

Original Article

# Laparoscopic Total Mesorectal Excision in Locally Advanced Rectal Cancer

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**Key Words**

Rectal cancer;  
Laparoscopic;  
Total mesorectal excision;  
Neoadjuvant chemoradiotherapy;  
Chemoradiation

**Purpose.** The efficacy of laparoscopic total mesorectal excision (TME) in locally advanced rectal cancer has not been demonstrated. The aim of the study is to evaluate the outcome of rectal cancer patients undergoing neoadjuvant chemoradiotherapy followed by laparoscopic TME in our hospital.

**Methods.** Between January 2006 and December 2013, 90 locally advanced rectal cancer patients that underwent neoadjuvant chemoradiotherapy followed by laparoscopic TME were enrolled. The clinicopathological and surgical data of these patients were collected and retrospectively analyzed.

**Results.** Of the 90 patients, 71.1% were men. The mean age of all patients was 59.2 years. The average distance of tumor location from the anal verge was 5.2 cm. The average interval between neoadjuvant chemoradiotherapy completion and surgery was 59 days. Only one patient required conversion (1.11%) to open surgery. Among 90 patients, 80% of the patients underwent sphincter-preserving operation. The 30-day mortality rate was 0%, and the mean hospital stay was 7.2 days. Three patients (3.3%) presented with anastomotic leakage. Local recurrence occurred in three patients (3.3%), whereas distant metastases occurred in 10 patients (11.1%). The 5-year overall survival rate was 75%, and the 5-year disease-free survival rate was 68%.

**Conclusions.** Laparoscopic surgery after neoadjuvant chemoradiotherapy in patients with locally advanced rectal cancer is feasible and appropriate. It can provide good short-term clinical and oncological outcomes.

[J Soc Colon Rectal Surgeon (Taiwan) 2015;26:150-156]

Several randomized controlled trials have demonstrated that laparoscopic colectomy is the standard treatment for colon cancer.<sup>1-4</sup> Total mesorectal excision (TME) became a widely adopted procedure for rectal surgery since Heald reported its association with decreased local recurrence in 1987. The COLOrectal cancer Laparoscopic or Open Resection (COLOR II) trial showed that laparoscopic rectal surgery shows re-

sults similar to open surgery in terms of safety, resection margins, and resection completeness with improved postsurgical recovery.<sup>6</sup> Therefore, this procedure has been considered to be safe and feasible when performed by experienced surgeons at specialized centers.

The National Surgical Adjuvant Breast and Bowel Project R-03 (NSABP R-03) trial showed improved

Received: April 13, 2015.

Accepted: September 15, 2015.

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disease-free survival with preoperative chemoradiotherapy. A German study (CAO/ARO/AIO-94 trial) revealed good local control and higher rates of sphincter-preserving surgery for rectal cancer after neoadjuvant chemoradiotherapy.<sup>7-9</sup>

The aim of this study is to evaluate the short- and long-term outcomes of rectal cancer patients undergoing neoadjuvant chemoradiotherapy followed by laparoscopic TME.

## Materials and Methods

### Patients

Between January 2006 and December 2013, 757 patients were diagnosed with rectal cancer. Among them, 176 patients presented with locally advanced rectal cancer. We excluded patients who underwent open surgery, robotic surgery, and transanal minimally invasive surgery (TAMIS). Patients who received reverse TME were included in the TAMIS group. The final sample consisted of 90 patients treated using laparoscopic techniques (Fig. 1).

Locally advanced rectal cancer was defined as

- (1) Tumor located within 15 cm from the anal verge
- (2) Clinical stage is (i) T3 and T4 stage or (ii) any N<sup>+</sup> stage.

We classified the rectum into low rectum ( $\leq 5$  cm from the anal verge), middle rectum (6-10 cm from the anal verge), and upper rectum (11-15 cm from the anal verge). We excluded patients with emergent operations or synchronous distant metastases. All of them received neoadjuvant chemoradiation.

Each patient received digital rectal examination to evaluate sphincter function and tumor location. Colonoscopy was performed with biopsy. Clinical stage was determined before neoadjuvant chemoradiotherapy using computed tomographic (CT) scans of the abdomen and pelvis combined with transrectal ultrasound or magnetic resonance imaging (MRI). Pelvic MRI was used for re-evaluation of clinical staging before the operation. Chest X-ray or chest CT scan and liver ultrasound were performed to exclude distant metastases. We analyzed clinicopathological features such

as age, sex, neoadjuvant regimen, pathological T and N stage, tumor response, histologic grade, hospital stay, perioperative morbidity, overall survival, and disease-free survival.

### Neoadjuvant chemoradiation protocol

All patients received preoperative, long-course radiotherapy, consisting of a total of 5040 cGy. During radiotherapy, patients also received intravenous 5-FU or oral capecitabine as a form of chemotherapy.

### Surgical technique

Preoperative bowel preparation was performed in all patients with monobasic and dibasic Sodium Phosphate (90 mL) or polyethylene glycol (2 L). All laparoscopic TMEs were performed by experienced surgeons. The splenic flexure was mobilized to ensure a tension-free anastomosis, and the inferior mesentery artery was ligated and divided at its origin. The rectum was sharply mobilized along the anatomic plane to maintain the integrity of the mesorectum. A temporary ileostomy or T-loop stoma was performed, depending on the surgeon's evaluation of the quality of anastomosis.

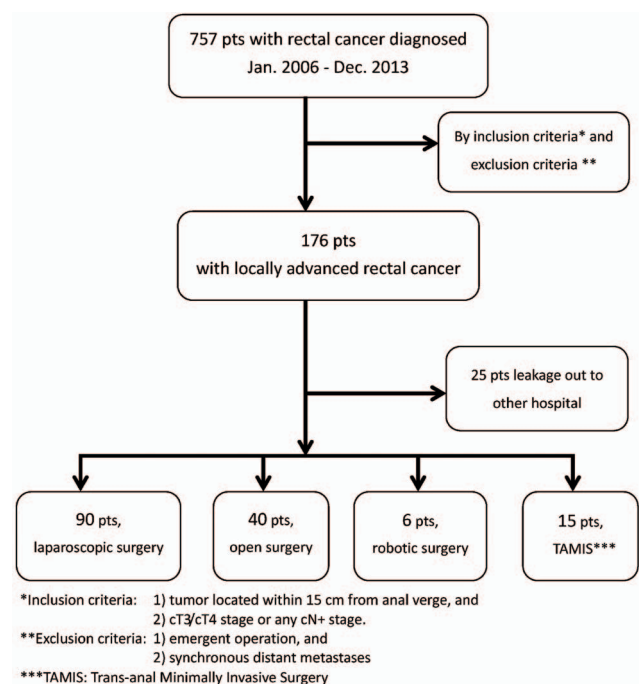


Fig. 1. Flow chart of the patient collection.

## Statistical analysis

All data are presented as median values with ranges. Disease-free survival and overall survival after treatment were analyzed using the Kaplan-Meier method, and statistically significant differences in survival were identified by the log rank test. All statistical analyses were performed using SPSS version 14.0 (SPSS Inc., Chicago, IL, USA).

## Results

### Preoperative

Our final sample had an average age of 59.2 years, with male predominance (71.1%). The basic patient characteristics including body mass index, American Society of Anesthesiologist (ASA) score, and comorbidities are presented in Table 1. There were four patients with other primary cancers and one patient with synchronous colon cancer (at the splenic flexure). The duration between completion of radiation and operation was an average of 59 days. One patient (1.1%) had upper rectal cancer, 33 (36.7%) had middle rectal cancer, and 56 (62.2%) had lower rectal cancer. The mean distance of the tumor from the anal verge was 5.2 cm. Five patients (5.6%) were at cT2 stage, 82 (91.1%) at cT3 stage, and three (3.3%) at cT4 stage. Forty-three patients (47.8%) were at cN0 stage and 47 (52.2%) at cN+ stage (Table 1).

### Perioperative

Laparoscopic techniques were initiated in all 90 patients. One patient required conversion to open TME (1.11%) because of severe local invasion. TME with staple anastomosis or coloanal anastomosis was performed in 80% of the patients (72/90). The remaining patients were treated with laparoscopic abdominopereineal resection. Of all TMEs performed, 71 patients (98.6%) had a temporary stoma. The sphincter-preserving rates for the different parts of the rectum were 100% (upper rectum), 97% (middle rectum), and 69.7% (lower rectum; Table 3). Mean operative time was 192

min (range: 115-242 min), and the mean estimated blood loss was 135 mL (range: 30-600 mL). Two patients required blood transfusion in the operating room (Table 2).

### Postoperative

The mean duration of hospital stay was 7.2 days

**Table 1.** The basic characteristics of 90 patients who underwent laparoscopic TME

Age (mean), years	59.2 (32-85)
Sex	71.1% male
BMI (mean), kg/m <sup>2</sup>	23.5 (15.7-35.7)
ASA score	
1-2	85.6%
3	14.4%
Comorbidity	
Diabetes mellitus	12.2%
Hypertension	18.9%
Old cerebral vascular accident	2.2%
End-stage renal disease	2.2%
Chronic hepatitis	3.3%
Chronic obstructive pulmonary disease	3.3%
Other primary cancer	4
Synchronous colon cancer	1 (at splenic flexure)
Preoperative CEA (Mean), ng/mL	9.7 (0.57-145.78)
Distance of tumor FAV (cm)	5.2 (1-12)
Tumor location	
Upper rectum (11-15 cm FAV)	1 (1.1%)*
Middle rectum (6-10 cm FAV)	33 (36.7%)
Low rectum (≤ 5 cm FAV)	56 (62.2%)
Image tool for pre-nCRT staging**	
CT + TRUS	40
MRI	12
Only CT	38
Clinical T stage	
cT2	5 (5.6%)
cT3	82 (91.1%)
cT4	3 (3.3%)
Clinical N stage	
cN0	43 (47.8%)
cN1	37 (41.1%)
cN2	10 (11.1%)
Interval between nCRT and operation (Mean), days	59 (19-172)

BMI = Body Mass index; ASA = American Society of Anesthesiologist; CEA = carcinoembryonic antigen; FAV = from the anal verge; nCRT = neoadjuvant chemoradiotherapy.

\* The tumor is located at 12 cm FAV.

\*\* nCRT = neoadjuvant chemoradiotherapy.

(range: 1-31 days), and no postoperative 30-day mortality was noted. Three patients (3.3%) had anastomotic leakage, as evidenced by an infected pelvic Jason-Patt drain. The intra-abdominal infection was controlled after intravenous antibiotics treatment. Five patients (5.6%) presented with postoperative complications: one each with prolonged ileus, intra-abdominal abscess, postoperative hemorrhage, internal herniation, and perineal wound infection (Table 2).

The mean follow-up period was 40.4 months (range: 2.4-87.1 months). Local recurrence occurred in three patients (3.3%), and distant metastases occurred in 10 patients (11.1%). Fourteen patients died during the follow-up period; of them, died of the rectal cancer. The 5-year overall survival rate was 75%. The 5-year

disease-free survival rate was 68% (Fig. 2).

The mean follow-up period was 40.4 months (range: 2.4-87.1 months). Local recurrence occurred in three patients (3.3%), and distant metastases occurred in 10 patients (11.1%). Fourteen patients died during the follow-up period.

### Discussion

The NSABP R-03 trial had compared preoperative chemoradiotherapy with postoperative chemoradiotherapy and reported that the former significantly improved 5-year disease-free survival (64.7%) rates and showed a trend toward improvement of 5-year overall survival (74.5%) rates<sup>7</sup>. From our results, 5-year disease-free survival and 5-year overall survival

**Table 2.** Perioperative and short-term outcome of patients with laparoscopic TME

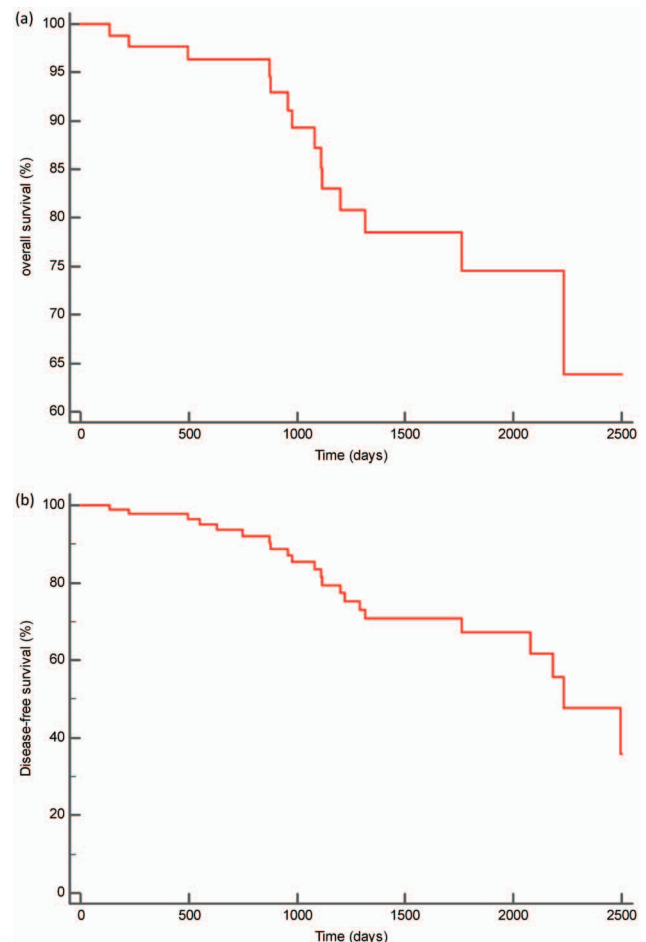
Perioperative	
Procedure	
Sphincter-preserving surgery, n (%)	72 (80%)
APR, n (%)	18 (20%)
Operative time (Mean), min	192 (115-242)
Conversion, n (%)	1
Temporary stoma, n (%)	71
Blood loss (Mean), mL	135 (30-600)
Need to blood transfusion, n (%)	2
Short-term outcome	
Hospital stay, (mean) days	7.2 (1-31)
30-day surgical mortality, n (%)	0 (0%)
Anastomotic leakage, n (%)	3 (3.3%)
Other complications, n (%)	5 (5.6%)
Prolonged ileus	1
Intraabdominal abscess	1
Internal herniation	1
Postoperative hemorrhage	1
Perineal wound infection	1

APR = abdominoperineal resection.

**Table 3.** Sphincter-preserving rate for different parts of the rectum

	Sphincter-preserving, n (%)	APR, n (%)
Upper rectum (n = 1)	1 (100%)	0 (0%)
Middle rectum (n = 33)	32 (97%)*	1 (3%)
Low rectum (n = 56)	39 (69.7%)	17 (30.3%)

\* One patient encountered conversion.



**Fig. 2.** (a) Overall survival curve; (b) Disease-free survival curve.

rates of 68% and 75% were achieved, respectively. In our sample, the interval from the end of radiation to surgery was an average of 59 days, and the complete response rate was 14.4% (Table 4). These results are similar to the complete response rate (16.5%) and interval (within 8 weeks) of the NSABP R-03 trial.<sup>7</sup>

In our study, 62 (68.9%) patients had ypN0 stage, similar to the 66.7% of preoperative chemoradiation patients with ypN0 stage in the NSABP R-03 trial. We also observed that more than half (59.6%) of patients with clinical positive N stage present with pathologic negative N stage, even with partial or poor response for T stage (Table 5). For the 13 patients with complete response, the interval between radiation and surgery was an average of 53 days. Therefore, the association between longer intervals and higher complete response rates remains unclear.

The Conventional versus Laparoscopic Assisted Surgery In Colorectal Cancer (CLASSIC) trial reported high conversion rates (34%) and high positive circumferential radial margins (16%) in laparoscopic rectal surgery.<sup>5</sup> However, further analysis revealed that we noted that intraoperative conversion rates fell by year.<sup>5</sup> After long-term follow-up (10 years), the CLASSIC trial reported that there were no differences in overall survival and disease-free survival rates be-

tween the open and laparoscopic groups.<sup>13</sup> The COLOR II trial reported a conversion rate of 16%, no differences in circumferential radial margin between the laparoscopic group and open group, faster bowel recovery, and shorter hospital stay.<sup>6</sup> Therefore, although laparoscopic TME is technically more difficult than laparoscopic colectomy, these randomized clinical trials corroborate the utility of laparoscopic surgery for rectal cancer.<sup>5,6,10,13</sup>

Though after the neoadjuvant chemoradiotherapy, the pelvic fibrosis and unobvious anatomic plain let the rectal surgery tough. Now The randomized Comparison of Open versus laparoscopic surgery for mid and low REctal cancer After Neoadjuvant chemoradiotherapy (COREAN) is the randomized trial which evaluates the difference between laparoscopic approach and open approach for locally advanced rectal cancer. This trial demonstrated that laparoscopic surgery after neoadjuvant chemoradiotherapy for mid or low rectal cancer is safe, and has greater short-term benefits compared with open surgery.<sup>11</sup> Moreover, the follow-up results of the COREAN trial revealed that laparoscopic surgery after neoadjuvant chemoradiotherapy yielded the same outcomes for disease-free survival as open resection.<sup>12</sup>

The COREAN trial reported sphincter-preserving rate of 88.8%, complication rate of 21.2%, 5-year disease-free survival rate of 70%, and 5-year overall survival rate of 80%. The results of our study showed sphincter-preserving rate of 80%, anastomotic leakage rate of 3.3%, other complication rates of 5.6%, 5-year overall survival rate of 75% and 5-year disease-free survival rate of 68%. However, our study

**Table 4.** Pathology outcome

Complete response, n (%)	13 (14.4%)
Tumor differentiation, n (%)	
Well differentiated	13 (14.4%)
Moderate differentiated	65 (72.2%)
Poorly differentiated	12 (13.3%)
ypT stage, n (%)	
ypT0	13 (14.4%)
ypTis	2 (2.2%)
ypT1	6 (6.7%)
ypT2	24 (26.7%)
ypT3	43 (47.8%)
ypT4	2 (2.2%)
ypN stage, n (%)	
ypN0	62 (68.9%)
ypN1	18 (20%)
ypN2	10 (11.1%)
Harvested lymph node, (mean)	16 (5-31)
Distal resection margin, (mean) cm	2.6 (0.5-6)
Circumferential margin, (mean) mm	7.9 (1.0-20)

**Table 5.** Down-staging rate at different part of rectum

	T category			N category*
	Complete, n (%)	Partial, n (%)	Poor, n (%)	
Upper rectum	0 (0%)	0 (0%)	1 (100%)	0%
Middle rectum	5 (15.2%)	7 (21.2%)	21 (63.6%)	11/17 (64.7%)
Low rectum	8 (14.3%)	27 (48.2%)	21 (37.5%)	17/30 (56.7%)

\* The ratio = the numbers of patients who became ypN-/the numbers of patients with cN+.



was retrospective in nature. We can obtain similar outcome as laparoscopic group in COREAN trial. Our study also revealed that laparoscopic TME for advanced rectal cancer should be performed by experienced surgeons to obtain acceptable short-term outcomes and oncological outcomes.

There were some limitations to this study. Although there are inherent weaknesses in the case series, we attempted to control several variables. The transrectal ultrasound was performed by the same surgeon, and the operating team, pathology team, and therapeutic radiology team were kept consistent. However, this was a retrospective study and the sample size is relatively small.

## Conclusions

In conclusion, laparoscopic surgery after neoadjuvant chemoradiotherapy in patients with locally advanced rectal cancer is feasible and appropriate. It can provide good short-term clinical and oncological outcomes.

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原 著

## 腹腔鏡全直腸系膜切除術治療 局部侵犯性的直腸癌

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**目的** 評估以局部侵犯性直腸癌的病人接受新輔助性電化療後，接受腹腔鏡全直腸系膜切除術治療的結果。

**方法** 從 2006/01 至 2013/12，我們收集了 90 位局部侵犯性直腸癌病人，全部接受新輔助性電化療併腹腔鏡全直腸系膜切除術，回溯性收集相關臨床和病理資料併分析。

**結果** 90 位病人中，71.1% 的病患為男性，平均年紀為 59.2 歲，腫瘤平均距離肛門 5.2 公分，平均在電療結束後 59 天進行手術。沒有病患因手術死亡，有 1 人術中轉成剖腹手術。共 80% 的病患可以保留肛門括約肌，術後住院天數平均為 7.2 天。局部復發率為 3.3%，遠端轉移率為 11.1%，5 年整體存活率為 75%，5 年無腫瘤復發存活率為 68%。

**結論** 局部侵犯性直腸癌的病人接受新輔助性電化療後，以腹腔鏡全直腸系膜切除術治療是可行且適宜的，可以達到好的短期臨床結果和長期腫瘤學結果。

**關鍵詞** 直腸癌、腹腔鏡手術、全直腸繫膜切除、新輔助性化學治療、新輔助性放射治療。