RAPID COMMUNICATION



Prognostic value of lateral lymph node metastasis for advanced low rectal cancer

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Abstract

AIM: To evaluate the risk factors for lateral lymph node metastasis in patients with advanced low rectal cancer, in order to make the effective selection of patients who could benefit from lateral lymph node dissection, as well as the relationship of lateral lymph node metastasis with local recurrence and survival of patients with advanced low rectal cancer.

METHODS: A total of 96 consecutive patients who underwent curative surgery with lateral pelvic lymphadenectomy for advanced lower rectal cancer were retrospectively analyzed. The relation of lateral lymph node metastasis with clinicopathologic characteristics, local recurrence and survival of patients was identified.

RESULTS: Lateral lymph node metastasis was observed in 14.6% (14/96) of patients with advanced low rectal cancer. Lateral lymph node metastasis was detected in 10 (25.0%) of 40 patients with tumor diameter \geq 5 cm and in 4 (7.1%) of 56 patients with tumor diameter < 5 cm. The difference between the two groups was statistically significant (χ^2 = 5.973, *P* = 0.015). Lateral lymph node metastasis was more frequent in patients with 4/4 diameter of tumor infiltration (7 of 10 cases, 70.0%), compared with patients with 3/4, 2/4 and 1/4 diameter of tumor infiltration (3 of 25 cases, 12.0%; 3 of 45 cases, 6.7%; 1 of 16 cases, 6.3%) (χ^2 = 27.944, *P* = 0.0001). The lateral lymph node metastasis rate was 30.0% (9 of 30 cases), 9.1% (4 of 44 cases) and 4.5% (1 of 22 cases) for poorly, moderately and well-differentiated carcinoma, respectively. The difference between the three groups was statistically significant ($\chi^2 = 8.569$, P = 0.014). Local recurrence was 18.8% (18 of 96 cases), 64.3% (9 of 14 cases), and 11.0% (9 of 82 cases) in patients with advanced low rectal cancer, in those with and without lateral lymph node metastasis, respectively. The difference between the two groups was statistically significant ($\chi^2 = 22.308$, P = 0.0001). Kaplan-Meier survival analysis showed significant improvements in median survival (80.9 ± 2.1 m, 95% CI: 76.7-85.1 m *vs* 38 ± 6.7 m, 95% CI: 24.8-51.2 m) of patients without lateral lymph node metastasis compared with those with lateral lymph node metastasis (loq-rank, P = 0.0001).

CONCLUSION: Tumor diameter, infiltration and differentiation are significant risk factors for lateral lymph node metastasis. Lateral pelvic lymphadenectomy should be performed following surgery for patients with tumor diameter \geq 5 cm. Lateral lymph node metastasis is an important predictor for local recurrence and survival in patients with advanced low rectal cancer.

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Key words: Low rectal cancer; Lateral lymph node metastasis; Local recurrence; Prognosis

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INTRODUCTION

It is well known that rectal carcinoma is one of the most common carcinomas in China. Since total mesorectal excision was adopted as the standard treatment of patients with rectal carcinoma, improvements have been made in decreasing its local recurrence and prolonging survival of patients^[1-8]. However, even having undergone radical resection with total mesorectal excision, about 5%-40% of patients with rectal carcinoma have local recurrence^[9-14]. The survival of patients with advanced low rectal cancer

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still remains poor. It was reported that lateral lymph node metastasis may be the most important factor for local recurrence and poor prognosis of advanced low rectal cancer^[15-18]. In the current study, the data on 96 consecutive patients who underwent curative surgery with total mesorectal excision and lateral lymph node dissection for advanced low rectal cancer at the Department of General Surgery of Guangdong Provincial People's Hospital were retrospectively analyzed. The relationship of lateral lymph node metastasis with local recurrence was identified. The prognostic value of lateral lymph node metastasis for advanced low rectal cancer was also evaluated. Moreover, the risk factors for lateral lymph node metastasis and indications of lateral lymph node dissection remain unclear. Therefore, this study was to explore the risk factors for lateral lymph node metastasis in order to make effective selection of patients who could benefit from lateral pelvic lymphadenectomy. The relation of lateral lymph node metastasis with clinicopathologic characteristics of advanced low rectal cancer was analyzed.

MATERIALS AND METHODS

Patients and methods

A total of 96 consecutive patients who underwent curative surgery with total mesorectal excision and lateral lymph node dissection for advanced low rectal cancer at the Department of General Surgery of Guangdong Provincial People's Hospital were retrospectively analyzed. There were 46 men and 50 women, ranging in age from 25 to 86 years, with a mean age of 65 years. None of these patients received preoperative chemotherapy or radiotherapy. Twenty-one patients (21.9%) had a family history, 40 patients (41.6%) had a high cancer embryonic antigen (CEA) level and a tumor diameter \geq 5 cm, 56 had a tumor diameter < 5 cm. According to the Ming's criteria, 42 tumors were classified as expansive type carcinoma, 54 tumors as infiltrative type carcinoma. Fifty-six patients (58.3%) had positive lymph node metastases and 36 patients (37.5%) had positive vessel cancerous emboli. Thirty patients had a poorly differentiated carcinoma, 44 patients had a moderately differentiated carcinoma, 22 patients had a well-differentiated carcinoma. Low anterior resection was performed in 68 patients and abdominal perineal resection in 28 patients. A total of 1776 lymph nodes were dissected from these 96 patients (average 18.5 lymph nodes per patient). Two pathologists who were blinded to the clinicopathological data observed the specimens independently.

Statistical analysis

Statistical analysis was performed by chi-square test to examine the association of lateral lymph node metastasis with clinicopathologic characteristics and local recurrence of advanced low rectal cancer. The relationship between lateral lymph node metastasis and survival in patients with advanced low rectal cancer was evaluated by Kaplan-Meier survival analysis and log-rank test. P < 0.05 was considered statistically significant.

RESULTS

Correlation between lateral lymph node metastasis and clinicopathologic characteristics of advanced low rectal cancer

Lateral lymph node metastasis was observed in 14.6 (14/96)of patients with advanced low rectal cancer. Lateral lymph node metastasis was detected in 10 (25.0%) of 40 patients with tumor diameter ≥ 5 cm and in 4 (7.1%) of 56 patients with tumor diameter < 5 cm. The difference between the two groups was statistically significant (χ^2 = 5.973, P = 0.015). Lateral lymph node metastasis was more frequent in patients with 4/4 diameter of tumor infiltration (7 of 10 cases, 70.0%), compared with patients with 3/4, 2/4 and 1/4 diameter of tumor infiltration (3 of 25 cases, 12.0%; 3 of 45 cases, 6.7%; 1 of 16 cases, 6.3%) (χ^2 = 27.944, P = 0.000). The lateral lymph node metastasis rate for poorly, moderately and well differentiated carcinoma was 30.0% (9 of 30 cases), 9.1% (4 of 44 cases) and 4.5% (1 of 22 cases), respectively. The difference between the three groups was statistically significant ($\chi^2 = 8.569$, P = 0.014). No significant correlation was found between lateral lymph node metastasis and other variables such as gender ($\chi^2 = 0.168$, P = 0.682), age ($\chi^2 = 0.103$, P = 0.749), family history ($\chi^2 = 0.430$, P = 0.512), high CEA level (χ^2 = 0.468, P = 0.494), Ming's classification ($\chi^2 = 0.430$, P =0.512), lymph node metastases ($\chi^2 = 0.239$, P = 0.625) and vessel cancerous emboli ($\chi^2 = 0.201$, P = 0.654) (Table 1).

Correlation between lateral lymph node metastasis and local recurrence of advanced low rectal cancer

Local recurrence was 18.8% (18 of 96 cases), 64.3% (9 of 14 cases), and 11.0% (9 of 82 cases) in patients with advanced low rectal cancer and those with and without lateral lymph node metastasis The difference between the two groups was statistically significant ($\chi^2 = 22.308$, P = 0.0001).

Correlation between lateral lymph node metastasis and survival in patients with advanced low rectal cancer

In a median follow-up period of 73 (range 16-90) mo, Kaplan-Meier survival analysis showed a significantly improved median survival (80.9 \pm 2.1 m, 95% CI: 76.7-85.1 m vs 38 \pm 6.7 m, 95% CI: 24.8-51.2 m) in patients without lateral lymph node metastasis compared with those with lateral lymph node metastasis. The difference between the two groups was statistically significant (log-rank, P =0.0001) (Figure 1).

DISCUSSION

Lateral pelvic lymphadenectomy for advanced low rectal cancer is controversial^[19-25]. In Japan, lateral pelvic lymphadenectomy is routinely performed for patients with advanced low rectal cancer, whereas it is not frequently performed in the Western countries^[26-28]. In the current study, a retrospective analysis was performed in 96 patients with advanced low rectal cancer who underwent curative surgery with lateral lymph node dissection. The relations of lateral lymph node metastasis with clinicopathologic

Table 1 Relations between lateral lymph node metastasis and clinicopathologic characteristics of patients with advanced low rectal cancer

Variable	п	Lateral lymph node metastasis		
		Positive (%)	Negative (%)	χ^2/P value
Gender				
Male	46	6 (13.0)	40 (87.0)	
Female	50	8 (16.0)	42 (84.0)	$\chi^2 = 0.168/P = 0.682$
Age (yr)				
< 60	38	5 (13.2)	33 (86.8)	
≥ 60	58	9 (15.5)	49 (84.5)	$\chi^2 = 0.103 / P = 0.749$
Family history				
Yes	21	4 (19.0)	17 (81.0)	
No	75	10 (13.3)	65 (86.7)	$\chi^2 = 0.430/P = 0.512$
CEA level				
High	40	7 (17.5)	33 (82.5)	
Normal	56	7 (14.6)	49 (85.4)	$\chi^2 = 0.468 / P = 0.494$
Superficial diameter (cm)				
< 5	56	4 (7.1)	52 (92.9)	
≥ 5	40	10 (25.0)	30 (75.0)	$\chi^2 = 5.973 / P = 0.015$
Diameter of infiltration				
1/4	16	1 (6.3)	15 (93.7)	
1/2	45	3 (6.7)	42 (93.3)	
3/4	25	3 (12.0)	22 (88.0)	
4/4	10	7 (70.0)	3 (30.0)	$\chi^2 = 27.944/P = 0.000$
Ming's classification				
Expansive	42	5 (11.9)	37 (88.1)	
Infiltrative	54	9 (16.7)	45 (83.3)	$\chi^2 = 0.430/P = 0.512$
Histologic differentiation				
Well	22	1 (4.5)	21 (95.5)	
Moderate	44	4 (9.1)	40 (90.9)	
Poorly	30	9 (30.0)	21 (70.0)	$\chi^2 = 8.569/P = 0.014$
Lymph node metastasis				
Positive	56	9 (16.1)	47 (83.9)	
Negative	40	5 (12.5)	35 (87.5)	$\chi^2 = 0.239 / P = 0.625$
Vessel cancerous emboli				
Positive	36	6 (16.7)	30 (83.3)	
Negative	60	8 (13.3)	52 (86.7)	$\chi^2 = 0.201/P = 0.654$

CEA: Carcinoma embryonic antigen.

characteristics, local recurrence and survival of advanced low rectal cancer were analyzed.

In our study, lateral lymph node metastasis was observed in 14.6% (14/96) of patients with advanced low rectal cancer, showing a significant correlation with tumor diameter, infiltration and differentiation. Lateral lymph node metastasis was found in 10 (25.0%) of 40 patients with tumor diameter ≥ 5 cm and in 4 (7.1%) of 56 patients with tumor diameter < 5 cm (χ^2 = 5.973, P = 0.015). Lateral lymph node metastasis was more frequent in patients with 4/4 diameter of tumor infiltration (7 of 10 cases, 70.0%) than in patients with 3/4, 2/4 and 1/4 diameter of tumor infiltration (3 of 25 cases, 12.0%; 3 of 45 cases, 6.7%; 1 of 16 cases, 6.3%) ($\chi^2 = 27.944$, P =0.000). The lateral lymph node metastasis rate of poorly, moderately and well differentiated carcinoma was 30.0% (9 of 30 cases), 9.1% (4 of 44 cases) and 4.5% (1 of 22 cases), respectively ($\chi^2 = 8.569$, P = 0.014), indicating that tumor diameter ≥ 5 cm, tumor infiltration and differentiation are risk factors for lateral lymph node metastasis of advanced low rectal cancer. Therefore, lateral pelvic lymphadenectomy should be performed following the management of patients with tumor diameter \geq 5 cm, tumor infiltration or differentiation.

It is well known that local recurrence is the most important prognostic factor for rectal carcinoma^[29-31]. It was reported that local recurrence can be found in 4%-50% of patients with rectal carcinoma after curative resection, and lateral lymph node metastasis may be the important factor for local recurrence^[15,16]. Ueno et al^[15] reported that patients with lateral node metastases have an increased risk for local recurrence (44% vs 11.7%; P < 0.001) compared with those without lateral node metastases. Sugihara et al^[16] also reported that positive lateral lymph nodes are significantly associated with increased local recurrence of rectal cancer. Similarly in this study, lateral lymph node metastasis was significantly correlated with local recurrence of advanced low rectal cancer. The local recurrence rate of advanced low rectal cancer was 64.3% (9 of 14 cases) and 11.0% (9 of 82 cases) in patients with and without lateral lymph node metastasis ($\chi^2 = 22.308$, P = 0.000), respectively, indicating that lateral pelvic lymphadenectomy can significantly reduce local recurrence of advanced low rectal cancer.

In the present study, patients without lateral lymph node metastasis had significant improvements in median survival ($80.9 \pm 2.1 \text{ m}$, 95% CI: 76.7-85.1 m vs 38 ± 6.7 m, 95% CI: 24.8-51.2 m) compared to those with lateral



Figure 1 Relations between lateral lymph node metastasis and survival of patients with advanced low rectal cancer (Kaplan-Meier survival analysis). LNM: Lymph node metastasis.

lymph node metastasis. The difference between the two groups was statistically significant (log-rank, P = 0.0001), supporting that lateral lymph node metastasis has a significant prognostic value for advanced low rectal cancer. Lateral pelvic lymphadenectomy may effectively improve the survival of patients with advanced low rectal cancer. Ueno *et al*^[32] also reported that advanced low rectal cancer patients having lymph node involvement in the lateral pelvic area are likely to benefit from lymphadenectomy.

COMMENTS

Background

Even having undergone radical resection with total mesorectal excision, about 5%-40% of patients with rectal cancer have local recurrence. The survival of patients with advanced low rectal cancer remains poor. Whether patients with advanced low rectal cancer could benefit from lateral lymph node dissection is still controversial.

Research frontiers

At present, lateral lymphadenectomy for advanced low rectal cancer is controversial. However, lateral lymph node metastasis is significantly associated with local recurrence and poor prognosis of advanced low rectal cancer.

Innovations and breakthroughs

The results of this study indicate that tumor diameter \ge 5 cm, tumor infiltration and differentiation are risk factors for lateral lymph node metastasis of advanced low rectal cancer. Lateral lymph node metastasis is significantly correlated with local recurrence and prognosis of advanced low rectal cancer.

Applications

Lateral pelvic lymphadenectomy may effectively reduce local recurrence and improve the survival in patients with advanced low rectal cancer.

Peer review

The present study investigated the relations of lateral lymph node metastasis with local recurrence and survival in patients with advanced low rectal cancer. The study design is good and data analysis is extensive. The manuscript is well written.

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