

Report about the clinical meaning of patients with pathologic metastasis of lateral lymph nodes but no metastasis of mesenteric lymph nodes after lateral lymph node dissection in low rectal cancer

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Abstract

Purpose The aim of this study is to investigate the clinical significance of lateral lymph node metastasis with no mesenteric lymph node metastasis after lateral lymph node dissection in middle and low rectal cancer .

Methods Retrospective analysis was performed on the clinical data of 5 consecutive patients who were pathologically diagnosed with lateral lymph node metastasis, while mesenteric lymph node metastasis was not observed after laparoscopic lateral lymph node dissection underwent for advanced low rectal cancer from July 2017 to August 2019.

Results All the 5 patients were successfully completed laparoscopic lateral lymph node dissection, and no cases were transferred to laparotomy. The mean age was 58.80 ± 6.53 years, Two Miles surgeries and three Dixon surgeries were performed.

Conclusion We found that some patients had lateral lymph node metastasis, while mesenteric lymph nodes had no metastasis after lateral lymph node dissection. This phenomenon suggests that lateral lymph nodes are one of the important metastasis pathways of low rectal cancer, a new N stage is needed to distinguish it from other types of lymph node metastasis. In addition, LLND is of great significance for the pathological diagnosis of lateral lymph nodes.

Introduction

Previous studies have shown that the lateral lymphatic metastasis in rectal cancer is 8-12%. For low rectal cancer up to 5 cm from the dentate line, the lateral lymph node metastasis rate is 16-23%. [1] In Japanese, researchers think the lateral lymph node metastasis should be classified as local metastasis, so Japanese guidelines recommend that LLND should be performed regularly in stageⅡor stageⅢ rectal cancers [2], while in European and American lateral lymph node metastasis is regarded as distant metastases, CRT + TME treatment strategy has been suggested. [3] A recent study shows that the CRT alone cannot effectively take control of local recurrence, the local recurrence rate of CRT alone and CRT plus LLND was 19.5% and 5.5% ,respectively ($p = 0.042$). [4] Whether lateral lymph nodes metastasis belongs to local metastasis makes significant difference between the East and the West. It is significant for treatment guidance of lateral lymph node metastasis to make it clear that Whether lateral lymph nodes metastasis belongs to local metastasis or distant metastasis.

In this study we retrospectively analyzed 42 routine clinicopathological data of lateral lymph node dissection in our medical center. There are 5 cases who have lateral lymph node metastasis but no mesenteric lymph nodes metastasis. Clinical and pathological characteristics of such patients and the meaning of lateral lymph nodes in low rectal cancer spread and metastasis are discussed in this paper.

Patients And Methods

Clinical data of 5 patients who have lateral lymph node metastasis but no mesenteric lymph nodes metastasis confirmed by pathological examination after LLND from July 2017 to August 2019 in the colorectal surgery of Tianjin Union Medical Center were retrospectively analyzed. Table 1 shows the baseline data of patients. All patients took preoperative colonoscopy and were diagnosed with rectal cancer by pathology biopsy. Lateral lymph node metastasis has been verified through abdominal enhanced CT and MRI assessment. Neoadjuvant chemoradiation has been followed by surgery after 6 ~ 8 weeks. Patients with unilateral lateral lymph node metastasis underwent unilateral lateral lymph node dissection according to preoperative imaging evaluation and those with bilateral lateral lymph node metastasis underwent bilateral lateral lymph node dissection. All surgeries were performed by the same surgeon. Lateral lymph node metastasis has been confirmed by preoperative CT and MRI images (short diameter ≥ 7 mm). Neoadjuvant chemoradiotherapy was performed with the consent of the patients. Lateral lymph node metastasis was confirmed (short diameter ≥ 5 mm) after neoadjuvant chemoradiotherapy. There is no distant metastasis or distant metastasis which can be removed by radical resection. Patients with lateral lymph node metastasis invading the proximal sacrum, piriformis muscle, sciatic nerve, external iliac vessels or unresectable distant metastases are excluded.

Rectal tumors were eradicated by TME, and lateral lymph node dissection was performed by the technique of fascial space priority approach, which has been reported in our previous studies [5].

STATISTICAL ANALYSIS

Data were recorded in a SPSS Statistics Version 25.0 database. The normal distribution test has been carried out for every variable. They are expressed as $\bar{x} \pm s$ when they followed a normal distribution and median values (range) when they don't. Categorical data are presented as numbers (%).

Results

Table 1 shows the characteristics of the patients and the tumor. Five cases were enrolled, the average age is 58.80 ± 6.53 . All five surgeries are completed smoothly with laparoscopy with no cases converted to laparotomy, 3 cases underwent Miles surgery and 2 underwent Dixon surgery. Table 2 shows the pathological characteristics. The mean follow-up was 13 (1-31) months with no lateral lymph node recurrence.

Table 1. Patient Characteristics

| Variables | Value (n=5) |
|---|--------------------------|
| Age, y, (range) | 58.80 ± 6.53 (50-67) |
| Sex, n (%) | |
| Male | 2 (40.0) |
| Female | 3 (60.0) |
| BMI, (kg/m ²), | 25.56 ± 3.56 |
| Distance of tumor from AV, cm, <i>M</i> (range) | 4.8 [3- 5.5] |
| Preoperative CEA, ng/mL, <i>M</i> (range) | 5.96 [2.79-44.32] |
| ycT Stage, n (%) | |
| cT3 | 4 (80.0) |

| | |
|------------------|----------|
| cT4 | 1 (20.0) |
| ycN Stage, n (%) | |
| cN1 | 5 (100) |

Table 2. Surgical outcomes and clinicopathological characteristics

| Variables | Value (n=17) |
|--|-----------------|
| Surgical approach, n(%) | |
| Miles | 2 (40) |
| Dixon | 3 (60) |
| LLND dissection, n(%) | |
| Unilateral | 5 (100) |
| TNM Stage, n(%) | |
| I | 5 (100) |
| Mesenteric lymph nodes, <i>M</i> (range) | |
| No. of dissection per patient, unit | 12 (12-21) |
| Lateral Lymph Nodes, <i>M</i> (range) | |
| No. of metastasis per each side, unit | 1 (1-2) |
| No. of dissection per each side, unit | 8 (3-13) |
| Neoadjuvant chemoradiotherapy, n(%) | 2 (40) |
| Metastatic lymph node location, n(%) | |
| Iliac artery region | 3 (60) |
| Obturator region | 2 (40) |

Discussion

Our previous study reported the technique of fascial space priority approach in laparoscopy lateral pelvic lymph node dissection. [6] We found an interesting phenomenon, 5 cases in 42 patients (11.9%) showed lateral lymph node metastasis but no rectal mesenteric lymph nodes metastasis. This phenomenon shows that lateral lymph nodes could be one of the important ways of rectal lymph drainage, even one of the sentinel lymph nodes, lymph nodes should be brought to the equal attention with mesenteric lymph nodes. This phenomenon has been reported in previous studies. [7-9] Lymphatic drainage of the lower rectum passes to external pelvic (inguinal area) or pelvic (iliac vessels and anterior sacral) lymph nodes, or to the root of IMA (inferior mesenteric) along the superior rectal artery. Akiyoshi found that the prognosis of patients with lymph node metastasis in the external iliac artery region was not statistically different from that of N2a (OS: 45% vs 45%, $P = 0.9585$; CSS: 51% vs 49%, $P = 0.5742$), while the prognosis of patients with lateral lymph node metastasis in the internal iliac artery region was not statistically different from that of N2b (OS: 32% vs 29%, $P = 0.3342$). CSS: 37% vs 34%, $P = 0.4347$) [11]. This suggests that the lateral lymph nodes should belong to local lymph nodes. Our study also confirms this conclusion. Lymph nodes dyeing technology (lymphatic mapping technology) can be adopted to study drainage direction of low rectal cancer. [10]

Studies about prognosis of patients with lateral lymph node metastasis but no mesorectum lymph nodes metastasis is rare. Takahashi found that 5-year survival rate of patients with lateral lymph node metastasis but no mesorectum lymph nodes metastasis is 75%, and 5-year survival rate of those with no lateral lymph node metastasis and mesorectum metastasis, mesorectum metastasis but no lateral lymph

node metastasis, both lateral lymph node metastasis and mesorectum metastasis were 90.1% ,67.7% and 32%, respectively. This means that the prognosis of patients with lateral lymph node metastasis but no mesorectum metastasis may be worse than that of patients with no lateral lymph node metastasis and mesorectum metastasis but better than that of patients with both lateral lymph node metastasis and mesorectum metastasis. [7] Akiyoshi thought lymph node metastasis located in the medial of internal iliac artery should be classified as N2a and those located in the lateral of internal iliac artery should be classified as N2b [11]. However, the prognosis of patients with lateral lymph node metastasis but no mesorectum metastasis is far better than that of patients with both lateral lymph node metastasis and mesorectum metastasis. So lateral lymph node staging should be more specific to verify a more accurate prognosis and formulate postoperative treatment strategy. But more studies about survival of patients with lateral lymph node metastasis but no mesorectum lymph nodes metastasis are needed to confirm this.

In addition, the phenomenon patients with lateral lymph node metastasis but no mesorectum lymph nodes metastasis also illustrates that the lateral lymph node dissection is of great significance for postoperative pathological diagnosis. If the lateral lymph nodes dissection were not undergone, the lymph node staging would be N0, and the pathology of tumor staging in patients would be stage 0. If there were no risk factors, adjuvant chemotherapy after surgery might not even be recommended. But the postoperative pathology showed lateral lymph node metastasis patients actually existed, and the tumor staging should be classified as stage Ⅰ with a similar prognosis to N2a or N2b tumors [11] and standardized postoperative adjuvant chemotherapy after surgery. Misleading staging would affect the clinical doctors developing wrong postoperative adjuvant treatment plan and making wrong prognosis judgement. LLND can change the patient's pathological staging. For low rectal cancer, CRT should be adopted if preoperative imaging reveals lateral lymph node enlargement and no mesorectum lymph node enlargement, and LLND should follow the CRT if the lateral enlarged lymph nodes do not shrinkage. If postoperative pathology after TME shows no mesenteric lymph node metastasis, the possibility of postoperative follow-up of lateral lymph node enlargement still deserves attention. The principle of "watch and wait" was proposed in NCCN guideline update 2020, which suggested no surgery temporarily and strict observation and follow-up for patients with clinical tumor complete remission after neoadjuvant chemoradiation. Our study shows that lateral lymph node metastasis should be paid more attention after neoadjuvant chemoradiation in addition to focusing on local lesion and mesenteric lymph nodes metastasis. [3]

Lymph nodes in the iliac artery region are classified as regional lymph nodes by AJCC colorectal cancer staging guidelines^[12], but those in obturator artery region are regarded as distant metastasis lymph nodes, which means the tumor staging would be M1 if lymph node metastasis in obturator artery region exists. However, according to our study, there was 2 cases in the 5 patients with obturator lymph nodes metastasis but no iliac artery lymph nodes and mesenteric lymph nodes metastasis, which means lymph node metastasis in obturator region may be earlier than that in the iliac region. So according to our

finding, obturator lymph nodes should also be classified as regional lymph nodes, but more studies will be needed to confirm this conclusion.

However, there are some shortages of our study. We just found this phenomenon, conducted a retrospective study of a few cases. Our sample size is small and the follow-up time is short, and the prognosis of these patients is unable to evaluate. The studies about the characteristics and prognosis of the patients with lateral lymph node metastasis but no mesorectum lymph nodes metastasis remain rare, and a lot of researches will be needed to clarify these problems. And it is well worth studying whether LLND surgery can improve the survival of these patients.

Conclusion

We found there were some patients with lateral lymph node metastasis but no mesorectum lymph nodes metastasis by pathological diagnosis in patients undergone LLND. This phenomenon shows that lateral lymph nodes may be sentinel lymph nodes of low rectal cancer. New N staging is needed to distinct this type with other types of lymph node metastasis. LLND is significant to specify the pathological diagnosis.

Abbreviations

LLND: Lateral lymph node dissection; CRT: Chemo-radiotherapy; CT: Computed tomography; MRI: Magnetic resonance imaging;

Declarations

Acknowledgement

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Authors' contributions

Xipeng Zhang and Yi Sun conceptualized the study. Peng Li, Zhichun Zhang, Yuanda Zhou, and Qingsheng Zeng collected the data used for the analysis. Pengli performed the analysis. Peng Li drafted the manuscript. All authors reviewed, edited, and agreed on the final draft of the manuscript.

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Availability of data and materials

The dataset is available upon reasonable request to the corresponding author.

Competing interest

All authors have declared no potential competing interests.

Ethics approval and consent to participate

The study has been conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all participants. The study received the ethics approval by the Ethics Committee of Tianjin Union Medical Center.

Consent for publication

All authors have provided their consent for publication of the manuscript.

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