Original Article

Comparison of Functional Results between Lower Third Rectal Cancer Patients Underwent Trans-anal Total Mesorectal Excision (TaTME) Associated with Inter-sphincter Resection and Patients Had Laparoscopic Inter-sphincter Resection (ISR) — A Pilot Study

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Key Words
Low rectal cancer;
Trans-anal endoscopic total meso-rectal excision (TaTME);
Laparoscopic inter-sphincteric resection (ISR);
Stool incontinence

Purpose. To investigate the differences of functional results between low rectal cancer patients underwent TaTME + ISR and Laparoscopic ISR.
Patients and Methods. From January 2011 to June 2019, 29 patients with low rectal cancer who underwent neo-adjuvant concurrent chemo-radiotherapy, followed by TaTME + ISR or laparoscopic ISR in Taipei Wan-fang Hospital, were enrolled into our study. 13 patients had TaTME + ISR, as the TaATME + ISR group and 16 patients underwent laparoscopic ISR, as the control group. We used Kirwan grade, and Wexer incontinence score to evaluate the anal function of the rectal cancer patients, three months after their stoma was closed.
Results. There were no differences in age, gender, bowel movements per 24 hours, and the rate of anti-diarrhea drugs use between the two groups. There were also no differences in Wexer score and Kirwan grade between TaTME + ISR and laparoscopic ISR group. But, we found that there were better results of Kirwan grade in TaTME + ISR group. It seems a better trend about anal function in TaTME + ISR group ($p = 0.10$).
Conclusions. TaTME + ISR may be a sphincter-saving procedure with acceptable functional results in patients with low-lying rectal cancers. There was no difference between TaTME + ISR group and laparoscopic ISR group in functional results. But, there was a better trend towards the TaTME + ISR group in Kirwan grade.
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The treatment of low-lying rectal cancer is still a challenging problem in surgery, which must decrease local recurrence rate, increase survival rate and increase the sphincter preservation rate to improve life quality. In the past two decades, abdomino-perineal combined resection (APR) is the gold standard procedure in rectal adenocarcinoma lying within 6 cm from anal verge or less than 2 cm from the Dentate line.[1]

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However, the introduction of inter-sphincter resection (ISR) changed the previous concept. ISR is recommended as a safe sphincter-preserving procedure with acceptable oncological and functional results in low rectal cancer treatment, and a valuable alternative to APR.[2-4]

Recently, laparoscopic ISR have been reported to be a safe and efficient procedure for select patients and have been proved to be a procedure which may decrease hospital stay, reduce postoperative pain, just like other laparoscopic procedures.[5-7] But, laparoscopic rectal surgery is still a difficult procedure in low rectal cancer patients, and high conversion rate was reported up to 17% to 25% in some multi-institute randomized controlled trial,[8,9] which suggest that there are still some unsolved problems about laparoscopic rectal surgery.

Trans-anal total meso-rectal excision (TaTME) was an evolving surgery which achieve the dissection of TME with a down-to-up manner under the guidance of the endoscope, which make the procedure easier than before, especially in male, obese patients or patients with a narrow pelvis.[10-12] In very low rectal cancer, we must perform ISR first, and then close the anal orifice. Under the guidance of endoscopy, mobilization of rectum was done in a down-to-up manner. We call it TaTME + ISR. As our knowledge, there were few functional reports about TaTME and no functional reports about TaTME + ISR.

This study was designed to evaluate the differences of functional results between TaTME + ISR and laparoscopic ISR.

Patients and Methods

Patients selection

From January 2011 to June 2019, we enrolled 33 patients with histologically proven rectal adenocarcinomas that had been defined pre-operatively to have the lower tumor margin within 6 cm from the anal verge as measured by rigid sigmoidoscopy at the Taipei Medical University-Wan-Fang Medical Center. Our inclusion criteria were clinical stage II-III or stage IV with metastatic lesions can be curatively resected, who underwent neo-adjuvant concurrent chemo-radiotherapy, followed by TATME + ISR or laparoscopic ISR. Exclusion criteria were the patients undergoing local excision or APR and who had another malignant tumors. After operation, 4 patients whose stoma could not be closed due to heart failure, cerebral vascular accident or pneumonia, were excluded because their anal functional test cannot be completed. Overall 29 patients were enrolled into our study.

Protocol of pre-operative CCRT

Three-dimensional conformal radiotherapy or intensity modulated radiotherapy was planned on the PINNACLE treatment planning system (Philips, Amsterdam, Netherlands) using 10- or 6-MV X rays to advanced rectal cancer patients. Clinical target volumes (CTVs) included the primary rectal tumor lesions and the two end portions of the rectum; the perirectal tissues; the anterior sacral lymph, iliac lymph, obturator lymph and true pelvis internal iliac lymph drainage areas. The median total dose was 45 Gy delivered to the CTV in 25 fractions of 1.8 Gy without a boost dose. A 5.4-Gy boost comprising 3 fractions of 1.8 Gy to the GTV increased the total dose to 50.4 Gy. During the first and fifth weeks of radiotherapy, fluorouracil was given as a 120-hour continuous infusion at a dose of 1000 mg per square meter per day. In patients who were assigned to preoperative treatment, surgery was scheduled to take place four to six weeks after the completion of chemo-radiotherapy.

Surgery

In laparoscopic ISR group, the abdominal phase, the same as TME originally described by Heald et al.,[13] was performed including high ligation of inferior mesentery artery and mobilization of rectum by sharp dissection to the levator ani under laparoscopic guidance. The perineal phase of ISR, described by Schiessel et al.,[2] included that perineal surgeon entered the inter-sphincteric space at the level of the inter-sphincteric groove, and dissection was continued upwards

between the smooth and striated sphincters. The anal orifice was closed with purse-string suture and then dissection was performed upwards to enter the pelvic cavity to meet abdominal surgeon. Then, the rectum and sigmoid colon was pulled out from right lower quadrant wound. The sigmoid colon was clamped and divided, and then, laparoscopic ISR was completed.

In TaTME + ISR group, the abdominal phase was the same as laparoscopic ISR group. The perineal phase included that surgeon entered the inter-sphincteric space at the level of the inter-sphincteric groove, and the anal orifice was closed with purse-string suture. The Gelpoint path trans-anal platform (Applied Medical, USA) was inserted into anal canal. Carbon dioxide insufflation was applied with the pressure of 10-12 cmH2O. Endoscope was inserted into the platform to light up the retro-peritoneum of pelvic cavity to help the dissection upwards with mono-polar electro-cauterization. Under this condition, the dissection will be done more precisely than ISR. Under the guidance of endoscope, dissection was performed upwards along the endo-pelvic fascia and the perineal surgeon entered the pelvic cavity to meet the abdominal surgeon. Pulled the rectum out from the abdominal port, and the rectum was clamped and divided. TaTME + ISR was completed.

Colon-anal anastomosis was performed with a colonic J pouch or transverse colo-plasty pouch, using the trans-anal hand-sewn technique in all patients. A diverting ileostomy was established in all patients, with closure planned for 3-12 months later.

Functional assessment

Defecation function was evaluated clinically by asking the patient about frequency of bowel movements in 24 hours and continence was assessed by Kirwan classification[14] and Wexerscore,[15] 3 months after the stoma was closed.

Statistical analysis

Frequency tables are used for patients' presentations and treatment characteristics. We used the two-tailed chi-square test for differences in proportions and the Student's t-test for continuous numerical variables. Statistical significance was defined as a value of $p < 0.05$. We compared all study data with Statistical Package for the Social Sciences (SPSS) version 13.0 for Windows (SPSS Inc., Chicago, IL, USA).

Results

There were 13 patients undergo TaTME + ISR and 16 patients who had laparoscopic ISR. Characteristics of the two groups are summarized in Table 1. There were no post-operative deaths. Early complications included one patient had Grade A anastomotic leakage in ISR group, and two patients suffered from pneumonia and chylous ascites in TaTME + ISR group. None required re-operation.

All patients underwent stoma closure with a median of 3 (2-6) months after ISR. Defecation function was assessed 3 months after stoma was closed.

There were no difference about 24 hour bowel frequency and use of anti-diarrhea drug between the TaTME + ISR group and control group (Table 2).

Function results showed that 69% patients had good continence (Kirwan grade I and 2) in TaTME + ISR group and 68% patients had good continence in ISR group. Frequent major soiling (Kirwan grade 4) occurred in 4 patients (25%, 4/16) in ISR group and no patient suffered from frequent major soiling in

Table 1. Characteristics of patients and their tumor in two groups

	ISR	TaTME + ISR	*p*
Age (years)	66 ± 12	65 ± 12	1.0
Sex			1.0
Male	10	8	
Female	6	5	
Clinical stage II	7	7	0.337
Clinical stage III	7	6	
Clinical stage IV	2	0	
Location (cm from anal verge)	4 ± 1.4	4 ± 1.5	0.879
Colonic pouch (no)	6	3	0.454
Colonic pouch (yes)	10	10	
Morbidity	1	2	

Clinical stage, pre-CCRT clinical; CCRT, concurrent chemo-radiotherapy.

TaTME + ISR group (Table 2). There was better Kirwan grade in TaTME + ISR group than ISR group (0.10), but the difference is not statistically significant.

Discussion

As our knowledge, this study is the first report discussing about functional results of TaTME + ISR and the first report which compared functional results of TaTME + ISR with laparoscopic ISR. In TaTME + ISR group, 69% patients had normal or good continence (Kirwan grade 1 and 2) and no patient suffered from frequent major incontinence (Kirwan grade 4). Although the post-operative fecal dysfunction that are caused by excision of the internal anal sphincters and neo-adjuvant CCRT, was questioned, some studies showed relatively satisfactory defecation function after ISR (Table 3). Various researchers have reported a diverse continence level about ISR, which included normal continence (60-79%), major incontinence (0-25%) and need-for-colostomy (0-0.8%).[3,16-18] In our study, there was a relatively good continence level in TaTME + ISR group.

In our opinion, the differences between TaTME + ISR and laparoscopic ISR are perineal part of ISR. After closing anal orifice, the upward dissection was performed in a narrow anal canal and narrow pelvic cavity. This is a dark and narrow space. ISR is a difficult procedure because the space is too narrow to identify the anatomy of rectroperitoneum of the pelvic cavity and the inter-sphincter space. In TaTME + ISR group, the space was filled with CO2 insufflation, and endoscope can offer better vision to dissection than ISR. So, TaTME + ISR may provide more precise dissection than laparoscopic ISR. This is a reasonable result that the functional results of TaTME + ISR may be better than laparoscopic ISR. But the conclusion should be evaluated in some large trials.

Table 2. Functional results between the two groups

	ISR	TaTME + ISR	*p*
Bowel frequency (per 24 hours)	5.4 ± 6.4	3.9 ± 3.7	0.333
Anti-diarrhea drug (no)	5	6	0.468
Anti-diarrhea drug (yes)	11	9	
Wexer Score	5.4 ± 2.8	3.9 ± 3.7	0.593
Kirwan Grade I	10	8	0.10
Grade II	1	1	
Grade III	1	4	
Grade IV	4	0	
Grade V	0	0	

Conclusion

TaTME + ISR is a safe and sphincter-saving procedure in patients with low-lying rectal cancers. There was no difference of functional results between TaTME + ISR and laparoscopic ISR. But there was a better trend towards TaTME + ISR group.

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Table 3. Functional outcomes after an intersphincteric resection for patients with rectal cancer

Author	Year	Number of patients	Evaluation time after stoma closure (months)	Stool frequency	Normal or good continence (%)	Major incontinence (%)
Rullier[16]	2001	21	-	2.5	73%	9.5%
Saito[3]	2006	181	24	-	68%	7%
Yamada[18]	2007	35	12	3.6	60%	0
Chamlou[17]	2007	83	-	2.3	76%	24%
The present study-ISR	2019	16	3	5.4	68%	25%
The present study-TaTME + ISR	2019	13	3	3.9	69%	0

ISR, intersphincteric resection; TaTME, trans anal total mesorectal excision.

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原　著

低位直腸癌患者接受經肛門內視鏡全直腸繫膜切除術合併肛門括約肌間切除術者與接受腹腔鏡肛門括約肌間切除術者之間功能性結果之比較

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目的　探討低位直腸癌患者接受經肛門內視鏡全直腸繫膜切除術合併肛門括約肌間切除術與接受腹腔鏡肛門括約肌間切除術之間肛門功能性的差異。

方法　我們回顧萬芳醫院西元 2011 年 1 月至 2018 年 07 月期間的病歷記錄，共有 29 位病患符合研究條件。其中有 13 位接受經肛門內視鏡全直腸繫膜切除術合併肛門括約肌間切除術，有 16 位接受腹腔鏡肛門括約肌間切除術。我們使用 Kirwan 氏分級及 Wexer 氏肛門失禁指數來評估兩者間在造口關閉三個月後的肛門功能。

結果　兩者之間在年齡、性別、24 小時大便次數、使用抗腹瀉藥物之比例，無明顯差異。在 Wexer 氏肛門失禁指數及 Kirwan 氏分級檢定上，兩者亦無明顯差異。但是接受經肛門內視鏡全直腸繫膜切除術合併肛門括約肌間切除術這組病患，似乎在 Kirwan 氏分級上有較佳的表現 ($p = 0.10$)，但未達統計學上明顯差異。

結論　對於低位直腸癌患者而言，經肛門內視鏡全直腸繫膜切除術合併肛門括約肌間切除術是一個安全可保留肛門的手術治療方式，術後有可接受的肛門功能。在患者接受肛門內視鏡全直腸繫膜切除術合併肛門括約肌間切除術與接受腹腔鏡肛門括約肌間切除術者之間，在功能上無差異。不過前者似乎在 Kirwan 氏分級上有較佳之傾向。

關鍵詞　低位直腸癌、經肛門內視鏡全直腸繫膜切除術、腹腔鏡肛門括約肌間切除術、大便失禁。