SYSTEMATIC REVIEW AND META-ANALYSIS OF TRANSANAL ENDOSCOPIC MICROSURGERY VS ENDOSCOPIC SUBMUCOSAL DISSECTION FOR RECTAL ADENOMAS AND EARLY RECTAL CANCER

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BACKGROUND: transanal endoscopic microsurgery (TEM) is the standard procedure for organ-preserving treatment of large adenomas and early rectal cancer. Low rates of R1 resections and fragmentations and, as a result, low rate of local recurrences are benefits of TEM as compared with other transanal procedures for rectal tumors. Endoscopic submucosal dissection (ESD) is a novel technique for rectal adenomas and rectal cancer.
AIM: this systematic review and meta-analysis compare efficacy and safety of ESD and TEM for large rectal adenomas and rectal cancer.
PATIENTS AND METHODS: literature search and meta-analysis were performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Checklist (PRISMA) [13] through MEDLINE publications in English without any limitations in publication date (until December 18, 2018) and using combinations of keywords "endoscopic submucosal dissection", "ESD", "endoscopic dissection", "TEM", "TAMIS", "transanal endoscopic microsurgery", "transanal resection", "TEO", "transanal endoscopic microsurgical excision". Systematic review included all studies which compared TEM and ESD for large rectal adenomas and early rectal cancer. Statistical analysis was performed using Review Manager 5.3 software.
RESULTS: four retrospective comparative studies were included in the analysis. The groups were similar in the number of tumors (OR=1.19, 95% CI 0.23–6.16) and their sizes (p=0.55) as well as the rates of intraoperative complications, i.e., hemorrhage (p=0.54) and perforation (p=0.32). Surgical time was greater (by 32 minutes) for ESD as compared with TEM (OR=16.1, 95% CI 17.7–47.4, p<0.0001). Postoperative hospital stay after TEM was 1.6-fold greater than after ESD (OR=16.1, 95% CI 1.5–30.1, p=0.03). Antibiotic prescription rate, (p=0.33), en bloc resection rate (p=0.66), R1 resection rate (p=0.74), and local recurrence rate (p=0.95) were similar as well.
CONCLUSION: ESD and TEM are safe and effective procedures for local removal of rectal adenomas and early rectal cancer. However, further randomized studies are required to obtain objective results.

[Keywords: rectal adenoma, early rectal cancer, transanal endoscopic microsurgery, endoscopic submucosal dissection, systematic review, meta-analysis]

INTRODUCTION

Diagnosis and treatment of rectal adenomas and early rectal cancer are an urgent issue of recent colorectal surgery. Minimally invasive organ saving procedures provide oncological outcomes similar to that of surgical resection with minimal functional loss [10].

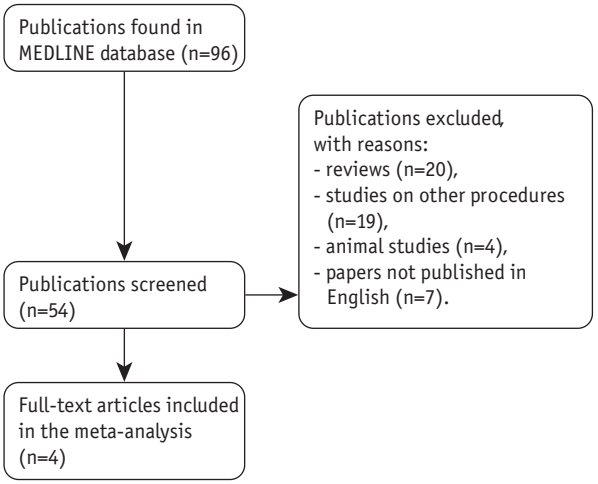

Figure 1. *Flow diagram of literature search*

Currently, transanal endoscopic microsurgery (TEM) is the gold standard in organ saving surgery forlarge rectal adenomas and early rectal cancer [10]. Low rate of R1 resections and fragmentations (which results inlow local recurrence rate) is an obvious advantage of TEM as compared with other transanal techniques of rectal tumor removing [1,4].

Endoscopic submucosal dissection (ESD) was developed in early 2000s to provide *en bloc* removal of non-invasive gastrointestinal tumors. ESD was firstly applied to remove gastric tumors [17] and, later, colorectal tumors [20]. Considering low complication rates and similar to TEM radicalism, ESD is an attractive option for rectal adenomas.

Meta-analysis published by Arezzo et al. included 11 studies on ESD and 10 studies on TEM (a total of 2077 patients). However, this meta-analysis did not provide direct comparisons while excised tumors were non-invasive only.

This systematic review and meta-analysis included all available comparative studies on two techniques for local removal of rectal tumors, i.e., TEM and ESD.

PATIENTS AND METHODS

Literature search and meta-analysis were performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Checklist (PRISMA) [13] through MEDLINE publications in English without any limitations in publication date (until December 18, 2018) and using combinations of keywords “endoscopic submucosal dissection”, “ESD”, “endoscopic dissection”, “TEM”, “TAMIS”, “transanal endoscopic microsurgery”, “transanal resection”, “TEO”, “transanal endoscopic microsurgical excision”. Systematic review included all studies which compared TEM and ESD forlarge rectal adenomas and early rectal cancer. Statistical analysis was performed using Review Manager 5.3 software.

SEARCH RESULTS

296 studies were found in MEDLINE database using PubMed search engine. After screening, 54 studies were proved eligible. 20 reviews, 19 papers on other procedures for early rectal cancer, 4 animal studies, and 7 papers not published in English were excluded. Currently, no randomized clinical trials which compare efficacy of TEM and ESD forlarge rectal adenomas and early rectal cancer are available. Finally, meta-analysis included 4 retrospective studies which compared the efficacy of these procedures in 95 patients after TEM and 120 patients after ESD (see Fig. 1) [11,12,15,18].

RESULTS

Table 1 shows the characteristics of studies included in the meta-analysis.

One-third of the tumors after TEM (34 of 95) and ESD (40 of 120) were adenocarcinomas. No significant differences in the size (p=0.83) and histology (p=0.55) of the tumors were found between the groups, therefore, the groups were homogenous (see Fig. 2).

No significant differences in intraoperative complications, i.e., hemorrhages (p=0.54) and colon perforations (p=0.32) were found between the groups as well. However, surgical time of ESD was significantly (by 32 minutes) greater than that of TEM (95% CI 17-47, p<0.0001). Meanwhile, postoperative hospital stay after TEM was 1.6-fold greater (95% CI 0.14-3.06, p=0.03). Nonetheless, antibiotic use rate was similar in both groups (p=0.33) (see Fig. 3).

Morphological study has demonstrated that en bloc resection rates were similar in both groups (p=0.66). R1 resection rates were similar as well (p=0.74) (see Fig. 4).

No significant difference inlocal recurrence rates was found between TEM and ESD (p = 0.95) (see Fig. 5).

DISCUSSION

TEM and ESD are both effective forlocal rectal adenomas and early rectal cancer and are an alternative to the traditional surgical resection [5,14,19]. Local removal is safer as compared with the surgical resection, does not provide poorer functional outcomes or

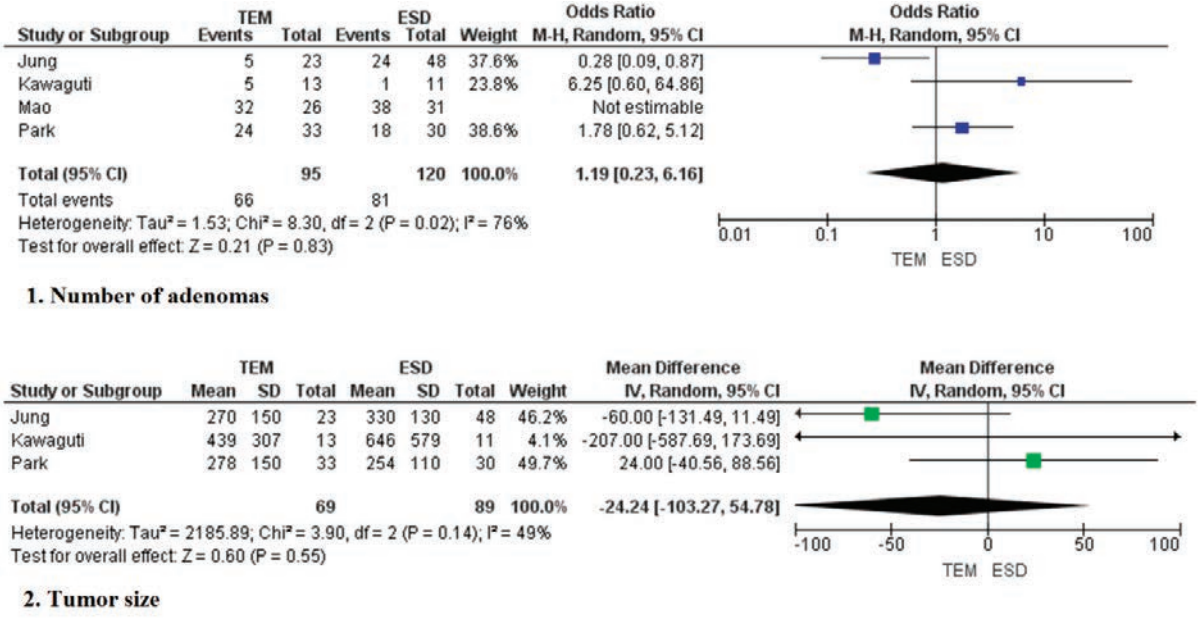

Figure 2. *Characteristics of tumors*

alter urogenital functions, and maintain the quality of life after the treatment [5,18].

It was established that positive R1 resection margin and tumor fragmentation are relevant risk factors for local recurrences [3,4,16]. Considering this, systematic review published by Barendse et al. [6] is of interest. The authors analyzed and compared recurrence rate of rectal adenomas after TEM and endoscopic mucosal resection (EMR). After 3 months, recurrence rate was 11.2% (95% CI 6.0–19.9) for EMR and 5.4% (95% CI 4.0–7.3) for TEM (p=0.04). The authors account these findings for tumor fragmentation in EMR group. However, early detection of continuous tumor growth in the area of prior EMR and tumor re-excision reduce

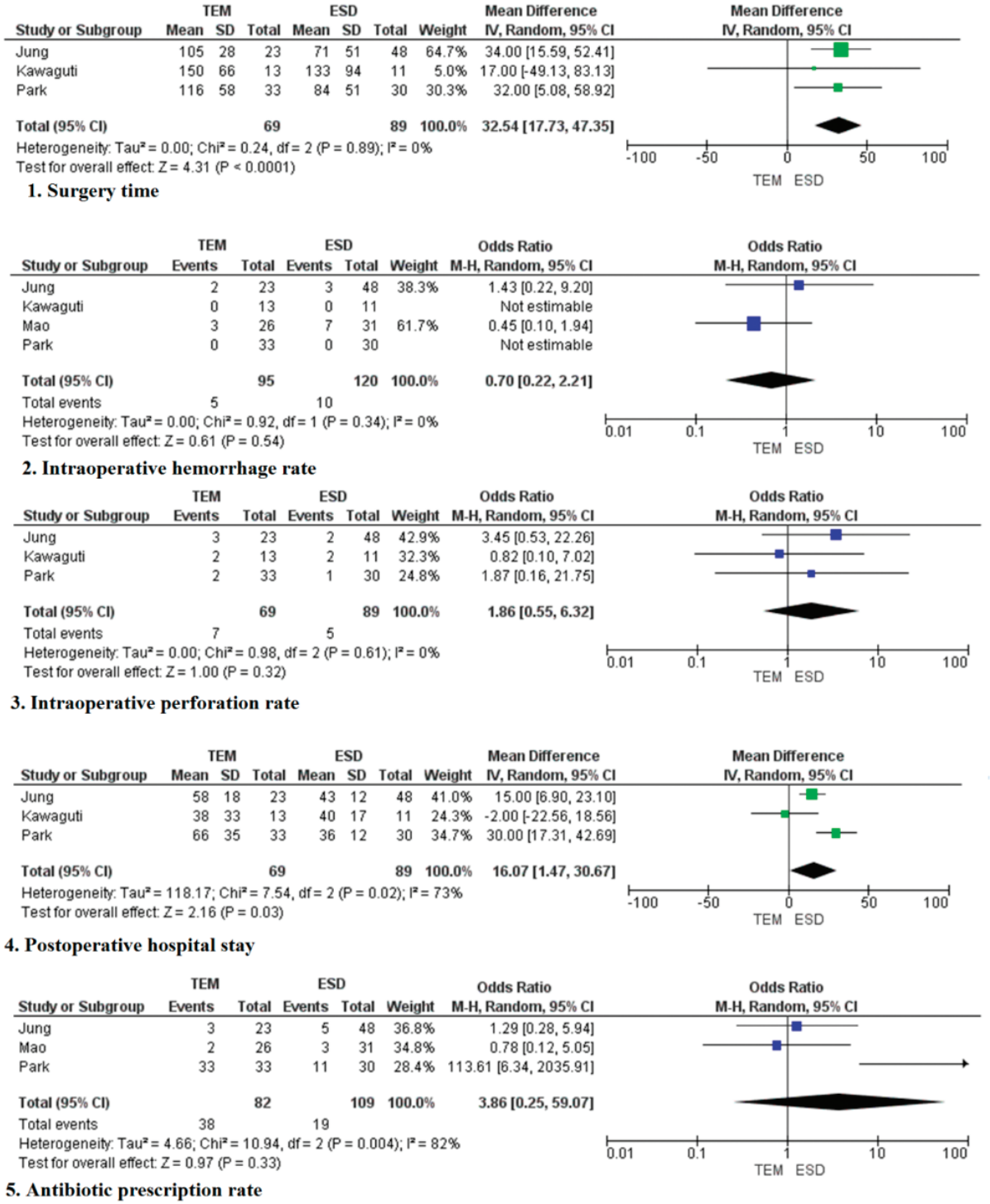

Figure 3. *Immediate surgical outcomes*

second recurrence rate to 1.5% (95% CI 0.6–3.9) which is similar to that of TEM (p=0.29).

Postoperative complication rate was 3.8% (95% CI 2.8–5.3) after EMR but 13.0% (95% CI 9.8–17.0) after TEM (p<0.001). This phenomenon presumably results from full-thickness tumor excision during TEM. The authors conclude that these techniques are comparable in their efficacy and safety but in patients with rectal adenomas only. In occult malignancies, the findings arelikely not to be similar. Despitelow risk of regional metastasis, tumor fragmentation and EMR are unacceptable. Therefore, TEM is the preferable option since alllayers of the rectal wall are excised [9].

Meta-analysis published by Clancy C. et al. included six comparative studies in a total of 927 patients who underwentlocal resection of rectal tumors. No significant difference in postoperative complication rate was found between TEM and transanal excision (TAE) (OR=1.018, 95% CI 0.658–1.575, p=0.937). However, both R1 resection rate (OR=5.281, 95% CI 3.201–8.712, p<0.001) and tumor fragmentation rate (OR=0.096, 95 CI 0.044–0.209, p<0.001) were significantly higher after TAE. As a result, local recurrence rate was significantly higher after TAE (OR = 0.248, 95% CI 0.154–0.401, p<0.001) [7].

Therefore, considering high risk of false negative preoperative tumor staging [8] and potential occult malignancies [2], procedures involving tumor fragmentation or R1 resection are unacceptable. Thus, Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines recommend *en bloc* removal of colon tumors sized more than 2 cm in diameter [21].

Randomized controlled studies are scarce. Therefore, we have analyzed retrospective studies which compare TEM and ESD. Our meta-analysis demonstrates that these procedures are similar in the rate and structure of intra- and postoperative complications, surgical radicalism confirmed by morphology, and tumor recurrence rate.

CONCLUSION

Choice for rectal adenomas and rectal adenocarcinomaslocalized within submucosa is still an enigma. TEM

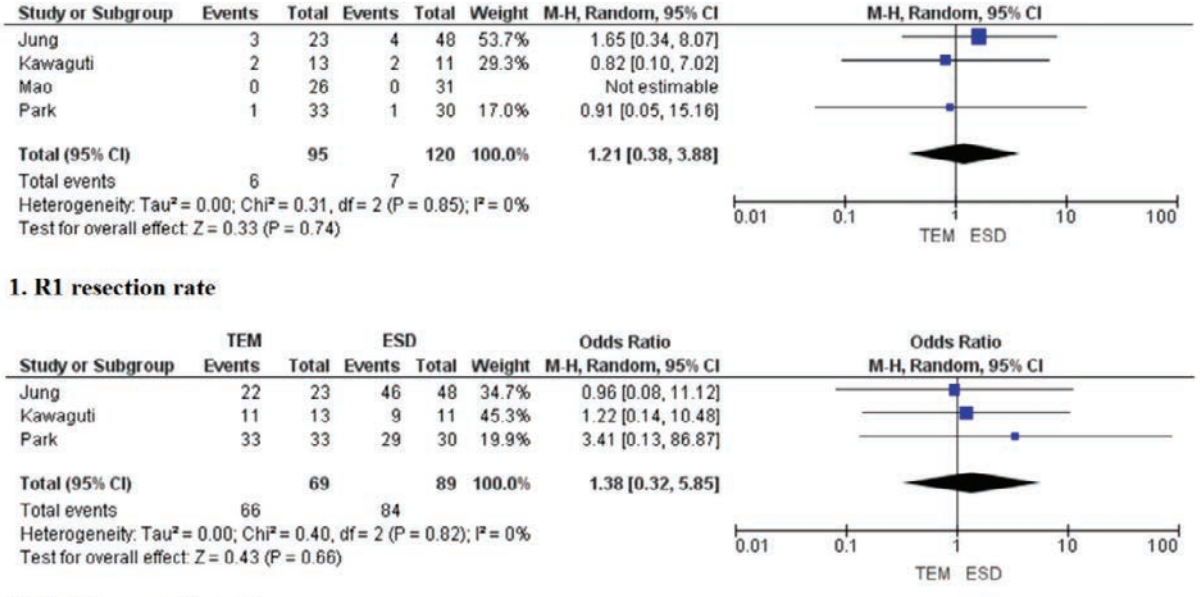

Figure 4. *Morphological study results*

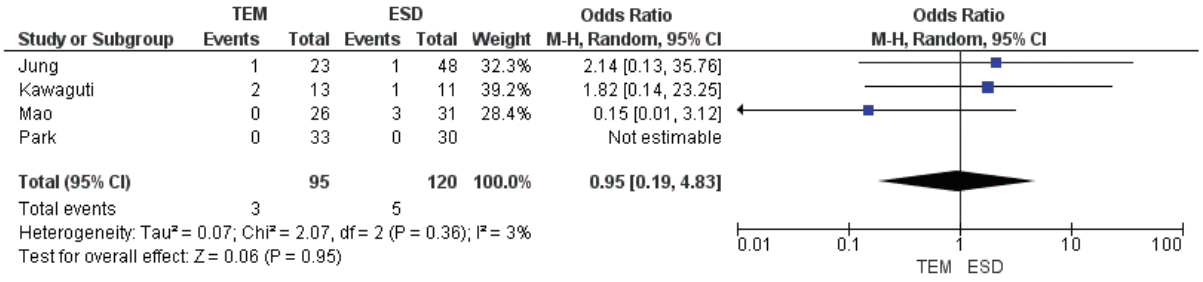

Figure 5. *Local recurrence rates after TEM and ESD*

and ESD are safe techniques for local tumor resection characterized by low fragmentation and R1 resection rates. However, considering poor evidences from the comparative studies on these procedures, further randimized trials are required.

Conflict of interests: The authors declare that there is no conflicts of interest.

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