

Long-term outcomes in patients with ypT0 rectal cancer after neoadjuvant chemoradiotherapy and curative resection

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Abstract

Objective: For patients with locally advanced rectal cancer treated with neoadjuvant chemoradiotherapy (NCRT), significant pathological response of the primary tumor has been proposed to identify candidates for organ preservation. However, this does not address metastatic lymph nodes in the mesorectum. The aim of this study was to assess the incidence of lymph node metastases in ypT0 patients treated with NCRT and curative resection and to explore risk factors associated with survival.

Methods: This was a retrospective study of patients with ypT0 rectal cancer after NCRT and curative resection at a tertiary care center in China from 2005 to 2014.

Results: A total of 60 (18.6%) patients who underwent surgery after NCRT and achieved ypT0 were enrolled in this study; one patient was excluded owing to lack of follow-up. Of these 59 patients, lymph node metastases were found in the mesorectum (ypT0N+) in eight (13.6%) patients. After a median follow-up of 52 months, 5-year recurrence-free survival (82.7% vs. 62.5%, $P=0.014$) and overall survival (OS) (90.9% vs. 70.0%, $P=0.032$) were much higher in ypN0 than ypN+ patients. Multivariate analyses showed that ypN+ status ($P=0.009$) and perioperative blood transfusion (BT) ($P=0.001$) were significantly independent risk factors associated with recurrence; however, no factor was correlated with 5-year OS.

Conclusions: Patients with ypT0N0 rectal cancer can achieve excellent long-term outcomes; however, positive lymph nodes or tumor deposits can still be found in 13.6% of ypT0 patients. Nodal positivity in the mesorectum and perioperative BT are independent risk factors for recurrence.

Keywords: Rectal cancer; neoadjuvant chemoradiotherapy; pathological response; lymph node; risk factor

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Introduction

In China, colorectal cancer is the fourth most common cancer with new cases of 60,900, and its incidence is increasing (1). Currently, the standard management for locally advanced rectal cancer (LARC), clinically staged as T3, T4, and/or N+, is neoadjuvant chemoradiotherapy (NCRT) combined with curative resection (2,3). NCRT may induce tumor down-sizing and down-staging, and

good responders are thought to achieve a pathological complete response (pCR) which means the absence of residual viable tumor cells in the surgical resection specimens (ypT0N0). The incidence of pCR has been reported in 10%–27% of patients, who show excellent survival rates with 5-year disease-free survival (DFS) of 83%–96% (4-8). In principle, curative surgery with total mesorectal excision (TME) is still routinely carried out in LARC patients after NCRT, regardless of the clinical

response. However, in view of the potential morbidity and mortality, and the permanent stoma associated with curative resection, there has been an increasing interest in recent years in a watchful waiting strategy or local excision (LE) of rectal cancer for patients who show a good response to NCRT (9-13).

However, non-operative management or LE does not address metastatic lymph nodes in the mesorectum. Although complete pathological response of the primary tumor (ypT0) can achieve excellent outcomes, there is still the risk of metastatic lymph nodes in the mesorectum associated with tumor recurrence (14). Several reports have shown that the incidence of metastatic lymph nodes in ypT0 disease ranges from 6.6% to 16%, and that ypN+ status is a significantly independent risk factor correlated with decreased 5-year DFS and overall survival (OS) (15-20).

Therefore, we conducted this study to assess the incidence of lymph node metastases in patients with ypT0 rectal cancer treated with NCRT and curative resection, and to explore risk factors associated with survival.

Materials and methods

Patient cohort

We conducted a retrospective consecutive cohort study of patients with rectal cancer who had undergone curative resection following NCRT at the Cancer Hospital, Chinese Academy of Medical Sciences, between 2005 and 2014. Eligible patients were selected according to the following inclusion criteria: 1) had pathologically confirmed rectal cancer; 2) were clinically staged as T3, T4, and/or N+; 3) were classified on pathological examination as ypT0 (no viable tumor cells in the rectal wall) after NCRT and curative resection; 4) no distant metastases; and 5) had undergone R0 resection. Patients were excluded if they had other malignancies or had a previous history of malignant disease or recurrence, or had undergone local resection. The study was approved by the Institutional Review Board Committee of the Cancer Hospital, Chinese Academy of Medical Sciences.

Treatment

Colonoscopic biopsy was performed for all patients before NCRT to confirm the pathology and to classify differentiation of tumor into the following categories: well, moderately, poorly differentiated, and unknown. The clinical stage prior to NCRT was decided by a digital rectal

examination, rectal magnetic resonance imaging (MRI), and/or endorectal ultrasound (EUS), and pulmonary and abdominopelvic contrast-enhanced computed tomography (CT) scans. Patients were treated with NCRT with a total radiotherapy dose of 42 to 50 Gy in 21 to 25 fractions with concurrent chemotherapy (single-agent capecitabine with or without oxaliplatin). Operations were generally performed 6 to 8 weeks following the completion of NCRT by an experienced colorectal surgical team according to the principles of the TME technique. All patients were generally recommended to receive adjuvant chemotherapy. A pathology assessment by two gastrointestinal pathologists was performed on all surgical specimens, and they were staged according to the 7th edition of the American Joint Committee on Cancer (AJCC) tumor-node-metastasis (TNM) staging system.

Follow-up

All patients were followed up at 3-month intervals for 2 years, at 6-month intervals for the next 3 years, and annually thereafter. The follow-up examinations included a clinical history, physical examination, serum carcinoembryonic antigen (CEA), stool occult blood test, chest X-ray, abdominal ultrasonography, colonoscopy, abdominopelvic CT or MRI, and positron emission tomography (PET) scanning if available. Determination of recurrence was made by clinical and radiological examinations or by histological confirmation. All patients included in this study were contacted at the time of the study to confirm their survival and recurrence status. The end point of the follow-up was 1 September 2017.

Statistical analysis

Categorical variables were reported as number (frequency); and quantitative variables were reported as median (interquartile range; IQR) and $\bar{x} \pm s$ and compared by the Wilcoxon rank sum test. Recurrence-free survival (RFS) was defined as the time between the date of surgery and the first tumor recurrence (local or distant metastases), and OS was defined as the time between the date of surgery and the date of death from any cause or the last follow-up. Survival was assessed using the Kaplan-Meier method and compared using the log-rank test. Multivariate Cox regression analyses were performed to verify the effects of prognostic factors found with $P < 0.2$ in univariate analyses on RFS and OS; however, the factor "Tumor differentiation" was excluded to test its value on OS

because tumor differentiation was available for just 59.3% of patients, which might decrease the statistical power. All tests were two-sided, and a P-value of less than 0.05 was considered to be statistically significant. All statistical analyses were performed with IBM SPSS software (Version 22.0; IBM Corp., New York, USA).

Results

Patient characteristics

A total of 323 patients were reviewed. Upon review of the clinical records, ypT0 was achieved in 60 (18.6%) patients and one patient was excluded due to lack of follow-up. The vast majority of these remaining 59 patients enrolled were males (64.4%), their mean age was of 55.0 years, and tumors were mainly located in the low-rectum (mean distance from the anal verge 4.4 cm). The majority of the tumors were clinically staged as cT3 (78.0%) and cN+ (81.4%). Fifty patients (84.7%) received a total radiotherapy dose of 50 Gy in 25 fractions. Twenty-six patients (44.1%) were treated with radiotherapy and concurrent single-agent capecitabine, while thirty-three patients (55.9%) received radiotherapy and concurrent capecitabine with oxaliplatin. Surgery was performed at a median of 7.7 (IQR, 6.6–9.4) weeks after completion of NCRT. All patients underwent R0 resection with negative distal and circumferential margins. During the perioperative period, 10 patients (16.9%) received blood transfusion (BT; mean volume 3.5 IU). Twenty-seven (45.8%) patients received postoperative chemotherapy with regimens including: single agent capecitabine (n=5); capecitabine and oxaliplatin (XELOX) (n=21); 5-fluorouracil, leucovorin and oxaliplatin (FOLFOX) (n=1). Thirty-two (54.2%) patients did not accept any adjuvant chemotherapy. The median total number of lymph nodes harvested was 12 (IQR, 9–16) and did not differ between the ypN0 and ypN+ patients (Table 1).

Pathological evaluation of specimens from the 59 patients showed that 51 patients (86.4%) had a complete pathological response to NCRT (ypT0N0), and eight patients (13.6%) had lymph node metastases in the mesorectum (ypT0N+). Of the eight patients with ypT0N+ disease, three patients had metastasis in only one lymph node, two patients had two metastatic lymph nodes, one patient had seven metastatic lymph nodes, one patient had 16 metastatic lymph nodes, and one patient showed one tumor deposit in the mesorectum.

Table 1 Demographic and clinical characteristics of patients with ypT0 rectal cancer (N=59)

Variables	n (%)
Sex	
Male	38 (64.4)
Female	21 (35.6)
Age ($\bar{x}\pm s$) (year)	55.0 \pm 12.0
Distance from anal verge ($\bar{x}\pm s$) (cm)	4.4 \pm 2.3
Tumor diameter ($\bar{x}\pm s$) (cm)	4.3 \pm 1.5
CEA ($\bar{x}\pm s$) (ng/mL)	7.5 \pm 10.8
>5	19 (32.2)
T status before treatment	
cT2	3 (5.1)
cT3	46 (78.0)
cT4	10 (16.9)
N status before treatment	
cN–	11 (18.6)
cN+	48 (81.4)
Treatment regimens before surgery	
Radiotherapy and capecitabine	26 (44.1)
Radiotherapy and capecitabine with oxaliplatin	33 (55.9)
Interval between NCRT and surgery (weeks)	
<6	11 (18.6)
6–8	23 (39.0)
>8	25 (42.4)
Perioperative BT	10 (16.9)
BT volume ($\bar{x}\pm s$) (IU)	3.50 \pm 0.85
Tumor differentiation	
Good	2 (3.4)
Moderate	22 (37.3)
Poor	11 (18.6)
Unknown	24 (40.7)
Harvested lymph nodes [median (IQR)]	12 (9–16)
Adjuvant chemotherapy	
Yes	27 (45.8)
No	32 (54.2)

CEA, carcinoembryonic antigen; NCRT, neoadjuvant chemotherapy; BT, blood transfusion; IQR, interquartile range.

Oncological outcomes

The median follow-up was 52 (IQR, 37–67; range, 29–136) months. Overall, tumor recurrence was observed in nine

(15.3%) of the 59 patients, eight had distant recurrence, and one had both local and distant recurrences (Table 2). The mean interval from surgery to recurrence was 33.9 ($\bar{x}\pm s$, 16.4; range, 11.0–60.0) months. Of the 59 patients, five patients (8.5%) died: four from recurrence and one from other causes. The mean interval from surgery to death was 42 ($\bar{x}\pm s$, 7.6; range, 32.0–53.0) months.

Of the 51 patients with ypT0N0 disease, six (11.8%) developed distant recurrence, with one patients having both local and distant recurrences. Of the eight patients with ypT0N+ disease, three (37.5%) developed distant recurrence. Of the four patients who died of distant disease, two were classified as ypT0N0 and ypT0N+, respectively. The 5-year RFS rate was 82.7% in ypT0N0 patients and 62.5% in ypT0N+ patients (P=0.014). The 5-year OS rate was 90.9% for ypT0N0 and 70.0% for ypT0N+ (P=0.009).

As shown in Table 3, the results of univariate analyses showed that RFS was significantly associated with ypN+ status (P=0.014) and perioperative BT (P<0.001). OS was significantly associated with interval between NCRT and surgery (P=0.038), ypN+ status (P=0.032), and perioperative BT (P=0.037). Multivariate analyses showed ypN+ status and perioperative BT to be independent prognostic factors correlated with decreased 5-year RFS; however, no factor was associated with OS (Tables 4 and 5).

Discussion

Over the past three decades, crucial improvements in the treatment of rectal cancer have been achieved with the introduction of NCRT and the standardization of the

TME surgical technique (21,22). Currently, the guidelines of both the European Society of Medical Oncology and the National Comprehensive Cancer Network recommend performing NCRT in patients with LARC (2,3). This approach has several advantages, including down-sizing and down-staging of the primary tumor and a decreased local recurrence rate. The best outcome of NCRT is to obtain a pCR, which means complete eradication of all viable tumor cells from the rectal wall and mesorectum. Interestingly, NCRT leads to pCR rates varying from 10% to 27% (5-7), and we reported a pCR rate of 15.8% in the present study.

Currently, curative surgery with TME is still considered the standard surgical approach in patients with LARC after completion of NCRT. Although NCRT-induced inflammation, fibrosis and tissue edema might have adverse effects on the operation, several reports have indicated that NCRT in patients with LARC treated with radical surgery was not correlated with a higher incidence of postoperative complications, including anastomotic leakage (23,24). Moreover, radical surgery to obtain a final pCR is associated with favorable oncological outcomes. An Italian study analyzed 566 ypT0N0 patients from 36 centers and found that, after a median follow-up of 46.4 months, locoregional relapse, distant metastasis, 5-year DFS, OS, and cancer-specific survival rates were 1.6%, 8.9%, 85%, 90%, and 94%, respectively (5). A pooled analysis including 484 pCR patients with a median follow-up of 48 months found that patients with pCR after NCRT and surgery achieved favorable oncological outcomes compared with those with residual disease (DFS: 83.3% vs. 65.6%, P<0.0001) and the survival benefits of pCR on survival

Table 2 Clinicopathological details of nine patients with tumor recurrence

Patient	Sex	Age	Stage	CEA	Surgery	Perioperative BT	ypN	Metastatic site	RFS (months)	Follow-up (months)	Outcome
1	M	66	cT3N1	34.58	APR	No	N0	Distant LN	49	66	Alive
2	M	57	cT3N2	1.28	LAR	Yes	N0	Liver	60	67	Alive
3	F	51	cT3N1	5.59	APR	Yes	N0	Lung	44	50	Alive
4	F	46	cT3N0	4.29	LAR	Yes	N0	Liver, lung	11	42	Dead
5	M	48	cT3N2	16.38	APR	Yes	N0	Local, distant LN, lung, bone	37	53	Dead
6	M	45	cT3N2	1.56	LAR	No	N0	Distant LN, lung	38	69	Alive
7	F	72	cT3N1	12.76	APR	Yes	N1a	Lung	12	39	Dead
8	F	56	cT3N2	4.34	APR	Yes	N2b	Distant LN	28	72	Alive
9	M	28	cT3N1	14.48	APR	No	N2b	Bladder, peritoneum	26	32	Dead

CEA, carcinoembryonic antigen; BT, blood transfusion; RFS, recurrence-free survival; M, male; F, female; APR, abdominoperineal resection; LAR, low anterior resection; LN, lymph nodes.

Table 3 Univariate analyses of prognostic factors for recurrence and decreased survival of ypT0 patients (N=59)

Variables	Total	5-year RFS			5-year OS		
		n	%*	P	n	%	P
Sex				0.462			0.752
Male	38	33	80.2		35	88.9	
Female	21	17	77.9		19	86.2	
Age (year)				0.459			0.535
<60	39	32	76.7		35	85.5	
≥60	20	18	84.4		19	92.9	
Distance from anal verge (cm)				0.408			0.249
≤5	45	37	76.8		40	85.0	
>5	14	13	87.5		14	100	
CEA (ng/mL)				0.113			0.188
≤5	40	36	86.3		38	92.6	
>5	19	14	65.6		16	77.4	
T status before treatment				0.423			0.246
cT2	3	3	100		2	66.7	
cT3–4	56	47	78.2		52	89.6	
N status before treatment				0.458			0.948
cN–	11	10	90.9		10	88.9	
cN+	48	40	75.9		44	87.7	
Treatment regimens before surgery				0.940			0.456
Radiotherapy and capecitabine	26	23	80.8		24	85.2	
Radiotherapy and capecitabine with oxaliplatin	33	27	79.3		30	89.8	
Interval between NCRT and surgery (weeks)				0.669			0.038
≤8	34	29	81.8		33	96.2	
>8	25	21	74.7		21	73.7	
Type of surgery				0.596			0.337
APR	34	28	78.2		30	83.9	
LAR	25	22	81.8		24	94.1	
Laparoscopic vs. open surgery				0.759			0.556
Fully laparoscopic	35	30	73.7		32	82.6	
Open from the beginning	24	20	82.4		22	90.9	
Number of LN retrieval				0.475			0.332
<12	28	22	75.4		24	83.6	
≥12	31	28	87.3		30	96.6	
ypN category				0.014			0.032
N–	51	45	82.7		48	90.9	
N+	8	5	62.5		6	70.0	
Perioperative BT				<0.001			0.037
No	49	46	90.7		47	94.7	
Yes	10	4	40.0		7	68.6	

Table 3 (continued)

Table 3 (continued)

Variables	Total	5-year RFS			5-year OS		
		n	%*	P	n	%	P
Tumor differentiation**				0.768			0.164
Good and moderate	24	21	85.6		23	94.1	
Poor	11	9	75.8		9	76.2	
Pathological type				0.282			0.593
Adenocarcinoma	56	48	80.3		51	87.3	
Others***	3	2	66.7		3	100	
Adjuvant chemotherapy				0.987			0.813
No	32	27	76.6		29	85.6	
Yes	27	23	84.0		25	90.8	

RFS, recurrence-free survival; OS, overall survival; CEA, carcinoembryonic antigen; NCRT, neoadjuvant chemoradiotherapy; APR, abdominoperineal resection; LAR, low anterior resection; BT, blood transfusion; LN, lymph nodes; *, cumulative 5-year survival calculated using Kaplan-Meier analysis; **, tumor differentiation available for 35 patients; ***, including two mucinous adenocarcinoma and one signet ring cell carcinoma.

Table 4 Multivariate analyses of factors associated with RFS in ypT0 patients

Factors	Total	HR	95% CI	P
CEA (ng/mL)				0.088
≤5	40	1		
>5	19	3.41	0.83–13.95	
ypN category				0.009
N–	51	1		
N+	8	10.15	1.76–58.41	
Perioperative BT				0.001
No	49	1		
Yes	10	11.77	2.78–49.90	

RFS, recurrence-free survival; CEA, carcinoembryonic antigen; BT, blood transfusion; HR, hazard ratio; 95% CI, 95% confidence interval.

were not affected by clinical T or N status, administration of adjuvant chemotherapy, tumor location, or type of surgery (6). Another meta-analysis conducted by Zorcolo *et al.*, analyzed the data for 1,913 patients from twelve studies and found that the 300 patients with pCR had better OS and DFS than those with partial or no response (OS: 92.9% vs. 73.4%, P=0.002; DFS: 86.9% vs. 63.9%, P=0.002) (7). The results of our study were similar to the above-noted studies, with 5-year RFS and OS rates of 82.7% and 90.9%, respectively, for ypT0N0 patients.

All of the studies mentioned above indicate that pCR translates to favorable oncological survival for patients. Based on this observation, and in an effort to preserve continence and long-term functional outcomes, avoid a

Table 5 Multivariate analyses of factors associated with OS in ypT0 patients

Factors	Total	HR	95% CI	P
CEA (ng/mL)				0.395
≤5	40	1		
>5	19	2.43	0.32–18.64	
Interval between neoadjuvant therapy and surgery (weeks)				0.095
≤8	34	1		
>8	25	7.25	0.71–74.37	
ypN category				0.105
N–	51	1		
N+	8	5.62	0.70–45.15	
Perioperative BT				0.087
No	49	1		
Yes	10	5.42	0.78–37.49	

OS, overall survival; CEA, carcinoembryonic antigen; BT, blood transfusion; HR, hazard ratio; 95% CI, 95% confidence interval.

permanent stoma, and reduce the morbidity and length of hospital stay associated with radical surgery, there has been a great interest in LE of the primary tumor or a watchful waiting strategy for patients who show a good clinical response to NCRT. In 2001, Kim *et al.* reported that 17 patients who underwent LE of their primary tumor after NCRT to achieve ypT0 disease did not experience recurrence, with a mean follow-up of 24 months (9). In 2004, Habr-Gama *et al.* indicated that omission of radical

surgery with a watchful waiting policy might be workable in selected patients who achieved a clinical complete response (cCR) to NCRT (10). Increasing evidence suggests that these methods are feasible in less advanced tumors (11-13).

However, when considering LE or a watchful waiting policy, these questions should be taken into account. Firstly, how should appropriate imaging technology be selected to characterize cCR or a complete response of the primary tumor? In 2013, Guillem *et al.* found that neither PET nor CT scans had adequate predictive ability to identify a pCR from an incomplete response (25). Even using combined tools (EUS and MRI), the sensitivity to select a pCR or sustained cCR patients was just 18.2% (26). Secondly, how should regrowths or recurrences be managed after NCRT and LE of the primary tumor or a watchful waiting policy? In review of the medical literature, the incidence of patients with rectal cancer who develop local regrowths after a watchful waiting strategy following NCRT ranges from 15% to 60% (12,13,27-30). Although most of these patients receive salvage resection, it is unclear whether NCRT-induced fibrosis limits the feasibility of salvage surgery, and whether salvage surgery is associated with increased postoperative complications. Moreover, the long-term outcomes of salvage surgery are also unclear. Recently, Perez *et al.* suggested that salvage resection for local recurrences after NCRT and transanal endoscopic microsurgery (TEM) was correlated with a high rate of R1 resection with positive circumferential margin in 87% of patients. Even if salvage surgery was carried out, the 2-year local re-RFS was just 60% (31). Another issue that should not be ignored is the status of mesorectal lymph nodes, which may be an important prognostic factor for local and distant recurrences. Several studies have shown that nodal metastasis in the mesorectum is recognized to be one of the most independent risk factors for recurrence (32,33). Although patients with lower ypT classifications following NCRT were less likely to have ypN+ status, the incidence of metastatic lymph node involvement among patients with ypT0 status after NCRT and surgery in prior reports varies from 6.6% to 16% (15-20).

In our study, 13.6% of patients with ypT0 rectal cancer after NCRT and curative surgery were ypN+ disease, consistently with prior results, and distant recurrence occurred more frequently in the ypN+ than the ypN0 patients. Recently, an Italian study of 261 patients who presented a complete or nearly complete response of primary tumor from 13 centers showed that nodal

positivity accounted for 8.7% of patients, and multivariate analyses identified nodal metastasis in the mesorectum as the only risk factor independently associated with a decreased OS (20). In accordance with this, Loftås *et al.* analyzed 161 ypT0 patients at a national level, revealing that survival was significantly better in ypT0N0 patients compared with ypT0N+ patients, and concluding that the survival benefits of primary tumor complete response were contingent upon ypN status (19). Similarly, according to the Korean Radiation Oncology Group study, residual nodal disease in ypT0 patients was associated with decreased DFS and OS (16). Another smaller cohort study of 91 ypT0 patients conducted by Jang *et al.* also suggested that ypN+ status was a significant prognostic factor correlated with distant metastases (17).

In summary, long-term outcomes in patients with ypT0N0 rectal cancer are excellent. However, patients with residual disease in the mesorectum even after complete regression of primary tumor have a poorer outcome. Thus, caution should be taken when using LE of primary tumor or a watchful waiting management approach for these patients.

For many years, BT has been an indispensable part of the standard treatment used alongside the surgery in cancer patients. Although BT has been recognized to improve oxygen delivery and tissue perfusion, it is also associated with a poorer outcome in cancer patients, especially in colorectal cancer. According to the results of the American College of Surgeons National Surgical Quality Improvement Program, 14.07% of patients received BT, and BT was correlated with worse short-term outcomes, for example, increased mortality and morbidity, longer hospital stay, and higher incidence of pulmonary and wound infection (34). Several studies also suggested that for patients with colorectal liver metastases undergoing liver resection, 5-year OS and RFS were worse in patients who received blood (35,36). However, the possible mechanism by which BT is associated with worse outcomes is unclear. Some deem that the immunomodulatory effect of BT might induce decreased macrophage function, lower CD4/CD8 ratios, and reduced natural killer cells function which may contribute to a reduced immune surveillance, thereby stimulating tumor growth, tethering, and dissemination (37,38). On the contrary, others have suggested that worse survival after rectal surgery in patients receiving BT was due to the clinical circumstances requiring transfusion, not because of the BT itself (39). In the present study, 16.9% of patients received BT and BT

was significantly associated with reduced RFS and OS. After adjustment for prognostic factors, BT was independently correlated with decreased RFS [hazard ratio (HR): 11.77; 95% confidence interval (95% CI): 2.78–49.90; $P=0.001$]. Although most patients with LARC after NCRT have poor performance status, it is unclear whether BT is more likely to affect immune defense, or to stimulate tumor growth, tethering, and dissemination in these patients. Future studies are warranted to illuminate this point.

This study had several limitations. First, the sample size for patients in the ypN0 and ypN+ groups was small which may limit the statistical analysis. Second, being a retrospective study and based on a single-center setting, it might be susceptible to selection bias. Besides, due to pCR of primary tumor after NCRT and surgery, tumor differentiation was not available for 40.7% of patients, although pretreatment pathological examination was performed for all patients before NCRT, which might decrease the statistical power owing to the high percentage of unknown data. Although we documented perioperative BT as an independent risk factor for recurrence, we did not further identify predictive factors independently associated with the necessity for transfusion.

Conclusions

Long-term outcomes in patients with ypT0N0 rectal cancer are excellent; however, positive lymph nodes or tumor deposits can still be found in 13.6% of patients who show complete pathological response in the rectal wall and are independently associated with decreased 5-year RFS. Additionally, perioperative BT is also one variable independently correlated with a worse RFS, so effective ways to rationalize blood utilization in rectal cancer surgery following NCRT are warranted to minimize the adverse effect on survival.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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