Original Article

Oncological Outcomes of Patients with Rectal Cancer Who Received Surgery after Clinically Complete Response to Neoadjuvant Chemoradiotherapy

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Key Words
Rectal cancer;
Neoadjuvant chemoradiotherapy (nCRT);
Clinically complete response (cCR);
Pathological complete response (pCR)

Purpose. To investigate the oncological outcomes of rectal cancer patients who received surgery after clinically complete response to neoadjuvant chemoradiation therapy.
Methods. We retrospectively analyzed 25 patients with rectal cancer who achieved clinically complete response after neoadjuvant chemoradiation therapy and subsequently underwent surgical treatment from January 1, 2007, to December 31, 2018, at a single medical center. Their demographic and clinicopathological data were recorded, and the oncological outcomes were analyzed.
Results. 25 patients with cT2-3N0-2 rectal cancer were enrolled. Of 25 patients, 5 (20%) had residual cancer cells after neoadjuvant chemoradiation therapy followed by surgical treatment. The mean age of all patients was 57.7 years, and 68% were men. Elevated carcinoembryonic antigen levels (> 5 ng/mL) were found in 28% patients at the time of initial diagnosis. The median follow-up time was 65 (range: 5.7-164) months. The 5-year overall survival and disease-free survival rates were 82.3% and 80.1%, respectively. A subgroup analysis revealed that patients with ypN0 might show a better outcome.
Conclusions. The oncological outcomes of the present study were favorable. There were 20% of patients who had residual cancer and may benefit from radical surgery. However, there were still 16% patients who received abdominoperineal resection, even with pathologically complete response. Hence, careful considerations from clinicians to ascertain whether patients with radical surgery, especially among those who have achieved clinically complete response, would be essential.

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Colorectal cancer is the third most common type of cancer and is the fifth frequent cause of cancer-related mortality worldwide.[1-4] In Taiwan, colorectal cancer is the third most common cause of cancer-related mortality in 2017.[1] With the current standard treatment for colorectal cancer, reducing the incidence of metastases and achieving a promising quality of life remain a challenge.[5] To date, neoadjuvant che-

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moradiotherapy (nCRT) plus total mesorectal excision (TME) with a free tumor margin (R0 resection) is the standard curative method for locally advanced-stage rectal cancer.

The watch-and-wait approach is the recommended non-standard method for patients with rectal cancer who achieve clinically complete response (cCR). Further, its use has become more common with the advent of total neoadjuvant therapy and with the increasing demand among patients who achieve cCR.[6,7] Some patients could benefit from nCRT and achieve cCR, which is associated with a better local control rate and sphincter preservation. Moreover, nCRT is advantageous for patients who achieve pathological complete response (pCR). However, the pCR rates significantly vary, and some patients with cCR could not achieve pCR. The definition of cCR is inconsistent, and surveillance recommendations differ. The optimal management of patients based on recurrence risk with observation alone and the impact of surgery on quality of life is still debated.

Several studies assessed the oncological outcomes of patients with cCR who received different treatments for cancer recurrence, which included surgery, additional chemotherapy, and other methods for disease control. Nevertheless, only a few studies have shown cCR in patients who are radically disease-free. Therefore, the current study aimed to assess the oncological outcome of patients with cCR and whether patients with cCR are radically disease-free.

Materials and Methods

Patient population and data collection

This was an observational retrospective study conducted at National Taiwan University Hospital. In total, 25 patients with rectal cancer achieved locoregional cCR after nCRT. Patients who had unresectable metastatic rectal cancer were excluded. All 25 patients underwent curative surgical treatment from January 1, 2007, to August 10, 2018, were included in the analysis. Next, their medical data were recorded. To determine tumor and nodal staging, all patients underwent colonoscopy, pelvic magnetic resonance imaging, and computed tomography (CT) of the abdomen. Distant metastasis was detected via CT of the thorax and abdomen. The application of positron emission tomography was dependent on the clinical condition of patients. Disease stage was determined using the American Joint Committee on Cancer staging system (7th edition), which utilizes the TNM scoring system.

Neoadjuvant chemoradiotherapy

Patients (n = 24) with cT2-3 rectal cancer received 5-fluorouracil 1600-2800 mg/m^2, oxaliplatin 40-85 mg/m^2, and leucovorin 300 mg/m^2 (FOLFOX) every 2-3 weeks at a median of five cycles with or without anti-VEGF regimen. Thus, FOLFOX treatment required a bi-weekly schedule. Moreover, they received one or two cycles of induction FOLFOX prior to radiotherapy, followed by two cycles of FOLFOX concomitantly administered during radiotherapy and an additional three or four cycles of consolidation FOLFOX after radiotherapy. A patient was referred from another hospital, who had received capecitabine for nCRT, however detailed data were unavailable.

The definition of clinically and pathological complete responses

Post nCRT evaluation was conducted at the same admission course for surgical treatment. The cCR was defined as no visible tumor and rectal mucosa and rectal wall supple or the presence of a small residual scar with no suspicious induration or ulceration on digital rectal examination and rigid or flexible rectoscopy.[8] Random biopsy of the tumor site was also considered. Similar to a previous study, we did not include pelvic MRI for cCR assessment due to inconsistency and incompleteness of image interpretation.[8] We defined pCR as the absence of viable tumor cells in the surgical specimen.

Surgical treatment

All patients received transabdominal TME surgery after discussion and patient preference, except

one who received transanal tumor excision. Abdominoperineal resection was conducted if a negative distal margin of 1 cm could not be achieved. Surgery was performed 8-12 weeks after nCRT for curative intent. Tumor size, nodal metastasis, and margin status were identified based on the patient's histological records.

Follow-up

After the completion of nCRT and surgery, all patients were followed-up postoperatively via physical examination and carcinoembryonic antigen (CEA) blood tests every 3 months within the first 2 years, every 6 months within 3-5 years, and annually thereafter. To screen for local recurrence or distant metastasis, patients underwent CT scan of the chest, abdomen, and pelvis annually. Postoperative colonoscopy was performed at 1, 3, and 5 years for surveillance based on the National Comprehensive Cancer Network guidelines.

Adjuvant therapy

Adjuvant chemotherapy was indicated for patients with one of the following pathological parameters: pathologic nodal metastasis, positive resection margins, preoperative distant metastasis, and pathologically residual cancer cells in specimen. Adjuvant chemotherapy was not given to patients who had pCR. The chemotherapy regimen was selected after a discussion with the oncologist.

Statistical analysis

All results were expressed as means ± standard deviations for continuous data and as frequencies or percentages for categorical data. The Kaplan-Meier curves were plotted to provide an overview of the disease-free survival and the overall survival rates of all patients. All analyses were performed using R software (version 4.1.2). A p value of < 0.05 was considered statistically significant.

Results

Demographic and baseline characteristics of patients

In total, 25 patients had clinically staged T2-3, N0-2 adenocarcinoma of the rectum. The treatment plan included nCRT followed by surgery. All patients achieved cCR (Fig. 1). Approximately 68.0% of patients were men, and the average age at diagnosis was 57.7 (range: 28-72) years. The median height and weight were 162.8 cm and 63.2 kg, respectively. Before treatment, the median length between the tumor and anal verge was 4.0 cm. Elevated CEA levels (> 5 ng/mL) were found in 28% patients at the time of initial diagnosis and significantly differed from 1.16 to 93.6 ng/mL. Approximately 84% of patients had cT3

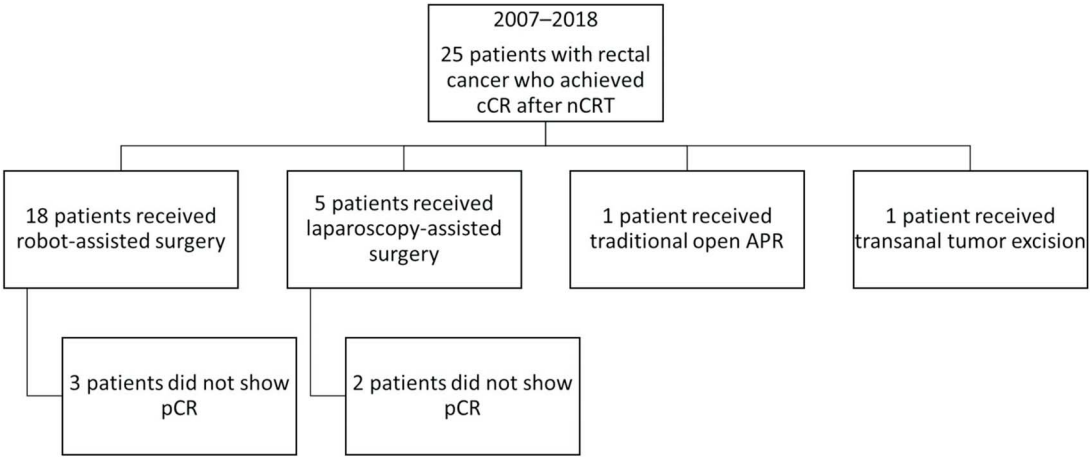

Fig. 1. Patient recruitment algorithm.

disease, and 56% had no lymph node involvement. Three patients presented with resectable distant metastasis to the lung or liver (Table 1).

Treatment course and perioperative outcome

During the treatment course, all patients received nCRT. The nCRT data of 4 patients were lost. The dose range of radiation therapy was between 4500 and 5500 cGy. In total, 21 patients received FOLFOX, and 17 patients received the combined FOLFOX and anti-VEGF agent. All patients achieved cCR preoperatively and underwent surgery. Among them, 18 had robot-assisted surgery (n = 14, TME and n = 4 abdominoperineal resection). One (4.0%) patient underwent transanal local excision (Fig. 1). The median period from end-radiation to surgery was 64 days. The median length of hospital stay after surgery was 15.6 (range: 5-32) days. In terms of operative outcomes, the median length of the specimen was 26.3 (range: 9-32) cm. The median number of lymph nodes dissected was 13.8. Table 2 depicts the final TNM stage. In total, 23 (92.0%) patients presented with ypT0 and 21 (84.0%) with ypN0 disease. 9 of the 12 patients

Table 1. Baseline characteristics of patients

Characteristics	Values (N = 25)	Range or %
Age, years	57.7 ± 11.6	28-72
Male sex	17	68.0%
Height, cm	162.8 ± 8.9	146.0-179.9
Weight, kg	63.2 ± 11.6	43.8-85.0
BMI, kg/m^2	23.8 ± 3.6	17.6-32.4
Source		
First visit	12	52.2%
Referral	11	47.8%
Above anal verge, cm (n = 21)[a]	4.0 ± 2.8	0-10
Pre-treatment CEA level, ng/mL	9.6 ± 19.4	1.16-93.6
Pre-OP TNM stage		
T category		
T2	4	16.0%
T3	21	84.0%
N category		
N0	11	44.0%
N1	6	24.0%
N2	8	32.0%
M category		
M0	22	88.0%
M1	3	12.0%

[a] Data of remaining 4 patients were lost.

Table 2. Treatment course and outcome

Characteristics	Value (N = 25)	Range or %
Radiation therapy regimen (n = 22) [a]	28.3 ± 7.0	25-52
Dosage of radiotherapy, cGy (n = 22) [a]	4772.7 ± 335.5	4500-5500
Time from end-radiation to surgery, days (n = 23) [a]	64.7 ± 15.2	45-96
Operation type		
LTME	4	16.0%
LTME + metasectomy	1	4.0%
RAPR	4	16.0%
RTME	14	56.0%
APR + metasectomy	1	4.0%
Transanal excision	1	4.0%
Length of hospital stay, days	15.6 ± 5.9	5-32
Surgical outcomes		
Length of the specimen, cm (n = 24) [a]	26.3 ± 8.7	9-42
Number of LNs dissected	13.8 ± 8.2	0-32
Metastatic LN	0.6 ± 1.8	0-8
Pathological TNM staging		
ypT category		
ypT0	23	92.0%
ypT2	1	4.0%
ypT3	1	4.0%
ypN category		
ypN0	21	84.0%
ypN1	3	12.0%
ypN2	1	4.0%
ypM category		
ypM0	23	92.0%
ypM1	2	8.0%
Margin involvement	0	

LTME, laparoscopic total mesorectal excision; RAPR, robotic-arm abdominoperineal resection; RTME, robotic-arm total mesorectal excision; LN, lymph node.
[a] Data of remaining patients were lost.

who were clinically nodal positive achieved nodal downstaging to ypN0 (Table 3). Tw opatients had ypM1 disease because of previous lung metastasis; they underwent curative resection at the same surgical course. One patient had previous liver metastasis and was managed with radiofrequency ablation. The patient who received local excision achieved pCR. None of the specimens presented with margin involvement.

Pathologically positive findings among patients with cCR

Three male and two female participants had pathologically positive findings, and all presented with cT3 disease preoperatively. Only one patient (No. 2) had lung metastasis, which received curative resection. Only one patient received abdominoperineal resection surgery (No. 3). After operation, all 5 patients received adjuvant chemotherapy (Table 3, 4).

Follow-up

Between January 1, 2007, and January 30, 2021, the median follow-up time of the patients was 65 (range: 5.7-164) months. During this period, 4 patients (16%) died, and 6 (24%) patients developed recurrence; 5 (20%) of which were distant metastasis, and another one (4%) was a local recurrence. In 5 distant metastasis cases, 4 patients were ypT0N0, whereas the remaining one was ypT0N1. The staging of local recurrence case was ypT0N1. The 5-year OS and DFS were 82.3% and 80.1%, and the 3-year OS and DFS were 93.0% and 80.1%, respectively (Fig. 2).

The patients were divided into the ypN0 and ypN ≠ 0 groups. The ypN0 group (89.3%) had a significantly higher 5-year OS rate than the ypN ≠ 0 group (55.6%). However, there was no statistically significant difference between the ypN0 and ypN ≠ 0 groups in terms of 5-year DFS (84.0% vs. 62.5%) (Fig. 3).

Table 3. Comparison of clinical staging with pathologic T and N staging

Clinical staging	Pathologic T staging			ypN negative	ypN positive	Total
	ypT0	ypT2	ypT3			
cT2	4 (17.4)	0 (0)	0 (0)			4 (17.4)
cT3	17 (73.9)	1 (4.3)	1 (4.3)			19 (82.6)
cN negative				10 (43.5)	1 (4.3)	11 (47.8)
cN positive				9 (39.1)	3 (13.0)	12 (52.2)
Total	21 (91.3)	1 (4.3)	1 (4.3)	19 (82.6)	4 (17.4)	23 (100)

N = 23, patients with distant metastasis were excluded.

Table 4. Treatment courses of patients with clinical complete response but pathological stage positive

N	Sex	CEA level, ng/mL	Clinical stage	Neoadjuvant chemoradiation therapy	Operative type	Pathological stage
1	M	3.34	T3N2M0	Radiation dose: 4500 cGy Chemotherapy: Oxaliplatin, 5-FU, Rescuvolin	LTME	ypT0N2
2	M	15.4	T3N0M1	Radiation dose: Datamissing Chemotherapy: Datamissing	LTME + metastasectomy	ypT3N1
3	F	36.2	T3N0M0	Radiation dose: 4500 cGy Chemotherapy: Capecitabine	RTME	ypT2N0
4	M	2.98	T3N1M0	Radiation dose: 4500 cGy Chemotherapy: Oxaliplatin, 5-FU Rescuvolin, Avastin	RAPR	ypT0N1
5	F	1.55	T3N2M0	Radiation dose: 5000 cGy Chemotherapy: Oxaliplatin, 5-FU, Rescuvolin, Avastin	RTME	ypT0N1

5-FU, 5-fluorouracil; LTME, laparoscopic total mesorectal excision; RAPR, robot-assisted abdominoperineal resection; RTME, robot-assisted total mesorectal excision.

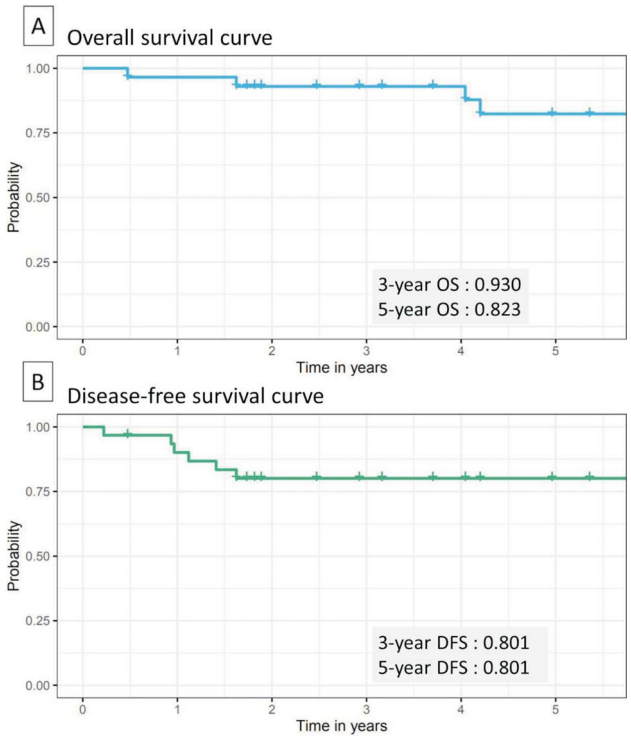

Fig. 2. Kaplan-Meier curve of all patients. (A) The 3-year OS and 5-year OS rates were 93% and 82.3%. (B) The 3-year DFS and 5-year DFS rates were 80.1% and 80.1%.

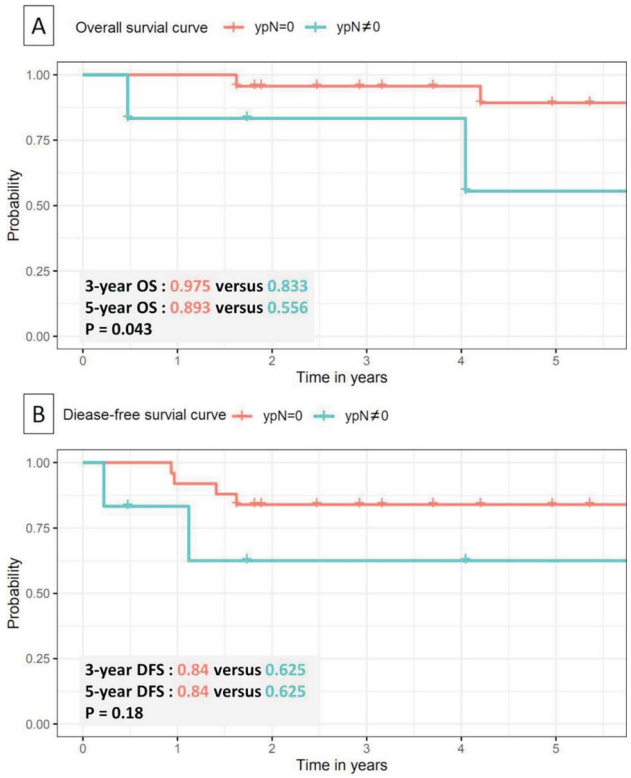

Fig. 3. Kaplan-Meier curve of the ypN = 0 and ypN ≠ 0 groups. (A) The 3-year OS and 5-year OS rates of the ypN = 0 group were 97.5% and 89.3%, and that of the ypN ≠ 0 group were 83.3% and 55.6%. The *p* value was 0.043. (B) The 3-year DFS and 5-year DFS rates of the ypN = 0 group were 84.0% and 84.0%, and that of the ypN ≠ 0 group were 62.5% and 62.5%. The *p* value was 0.18.

Discussion

The development of improved nCRT protocols has increased the number of patients achieving a cCR, which determined a cCR in up to 26.8% of cT2-4N0-2M0 patients.[9,10] Furthermore, in a series 231 patients with cT1-2N0M0 distal rectal cancer managed by neoadjuvant therapy, 135 (58.4%) achieved cCR (76.1% in cT1N0 patients and 51.2% in cT2N0 patients).[11] According to a recent meta-analysis, nCRT development can achieve a pCR in 22.4% (95% CI 19.4%-25.7%) patients undergoing total neoadjuvant therapy.[12] The above promoted a higher overall survival rate following surgical resection in patients with pCR than those without pCR.[13,14] The result above also raised some questions, such as whether a cCR can accurately predict pCR and the effect of inconsistency between cCR and pCR on oncological outcomes. Our results showed that 5 patients (20%) with cCR did not achieve pCR. Thus the achievement of pCR after surgery is inconsistent among patients with cCR after nCRT. The accuracy of pCR diagnosis is crucial to optimize organ preservation and oncological result. Unfortunately, pCR cannot be established before rectal resection. In the surgery group of a cohort study included 92 cases, the inconsistency of cCR and pCR was 12%.[15] Moreover, the rate of this inconsistency varied largely between different series, 5-53% of patients with cCR still had viable tumor cells, depending on the modality of cCR assessment. Another study showed that 33%-81% of patients had inconsistent cCR and pCR.[16,17] The reason for the above discrepancy may be related to different cCR assessment modalities. Thus, further study is required.[18]

In this study, two patients with cT3 stage (Nos. 2 and 3) had cCR and presented with residual cancer after nCRT based on tumor (T) staging. Hasan et al. re-

vealed that in the lower cT stage, the chance of pCR (cT1/T2 vs. cT3: odds ratio (95% CI) = 0.60 (0.41-0.87), $p = 0.01$) was significantly higher.[14] The findings of our study are in concordance with the above published in the literature. Moreover, the nodal staging of one patient (No. 2) after surgery changed from cN0 to ypN1, indicating that the preoperative evaluation of cCR had false negative findings. Due to the different cCR diagnostic strategies, current methods cannot predict pCR with high consistency. Nevertheless, it remains unclear whether radical surgery is required for a definitive pCR in cCR patients. For patients who achieved cCR, the National Comprehensive Cancer Network guidelines state that an initial watchful waiting may be considered with an experienced multidisciplinary team. However, guidelines from the American Society of Colon and Rectal Surgeons suggest that patients with an cCR should be offered radical resection. Several prospective randomized trials of nonoperative therapy in cCR patients are underway (NCT01047969, NCT03426397), which may resolve the above concerns.

In our study, all 25 cCR patients had received surgical treatment, and 5-year OS/DFS were 82.3% and 80.1%. The results were similar to the previous study by Habr-Gama et al., with the 5-year OS/DFS 88% and 83% in the TME group.[10] From a recent study that included 212 cases who had cCR after nCRT, 160 (75.5%) cases were treated by TME, revealing a 5-year OS 95.9%.[19] Moreover, low-risk patients had significantly better 5-year OS (99.0% vs. 92.3%, $p = .050$), DFS (95.9% vs. 75.3%, $p < .001$) when they were treated with TME versus the watch and wait strategy. However, high-risk patients acquired no such survival benefit from TME.[19] Hence, whether patients will benefit from radical surgery require careful consideration by clinicians, especially among those who achieved cCR.

As for neoadjuvant therapy, we arranged an aggressive nCRT protocol, which included anti-VEGF therapy. The efficacy of adding bevacizumab in nCRT was shown by a recent meta-analysis, which the pooled pCR rate for bevacizumab-relevant cohorts was 21%, superior to the current benchmark of 15%.[20] Similar results have also been reported by Zhong et al.[21] The above results showed some degree of variation, possibly related to different predefined criteria for a cCR, nCRT protocols, and retrospective setting.

As for local recurrence, the individual data of only one case did not help to explain this local recurrence. The cCR of this case might be attributed to faulty cCR assessment or the fact that the tumor was left in the patient (e.g., lateral lymph nodes). In a recent prospective cohort study, 26 of the 84 cCR cases were divided into TME group, and 6 cases (23.1%) had residual tumors. The tumor recurrence rate of the pCR subgroup was 5% (1/20), which was significantly lower than that of the non-pCR subgroup (50%, 3/6, $p = 0.028$).[22]

In this study, the ypN0 group had a significantly higher 5-year OS than the ypN ≠ 0 group. Hence, even in a patient with cCR, the achievement of pCR can affect overall survival. Similar result was also obtained by the study conducted by Mass et al. in 465 patients with pCR, wherein the 5-year OS rate was 87.6%. Conversely, for patients without pCR who received radical surgery, the OS rates were significantly lower (76.4%, respectively) than those observed in patients with pCR ($p < 0.0001$).[23]

Organ preservation was one of our major concerns. Our results revealed that 5 (20%) patients received APR, which was mostly practiced before 2016 and rarely now. Unfortunately, of the 5 patients who underwent APR, 4 (16%) patients had proven pCR postoperatively. In a cohort study,[15] 122 patients who had cCR were divided into wait-and-see and radical surgery. There were 92 patients received radical surgery, and 40 (43.5%) patients had received APR, which was higher than our result. Though there were several studies compared the OS and DFS of patients who had cCR followed by wait-and-see or radical surgery. A comparison of proportions of the APR in either wait-and-see or radical surgery group is still lacking. In the era of nonoperative management, whether patients will benefit from APR require careful consideration by clinicians, especially among those who achieved cCR.

Local excision represents a surgical alternative to radical surgery for selected patients. Our study had only one case that received local excision, who achieved pCR. This case had cT3N1 preoperatively, and

had cCR after nCRT. However, in the GRE3CCAR2 trial, patients with cT2-3N0-1M0 stage at baseline received nCRT, revealing that almost 46% of patients who received local excision requided further radical surgery.[24] Even though, local excision in the GRECCAR2 trial seems to be oncologically safe. The 3-year DFS and OS rates were 78.3% and 91.9%, respectively. Additionally, a perprotocol analysis found similar 3-year local recurrence rates after local excision and radical surgery (6% vs. 3%, respectively; $p = 0.63$).[24]

The current study had several limitations. First, it had a small sample size with one arm setting and was retrospective in nature. Hence, it was challenging to identify factors causing the difference between cCR and pCR and treatment strategies. Second, lacking of pelvic MRI for assessment of cCR in this study could not meet current treatment consensus. Finally, we included patients who had resectable metastatic rectal cancer with locally cCR after nCRT, which may affect the results of OS and DFS.

Conclusion

The oncological outcomes of patients with rectal cancer who received radical surgery after cCR to nCRT were favorable. Moreover, a significant of percentage of patients (n = 5, 20%) was histologically proven to have residual cancer and benefited from radical surgery. This implies the inconsistency between the cCR and final pathology. However, 16% of patients receive APR, even with pCR. Hence, in the era of nonoperative management, whether patients will benefit from radical surgery require careful consideration by clinicians, especially among those who achieved cCR.

Financial Disclosure

None.

References

1. Yeh KH, Yang TS, Hsu TC, et al. Real-world evidence of the safety and effectiveness of regorafenib in Taiwanese patients with metastatic colorectal cancer: CORRELATE Taiwan. *J Formos Med Assoc* 2021;120:2023-31.
2. Tsai CE, Wu KL, Chiu YC, et al. The incidence and clinical associated factors of interval colorectal cancers in Southern Taiwan. *J Formos Med Assoc* 2018;117:185-90.
3. Wang YW, Chen HH, Wu MS, Chiu HM; Taiwanese Nationwide Colorectal Cancer Screening P. Current status and future challenge of population-based organized colorectal cancer screening: lesson from the first decade of Taiwanese program. *J Formos Med Assoc* 2018;117:358-64.
4. Huang X, Liu H, Liao X, et al. Prognostic factors for T1-2 colorectal cancer after radical resection: lymph node distribution is a valuable predictor of its survival. *Asian J Surg* 2021; 44:241-6.
5. Smith JJ, Strombom P, Chow OS, et al. Assessment of a watch-and-wait strategy for rectal cancer in patients with a complete response after neoadjuvant therapy. *JAMA Oncol* 2019;5:e185896.
6. Cercek A, Goodman KA, Hajj C, et al. Neoadjuvant chemotherapy first, followed by chemoradiation and then surgery, in the management of locally advanced rectal cancer. *J Natl Compr Canc Netw* 2014;12:513-9.
7. Smith JJ, Garcia-Aguilar J. Advances and challenges in treatment of locally advanced rectal cancer. *J Clin Oncol* 2015; 33:1797-808.
8. Smith JD, Ruby JA, Goodman KA, et al. Nonoperative management of rectal cancer with complete clinical response after neoadjuvant therapy. *Ann Surg* 2012;256:965-72.
9. Habr-Gama A, Perez RO, São Julião GP, Proscurshim L, Gama-Rodrigues J. Nonoperative approaches to rectal cancer: a critical evaluation. *Radiat Oncol* 2011;21:234-9.
10. Habr-Gama A, Perez RO, Nadalin W, et al. Operative versus nonoperative treatment for stage 0 distal rectal cancer following chemoradiation therapy: long-term results. *Ann Surg* 2004;240:711-7.
11. Peng HH, Liao ZW, Lin XD, et al. Definitive radiotherapy or chemoradiotherapy for distal rectal cancer with early stage of cT1-2N0. *Cancer Manag Res* 2019;11:5221-9.
12. Petrelli F, Trevisan F, Cabiddu M, et al. Total neoadjuvant therapy in rectal cancer: a systematic review and meta-analysis of treatment outcomes. *Ann Surg* 2020;271:440-8.
13. Sinukumar S, Patil P, Engineer R, Desouza A, Saklani A. Clinical outcome of patients with complete pathological response to neoadjuvant chemoradiotherapy for locally advanced rectal cancers: the Indian scenario. *Gastroenterol Res Pract* 2014;2014:867-41.
14. Hasan S, Renz P, Wegner RE, et al. Microsatellite instability (MSI) as an independent predictor of pathologic complete response (PCR) in locally advanced rectal cancer: a National Cancer Database (NCDB) analysis. *Ann Surg* 2020;271: 716-23.
15. Li J, Liu H, Yin J, et al. Wait-and-see or radical surgery for rectal cancer patients with a clinical complete response after

neoadjuvant chemoradiotherapy: a cohort study. *Oncotarget* 2015;6:42354-61.
16. Habr-Gama A. Assessment and management of the complete clinical response of rectal cancer to chemoradiotherapy. *Colorectal Dis* 2006;8:21-4.
17. Maggiori L, Bretagnol F, Aslam MI, et al. Does pathologic response of rectal cancer influence postoperative morbidity after neoadjuvant radiochemotherapy and total mesorectal excision? *Surgery* 2014;155:468-75.
18. Garcia-Aguilar J, Shi Q, Thomas CR Jr, 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.
19. Zhang S, Zhang R, Li RZ, et al. Beneficiaries of radical surgery among clinical complete responders to neoadjuvant chemoradiotherapy in rectal cancer. *Cancer Sci* 2021;112:3607-15.
20. Zhou Y, Guo Z, Wu Z, et al. The efficacy and safety of adding bevacizumab in neoadjuvant therapy for locally advanced rectal cancer patients: a systematic review and meta-analysis. *Transl Oncol* 2021;14:100964.
21. Zhong X, Wu Z, Gao P, et al. The efficacy of adding targeted agents to neoadjuvant therapy for locally advanced rectal cancer patients: a meta-analysis. *Cancer Med* 2018;7:565-82.
22. Han Z, Li M, Chen J, et al. Surgery may not benefit patients with locally advanced rectal cancer who achieved clinical complete response following neoadjuvant chemoradiotherapy. *Asian J Surg* 2022;45:97-104.
23. Maas M, Nelemans PJ, Valentini V, et al. Long-term outcome in patients with a pathological complete response after chemoradiation for rectal cancer: a pooled analysis of individual patient data. *Lancet Oncol* 2010;11:835-44.
24. Rullier E, Rouanet P, Tuech JJ, et al. Organ preservation for rectal cancer (GRECCAR2): a prospective, randomised, open-label, multicentre, phase 3 trial. *Lancet* 2017;390:469-79.

原　著

經前導性治療後臨床完全緩解之直腸癌病患接受手術之預後探討

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目的　探討經前導性治療後完全緩解之直腸癌病患接受手術治療之腫瘤學預後。

方法　本回溯性研究分析 25 位經前導性化學治療及放射線治療後達成臨床完全緩解且接受手術之直腸癌病患。個案來源於單一醫療中心，蒐集期間為 2007 年 1 月至 2018 年 12 月，並追蹤至 2021 年。我們整理病患臨床資訊、腫瘤分期與病理結果，並分析三年及五年之無疾病存活率與五年整體存活率。

結果　本研究收案 25 位直腸癌臨床分期 cT2–3N0–2 之病患，有 5 位病患於前導性治療及手術後發現殘餘癌細胞。平均年齡為 57.7 歲，68% 的病患為男性。28% 的病患於診斷時有異常之癌胚胎抗原 (carcinoembryonic antigen > 5 ng/mL)。術後追蹤時間中位數為 65 個月。五年整體存活率與五年無疾病存活率各為 82.3% 及 80.1%。術後病理無殘留淋巴轉移者有較佳之預後。

結論　本研究之預後為可接受的。有 20% 病患達成臨床完全緩解後仍有殘餘之癌細胞，且可能因手術而得到較佳預後。然而，有 16% 病患接受腹部會陰切開術，且術後診斷為病理完全緩解。因此，對於臨床完全緩解之直腸癌病患，臨床醫師須謹慎考慮根治性手術是否會使病患受益。

關鍵詞　直腸癌、前導性治療、臨床完全緩解、病理完全緩解。