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RAPID COMMUNICATION

Risk factors for local recurrence of middle and lower rectal carcinoma after curative resection

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Abstract

AIM: To explore the risk factors for local recurrence of middle and lower rectal carcinoma after curative resection.

METHODS: Specimens of middle and lower rectal carcinoma from 56 patients who received curative resection 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. The relations between clinicopathologic characteristics, mesorectal metastasis and circumferential resection margin status were identified in patients with local recurrence of middle and lower rectal carcinoma.

RESULTS: Local recurrence of middle and lower rectal carcinoma after curative resection occurred in 7 of the 56 patients (12.5%), and was significantly associated with family history (χ^2 = 3.929, P = 0.047), high CEA level (χ^2 = 4.964, P = 0.026), cancerous perforation (χ^2 = 8.503, P = 0.004), tumor differentiation (χ^2 = 9.315, P = 0.009) and vessel cancerous emboli (χ^2 = 11.879, P = 0.001). In contrast, no significant correlation was found between local recurrence of rectal carcinoma and other variables such as age (χ^2 = 0.506, P = 0.477), gender (χ^2 = 0.102, χ^2 = 0.749), tumor diameter (χ^2 = 0.421, P = 0.516), tumor infiltration (χ^2 = 5.052, P = 0.168), depth of tumor invasion (χ^2 = 4.588, P = 0.101), lymph node metastases (χ^2 = 3.688, P = 0.055) and TNM staging system (χ^2 = 3.765, P = 0.152). The local recurrence rate of middle and lower rectal carcinoma was 33.3% (4/12) in patients with positive circumferential resection margin and 6.8% (3/44) in those with negative circumferential resection margin. There was a significant difference between the two groups (χ^2 = 6.061, P = 0.014). Local recurrence of rectal carcinoma occurred in 6 of 36 patients (16.7%) with mesorectal metastasis, and in 1 of 20 patients (5.0%) without mesorectal metastasis. However, there was no significant difference between the two groups (χ^2 = 1.600, P = 0.206).

CONCLUSION: Family history, high CEA level, cancerous perforation, tumor differentiation, vessel cancerous emboli and circumferential resection margin status are the significant risk factors for local recurrence of middle and lower rectal carcinoma after curative resection. Local recurrence may be more frequent in patients with mesorectal metastasis than in patients without mesorectal metastasis.

Key words: Middle and lower rectal carcinoma; Local recurrence; Circumferential resection margin; Mesorectal metastasis

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INTRODUCTION

It is well known that local recurrence is of rectal carcinoma plays an important role in its prognosis[1-3]. However, local recurrence of rectal carcinoma occurs in about 4%-50% of patients even after radical resection of primary tumors and lymph nodes[4-8]. The risk factors

for local recurrence of rectal carcinoma remain unclear. Therefore, the aim of the current study was to explore the risk factors for local recurrence of middle and lower rectal carcinoma after curative resection. Specimens of middle and lower rectal carcinoma from 56 patients who underwent total mesorectal excision (TME) at the Department of General Surgery, Guangdong Provincial People's Hospital, from November, 2001 to July, 2003, were studied. A large slice technique was used to detect mesorectal metastasis and evaluate circumferential resection margin status. The relationship between mesorectal metastasis, local recurrence and circumferential resection margin status of rectal carcinoma was observed. The clinicopathologic characteristics of middle and lower rectal carcinoma were also evaluated.

MATERIALS AND METHODS

Patients and specimens

Specimens of middle and lower rectal carcinoma from 56 patients who underwent TME at the Department of General Surgery, 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 received preoperative chemotherapy or radiotherapy. Twenty-six patients had lower rectal carcinoma and 30 had middle rectal carcinoma. Tumors $\geqslant$ 5 cm and in < 5 cm diameter were found in 18 and 38 patients, respectively. Low anterior resection was performed in 40 patients and abdominoperineal resection in 16 patients. TNM stages were as followa: stage I in 5 patients, stage Ⅱ in 22 patients, and stage Ⅲ in 29 patients poorly-differentiated carcinoma was observed in 14 patients, moderately-differentiated carcinoma in 37 patients, and well-differentiated carcinoma in 5 patients, respectively. A large slice technique was used to detect mesorectal metastasis and evaluate circumferential resection margin status. Two pathologists who were blinded to the clinicopathological data observed the specimens independently. If tumor cells were detected within 1 mm of circumferential margin, they were classified to have a positive circumferential resection margin as previously described[9-11].

Statistical analysis

Statistical analysis was performed by the Pearson χ^2 test to examine the association between local recurrence, circumferential resection margin status and mesorectal metastasis of rectal carcinoma. Clinicopathologic characteristics of the patients with middle and lower rectal carcinoma were also analyzed. $P < 0.05$ was considered statistically significant.

RESULTS

Correlation between local recurrence and clinicopathologic characteristics of patients with middle and lower rectal carcinoma

Local recurrence of middle and lower rectal carcinoma after curative resection was found in 7 of 56 patients (12.5%), which was significantly related with family history ($\chi^2 = 3.929$, $P = 0.047$), high CEA level ($\chi^2 = 4.964$, $P = 0.026$), cancerous perforation ($\chi^2 = 8.503$, $P = 0.004$), tumor differentiation ($\chi^2 = 9.315$, $P = 0.009$) and vessel cancerous emboli ($\chi^2 = 11.879$, $P = 0.001$). In contrast, no significant correlation was found between local recurrence and other variables such as age ($\chi^2 = 0.506$, $P = 0.477$) and gender ($\chi^2 = 0.102$, $P = 0.749$), tumor diameter ($\chi^2 = 0.421$, $P = 0.516$), tumor infiltration ($\chi^2 = 5.052$, $P = 0.168$), depth of tumor invasion ($\chi^2 = 4.588$, $P = 0.101$), lymph node metastases ($\chi^2 = 3.688$, $P = 0.055$) and TNM staging system ($\chi^2 = 3.765$, $P = 0.152$) (Table 1).

Correlation between circumferential resection margin status and local recurrence of middle and lower rectal carcinoma

A positive circumferential resection margin of middle and lower rectal carcinoma was observed in 12 of 56 patients (21.4%). Local recurrence of middle and lower rectal carcinoma was found in 4 of 12 patients (33.3%) with a positive circumferential resection margin and in 3 of 44 patients (6.8%) with a negative circumferential resection margin. There was a significant difference between the two groups ($\chi^2 = 6.061$, $P = 0.014$) (Table 1).

Correlation between mesorectal metastasis and local recurrence of middle and lower rectal carcinoma

Mesorectal metastasis of middle and lower rectal carcinoma was detected in 36 of 56 patients (64.3%). The local recurrence rate of mesorectal metastasis was 16.7% (6 of 36 patients) and 5.0% (1 of 20 patients), respectively. However, there was no significant difference between the two groups ($\chi^2 = 1.600$, $P = 0.206$) (Table 1).

DISCUSSION

It is well known that middle and lower rectal carcinoma is one of the most common carcinomas in China. Local recurrence of middle and lower rectal carcinoma after curative resection has significant morbidity and mortality[4,12-15] and its recurrence rate varies from less than 4% to greater than 50%. Since TME was adopted as the standard treatment of patients with rectal carcinoma, a significant decrease in local recurrence and a trend to improve relative survival have been reported[16-18]. In our sturdy, local recurrence of middle and lower rectal carcinoma occurred in 7 of 56 patients (12.5%) after TME, indicating that TME can significantly reduce the local recurrence rate of middle and lower rectal carcinomas.

The correlation between circumferential resection margin status and local recurrence of rectal carcinoma is still controversial[10,11,19-21]. Wibe *et al*[10] reported that a positive circumferential resection margin has a significant and major prognostic impact on the local recurrence rate of rectal carcinoma after TME. However, Luna-Perez *et al*[19] reported that circumferential resection margin involvement is not correlated significantly with

Table 1 Local recurrence and circumferential resection margin status, mesorectal metastasis, and clinicopathologic characteristics of middle and lower rectal carcinoma

Clinicopathologic variable	Patients (*n*)	Local recurrence		χ^2	*P*
		Positive (%)	Negative (%)		
Gender					
Male	37	5 (13.5)	32 (86.5)		
Female	19	2 (10.5)	17 (89.5)	0.102	0.749
Age					
< 60 yr	25	4 (16.0)	21 (84.0)		
⩾ 60 yr	31	3 (9.7)	28 (90.3)	0.506	0.477
Family history					
Yes	21	5 (23.8)	16 (76.2)		
No	35	2 (5.7)	33 (94.3)	3.929	0.047
CEA level					
High	26	6 (23.1)	20 (76.9)		
Normal	30	1 (3.3)	29 (96.7)	4.964	0.026
Cancerous perforation					
Yes	3	2 (33.3)	1 (66.7)		
No	53	5 (9.4)	48 (90.6)	8.503	0.004
Superficial diameter					
< 5 cm	38	4 (10.5)	34 (89.5)		
⩾ 5 cm	18	3 (16.7)	15 (83.3)	0.421	0.516
Diameter of infiltration					
1/4	8	0 (0)	8 (100)		
1/2	16	1 (6.3)	15 (93.7)		
3/4	18	2 (11.1)	16 (88.9)		
4/4	14	4 (28.6)	10 (71.4)	5.052	0.168
Depth of invasion					
T_1	6	0 (0)	6 (100)		
T_2	23	1 (4.3)	22 (95.7)		
T_3	27	6 (22.2)	21 (77.8)	4.588	0.101
Histologic differentiation					
Well	5	0 (0)	5 (100)		
Moderate	37	2 (5.4)	35 (94.6)		
Poorly	14	5 (35.7)	9 (64.3)	9.315	0.009
Lymph node metastasis					
Positive	29	6 (20.7)	23 (79.3)		
Negative	27	1 (3.7)	26 (96.3)	3.688	0.055
Vessel cancerous emboli					
Positive	12	5 (41.7)	7 (58.3)		
Negative	44	2 (4.5)	42 (95.5)	11.879	0.001
Circumferential resection margin					
Positive	12	4 (33.3)	8 (66.7)		
Negative	44	3 (6.8)	41 (93.2)	6.061	0.014
Mesorectal metastasis					
Positive	36	6 (16.7)	30 (83.3)		
Negative	20	1 (5.0)	19 (95.0)	1.6	0.206
TNM staging					
Ⅰ	5	0 (0)	5 (100)		
Ⅱ	22	1 (4.5)	21 (95.5)		
Ⅲ	29	6 (20.7)	23 (79.3)	3.765	0.152

local recurrence of rectal adenocarcinoma (P = 0.33). Hall *et al*[11] reported that the local recurrence rate of rectal carcinoma with a positive circumferential resection margin is 15% and 11% in of those with a negative circumferential resection margin. The difference between the two groups was not significant. Our results demonstrate that circumferential resection margin involvement had a significant correlation with local recurrence of middle and low rectal carcinoma. Local recurrence was more frequently observed in rectal carcinomas with a positive circumferential resection margin (4 of 12 patients, 33.3%) than in those with a negative circumferential resection margin (3 of 44 patients, 6.8%) (P = 0.014), suggesting that circumferential resection margin status is an important predictor for the local recurrence of middle and low rectal carcinoma. It has been shown that residual mesorectal metastasis observed in rectal surgery may be the most important factor for local recurrence of rectal carcinoma[22,23]. In the current study, the local recurrence of rectal carcinoma was more frequent in patients with mesorectal metastasis than in those without mesorectal metastasis (16.7% *vs* 5.0%). However, there was no significant difference between the two groups (P = 0.206). TME may be also a plausible explanation for the observation.

Sugihara *et al*[24] investigated the correlation between local recurrence and clinicopathologic characteristics of rectal carcinoma by multivariate analysis, and found that local recurrence of lower rectal cancer is significantly associated lymph node metastasis. It has been demonstrated that pathologic stages T and N are the significant predictors for the local recurrence of rectal carcinoma[25]. In the present study, local recurrence of poorly- and moderately- differentiated rectal carcinomas was found in 5 of 34 patients (35.7%) and in 2 of 37 patients (5.4%), respectively ($P = 0.009$), while no local recurrence of well-differentiated rectal carcinoma was observed in any patients, suggesting that local recurrence of rectal carcinoma is significantly correlated with tumor differentiation. We also found that the local recurrence rate of rectal carcinoma was also correlated with the depth of tumor invasion. Local recurrence of T_3, and T_2 tumors was observed in 6 of 27 patients (22.2%) and in 1 of 23 patients (4.3%), respectively, while no local recurrence of T_1 tumors was observed ($P = 0.101$). Local recurrence of rectal carcinoma developed in 6 (20.7%) of the 29 patients with lymph node metastasis and in 1 (3.7%) of 27 patients without lymph node metastasis ($P = 0.055$). These observations may be explained by the fact that the number of patients in our study was comparatively small. Further study with a larger sample size is needed.

Park *et al*[26] reported that change in perioperative serum CEA is a useful prognostic predictor for the occurrence of stage Ⅲ rectal cancer and the survival of such patients. Oh *et al*[27] reported that vascular invasion is significantly associated with local recurrence of rectal cancer. Our results also demonstrate that local recurrence of rectal carcinoma had a significant correlation with high CEA level ($P = 0.026$) and vessel cancerous emboli ($P = 0.001$). We also found that family history and cancerous perforation were significantly correlated with local recurrence of rectal carcinoma ($P < 0.05$).

In conclusion, extensive mesorectal excision and postoperative adjuvant chemotherapy should be used in the treatment of middle and lower rectal carcinoma.

COMMENTS

Background

It is well known that local recurrence is the most important prognostic factor for rectal carcinoma. However, local recurrence of rectal carcinoma occurs in about 4%-50% of patients even after radical resection of primary tumors and lymph nodes. The risk factors for local recurrence of rectal carcinoma remain unclear.

Research frontiers

Since total mesorectal excision (TME) was adopted as the standard treatment of rectal carcinoma, a significant decrease in its local recurrence and a trend to improve the relative survival of rectal carcinoma patients have been reported. However, the local recurrence rate of rectal carcinoma is still high. The correlation between circumferential resection margin status and local recurrence of rectal carcinoma is still controversial.

Innovations and breakthroughs

The aim of the current study was to explore the risk factors for local recurrence of middle and lower rectal carcinoma after curative resection. A large slice technique was used to detect its mesorectal metastasis and evaluate its circumferential resection margin status. The relationship between mesorectal metastasis and circumferential resection margin status with local recurrence was identified. The clinicopathological characteristics of rectal carcinoma were described.

Applications

Family history, high CEA level, cancerous perforation, tumor differentiation, vessel cancerous emboli and circumferential resection margin status are the significant risk factors of local recurrence of middle and lower rectal carcinoma after curative resection. Local recurrence of middle and lower rectal carcinoma may be more frequent observed in patients with mesorectal metastasis than in those without mesorectal metastasis.

Terminology

Local recurrence of middle and lower rectal carcinoma was defined as any recurrence diagnosed or suspected in the pelvis (tumor bed, pelvic nodes, anastomosis, drain site, or perineum).

Peer review

The authors explored the risk factors for local recurrence of middle and lower rectal carcinoma after curative resection, demonstrating that family history, high CEA level, cancerous perforation, tumor differentiation, vessel cancerous emboli and circumferential resection margin status are the significant risk factors for the local recurrence of middle and lower rectal carcinoma. The study was well designed. The data provided in the paper are interesting and valuable.

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