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ORIGINAL ARTICLE

Comparison of the short-term outcomes in lower rectal cancer using three different surgical techniques: Transanal total mesorectal excision (TME), laparoscopic TME, and open TME

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KEYWORDS
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Circumferential margin

Summary *Background:* Total mesorectal excision (TME) is the standard surgical principle in the treatment of rectal cancer. However, in recent years, there has been an increasing debate about how to obtain better results in circumferential margin (CRM) and distal margins of the surgical specimen. The CRM and distal margin involvement rates have been linked to local recurrence and disease-free survival rates. In this study, we compared three surgical techniques for the treatment of lower rectal cancer.
Methods: From July 2008 to April 2018, we identified consecutive patients with lower rectal cancer who underwent TME. According to the surgical technique, we divided the patients into three groups: transanal TME (TaTME), laparoscopic TME (LaTME), and open TME (OpTME).
Results: A total of 126 patients underwent TME; 39, 64 and 23 patients underwent TaTME, LaTME, and OpTME respectively. Tumor location was lower in the TaTME group than the other groups ($p < 0.01$). TaTME resulted in longer operation time than the other two groups

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($p < 0.01$). In pathological outcomes, no patients with a CRM <1 mm were observed in the TaTME group compared with five (7.8%) and three patients (13.0%) with CRM <1 mm in the LaTME and OpTME group respectively ($p = 0.035$). Patients in the TaTME and LaTME groups also had a better disease-free survival than OpTME group ($p < 0.01$).
Conclusion: TaTME provides surgeons with a novel and effective method to treat lower rectal cancer. In the short-term outcomes, TaTME achieved better pathological results and disease free survival than OpTME but not significantly superior to LaTME. Further studies are necessary to evaluate the long-term oncological results.

1. Introduction

Total mesorectal excision (TME) is the standard principle in rectal cancer treatment.[1–3] Transanal TME (TaTME) was proposed by Lacy in 2010 to address mid and lower rectal cancer.[4] Currently, TME is performed open (OpTME) or laparoscopically (LaTME), and both techniques have a similar execution during the transabdominal phase of the surgery, that is, cephalic to caudally when entering the narrowing pelvic space. The quality of the distal margin and circumferential margin (CRM) is uncertain due to the limited working space during the transection of the distal part of the rectum. For this reason, obtaining an adequate CRM and distal margin is a major issue that has a direct impact on the local recurrence of rectal cancer.[5,6] Before TaTME was proposed, a randomized controlled trial (Color II) compared the pathological outcomes between LaTME and OpTME. In the Color II clinical trial, the 3-year local recurrence rate was similar in both groups. The disease-free and overall survival rates did not show significant differences.[7] In contrast, the ACOSOG Z6051 randomized clinical trial revealed that pathological outcomes in LaTME failed to meet the non-inferiority criteria, compared with those in OpTME.[8] A negative CRM >1 mm was obtained in 87.9% of patients who underwent LaTME and in 92.3% who underwent OpTME. In ALaCaRT, a randomized clinical trial in 2015, it still couldn't be established that laparoscopic resection has more clearance of CRM and distal margin (CRM: 93% in LaTME vs 97% in OpTME).[9] As mentioned, the difference between the locoregional recurrence rate could reach 12.7% and 37.6% if CRM is involved.[10] Currently, CRM is the main quality indicator, particularly for mid and lower rectal cancer.

Until now, there have been many studies focusing on the comparison between TaTME and LaTME, and most of them have shown that TaTME has a better pathological outcome and equal or better oncological outcome.[11–15] However, few studies have compared OpTME and TaTME. In this present study, we use retrospective methods to investigate and analyze these three surgical techniques for the treatment of lower rectal cancer.

2. Methods

2.1. Patient selection

Between July 2008 and April 2018, a total of 175 patients with lower rectal cancer underwent surgical treatment at one single center. All the patients included in our study signed the informed consent, which was documented by the respective institution's Internal Review Board. The inclusion criteria were rectal adenocarcinoma within 7 cm from the anal verge and a preoperative clinical staging of I—III (T0-3, N0-1, M0). Patients with cancer perforation, local invasion to adjacent organs, distant metastasis, or patients who underwent abdominal perineum resection were excluded from our study (Fig. 1). We documented the patients' age, gender, body mass index (BMI), and American Society of Anesthesiology (ASA) level.

The pre-operation work-up included the following: digital examination, colonoscopy, a lower gastrointestinal series X-ray with double contrast, chest X-ray, abdominal and pelvic computed tomography, and a pelvic magnetic resonance imaging. After the patients were placed in the operation room and anesthetized, we examined the precise location of the tumor using rigid proctoscopy from the anal verge.

2.2. Surgical techniques

TaTME group: Only one surgical team performed TaTME in all the patients. First, we ligated the inferior mesenteric

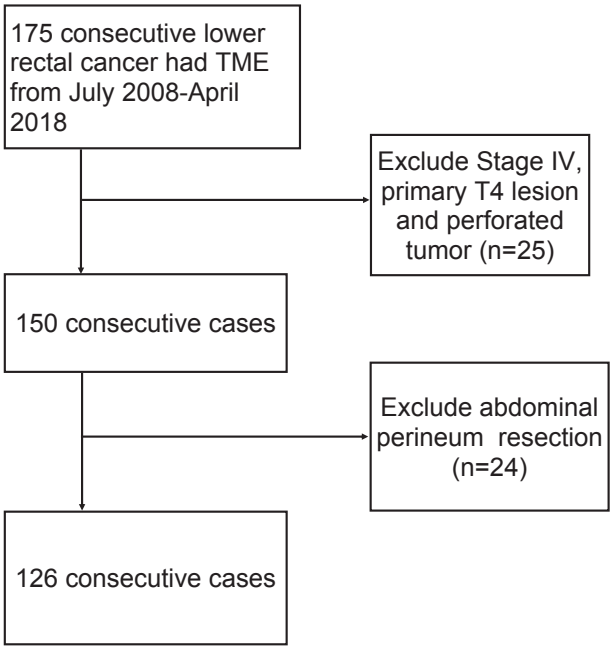

Figure 1 Patient selection flow diagram.

artery and vein at a high level and take down the splenic flexure of colon; then, we mobilized the sigmoid colon to the upper rectum using 2—4 working ports. Following this, we moved to the transanal part and inserted the GelPoint Path Transanal Platform (Applied Medical, Rancho Santa Margarita, CA). Under direct vision, we performed a purse-string suture 1—2 cm distal to the tumor. The lumen was then rinsed with an antiseptic solution. Carbon dioxide insufflation was started with an intraluminal pressure of 8—10 mmHg. A full-thickness rectum transection approximately 1 cm below the purse-string suture was performed using a monopolar electrocauterizer. We proceeded with dissection in the avascular plane between the mesorectum and presacral fascia by either monopolar diathermy or using the Sonicision (Covidien, Mansfield, MA) and then anteriorly and laterally from caudal to cephalic dissection. Finally, we completed the dissection until we entered the peritoneal cavity. Depending on its size, the specimen was retrieved from the anus or the extended umbilical wound. A purse-string suture was performed at the stump of the rectum, and finally, end-to-end colorectal or coloanal anastomosis was made using a curved intraluminal stapler (Ethicon Endo-Surgery, Cincinnati, OH).

LaTME group: We performed LaTME using 3—4 working ports following a standard method. This included medial to lateral dissection, high ligation of the inferior mesenteric vessels, take down the splenic flexure of the colon, mobilizing of the sigmoid colon TME, and bowel transection by stapling. We retrieved the specimen from the extended umbilical wound and performed end-to-end anastomosis by stapling.

2.3. Statistical analysis

Data was analyzed using the SPSS package (Statistical Product and Service Solutions 20.0 for Macintosh; SPSS, Inc., Chicago, IL). Data was presented as mean ± standard deviation. Comparisons were made using the χ^2 test or one-way analysis of variance for categorical or continuous variables, respectively, and a *P*-value <0.05 was considered statistically significant.

3. Results

From July 2008 to April 2018, a total of 126 patients were included in this study. The median follow-up time was 26.3 months (range: 1—102 months). Thirty-nine patients with lower rectal cancer underwent TaTME and another 64 and 23 patients with lower rectal cancer treated with LaTME and OpTME were included for comparison. The tumor location from the anal verge was lower in the TaTME (4.3 ± 1.4 cm) group than the LaTME (5.8 ± 1.2 cm) and OpTME (5.6 ± 1.3 cm) groups ($p < 0.01$). The demographic data showed that there was no difference in age, gender, BMI, ASA score, clinical TNM staging, and preoperative CCRT rate (Table 1).

In the TaTME group, four patients received inter-sphincter dissection and coloanal anastomosis but it was not performed in the LaTME and OpTME groups. In these three groups, TaTME had the longest operation time (210 ± 57 min), followed by LaTME (184 ± 55 min) and OpTME (153 ± 42 min) ($p < 0.01$). TaTME and LaTME both had less blood loss (63 ± 102 ml and 42 ± 59 ml) than OpTME (113 ± 129 ml) ($p < 0.01$). There was one conversion case in the TaTME group for the transabdominal phase due to adhesion related to previous operations; however, the total mesorectal excision was still performed by transanal approach. There was one patient in the LaTME group who needed conversion to OpTME due to a bulky mass lesion resulting in poor vision found during the laparoscopic visualization of the pelvic area. Anastomotic site leakage was observed in one case in the TaTME group and none in the

Table 1 Clinical characteristics of two group of patients.

	TaTME	LaTME	OpTME	*p* Value
Patient number	39	64	23	
Sex n				0.11
Male	29	42	11	
Female	10	22	12	
Age (years)	62.0 ± 14.9	64.0 ± 12.2	67.0 ± 10.5	0.44
BMI (kg/m^2)	25.4 ± 4.0	24.6 ± 3.3	22.7 ± 4.1	0.19
ASA score				0.41
I	5	5	3	
II	28	53	17	
III	6	6	3	
Tumor distance from anal verge (cm)	4.3 ± 1.4	5.8 ± 1.2	5.6 ± 1.3	**<0.01** (TaTME vs. LaTME, $p < 0.01$, TaTME vs. OpTME, $p < 0.01$, LaTME vs. OpTME, $p = 0.60$)
Range (median)	2—7 (4)	2—7 (5)	3—7 (5)	
Neoadjuvant therapy n (%)	15 (39%)	31 (48%)	8 (35%)	0.43
Clinical staging				
T1-2N0M0	11	19	6	0.78
T3N0M0	11	18	5	
T1-3N1-2M0	17	37	12	
Follow time (month)	17.5 ± 8.8	37.5 ± 23.7	41.6 ± 29.1	**<0.01** (TaTME vs. LaTME, $p < 0.01$, TaTME vs. OpTME, $p < 0.01$, LaTME vs. OpTME, $p = 0.50$)

A *p* value <0.05 indicates statistical significance.

other two groups. This leakage was resolved by prolonged intra-abdominal well drainage and protective stoma use. The postoperative complication rate was 10.2%, 10.9%, and 8.7% in the three subgroups. There was one patient who had a stroke attack 5 days after surgery in the LaTME group. Perioperative mortality rate at 30 days was negative in all three groups (Table 2).

The pathological TNM staging is shown in Table 3. There were four and four patients in the TaTME and LaTME groups with complete remission due to the concurrent chemo-radiotherapy. There were five (7.8%) and three (13.0%) patients in the LaTME and OpTME groups with CRM <1 mm compared with no patient in the TaTME group ($p = 0.035$). The amount of harvested lymph nodes did not differ in all the three groups. Patients with local recurrence were noted only in the LaTME and OpTME groups.

The 2-year disease-free survival rates were 90%, 91%, and 65% in the TaTME, LaTME, and OpTME groups (Table 3 and Fig. 1, $p = 0.01$). The 2-year overall survival rates were 97%, 89%, and 89% in the TaTME, LaTME, and OpTME groups (Table 3 and Fig. 2, $p = 0.56$).

4. Discussion

Although the Color III clinical trial has not completed its prospective data collection between TaTME and LaTME in mid and lower rectal cancer, there is a trend toward using

Table 2 Peri-operative characteristics.

	TaTME (N = 39)	LaTME (N = 64)	OpTME (N = 23)	*p* value
Operation procedure				**<0.01** (TaTME vs. LaTME, $p < 0.01$, TaTME vs. OpTME, $p < 0.01$, LaTME vs. OpTME, $p = 1.0$)
LAR	35	64	23	
Intersphincter dissection	4	0	0	
Operation time (min)	210 ± 57	184 ± 55	153 ± 42	**<0.01** (TaTME vs. LaTME, $p = 0.03$, TaTME vs. OpTME, $p < 0.01$, LaTME vs. OpTME, $p = 0.01$)
Blood loss (ml)	63 ± 102	42 ± 59	113 ± 129	**<0.01** (TaTME vs. LaTME, $p = 0.19$, TaTME vs. OpTME, $p = 0.01$, LaTME vs. OpTME, $p < 0.01$)
Postoperative hospital stay (day)	9.2 ± 2.7	9.6 ± 4.6	9.4 ± 2.4	0.87
Conversion n (%)	1 (2.5%)	1 (1.6%)	0	
Complication n (%)	4 (10.2%)	7 (10.9%)	2 (8.7)	0.95
Anastomotic leakage	1	0	0	
Postoperative ileus	1	3	1	
Stroke	0	1	0	
Urinary dysfunction on discharge	2	3	1	
Mortality (post OP 30 days)	0	0	0	1

A *p* value <0.05 indicates statistical significance.

Table 3 Pathological characteristics.

	TaTME (n = 39)	LaTME (n = 64)	OpTME (n = 23)	*p* value
Tumor size (cm)	3.6 ± 2.2	3.2 ± 1.5	4.1 ± 1.5	0.08
Pathological staging				0.06
Complete remission	4	4	0	
T1-2N0M0	16	20	4	
T3N0M0	7	13	8	
T1-3N1-2M0	12	27	11	
Distal margin (cm)	1.6 ± 1.4	1.9 ± 1.3	1.6 ± 0.9	0.30
Circumferential margin (mm)				**0.035** (TaTME vs. LaTME, $p = 0.08$, TaTME vs. OpTME, $p < 0.01$, LaTME vs. OpTME, $p = 0.2$)
<1 mm n (%)	0	5 (7.8%)	3 (13.0)	
≥1 mm n	39	59	20	
Harvested lymph node	20.8 ± 9.0	18.8 ± 8.1	23.5 ± 8.2	0.07
Local recurrence	0	3 (4.7%)	2 (8.7%)	
Two years disease free survival rate	0.90	0.91	0.65	**0.01** (TaTME vs. LaTME, $p = 0.70$, TaTME vs. OpTME, $p = 0.01$, LaTME vs. OpTME, $p = 0.01$)
Two year overall survival rate	0.97	0.89	0.89	0.56

A *p* value <0.05 indicates statistical significance.

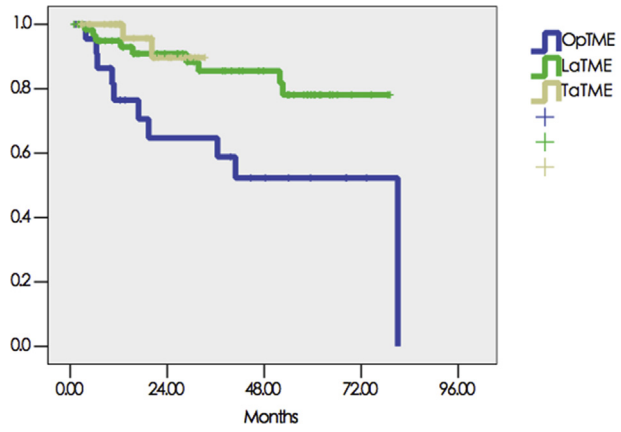

Figure 2 Disease free survival curve in three groups.

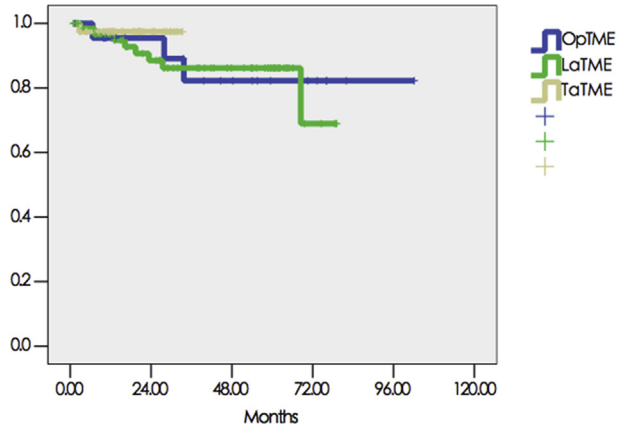

Figure 3 Overall survival curve in two groups.

TaTME due to the comfortable working visualization and working space when dissecting the distal part of the mesorectum.[16] TaTME not only provides nerve-sparing, sphincter-saving properties but also attains a better pathological CRM uninvolvement rate.[13] Many large prospective randomized studies have compared OpTME with LaTME in short- and long-term outcomes, showing equivalent results in pathological outcome. However, few studies have analyzed between TaTME and OpTME once TaTME became popular worldwide.

Comparing the dissection and transection rectum when using LaTME and OpTME in lower rectal cancer, we find a better vision for the distal margin of the tumor using the TaTME technique. In addition, the air-dissection caused by inflation with carbon dioxide would help us in entering the presacral space more easily.[14] Conversely, the poor vision field makes the pelvic dissection more difficult during the abdominal part of the surgery in both LaTME and OpTME, particularly in men and obese patients.[17,18] The pathological margin clearance can be achieved more completely by using TaTME. The CRM uninvolvement rate in the TaTME group was not significantly better than that in the LaTME group, only better than it in OpTME group. The uninvolvement of CRM reflected the better outcome and there was no local recurrence in the TaTME group, and the other two groups were both positive in some patients.

In the past studies, TaTME had a shorter operation time than LaTME. This was mainly because the operation was performed simultaneously by two teams including the trans-abdominal part and trans-anal part, thus saving time for surgery.[15,19] However, we performed trans-abdominal first and followed trans-anal by one team. This is the reason that the operation time will be longer than the other two groups. Although the operation time was slightly longer, it did not affect the results of our post-operative short-term outcomes.

The first step of the trans-anal part in TaTME is to make an air proof purse-string in the rectum. It is relatively difficult to perform purse-string and initial dissection in middle or upper rectum due to a long distance from the anus. The long distance from the anus sometimes forces the surgeon to sacrifice an overly long section of healthy rectum in upper or middle rectal cancer, and it is relatively easy to perform purse-string and dissection from the lower rectum in lower rectal cancer treatment.[20] Therefore, we believe that TaTME can directly visualize the lower edge of the tumor for dissection. In the treatment of lower rectal cancer, it will be better than the other two top-down methods for handling the distal margin and CRM. In our study, the tumor location in the TaTME group was closer to the anus than the other two groups, and its CRM clearance was relatively better than the other two groups, which also showed TaTME has more advantages than LaTME and OpTME in the treatment of low rectal cancer.

In the TaTME group, one patient changed to open surgery because of severe adhesion in the abdominal cavity, but we still did the TaTME procedure trans-anally. The adhesion in the abdominal cavity did not affect the procedure of TaTME but it also provided an air proof barrier in the pelvis to prevent air leakage during Carbon dioxide insufflation. Trépanier et al reported that patients with a second rectal surgery and intra-abdominal adhesions, rectal resection via TaTME may be a better surgical option than via the trans-abdominal method to prevent patients from more operation risk resulting from difficult dissection in the pelvis from abdominal cavity.[21]

Robotic surgery was proposed for the treatment of lower rectal cancer because its visualization of the surgical field in 3-D and dedicated movements in a limited space could be helpful when performing dissection in the pelvic cavity. In one large randomized study in 2017, there was no significant difference in the CRM involvement rate between the robotic-assisted laparoscopic group and the conventional laparoscopic group among patients with rectal cancer (5.7% vs 5.1%, $p = 0.16$; defined as <1 mm).[22] However, only a few studies comparing the result between TaTME and robotic surgery in rectal cancer were reported recently.[23] In our experience, during the cephalic to caudal approach in robotic surgery, the surgeons face the same difficulty when determining the adequate distal margin and CRM.

The most important complications for TaTME are urinary dysfunction and urethral injury, urethral injuries were reported in some early series, the urethral injury rate is 2.5–6.6%.[11,24] We suggest that it is safe and quick to perform dissection from the posterior wall of the rectum in TaTME, and then dissection from the lateral side to the anterior wall of the rectum. Dissection from the posterior to anterior wall can avoid urinary system injury in men,

because the Denonvilliers fascia between the anterior rectal wall and prostate is too thin at the lower rectum level, and it is easy to injure the urinary system (such as the prostate or urethra) if dissection begins from the anterior wall initially. Urinary dysfunction is another concern of TaTME. Although acute urinary dysfunction rate was 8.9%—16%[25,26] after TaTME, Koedam et al reported there is no difference in the bladder function after TaTME or LaTME in short-term and long-term functional outcome.[27] These conflicting results indicate that there will be some study to evaluate the urinary and sexual function in the future.

There are some limitations in our study. First, we initiated the TaTME technique in our hospital from the end of 2014, and the follow-up periods among the three groups were significant difference. The different follow up time may cause some bias in disease free survival and overall survival rate. Second, although there were no significant differences between the three groups in clinical staging and pathological staging, no patient with complete remission and relatively smaller patient number of stage I in OpTME group were noted in our study. It may be that patients in OpTME group are more serious in their own condition, or they have a poor response after pre-operative radiotherapy. Therefore these patients were selected for conventional open surgery, and it made some bias in our oncological and survival results. Third, all TaTME procedures are performed by a single surgeon, in the opposite, LaTME and OpTME are performed by multiple surgeons, and this made some patient selection bias in our study. Finally, the expense of instruments of TaTME and LaTME is not covered by the National Health Insurance in Taiwan; this could result in some degree of selection bias.

In conclusion, TaTME had better pathological and oncological results than OpTME, but it is not superior to LaTME. However TaTME is feasible and safe procedure and it provides surgeons with an effective sphincter-saving method for lower rectal cancer treatment.

Conflict of interest

Drs Yu-Ting Chen, Kee-Thai Kiu, Min-Hsuan Yen and Tung-Cheng Chang have no conflicts of interest or financial ties to disclose.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.asjsur.2018.09.008.

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