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BRIEF ARTICLE

Patterns of lymph node metastasis are different in colon and rectal carcinomas

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Abstract

AIM: To describe patterns of lymph node metastasis in invasive colon and rectal carcinomas.

METHODS: Clinical data of 2340 patients with colorectal carcinoma (stage Ⅰ to Ⅲ) who received radical resection, was retrospectively reviewed. Of the 2340 patients, 1314 patients suffered from rectal carcinoma and 1026 from colon carcinoma. Patients with rectal cancer who received neoadjuvant chemoradiation therapy were excluded. Statistical analysis was performed using Mann-Whitney, χ^2 and Cochran's and Mantel-Haenszel tests (SPSS 15.0). A two-tailed $P < 0.05$ was considered statistically significant.

RESULTS: Lymph node retrieval in the rectal carcinoma group was significantly lower than that in the colon carcinoma group ($P < 0.001$), while positive lymph node retrieval in the rectal carcinoma group was significantly higher than that in the colon carcinoma group ($P < 0.001$). The proportion of lymph node positive (N+) cases was higher (patients with one or more positive lymph nodes) in the rectal carcinoma group ($P = 0.004$). The number of N+ cases was compared at different T stages (T1-T4) to eliminate background bias and the results were confirmed ($P < 0.001$). In addition, the lymph node ratio (the ratio of number of positive lymph nodes over the number of lymph nodes examined) of stage Ⅲ cases in the rectal carcinoma group was significantly higher than that in the colon carcinoma group ($P < 0.001$).

CONCLUSION: Rectal carcinomas seem more prone to metastasize to the lymph nodes than colon carcinomas, which may be of potential clinical significance.

Key words: Lymph node; Metastasis; Colon; Rectum; Neoplasms

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INTRODUCTION

Lymph node metastasis in colorectal cancer significantly in-

fluences patient management and prognosis[1-4]. Therefore, the number of positive lymph nodes is regarded as an index to determine different N stages in the extensively accepted colorectal cancer tumor node metastasis (TNM) staging[5,6]. As to the issues of the minimal number of lymph nodes examined[6-9] and lymph node metastasis[6,10,11], colon cancers and rectal cancers are usually treated as a single entity. Some researchers pointed out that the rate of lymph node metastasis in colon cancer and rectal cancer might be different[12,13]. The present study was attempted to describe the possible differences in patterns of lymph node metastasis between colon and rectal tumors so as to provide useful information for more effective clinical treatment and prognostic assessment of colon and rectal carcinomas.

MATERIALS AND METHODS

Patient selection

Patients with invasive colorectal cancer who received surgical treatment at Changhai Hospital between January 2000 and June 2008 were identified from our prospectively collected database as approved by the Institutional Review Board (IRB). Patient characteristics, examination records, operative and pathologic reports were reviewed. The following data were collected from the patients' charts: (1) Demographic data (age and gender); (2) Preoperative examinations including colonoscopy, abdominal ultrasound and chest X-ray; (3) Preoperative adjuvant treatment; (4) Operative records; and (5) Postoperative pathology: tumor grade [low grade (equal to well and moderately differentiated) or high grade (equal to poorly differentiated and undifferentiated)]; tumor size (refers to the maximum dimension of the primary tumor measured in the operative specimen), T stage (depth of invasion), and N stage (the number of total and positive lymph nodes)[5]. Based on the lymph node status, the patients were divided into node positive (N+) and node negative (N-). N+ patients included all patients with one or more positive lymph nodes (N1 and N2), and N- patients included all patients without positive lymph nodes on final pathological analysis.

Inclusion criteria

Inclusion criteria were primary invasive colorectal cancer confirmed by preoperative pathology and treated with radical operation.

Exclusion criteria

Exclusion criteria were recurrent colorectal tumors, Tis tumors, R1 or R2 resection [The resection margin was considered positive (R1 resection) when the invasive tumor was present in the resection margin or the distance between the tumor and the resection margin was less than 1 mm; R2 resection refers to incomplete tumor resection with gross residual tumor that was not resected]. Patients with rectal cancer who received neoadjuvant chemoradiation or with stage Ⅳ colorectal carcinoma, patients who lacked complete information, and patients with synchronous diseases (such as total colectomy for familial adenomatous polyposis) that might affect lymph node harvest were also excluded.

Procedures

For rectal carcinoma, surgery was performed using a standardized surgical procedure with sharp mesorectal dissection techniques as described by Heald *et al*[14]. Standard colectomy and regional lymphadenectomy (right hemicolectomy, transverse colectomy, left hemicolectomy and sigmoid colectomy) were performed according to the location of colon cancer.

Pathology

The surgical specimens were fixed in 10% buffered neutral formalin. The traditional inspection and palpation method was applied for lymph node harvest. No adjuvant technique such as fat clearance was used to help identify lymph nodes.

Statistical analysis

Statistical analysis was performed using SPSS Software system (version 15.0, Chicago, IL). Mann-Whitney test was employed to numerical data that did not show a normal distribution (age, total number of lymph node examined, the number of positive lymph node) or ordinal variables (T stage and N stage). Comparison of proportions was analyzed by χ^2 test. Cochran's and Mantel-Haenszel tests were applied to compare the difference in the number of N+ patients in different tumor groups to stratify the data by T stage. Results were expressed as median (range). A two-tailed P value of < 0.05 was considered statistically significant. The study was reviewed and approved by Changhai Hospital IRB.

RESULTS

Patient population

A total of 2340 patients were identified, including 1314 patients with rectal carcinoma, and 1026 patients with colon carcinoma involving the cecum in 63 cases, ascending colon in 242 cases, hepatic flexure in 118 cases, transverse colon in 67 cases, splentic flexure in 40 cases, descending colon in 79 cases, and sigmoid colon in 417 cases.

There were 977 females (41.8%) and 1363 males (58.2%) with a median age of 61 (51-71) years. The median tumor size was 4.5 (3.5-6.0) cm. The percentages of stage Ⅰ, Ⅱ and Ⅲ tumors were 19.5%, 41.7% and 38.8% respectively.

Comparison of tumor characteristics and the total number of lymph nodes examined between rectal and colon carcinoma groups

The tumors in the rectal carcinoma group were smaller than those in the colon carcinoma group ($P < 0.001$). In addition, there were more low-grade tumors in the rectal carcinoma group ($P = 0.002$). The total lymph node number in the rectal carcinoma group was lower than that in the colon carcinoma group ($P < 0.001$).

Table 1 Comparison between rectal cancer and colon cancer groups *n* (%)

Clinicopathologic factors	Rectal cancer (*n* = 1314)	Colon cancer (*n* = 1026)	*P* value
Gender			
Male	797 (60.7)	566 (55.2)	0.008
Female	517 (39.3)	460 (44.8)	
Age (yr)	59 (50-68)	64 (53-72)	< 0.001
Grade			
Low	1125 (85.6)	830 (80.9)	0.002
High	189 (14.4)	196 (19.1)	
Tumor size (cm)	4.0 (3.0-5.5)	5.0 (4.0-6.0)	< 0.001
Total nodes	9 (7-12)	10 (8-13)	< 0.001
Positive nodes	3 (1-5) (*n* = 544)	2 (1-4) (*n* = 364)	< 0.001
LNR	0.31 (0.14-0.60) (*n* = 544)	0.22 (0.13-0.50) (*n* = 364)	< 0.001
N stage			
N0	770 (58.6)	662 (64.5)	< 0.001
N1	338 (25.7)	267 (26.0)	
N2	206 (15.7)	97 (9.5)	
N+ stage			
N0	770 (58.6)	662 (64.5)	0.004
N+	544 (41.4)	364 (35.5)	
T stage			
T1	49 (3.7)	23 (2.2)	< 0.001
T2	377 (28.7)	121 (11.8)	
T3-4	888 (67.6)	882 (86.0)	

LNR: Lymph node ratio.

Number of positive lymph nodes, N stage and lymph node ratio between the two groups

The number of positive lymph nodes in the rectal carcinoma group was larger than that in the colon carcinoma group ($P < 0.001$). This was confirmed by comparison of N stage between the two groups. It was found that the patients in the rectal carcinoma group had a significantly higher N stage ($P < 0.001$) (Table 1).

The number of N+ patients in the rectal carcinoma group was significantly larger than that in the colon carcinoma group ($P = 0.004$) (Table 1). In addition, comparison of the lymph node ratio (LNR) of the stage Ⅲ cases between the two groups showed that LNR was higher in the rectal carcinoma group ($P < 0.001$).

Comparison of N+ stage stratified by T stage between the two groups

Advanced T stage was more likely to be associated with positive lymph nodes. A comparison of T stage between the two groups was undertaken to explore any possible impact of T stage on positive lymph node harvest. T3 and T4 tumors were taken together because most colon cancers were inherently located intraperitoneally, while more than half rectal cancers presented as extraperitoneal tumors. Considering the different definition of T3 and T4 stage of intraperitoneal and extraperitoneal tumors, it is more reasonable and comparable to put T3 and T4 tumors together to avoid location bias. It was noted that T stage was more advanced in the colon carcinoma group ($P < 0.001$). Moreover, Cochran's and Mantel-Haenszel statistics were used to compare patients with N+ stage between the two groups further stratified by T stage level. The N stage was significantly higher ($P < 0.001$) in the rectal carcinoma group, with an odds ratio (OR) of 1.617 (95% confidence interval: 1.355-1.931) (Table 2).

Table 2 Comparison between the percentage of patients with N+ stage

T stage[1]	N+ stage proportion (%)		*P* value
	Rectal cancer (*n* = 1314)	Colon cancer (*n* = 1026)	
T1	5/49 (10.2)	1/23 (4.3)	< 0.001
T2	84/377 (22.3)	23/121 (19.0)	
T3-4	455/888 (51.2)	340/882 (38.5)	

[1]Stratified by T stage.

DISCUSSION

Lymph node metastasis is an important prognostic factor for patients suffering from colorectal carcinoma without distant metastasis, as well as a risk factor for recurrence and distant metastasis of colorectal carcinoma[1-3]. The five-year survival rate of N+ patients was lower than that of N- patients[4]. In addition, the higher the number of positive lymph nodes examined, the poorer the prognosis would be. So in the colorectal TNM staging system[5,6], the node status was applied as the parameter to determine the stage Ⅲ tumors from the stage Ⅱ lesions, while the number of positive nodes indicated different N stages. In recent studies, LNR was recommended as a significant prognostic factor for both colon and rectal cancer patients[15,16], and thought to optimize staging in colorectal cancer[17]. Lymph node metastasis also affects patient management. It is generally accepted that adjuvant treatment is beneficial to N+ patients, but whether it is appropriate for N- patients remains controversial.

With respect to lymph node metastasis, colon cancer and rectal cancer were not often discussed independently[6,10,11]. Several studies compared the rates of lymph node metastasis between early rectal and colon cancers and found that they were different[12,13]. But the patient population in these studies was too small to draw a convincing conclusion. The present study explored possible differences in the lymph node metastasis pattern between colon and rectal carcinomas using strict inclusion criteria to eliminate patients who received neoadjuvant therapy, and those with stage Ⅳ tumors and incomplete information for the sake of minimizing influences of these factors on lymph node harvest. As several studies including our previous study had shown that neoadjuvant therapy decreased lymph node harvest and down-staged tumors[18], we excluded all patients who received neoadjuvant therapy in the present study. All procedures were performed by seven experienced colorectal surgeons with standard technique in one surgical section, and all specimens were treated in one pathology department to minimize interpretation variability.

In the present study, there was a higher percentage of

positive lymph node retrieval and N+ patients in the rectal carcinoma group in spite of a lowered total lymph node harvest. It is well established that T stage correlates with N stage[19,20], so T stage was investigated between the two groups to decrease background bias. Comparison of the overall lymph node status (N+) between the two groups based on T stage level also confirmed that there were more N+ patients in the rectal carcinoma group. Then the tumor size and grade were compared. Our data showed that the tumors in the rectal carcinoma group were smaller than those in the colon carcinoma group. In addition, there were more low-grade tumors in the rectal carcinoma group. Considering that high-grade big tumors harbored more metastatic lymph nodes[19,21], the primary tumor characteristics of the two groups enforced the hypothesis that rectal cancer is prone to metastasize to lymph nodes as compared with colon cancer. Furthermore, LNR of stage Ⅲ tumors was higher in the rectal carcinoma group than that in the colon carcinoma group.

Nevertheless, there were still some sources of bias in our retrospective study. The median number of total lymph nodes examined fell below 12, which would affect the accuracy of N stage. No long-term clinical follow-up was included, which may limit the ability to interpret the oncological significance of our findings. Further study is, therefore, required.

Different incidences of lymph node metastasis between colon and rectal cancers have several clinical implications. First, the minimal number required for lymph nodes retrieval remains controversial with a range from 7 to 21 in the literature[7-9]. Most of these studies combined colon and rectal cancers and the AJCC and College of American Pathologists recommend a minimum of 12 lymph nodes to be examined for both colon and rectal cancer[6,22]. In our study, the number of lymph nodes was significantly lower in the rectal cancer group compared with the colon cancer group. So the question arises whether the minimal number of lymph node harvest for colon and rectal cancer should be different. Second, the incidence of lymph node metastasis should be taken into account in choosing therapeutic strategies: a more aggressive strategy may be justified in treating rectal cancers than in colon cancers. As rectal carcinomas are more prone to metastasize to lymph nodes and the involved nodes might be the main reason of recurrence following local excision, radical resection rather than local excision seems to be a more reasonable recommendation for early rectal cancer as compared with colon cancer of similar primary tumor characteristics. For the same reason, adjuvant chemotherapy should be more suggestive for rectal cancer after local excision. Third, it is well known that the overall survival rate is lower and the local recurrence rate is higher in rectal caner following radical resection as compared with colon cancer. As we discussed earlier, the lymph node status is a key predictor for the prognosis of colorectal cancer. The differences seen in our study may explain the discrepancy in survival and local recurrence typically observed between colon and rectal cancers.

In conclusion, our study shows that the incidence of lymph node metastasis of rectal cancer is significantly higher than that of colon cancer as stratified by T stage, which may be attributed to different oncological and anatomic characteristics. This finding carries potential clinical significance related to treatment decision making, such as local excision or adjuvant therapy, as well as to prognostic assessment of rectal carcinoma.

COMMENTS

Background

Lymph node metastasis in colorectal cancer significantly influences patient management and prognosis. As to the issue of lymph node metastasis, colon cancers and rectal cancers are usually treated as a single entity.

Research frontiers

This paper essentially audits the colorectal cancer practice in one hospital over an 8-year period. The authors identified 2340 patients (1314 rectal, 1026 colonic) and retrospectively reviewed the pathological data related to these with particular respect to the number and distribution of lymph node metastases.

Applications

The rectal carcinoma seems more prone to metastasize to lymph nodes than colon carcinoma, which harbors potential clinical significance related to treatment decision making and prognosis interpretation.

Peer review

The authors analyzed the different patterns of lymph node metastasis in colon and rectal cancers. Although it is retrospective, the study involves a large patients' population over a relatively short period of time.

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