

Original Article

Transanal Endoscopic Operation (TEO) in Advanced Rectal Cancer Following Neoadjuvant Chemoradiotherapy: Is It Safe?

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Key Words

Transanal endoscopic operation;
Advanced rectal cancer;
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Purpose. Transanal endoscopic resection has been proposed as an alternative to radical surgery for selected patients but there is still debate with regard to local recurrence and outcomes after neoadjuvant therapy. The aim of this study was to evaluate the oncologic outcome of transanal endoscopic resection for local excision of rectal cancer, and compare patients who had neoadjuvant chemoradiotherapy to those who did not.

Methods. Retrospective analysis of p hod was used to estimate overall survival and disease-free survival. Univariate analysis was included in a stepwise multivariate logistic regression analysis to evaluate the risk factors associated with recurrence.

Results. Of 67 patients undergoing transanal endoscopic resection, 28 patients had neoadjuvant chemoradiotherapy and 39 patients did not. Fragmented specimens (28.6% vs. 10.3%, $p = 0.05$) and suture dehiscence (17.9% vs. 2.6%, $p = 0.031$) were higher in neoadjuvant chemoradiotherapy group vs. no chemoradiotherapy group. After a mean follow-up of 41.5 months, 11 out of 67 patients (16.4%) sustained a local recurrence but no statistically significant difference was found between the two groups (21.4% vs. 12.8%, $p = 0.35$). Pathology T stage ($p < 0.01$), suture dehiscence ($p = 0.01$) and margin positivity ($p = 0.01$) were independent predictors of tumor recurrence.

Conclusion. Transanal endoscopic resection in advanced rectal cancer following neoadjuvant chemotherapy was associated with high suture dehiscence and specimen fragmentation rates and high local recurrence rate after a mean follow up of 41 months. These results imply that transanal endoscopic resection should be reserved to highly selected patients.

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The gold standard management for rectal cancer with regard to oncologic control is total mesorectal excision (TME).¹ Transanal excision (TAE), first proposed by Parks in 1968, is an attractive alternative to radical surgery as it is less invasive, can preclude the need for stoma, preserves organ function and can be achieved with less morbidity and better quality

of life compared with TME.² However, high rates of positive margins and specimen fragmentation have been reported following TAE and this may be a factor of tumor recurrence.³

In 1983, Gerhard Buess innovated transanal endoscopic microsurgery (TEM), which allowed full thickness tumor excision in the middle and upper rectum

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while reducing the need for radical surgery in selected cases.⁴ The purported advantages of TEM included stable visualization, better exposition because of CO₂ pneumorectum, resulting in better specimen quality, lower rates of local recurrence and positive surgical margins compared with TAE.⁵ However, TEM has not gained universal use within the surgical community because of the steep learning curve, the need for specific and complex equipment and high costs.⁶ In the past decade, transanal endoscopic operations (TEO[®] Karl Storz, Germany), a derivative of TEM, have emerged.

In 1988, Marks et al. first reported that local excision was feasible in early rectal cancer after neoadjuvant radiotherapy.⁷ Later Lezoche et al. reported in a randomized clinical trial of TEM versus laparoscopic TME for T2 rectal cancer after neoadjuvant chemoradiotherapy (n-CRT) that oncologic outcomes were comparable in selected patients.⁸ Recently, ACOSOG Z6041 trial showed that local excision was attractive organ-preserving alternative in T2N0 rectal cancer following n-CRT.⁹ However, these trials were limited in highly selective patients and the study of transanal endoscopic resection in advanced rectal cancer following n-CRT was rare.^{10,11}

The aim of this study was to evaluate the feasibility of transanal endoscopic resection by TEO[®] for advanced rectal cancer following n-CRT and report our outcomes, comparing patients who had n-CRT to those who did not.

Material and Methods

From December 2012 through December 2016, all patients undergoing rectal cancer excision by transanal endoscopic resection were prospectively and consecutively enrolled in this study. Data included patient demographics, medical history, tumor size, distance of lower edge of the tumor from the anal verge, circumferential involvement of the lesion, perioperative details, histopathologic findings, postoperative suture dehiscence, tumor recurrence and duration of follow-up. The indications for transanal endoscopic resection in this series included (a) malignant rectal polyp with

margin involvement after colonoscopic mucosal resection, (b) early rectal cancer < cT2N0M0 and tumor size < 1/3 circumference, (c) advanced rectal cancer after n-CRT with clinical complete response or cyT0~2N0M0 and tumor size < 1/3 circumference and (d) patients with cT3N0M0 with poor performance status and deemed unfit for radical surgery. All patients were informed of the possibility of recurrent disease, lymph node or distant metastasis (DM) after local excision by transanal endoscopic resection. Due to the retrospective nature of the study, formal approval was not required and each patient gave informed consent at the outpatient ward after multidisciplinary team discussion. In preoperative workup, the rectal tumor was located and biopsied by colonoscopy. The preoperative staging modality included magnetic resonance imaging (MRI) and/or endorectal ultrasound (EUS) for determining T and N stages in accordance with National Comprehensive Cancer Network guidelines. Computed tomography (CT) or positron emission tomography (PET) were used to assess distant metastasis. Locally advanced rectal cancer was defined as cT3~4 or N1~2 and lower rectum was defined as 0~5 cm from anal verge, middle rectum was 5~10 cm, upper rectum was 10~15 cm. Locally advanced rectal cancer located within 10 cm from the anal verge were indicated for n-CRT in our institution (50.4 Gy radiation divided into 25 fractions and 5-fluorouracil based chemotherapy). Tumor status was re-evaluated in all patients 8 weeks after completion of n-CRT by digital rectal examination, sigmoid fibroscopy, MRI, EUS and carcinoembryonic antigen (CEA).

All surgeries were performed by the same surgical team (eight attending surgeons). All patients were admitted the day before surgery and underwent antegrade mechanical bowel preparation. We used Monobasic & Dibasic Sodium Phosphate 90 ml with single dose for bowel preparation the day before surgery. Prophylactic antibiotics (Cefmetazole 1g) was administered thirty minutes before surgery. Patients were positioned in the lithotomy position regardless of tumor location and all surgeries were performed under general anesthesia. The trans-anal platform was the TEO[®] (Karl Storz Germany) with a 5 mm 30-degree angled scope (Karl Storz Germany). After the TEO[®]

was inserted into the anal canal, a 12 mm Hg pneumorectum was created and then the resection margin was marked by an electrocautery hook 1 cm from the distal tumor border. Partial or full thickness resection, depending on the depth of tumor invasion was performed with the monopolar electrocautery hook. The wound was irrigated with saline and carefully checked for bleeding before closing the defect with a 3-0 V-lock. Patients were allowed to eat normally immediately after operation and scheduled for discharge on post-operative day 1. Post-operatively, follow up included digital rectal examination, CEA, chest X-ray, abdomen and pelvic CT scan every three months, sigmoid fibroscopy six months after operation, and colonoscopy one, three and five years after operation.

Our goal was to compare outcomes between patients who underwent TEO[®] rectal tumor ablation according to whether they had n-CRT or not. The primary endpoint was long-term oncologic outcome while secondary endpoints were margin status, specimen quality and suture dehiscence. Local recurrence (LR) was defined as pelvic lymph node or TEO[®] wound recurrence as determined by clinical, radiological or histological findings. Distal metastasis (DM) was defined as tumor recurrence outside the pelvis with or without LR.¹²

Categorical data is presented as a numbers (percentages), and were compared with the Chi-square or Fisher's exact test as appropriate. Continuous data is expressed as means \pm standard deviations (SD), and were compared with the Student t-test. The Kaplan-Meier method was used to estimate overall survival (OS) and disease-free survival (DFS). *p* values less than 0.05 were considered to be statistically significant. Variables with *p* values $<$ 0.05 from univariate analysis were included in a stepwise multivariate logistic regression analysis to evaluate the risk factors associated with recurrence. All statistical analyses were performed with SPSS for Windows (version 19.0; IBM-SPSS Inc., Armonk, NY).

Results

Between December 2012 and December 2016,

532 consecutive patients with rectal cancer underwent surgery at China Medical University Hospital, Taichung, Taiwan. Of these, 67 patients with rectal cancer undergoing TEO[®] were divided into two groups according to whether they underwent n-CRT (*n* = 28) or not (*n* = 39) and form the population of this study. Patient and tumor characteristics for each group are indicated in Table 1. There were no statistically significant differences in patient characteristics (age, sex, BMI and ASA) between the two groups. With regard to tumor characteristics, the only statistically significant differences between the two groups were the distance between the tumor and anal verge (4.5 ± 1.7 cm vs. 6.5 ± 3.2 , *p* = 0.03) and the number of patients cN+ (8 (28.6%) vs. 0 (*p* = 0.02) in n-CRT vs. non n-CRT, respectively).

Pathology characteristics are given in Table 2. The only statistically significant differences were in the rate of fragmented specimens, higher in n-CRT than in no CRT (28.6% vs. 10.3%, *p* = 0.05).

Operative characteristics are given in Table 3. Statistically significant differences were found in mean operative time (122.8 ± 60.3 vs. 93.6 ± 55.0 , *p* = 0.05) and suture dehiscence (17.9% vs. 2.6%, (*p* = 0.031) in n-CRT vs. non n-CRT, respectively. Among the patients with suture dehiscence, three were treated conservatively while three patients required reoperation including one diverting colostomy while two patients underwent laparoscopic total mesorectal excision. Seven patients underwent further radical surgery 3 months after TEO[®] and five patients had salvage radical surgery for LR. At a mean follow-up of 41.5 ± 14.6 months, there were 15 patients having tumor recurrence and details were described in Table 4. 11 out of 67 patients (16.4%) sustained a LR but no statistically significant difference was found between the two groups (21.4% vs. 12.8%, *p* = 0.35).

Overall mortality was statistically significantly higher in patients undergoing n-CRT (21.4% vs. 5.1%, *p* = 0.04) but there was no statistically significant difference in cancer specific mortality (7.1% vs. 2.6%, *p* = 0.37) (Table 3), 3-year OS (85% vs. 96%), 3-year cancer specific survival (95% vs. 98%), or 3-year DFS (74% vs. 79%) (Figs. 1-3) in patients undergoing n-CRT vs. non n-CRT, respectively.

Table 1. Patient and tumor characteristics

	All (n = 67)	n-CRT (n = 28)	Non n-CRT (n = 39)	p value
Age (years)	62.7 ± 12.7	64.3 ± 13.2	61.5 ± 12.3	0.62
Sex				0.23
Male	35 (52.2%)	13 (46.4%)	22 (56.4%)	
Female	32 (47.8%)	15 (53.6%)	17 (43.6%)	
BMI (kg/m ²)	25.2 ± 4.1	25.1 ± 3.4	25.2 ± 4.6	0.68
ASA				0.55
1	12 (17.9%)	4 (14.3%)	8 (20.5%)	
2	30 (44.8%)	13 (46.4%)	17 (43.6%)	
3	25 (37.3%)	11 (39.3%)	17 (35.9%)	
Distance from anal verge (cm)	5.7 ± 2.8	4.5 ± 1.7	6.5 ± 3.2	0.03
Tumor site				0.14
Lower rectum	41 (61.2%)	20 (71.4%)	21 (53.8%)	
Middle rectum	19 (28.4%)	8 (28.6%)	11 (28.2%)	
Upper rectum	7 (10.4%)	0	7 (17.9%)	
Tumor location				0.83
Anterior	14 (20.9%)	5 (17.9%)	9 (23.1%)	
Right lateral	18 (26.9%)	8 (28.6%)	10 (25.6%)	
Left lateral	12 (17.9%)	5 (17.9%)	7 (17.9%)	
Posterior	23 (34.3%)	10 (35.7%)	13 (33.3%)	
Clinical stage				0.01
cTx	10 (14.9%)	0	10 (25.6%)	
cT0	3 (4.4%)	0	3 (7.7%)	
cT1	13 (19.4%)	0	13 (33.3%)	
cT2	13 (19.4%)	3 (10.7%)	10 (25.6%)	
cT3	27 (40.2%)	24 (85.7%)	3 (7.7%)	
cT4	1 (1.5%)	1 (3.5%)	0	
cN				0.02
Negative	59 (88%)	20 (71.4%)	39 (100%)	
Positive	8 (12%)	8 (28.6%)	0	
Interval between CRT and surgery (days)		73.7 ± 36.0		

n-CRT, neoadjuvant chemoradiotherapy.

Table 2. Pathology characteristics

	All (n = 67)	n-CRT (n = 28)	Non n-CRT (n = 39)	p value
Tumor size (cm)	1.38 ± 1.51	0.88 ± 0.86	1.73 ± 1.78	0.39
Pathology T stage				
Tx (no residual tumor)			10 (25.6%)	
Tis			5 (12.8%)	
T1			13 (33.3%)	
T2			8 (20.5%)	
T3			3 (7.7%)	
T4			0	
ypTx (complete response)		10 (35.7%)		
ypTis		1 (3.5%)		
ypT1		7 (25.0%)		
ypT2		5 (17.8%)		
ypT3		5 (17.8%)		
Margin positive	12 (17.9%)	7 (25.0%)	5 (12.8%)	0.21
Fragmentation	12 (17.9%)	8 (28.6%)	4 (10.3%)	0.05
Cell differentiation				0.90
Well	19 (28.4%)	9 (32.1%)	10 (25.6%)	
Moderate	37 (55.2%)	18 (64.3%)	19 (48.7%)	
Poor	3 (4.5%)	1 (3.6%)	2 (5.1%)	
Lymphovascular invasion	2 (3%)	0	2 (5.1%)	0.22
Perinural invasion	3 (4.5%)	1 (3.6%)	2 (5.1%)	0.76

Table 3. Perioperative characteristics and oncologic outcome

	All	n-CRT	Non n-CRT	<i>p</i> value
Duration of operation (min)	105.8 ± 58.7	122.8 ± 60.3	93.6 ± 55.0	0.05
Blood loss (cc)	7.3 ± 32.6	4.0 ± 19.0	9.7 ± 40.0	0.99
Hospital stay (days)	2.42 ± 2.27	3.04 ± 3.00	1.97 ± 1.44	0.09
Suture dehiscence	6 (9%)	5 (17.9%)	1 (2.6%)	0.03
Reoperation	3 (4.5%)	3 (10.7%)	0	0.04
Radical surgery	12 (17.9%)	7 (25.0%)	5 (12.8%)	0.20
Local recurrence	11 (16.4%)	6 (21.4%)	5 (12.8%)	0.35
Distal metastases	10 (14.9%)	6 (21.4%)	4 (10.2%)	0.21
Follow up duration (months)	41.46 ± 14.59	42.89 ± 16.25	40.44 ± 13.40	0.32
Delay to recurrence time (months)	18.50 ± 10.58	15.1 ± 9.73	21.47 ± 11.00	0.85
Overall mortality	8 (13.4%)	6 (21.4%)	2 (5.1%)	0.04
Cancer specific mortality	3 (4.5%)	2 (7.1%)	1 (2.6%)	0.37

Table 4. Patients with tumor recurrence

Case number	Image stage	pT	Margin status	n-CRT	Radical surgery	Time to recurrence (months)	LR	DM	Suture dehiscence
1	II	3	Positive	Yes	No	5	Intraluminal	Adrenal	No
2	I	1	Negative	No	No	17	Intraluminal	Nil	Yes
3	I	2	Negative	No	No	19	Intraluminal + lymph node	Nil	No
4	II	2	Negative	No	No	36	Intraluminal	Carcinomatosis	No
5	II	3	Positive	Yes	Yes	6	Intraluminal	Lung, Liver, Bone	Yes
6	II	3	Negative	Yes	No	16	Lymph node	Lung	Yes
7	I	2	Negative	No	Yes	22	Nil	Liver	No
8	I	1	Negative	No	No	10	Intraluminal	Nil	No
9	II	1	Negative	Yes	No	12	Intraluminal	Lung	No
10	I	CR	Negative	Yes	No	8	Nil	Lung	Yes
11	II	3	Positive	Yes	No	10	Intraluminal	Lung	No
12	II	3	Negative	No	No	29	Intraluminal	Nil	No
13	II	2	Positive	No	No	4	Nil	Lung	No
14	I	2	Positive	No	No	14	Nil	Liver	No
15	I	2	Positive	Yes	No	12	Intraluminal	Nil	No

Univariate analysis identified pathology T stage ($p < 0.01$), suture dehiscence ($p = 0.01$) and margin positivity ($p = 0.01$) as being statistically significantly associated with tumor recurrence. After multivariate analysis, pathology T stage (OR = 6.782), suture dehiscence (OR = 7.910) and margin positivity (OR = 4.764) remained statistically significant for tumor recurrence (Table 5).

Discussion

In this single center series of 67 patients, morbidity (suture dehiscence) and mortality occurred more

frequently in patients undergoing n-CRT (compared to those who did not), while pathology T stage (OR = 6.782), suture dehiscence (OR = 7.910) and margin positivity (OR = 4.764) were found to be independent predictive factors of tumor recurrence.

Radical surgery for rectal cancer has been associated with high postoperative morbidity leading surgeons to search for alternatives such as local excision while also preserving organ function. Some authors reported that oncologic outcomes after local excision seemed acceptable in highly selected patients with rectal cancer,^{13,14} and one prospective study showed that n-CRT followed by TEM offered comparable oncologic outcome to initial TME.⁸ However, for

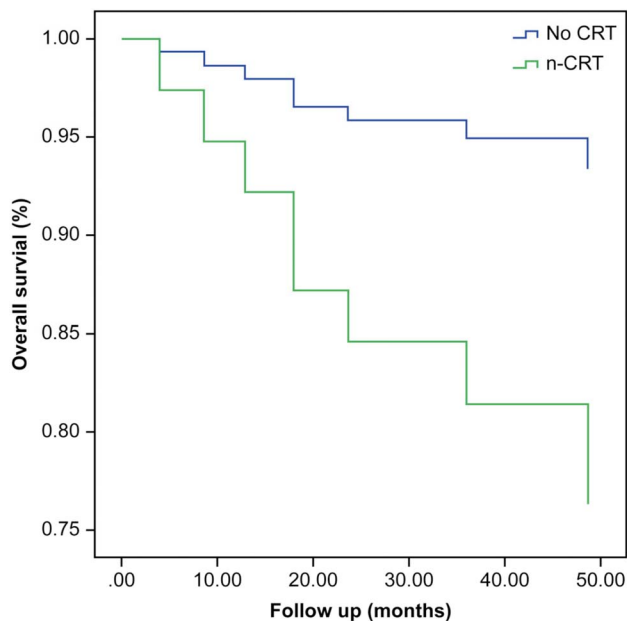


Fig. 1. 3-year overall survival.

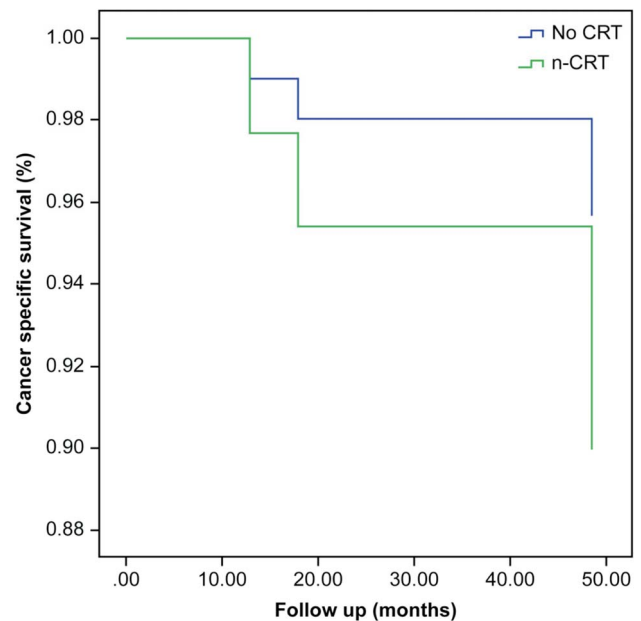


Fig. 2. 3-year cancer specific survival.

others, the oncologic outcome after local excision is still debatable because of potential occult lymph node metastasis,^{10,15} aggressive tumor characteristics,¹⁶ incomplete resection^{12,17} or high morbidity in case of recurrence.¹⁸ Most of these studies concerned TEM.

Among the studies on n-CRT followed by TEM, Lezoche et al. reported a 13% complication rate including a 8% suture dehiscence.¹⁹ Wound dehiscence following TEM after n-CRT is a major concern. Several authors have implied that dehiscence is associated with LR, residual pain and hospital readmission.^{10,18,20-22} Perez et al. reported a 70% wound dehiscence rate after n-CRT compared with 23% in the control group ($p = 0.03$).¹⁸ Possible explanations for high suture dehiscence rates could be compromised wound healing in irradiated tissue and the usage of rigid rectoscope causing trauma of surrounding tissues. In our study, six patients had suture dehiscence (17.9% vs. 2.6%, $p = 0.03$ for n-CRT vs. no CRT) while three patients needed a second operation for pelvic abscess. Among these, four patients developed tumor recurrence (local recurrence ($n = 1$), distal metastasis ($n = 1$), LR and DM ($n = 2$)). Of note, one patient had a complete response on pathology but developed LR and lung metastasis eight months after suture dehiscence. In contrast to previous series in the literature, we found that

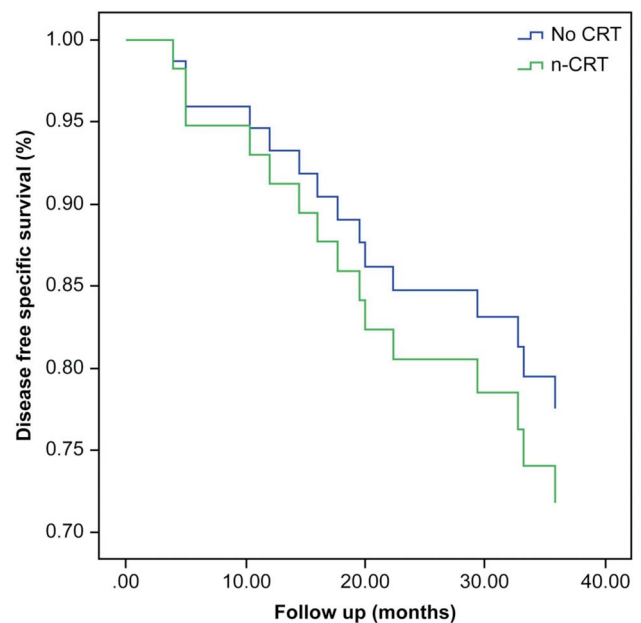


Fig. 3. 3-year disease free survival.

patients with suture dehiscence were more likely to have tumor recurrence (26.7% vs. 3.8%, $p = 0.01$). One possible explanation is that suture dehiscence may lead to extraluminal implantation of viable cancer cells and the increased systemic inflammatory response might enhance tumor spread.^{23,24}

Of 67 patients in our series, 11 had LR (10 were intraluminal, one was extraluminal (presacral lymph

Table 5. Predictors of tumor recurrence

	Recurrence (n = 15)	No recurrence (n = 52)	<i>p</i> value	OR (95% CI) Multivariate analysis
Age	62.93 ± 13.03	62.58 ± 12.66	0.09	
Sex			0.62	
Male	7 (46.7%)	28 (53.8%)		
Female	8 (53.3%)	24 (46.2%)		
BMI		24.94 ± 3.96	0.30	
ASA			0.68	
1	2 (13.3%)	10 (19.2%)		
2	6 (40.0%)	24 (46.2%)		
3	7 (46.7%)	18 (34.6%)		
Distance from anal verge (cm)	5.27 ± 3.11	5.79 ± 2.77	0.49	
Tumor site			0.55	
Lower rectum	11 (73.3%)	30 (57.7%)		
Middle rectum	3 (20.0%)	16 (30.8%)		
Upper rectum	1 (6.7%)	6 (11.5%)		
Tumor location			0.15	
Anterior	0	14 (26.9%)		
Right lateral	5 (33.3%)	13 (25.0%)		
Left lateral	4 (26.7%)	8 (15.4%)		
Posterior	5 (40.0%)	17 (32.7%)		
Clinical stage			0.78	
cTx	1 (6.7%)	9 (17.3%)		
cT0	0	3 (5.8%)		
cT1	2 (13.3%)	11 (21.2%)		
cT2	4 (26.7%)	9 (17.3%)		
cT3	8 (53.3%)	19 (36.5%)		
cT4		1 (1.9%)		
cN			0.16	
cN (-)	15 (100%)	44 (84.6%)		
cN (+)	0	8 (15.4%)		
Tumor size (cm)	3.31 ± 1.65	2.32 ± 1.88	0.697	
n-CRT			0.664	
Yes	7 (46.7%)	21 (40.4%)		
No	8 (53.3%)	31 (59.6%)		
Pathology T stage			< 0.01	6.782 (1.114-41.699)
T0, TIS, T1	4 (26.7%)	41 (78.8%)		
T2, T3	11 (73.3%)	11 (21.2%)		
Cell differentiation			0.23	
Well	3 (20%)	16 (30.8%)		
Moderate	12 (80%)	25 (48.1%)		
Poor	0	3 (5.8%)		
LVI	0	2 (3.8%)	0.44	
PNI	1 (6.7%)	2 (3.8%)	0.64	
Duration of operation (min)	124.53 ± 75.68	100.40 ± 52.41	0.85	
Blood loss (cc)	10.00 ± 38.73	6.54 ± 30.93	0.83	
Suture dehiscence	4 (26.7%)	2 (3.8%)	0.01	7.910 (0.348-114.630)
Fragmentation	4 (26.7%)	8 (15.4)	0.32	
Positive margins	6 (40%)	6 (11.5%)	0.01	4.764 (0.236-96.264)

node recurrence)). Of note, all 11 were considered as LN-on preoperative MRI. Conversely, none of the patients who were LN+ had local recurrence. This is in line with Junginger et al. who reported 100 patients with pT1 rectal cancer treated with TEM: all LR were

intraluminal.¹³ In this study the authors incriminated minimal clearance margins < 1 mm as the main cause of LR. The authors concluded that LR was related to viable cancer implantation in the excision site rather than undetected lymph node metastasis. In our study,

there were 12 patients with positive margins and 6 out of 12 had tumor recurrence vs. 9/55 (16.3%) after complete resection. Univariate and multivariate logistic regression analysis found that positive margins were an independent risk factor of tumor recurrence in our study.

Another major concern with regard to surgical quality is specimen fragmentation potentially resulting in incomplete microscopic examination of margin status. Our specimen fragmentation rate was relatively high (17.9%) compared to the TEO[®] literature (1.4%-6.5%).^{25,26} Moreover, fragmentation was higher in n-CRT vs. no CRT (28.6% vs. 10.3%, $p = 0.05$). In our institution, TEO[®] was performed by eight well-experienced laparoscopic surgeons. One must remember that TEO[®] is single port laparoscopic surgery, uses a rigid rectoscope, more difficult to handle than “soft” platforms with a steep learning curve:²⁶ in the study by Hur, the fragmentation rate was 12% for the first 17 consecutive cases and then decreased to 3% in the last 29 cases. In accordance to the outcome of this study, possible explanations of the high fragmentation rate in our study could be unfamiliar with the TEO[®] system meaning it should be performed by surgeons who are well-trained in laparoscopic single port surgery.

Lezoche et al. reported a 5% local failure rate and an 89% cancer specific survival rate at 90 months follow up in patients with T2-3 N0 distal rectal cancer undergoing n-CRT followed by local excision.²⁰ The same authors also reported that oncologic outcomes did not differ between patients undergoing endoluminal locoregional resection versus laparoscopic total mesorectal excision for T2 rectal cancer after n-CRT in a randomized trial:⁸ similar oncologic results were found in the ACOSOG Z6041 trial, 3-year disease free survival was 88.2% for patients with cT2N0 rectal adenocarcinoma measuring less than 4 cm in greatest diameter and involving no more than 40% of the rectal circumference, located within 8 cm of the anal verge, and with an Eastern Cooperative Oncology Group performance status of no less than 2.⁹ The outcome of these studies suggest that local excision might be an attractive alternative for highly selective patients with T2-3, N0 rectal cancer after CRT. Conversely, the literature on oncologic outcome after lo-

cal excision for local advanced rectal cancer (T3~4 or N+) following CRT is limited. Perez et al. reported the outcomes of TEM for residual rectal cancer (ypT0-2) following CRT: local failure was 15% after a median follow up of 15 months.¹⁰ Of the 27 patients in this study, 15 were cT3 while five were N+. In our study, 24 patients had cT3 tumors and eight were N+. Our LR rate was 16.4% and the DM rate was 14.9% after mean follow up time of 41 months, similar to the outcomes reported by Perez et al.¹⁰

Our study has several limitations. It is a retrospective analysis of a single institution case series, the sample is small, and it is possible that poor performance status of patients deemed unfit for more radical surgery may have biased the survival rate. In our study, suture dehiscence was higher in patients undergoing n-CRT which in turn was performed in patients with higher T and N stage, and therefore the relationship between suture dehiscence on tumor recurrence may be multifactorial. There were eight attending surgeons that contributed to our study, and different specimen quality may be led to different oncologic outcomes.

In conclusion, transanal endoscopic resection performed for advanced rectal cancer after n-CRT was associated with high suture dehiscence and specimen fragmentation rates with high LR and DM rates after mean follow up time of 41 months. Pathology T stage, suture dehiscence and positive margins were strong predictors of tumor recurrence in our study. Although this was a single center case series, our results suggest that transanal endoscopic resection may not be suitable for locally-advanced rectal cancer after n-CRT and should only be proposed to highly selected patients with complete response, duly warned of possible unfavorable outcomes.

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References

- MacFarlane JK, Ryall RDH, Heald RJ. Mesorectal excision for rectal cancer. *Lancet* 1993;341:457-60.
- Parks AG. A technique for excising extensive villous papillomatous change in the lower rectum. *Proc R Soc Med* 1968; 61:441-2.
- Sakamoto GD, MacKeigan JM, Senagore AJ. Transanal excision of large, rectal villous adenomas. *Dis Colon Rectum* 1991;34:880-5.
- Buess G, Hutterer F, Theiss J, Pichlmaier H. A system for a transanal endoscopic rectum operation. *Chirurg* 1984;55: 677-80.
- Clancy C, Burke JP, Albert MR, O'Connell PR, Winter DC. Transanal endoscopic microsurgery versus standard transanal excision for the removal of rectal neoplasms: a systemic review and meta-analysis. *Dis Colon Rectum* 2015;58:254-61.
- Maslekar S, Pillinger SH, Sharma A, Taylor A, Monson JRT. Cost analysis of transanal endoscopic microsurgery for rectal tumors. *Colorectal Dis* 2007;9:229-34.
- Marks G, Mohiuddin M, Goldstein SD. Sphincter preservation for cancer of the distal rectum using high-dose preoperative radiation. *Int J Radiat Oncol Biol Phys* 1988;15:1065-8.
- Lezoche E, Baldarelli M, Lezoche G, Paganini AM, Gesuita R, Guerrieri M. Randomized clinical trial of endoluminal locoregional resection versus laparoscopic total meso rectal excision for T2 rectal cancer after neoadjuvant therapy. *Br J Surg* 2012;99:1211-8.
- Garcia-Aguilar J, Renfro LA, Chow OS, et al. Organ preservation for clinical T2N0 distal rectal cancer using neoadjuvant chemoradiotherapy and local excision (ACOSOG Z6014): results of an open-label, single arm, multi-institutional phase 2 trial. *Lancet Oncol* 2015;16:1537-46.
- Perez RO, Habr-Gama A, Lynn PB, et al. Transanal endoscopic microsurgery for residual rectal cancer (yp T0-2) following neoadjuvant chemoradiation therapy: another word of caution. *Dis Colon Rectum* 2013;56:6-13.
- Rizzo G, Zaccone G, Magnocavallo M, et al. Transanal endoscopic microsurgery after neoadjuvant radiotherapy for locally advanced extraperitoneal rectal cancer. *EJSO* 2017;43: 1488-93.
- Junginger T, Goenner U, Hitzler M, et al. Analysis of local recurrence after transanal endoscopic microsurgery for low risk carcinoma. *Int J Colorectal Dis* 2017;32:265-71.
- Lezoche G, Guerrieri M, Baldarelli M, et al. Transanal endoscopic microsurgery for 135 patients with small non-advanced low rectal cancer (iT1-iT2, iN0): short- and long-term results. *Surg Endosc* 2011;25:1222-9.
- Tsai BM, Finne CO, Nordenstam JF, Christoforidis D, Madoff RD, Mellgren A. Transanal endoscopic microsurgery resection of rectal tumors: outcomes and recommendations. *Dis Colon Rectum* 2010;53:16-23.
- Landmann RG, Wong WD, Hoepfl J, et al. Limitation of early rectal cancer nodal staging may explain failure after local excision. *Dis Colon Rectum* 2007;50:1520-5.
- Junginger T, Goenner U, Hitzler M, et al. Long-term results of transanal endoscopic microsurgery after endoscopic polypectomy of malignant rectal adenoma. *Tech Coloproctol* 2017;21:225-32.
- Bach SP, Hill J, Monson JRT, et al. A predictive model for local recurrence after transanal endoscopic microsurgery for rectal cancer. *Br J Surg* 2009;96:280-90.
- Perez RO, Habr-Gama A, São Julão GP, Proscurshim I, Neto AS, Gama-Rodrigues J. Transanal endoscopic microsurgery for residual rectal cancer after neoadjuvant chemoradiation therapy is associated with significant immediate pain and hospital readmission rates. *Dis Colon Rectum* 2011;54:545-51.
- Lezoche E, Guerrieri M, Paganini AM, Baldarelli M, Sanctis AD. Long-term results in patients with T2-3 N0 distal rectal cancer undergoing radiotherapy before transanal endoscopic microsurgery. *Br J Surg* 2005;92:1546-52.
- Garcia-Aguilar J, Shi Q, Thomas CR, et al. A phase II trial of neoadjuvant chemoradiation and local excision for T2N0 rectal cancer: preliminary results of the ACOSOG Z6041 trial. *Ann Surg Oncol* 2012;19:384-91.
- Lee BC, OH S, Lim SB, Yu CS, Kim JC. Transanal minimally-invasive surgery for treating patients with regressed rectal cancer after preoperative chemoradiotherapy. *Ann Coloproctol* 2017;33:52-6.
- Marks JH, Valsdottir EB, DeNittis A, et al. Transanal endoscopic microsurgery for the treatment of rectal cancer: comparison of wound complication rates with and without neoadjuvant radiation therapy. *Surg Endosc* 2009;23:1081-7.
- Walker KG, Bell SW, Matthew J, et al. Anastomotic leakage is predictive of diminished survival after potentially curative resection for colorectal cancer. *Ann Surg* 2004;240:255-9.
- Mirnezami A, Mirnezami R, Chandrakumaran K, et al. Increased local recurrence and reduced survival from colorectal cancer following anastomotic leak: systematic review and meta-analysis. *Ann Surg* 2011;253:890-9.
- Han J, Noh GT, Cheong C, et al. Transanal endoscopic operation versus conventional transanal excision for rectal tumors: case matched study with propensity score matching. *World J Surg* 2017;41:2387-94.
- Hur H, Bae SU, Han YD, Kang J, Min BS, Baik SH, Lee KY, Kim NK. Transanal endoscopic operation for rectal tumor: short-term outcomes and learning curve analysis. *Surg Laparosc Endosc Percutan Tech* 2016;26:236-43.

原 著

經肛門內視鏡手術運用於侵犯性直腸癌 新輔助化放療後

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目的 經肛門內鏡切除術已被作為特定患者根治性手術的替代方案，但仍然存在較高復發率的爭論。本研究的目的是評估經肛門內鏡切除術治療局部切除直腸癌，並比較接受新輔助放化療的患者與未接受新輔助放化療的患者。

方法 病人收集於 2012 年至 2016 年區間。Kaplan-Meier method 運算存活率和復發率。使用單因素分析包括在逐步多變量邏輯回歸分析中，以評估與復發相關的風險因素。

結果 67 例接受經肛門內鏡切除術的患者中，28 例接受新輔助放化療，39 例未接受新輔助放化療。新輔助放化療組與未放化療組相比，碎片標本 (28.6% 對比 10.3%， $p = 0.05$) 和縫合開裂 (17.9% 對 2.6%， $p = 0.031$) 更高。平均術後追蹤為 41.5 個月，67 例患者中有 11 例 (16.4%) 出現局部復發，但兩組之間無統計學差異 (21.4% 對 12.8%， $p = 0.35$)。病理學 T 分期 ($p < 0.01$)，縫線裂開 ($p = 0.01$) 和邊緣陽性 ($p = 0.01$) 是腫瘤復發的獨立預測因子。

結論 新輔助化放療後經肛門內鏡下切除術與高位縫合開裂和標本碎裂率有關，平均術後追蹤 41 個月後局部復發率較高。這些結果意味著經肛門內視鏡切除術應保留給高度選擇的患者。

關鍵詞 經肛門內視鏡切除術、侵犯性直腸癌、新輔助化放療。