

or LRs in his TaTME-series (59).

Discussion

This is the latest systematic review of all the cohorts larger than 15 patients, describing the short-term results of TaTME. Because the comparison with LaTME is most important in evaluating the potential benefits of TaTME and comparative prospective clinical trial are still lacking we have added the result of the 4 latest randomized trials evaluating LaTME. TaTME compared to LaTME is beneficial in terms of conversion rate and clinico-pathological outcomes, morbidity and anastomotic leakage seems comparable. End colostomy (APR) rate and LRs could was not reliably reported by the retrieved studies, due to design and lack of long-term follow-up (37,38,42-62). Before widespread implementation can be justified, careful evaluation is warranted because morbidity has not decreased, and the rate of LR is still a concern and needs thorough evaluation in an RCT with quality control of surgery and data (63).

The short-term overall morbidity in TaTME was 31.5% which is beneficial compared to the registry data of 34.8% and pooled LaTME of 39.6%. This 31.5% rate

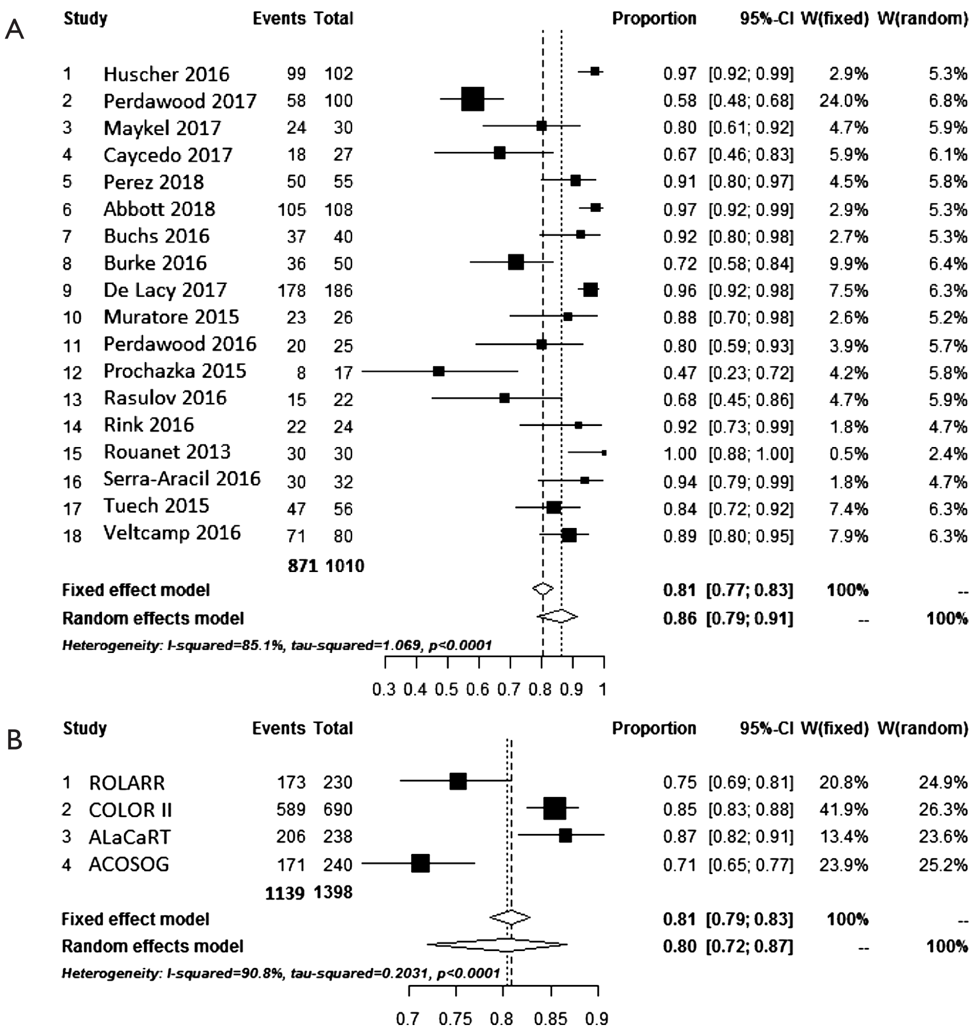

Figure 5 Meta-analysis of the single proportions by inverse variance with a random effects model. Proportions are shown with 95% CI. (A) TaTME mesorectum complete; (B) LaTME mesorectum complete. TaTME, transanal total mesorectal excision; LaTME, laparoscopic TME.

of the TaTME cohorts must be interpreted with caution since morbidity was not reported in a standardized way such as the Clavien-Dindo classification. A concern in (laparoscopic) rectal cancer surgery remains anastomotic leakage which was 8% in the latest laparoscopic RCT data. It was imposed that leakage could be decreased by TaTME as a consequence of a new way of making an anastomosis without the need for cross stapling leaving dog-ears which are prone to ischemia (25,64). However, the current data do not suggest a decrease with a reported 30-day leak rate 7%. The open rectal stump which results after the dissection needs to be fused with the descending colon to create the anastomosis. This can be performed either by a hand sewn colo-anal anastomosis for very low anastomosis or by a stapled colo-rectal anastomosis with a circular stapling technique with the aid of a second purse string to close up the open rectal stump, which is described in detail in the 2016 paper in Techniques of coloproctology (64). TaTME potentially leads to more bacterial load as showed by Velthuis *et al.* and needs further investigation of the rate of anastomotic failure or pelvic abscess (65). The registry reported an anastomotic failure rate of 15.7% when late complications of the anastomosis such as fistula, chronic abscess or presacral sinuses were included (25). These numbers are comparable to the anastomotic leak rate, defined as not only early dehiscence but include presacral

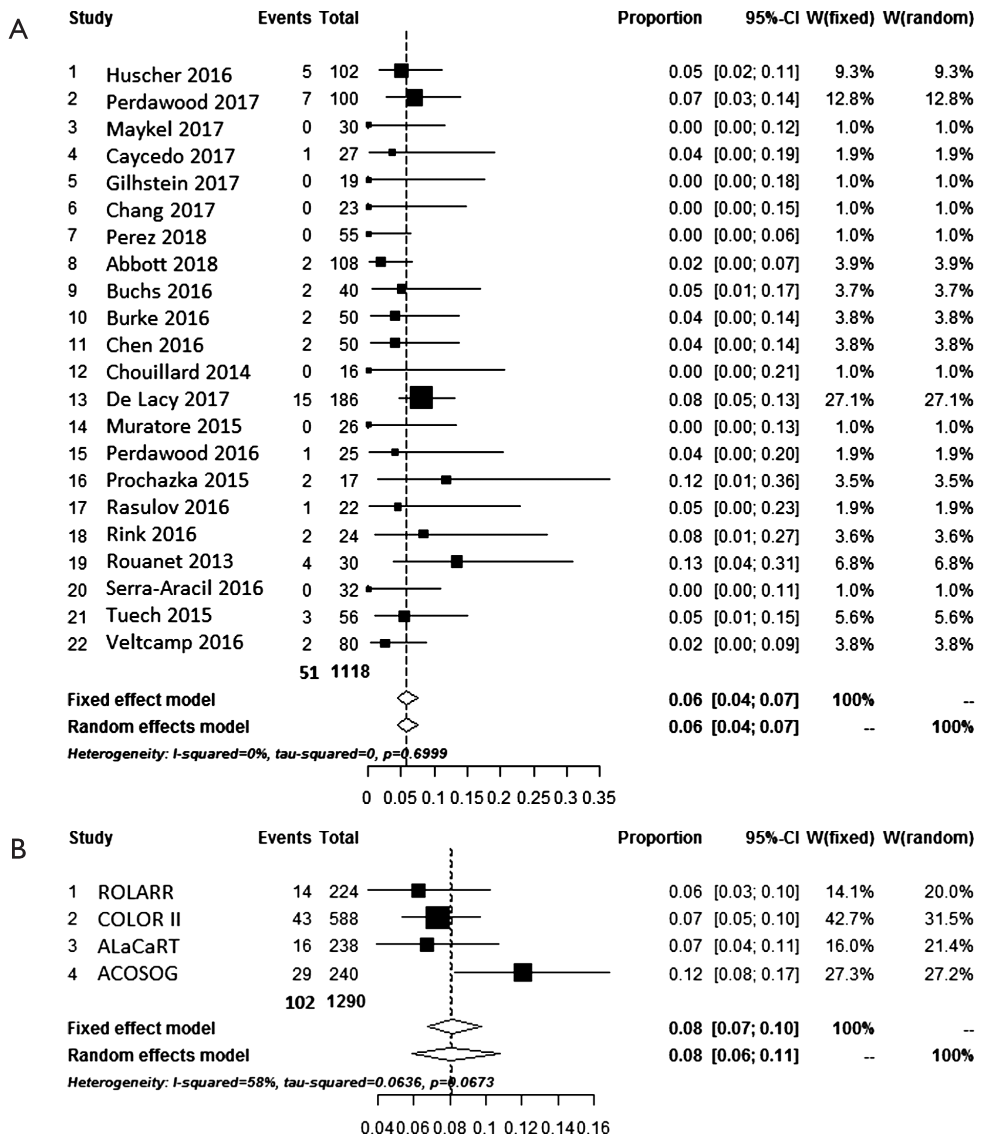

Figure 6 Meta-analysis of the single proportions by inverse variance with a random effects model. Proportions are shown with 95% CI. (A) TaTME CRM+; (B) LaTME CRM+. TaTME, transanal total mesorectal excision; LaTME, laparoscopic TME.

abscess or sinus, which builds up to 20% beyond the 30-day cut-off (6).

This paper shows a promising conversion rate of 2% in TaTME in the cohort series compared to 5.6% in the TaTME registry compared to 12.2–16.6% for LaTME as reported in the ROLARR and laparoscopic arms of the COLOR II, ALaCaRT and ACSOG-Z6501 trials (8,9,40,41). The main reasons for conversion to open surgery are extensive adhesions, intra-operative complications such as major bleeding, the inability to make progress in sharp dissection of the mesorectal envelope or to achieve a clear distal margin below the tumor (12). Risk-factors that contribute to difficulty are male sex, high BMI, visceral obesity, narrow pelvis, bulky tumours or more advanced stage of the tumours and these patients might be candidates for a down to up approach of mesorectal excision (10,11,66).

The average 20% APR-rate in LaTME surgery for rectal cancer as stated before impacts quality of life. This extensive procedure with resection of the sphincter complex is not always required from oncological point of view, which is mostly the risk of CRM+ due to ingrowth in the sphincter complex or levator ani, but is also performed for technical reasons such as the inability to get a satisfactory distal margin intraoperatively (16). Definitive colostomy-rate is even higher, adding some sphincter sparing Hartmann procedures without restoration of bowel continuity. TaTME enables lower sphincter saving, or intersphincteric, dissections with a colo-anal anastomosis in selected cases (16). Unintended APR rate resulting in end colostomy was an endpoint which could not be evaluated. The RCT series did not report the incidence of planned versus unplanned; one study reported an end colostomy rate of 79.7% in LaTME for the low rectum (0–5 cm from the AV) (9).

The CRM positivity, an important predictor of LR, was found to be less frequently involved in TaTME (67). This can be contributed by improved visualization of the surgical plane and improved ergonomics in the dissection of especially the lower (meso)rectum (1,2).

The integrity of the mesorectal envelope surrogates surgical quality by pursuing a smooth specimen which is correlated to LR (68). This review shows that TaTME results in better mesorectal integrity for TaTME as shown in *Table 1*. Positive distal resection margins are rarely encountered since the tumor can be directly visualized by the transanal endoscopic view (4). Furthermore, in case of a stapled anastomosis, the donuts of the EEA-31 hemorrhoid stapler add an extra 16 mm margin in addition to the original specimen (64). LRs are not well reported in the TaTME cohorts. Overall, 17 LRs were reported with a varying follow-up (9.7–29.0 months). The registry has not reported long-term oncological outcome and will probably underreport this fact because of the voluntary non-audited design. The trial data of LaTME reports a 5% LR rate at 3-year follow-up (39).

The lack of long-term outcome underlines the importance of a prospective trial with quality assurance and with auditing of the long-term data. Potentially tumor spill due to inadequate closure of the rectum or due to seeding due to manipulation could be a concern of the TaTME technique.

The cohorts and registry contain unaudited data and publication bias, therefore concern has risen about unreported poor outcomes. Urethral injuries have been mentioned at symposia and training sessions frequently, but fail to be equivalently reported in manuscripts (4,25,69). Other potential injuries such as side wall injury with the risk at major haemorrhage or autonomous nerve injury and a too low stapled anastomosis resulting in poor outcomes are also concerns especially in the learning curve. These potential disastrous complications warrant restraint of wide-spread rigorous implementation of the technique without proper training and auditing (22,70,71).

Although this review contains the most up-to-date overview of the available data substantial limitations are present which precludes any conclusion about the value of TaTME. Only cohort data with selection bias, publication bias and lack of audit. The registry data contains similar bias since data is missing and no audit of the data is present. Comparing RCT with cohort data is only presented due to lack of other comparative data and only serves as an indication. RCT's often have better results compared to registries since the learning curve is less an issue whereas the TaTME data is biased by a learning curve which has shown to be associated with increased morbidity and worse specimens. The learning curve of laparoscopy has been set at 50–60 patients previous decade, measured by conversion and morbidity (72,73). Koedam *et al.* analyzed the individual learning curve of a surgeon starting TaTME, and concluded is achieved after 40 cases and 60 more are required to get to the level competent to teach others (Koedam *et al. Tech coloproctology* 2018, Accepted).

To shorten this learning curve, a training pathway has been designed which covers e-learning, live surgery, hands on cadaver course and on-site proctoring (32,70,71). The international TaTME consensus meeting on the design of a training-pathway concluded due to the technical demanding aspect of TaTME this approach should be reserved for dedicated colorectal surgeons who have extensive experience in both laparoscopic colorectal surgery and TAMIS for local excision (70). The results of the Australian & New Zealand training and implementation program that were included in this review reported the outcomes of 12 surgeons that performed 108 cases TaTME for rectal cancer with a 5.4% anastomotic leak rate, 1.9% CRM+, 0% DRM+ and an intact TME specimen in 107 cases (98.2%) suggesting high quality surgery (49).

Another need is quality assurance to ensure proficiency and safety and avoid patients and results of trials to be hampered by suboptimal performance of not sufficiently trained surgeons (74,75). A well designed trial with these components, in order to capture the real advantage and potential harms of a technique within a training pathway and a patient safety environment, avoids underreporting of poor outcomes and a randomized trial is best suited to rule out bias of excellence centers.

It is well recognized that randomization often discourages patients and surgeons which are in favor of one technique but no other trial design yet has been able to reproduce the level of evidence an adequately powered and executed RCT provides (76).

Conclusions

Continuous cohort reports on TaTME indicate a benefit in conversion rate compared to LaTME and potential increase in sphincter preservation. However, morbidity including anastomotic leakage and by this novel approach introduced specific complications as urethral or pelvic side-wall injury need prospective audit. A significant learning curve is present in the implementation and hampers fair comparison. Long-term oncological outcome does not seem to improve so far but randomized controlled trial with proper quality assurance is best suited to provide data on short-term outcomes as well long-term oncological safety.

The following URL shows supplementary data from the TaTME series: http://ales.amegroups.com/public/system/ales/supp-ales.2018.04.02-2.pdf

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/ales.2018.04.02). The authors have no conflicts of interest to declare.

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Supplementary

Table S1 Search results 25-01-2018

Search	Query	Items found
#1	Search (((excision*[tiab] OR resection*[tiab] OR TME[tiab] OR TaTME[tiab] OR TAMIS[tiab] OR NOTES[tiab] OR proctectom*[tiab]) AND (transanal*[tiab] OR trans-anal*[tiab])) OR ((excision*[ot] OR resection*[ot] OR TME[ot] OR TaTME[ot] OR TAMIS[ot] OR NOTES[ot] OR proctectom*[ot]) AND (transanal*[ot] OR trans-anal*[ot]))) AND ((((“Neoplasms”[Mesh] OR neoplas*[tw] OR tumor*[tw] OR tumour*[tw] OR cancer*[tw] OR malignan*[tw] OR oncolog*[tw] OR carcinom*[tw] OR adenocarcinom*[tw]) AND (“Rectum”[Mesh] OR rectum[tiab] OR rectal[tiab] OR colorect*[tiab] OR mesorect*[tiab])) AND (“surgery”[Subheading] OR surgery[tiab] OR surgical[tiab] OR operati*[tiab])) OR (“Rectal Neoplasms/surgery”[Mesh:noexp]))	1,521
#2	Search #1 AND (“2005/01/01”[Date-Entrez] : “2016/07/01”[Date-Entrez])	896
#3	Search #1 AND (“2005/01/01”[Date-Entrez] : “2018/01/25”[Date-Entrez])	1,093
#4	Search #3 NOT #2	197

Table S2 LaTME

Outcome	ROLARR	COLOR II	ALaCaRT	ACOSOG
Inclusion criteria	<15 cm, curative intent, no T4, M0	<15 cm, cT1-T3, CRM-, no T4, M0	<15 cm, cT1-T3, CRM-, no T4	<12 cm, T3N0M0, Tany N1 or 2, M0, and no T4
N	234	699	238	240
Male sex (%)	67.9% 159/234	64.1% 448/699	67.2% 160/238	64.5% 156/240
Age mean (SD)	65.5 (11.93)	66.8 (10.5)	65 (56.0–74.0)*	57.7 (11.5)
BMI mean (SD)	NR	26.1 (4.5)	27 (24.0–30.0)	26.4 (4.0)
Neoadjuvant therapy	46.2% 108/234	58.9% 412/699	50% 119/238	98.3% 235/240
Surgical procedure				
High anterior Resection	8.3% 19/230	10% 72/699	n.s.	n.s.
Low anterior Resection	71.7% 165/230	60% 418/699	89% 212/238	74.6% 179/240
APR	19.6% 45/230	29% 200/699	11% 25/238	24.2% 58/240
Missing/other	0.4% 1/230	1% 9/200	0.4% 1/238	1.2% 3/240
Stoma				
Temporary	68.3% 157/230	35% 243/690	68% 162/238	71.3% 171/240
Definitive	21.3% 49/230	34% 236/690	13% 30/238	26.3% 63/240
No	10.4% 24/230	35% 245/690	19% 46/238	2.4% 6/240
Quality of the mesorectum (Quirke)				
Complete	77.6% 173/230	84% 589/690	87% 206/238	72.9% 175/240
Near/partial	17.0% 38/230	8% 58/690	10% 24/238	19.2% 46/240
Incomplete	5.4% 12/230	3% 19/690	3% 8/238	7.9% 19/240
Missing (n)	7	33	–	–
CRM+	6.3% 14/224	7.3% 43/588	6.7% 16/238	12.1% 29/240
DRM+	0.4% 1/224	NR	0.8% 2/238	1.7% 4/240
Conversion	12.2% 28/230	16.6% 114/695	8.8% 21/238	11.2% 27/240
Duration of surgery minutes mean(SD)	261 (83.24)	240 (184.0–300.0)*	210 (163.0–253.0)*	266.2 (101.9)
Intraoperative complications	14.8% 34/230	12% 81/694	NR	10.8% 26/240
Bleeding	4.8% 11/230	3% 22/694	NR	3.3% 8/240
Length of stay days mean (SD)	8.2 (6.03)	8.0 (7.3–8.2)*	8 (4.44)	7.3 (5.4)
Short-term morbidity	31.7% 73/230	40% 278/697	NR	46.3% 111/240
Anastomotic leak	9.9% 18/181	12.6% 58/461	3.1% 7/222	2.2% 5/240
Mortality (<30 days)	0.9% 2/230	1% 8/699	0.6% 1/238	0.8% 2/240
Local recurrence (3 yr)	NR	5% 31/588	NR	NR

*, median (inter quartile range). NR, not reported; n.s., not specified; APR, abdominoperineal resection; SD, standard deviation; CRM+, circumferential resection margin involved; DRM+, distal resection margin involved; 3 yr, three years.