REVIEW

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Comparison between endoscopic resection and transanal surgery for treatment of rectal tumors: a systematic review and meta-analysis

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Background/Aims: Both endoscopic resection (ER) and transanal surgery (TAS) are minimally invasive treatment options that allow organ preservation in early rectal tumors. We conducted a meta-analysis to compare treatment outcomes between the 2 treatments. **Methods:** We searched all relevant studies published until January 2024 that examined the comparative outcomes between ER and TAS for rectal tumors, including adenoma, adenocarcinoma, and neuroendocrine tumor (NET). TAS included transanal excision, transanal endoscopic microsurgery, and transanal minimally invasive surgery. **Results:** Seventeen studies with a total of 1,569 patients were included in this meta-analysis. For adenoma/adenocarcinoma, the R0 resection rate did not differ between ER and TAS (risk ratio [RR], 0.99; 95% confidence interval [CI], 0.94–1.03). For NET, the R0 resection rate was lower in the ER group than in the TAS group (RR, 0.76; 95% CI, 0.68–0.84) and the procedure time for ER was shorter than that for TAS. For both adenoma/adenocarcinoma and NET, ER and TAS did not differ in terms of complication rates, additional surgery, and recurrence. **Conclusions:** ER and TAS showed similar treatment outcomes for adenoma/adenocarcinoma. Considering that TAS typically incurs higher costs than ER, ER may be favored in the treatment of rectal adenoma/adenocarcinoma. For rectal NET, TAS showed a superior R0 resection rate than ER. However, given that TAS requires a long procedure time, expensive equipment, and complex manipulations, TAS may be considered selectively for large NETs with suspected deep tumorous infiltration. **(Intest Res, Published online)**

Key Words: Rectal tumor; Rectal neuroendocrine tumor; Endoscopic resection; Transanal surgery

INTRODUCTION

Despite detailed guidelines for screening and surveillance, colorectal cancer (CRC) still has a high incidence and remains the leading cause of cancer-related death.[1-5] According to 2020 global cancer statistics, CRC is the third most frequently diagnosed cancer and the second most common cause of cancer death.[1,6] In particular, the proportion of rectal cancer in the incidence and mortality rates of CRC is high at 38.9% and 37.0%, respectively.[1] Early rectal cancer or rectal premalignant lesions can be removed using minimally invasive techniques, such as transanal surgery (TAS), instead of performing major surgeries, such as low anterior resection or abdominoperineal resection, which can cause significant morbidity and greatly impact the quality of life.

TAS includes transanal excision (TAE), transanal endoscopic microsurgery (TEM), and transanal minimally invasive sur-

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gery (TAMIS). TAE is a method initially developed to remove lesions by direct visualization using standard retractors.[7] Therefore, this method does not allow sufficient visualization of the mid and upper rectum, allowing resection of only distal rectal lesions. TEM, introduced in the 1980s, uses special instruments, including proctoscopes, laparoscopic camera, and laparoscopic instruments, to allow the operator to reach lesions in the mid and upper rectum.[7] However, this method presents challenges when the lesion is located where it cannot be properly removed in standard patient positioning. TAMIS, developed in 2009 as an alternative technique, uses a single multichannel port inserted into the anus, enabling more flexibility in patient positioning.[8]

Another minimally invasive technique to remove early rectal cancer or rectal premalignant lesions is endoscopic resection (ER), such as endoscopic submucosal dissection (ESD) and endoscopic mucosal resection (EMR).[9] ER is less invasive and has lower morbidity; however, sometimes resection margins, especially deep margins, cannot be accurately determined, requiring additional surgical treatment. In these cases, TAS, which allows for full-thickness resection of the rectal wall can be a more curative method. However, TEM and TAMIS require special equipment and general anesthesia or epidural anesthesia, and can place economic and psychological burdens on patients.

Clinicians often encounter lesions that are difficult to determine which method is more appropriate, ER or TAS. To address this concern, several studies have compared ER and TAS, and recently, a meta-analysis was performed on this topic.[10] A meta-analysis of 11 studies searched until January 2020 demonstrated that TAS has a higher R0 resection rate for early rectal neoplasms than ER.[10] However, this meta-analysis presented the results of combining these lesions without distinguishing between adenoma/adenocarcinoma and neuroendocrine tumor (NET). Most rectal NETs are < 1 cm in size and appear as small yellowish submucosal lesions with intact overlying mucosa.[11] As with rectal adenoma/adenocarcinoma, treatment options for rectal NET include ER and TAS; however, since the 2 tumors have different characteristics, analyzing them separately is reasonable. Moreover, several relevant studies have been published and accumulated since then. Therefore, complementing and updating the information on this topic is necessary.

In this study, we conducted a systematic review and meta-analysis to analyze the comparative outcomes between ER and TAS for rectal tumors, including adenoma/adenocarcinoma and NET. In contrast to previous meta-analysis, our study compared adenoma/adenocarcinoma and NET separately.

METHODS

1. Search Strategy

We searched for all relevant studies published between January 1990 and January 2024 that compared clinical outcomes between ER and TAS in patients with rectal adenoma, adenocarcinoma, or NET through MEDLINE, EMBASE, and Cochrane Library databases. The following search string was used: ([endoscopic submucosal dissection] OR [endoscopic submucosal dissections] OR [ESD] OR [endoscopic mucosal resection] OR [endoscopic mucosal resections] OR [EMR] OR [endoscopic resection] OR [endoscopic resections]) AND ([transanal surgery] OR [transanal surgeries] OR [TAS] OR [transanal excision] OR [transanal excisions] OR [TAE] OR [local excision] OR [local excisions] OR [transanal resection] OR [transanal resections] OR [transanal endoscopic microsurgery] OR [transanal endoscopic microsurgeries] OR [TEM] OR [transanal endoscopic surgery] OR [transanal endoscopic surgeries] OR [transanal minimally invasive surgery] OR [transanal minimally invasive surgeries] OR [TAMIS]) AND ([rectal] OR [rectum] OR [colorectal] OR [colorectum]). The detailed search strategies used for each database are shown in Appendix 1.

2. Inclusion/Exclusion Criteria

The inclusion criteria were as follows: (1) patients—patients who underwent ER or TAS for rectal adenoma, adenocarcinoma, or NET; (2) intervention—ER, including EMR and ESD; (3) comparator—TAS, including TAE, TEM, and TAMIS; and (4) outcome—procedure time, *en bloc* resection, R0 resection, complications (including bleeding and perforation or postoperative leakage), additional surgery, and recurrence. Nonoriginal studies, nonhuman studies, abstract-only publications, and non-English publications were excluded. In addition, studies in which more than 25% of the study participants had rectal tumors other than adenoma, adenocarcinoma, or NET were excluded from the analysis.

3. Study Selection

We conducted a comprehensive review of the identified studies through our keyword search methodology. Initially, we excluded duplicates obtained from various search engines. Subsequently, we applied our predetermined inclusion and exclu-

sion criteria to eliminate irrelevant studies based on a thorough assessment of their titles and abstracts. Following this, we meticulously examined the full texts of the remaining studies. Eligibility evaluation was independently carried out by 2 investigators (C.H.P. and Y.S.J.), and any disagreements were resolved through discussion and consensus. In cases where consensus could not be reached, a third investigator (B.W.J.) made the final determination. Furthermore, we conducted a manual search of potentially relevant literature by scrutinizing the references of the included studies.

4. Quality Assessment

Two investigators (C.H.P. and Y.S.J.) independently performed a formal quality assessment of observational studies using the Newcastle–Ottawa Scale.[12] The scoring encompassed 3 categories: selection (4 points), comparability of study groups (2 points), and ascertainment of exposure or outcome (3 points). Studies with a cumulative score of ≥7 points were classified as high-quality studies. We used the Cochrane risk of bias assessment tool for randomized controlled trials (RCTs), to evaluate the risk of bias in individual studies.[13]

5. Data Extraction

Data extraction was executed using a predeveloped form. Two investigators (C.H.P. and Y.S.J.) independently extracted information, including the first author, year of publication, study design, country, study period, publication language, tumor size and location, and clinical outcomes (including procedure time, *en bloc* resection, R0 resection, complications, additional surgery, and recurrence).

6. Study Endpoints

The primary endpoint of our meta-analysis was R0 resection. R0 resection was defined as complete resection with a pathologically negative margin. The secondary endpoint included procedure time, *en bloc* resection, complications (bleeding and perforation or postoperative leakage), additional surgery, and recurrence. Baseline lesion characteristics, including tumor size and location (distance from anal verge), were compared between ER and TAS. Additional surgery was defined as surgery due to noncurative resection; however, surgery due to recurrence was not considered.

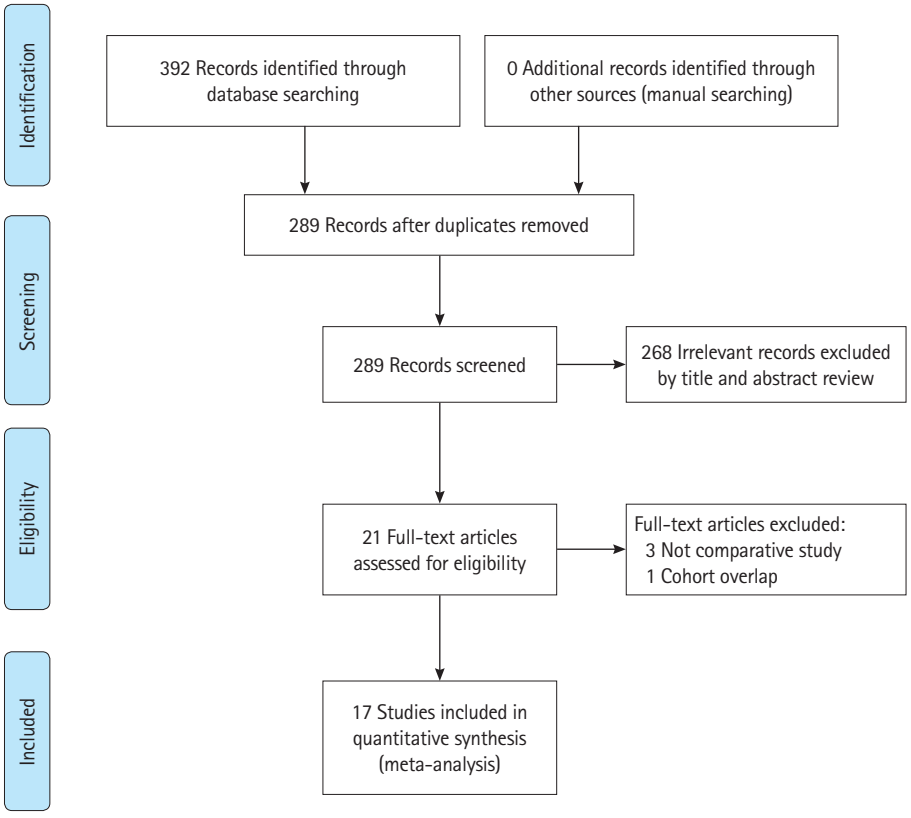

Fig. 1. Study flow diagram.

Table 1. Baseline Characteristics of Included Studies

Publication year	First author	Country	Study period	Study design	No. of patients	Age (yr), mean±SD	Male sex (%)	Histology (%)	Tumor size (mm), mean±SD	Distance from anal verge (cm), mean±SD	Follow-up period (mo), mean±SD	NOS (selection/ comparability/ outcome)
2009	Lee[18]	South Korea	1999–2007	Retrospective observational study	ER: 16 TAE: 16	ER: 59.4±8.9 TAE: 57.0±12.7	ER: 46.7 TAE: 50.0	Adenocarcinoma 100	ER: 18±10 TAE: 20±10	ER: 9.6±6.5 TAE: 5.2±2.2	ER: median 12.0 TAE: median 21.5	4/2/3
2011	Hon[19]	China	2000–2010	Retrospective observational study	ESD: 14 TAE: 30	ESD: 65.3±14.7 TAE: 66.0±14.4	ESD: 35.7 TAE: 56.7	ESD: adenoma 85.7, hyperplastic polyp 7.1, NET 7.1 TAE: adenoma 73.3, adenocarcinoma 6.7, hyperplastic polyp 3.3, NET 16.7	ESD: 29±10 TAE: 26±12	ESD: 8.6±3.6 TAE: 5.0±2.9	NA	4/2/3
2011	Kiriyama[20]	Japan	1998–2006	Retrospective observational study	ESD: 52 TAE: 33	ESD: 61±11 TAE: 64±13	NAc	ESD: adenoma 17.3, adenocarcinoma 82.7 TAE: adenoma 6.1, adenocarcinoma 93.9	ESD: 40±21 TAE: 39±24	NA	NA	4/2/3
2012	Barendse[21]	Netherlands	2004–2008	Retrospective observational study	EMR: 73 TEM: 219	EMR: 67±11.0 TEM: 66±11.3	EMR: 47.9 TEM: 48.9	EMR: adenoma 100 TEM: adenoma 98.6, no abnormality 0.9, GIST 0.5	EMR: median 30 (range, 20–80) TEM: median 40 (range, 20–160)	EMR: 8.2±5.0 TEM: 6.5±4.1	EMR: median 12.2 TEM: median 12.9	4/2/3
2012	Park[22]	South Korea	2007–2011	Retrospective observational study	ESD: 30 TEM: 33	ESD: 58.6±8.3 TEM: 59.5±11.0	ESD: 46.7 TEM: 51.5	ESD: HGD 60.0, SM cancer 40.0 TEM: HGD 72.8, SM cancer 27.3	ESD: 25.4±11.0 TEM: 27.8±15.0	ESD: 10.5±4.6 TEM: 6.0±3.6	ESD: 20.1±14.1 TEM: 27.2±11.6	4/2/3
2013	Son[23]	South Korea	2001–2010	Retrospective observational study	Strip biopsy: 28 EMR: 27 EMR-C: 53 ESD: 47 TEM or TAE:11	52.7±10.2	59.6	NET 100	5.5±2.4	6.8 (range, 2–15)	Median 31 (range, 1–105)	4/1/3
2014	Jeon[24]	South Korea	2007–2011	Retrospective observational study	EMR: 29 ESD: 23 TEM: 14	EMR: 47.6±9.6 ESD: 51.0±12.3 TEM: 48.5±14.4	EMR: 79.3 ESD: 65.2 TEM: 64.3	NET 100	EMR: 6.1±2.3 ESD: 6.7±1.8 TEM: 8.2±3.0	EMR: 6.3±2.5 ESD: 6.6±2.8 TEM: 6.7±2.8	EMR: 20.4±14.5 ESD: 29.1±12.3 TEM: 13.2±6.1	4/1/3
2016	Yan[25]	China	2007–2012	Retrospective observational study	ESD: 31 TAE: 23	ESD: 52.2±10.2 TAE: 47.9±11.7	ESD: 71.0 TAE: 60.9	NET 100	ESD: 8±2 TAE: 11±5	ESD: 5.9±2.3 TAE: 5.4±1.5	ESD: median 16.4 (range 8–31), TAE: median 28.4 (range, 8–68)	4/1/3
2017	Mao[26]	China	2012–2016	Retrospective observational study	ESD: 31 TAMIS: 26	ESD: 52.1 (range, 32–74) TAMIS: 54.8 (range, 34–75)	ESD: 54.8 TAMIS: 57.7	ESD: adenoma 93.5, adenocarcinoma 6.5 TAMIS: adenoma 96.2, adenocarcinoma 3.8	ESD: 35 (range, 20–40) TAMIS: 32 (range, 20–40)	NA	ESD: range, 24–36 TAMIS: range, 10–32	4/2/3
2018	Barendse[27]	Netherlands and Belgium	2009–2013	RCT	EMR: 88 TEM: 89	EMR: 67.4±11.3 TEM: 67.5±10.0	EMR: 54.5 TEM: 52.8	EMR: adenoma 83.0, adenocarcinoma 17.0 TEM: adenoma 86.5, adenocarcinoma 13.5	EMR: 48±15 TEM: 45±17	EMR: 4.9±3.8 TEM: 5.5±4.4	24 mo	[a]

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Table 1. Continued

Publication year	First author	Country	Study period	Study design	No. of patients	Age (yr), mean ± SD	Male sex (%)	Histology (%)	Tumor size (mm), mean ± SD	Distance from anal verge (cm), mean ± SD	Follow-up period (mo), mean ± SD	NOS (selection/ comparability/ outcome)
2018	Jung[28]	South Korea	2013–2015	Retrospective observational study	Epithelial tumor -ESD: 40 -TEM: 16 Subepithelial tumor -ESD: 8 -TEM: 7	Epithelial tumor -ESD: 67.4 ± 9.3 -TEM: 68.4 ± 8.9 Subepithelial tumor -ESD: 53.1 ± 16.8 -TEM: 52.2 ± 8.2	Epithelial tumor -ESD: 55.0 -TEM: 56.3 Subepithelial tumor -ESD:62.5 -TEM: 100.0	Epithelial tumor -ESD: adenoma 60.0, adenocarcinoma 40.0 -TEM: adenoma 31.3, adenocarcinoma 68.8 Subepithelial tumor -ESD: NET 100 -TEM: NET 42.9, GIST 28.6, leiomyoma 14.3, mucinous cystadenoma: 14.3	Epithelial tumor -ESD:33.0 ± 13.0 -TEM: 27.0 ± 15.0 Subepithelial tumor -ESD: 13.7 ± 5.1 -TEM: 18.5 ± 17.6	Epithelial tumor -ESD: mid lower rectum 92.5%, upper rectum 7.5% -TEM: mid lower rectum 81.3%, upper rectum 18.8% Subepithelial tumor -ESD: mid lower rectum 100% -TEM: mid lower rectum 85.7%, upper rectum 14.3%	NA	4/2/3
2020	Bisogni[29]	Italy	2014–2019	Retrospective observational study	ESD: 13 TEM: 36	ESD: 74.9 ± 7.8 TEM: 69.2 ± 12.7	ESD: 61.5 TEM: 52.8	ESD: adenoma 92.3, adenocarcinoma 7.7 TEM: adenoma 52.8, adenocarcinoma 27.8, squamous cell carcinoma 5.6, phlogistic tissue 2.8, sclerotic tissue 11.1	ESD: 49.1 ± 17.5 TEM: 36.3 ± 23.8	ESD: lower rectum 30.8%, mid-rectum 23.1%, upper rectum 46.2% TEM: lower rectum 72.2%, mid-rectum 22.2%, upper rectum 5.6%	NA	4/1/3
2020	Shen[30]	China	2014–2019	Retrospective observational study	EMR: 53 TAMIS: 44	EMR: 60.7 ± 10.4 TAMIS: 64.3 ± 10.9	EMR: 56.6 TAMIS: 47.7	EMR: adenoma or polyp 86.8, NET 13.2 TAMIS: adenoma or polyp 77.3, NET 22.7	EMR: 11.4 ± 5.3 TAMIS: 14.7 ± 9.6	EMR: 8.8 ± 3.0 TAMIS: 7.4 ± 1.9	NA	4/1/3
2021	Kimura[31]	Brazil	2008–2017	Retrospective observational study	ESD: 71 TEM: 27	ESD: 65.5 ± 10.0 TEM: 64.9 ± 11.8	ESD: 49.3 TEM: 40.7	ESD: adenoma 28.2, intramucosal adenocarcinoma 64.8, SM adenocarcinoma 7.0 TEM: adenoma 33.3, Intramucosal adenocarcinoma 44.4, SM adenocarcinoma 22.2	ESD: 68.5 ± 39.3 TEM: 44.5 ± 30.8	ESD: 5.4 ± 4.0 TEM: 3.3 ± 2.3	ESD: 31.0 ± 16.0 TEM: 53.9 ± 24.8	4/1/3
2021	Park[32]	South Korea	2008–2017	Retrospective observational study	ESD: 52 TEM: 52	ESD: 49.5 ± 9.6 TEM: 51.0 ± 11.7	ESD: 59.6 TEM: 67.3	NET 100	ESD: median 6 (range, 2–13) TEM: median 6.5 (range, 2–25)	ESD: median 6 (range, 3–10) TEM: median 6 (range, 3–13)	Median 48 (range, 0–194)	4/2/3
2023	Jin[33]	China	2010–2021	Retrospective observational study	ESD: 55 TEM: 59	ESD: 52.9 ± 11.7 TEM: 51.1 ± 12.1	ESD: 36.4 TEM: 30.5	NET 100	ESD: median 6 (range, 3–20) TEM: median 6 (range, 2–20)	ESD: median 8 (range, 3–15) TEM: median 7 (range, 3–10)	ESD: median 19 (range, 2–75) TEM: median 28 (range, 2-117)	4/2/3

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Table 1. Continued

Publication year	First author	Country	Study period	Study design	No. of patients	Age (yr), mean ± SD	Male sex (%)	Histology (%)	Tumor size (mm), mean ± SD	Distance from anal verge (cm), mean ± SD	Follow-up period (mo), mean ± SD	NOS (selection/ comparability/ outcome)
2023	Kim[34]	USA, Greece, Switzerland, and Mexico	2016–2019	Retrospective observational study	ESD: 101 TEM: 103	ESD: 63 ± 12 TEM: 60 ± 11	ESD: 49.5 TEM: 43.7	ESD: adenoma 74.0, adenocarcinoma 19.0, subepithelial tumor 7.0 TEM: adenoma 86.4, adenocarcinoma 13.6	ESD: median 40 (SD, 23.9) TEM: median 56 (SD, 27.9)	ESD: 6.6 ± 3.3 TEM: 4.1 ± 0.9	<6	4/1/3

[a]Barendse et al.'s study in 2018 was assessed via the risk of bias assessment tool instead of NOS scale since it is an RCT. The study has low risk of bias for all domains, including selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias.[27]

SD, standard deviation; NOS, Newcastle–Ottawa Scale; ER, endoscopic resection; TAE, transanal excision; NET, neuroendocrine tumor; NA, not available; EMR, endoscopic mucosal resection; TEM, transanal endoscopic microsurgery; GIST, gastrointestinal stromal tumor; ESD, endoscopic submucosal dissection; HGD, high-grade dysplasia; SM, submucosal; EMR-C, endoscopic mucosal resection with cap; TAMIS, transanal minimally invasive surgery; RCT, randomized controlled trial.

7. Statistical Analyses

We conducted meta-analyses to calculate pooled odds ratios or mean differences (MDs) with 95% confidence intervals (CIs) using a random-effects model. Meta-analyses were performed according to the predominant histology (>75%) of rectal tumors in each individual study (adenoma/adenocarcinoma vs. NET). Individual studies that included rectal tumors with various histological types but with no predominant histology were excluded from the meta-analyses. The primary comparison groups were ER and TAS. However, short-term outcomes, including procedure time, *en bloc* resection, and R0 resection, were further compared between ESD and TAS as sensitivity analyses.

Heterogeneity was assessed through Cochran's Q test, with *P*-values <0.1 indicating significant heterogeneity and I^2 statistics, with values >50% suggesting significant heterogeneity.[14] We qualitatively examined funnel plots to assess any publication bias. Additionally, we conducted a quantitative assessment of publication bias using Egger's test, considering *P*-values < 0.1 as statistically significant.[15] Based on the recommendations of the Cochrane group, the funnel plot asymmetry test was not conducted when <10 studies were included.[16] All *P*-values were two-tailed, and significance was set at $P<0.05$ for all tests, except heterogeneity and publication bias tests. The analysis and reporting adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[17] All statistical analyses were conducted using Review Manager 5.3 (version 5.3.5; Cochrane Collaboration, Copenhagen, Denmark).

RESULTS

1. Study Selection and Characteristics

Seventeen studies, involving a total of 1,569 participants, met the inclusion criteria for this meta-analysis (Fig. 1). Table 1 provides a summary of the baseline characteristics of these included studies.[18-34] Their publication dates span between 2009 and 2023, with enrollment periods ranging from 1998 to 2021.[18-34] Among the 17 studies, 1 was a RCT,[27] while the remaining 16 were retrospective observational studies.[18-26,28-34] Eleven studies predominantly included patients with adenoma/adenocarcinoma,[18-22,26,27,29-31,34] whereas 5 studies exclusively enrolled patients with NET.[23-25,32,33] The remaining 1 study reported results for both epithelial tumors (adenoma/adenocarcinoma) and subepithelial tumors.[28] However, the subepithelial tumor groups exhibited heterogeneity due to the inclusion of various

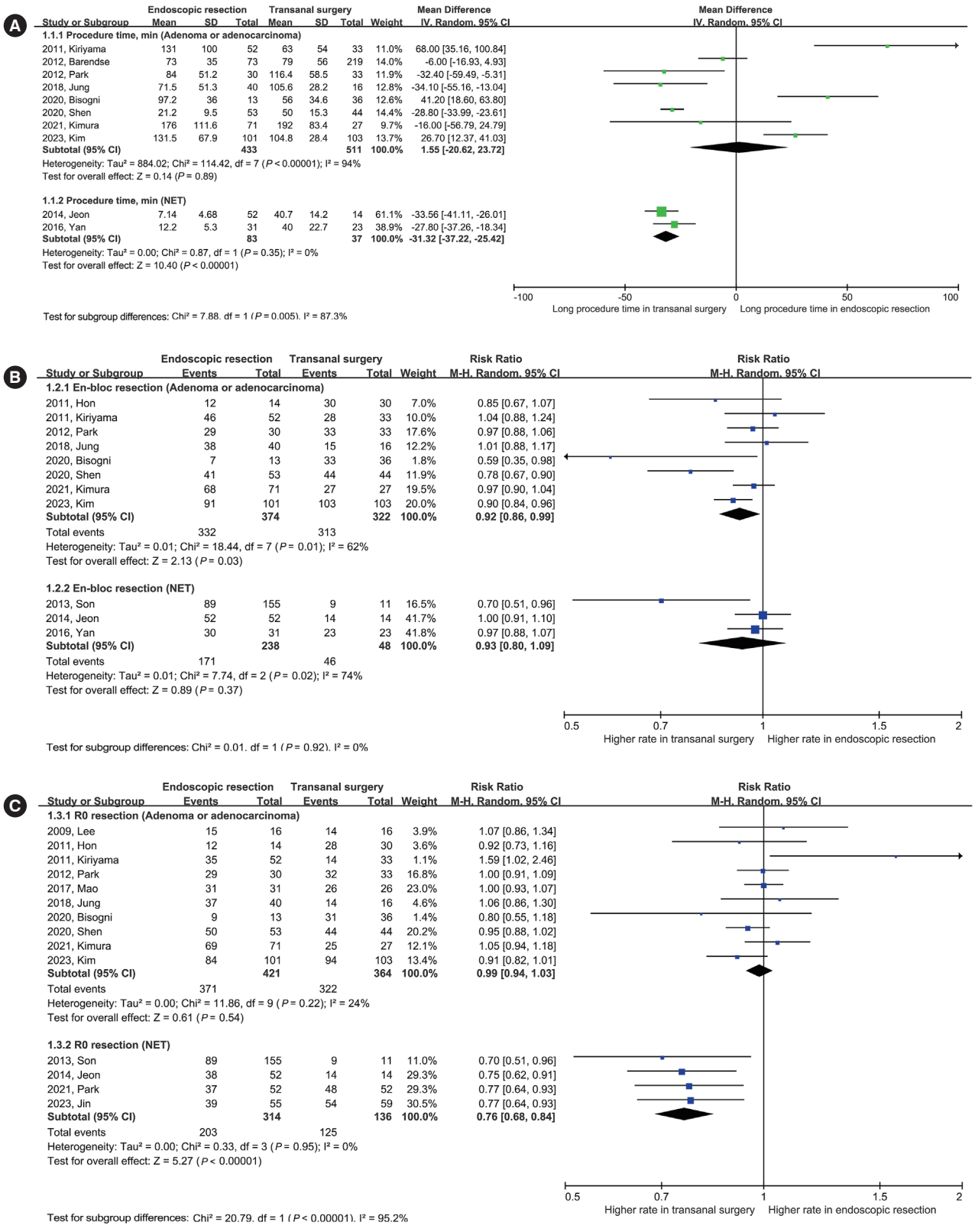

Fig. 2. Forest plots for short-term clinical outcomes between endoscopic resection and transanal surgery. (A) Procedure time, (B) *en bloc* resection, and (C) R0 resection. SD, standard deviation; IV, inverse variance; CI, confidence interval; NET, neuroendocrine tumor; M-H, Mantel–Haenszel.

histology types: 42.9% NET, 28.6% gastrointestinal stromal tumor, 14.3% leiomyoma, and 14.3% mucinous cystadenoma. Consequently, only results related to adenoma/adenocarcinoma were incorporated into the meta-analysis.

The Newcastle–Ottawa Scale quality scores for the included studies are shown in Table 1. All observational studies were rated as high quality. The single RCT was deemed to have a low risk of bias across all domains, encompassing selection, performance, detection, attrition, reporting, and other biases.[27]

2. Baseline Lesion Characteristics between ER and TAS

Supplementary Fig. 1A shows the difference in tumor size between ER and TAS groups. For adenoma/adenocarcinoma, the tumor size did not differ between the 2 groups (ER vs. TAS: MD, 2.55 mm; 95% CI, –1.42 mm to 6.53 mm), with significant heterogeneity (df = 8, $P < 0.01$, $I^2 = 66\%$). However, for NET, the tumor size was smaller in the ER group than in the TAS group (ER vs. TAS: MD, –2.25 mm; 95% CI, –3.56 to –0.93 mm).

The difference in the distance from the anal verge is shown in Supplementary Fig. 1B. In the adenoma/adenocarcinoma subgroup, the lesions were located further away from the anal verge in the ER group, compared to that in the TAS group (ER vs. TAS: MD, 2.14 cm; 95% CI, 1.15 to 3.13 cm). Significant heterogeneity was observed in this comparison (df = 7, $P < 0.01$, $I^2 = 78\%$). In contrast, for NET, the distance from the anal verge did not differ between ER and TAS (ER vs. TAS: MD, 0.28 cm; 95% CI, –0.59 to 1.14 cm), without significant heterogeneity (df = 1, $P = 0.41$, $I^2 = 0\%$).

3. Short-term Clinical Outcomes

Short-term clinical outcomes, including procedure time, *en bloc* resection, and R0 resection, are demonstrated in Fig. 2. For adenoma/adenocarcinoma, the procedure time did not differ between ER and TAS (ER vs. TAS: MD, 1.55 minutes; 95% CI, –20.62 to 23.72 minutes) (Fig. 2A). However, the result should be interpreted cautiously because a significant heterogeneity was observed (df = 7, $P < 0.001$, $I^2 = 94\%$). For NET, on the contrary, the procedure time was shorter in the ER group than in the TAS group, without heterogeneity (ER vs. TAS: MD, –31.32 mm; 95% CI, –37.22 to –25.42 mm; df = 1, $P = 0.35$, $I^2 = 0\%$).

For adenoma/adenocarcinoma, the *en bloc* resection rate was lower in the ER group than in the TAS group (ER vs. TAS: risk ratio [RR], 0.92; 95% CI, 0.86–0.99), with significant heterogeneity (df = 7, $P = 0.01$, $I^2 = 62\%$) (Fig. 2B). For NET, the *en bloc* resection rate tended to be lower in the ER group than in the TAS group (ER vs. TAS: RR, 0.93; 95% CI, 0.80–1.09), with significant heterogeneity (df = 2, $P = 0.02$, $I^2 = 74\%$).

The R0 resection rate, the primary endpoint of the current study, is shown in Fig. 2C. For adenoma/adenocarcinoma, the R0 resection rate of ER was comparable with that of TAS (ER vs. TAS: RR, 0.99; 95% CI, 0.94–1.03), without significant heterogeneity (df = 9, $P = 0.22$, $I^2 = 24\%$). However, for NET, the R0 resection rate was lower in the ER group than in the TAS group (ER vs. TAS: RR, 0.76; 95% CI, 0.68–0.84), without significant heterogeneity (df = 3, $P = 0.95$, $I^2 = 0\%$).

We further performed meta-analyses for short-term clinical outcomes between ESD and TAS (Supplementary Fig. 2). Overall, the results of ESD and TAS were similar to those of ER and TAS. However, no significant differences in *en bloc* resection rate between ER and TAS for adenoma/adenocarcinoma were observed in the comparison of ESD and TAS (ESD vs. TAS: RR, 0.95; 95% CI, 0.89–1.01).

4. Adverse Events

Adverse events, including bleeding and perforation or postoperative leakage, are shown in Fig. 3. For adenoma/adenocarcinoma, the risk of bleeding did not differ between the 2 groups, without significant heterogeneity (ER vs. TAS: RR, 1.17; 95% CI, 0.78–1.77). For NET, the risk of bleeding also did not differ between ER and TAS, without significant heterogeneity (ER vs. TAS: RR, 1.49; 95% CI, 0.27–8.31). The risk of perforation or postoperative leakage did not differ between ER and TAS for adenoma/adenocarcinoma, without significant heterogeneity (ER vs. TAS: RR, 1.05; 95% CI, 0.40–2.77). For NET, only 1 study was included in the meta-analysis for perforation or postoperative leakage, and it did not show a significant difference in the risk (ER vs. TAS: RR, 3.21; 95% CI, 0.13–77.28).

5. Additional Surgery and Recurrence

Additional surgery due to noncurative resection from the initial ER or TAS is shown in Supplementary Fig. 3A. The additional surgery did not differ between ER and TAS for both adenoma/adenocarcinoma and NET (ER vs. TAS: RR, 1.15; 95% CI, 0.39–3.36 for adenoma/adenocarcinoma; RR, 1.46; 95% CI, 0.64–3.34 for NET). Supplementary Fig. 3B shows the difference in recurrence between ER and TAS. For adenoma/adenocarcinoma, the risk of recurrence did not differ between the groups (ER vs. TAS: RR, 1.15; 95% CI, 0.17–7.61). For NET, only 1 study was included in the analysis of the recurrence, and it did not show any difference between ER and TAS (ER vs. TAS: RR, 0.27; 95% CI, 0.03–2.33).

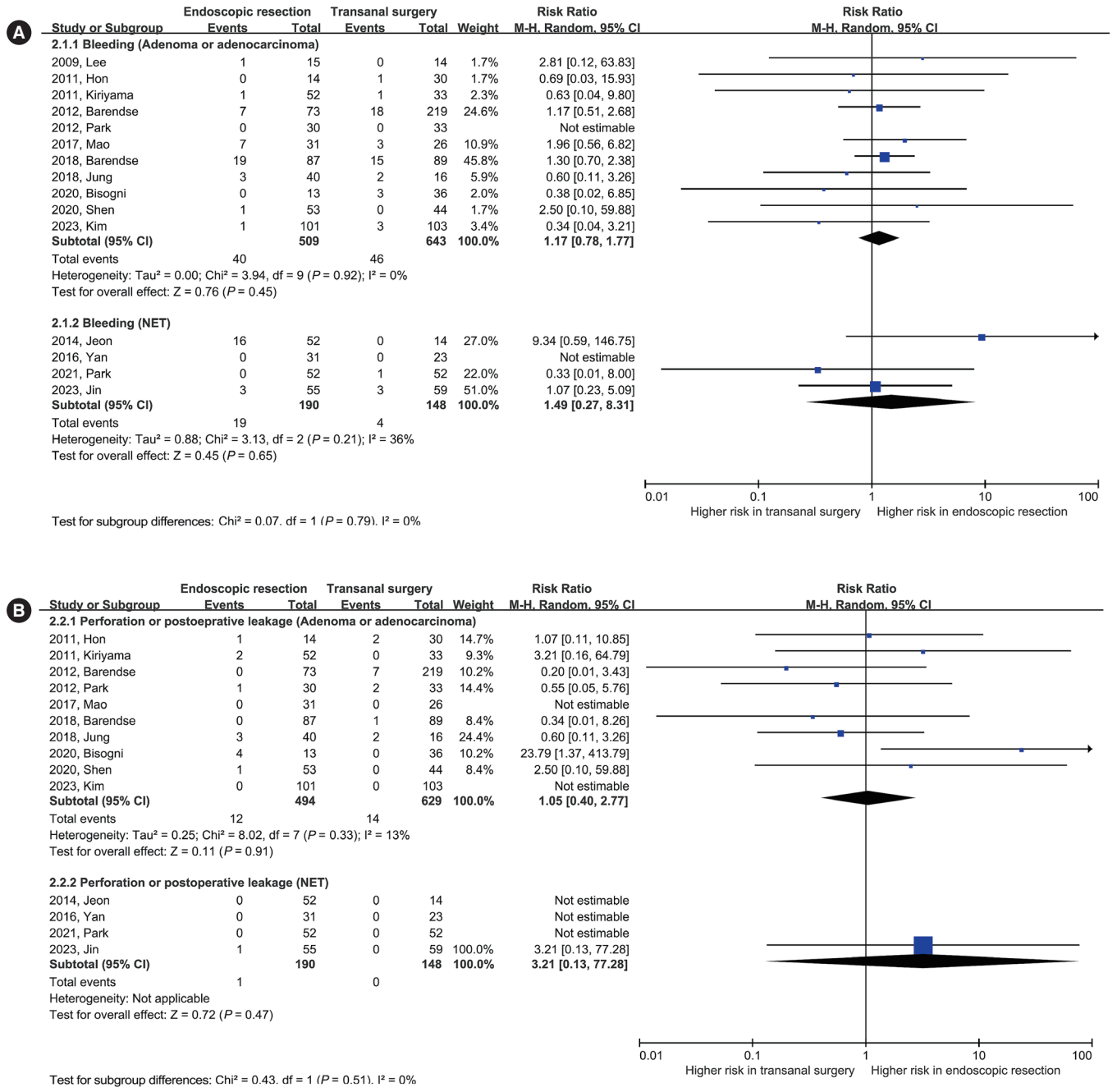

Fig. 3. Forest plots for adverse events between endoscopic resection and transanal surgery. (A) Bleeding and (B) perforation or postoperative leakage. M-H, Mantel–Haenszel; CI, confidence interval; NET, neuroendocrine tumor.

6. Publication Bias

Publication bias was assessed for R0 resection and bleeding in the individual studies on adenoma/adenocarcinoma (Supplementary Fig. 4). Asymmetry of funnel plots was not identified. Additionally, no significant publication bias was identified using Egger test (P=0.449 for R0 resection, P=0.303 for bleeding).

DISCUSSION

In this study, we performed meta-analyses for rectal adenoma/adenocarcinoma and NET. In the meta-analysis for adenoma/adenocarcinoma, the TAS group had a superior *en bloc* resection rate than the ER group; however, no difference was observed between the 2 groups in terms of R0 resection rate

and procedure time. For NET, the R0 resection rate was higher in the TAS group than in the ER group, and the *en bloc* resection rate also tended to be higher in the TAS group than in the ER group. However, TAS showed a longer procedure time than that for ER. For both adenoma/adenocarcinoma and NET, the rates of complications (such as bleeding and perforation), additional surgery, and recurrence, did not differ between TAS and ER.

For adenoma/adenocarcinoma, the *en bloc* resection rate was lower in the ER group than in the TAS group, with 88.8% in the ER group and 97.2% in the TAS group. A reason for this result may be that ER included EMR. This is supported by the finding of no difference in the *en bloc* resection rate when comparing the ESD (90.7%) and TAS (96.8%) groups (Supplementary Fig. 2). However, the R0 resection rates were similar between the ER and TAS groups, with 88.1% and 88.5%, respectively. Clinically, when deciding whether to perform additional surgery for endoscopically resected adenoma/adenocarcinoma lesions, R0 resection, especially the negative vertical resection margin, is more important than *en bloc* resection. Similar R0 resection rates between the 2 groups likely resulted in no differences in additional surgery and recurrence rates.

A previous meta-analysis study comparing ESD and TEM/TAMIS for the treatment of early rectal tumor is consistent with our results. The meta-analysis study, which included 4 original articles and 2 abstracts searched until November 2018, demonstrated that there were no significant differences between the 2 groups for all outcomes, including R0 resection, *en bloc* resection, local recurrence, procedure duration, and complications.[35] Our meta-analysis additionally included studies published after 2018 and compared ER and TAS more comprehensively than the aforementioned meta-analysis study. Our results strengthen the evidence that there is no difference in outcomes and safety between ER and TAS for the treatment of adenoma/adenocarcinoma. Although our study did not evaluate cost-effectiveness, several studies have reported that ER is more cost-effective than TAS.[36,37] A previous study using the Markov model reported that ER was less expensive than TEM in the management of benign rectal polyps.[36] Another study revealed that median total hospital costs for the treatment of rectal tumors were significantly lower for ESD than for TEM (1,214 United States dollars [USD] vs. 1,686 USD).[37] Given the similar treatment outcomes between ER and TAS and the high cost of TAS, considering ER over TAS as a primary treatment for rectal adenoma/adenocarcinoma may be reasonable. Guidelines also recommend that ER should be considered as the standard treatment for colorectal neoplasms with dysplasia confined to the mucosa, while ESD should be considered for *en bloc* resection of colorectal (but particularly rectal) lesions with suspicion of superficial submucosal invasion.[38-40] However, although ESD is a commonly used technique for the treatment of early-stage CRC in Asian countries, its use is still quite limited in Western countries. The management for early rectal adenocarcinoma should be determined by comprehensively considering local expertise, the endoscopist's skill, equipment availability, and cost. For lesions where determining the direction of treatment is difficult, it may be wise to make a decision on an individual basis through a multidisciplinary team.

For NET, the R0 resection rate was higher in the TAS group than in the ER group, with 91.9% and 64.6% in the TAS and ER groups, respectively. Given that adenoma/adenocarcinoma originates from the mucosal layer, whereas rectal NET originates from the submucosal layer, the higher R0 resection rate of TAS is due to the full-thickness resection of TAS. The R0 resection rate was also significantly higher in the TAS group than in the ESD group, although the difference narrowed (ESD 72.9%) (Supplementary Fig. 2). These results suggest that ESD may be more appropriate than EMR for complete resection of NETs. However, the procedure time in the TAS group was longer than that in the ER group by a mean of 31 minutes. When compared to the ESD group, the procedure time in the TAS group was also longer, with a mean of 25 minutes. The longer procedure time for TAS is because TAS requires general or spinal anesthesia in the operating room. Specifically, TEM requires learning curves, relatively higher expertise, and expensive specialized instruments.[41,42] Although the R0 resection rate for rectal NET was higher in the TAS group, ER may be more advantageous considering its cost-effectiveness. Furthermore, unlike in adenoma/adenocarcinoma, R0 resection may be less important in the prognosis of rectal NETs smaller than 10 mm without lymphovascular invasion and atypical features. When the margins are positive after ER of rectal NETs < 1 cm in size, the positive vertical margin rate is much higher than the positive lateral margin rate.[43] Rectal NET exists in the submucosal layer and ER has limitations in resecting the deep submucosal layer; therefore, it is not uncommon for vertical resection margins to be positive even after complete ER. However, this may not necessarily mean that there are residual lesions. A multicenter study examining long-term clinical outcomes of endoscopically resected rectal NETs supports this.[44] The study showed that

among 137 patients with positive or indeterminate resection margins, local recurrence occurred in only 2 patients (1.5%).[44] Similarly, our study also revealed that despite the lower R0 resection rate in the ER group, the recurrence rate was not different from that in the TAS group. In particular, among 338 patients who underwent ER, recurrence occurred in only 1 patient (Supplementary Fig. 3B). Of note, majority of the rectal NETs analyzed in the aforementioned study and in our study were <1 cm. In summary, ER should be chosen as the primary treatment for small rectal NETs. However, for large NETs with suspected deep tumorous infiltration where performing ER is challenging, TAS may be preferred.

Our meta-analysis provides a better understanding of the outcomes of ER and TAS for the treatment of rectal tumors. Nevertheless, our study has several limitations. First, although TAE, TEM, and TAMIS are different surgical techniques, they were analyzed together as TAS. Only 2 studies used TAMIS; therefore, the number of studies was too small to analyze each. As more relevant papers are accumulated in the future, ranking them using network meta-analysis seems necessary. Second, although no significant difference in recurrence was observed between the ER and TAS groups, there were limitations in accurately comparing recurrence because the follow-up period differed between studies. Third, differences in procedural or surgical skills among endoscopists and surgeons were not considered, even though these could greatly affect the outcomes. Fourth, the size of the resected lesions between the studies was heterogeneous. Lastly, all studies included in the meta-analysis, except one, were retrospective observational studies; therefore, there are concerns about selection bias, important variables could not be controlled, and the level of evidence was lowered. In the future, more RCTs on this topic should be conducted.

In conclusion, TAS had a superior *en bloc* resection rate in rectal adenoma/adenocarcinoma and a superior R0 resection rate and longer procedure time in rectal NET; other treatment outcomes and safety were comparable between ER and TAS. Given the cost-effectiveness, prioritizing ER as a treatment for early rectal tumors and considering TAS only for lesions that are large and suspected to have deep tumorous infiltration seems desirable. However, the medical environment may be different in each country and hospital; therefore, the choice of treatment modality should be made carefully by comprehensively considering local expertise, the endoscopist's skill, and equipment availability.

ADDITIONAL INFORMATION

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Conflict of Interest

Jung YS is an editorial board member of the journal but was not involved in the peer reviewer selection, evaluation, or decision process of this article. No other potential conflicts of interest relevant to this article were reported.

Data Availability Statement

Data sharing is not applicable as no new data were created or analyzed in this study.

Author Contributions

Conceptualization; Data curation: Park CH, Jung YS. Data interpretation: Jung BW. Formal analysis: Park CH. Investigation: all authors. Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization: Park CH, Jung YS. Writing–original draft: Park CH, Jung YS. Writing–review & editing: all authors. Approval of final manuscript: all authors.

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Supplementary Material

Supplementary materials are available at the Intestinal Research website (https://www.irjournal.org).

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Appendix 1. Detailed search strategy

MEDLINE (Search interface: PubMed)

(endoscopic submucosal dissection[tw] endoscopic submucosal dissections[tw] OR ESD[tw] OR endoscopic mucosal resection[tw] OR endoscopic mucosal resections[tw] OR EMR[tw] OR endoscopic resection[tw] OR endoscopic resections[tw]) AND (transanal surgery[tw] OR transanal surgeries[tw] OR TAS[tw] OR transanal excision[tw] OR transanal excisions[tw] OR TAE[tw] OR local excision[tw] OR local excisions[tw] OR transanal resection[tw] OR transanal resections[tw] OR transanal endoscopic microsurgery[tw] OR transanal endoscopic microsurgeries[tw] OR TEM[tw] OR transanal endoscopic surgery[tw] OR transanal endoscopic surgeries[tw] OR transanal minimally invasive surgery[tw] OR transanal minimally invasive surgeries[tw] OR TAMIS[tw]) AND (rectal[tw] OR rectum[tw] OR colorectal[tw] OR colorectum[tw]) AND ("1990/01/01"[Date - Publication]: "3000"[Date - Publication]) NOT review[Publication Type] NOT meta-analysis[Publication Type]

EMBASE (Search interface: Ovid)

1: ((endoscopic submucosal dissection or endoscopic submucosal dissections or ESD or endoscopic mucosal resection or endoscopic mucosal resections or EMR or endoscopic resection or endoscopic resections) and (transanal surgery or transanal surgeries or TAS or transanal excision or transanal excisions or TAE or local excision or local excisions or transanal resection or transanal resections or transanal endoscopic microsurgery or transanal endoscopic microsurgeries or TEM or transanal endoscopic surgery or transanal endoscopic surgeries or transanal minimally invasive surgery or transanal minimally invasive surgeries or TAMIS) and (rectal or rectum or colorectal or colorectum)).ab,ti.

2: limit 1 to (english language and embase and yr = "1990 -Current" and (article or article in press))

Cochrane library

#1: endoscopic submucosal dissection or endoscopic submucosal dissections or ESD or endoscopic mucosal resection or endoscopic mucosal resections or EMR or endoscopic resection or endoscopic resections

#2: transanal surgery or transanal surgeries or TAS or transanal excision or transanal excisions or TAE or local excision or local excisions or transanal resection or transanal resections or transanal endoscopic microsurgery or transanal endoscopic microsurgeries or TEM or transanal endoscopic surgery or transanal endoscopic surgeries or transanal minimally invasive surgery or transanal minimally invasive surgeries or TAMIS

#3: rectal or rectum or colorectal or colorectum

#4: #1 and #2 and #3 (with Publication Year from 1990 to 2024, in Trials)