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Meta-Analysis of Transanal *vs*. Robotic Total Mesorectal Excision for Rectal Cancer

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Abstract

Background/Aim: A meta-analysis was conducted to evaluate and compare the short- and long-term outcomes of transanal total mesorectal excision and robot-assisted total mesorectal excision for rectal cancer.

Methods: We searched MEDLINE et al. for relevant papers published between 2010 and February 2020 by using specific search terms. For the short-term analysis, we collected data on the perioperative period, clinical course, postoperative complications, and pathological findings. For the long-term analysis, the rates of overall, distant, and local recurrence were examined.

Results: We identified 5 papers reporting results that compared transanal total mesorectal excision for rectal cancer with robot-assisted total mesorectal excision. Our meta-analysis included 863 patients with rectal cancer; 348 had undergone transanal total mesorectal excision, and 515 had undergone robot-assisted total mesorectal excision. No significant difference was found in the operative time, conversion rate to laparotomy, and circumferential resection margin between the two groups. The rates of overall recurrence, distant recurrence, and local recurrence were not significantly different. Transanal total mesorectal excision results in almost similar outcomes in the short-term and in the long-term, compared to robot-assisted total mesorectal excision.

Conclusion: Transanal total mesorectal excision and robot-assisted total mesorectal excision may be as incomparable as each other as surgical procedures for rectal cancer.

Keywords: Rectal Cancer; Robot-assisted Total Mesorectal Excision; Transanal Total Mesorectal Excision; Meta-analysis

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Introduction

In the surgery for rectal cancer, the age of blunt dissection were associated with 27% to 85% local recurrence rate [1,2]. In 1982, Head RJ introduced Total Mesorectal Excision (TME) [3], in other words, sharp dissection for the rectal tumor and posterior sheath of the endopelvic fascia en bloc to the levator ani muscle along the visceral pelvis fasciation that is named the "holy plane" [4]. Heald described the "holy plane" to indicate an adjustable anatomic dissection plan to minimize residual tumor. The essence of the TME hypothesis is that lymph nodes, which are not all visible or palpable, are randomly distributed. The posterior surgical plan lies between the fascia of the mesorectum (visceral fascia) and the transverse fascia (parietal fascia) covering the sacrum, the coccygeum, the central sacral artery and the transverse vein. This potential space between the visceral fascia covering the mesorectum and the parietal fascia (endopelvic fascia) is the area, relatively speaking without blood vessels of the TME dissection (holy plane). After the introduction of TME, the local recurrence rate at 5 years of rectal surgery decreased to 3.7% to 10.9% [5,6].

The rate of local recurrence was higher for patients with positive Circumferential Resection Margin (CRM) than those with negative CRM [7]. CRM, which is radical, lateral, or mesorectal resection margin, is reported to be a prognostic factor for patients with rectal cancer [8]. Positive CRM is defined as a tumor extension (continuous or discontinuous) or the presence of positive lymph nodes <1 mm from the radial, non-peritonealized soft tissue border. Patients who have an edge <1 mm have an increased risk of distant metastases [9,10]. In patients with positive CRM, the rate of incomplete TME was 44%, while in patients with negative CRM, incomplete TME was only 11%. In treatment of rectal surgery, pre- or postoperative (chemo) radiation decreased local

Table 1: Characteristics of all the trials.

S.No	Author	Year	Reference number	Style of Study	Number of patients		Conversion to laparotomy		Reasons for conversion		Number of the team for TaTME	Type of robot system	Neoadjuvant Chemoradiotherapy (CRT)			Follow-up period (months)	
					TaTME	RTME	TaTME	RTME	TaTME	RTME			TaTME	RTME	Entire	TaTME	RTME
1	Lee L, et al. [16]	2018	16	matched-cohort	226	370	3 (1.3%)	4 (1.1%)	U	U	-	da Vinci Si or Xi	160 (70.7%)	256 (69.2%)	U	U	U
2	Perez D, et al. [17]	2017	17	Retro-spective	55	60	2 (3.6%)	6 (10.0%)	U	U	two (65%)	da Vinci Si	35 (63.6%)	42 (70%)	U	U	U
											one (35%)						
3	Lee KY, et al. [18]	2018	18	case-matched	21	24	0 (0%)	1 (4.2%)	-	U	one	da Vinci S or Si	14 (66.7%)	12 (50.0%)	21.3	20.1	22
4	Law WL, et al. [19]	2019	19	propensity score Matching	40	40	2 (5%)	2 (5%)	adhesions in the pelvic cavity	pelvic bleeding	two	da Vinci S	27 (67.5%)	22 (55%)	U	U	U
									inadequate perfusion to the descending colon	inability to insert the stapler							
5	Seow-En I, et al. [20]	2018	20	Retro-spective	6	21	0 (0%)	1 (4.8%)	-	locally advanced disease	one	da Vinci Si	2 (33%)	7 (33%)	U	30 (29-35)	28 (22-38)

-: Not Stated; U: Unknown

recurrence rate [1].

As a minimally invasive surgery, laparoscopic surgery for Colorectal Cancer (CRC) was first described in 1991 [11] and has since been widely applied by surgeons to treat patients with CRC. Laparoscopic TME for rectal cancer has technical disadvantages such as inadequate two-dimensional view with a movable video camera, a limited range for maneuver of the long, straight and rigid laparoscopic instruments in the narrow pelvic cavity, and is difficult particularly for bulky and low tumors, male gender and obesity. Innovative approaches to compensate these disadvantages of laparoscopic TME are Transanal TME (TaTME) and Robotic TME (RTME).

Several studies describe safety and feasibility of RTME for rectal cancer after it was first reported in 2002 [12]. We reported that RTME for rectal cancer may have some favorite points over laparoscopic TME [13].

TaTME is said to be a beneficial treatment in male patients with a narrow pelvis and in obese patients with a bulky tumor, since it was first reported in 2010 [14]. There were few studies comparing TaTME with RTME for rectal cancer. However, there were no randomized controlled trials comparing the 2 groups. The Methodological Index for Non-Randomized Studies (MINORS) is a valid instrument for assessing the methodological quality of non-randomized studies, especially for the purposes of meta-analysis [15]. Here, we conducted a meta-analysis of previously conducted non-randomized controlled trials [16-20]. The outcomes of each of the surgical procedures were analyzed.

Methods

Literature search

To identify papers relevant to our study, we searched the major medical databases-MEDLINE, EMBASE, Science Citation Index, and the Cochrane Controlled Trial Register-for studies published between 2010 and February 2020. The following search terms were used: "robotic", "robot-assisted", "transanal", "total mesorectal excision", "TME", "surgery", and "rectal cancer". Appropriate data from the studies were used for this meta-analysis. This meta-analysis was prepared in accordance with the Preferred Reporting Items for Systemic reviews and Meta-Analysis (PRISMA) statement (Figure 1) [21].

Inclusion criteria

To enter this meta-analysis, studies had to: (1) be written in English; (2) compare TaTME with RTME for rectal cancer; and (3) report on at least one of the outcome measures mentioned below.

Exclusion criteria

Studies were excluded from this analysis if the outcomes of interest were not reported for the two surgical techniques.

Study quality

The MINORS was used to evaluate the methodological quality of the non-randomized studies. Two reviewers independently appraised the studies. Disagreements were resolved by discussion and consensus.

Data extraction

Three researchers (H.O., S.N., and H.N.) extracted data from each article by using a structured sheet and entered the data into a database. We conducted meta-analyses for short- and long-term. For the short-term analysis, we collected data on the perioperative period, clinical course, postoperative complications, and pathological findings. For the perioperative period, we collected data on operation time, estimated blood loss, conversion rate to open surgery, mean height from anal verge, the rate of the patients undergoing the neoadjuvant radiochemotherapy and having diverting ileostomy. The rate of stapled anastomosis, BMI, the number of males, the patient ages and the number of the patients with lower rectal tumor were studied. The postoperative mortality, the rate of reoperation and duration of hospital stay were examined as the data of clinical course. For the postoperative complications, overall complications, anastomotic leakage, ileus, urinary retention, superficial surgical site infection and, the number of complications that are Clavien-Dindo III or higher, were analyzed. Number of retrieved lymph nodes, Circumferential Resection Margin (CRM), Proximal Margin (PM), the distance and involvement of Distal Margin (DM), number of cases with complete TME, and tumor size of the specimen, were examined for the pathological data. For the long-term analysis, we used data on the rate of overall recurrence and local recurrence.

Statistical analysis

Weighted Mean Differences (WMDs) and odds ratios were used for the analysis of continuous and dichotomous variables, respectively.

Table 2: The revised and validated version of MINORS.

		Methodological items for non-randomized studies								Additional criteria in the case of comparative study				
S.No		A clearly stated aim	Inclusion of consecutive patients	Prospective collection of data	Endpoints appropriate to the aim of the study	Unbiased assessment of the study endpoint	Follow-up period appropriate to the aim of study	Loss to follow up less than 5%	Prospectve calculation of the study size	An adequate control group	Contemporary groups	Baseline equivalence of groups	Adequate statistical analyses	Score
1	Lee L, et al. [16]	2	2	0	2	1	0	2	0	2	2	2	2	17
2	Perez D, et al. [17]	2	2	0	2	0	0	2	0	2	2	2	2	16
3	Lee KY, et al. [18]	2	2	0	2	1	1	2	0	2	2	2	2	18
4	Law WL, et al. [19]	2	2	1	2	1	0	2	0	2	2	2	2	18
5	Seow-En I, et al. [20]	2	2	0	2	0	1	2	0	2	2	2	2	17

The items are scored 0 (not reported), 1 (reported but inadequate) or 2 (reported and adequate). The global ideal score being 16 for non-comparative studies and 24 for comparative studies.

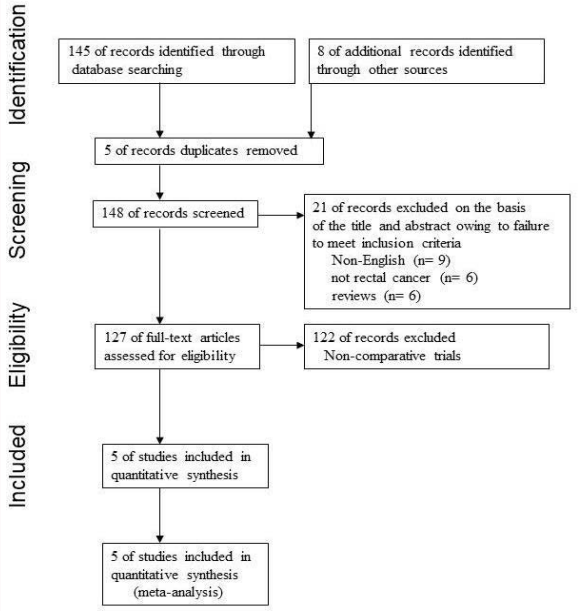

Figure 1: Flow diagram of this meta-analysis in accordance with PRISMA Statement.

Random effects models were used to identify heterogeneity between the studies, and the degree of heterogeneity was assessed using the χ^2 test. For the analysis of the conversion rate, the χ^2 test was used. The Confidence Interval (CI) was established at 95%, and *p* values of less than 0.05 were considered to indicate statistical significance. For the computation of the CI, estimates of the mean and standard deviation were obtained using formulas proposed by Hozo et al. [22]. Statistical analyses were performed using the Review Manager (RevMan) software, version 5.3, provided by the Cochrane Collaboration, Copenhagen, Denmark.

Results

Search results

The present meta-analysis met the PRISMA statement. Overall, 145 citations were retrieved from the search strategy. Eight additional articles were identified by contacting clinical experts and searching bibliographies. Five studies were excluded because of duplicate reports. Twenty-one studies were removed from the 148 because they were not written in English, reported carcinomas of the other organs except the rectum, and were described in the form of review. One hundred and twenty-two studies were excluded on account of non-comparative trials.

We identified 5 trials that compared TaTME with RTME for rectal cancer for this meta-analysis. The characteristics of each trial are presented in Table 1. Our meta-analysis included 863 patients with rectal cancer; of these, 348 had undergone TaTME, and 515 had undergone RTME. Short- and long-term results are shown in Figure 2 and 3, respectively. The study quality by using the MINORS was shown in Table 2.

Clinicopathological characters of the patients

There were no significant differences in age, gender, BMI, the number of patients with lower rectal tumor and patients undergoing the neoadjuvant chemoradiotherapy between the TaTME group and the RTME group (Figure 2c). No differences were found in pathological TNM stage 0, I, II, III, pT0, pTis, pT1, pT2, and pT4, while there were more cases with pT3 tumors in RTME than in TaTME.

Short-term outcomes

No significant difference was found in the operative time, intraoperative estimated blood loss, mean tumor height from anal verge, and number of the patients undergoing diverting ileostomy and stapled anastomosis between TaTME and RTME from the analysis (Figure 2a). The occurrence rate of overall postoperative complications, anastomotic leakage, ileus, superficial surgical site infection, urinary retention, and the complications that are Clavien-Dindo III or higher, did not differ significantly between the two procedures (Figure 3a,b). Examining 703 resections (272 TaTME and 431 RTME), 0 and 3 perioperative mortality occurred among patients who underwent TaTME and RTME, respectively. No significant difference was found in the rate of mortality between the 2 groups. The cause of death in the 3 cases of RTME was unknown There were no significant differences in the rate of reoperation and duration of hospital stay.

In resected specimen, no significant difference was found in tumor size, number of retrieved lymph nodes, length of DM and PM, and number of cases with CRM and DM involvement between TaTME and RTME. There was no significant difference in number of cases with complete, nearly complete, and incomplete TME between the 2 groups.

Conversion rate

The conversion rate from TaTME to open surgery, and RTME

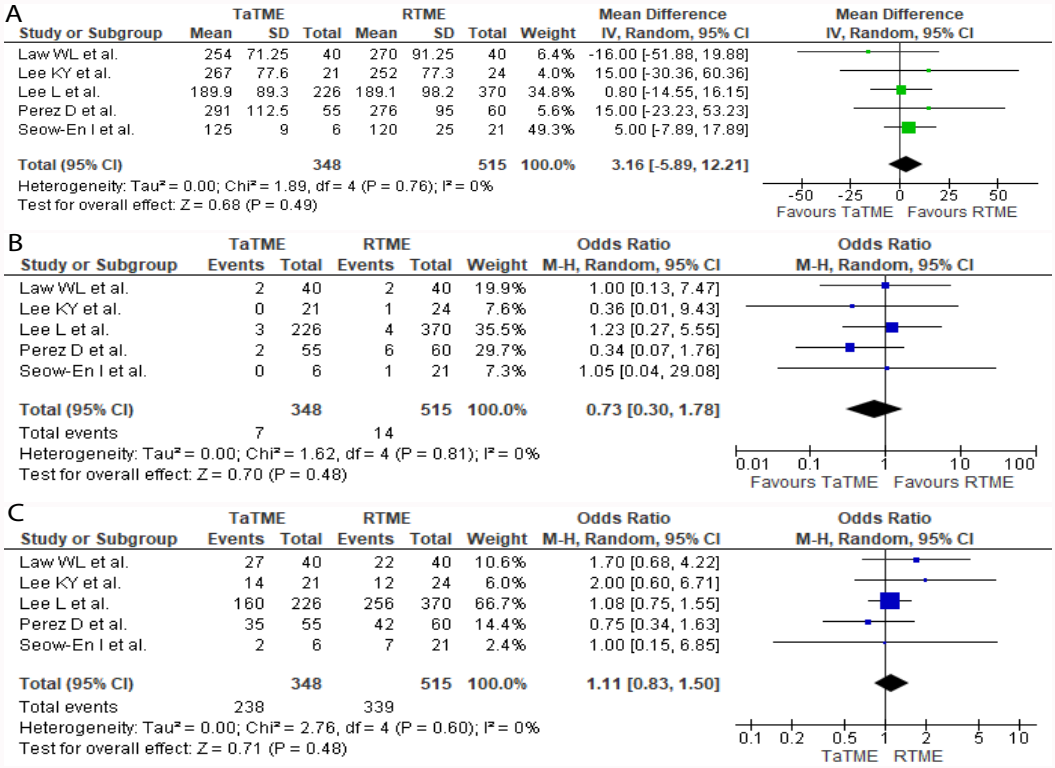

Figure 2: Meta-analysis of the short-term outcomes.
Figure 2a: Operative time (minutes).
Figure 2b: Conversion rate to laparotomy.
Figure 2c: Number of the patients undergoing neoadjuvant chemoradiotherapy (CRT).

to open surgery ranged from 0% to 5.0%, and 1.1% to 10.0% in the analysis of 5 studies (Table 1). The conversion rate had no significant difference between the 2 groups (Figure 2b). Seven (2.0%) of 348 cases of TaTME and 14 (2.7%) of 515 RTME were converted to open surgery, respectively.

Long-term outcomes

Tumor recurrence: The rates of overall recurrence, distant recurrence, and local recurrence were not significantly different between TaTME and RTME, from the analysis of 72 resections (27 TaTME and 45 RTME). Examining 72 resections (27 TaTME and 45 RTME), 1 (3.7%) and 3 (6.7%) local recurrence occurred among patients who underwent TaTME and RTME, respectively.

Heterogeneity: In the short-term period, significant heterogeneity was found between studies with respect to mean height from anal verge, distal margin, number of cases undergoing diverting ileostomy, and overall complications. In the long-term period, we found no significant heterogeneity in all the types of recurrence between studies.

Discussion

TaTME and RTME were introduced to compensate disadvantages of laparoscopic TME for rectal cancer [19,23]. The short and long-term outcomes of TaTME and RTME were primarily compared in this meta-analysis. While there have been few randomized trials comparing TaTME to RTME for rectal cancer, 5 non-randomized trials have been reported [16-20].

In the short-term period, there was no significant difference in the operative time and intraoperative estimated blood loss. Several papers report that TaTME requires less operating time than laparoscopic TME [24,25]. On the other hand, there are many reports that operative time is longer in RTME than in laparoscopic TME [13,26,27]. There was no significant heterogeneity of the operation time between studies. Two of five literatures report that the technical skills of surgeons for TaTME are still in the early stages. The learning curve of TaTME and RTME for rectal cancer is described to be from 30 to 40 cases [28,29], and from 15 to 35 cases [30,31], respectively. The operation time for TaTME will be expected to decrease in future, as surgeons experience TaTME. The operative time of TaTME can be shorter for two-team approach than one-team approach [24,25]. Four of the five literatures in this study reported the number of the team for TaTME. One literature and two literatures described that the surgery of TaTME was performed by two-team and one-team, respectively. The rest one literature reported that TaTME was done by one-team or two-team. Tumor size, mean tumor height, number of retrieved lymph nodes, length of DM and PM, number of cases with CRM and DM involvement, and the quality of TME by Quirke classification were similar between TaTME and RTME [32]. These suggest that the quality of TME may remain the same between the 2 groups. CRM is a prognostic factor, but there is no significant difference between TaTME and RTME groups [8].

The conversion rate from RTME to laparotomy in this study was 1.1% to 10.0%, which was not much different from the conversion rate in ROLARR trial (8.1%) [33]. On the other hand, the conversion rate from TaTME to open surgery in this study was 0 to 5.0%, which was similar to other literatures (0% to 7.5%) [34-36]. It is presumed that surgeon's skill in this study is excellent.

There was no significant difference in the occurrence rate of

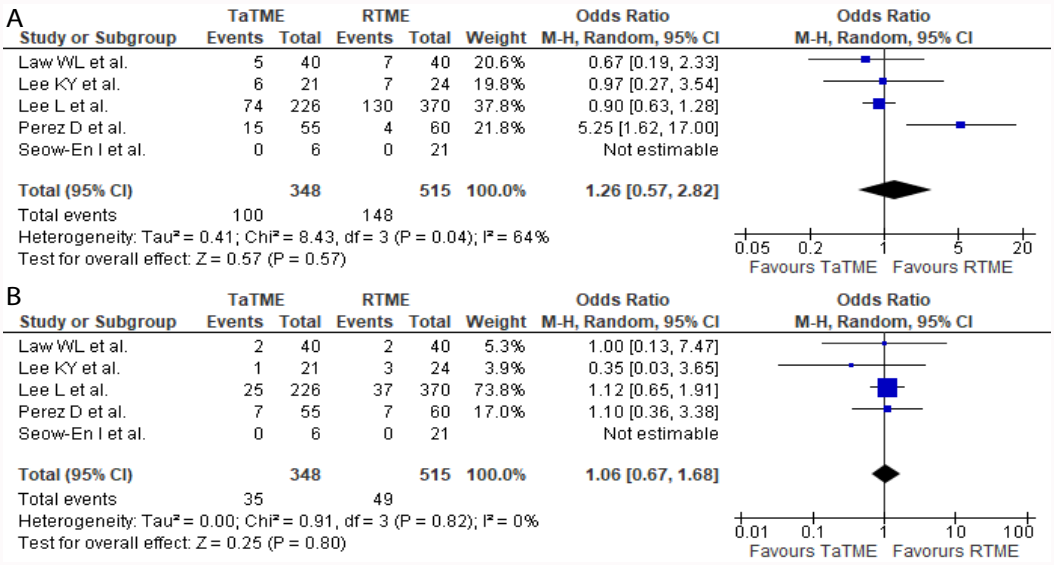

Figure 3: Meta-analysis of the postoperative complications.
Figure 3a: Overall postoperative complications.
Figure 3b: Anastomotic leakage.

overall postoperative complications. A single-stapling anastomosis or a hand-sewn anastomosis was performed in TaTME, while double or more staple anastomosis or a hand-sewn anastomosis was performed in RTME. There was no difference in the rate of anastomotic leakage. All the five papers referred to the rate of anastomotic leakage, with rates of 5.2% to 12.7% for TaTME and 5.0% to 12.5% for RTME. The reported anastomotic leakage rates suggest that both TaTME and RTME may be feasible procedures. The important intraoperative complication of TaTME is urethral injury, which was not mentioned in these five literatures [37].

Significant heterogeneity of the mean height from anal verge, distal margin, number of cases undergoing diverting ileostomy, and number of overall complications between studies may be depend on the difference of points on learning curve of the surgeons, surgical procedures, tumor condition, and the factors of patients which are obesity, and so on.

In the long-term period, we found that the rates of overall recurrence, metastatic recurrence and local recurrence are not significantly different between TaTME and RTME. The above mentioned may be related to no significant difference in CRM involvement and quality of TME between the two groups. This finding suggests that TaTME may be comparable to RTME with respect to long-term oncologic results.

There are several limitations in this study. First, all of the 5 articles are non-randomized clinical trials, which may bias to estimating the results. Second, the five articles reported the preoperative chemoradiation for rectal cancer. The influence of preoperative chemoradiation to selection for the surgical procedures or prognosis could not be discussed. Third, as TaTME is a relatively recent procedure, duration of following up patients is not adequate. Data for 5-year follow-up may be requested.

In conclusion, although there are several limitations, this meta-analysis showed that TaTME for rectal cancer result in almost similar outcomes in the short-term and in the long-term oncologic outcomes, compared to RTME. It has been suggested that TaTME and RTME may be as incomparable as each other as surgical procedures for rectal cancer.

If possible, some prospective randomized trials comparing TaTME to RTME for rectal cancer should be performed in the near future.

Authorship Contributions

Protocol/project development: Ohtani, Ohno, Maeda, Nagahara, Hirakawa, Ohira.

Data collection or management: Ohtani, Ohno, Nomura, Yamakoshi, Nakagawa, Nagamori.

Data analysis: Ohtani, Shibutani, Fukuoka, Iseki.

All Authors meet the International Committee of Medical Journal Editors authorship criteria.

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