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REVIEW

Should the rectal defect be closed following transanal local excision of rectal tumors? A systematic review and meta-analysis

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Abstract
Background Transanal local excision (TLE) has become the treatment of choice for benign and early-stage selected malignant tumors. However, closure of the rectal wall defect remains a controversial point and the available literature still remains unclear. Our aim was to determine through a systematic review of the literature and a meta-analysis of relevant studies whether or not the wall defect following TLE of rectal tumors should be closed.
Methods Medline and the Cochrane Trials Register were searched for trials published up to December 2016 comparing open versus closed management of the surgical rectal defect after TLE of rectal tumors. Meta-analysis was performed using Review Manager 5.0.
Results Four studies were analyzed, yielding 489 patients (317 in the closed group and 182 in the open group). Meta-analysis showed no significant difference between the closed and open groups regarding the overall morbidity rate (OR 1.26; 95% CI 0.32–4.91; $p = 0.74$), postoperative local infection rate (OR 0.62; 95% CI 0.23–1.62; $p = 0.33$), postoperative bleeding rate (OR 0.83; 95% CI 0.29–1.77; $p = 0.63$), and postoperative reintervention rate (OR 2.21; 95% CI 0.52–9.47; $p = 0.29$).
Conclusions This review and meta-analysis suggest that there is no difference between closure or non-closure of wall defects after TLE.

Keywords Transanal local excision · Rectal tumor · Transanal endoscopic microsurgery · Transanal minimally invasive surgery · Defect closure

Introduction

Abdominal rectal resection combined with total mesorectal excision (TME) is the current standard of care for the treatment of rectal cancer [1, 2]. However, postoperative morbidity rates are high and functional sequelae are common [3, 4]. During the past 20 years, several studies have highlighted the role of transanal local excision (TLE) for the treatment of early rectal cancer [5], even though this treatment remains controversial because of the lack of adequate lymphadenectomy [6]. The current evidence supports the use of TLE with a curative intent only in selected T1 rectal cancers (i.e., diameter ≤ 3 cm, rectal circumferential involvement ≤ 30%, low submucosal tumor invasion (≤ Sm2), good histological differentiation, absence of either mucinous adenocarcinoma, or positive deep or peripheral margins, absence of either involved lymph nodes, or lymphovascular and perineural invasion [1, 2, 7]. Furthermore, surgical techniques have improved with the introduction of transanal endoscopic microsurgery (TEM) instead of traditional local excision (LE). TEM significantly reduced local recurrence rate when compared to local excision (LE), due to a higher rate of whole specimens with free resection margins [8, 9]. However, TEM equipment is not available in most centers [10] and transanal minimal invasive surgery (TAMIS) is an efficient alternative [11]. Closure of the rectal defect below

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the peritoneal reflection remains a controversial point. Some authors have recommended suturing on the basis of earlier wound healing, better bleeding control, and less stenosis of the lumen [12–15], whereas others have maintained that routine closure is not advisable because closure increases mean operative time [16–18]. To our knowledge, only one randomized controlled trial has compared these two strategies after either TEM or conventional LE and suggested that there was no difference in terms of intraoperative results and outcomes [16]. However, the sample size of the study affected the level of evidence. There is no consensus among colorectal surgeons regarding this question. For this reason, we decided to perform a meta-analysis to determine whether or not the rectal defect following TLE of rectal tumors should be closed.

Materials and methods

Search strategy

We performed a systematic review of the literature published up to December 2016 by searching abstracts in Medline, the Cochrane database and Cochrane Clinical Trials Registry. The medical subject headings (MeSH) and keywords searched for individually and in combination were as follow: «transanal local excision», «transanal endoscopic microsurgery», «transanal minimal invasive surgery», «rectal tumor», «defect closure», and «defect suture». References cited in an identified article were searched manually to retrieve other suitable studies. We also screened the references of the relevant studies to check for potentially relevant articles.

Inclusion and exclusion criteria

Criteria for inclusion in the meta-analysis were (1) studies that compared open versus closed management of the surgical defect after TLE (i.e., LE, TEM, TAMIS) of rectal tumors; (2) studies that reported at least one of the outcome measures (i.e., postoperative complications such as reintervention, bleeding, abscess formation, wound dehiscence, bladder dysfunction).

Exclusion criteria included (1) studies that involved pediatric patients (< 18 years of age); (2) studies that included TLE after chemoradiotherapy; (3) non-English papers; iv) articles that were not full-text and non-comparative studies and which included less than 10 patients; or (4) animal or laboratory studies.

Data extraction and review

Critical appraisal and data extraction were conducted independently by two reviewers (BM, JL), and discrepancies were resolved by consensus intervention of a third investigator (AA).

The following individual data were independently extracted for each included study using standardized extraction forms: general data (study design, year, sample size), characteristics of patients (age, gender, indication for the index operation including size and location of the rectal tumor), main features of the intervention [surgical technique (i.e., LE, TEM, TAMIS), methods of rectal defect suturing]. Primary outcome includes overall postoperative morbidity as defined as any complication occurring during the hospital stay or within 30 days after TLE. Secondary outcomes included reintervention (including surgical and/or endoscopic intervention), and specific surgical complications such as bleeding with or without blood transfusion requirement, local postoperative infection (i.e., abscess or pelvic pain and either fever or leukocytosis).

The quality of the studies was checked with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement for non-randomized comparative studies and the Jadad scale for randomized controlled trials [19, 20].

Statistical analysis

All statistical analyses were performed using Review Manager 5.0 software (Cochrane Collaboration, Oxford, UK). A fixed model was used if there was no evidence of heterogeneity, and otherwise a random effects model was used. Heterogeneity was assessed using the I^2 statistic, with values > 50% considered to indicate significant heterogeneity. Odds ratios (ORs) were calculated for each trial from the number of evaluable patients, and 95% confidence intervals (CIs) were calculated to confirm the effect size estimation and test criteria. The Mantel–Haenszel OR was calculated for dichotomous variables (or Peto OR when necessary, i.e., because there was an event scored to 0, where a random effect with Mantel–Haenszel OR is not appropriate). In this meta-analysis, OR was calculated using the Mantel–Haenszel test for dichotomic factors such as overall morbidity. For the other outcomes (infection rate, bleeding rate, and reintervention rate), a Peto model was used.

The p value for the overall effect was calculated using the Z test, with significance set at $p < 0.05$. Sensitivity analysis and estimation of publication bias were also performed.

Results

Population characteristics

Details of the initial search results and refined inclusion are presented in the flowchart (Fig. 1). Two hundred and

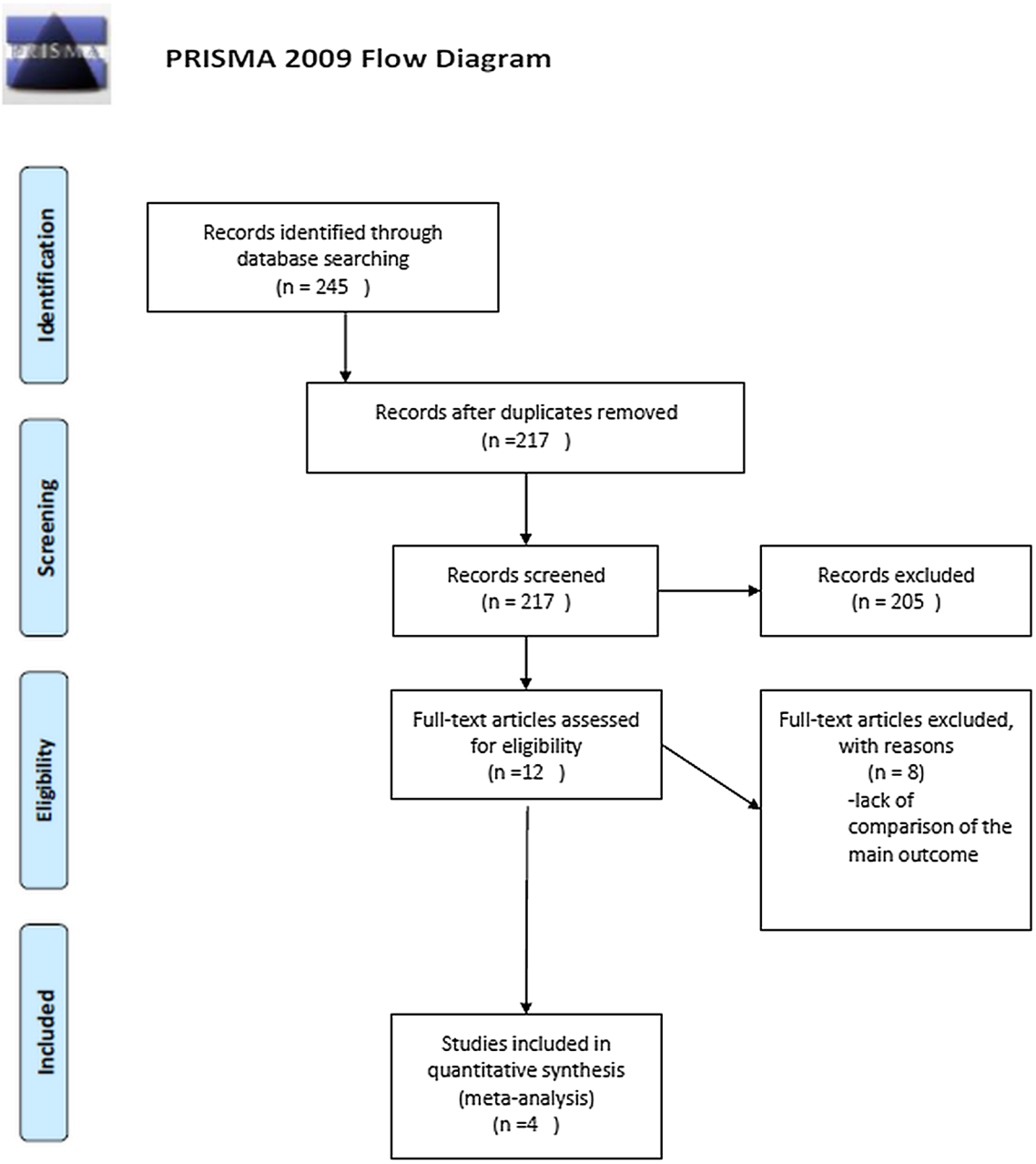

Fig. 1 PRISMA flowchart

forty-five articles were reviewed, and 12 appropriate studies were assessed to be potentially included in the meta-analysis. Eight of these were excluded because they did not compare open versus closed management of the surgical defect after TLE [21–28]. The remaining four studies analyzed, yielding 489 patients (317 in closed group and 182 in open group, respectively) included one randomized controlled trial (RCT) [16], two prospective case series [15, 18], and one retrospective case series [17]. Characteristics of the included studies are outlined in Table 1. Mechanical bowel preparation was performed preoperatively in all four studies. Rectal tumors (i.e., low- and high-grade rectal adenoma and early rectal cancer) were eligible for TLE including LE, TEM, and TAMIS. Except for one RCT (16), the decision about defect closure depended on the operator's assessment. Several techniques of defect closure were used, including running suture and/or single stitches and/or suture clip forceps. In one study [15], patients were excluded if the peritoneal cavity was entered during the procedure.

Table 1 Characteristics of the studies

Trial	Year	Study period	Type of study	*N*	Indications	Surgical technique	Surgical suture	Carcinoma (%)	Colorectal preparation	Single center	Clavien–Dindo
Ramirez	2002		RCT	44	Benign sessile adenomas or early rectal carcinomas μT1, low risk located below peritoneal reflection	Local excision with a Park's retractor and/or transanal endoscopic microsurgery	Running suture of 3.0 absorbable microfilament	20.5	Full mechanical bowel preparation	Y	N
Hahnloser	2015	2009–2012	PCS	75	Low- and high-grade rectal adenoma; rectal carcinomas and carcinoid tumor	Transanal minimally invasive surgery (TAMIS) which combined TEM and single-port laparoscopic surgery	Single stitches or running suture of Vicryl 3-0 or V-loc 3.0	43	Rectal enema and/or full mechanical bowel preparation	N	Y
Brown	2016	2007–2014	PCS	341	Defunctioning low colorectal anastomoses	Transanal endoscopic microsurgery (TEM)[a]	Running suture of2-0 PDS and secured with suture clip forceps	40	Full mechanical bowel preparation	Y	N
Noura	2016	2004–2015	RCS	43	Defunctioning low colorectal anastomoses	Local excision with a Park's retractor or TAMIS	NA	95	Full mechanical bowel preparation	Y	Y

Y yes, *N* no, *RCT* randomized controlled trial, *PCS* prospective controlled study, *RCS* retrospective controlled study; *NA* not available

[a]Exclusion if the peritoneal cavity was interested instead of Hanloser et al.

Results of meta-analysis

Overall postoperative morbidity All studies reported the postoperative overall morbidity rate. The overall postoperative morbidity rate was 11% (35/317) in the closed group and 15.4% (28/182) in the open group. Meta-analysis showed no significant difference in postoperative overall morbidity rate between the groups (OR 1.26; 95% CI 0.32–4.91; $p = 0.74$ (Fig. 2).

Local postoperative infection rate All studies reported the local postoperative infection rate. The overall postoperative infection rate was 3.1% (10/317) in the closed group and 4.9% (9/182) in the open group. Meta-analysis showed no significant difference in the local postoperative infection rate between the groups (OR 0.62; 95% CI 0.23–1.62; $p = 0.33$) (Fig. 3).

Postoperative bleeding rate All studies reported the postoperative bleeding rate. The overall postoperative bleeding rate was 5.6% (18/317) in the closed group and 7.7% (14/182) in the open group. Meta-analysis showed no significant difference in the postoperative bleeding rate between the groups (OR 0.83; 95% CI 0.29–1.77; $p = 0.63$) (Fig. 4).

Reintervention rate All studies reported the postoperative reintervention rate. The overall reintervention rate was 1.9% (6/317) in the closed group and 1.1% (2/182) in the open

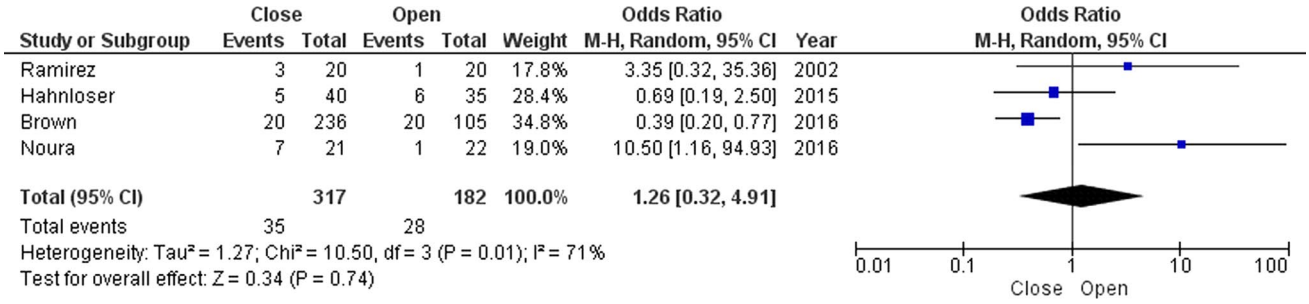

Fig. 2 Postoperative overall morbidity rate

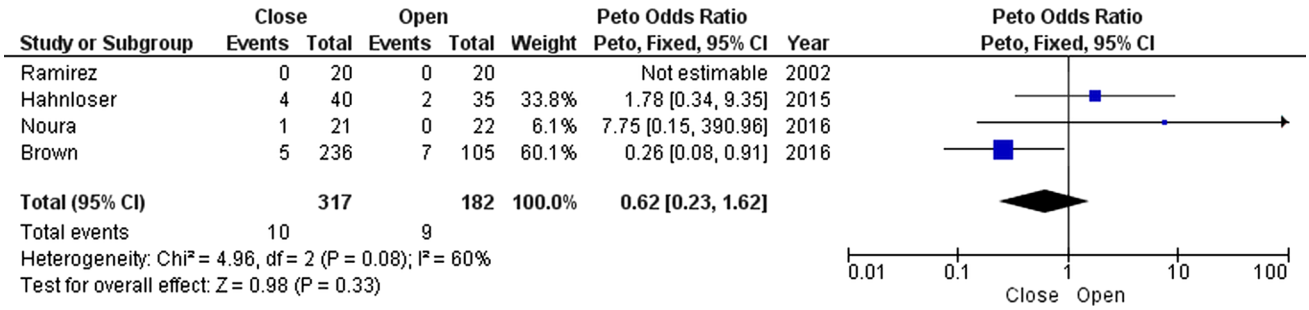

Fig. 3 Incidence of postoperative infections

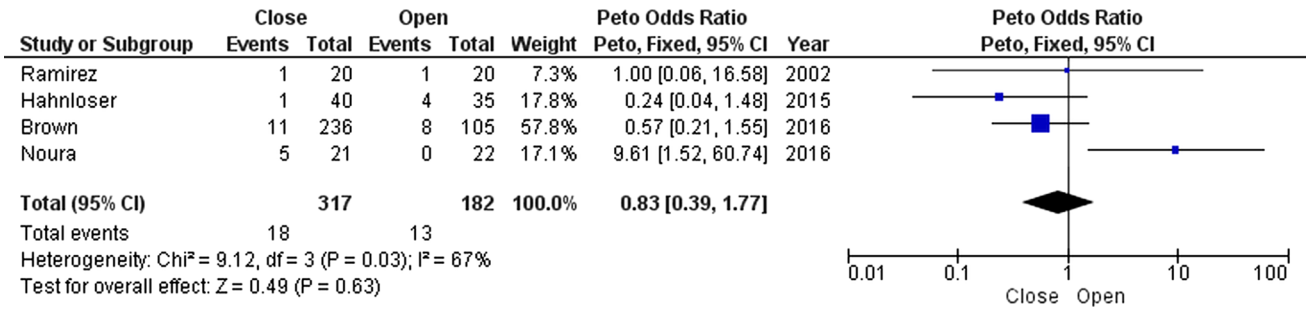

Fig. 4 Postoperative bleeding

group. Meta-analysis showed no significant difference in the postoperative reintervention rate between the groups (OR 2.21; 95% CI 0.52–9.47; $p = 0.29$) (Fig. 5).

Sensitivity analysis and publication bias Sensitivity analysis and estimation of publication bias were performed with the aim of determining the significance of results. For postoperative overall morbidity, the combined OR was calculated using both fixed effects and random effects model, and the results were compared. Because statistically significant data are published more frequently than nonsignificant data, our results may be influenced by publication bias.

Discussion

This meta-analysis suggests that there is no difference between closure and non-closure of the wall defect in terms of postoperative outcomes after TLE.

The major advantage of TLE is the significantly lower morbidity and mortality compared with the traditional treatment for malignant rectal tumors [5, 7]. TEM has revolutionized the approach to TLE and became the treatment of choice for benign and early-stage malignant tumors [8, 9]. Since 2010, TAMIS appears to have equivalent indications and outcomes when compared to TEM [11].

The morbidity rate following TLE reported in the recent literature ranges from 2 to 21% [29–32]. Most of complications are generally grades I or II according to the Clavien–Dindo classification [31]. The overall complications rate after TEM has been showed to be linked to the location of the rectal tumor (lateral, distal) [29, 33, 34]. A defect size of 2 cm was the cutoff for some authors [32, 33]. Marques et al. have recently reported that wound closure using TEM techniques had a lower risk of grade III [35] Clavien–Dindo complications when compared to open techniques [33].

The decision whether to close the rectal defect during TLE or not remains an unanswered question. Whichever the method used, it may be technically challenging as the space inside the rectum is limited. Instruments obstruct each other, and it is difficult to produce adequate tissue tension around the lesion [11]. The procedure may become lengthy. TAMIS, using a SILS trocar, makes it possible to decrease the diameter (30 mm) and increase the pliability as compared with the rigid proctoscope use in the TEM (40 mm). Despite potential advantages, it may not be possible to close the rectal defect in some instances, and in up to 30% in the report by Hahnloser [18].

The results of this meta-analysis suggest that the overall morbidity rate was comparable between the two procedures, including postoperative bleeding (5.6 vs. 7.7%) and local infection rates (3.1 vs. 4.9%). There are several limitations in each study included, with differences in perioperative management, surgeon experience, and operative technique used (for instance energy sources). Another cause of variation between included studies affecting the decision to close the defects was distance from the anal verge (with associated risk for peritoneal contamination), but this was not adequately reported.

Finally, there might be publication bias because statistically significant results are more often published than nonsignificant data and might influence the results. So publication bias cannot be adequately assessed.

Few studies have evaluated the risk factors related to incidence and severity of postoperative complications [29, 32]. It is largely agreed that postoperative complications after TLE occur more frequently and more severely after neoadjuvant chemoradiotherapy [11, 31, 32, 36]. We decided to exclude studies including neoadjuvant treatment because this therapeutic strategy is not currently recommended and may lead to heterogeneous results [37]. In a study by Marqes et al. [32], linear regression analysis showed a fourfold increased risk of complication occurrence in the CRT group and also revealed a threefold lower risk of complications among patients with lesions above the first rectal valve. Multimodal logistic regression analysis also demonstrated that wound closure using TEM techniques had a 16.6-fold lower risk of grade III (Clavien–Dindo) complications in comparison with open techniques ($p = 0.04$).

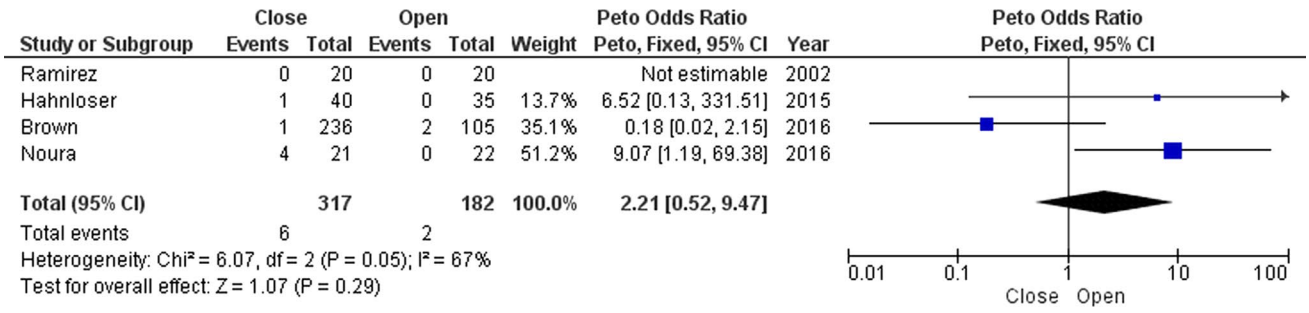

Fig. 5 Reintervention rate

Lateral position of the rectal tumor has been previously associated with an increased risk of intraoperative bleeding and overall complications after TEM [29, 34], and Kreissler–Haag et al. [33] reported that tumor diameter more than 2 cm and location on lateral wall of the rectum were associated with increased postoperative complications (such as bleeding), recommending that such defects should be closed. Posterior defects were associated with postoperative complications and may be left open, as it was suggested. Anterior and lateral defects may be associated with leakage and pelvic sepsis [29, 34]. Bignell et al. [33] showed that postoperative complications were more closely associated with more distal lesions.

This meta-analysis showed no significant difference in the overall morbidity rate between the groups ($p = 0.74$). According to Brown et al., overall postoperative morbidity (8.4 vs. 19%, $p = 0.03$) and readmission (4.7 vs. 12.4%, $p = 0.0$) rates were significantly lower following closure of the rectal defect [15]. Increased experience may, in this case, be a confounding factor with regard to complications because more than 50% of the procedures were performed by one experienced surgeon, who tended to close the rectal defect [15]. Furthermore, the height of the tumor, which has been previously reported as a risk factor for postoperative morbidity [32, 33], was significantly lower in the open group. Conversely, Noura et al. [17] found that both incidence (33.3 vs. 4.5%, $p = 0.02$) and severity (≥ IIIa 19 vs. 0%, $p = 0.04$) of postoperative complications were significantly associated with closure of the rectal defect. However, operative procedures using TAMIS and an energy source such as a vessel-sealing device were only used in the open group [17].

This meta-analysis showed no significant difference in local postoperative infection rate between the groups ($p = 0.33$). Hahnloser et al. reported a similar postoperative infection rate (10 vs. 6%, $p = 0.30$), but antibiotics were used significantly longer in the open group than in the closed group (5.5 vs. 8.5 days, $p = 0.001$).

This meta-analysis has some limitations. First of all, there is heterogeneity regarding type of studies (RCT and retrospective studies), although results were still the same when we analyzed only the RCT in sensitivity analysis [16]. Secondly, there were different definitions of postoperative complications, requiring reclassification according to the Clavien–Dindo system to make comparison between included studies possible.

In conclusion, this meta-analysis of available data suggests that there is no difference between closure and non-closure of the rectal wall defect after TLE.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants performed by any of the authors.

Informed consent For this type of study formal consent is not required.

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