



RAPID COMMUNICATION

Study of circumferential resection margin in patients with middle and lower rectal carcinoma

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Abstract

AIM: To clarify the relationship between circumferential resection margin status and local and distant recurrence as well as survival of patients with middle and lower rectal carcinoma. The relationship between circumferential resection margin status and clinicopathologic characteristics of middle and lower rectal carcinoma was also evaluated.

METHODS: Cancer specimens from 56 patients with middle and lower rectal carcinoma who received total mesorectal excision at the Department of General Surgery of Guangdong Provincial People's Hospital were studied. A large slice technique was used to detect mesorectal metastasis and evaluate circumferential resection margin status.

RESULTS: Local recurrence occurred in 12.5% (7 of 56 cases) of patients with middle and lower rectal carcinoma. Distant recurrence occurred in 25% (14 of 56 cases) of patients with middle and lower rectal carcinoma. Twelve patients (21.4%) had positive circumferential resection margin. Local recurrence rate of patients with positive circumferential resection margin was 33.3% (4/12), whereas it was 6.8% (3/44) in those with negative circumferential resection margin ($P = 0.014$). Distant recurrence was observed in 50% (6/12) of patients with positive circumferential resection margin; conversely, it was 18.2% (8/44) in those with negative circumferential resection margin ($P = 0.024$). Kaplan-Meier survival analysis showed significant improvements in median survival (32.2 ± 4.1 mo, 95% CI: 24.1-40.4

mo vs 23.0 ± 3.5 mo, 95% CI: 16.2-29.8 mo) for circumferential resection margin-negative patients over circumferential resection margin-positive patients (log-rank, $P < 0.05$). 37% T₃ tumors examined were positive for circumferential resection margin, while only 0% T₁ tumors and 8.7% T₂ tumors were examined as circumferential resection margin. The difference between these three groups was statistically significant ($P = 0.021$). In 18 cancer specimens with tumor diameter ≥ 5 cm 7 (38.9%) were detected as positive circumferential resection margin, while in 38 cancer specimens with a tumor diameter of < 5 cm only 5 (13.2%) were positive for circumferential resection margin ($P = 0.028$).

CONCLUSION: Our findings indicate that circumferential resection margin involvement is significantly associated with depth of tumor invasion and tumor diameter. The circumferential resection margin status is an important predictor of local and distant recurrence as well as survival of patients with middle and lower rectal carcinoma.

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Key words: Middle and lower rectal carcinoma; Circumferential resection margin; Prognosis

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INTRODUCTION

It is well known that middle and lower rectal carcinomas are of the most common carcinomas in China. However, even after undergoing radical resection of primary tumors and lymph nodes, about 5%-40% of patients with rectal carcinoma report with local recurrence^[1-5]. It has been reported that residual mesorectal metastasis may be the most important factor of local recurrence^[6,7]. In the current study, circumferential resection margin was detected by pathological observation in cancer specimens from 56 patients with middle and lower rectal carcinoma. The associations of circumferential resection margin status and local recurrence, distant recurrence as

well as clinicopathologic characteristics of patients with middle and lower rectal carcinoma were investigated. The relationships between circumferential resection margin status and clinicopathologic characteristics of middle and lower rectal carcinoma were also evaluated.

MATERIALS AND METHODS

Patients

Cancer specimens resected from 56 patients with middle and lower rectal carcinoma who received total mesorectal excision at the Department of General Surgery of Guangdong Provincial People's Hospital from November 2001 to July 2003 were studied. There were 37 men and 19 women, ranging in age from 30 to 86 years, with a mean age of 60.5 years. None of these patients had received preoperative chemotherapy or radiotherapy. There were 26 lower rectal carcinomas and 30 middle rectal carcinomas. Patients with tumor diameter ≥ 5 cm were in 18 cases, with tumor diameter < 5 cm in 38 cases. Low anterior resection was performed in 40 patients, abdominal perineal resection in 16 patients. According to the Ming's criteria, 15 tumors were classified as expansive type carcinomas, 41 tumors classified as infiltrative type carcinomas. TNM stage status: stage I in 5 patients, stage II in 22 patients, and stage III in 29 patients. There were 14 patients with poorly differentiated carcinoma, 37 patients with moderately differentiated carcinoma, and 5 patients with well-differentiated carcinoma.

Methods

Two pathologists who had no knowledge of the clinicopathological data observed the specimens independently. If tumor cells were detected within 1 mm of the circumferential margin, the status was classified as positive circumferential resection margin^[8].

Statistical analysis

Statistical analysis was performed by the Pearson Chi-square test to examine the associations of circumferential resection margin status and local recurrence, distant recurrence as well as clinicopathologic characteristics of patients with middle and lower rectal carcinoma. The relationship between circumferential resection margin status and survival of patients with middle and lower rectal carcinoma was evaluated by Kaplan-Meier survival analysis and log-rank test. Statistical significance was defined as $P < 0.05$.

RESULTS

Correlations between circumferential resection margin status and local recurrence, distant recurrence as well as survival of patients with middle and lower rectal carcinoma

Local recurrence occurred in 12.5% (7 of 56 cases) of patients with middle and lower rectal carcinoma. Distant recurrence occurred in 25% (14 of 56 cases) of patients with middle and lower rectal carcinoma. Twelve patients (21.4%) had positive circumferential resection margin. Local recurrence rate of patients with

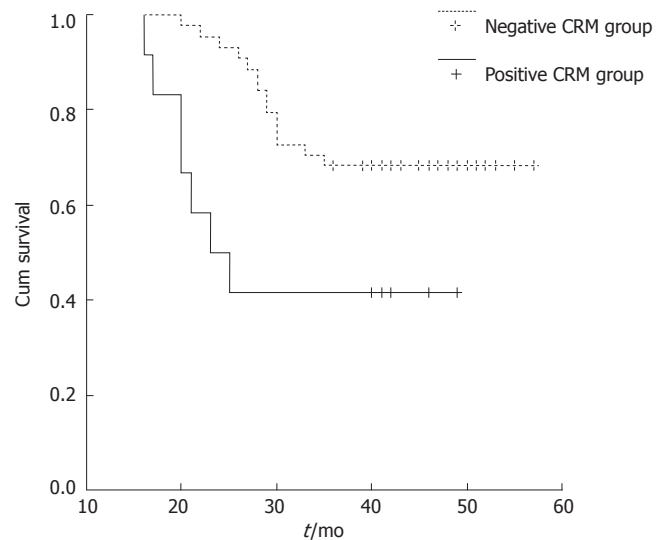


Figure 1 Correlation between circumferential resection margin status and survival of patients with middle and lower rectal carcinoma (Kaplan-Meier survival analysis).

positive circumferential resection margin was 33.3% (4/12), whereas it was 6.8% (3/44) in those with negative circumferential resection margin ($P = 0.014$). Distant recurrence was observed in 50% (6/12) of patients with positive circumferential resection margin; conversely, it was 18.2% (8/44) in those with negative circumferential resection margin ($P = 0.024$). Kaplan-Meier survival analysis showed significant improvements in median survival (32.2 ± 4.1 mo, 95% CI: 24.1-40.4 mo *vs* 23.0 ± 3.5 mo, 95% CI: 16.2-29.8 mo) for circumferential resection margin-negative patients over circumferential resection margin-positive patients (log-rank, $P < 0.05$) (Figure 1).

Correlations between circumferential resection margin status and clinicopathologic characteristics of patients with middle and lower rectal carcinoma

The circumferential resection margin involvement correlated significantly with depth of tumor invasion and tumor diameter. 37% T₃ tumors were examined as positive circumferential resection margin, while only 0% T₁ tumors and 8.7% T₂ tumors were examined as circumferential resection margin. The difference between these three groups was statistically significant ($P = 0.021$). In 18 cancer specimens with tumor diameter ≥ 5 cm 7 (38.9%) were detected positive circumferential resection margin, while in 38 cancer specimens with tumor diameter < 5 cm only 5 (13.2%) were positive circumferential resection margin ($P = 0.028$). No significant correlations were found between circumferential resection margin involvement and other variables such as age ($P = 0.815$), gender ($P = 0.961$), diameter of tumor infiltration ($P = 0.417$), tumor differentiation ($P = 0.074$), Ming's classification ($P = 0.372$) and lymph node metastases ($P = 0.609$) (Table 1).

DISCUSSION

After radical resection of rectal carcinoma, the circumferential resection margin on the non-peritonealized surface of the resected specimen is of critical importance.

Table 1 Correlation between circumferential resection margin involvement with clinicopathologic characteristics of patients with middle and lower rectal carcinoma

Variable	n	Circumferential resection margin involvement		P
		Negative (%)	Positive (%)	
Gender				
Male	37	29 (78.4)	8 (21.6)	P = 0.961
Female	19	15 (78.9)	4 (21.1)	
Age (yr)				
< 60	25	20 (80.0)	5 (20.0)	P = 0.815
≥ 60	31	24 (77.4)	7 (22.6)	
Superficial diameter (cm)				
< 5	38	33 (86.8)	5 (13.2)	P = 0.028
≥ 5	18	11 (61.1)	7 (38.9)	
Diameter of infiltration				
1/4	8	7 (87.5)	1 (12.5)	P = 0.417
1/2	16	14 (87.5)	2 (12.5)	
3/4	18	14 (77.8)	4 (22.2)	
4/4	14	9 (64.3)	5 (35.7)	
Ming's classification				
Expansive	15	2 (13.3)	13 (86.7)	P = 0.372
Infiltrative	41	10 (24.4)	31 (75.6)	
Depth of invasion				
T ₁	6	6 (100.0)	0 (0)	P = 0.021
T ₂	23	21 (91.3)	2 (8.7)	
T ₃	27	17 (63.0)	10 (37.0)	
Histologic differentiation				
Well	5	4 (80.0)	1 (20.0)	P = 0.074
Moderate	37	32 (86.5)	5 (13.5)	
Poorly	14	8 (57.1)	6 (42.9)	
Lymph node metastasis				
Positive	29	22 (75.9)	7 (24.1)	P = 0.609
Negative	27	22 (81.5)	5 (18.5)	

7.1%-35% of patients with rectal carcinoma were reportedly identified circumferential resection margin involvement^[3,8-10]. In the present study, circumferential resection margin involvement in patients with middle and lower rectal carcinoma who underwent radical resection and total mesorectal excision were evaluated. 21.4% (12 of 56 cases) of patients had positive circumferential resection margin.

The correlation between circumferential resection margin status and local recurrence of patients with rectal carcinoma is still controversial presently^[10-13]. Wibe *et al*^[13] reported that positive circumferential resection margin had a significant and major prognostic impact on the rates of local recurrence of patients with rectal carcinoma who underwent total mesorectal excision. After a median follow-up of 29 (range 14-60) mo, the overall local recurrence rate was 7% (46 of 686 patients): 22% among patients with a positive resection margin and 5% in those with a negative margin. However, Luna-Perez^[10] *et al* reported that circumferential resection margin involvement was not correlated significantly with local recurrence of patients with rectal adenocarcinoma ($P = 0.33$). Hall *et al*^[11] reported that local recurrence rate of patients with positive circumferential resection margin was 15%, whereas it was 11% in those with negative circumferential resection margin. The difference between these two groups was not statistically significant ($P = 0.38$). Our results demonstrated that circumferential resection margin involvement had significant correlation with local recurrence of patients with middle and low rectal carcinoma. Local recurrence

was more frequent in patients with positive circumferential resection margin (4 of 12 cases, 33.3%), compared with patients with negative circumferential resection margin (3 of 44 cases, 6.8%) ($P = 0.014$). We conclude that the circumferential resection margin status is an important predictor of local recurrence of patients with middle and low rectal carcinoma.

We also found that circumferential resection margin involvement was significantly correlated with distant recurrence and survival of patients with middle and low rectal carcinoma. Distant recurrence was observed in 50% (6/12) of patients with positive circumferential resection margin; conversely, it was 18.2% (8/44) in those with negative circumferential resection margin ($P = 0.024$). Kaplan-Meier survival analysis showed significant improvements in median survival for circumferential resection margin-negative patients over circumferential resection margin-positive patients (log-rank, $P < 0.05$). The consequences indicate that the circumferential resection margin status is an important predictor of local and distant recurrence as well as survival. For this reason, the circumferential resection margin status should be considered a major prognostic factor and should be validated in future trials as an early alternative clinical endpoint. Our results also support that histopathological examination of resected specimens must include careful assessment of the circumferential resection margin.

Many clinical studies reported the existence of circumferential resection margin involvement in patients with rectal carcinoma^[8-15]. However, the relationships between circumferential resection margin status and clinicopathologic characteristics have not yet been explored. Therefore, the main objective of this study was to examine circumferential resection margin involvement and explore its relationship with clinicopathologic characteristics of patients with middle and lower rectal carcinoma. The circumferential resection margin involvement correlated significantly with depth of tumor invasion and tumor diameter. Positive circumferential resection margin was more frequent in T₃ tumors (20 of 27 cases, 37%), compared with T₂ tumors (2 of 23 cases, 8.7%) and T₁ tumors (0 of 6 cases, 0%). The difference between these three groups was statistically significant ($P = 0.021$). 38.9 per cent (7 of 18 cases) of patients with tumor diameter ≥ 5 cm were detected as positive circumferential resection margin, while only 13.2% (5 of 38 cases) of patients with tumor diameter < 5 cm had circumferential resection margin involvement ($P = 0.028$). The result indicates that wider mesorectal excision should be followed in the management of patients with T₃ tumors or tumor diameter ≥ 5 cm.

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