Should the rectal defect be sutured following TEMS/TAMIS carried out for neoplastic rectal lesions? A meta-analysis

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ABSTRACT

INTRODUCTION Management of the rectal defect following transanal endoscopic microsurgery (TEMS) or minimally invasive surgery (TAMIS) carried out for excision of neoplasm in the lower rectum is controversial. We aimed to extract evidence by carrying out a meta-analysis to compare the peri- and postoperative outcomes following rectal neoplasm excision carried out by TEMS and/or TAMIS, whereby the defect is either sutured or left open.

METHODS A literature search of Ovid MEDLINE and EMBASE was performed. Full-text comparative studies published until November 2019, in English and of adult patients, whereby TEMS or TAMIS was undertaken for rectal neoplasms were included. The main outcome measures were postoperative bleeding, infection, operative time and hospital stay.

FINDINGS Three studies (one randomised controlled trial and two comparative case series) yielded 555 cases (283 in the sutured group and 272 in the open group). The incidence of postoperative bleeding was higher and statistically significant ($p = 0.006$) where the rectal defect was left open following excision of the neoplasm (19/272, 6.99% vs 6/283, 2.12%). There was no statistical difference between the sutured and open groups regarding infection ($p = 0.27$; (10/283, 3.53% vs 5/272, 1.84%, respectively), operative time ($p = 0.15$) or length of stay ($p = 0.67$).

CONCLUSION Suturing the rectal defect following excision of rectal neoplasm by TEMS/TAMIS reduces the incidence of postoperative bleeding in comparison to leaving the defect open. However, suturing makes the procedure slightly longer but there was no statistical difference between both groups when postoperative infection and length of hospital stay were compared.

KEYWORDS

Transanal endoscopic microsurgery – TEMS – Transanal minimally invasive surgery – TAMIS – Rectal neoplasm

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Introduction

Whether to suture or to leave the rectal defect open following excision of a rectal neoplasm carried out by transanal endoscopic microsurgery (TEMS) or minimally invasive surgery (TAMIS) is widely debated. Management of the rectal defect below the peritoneal reflection is influenced by the surgeon's preference.^{1–5} Proponents of suturing the surgical defect recommend it because of its improved haemostasis, accelerated wound healing rates and low risk of rectal lumen stenosis.^{4,5} Others prefer to leave rectal defect open, as suturing makes no difference to the surgical or oncological outcomes but increases operating time.⁶

TEMS is a minimally invasive technique. Since its inception in 1983, it has been proven as a viable alternative to radical surgery and endoscopic resections to treat selected early rectal cancers and large rectal neoplasms. Total mesorectal excision surgery is the gold standard surgical

treatment for rectal cancer.⁷ To treat early rectal cancers, surgeons prefer organ-preserving minimally invasive and curative TEMS, which aims to reduce the impact of treatment on quality of life by preserving normal physiological rectal and genitourinary functions, as well as reducing the morbidities associated with major resectional surgery.⁸ In the UK, TEMS has been employed to treat early rectal cancers (T1 tumours) involving less than 30% of luminal circumference with no evidence of lymphovascular or perineural invasion and absence of lymph node metastasis.^{9,10} TAMIS was introduced in 2009 and has been shown to have similar outcomes to TEMS.^{11,12}

Closure of the defect following excision of rectal neoplasm by TEMS or TAMIS above the peritoneal reflection is a standard of care. However, where excision is carried out below the reflection, there is lack of consensus among colorectal surgeons. We aimed to extract evidence by carrying out a meta-analysis to estimate and compare

the peri- and postoperative outcomes following rectal neoplasm excision after TEMS and TAMIS with and without suturing of the rectal defect.

Methods

Search strategy

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed to carry out this meta-analysis.¹⁵ We carried out an extensive computerised literature search of Ovid MEDLINE and EMBASE to evaluate whether suturing of the rectal defect would make a difference in postoperative outcomes following TEMS/TAMIS carried for excision of the rectal neoplastic lesion. We restricted our search strategy to humans and English language only. We used the PICO model to define terms used in our searches. Suitable keywords were selected for population, intervention, comparison and outcomes (PICO; Table 1).

Keywords searched for individually and in combination were transanal endoscopic microsurgery, transanal endoscopic microsurgery, transanal minimally invasive surgery, TEMS, TAMIS, defect (sutured or open). Results from the two databases were combined. Duplicate records were deleted. Relevant systematic reviews or meta-analyses were also scrutinised for additional studies. Screening of the reference list was carried out to retrieve further relevant studies.

All comparative studies, including randomised controlled trials and comparative cohort studies, who reported postoperative outcomes on the rectal defect either being sutured or left open following TEMS/TAMIS carried out for rectal neoplasm were included. Additional criteria were adult patients, studies with at least one of the outcomes being reported, minimum of 30 days follow-up. Studies with transanal local excisions and robotic excisions, non-English papers and abstracts from conferences were excluded.

Data extraction and review

An independent screening of titles and abstracts was carried out by two investigators (KK, TM). Based on inclusion and exclusion criteria, data were extracted independently by both investigators. Any discordance was resolved by a third investigator (IAH).

The data extracted were general information (year of publication, study period, country of origin, number of cases in each group, bowel preparation, information regarding antibiotics, neoadjuvant therapy and postoperative follow-up); features of the intervention, surgical technique (TEMS/TAMIS); number of cases in the sutured and open groups. Outcomes included postoperative infection, postoperative bleeding (defined as whether patient needed blood transfusion and/or admission), operative time (in minutes) and length of hospital stay (in days).

Risk of bias and quality assessment

The Cochrane RoB2 risk of bias tool was used for assessing risk of bias in randomised controlled trials. This tool has five domains, in which helps in highlighting bias in results. Each domain judges the risk of bias as either 'low risk',

'some concerns' or 'high risk'. Following judgements at domain level, this assessment leads to an overall risk of bias in the included studies as 'low risk', 'some concerns' or 'high risk'.¹⁴

Where studies were non-randomised controlled trials, the Methodological Index for Non-randomized Studies tool was used. This tool is specifically used for the quality assessment of non-randomised controlled trials. It has 8 and 12 parameters for non-comparative and comparative studies, respectively. Each parameter can be scored from 0 to 2, where score 0 means 'not reported', 1 is 'reported but inadequate' and 2 means 'reported and adequate'. For non-comparative and comparative studies, the ideal score being 16 and 24, respectively. High-quality studies have an overall score of 12 or more points.¹⁵

Statistical analysis

The Review Manager software (RevMan, Version 5.3, Cochrane Collaboration, Oxford, UK) was used to conduct the meta-analysis. Data from all the studies were pooled. For continuous data, standard mean difference (SMD) and 95% confidence intervals (CI) were calculated using the inverse variance method. For dichotomous data, the odds ratio (OR) and 95% CI were generated by using Mantel-Haenszel method. Heterogeneity was determined by I² statistics; I² if calculated as 25%, 50% and 75%, were deemed to be low, moderate or high heterogeneity, respectively. Given that in surgical research every centre uses a different protocol, the random effect model was used to pool data. A *p*-value less than 0.05 was considered statistically significant. To visually evaluate pooled results, forest plots were generated for each individual outcome category.

Findings

Population characteristics

Our study selection process is outlined in the PRISMA flowchart (Fig 1). Our search strategy identified 130 studies. Total studies following deduplication were 99. Of these, five were considered eligible based on the title and abstract. One full-text study was excluded due to overlapping of the patient cohort with another study carried out by the same author, who was included in our analysis.¹⁶ A further study was excluded as had few cases of transanal local excisions with TEMS.

Table 1 Population, intervention, comparison and outcome of search strategy for this review

Population	Patients who underwent transanal endoscopic microsurgery or transanal minimally invasive surgery
Intervention	Defect sutured
Comparison	Defect left open
Outcome	Postoperative infection, bleeding, operative time, hospital stay

When screening the full texts, three studies met our inclusion and exclusion criteria. These three studies were then analysed. We included them for our risk of bias and methodological quality assessment. Following that we synthesised our results. These studies were carried out in Canada, Switzerland, Spain, Italy, the UK and the United States. There was one randomised controlled trial,¹⁷ one prospective comparative case series,⁶ and one multi-institutional retrospective matched case series.¹⁸ Table 1 shows the characteristics of the included studies.

Risk of bias and quality assessment

The RoB2 tool was used for the one randomised controlled trial included in our review. The study had 'low risk' of bias in all domains except the domain regarding deviation from the intended intervention, where the outcome was 'some concerns'. However, the overall risk of bias was 'low' for this study (Table 3).

To assess the quality of non-randomised trials, MINORS criteria were used. Given that both studies scored more

than 12, they were classed as high-quality studies. One study scored 18, while the other scored 22 (Table 4).

Main outcomes

We extracted data for 555 patients who underwent excision of rectal neoplasm by TEMS or TAMIS. Of these, 283 had the rectal defect sutured, while 272 had the rectal defect left open.

Our meta-analysis showed that there was a significant difference in postoperative bleeding between the two groups. The incidence of postoperative bleeding was 2.12% in sutured group (6/283) and 6.99% in the open group (19/272; OR 0.26; 95% CI 0.10–0.68; $p = 0.006$). Heterogeneity was low (I², 0%; Fig 2).

The synthesised results demonstrated an overall incidence of postoperative infection of 3.53% (10/283) in the sutured group and 1.84% (5/272) in the open group. There was no statistical difference for postoperative infection between the groups (OR 1.81; 95% CI 0.63–5.20; $p = 0.27$). The collected data had low heterogeneity (I², 0%; Fig 3).

Figure 1 PRISMA flowchart showing selection process

There was no statistical difference in the operative time (in minutes) between both groups ($p = 0.15$; SMD 0.35; 95% CI -0.12 to -0.82). However, on closer examination of the data and the forest plot (Fig 4), there is a noticeable trend towards shorter operative time in cases where the defect was left open. There was high heterogeneity of the collected data (I^2 , 76%).

On combining data of the included studies for hospital stay, there was no statistical difference between the groups ($p = 0.67$; SMD -0.06 , 95% CI -0.36 to -0.23). Heterogeneity was moderate for these data (I^2 , 45%) (Fig 5).

Discussion

The present meta-analysis synthesised results from comparative studies of patients who underwent TEMS/TAMIS for rectal neoplasia where the rectal defect was either sutured or left open. This study demonstrated a significant postoperative bleeding when the defect is left open. However, there was no statistical difference in postoperative infection, operative time and length of hospital stay between the two groups.

TEMS and TAMIS are minimally invasive and safe techniques with a mortality rate of 0–0.6%.¹⁹ The reported overall morbidity in the literature is 0–21%.^{20–22} This meta-analysis demonstrated no statistically significant difference in postoperative infection between the sutured and open groups (3.53% and 1.84%, $p = 0.27$). Infection rates correspond to reported rates in the literature between 1% and 10%.^{18,23} However, there were variations in patient selection and protocols across the included studies. Bowel preparation and prophylactic antibiotics were given in the randomised controlled trial.¹⁷ In the study by Lee *et al*,¹⁸ prophylactic antibiotics were given to all patients, but bowel preparation consisted of phosphate enemas for TEMS and full mechanical bowel preparation for TAMIS. Hahnloser *et al* included 32% of patients given an enema, and postoperative antibiotics were continued for seven days.⁶

We estimated an incidence of postoperative bleeding of 2.12% in the sutured group (6/285) and 6.99% (19/272) in the open group. These findings are statistically significant between the two groups ($p = 0.006$). All studies included cases with full thickness excision, but the study by Lee *et al* had also included a cohort of patients who underwent partial-thickness excision of the rectal wall containing the lesion. Our observations are contrary to previous meta-analysis, whereby there was no difference in the incidence of postoperative bleeding between open and closed groups.²¹ However, the meta-analysis conducted by Menaham *et al* included a mixture of interventions including TEMS/TAMIS and conventional transanal excisions, indicating that this study may not have represented a true comparison of minimally invasive transanal platforms.

Postoperative complications after TEMS may be adversely affected by neoadjuvant chemoradiotherapy.^{24,25} In our meta-analysis, one of the three studies stated that chemoradiotherapy was not used. The remaining two

Study (year of publication)	Study period (years)	Country	Design	Preoperative chemotherapy	Sample Size	Excision	Antibiotics	Bowel preparation	TEMS or TAMIS	Defect		Follow-up (days)
										Sutured	Open	
Brown (2019) ¹⁷	2012–2013	Canada	Randomised controlled trial	nil	50	FT	preop but not postop	mech	TEMS	28	22	30
Lee (2018) ²⁷	1997–2016	UK/USA	Retrospective matched case series	not mentioned	430	FT 220; PT 210	Yes	enema (TEMS); prep (TAMIS)	TEMS and TAMIS	215	215	30
Hahnloser (2015) ⁶	2009–2012	Switzerland, Spain, Italy	Prospective comparative case series	3	75	FT	preop; postop 7 days	mech 64%; enema 32%; no prep 4%	TAMIS	40	35	Median 388 (range 67–884)
FT, full thickness; mech, full mechanical bowel preparation; postop, postoperatively; preop, preoperatively; prep, bowel preparation; PT, partial thickness; TAMIS, transanal minimally invasive surgery; TEMS, transanal endoscopic microsurgery												

studies either did not mention chemoradiotherapy or did not describe it in detail. In the study by Hahnloser *et al*, the use of chemoradiotherapy was mentioned in at least three cases.

In our meta-analysis, we noticed a trend towards longer operating time in the sutured group, but this was not statistically significant. This represents the wide acceptance among colorectal surgeons that closure of a rectal defect in a confined place is accepted as a technically challenging skill with a steep learning curve.^{26,27} The decision to leave the rectal defect open may seem appealing, especially at the end of a long and difficult procedure. It has been reported that closure of the defect may not be possible in up to 30% of cases due to technical difficulties.⁶ The potential advantage of routine defect closure would be to maintain and develop the intraluminal suturing skills that would be needed in where an accidental peritoneal entry is made,

which has been reported in up to 6% of cases.^{28,29} Furthermore, repeat TEMS/TAMIS may be needed for recurrent rectal lesions. Ramkumar *et al*,⁵⁰ in their series of repeat TEMS procedures, discovered that where the defect was left open during the primary procedure, closure of the rectal defect proved almost impossible due to a lack of pliability and a fixed rectal wall.⁵⁰

The strength of this study is that it is the first meta-analysis on the management of rectal defects following surgical excisions of rectal neoplasms carried out by TEMS and TAMIS only. In addition, we conducted a comprehensive search and PICO strategy. We carried out an independent screening and studies quality assessments with consensus among fellow authors. On reviewing the studies, we had the data sourced from various geographical regions.

Our meta-analysis has some limitations. Our synthesised results were calculated from a relatively small dataset,

Author	1	2	3	4	5	6
Brown (2019) ¹⁷
1 Randomisation process. 2 Deviations from intended interventions. 3 Missing outcome data. 4 Measurement of the outcome. 5 Selection of the reported result. 6 Overall risk of bias.
Low risk; some concerns; high risk.						

Table 3 Risk of bias (RoB2)

Table 4 Methodological Index for Non-randomised Studies score													
Author	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII	Score
Hahnloser (2015) ⁶	2	2	2	2	2	2	2	0	2	2	2	2	22
Lee (2018) ²⁷	2	0	1	2	2	2	1	0	2	2	2	2	18

I: Clearly stated aim.
 II: Consecutive patients included.
 III: Prospective data collection.
 IV: Appropriate endpoints to the aim of the study.
 V: Unbiased end point assessment.
 VI: Appropriate follow-up period.
 VII: Less than 5% loss to follow-up.
 VIII: Prospective sample size calculation.
 IX: An adequate control group.
 X: Contemporary groups.
 XI: Equivalence of groups.
 XII: Appropriate statistical analyses.

originating from one randomised controlled trial and two comparative case series. The results across all outcomes were primarily driven by Lee *et al* ($n = 430$; weight of study, minimum 42% and maximum 54%), a matched comparative case series. In addition, the sample size of the included randomised controlled trial was small ($n = 50$) and calculated (power 0.80, $\alpha = 0.05$), based on anticipated visual analogue score, as postoperative pain was primary outcome measure, while postoperative complications were secondary.

Given that all the data were sourced from these multicentre studies, there could be differences in the surgical skills and experience of performing surgeons,

including their suturing techniques, antibiotic regimens, preoperative protocols and postoperative follow-up care. Furthermore, pooling of data, whereby some subjects might have received neoadjuvant chemoradiotherapy may create a potential selection bias. A propensity score matching was used by Lee *et al* to create balanced comparative groups of open and closed defects for both partial- and full-thickness excision. Pooling the data of patients who underwent full- and partial-thickness excisions of rectal neoplastic lesions creates another potential limitation of this review. Limiting the search strategy to the English language was a language bias. Finally, publication bias might be a possibility, as statistically significant results

Figure 2 Forest plot comparing postoperative bleeding between sutured and open rectal defects following transanal minimally invasive surgery or transanal endoscopic microsurgery

Figure 3 Forest plot comparing postoperative infections between sutured and open rectal defects following transanal minimally invasive surgery or transanal endoscopic microsurgery

Figure 4 Forest plot comparing operative time (in minutes) between sutured and open rectal defects following transanal minimally invasive surgery or transanal endoscopic microsurgery

Figure 5 Forest plot comparing hospital stay (in days) between sutured and open rectal defects following transanal minimally invasive surgery or transanal endoscopic microsurgery

seems like an attractive research to be published. Given the diversity of such studies, interpretation of results of such review should be read with caution.

Conclusion

We concluded from the synthesised results that following TEMS/TAMIS carried out for rectal neoplasm, suturing the rectal defect can be time consuming but it decreases the risk of postoperative bleeding. Furthermore, there are no significant differences in postoperative infection and length of hospital stay whether the rectal defect is sutured or left open.

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