University Library

A gateway to Melbourne's research publications

Minerva Access is the Institutional Repository of The University of Melbourne

Author/s:
Lau, SYC;Choy, KT;Yang, TWW;Heriot, A;Warrier, SK;Guest, GD;Kong, JC

Title:
Defining the learning curve of transanal total mesorectal excision: a systematic review and meta-analysis

Date:
2022-03-01

Citation:
Lau, S. Y. C., Choy, K. T., Yang, T. W. W., Heriot, A., Warrier, S. K., Guest, G. D. & Kong, J. C. (2022). Defining the learning curve of transanal total mesorectal excision: a systematic review and meta-analysis. ANZ Journal of Surgery, 92 (3), pp.355-364. https://doi.org/10.1111/ans.17262.

Persistent Link:
https://hdl.handle.net/11343/299113

Lau Steve (Orcid ID: 0000-0003-2819-9704)
Choy Kay Tai (Orcid ID: 0000-0001-5763-5742)
Heriot Alexander (Orcid ID: 0000-0001-9846-8776)
Kong Joseph (Orcid ID: 0000-0002-1392-2480)

Defining the Learning Curve of Transanal Total Mesorectal Excision (taTME): A Systematic Review and Meta-analysis

Steve Yee Chiang Lau, MBBS, FRACS,[1*] Kay T. Choy, MBBS,[2*] Tze Wei Wilson Yang, MBBS, MS(Sc), [3*] Alexander Heriot, MD, FRACS[4-6] Satish K Warrier, MS, FRACS,[3-6] Glenn D. Guest, MSc, FRACS,[1,7] Joseph C. Kong, MBChB, MS, FRACS, PhD[4-6]

[1]Department of Surgery, University Hospital Geelong, Geelong, Victoria, Australia

[2]Department of Surgery, Austin Hospital, Melbourne, Victoria, Australia

[3]Department of Colorectal Surgery, Alfred Hospital, Melbourne, Victoria, Australia

[4]Division of Cancer Surgery, [5]Division of Cancer Research, Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia

[6]Sir Peter MacCallum Department of Oncology, University of Melbourne, Parkville, Victoria, Australia

[7]Department of Surgery, Epworth Geelong Hospital and Deakin University, Geelong, Victoria, Australia

[*] SYCL, KTC and TWWY are co-first authors and have contributed to this study equally.

Correspondence to:

Kay Tai Choy

Tel: +614 05 680 879

Email: kay.choy@uqconnect.edu.au

Address: 145 Studley Rd, Heidelberg, VIC 3084, Australia

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/ans.17262

This article is protected by copyright. All rights reserved.

Author Manuscript

Author Manuscript

Disclaimer: We have no conflict of interest to declare.

Source of support: None

Manuscript word count: 3530

Abstract word count: 243

Author Manuscript

Author's contribution

Contributions	**By which author**
Substantial contributions to the conception and design, acquisition of data, or analysis and interpretation of data	All authors
Drafting and revising the article	All authors
Final approval of the version to be published	All authors

Appropriate category for the paper: Rectal neoplasia

Author Manuscript

Abstract

Background: Transanal total mesorectal excision (taTME) represents a novel approach to rectal dissection. Although many structured training programs have been developed worldwide to assist surgeons in implementing this new technique, the learning curve of taTME has yet to be conclusively defined. This is particularly important given the concerns regarding the complication profile and oncological safety of taTME.

Objectives: The aim of this review was to provide an up-to-date systematic review and meta-analysis of the learning curve for taTME, comparing the difference of outcomes between the learning curve (LC) and after learning curve (ALC) groups.

Data Sources: An up-to-date systematic review was performed on the available literature between 2010-2020 on PubMed, EMBASE, Medline and Cochrane Library databases.

Study Selection: All studies comparing taTME procedures before and after learning curve were analysed.

Results: Seven retrospective studies of prospectively collected databases were included, comparing 333 (51.0%) patients in the Learning Curve (LC) group and 320 (49.0%) patients in the after Learning Curve (ALC) group. There was a significantly reduced number of adverse intra-operative events, anastomotic leaks and improved quality of mesorectal excision in the ALC group.

Conclusion: This review shows that there is a significant improvement in clinical outcomes between the LC and ALC groups which supports the need for careful mastery and ongoing

technical refinement during the learning curve in taTME. This procedure should be performed on a subset of carefully selected patients in the hands of experienced and well-trained teams dedicated to ongoing audit.

Keywords:
Transanal TME, learning curve, proctorship

Author Manuscript

Author Manuscript

Introduction

Transanal total mesorectal excision (taTME) was designed as a solution to some of the technical shortcomings of the laparoscopic and open approach to rectal cancer surgery[1, 2], facilitating rectal dissection in the narrow android pelvis, at times made more challenging with obesity, a low rectal tumour and previous pelvic irradiation[3, 4]. In such cases, taTME allows direct visualisation of the tumour, facilitating placement of a purse-string distal to the tumour and allows the mesorectum to be dissected from both abdominal and transanal fields[5]. Reassuringly, early studies have shown that a high quality total mesorectal excision (TME) can be achieved with this technique[6-8].

However, the unique and unfamiliar viewpoint to rectal dissection can make this procedure challenging, even to the most experienced of surgeons. Complications that were previously not seen with the conventional approach to rectal dissection such as urethral injuries have been reported[2, 9]. More recently, several studies have also questioned the long-term oncologic safety of taTME[10, 11], raising further technical concerns about the performance of taTME.

To date, several countries have implemented a structured training program with proctorship to help introduce this procedure safely, albeit with varying degrees of supervision[2, 12, 13]. Although it is recognised that the learning curve of taTME is long and demanding, there is limited knowledge on the number of procedures required to achieve proficiency[1].

The present study aims to assess the learning curve of taTME by comparing clinicopathologic outcomes related to the procedure during the learning curve and after the learning curve. We

hypothesize that beyond the learning curve, taTME can be safely performed in a selected group of patients by surgeons who have undergone appropriate training.

Methods

Search Strategy

All relevant published studies were identified through a computer-assisted search of PubMed, EMBASE, Medline databases from 2010 to 2020. The following medical subject heading (MeSH) terms and text words were used for the search in all possible combinations: “taTME” AND “learning curve” OR “proctor*” OR “CUSUM”. The cited references in each retrieved paper were also checked for relevance. This systematic review was registered in The International Prospective Register of Systematic Reviews (PROSPERO) with the registration number CRD42021232942. The latest date for this search was 10 September 2020.

Selection of studies

The retrieved titles and abstracts of all studies were evaluated for their eligibility for inclusion according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines. Selection of articles was based on the following criteria: adult population undergoing oncological resection, studies comparing outcomes during learning curve (LC) versus after learning curve (ALC) with the outcomes of interest being overall morbidity, operating time, blood loss and oncological indicators such as involvement of Circumferential Resection Margin (CRM), lymph node yield as well as quality of Total Mesorectal Excision (TME) dissection. Intraoperative adverse events are defined as any unexpected or undesirable

Author Manuscript

events occurring as a result of surgery. All letters, perspectives, conference abstracts or studies focusing on paediatric population groups were excluded.

Data extraction

Two reviewers (KTC and TWWY) independently extracted the data from the included studies using a standard data extraction form. Any discrepancies were resolved by consensus and discussion between the two reviewers and the supervising author (JCK). In one of the included studies[7], the authors made four treatment groups in consecutive order of surgery with the cut-off for the learning curve proposed to be in the middle (i.e. between Group B and Group C). As their provided data were distinct to the individual groups, we were only able to compare the middle two groups instead (i.e. Group B vs Group C).

Statistical analysis

All the categorical data was collected as absolute numbers. In any data that reported zero events, this was replaced with 0.5 to allow for computation of statistical calculation. A pooled odds ratio (OR) was calculated based on Cochran-Mantel-Haenszel test. I^2 statistics was performed to assess for inter-study heterogeneity and the Newcastle-Ottawa scale (for non-randomised studies) or Jadad scale (for randomised control trial - RCTs) was used to assess quality of each non-randomised study. A p-value of <0.05 was considered significant. All data analysis was performed in R Studio Team (2015). RStudio: Integrated Development for R Studio, Inc., Boston, MA and using the metaphor package for meta-analysis.

Author Manuscript

Author Manuscript

Results

Search results and included studies

There were 247 citations identified from the initial search. Three additional studies were included from references of identified articles. After screening for full text reviews, a total of seven studies were included into the study. The characteristics of these studies are summarized in Table 1. This yielded a total of 653 patients, with 333 (51.0%) patients in the Learning Curve (LC) group and 320 (49.0%) patients in the after Learning Curve (ALC) group.

Study Design and Quality

All seven included papers were retrospective studies of prospectively collected databases. As shown in Table 1, all of them scored six or more on the Newcastle-Ottawa Scale, and therefore were deemed good quality studies.

Surgeon Experience, Learning Pathway and Proctorship

Five studies specified that surgeries were performed by at least 1 to 4 [15-18] sub-specialty trained colorectal surgeons[15, 17, 18] who were experienced in laparoscopic resection of rectal cancer[15, 12, 18, 19] and transanal minimally invasive surgery (TAMIS)[12, 15, 18]. Four studies described a detailed training program including education sessions [12, 18], observation of live cases [12, 18] and cadaveric workshops [12, 18, 19] with three out of these four studies including a proctorship component by having an surgeon experienced in taTME present intraoperatively[12, 15, 18, 19].

Patient Characteristics

The mean age for patients ranged between 56.6 to 67 years in the LC group and 55.8 to 70 years in the ALC group. There were more male patients in both groups with mean 64.8% and 67.7% in the LC and ALC group respectively. Six studies included patients who underwent neoadjuvant chemoradiotherapy (CRTx)[12, 15-19], with 185 (79.4%) patients in LC group and 133 (60.5%) patients in ALC group. Five studies reported on tumour staging [15-19] and there were 74 (42.8%) patients in LC group and 62 (38.8%) patients in ALC group who had at least Stage IIIa or Dukes C colorectal cancer.

Intra-Operative Outcomes

As shown in Table 2, the mean operative time ranged between 199 to 303 minutes in the LC group and 195 to 302.5 minutes in the ALC group. There was no significant difference identified with the standard mean difference (SMD) favouring ALC group (SMD: 0.51, 95% CI: -0.38-1.40, p = 0.262, see Fig 1).

Blood Loss

Four studies reported mean blood loss volumes ranging from 95.9 to 288 mls in the LC group and 63.2 to 150 mls in the ALC group [15, 16, 19, 20]. There was no significant difference identified with the SMD favouring ALC group (SMD: 0.51, 95% CI: -0.45-1.47, p = 0.299, Table 2).

Author Manuscript

Author Manuscript

Open Conversion

Four studies described open conversion rates, with six (3.4%) patients in the LC group and nine (5.0%) patients in the ALC group requiring open conversion [12, 15, 17, 18]. There was no significant difference identified between the groups (OR: 0.66, 95% CI: 0.23-1.84, p = 0.585, see Table 2).

Adverse Events

Five studies detailed intra-operative adverse events. These included vascular injuries causing excessive bleeding, bowel perforation as well as urological injuries to bladder/urethra. No case of carbon dioxide embolus was recorded. There were significantly more intra-operative adverse events in the LC group with 27 (9.7%) patients compared to 11 (4.2%) patients in the ALC group[12, 15-17, 20] (OR: 2.27, 95% CI: 1.11-4.64, p = 0.035, see Fig 2). Specifically in terms of urological injuries, there were three reported cases in the LC group compared to no cases in the ALC group.

Clinical Outcomes

Morbidity and Mortality

As shown in Table 3, five studies reported on total morbidities[15-19] and major morbidities (Clavien-Dindo classification III-IV) [12, 15-18]. There was no significant difference in total morbidity rates with 68 (39.3%) patients in the LC group and 47 (29.4%) patients in the ALC group (OR: 1.51, 95% CI: 0.92-2.49, p = 0.136, see Fig 3). Furthermore, no significant

difference was identified in major morbidity rates with 40 (18.3%) patients in the LC group and 25 (12.2%) patients in the ALC group (OR: 1.73, 95% CI: 0.99-3.02, $p = 0.072$, see Table 3).

Three studies reported on mortalities [12, 17, 18], with two (1.6%) deaths in the LC group and no fatalities in the ALC group.

Primary Anastomosis and Anastomotic leak

In six of the studies, there were 209 (76.6%) patients in the LC group and 215 (82.7%) patients in the ALC group who underwent primary anastomosis[15-20]. Anastomotic leaks were defined based on clinical, radiological or endoscopic evidence of disruption in the anastomosis. All leaks were recorded irrespective of its impact on clinical management[21]. Nevertheless, amongst these patients, there was significantly more anastomotic leaks in the LC group compared to ALC group with 32 (15.3%) patients and 16 (7.4%) patients respectively (OR: 2.30, 95% CI: 1.21-4.36, $p < 0.001$, see Table 3).

Pathological Outcomes

Distal and Circumferential margins involvement

As shown in Table 4, four and five studies reported on distal [12, 15, 17-19] and circumferential [12, 15, 17, 18, 20] margins involvement respectively. With regards to distal margins, both groups only had 1 (0.6%) patient with involvement. There was no significant difference in circumferential

Author Manuscript

margin involvement with 11 (4.0%) patients in the LC group and 11 (3.9%) patients in the ALC group (OR: 0.91, 95% CI: 0s.40-2.12, p = 0.996, see Table 4).

Quality of mesorectal excision

Six studies described the quality of mesorectal excision [12, 15-18, 20]. As shown in Figure 10, 240 (75.5%) patients had complete excision, 70 (22.0%) patients had nearly complete excision and 12 (3.8%) patients had incomplete excision in the LC group. In the ALC group, 255 (83.6%) patients had complete excision, 47 (15.4%) patients had nearly complete excision and 12 (3.9%) patients had incomplete excision. The LC group obtained significantly lower complete mesorectal excision rates compared to ALC group (OR: 0.56, 95% CI: 0.37-0.85, p = 0.008, see Table 4).

Lymph Node Harvest

Four studies recorded lymph nodes harvested [12, 15, 16, 20], with the mean number of nodes ranging from 9.6 to 25.6 in the LC group and 15.8 to 24.8 in the ALC group. There was no significant difference identified with the SMD favouring the LC group (SMD: -0.48, 95% CI: -1.16-0.21, p = 0.172, see Table 4)

Definition of Learning Curve

Four studies defined the learning curve utilizing Cumulative Sum (CUSUM) analysis. However, there was variation amongst them in the endpoints included to evaluate the learning curve. As seen in Table 5, three out of four used operating time and rates of postoperative

Author Manuscript

morbidity/intraoperative complications with one instead focusing on the pathological outcomes of high-quality TME dissection with negative distal/circumferential margins.

Six studies described the number of cases required to reach stabilization of learning curve and potentially proficiency. These ranged from 5 to 140, with the majority of cases (four out of six) settling on between 30 to 50 cases.

Author Manuscript

Discussion

This systematic review of 653 patients comparing the short-term outcomes of taTME during and after the learning curve has shown that following the learning phase, there is a significant reduction in the number of intra-operative adverse events, anastomotic leaks and an improvement in the quality of mesorectal excision.

In light of the recent concerns regarding the safety of taTME culminating in the Norwegian moratorium on this procedure, the analysed studies suggest that there is a significant learning curve during the uptake of taTME with the estimated number of procedures required to achieve proficiency in taTME ranging from 30-140 cases[12, 15, 16, 18-20]. The wide variation can be explained by many possible reasons. As described previously, there is heterogeneity in the endpoints used to measure proficiency in the calculation of learning curve. Some studies also chose to report institutional learning curve rather than single surgeon data which may influence the number of cases required to achieve taTME proficiency[15, 18, 20]. Moreover, early results in some studies included the outcomes of early adopters prior to introduction of structured training and proctorship programs which would have potentially shortened the learning phase[18]. This reflects the evolution of practice in taTME over the last decade since its introduction, and notably highlights the importance of overcoming the learning curve through structured training with proctorship, maintaining adequate case volume and ongoing audit.

Since its introduction in 2010, there has been a rapid uptake of taTME globally. The proposed benefits of this technique include improved visualization and access to deep pelvic structures, especially in the narrow android pelvis or in obese patients with bulky low rectal tumours and prior pelvic irradiation[22]. However, taTME is a technically demanding procedure. It requires

Author Manuscript

single port surgical skills, mastery of the placement of an air tight purse-string suture distal to the tumour and utilizes a ‘bottom-up’ viewpoint to rectal dissection, which introduces new anatomical landmarks compared to the conventional approaches to TME dissection[18, 23].

The early adopters of taTME have noted technique-specific complications such as urethral injuries and carbon dioxide embolism[9, 24]. In this study, urethral injuries were rare and no carbon dioxide embolism were reported. In fact, this review showed a significant reduction in intra-operative adverse events following the initial learning curve period (9.7 vs 4.2%; OR: 2.27, 95% CI: 1.11-4.64, $p = 0.035$). Similarly, there was also a significant reduction in the anastomotic leak rate before and after the initiated learning curve. This is consistent with the data presented from an international taTME registry[25].

Such a complication has significant short-term (sepsis and potential death) and long-term impact on the patient. Of particular concern is the known association between an anastomotic leak with higher rates of local and distant recurrence[26, 27]. However, in this review, a significant improvement was noted in the anastomotic leak rate following the initial learning curve (15.3 vs 7.4%; OR: 2.30, 95% CI: 1.21-4.36, $p < 0.001$). While possibly contributed to by the lower rates of neoadjuvant radiotherapy in the ALC group (see Table 1), this has also benefited from refinements to the technique during the learning phase and appropriate selection of patients for natural orifice extraction of a specimen. In the initial approach to taTME specimen extraction, the tumour is routinely extracted through the rectum and anus as described by Sylla and Lacy[28]. Although natural orifice extraction of the specimen has several benefits including reduced analgesic requirements compared to an abdominal extraction site, routine transanal extraction of the specimen may have several disadvantages.

Author Manuscript

Caycedo-Marulanda et. al. hypothesized that routine transanal extraction of specimen may contribute to anastomotic leak by tearing of the marginal artery, potentially devascularizing the colonic conduit[29].From their observation, the authors had advocated for transabdominal extraction for a select group of patients (bulky tumour, short mesentery, obese patients, male), as well as intracorporeal division of mesentery, abundant washing prior to transanal extraction (to reduce bacterial contamination in an open rectal stump), mandatory splenic flexure mobilisation if anastomosis is considered and regular use of indocyanine green (ICG) to assess vascularity of conduit to be instituted into the taTME protocol. These procedural refinements and resulted in a reduction of leak rate from 15% in the early cohort to 4.6% in the late cohort [29]

The lack of improvement in the operative time with progression from learning curve to after, while surprising, is in fact consistent with previous learning curve analyses such as those around robotic colorectal surgery[30]. Proposed reasons include a propensity to take on more challenging cases after the learning curve, or the transition from having a supportive proctor to performing these surgeries independently[30]. Indeed, these factors particularly apply to taTME where rectal cancer surgery, particularly the lower third is technically difficult no matter which technique is used (open, laparoscopic, robotic or taTME). This was reflected in studies showing improvement in operating time with change from a single surgeon to synchronous two surgeon approach, however, operating time did not improve with experience[15, 18].

Recently, there has been recurring concerns on the uptake of taTME within a surgeon's learning curve and the possible association with multifocal local recurrence[10, 31]. As a result of

Author Manuscript

these findings, taTME has been suspended in Norway pending completion of a national audit which confirmed not only unfavourable local recurrence rate but also a higher anastomotic leak rate)[10, 31].

The early and multifocal nature of local recurrence could potentially be explained by either a purse string failure or rectal perforation leading to aerosolization of tumour cells into the pelvis.[11] Accordingly, further modification to the standard taTME technique including placement of a second reinforcement purse-string followed by a rectal washout has been suggested to ensure complete occlusion of the rectum and an airtight seal[33]. It is also important to note that intraoperative complications such as purse string failure and rectal perforation may have significant bearing on the rate of local recurrence and can occur despite a high quality TME specimen. These events should be accurately documented along with specimen quality when reporting local recurrence rates.

Furthermore, as this technique requires a bottom-up approach to rectal dissection, the usual anatomical landmark from the abdominal approach cannot be relied upon. Therefore, the transanal view is foreign and requires re-orientation or re-adjustment to recognise new anatomical landmark that may not be obvious in the initial cases[34]. Recognizing the complexity of this procedure and to facilitate safe introduction of taTME locally, many countries have developed structured training programs encompassing didactic and hands-on components[2, 12, 35, 36]. Although not mandatory, it is highly recommended that surgeons complete a structured training program prior to implementing taTME into clinical practice[14]. Ongoing proctorship by a taTME expert was available in some programs albeit for a limited number of cases[12, 36, 37], and would be recommended. More recently, an international panel of experts have identified the importance of the inclusion of a formative assessment during proctorship to help monitor

Author Manuscript

learning and guide duration of proctorship[14]. Finally, in accordance with the IDEAL framework for safe introduction of new procedures, ongoing assessment and audit is vital in ensuring rigorous evaluation of the long-term outcomes of a procedure. Thus, the authors suggest that the learning curve is likely to include between 30 to 50 cases, which was reflected in the majority (four out of six) of the analysed studies. The reason for such a wide variation may reflect the surgeon's prior experience in rectal cancer surgery. Although the volume of cases is important during the learning curve, maintenance of a regular caseload, ongoing formative assessment and proctorship as well as ongoing contribution to audit/ national registry are important aspects to consider when adopting this novel technique.

There are several limitations to this study. Firstly, these are observational studies and therefore has its inherent bias including patient selection, particularly in the initial part of the learning curve. This is expected given that the primary outcome is the learning curve and outcome for these studies[18]. Additionally, the study heterogeneity makes comparison between studies challenging. Thirdly, all included studies did not study the effects of long-term oncological outcomes in patients who had taTME in the learning curve, a particularly important outcome after recent concerns culminating in the Norwegian moratorium[10]

While this meta-analysis of retrospective cohort studies has been weakened by the lack of important long-term functional and oncological measures due to inadequate length of follow-up, as well as the lack of significant difference in surrogate/actual oncological outcomes between LC and ALC groups, the results of the currently ongoing COLOR III and GRECCAR randomised controlled trials are eagerly anticipated, in order to provide clarity on the role of taTME in the management of middle and low rectal cancer[41, 42].

Author Manuscript

However, with the intermediate long-term data from a multicentre study in Europe by de Lacey showing a possible improvement in oncological results following taTME compared to LapTME [43], the authors believe that there is a role for taTME to complement existing approaches to rectal dissection, used selectively in patients with a challenging pelvis. Extreme caution should be exercised when taking up this procedure, perhaps for a subset of carefully selected patients in the hands of experienced and well-trained teams dedicated to ongoing audit.

Funding

There are no sources of funding to declare.

Author Manuscript

References

1. Adamina M, Buchs NC, Penna M, Hompes R. St. Gallen consensus on safe implementation of transanal total mesorectal excision. Surgical endoscopy. 2018;32(3):1091-103.
2. Atallah SB, DuBose AC, Burke JP, Nassif G, deBeche-Adams T, Frering T, et al. Uptake of transanal total mesorectal excision in North America: initial assessment of a structured training program and the experience of delegate surgeons. Diseases of the Colon & Rectum. 2017;60(10):1023-31.
3. Targarona EM, Balague C, Pernas JC, Martinez C, Berindoague R, Gich I, 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. Annals of surgery. 2008;247(4):642-9.
4. Shin DW, Shin JY, Oh SJ, Park JK, Yu H, Ahn MS, et al. The prognostic value of circumferential resection margin involvement in patients with extraperitoneal rectal cancer. The American Surgeon. 2016;82(4):348-55.
5. Atallah S, Sylla P, Wexner S. Norway versus The Netherlands: will taTME stand the test of time? : Springer; 2019.
6. de Lacy FB, van Laarhoven JJ, Pena R, Arroyave MC, Bravo R, Cuatrecasas M, et al. Transanal total mesorectal excision: pathological results of 186 patients with mid and low rectal cancer. Surgical endoscopy. 2018;32(5):2442-7.
7. Wolthuis AM. Transanal total mesorectal excision international registry results of the first 720 cases. ANNALS OF LAPAROSCOPIC AND ENDOSCOPIC SURGERY. 2017;2.
8. Helbach MV, Deijen C, Velthuis S, Bonjer H, Tuynman J, Sietses C. Transanal total mesorectal excision for rectal carcinoma: short-term outcomes and experience after 80 cases. Surgical endoscopy. 2016;30(2):464-70.
9. Sylla P, Knol JJ, D'Andrea AP, Perez RO, Atallah SB, Penna M, et al. Urethral injury and other urologic injuries during transanal total mesorectal excision: an international collaborative study. Annals of Surgery. 2020.
10. Wasmuth H, Faerden A, Myklebust T, Pfeffer F, Norderval S, Riis R, et al. Transanal total mesorectal excision for rectal cancer has been suspended in Norway. British Journal of Surgery. 2020;107(1):121-30.
11. Van Oostendorp S, Belgers H, Bootsma B, Hol J, Belt E, Bleeker W, et al. Locoregional recurrences after transanal total mesorectal excision of rectal cancer during implementation. British Journal of Surgery. 2020.
12. Helbach MV, van Oostendorp SE, Koedam T, Knol J, Stockmann H, Oosterling S, et al. Structured training pathway and proctoring; multicenter results of the implementation of transanal total mesorectal excision (TaTME) in the Netherlands. Surgical Endoscopy. 2020;34(1):192-201.
13. Peyser D, Hersh EH, Sylla P. Training and accreditation in transanal total mesorectal excision in the United States.
14. Hompes R, Adamina M, Aigner F, Araujo S, Arezzo A, Ashamalla S, et al. International expert consensus guidance on indications, implementation and quality measures for Transanal Total Mesorectal Excision (TaTME). Colorectal Disease. 2020.
15. Lee L, Kelly J, Nassif GJ, deBeche-Adams TC, Albert MR, Monson JR. Defining the learning curve for transanal total mesorectal excision for rectal adenocarcinoma. Surgical endoscopy. 2020;34(4):1534-42.
16. Rubinkiewicz M, Truszkiewicz K, Wysocki M, Witowski J, Torbicz G, Nowakowski MM, et al. Evaluation of the learning curve of transanal total mesorectal excision: single-centre experience. Videosurgery and Other Miniinvasive Techniques. 2020;15(1):36.

Author Manuscript

Author Manuscript

17. Caycedo-Marulanda A, Ma G, Jiang H. Transanal total mesorectal excision (taTME) in a single-surgeon setting: refinements of the technique during the learning phase. Techniques in coloproctology. 2018;22(6):433-43.
18. Koedam T, Helbach MV, Van de Ven P, Kruyt PM, van Heek N, Bonjer H, et al. Transanal total mesorectal excision for rectal cancer: evaluation of the learning curve. Techniques in coloproctology. 2018;22(4):279-87.
19. Kang L, Luo S, Chen W, Zhang X, Cai Y, Hou Y, et al. Learning curve of transanal total mesorectal excision for rectal cancer. Zhonghua wei chang wai ke za zhi= Chinese journal of gastrointestinal surgery. 2016;19(8):917-22.
20. Perdawood SK, Kroeigaard J, Eriksen M, Mortensen P. Transanal total mesorectal excision: the Slagelse experience 2013–2019. Surgical Endoscopy. 2020:1-11.
21. Rahbari NN, Weitz J, Hohenberger W, Heald RJ, Moran B, Ulrich A, et al. Definition and grading of anastomotic leakage following anterior resection of the rectum: a proposal by the International Study Group of Rectal Cancer. Surgery. 2010;147(3):339-51.
22. Kang L, Sylla P, Atallah S, Ito M, Wexner SD, Wang J-P. taTME: boom or bust? : Oxford University Press; 2020.
23. Deijen C, Tsai A, Koedam T, Helbach MV, Sietses C, Lacy A, et al. Clinical outcomes and case volume effect of transanal total mesorectal excision for rectal cancer: a systematic review. Techniques in coloproctology. 2016;20(12):811-24.
24. Shiraishi T, Nishizawa Y, Yamamoto H, Tsukada Y, Sasaki T, Ito M. Carbon dioxide embolism during transanal total mesorectal excision (taTME). Techniques in coloproctology. 2018;22(9):735-8.
25. Penna M, Hompes R, Arnold S, Wynn G, Austin R, Warusavitarne J, et al. Incidence and risk factors for anastomotic failure in 1594 patients treated by transanal total mesorectal excision: results from the international TaTME registry. Annals of surgery. 2019;269(4):700-11.
26. Lu ZR, Rajendran N, Lynch AC, Heriot AG, Warrier SK. Anastomotic leaks after restorative resections for rectal cancer compromise cancer outcomes and survival. Diseases of the Colon & Rectum. 2016;59(3):236-44.
27. Bell S, Walker K, Rickard M, Sinclair G, Dent O, Chapuis P, et al. Anastomotic leakage after curative anterior resection results in a higher prevalence of local recurrence. British journal of surgery. 2003;90(10):1261-6.
28. Sylla P, Rattner DW, Delgado S, Lacy AM. NOTES transanal rectal cancer resection using transanal endoscopic microsurgery and laparoscopic assistance. Surgical endoscopy. 2010;24(5):1205-10.
29. Caycedo-Marulanda A, Verschoor C. Experience beyond the learning curve of transanal total mesorectal excision (taTME) and its effect on the incidence of anastomotic leak. Techniques in coloproctology. 2020;24(4):309-16.
30. Bokhari MB, Patel CB, Ramos-Valadez DI, Ragupathi M, Haas EM. Learning curve for robotic-assisted laparoscopic colorectal surgery. Surgical endoscopy. 2011;25(3):855-60.
31. Larsen S, Pfeffer F, Kørner H, Group NCC. Norwegian moratorium on transanal total mesorectal excision. British Journal of Surgery. 2019;106(9):1120-1.
32. Hol JC, van Oostendorp SE, Tuynman JB, Sietses C. Long-term oncological results after transanal total mesorectal excision for rectal carcinoma. Techniques in coloproctology. 2019;23(9):903-11.
33. Koch M, Tanis P, Bemelman W, Tuynman J, Hompes R, Belgers H. Purse-string reinforcement in transanal total mesorectal excision: a further essential step to increase oncological safety–a video vignette. Colorectal Disease. 2020;22(2):219-20.

Author Manuscript

34. Bernardi M-P, Bloemendaal A, Albert M, Whiteford M, Stevenson A, Hompes R. Transanal total mesorectal excision: dissection tips using 'O's and 'triangles'. Techniques in coloproctology. 2016;20(11):775-8.
35. Bell SW, Stevenson A. Training and accreditation in transanal total mesorectal excision (taTME) (Australasia). Annals of Laparoscopic and Endoscopic Surgery. 2020;5.
36. Francis N, Penna M, Carter F, Mortensen NJ, Hompes R, Group APNTTIS, et al. Development and early outcomes of the national training initiative for transanal total mesorectal excision in the UK. Colorectal Disease. 2020.
37. Abbott S, Stevenson A, Bell S, Clark D, Merrie A, Hayes J, et al. An assessment of an Australasian pathway for the introduction of transanal total mesorectal excision (taTME). Colorectal Disease. 2018;20(1):O1-O6.
38. Caycedo-Marulanda A, Brown CJ, Chadi SA, Ashamalla S, Lee L, Stotland P, et al. Canadian taTME expert collaboration (CaTaCO) position statement. Surgical endoscopy. 2020;34(9):3748-53.
39. Soomro N, Hashimoto D, Porteous A, Ridley C, Marsh W, Ditto R, et al. Systematic review of learning curves in robot-assisted surgery. B JS open. 2020;4(1):27.
40. Khan N, Abboudi H, Khan MS, Dasgupta P, Ahmed K. Measuring the surgical 'learning curve': methods, variables and competency. BJU international. 2014;113(3):504-8.
41. Deijen CL, Velthuis S, Tsai A, Mavroveli S, de Lange-de Klerk ES, Sietses C, et al. COLOR III: a multicentre randomised clinical trial comparing transanal TME versus laparoscopic TME for mid and low rectal cancer. Surgical endoscopy. 2016;30(8):3210-5.
42. Lelong B, De Chaisemartin C, Meillat H, Cournier S, Boher JM, Genre D, 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(1):253.
43. de Lacy FB, Roodbeen SX, Ríos J, van Laarhoven J, Otero-Piñeiro A, Bravo R, et al. Three-year outcome after transanal versus laparoscopic total mesorectal excision in locally advanced rectal cancer: a multicenter comparative analysis. 2020.

Table 1 - Study characteristics, quality assessment and patient characteristics

Author and Year	Study Period	No. of centres, Country	Study Design	Quality Assessment			Surgeon experience, training (no. of surgeons)	No. of patients		Age				Male				Neoadjuvant CRTx				Advanced cancer (AJCC III or Duke C)			
				S	C	O		LC	ALC	LC	Range	ALC	Range	LC	Range	ALC	Range	LC	Range	ALC	Range	LC	Range	ALC	Range
Lee et al [1], 2020	2012-2017	1, United States	R,D	3	2	2	Colorectal surgeons proficient in LaTME and TAMIS. Proctorship - 1 senior surgeon present in all cases. (4)	51	36	59.8	9.4	61.9	10.3	35	68.6%	22	61.1%	43	84.3%	27	75.0%	38	74.5%	18	50.0%
Perdawood et al [2], 2020	2013-2019	1, Denmark	R,D	3	1	2	NR (NR)	100	100	67 (10.2)				73	73.0%	74	74.0%	44 (22%)				58 (29%)			
Rubinkiewicz et al [3], 2020	2014	1, Poland	R,D	3	2	2	Training program included cadaver based hands on practice. (1)	40	26	62.5	54.5-72.5	65	57-71	31	77.5%	13	50%	35	87.5%	19	73.1%	7	17.5%	11	42.3%
Veltcamp Helbach et al [4], 2020	2014-2018	12, Netherlands	R,D	3	2	2	Surgeons experienced in LaTME and TAMIS. Training program including e-learning, anatomy teaching, observation of live procedure, hands-on cadaver workshop and the first cases proctored by experts. (NR)	60	60	64.9	10.3	66	9.5	45	75.0%	46	76.7%	42	70.0%	35	58.3%	NR	NR	NR	NR
Caycedo-Marulanda et al [5], 2018	2015-2017	1, Canada	R,D	3	2	2	Sub-specialty trained colorectal surgeon. (1)	27	43	60.74	9.77	63.48	10.85	14	51.9%	29	67.4%	19	70.4%	27	62.8%	16	59.3%	20	46.5%
Koedam et al [6], 2018	2012-2017	1, Netherlands	R,D	3	2	3	Colorectal surgeons experienced in LAR and TAMIS. Training program included cadaveric courses, symposia, observership. Procedures proctored by senior surgeon. (3)	40	40	65.5	42-86	70	51-81	27	67.5%	26	65.0%	37	92.5%	21	52.5%	12	30.0%	11	27.5%
Kang et al [7], 2016	2014-2016	1, China	R,D	3	2	1	Surgeons skilled in laparoscopic resection of rectal cancer. Training program included specimen dissection and animal/cadaveric preparation courses. Procedures proctored by professor surgeon. (NR)	15	15	56.6	36-77	55.8	30-80	6	40.0%	12	80.0%	9	60.0%	4	26.7%	1	6.7%	2	13.3%

R retrospective, *D* prospective database, *S* selection, *C* comparability, *O* outcome, *LaTME* laparoscopic total mesorectal excision, *TAMIS* transanal minimally invasive surgery, *NR* not reported, *LC* learning curve, *ALC* after learning curve, *CRTx* chemoradiotherapy, *AJCC* American Joint Committee on Cancer

Author Manuscript

Author Manuscript

Table 2 - Intra-operative outcomes

Author and Year	Operative time (min)				Blood loss (ml)				Open conversion				Adverse events			
	LC	Range	ALC	Range	LC	Range	ALC	Range	LC	Range	ALC	Range	LC	Range	ALC	Range
Lee et al [1], 2020	278	84	270	73	150	75-200	100	50-100	1	2.0%	1	2.8%	6	11.8%	2	5.6%
Perdawood et al [2], 2020	289.4	63.5	281.7	63.2	95.9	121.0	63.2	127.6	NR	NR	NR	NR	13	13.0%	5	5.0%
Rubinkiewicz et al [3], 2020	270	240-300	210	170-240	100	50-200	150	50-200	NR	NR	NR	NR	5	12.5%	1	3.8%
Veltcamp Helbach et al [4], 2020	283.6	80.1	302.5	103.6	NR	NR	NR	NR	1	1.7%	4	6.7%	3	5.0%	3	5.0%
Caycedo-Marulanda et al [5], 2018	303	75.6	297.6	68.4	NR	NR	NR	NR	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Koedam et al [6], 2018	199	95-329	195	127-286	NR	NR	NR	NR	4	10.0%	4	10.0%	NR	NR	NR	NR
Kang et al [7], 2016	299	131	278	44.8	288	568.1	87	43.3	NR	NR	NR	NR	NR	NR	NR	NR

LC learning curve, *ALC* after learning curve, *NR* not reported

Author Manuscript

Table 3 - Clinical outcomes

Author and Year	Total Morbidity				Major Morbidity (CD III - IV)				Mortality				Primary Anastomosis				Anastomotic leak			
	LC	Range	ALC	Range	LC	Range	ALC	Range	LC	Range	ALC	Range	LC	Range	ALC	Range	LC	Range	ALC	Range
Lee et al [1], 2020	23	45.1%	15	41.7%	6	11.8%	2	5.6%	NR	NR	NR	NR	44	86.3%	32	88.9%	3	6.8%	0	0%
Perdawood et al [2], 2020	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	59	59.0%	81	81.0%	4	6.8%	9	11%
Rubinkiewicz et al [3], 2020	13	32.5%	2	7.7%	6	15.0%	1	3.8%	NR	NR	NR	NR	40	100.0%	26	100.0%	7	17.5%	1	4%
Veltcamp Helbach et al [4], 2020	NR	NR	NR	NR	12	20.0%	11	18.3%	0	0%	0	0%	NR	NR	NR	NR	9	NR	8	NR
Caycedo-Marulanda et al [5], 2018	4	14.8%	3	7.0%	4	14.8%	5	11.6%	0	0%	0	0%	26	96.3%	34	79.1%	4	15.4%	2	6%
Koedam et al [6], 2018	23	57.5%	25	62.5%	12	30.0%	6	15.0%	2	5.0%	0	0%	25	62.5%	27	67.5%	11	44.0%	2	7%
Kar[illegible] et al [7]																				

LC learning curve, *ALC* after learning curve, *CD* Clavien-Dindo, *NR* not reported

Author Manuscript

Table 4 – Pathological outcomes and quality of mesorectal excision

Author and Year	Distal margins involvement				Circumferential margins involvement				Complete				Nearly complete				Incomplete				LN harvest			
	LC	Range	ALC	Range	LC	Range	ALC	Range	LC	Range	ALC	Range	LC	Range	ALC	Range	LC	Range	ALC	Range	LC	Range	ALC	Range
Lee et al [1], 2020	1	2.0%	0	0%	2	3.9%	0	0.0%	37	72.5%	32	88.9%	17	33.3%	13	36.1%	1	2.0%	0	0.0%	19.7	10	19.6	11.7
Perdawood et al [2], 2020	NR	NR	NR	NR	6	6.0%	5	5.0%	67	67.0%	66	66.0%	23	23.0%	22	22.0%	10	10.0%	12	12.0%	NR	NR	NR	NR
Rubinkiewicz et al [3], 2020	N.S	N.S	N.S	N.S	N.S	N.S	N.S	N.S	34	85.0%	23	88.5%	6	15.0%	3	11.5%	0	0.0%	0	0.0%	NR	NR	NR	NR
Veltcamp Helbach et al [4], 2020	0	0%	0	0%	1	1.7%	5	8.3%	48	80.0%	59	98.3%	12	20.0%	1	1.7%	0	0.0%	0	0.0%	NR	NR	NR	NR
Caycedo-Marulanda et al [5], 2018	0	0%	1	2%	1	3.7%	1	2.3%	18	66.7%	36	83.7%	9	33.3%	7	16.3%	0	0.0%	0	0.0%	25.59	8.88	24.81	9.9
Koedam et al [6], 2018	0	0%	0	0%	1	2.5%	0	0%	36	90.0%	39	97.5%	3	7.5%	1	2.5%	1	2.5%	0	0.0%	15	7-27	16	4-66
Kang et al [7], 2016	NR	NRS	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	9.6	2.7	15.8	4.8

LN lymph nodes, *LC* learning curve, *ALC* after learning curve, *NR* not reported

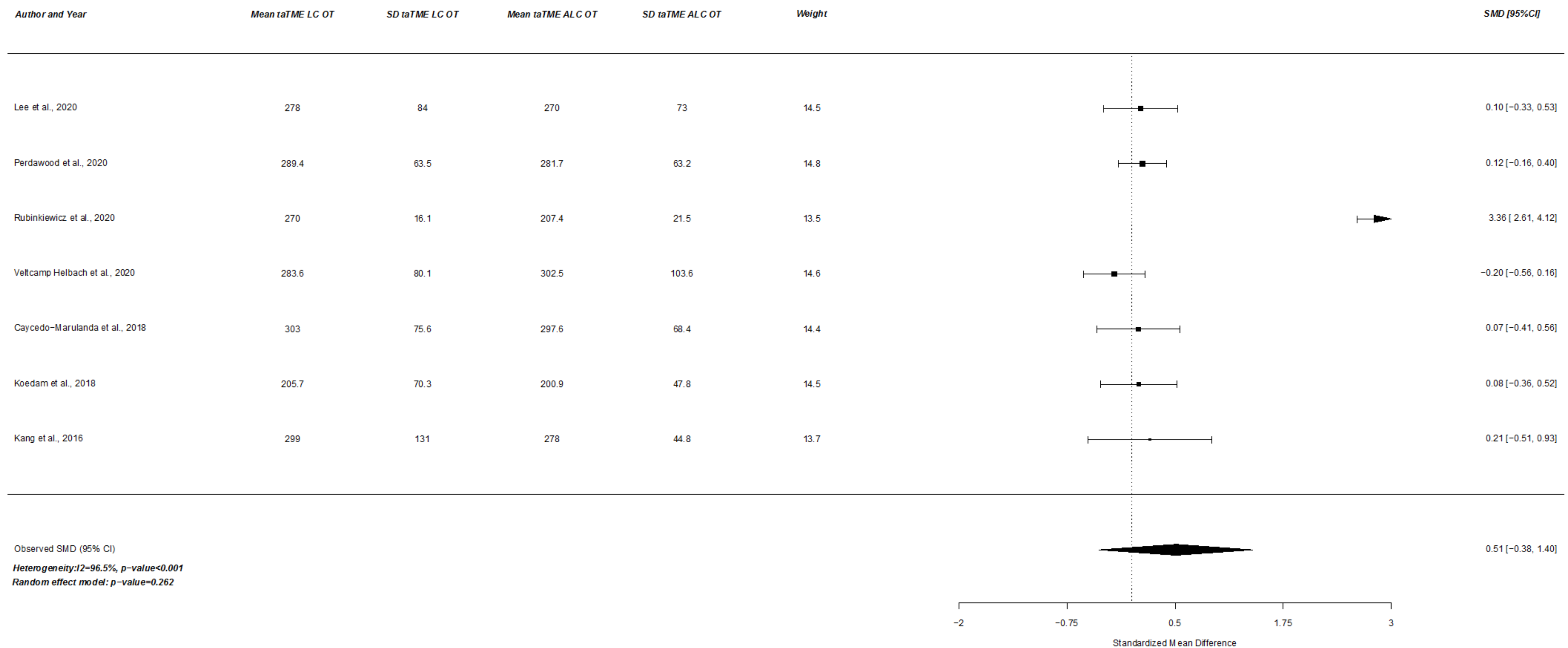
Table 5 – Definitions of Learning Curve

Study	Author	No. of procedures to reach stabilization of learning curve	Criteria used to define proficiency
1	Lee et al	45-51	Acceptable rates of high-quality TME (complete or near-complete mesorectal envelope (as defined in ACOSOG Z6051 trial), negative distal (DRM), and circumferential resection (> 1 mm; CRM) margin).
2	Perdawood et al	140	Operating time (transanal dissection), Blood loss, Intraoperative complications
3	Rubinkiewicz et al	40	Intraoperative complications, Postoperative morbidity, Operating time
4	Veltcamp Helbach et al	5*	This was an arbitrary number for comparison
5	Caycedo-Marulanda et al	NR	
6	Koedam et al	40	Postoperative morbidity, Operating time
7	Kang et al	30	Operating time, Blood loss, Lymph node harvest (Not based on CUSUM analysis)

Author Manuscript

Author Manuscript

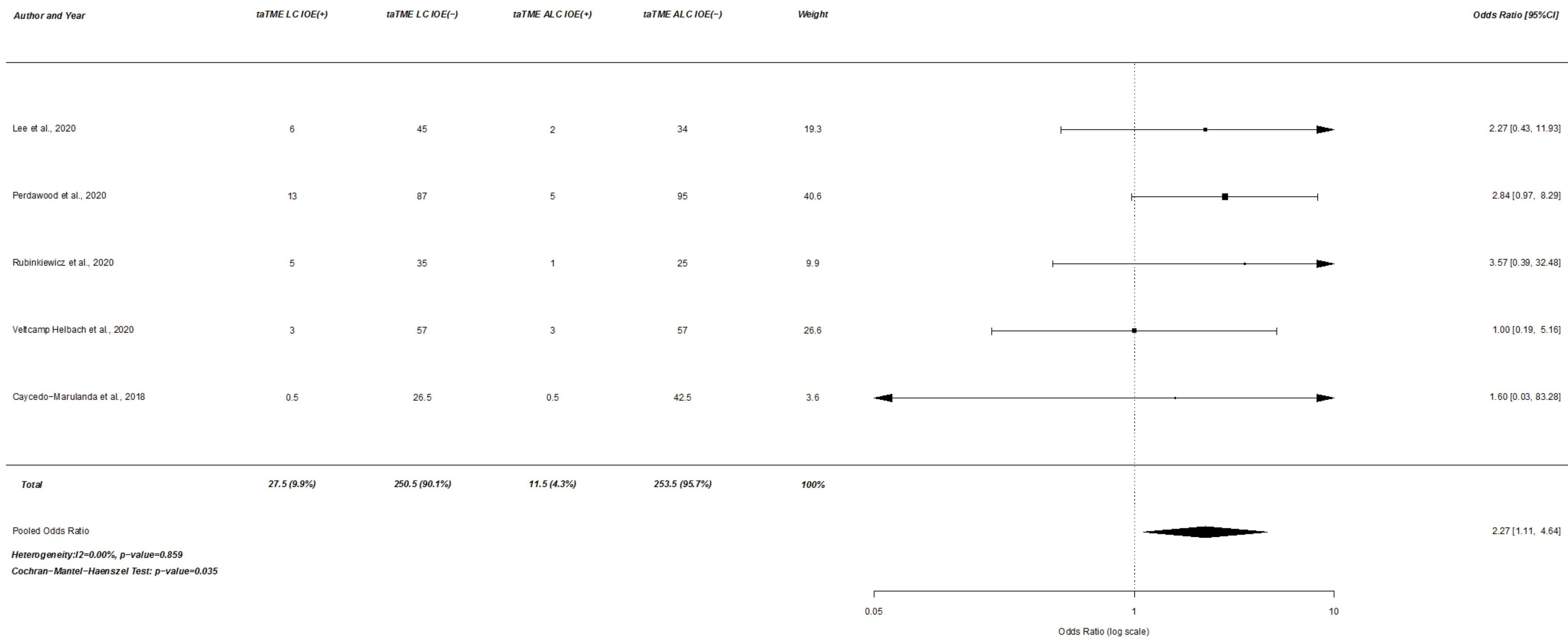
Figure 1 - Forest plot of all studies included for this meta-analysis with pool standardized mean difference for operative time



TaTME transanal total mesorectal excision, *LC* learning curve, *ALC* after learning curve, *OT* operative time

Author Manuscript

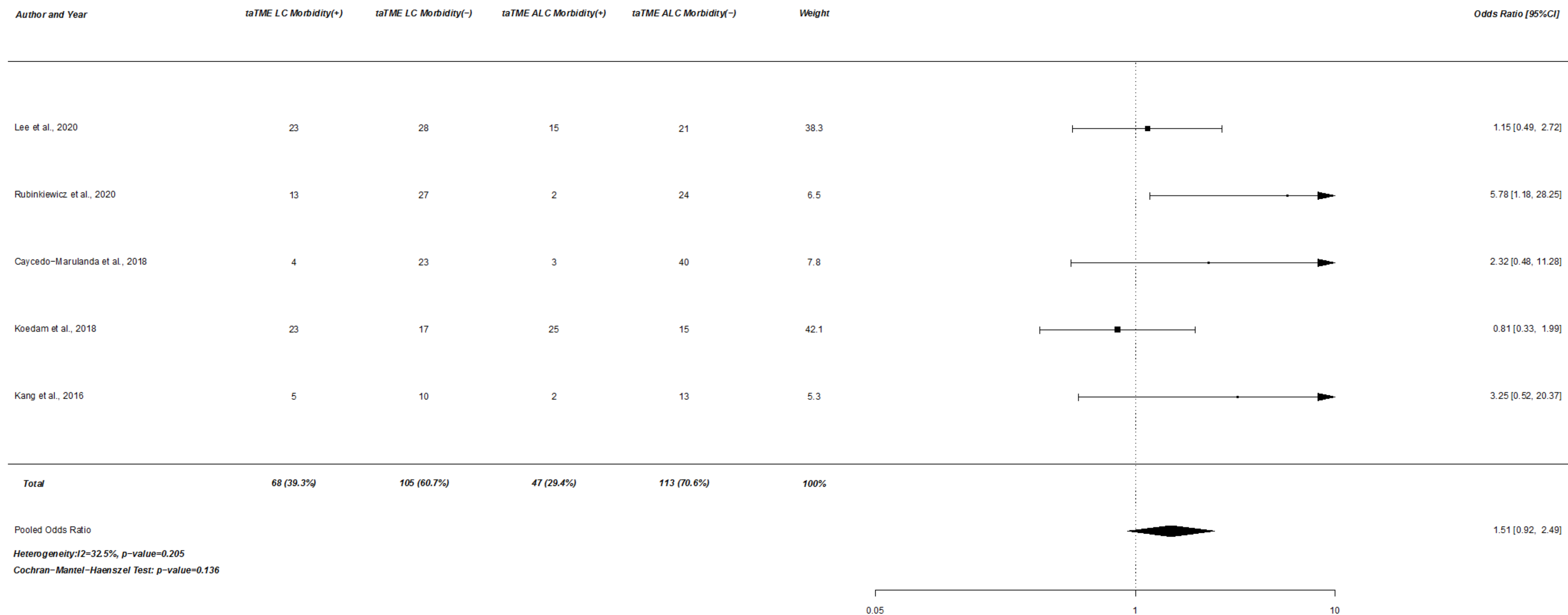
Figure 2- Forest plot of all studies included for this meta-analysis with pooled odds ratio for intra-operative adverse events



TaTME transanal total mesorectal excision, *LC* learning curve*, ALC* after learning curve, *IOE* intra-operative events

Author Manuscript

Figure 3 - Forest plot of all studies included for this meta-analysis with pooled odds ratio for total morbidity



TaTME transanal total mesorectal excision, *LC* learning curve, *ALC* after learning curve

Author Manuscript