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ORIGINAL ARTICLE

Assessment of lymph node metastasis in elderly patients with colorectal cancer by sentinel lymph node identification using carbon nanoparticles

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Summary

Purpose: *To evaluate the value of sentinel lymph node (SLN) identification using carbon nanoparticles in abdominal lymph node metastasis in elderly (>60 years old) patients with colorectal cancer.*

Methods: *Eighty patients admitted at Weihai Second Municipal Hospital affiliated to Qingdao University from November 2014 to February 2017 were selected and divided into the control group (n=40) and the observation group (n=40) using the random number method. The control group was treated with surgery, while the observation group was administered carbon nanoparticle tracer for intraoperative dye detection and positioning; the first to four black-stained lymph nodes were marked as SLN, then radical surgery for colorectal cancer was performed. Pathological examination of intraoperative specimens was performed to assess the effect of SLN in the abdominal lymph node metastasis.*

Results: *There were no statistically significant differences in the metastasis rate and lymph node metastasis rate between the two groups (p>0.05). The total number of lymph nodes and the number of lymph nodes with micrometastases (<2mm) in the observation group were larger than those in the control group (p<0.05); the ratio of fewer than 12 lymph nodes in the observation group was lower than that in the control group (p<0.05). In the observation group, 8 out of 40 cases had lymph node metastasis, the detection rate of SLN using carbon nanoparticles was 92.50%, the accuracy rate 94.59%, the specificity of diagnosis 87.50%, the false negative rate 12.50% and the negative predictive value 21.88%. There was no statistically significant difference in the metastasis rate of black-stained and non-black-stained lymph nodes in the observation group (p>0.05). The black-stained rate of micro lymph nodes was higher than the total black-stained rate (p<0.05); the rate of micro lymph node metastasis was lower than that of lymph node metastasis >5mm (p<0.05).*

Conclusion: *Preoperative SLN examination can evaluate the abdominal lymph node status in elderly patients with colorectal cancer, which is simple and accurate and can guide the clinical treatment, so it is worthy of popularization and application.*

Key words: *abdominal lymph node metastasis, carbon nanoparticles, elderly colorectal cancer patients, sentinel lymph node*

Introduction

Colorectal cancer is one of the most common malignancies, mostly occurring in elderly population and ranking fourth among the common malignancies all over the world, becoming thus an important reason affecting the health of elderly population among the top of common cancer [1]. According to several reports [2,3], the incidence of colorectal cancer is 46/100,000 in the United States, and 30/100,000 in China. In recent years, with the increasing aging of the population combined with changes in people's eating habits, the incidence of colorectal cancer in China has been

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increasing, showing a trend for younger ages [4,5]. At present, the clinical treatment for colorectal cancer in elderly patients is mainly radical surgery, which can resect the tumor, slow down the progression of disease, and improve the clinical results. Yet, some patients have already lymph node metastasis before operation, leading to high postoperative recurrence and mortality rates [6]. Therefore, it is of great significance to evaluate the lymph node metastasis in elderly patients with colorectal cancer which could lead to improved prognosis.

SLN represent the first nodal station. Researchers established the minimally invasive assessment method of lymph node metastasis via SLN biopsy in 1977, which was widely used in melanoma and breast cancer diagnosis and treatment [7,8]. However, no data are to be found on the evaluation of SLN in abdominal lymph node metastasis of elderly patients with colorectal cancer. Carbon nanoparticles are nano-sized carbon black particles developed based on nanotechnology, with a high degree of lymphatic system affinity and specificity, which can improve the detection of abdominal lymph node metastasis rate of elderly patients with colorectal cancer.

To investigate the assessment value of SLN identification using carbon nanoparticles on abdominal lymph node metastasis, patients admitted at the Weihai Second Municipal Hospital affiliated to Qingdao University from November 2014 to February 2017 were selected and evaluated.

Methods

Patients

Eighty patients admitted at Weihai Second Municipal Hospital from November 2014 to February 2017 were selected and divided into control group and observation group using the random number method.

There were 40 cases in the control group, including 23 males and 17 females aged 61-80 years (average 53.17±5.31). The tumor diameter ranged between 2.35 and 6.19 cm (average 3.59±2.15). Eight cases had Dukes stage I, 10 cases stage II, and 22 cases stage III . In 14 cases the tumor was in the ascending colon, in 10 in the descending colon, in 11 in the sigmoid colon, and in 5 cases in the rectum.

There were 40 cases in the observation group, including 22 males and 18 females aged 60-80 years (average 52.98±5.35); the tumor diameter ranged from 2.29 to 6.23 cm (average 3.60±2.21). In terms of tumor staging, there were 9 cases with Dukes stage I, 11 with stage II, and 20 cases with stage III.. In terms of tumor site, there were 13 cases in the ascending colon, 12 in the descending colon, 11 in the sigmoid colon, and 4 in the rectum.

Inclusion criteria: (1) elderly patients meeting the clinical diagnosis standards of colorectal cancer [9,10]; (2) patients diagnosed via surgery and pathological examination; (3) elderly patients fit for surgical treatment of colorectal cancer.

Exclusion criteria: (1) elderly patients not meeting the diagnosis and inclusion criteria for colorectal cancer; (2) elderly patients with incomplete data or who could not cooperate for surgery or radiotherapy; (3) patients with severe heart, liver or kidney dysfunction.

The study was approved and supervised by the Ethics Committee of Weihai Second Municipal Hospital, and the patients signed informed consent for the treatment.

Methods

The control group received carbon nanoparticles for intraoperative SLN detection and localization. The first to fourth black-stained lymph nodes were marked as SLN and then radical surgery of elderly colorectal cancer patients was performed.

1. Carbon nanoparticles (Chongqing Lummy Pharmaceutical Co., Ltd., China, each mL containing 50mg carbon nanoparticles); the diameter of carbon nanoparticles in the suspension was 150nm, and the patients in the observation group were injected with 0.15-0.25mL carbon nanoparticle suspension at 4 positions, 1-1.5cm below the tumor tissue, 1 day before the operation [11].
2. Surgical methods. Patients in both groups were treated with radical surgery for colorectal cancer, and all the operations were performed by the same surgeon. During the operation, under general anesthesia via tracheal intubation, patients with rectal and sigmoid colon cancer were placed in lithotomy position, while patients with right semi-colon and left semi-colon were placed in supine position. The 5-incision method was adopted, CO_2 artificial pneumoperitoneum was established during the perioperative period, appropriate pneumoperitoneum pressure was maintained and the location and size of the lesion were observed under laparoscope. The staining effects of the carbon nanoparticles on the tumor's surrounding lymph nodes were observed in the observation group, and laparoscopic radical surgery was performed [12].
3. Intraoperative observation. The staining effect of carbon nanoparticles on the tumor's surrounding lymph nodes was observed in the observation group; the black-stained lymph node closest to the tumor was marked as SLN, and the 1st, 2nd and 3rd lymph node dissection was performed according to the staining area. After the tumor resection, the lymph nodes in the control group were searched using palpation. In the observation group, SLN was firstly taken, then the black-stained lymph nodes were checked and counted [13,14].

Observation indicators

1. Comparison of lymph nodes dissected. The total number of detected lymph nodes, the number of micro lymph nodes, the rate of metastasis, the rate of lymph

node metastasis and the ratio of fewer than 12 lymph nodes were assessed.
2. SLN detection rate using carbon nanoparticle identification. The success rate, accuracy, specificity, false negative rate and negative predictive value of SLN in the observation group were assessed.

Statistics

The data was processed using SPSS 18.0 software (Strong-Vinda). Enumeration data were tested by chi-square test, and presented as [n (%)]. Quantitative data were tested by *t* test and presented as mean±SD. P<0.05 suggested that the difference was statistically significant.

Results

Comparison of lymph node dissected

There were no statistically significant differences in the metastasis rate and lymph node metastasis rate between the two groups (p>0.05). The total number of detected lymph nodes and the number of micro lymph nodes were higher in the observation group than in the control group (p<0.05). The ratio of fewer than 12 lymph nodes in the observation group was lower than that in the control group (p<0.05) (Table 1).

Detection rate of SLN using carbon nanoparticle identification

Out of 40 cases there were 8 cases of lymph node metastasis in the observation group, the detection rate of SLN using carbon nanoparticle was 92.50%, the accuracy rate was 94.59%, the specificity 87.50%, the false negative rate 12.50%, and the negative predictive value 21.88% (Table 2).

Comparison of black-stained lymph nodes in the observation group

There were no statistically significant differences in the metastasis rates of black-stained and non-black-stained lymph nodes in the observation group (p>0.05); the black-stained rate of micrometastatic lymph nodes was higher than the total black-stained rate (p<0.05); the rate of micrometastatic lymph nodes was lower than that of lymph node metastasis >5mm (p<0.05) (Table 3).

Discussion

Colorectal cancer is a common disease, which occurs mostly in the elderly population. With the increasing aging of population in China, the incidence of colorectal cancer has been increased and

Table 1. Comparison of lymph node dissection

Group	*n*	*Total lymph nodes* *n*	*Micro lymph nodes* *n*	*Metastasis rate of patients* *n (%)*	*Metastasis rate of lymph nodes* *n (%)*	*Ratio of <12 lymph nodes* *n (%)*
Observation	40	434	137	20 (50.00)	8 (20.00)	0 (0.00)
Control	40	340	56	16 (40.00)	9 (22.50)	13 (32.50)
	x^2	5.937	6.138	1.035	0.894	5.882
	p	<0.05	<0.05	>0.05	>0.05	<0.05

Table 2. SLN detection rate using carbon nanoparticle identification

Detection rate	*Rate* *n (%)*
Success rate	37/40 (92.50)
Accuracy	35/37 (94.59)
Specificity	7/8 (87.5)
False negative	1/8 (12.5)
Negative predictive value	7/32 (21.88)

Table 3. Comparison of black-stained lymph nodes in the observation group

	Observation group *n (%)*	*p value*
Black-stained rate of micro lymph nodes	104/137 (75.9)	<0.05
Black-stained rate of total lymph nodes	232/434 (53.5)	
Metastasis rate of black-stained lymph nodes	51/232 (22.00)	>0.05
Metastasis rate of non-black-stained lymph nodes	65/297 (21.90)	
Rate of micro lymph node metastasis	19/137 (13.9)	<0.05
Rate of lymph node metastasis >5mm	65/297 (21.9)	

is showing a trend for appearance in younger ages. At present, the treatment of colorectal cancer in the elderly is mainly surgical operation [15]. According to data [16], more than 45.3% of elderly patients have lymph node metastasis after colorectal radical surgery. With the detection of tumor markers by PCR it is observed that the 5-year overall survival rate is 91.0% for patients without lymph node metastases and the 5-year overall survival rate of patients with lymph node metastasis or micrometastasis is less than 50.0% [17]. Therefore, it is of great importance to assess the metastatic state of abdominal lymph nodes for the prognosis of elderly patients with colorectal cancer.

In recent years, carbon nanoparticle usage for identification of SLN in elderly colorectal cancer patients with abdominal lymph node metastasis has been applied, and the effect is ideal [18]. In this study, there were no statistically significant differences in metastasis rate and lymph node metastasis rate between the two groups ($p>0.05$). The total number of lymph nodes detected and the number of micrometastatic lymph nodes were higher in the observation group than in the control group ($p<0.05$), while the ratio of fewer than 12 lymph nodes in the observation group was lower than in the control group ($p<0.05$). It is suggested that the SLN identification using carbon nanoparticle can improve the detection rate of metastatic lymph nodes [19]. SLN identification using carbon nanoparticles was firstly developed in 1997 [20] and refers to the first or first group of lymph nodes that receive the primary tumor drainage; the pathological state can reflect the state of lymph nodes in the entire area. A study has shown that SLN status can effectively predict the regional lymph node metastasis with high specificity [21]. The effect of surgical treatment in elderly patients with colorectal cancer can be determined based on SLN pathological results, in the sense that it can help discriminate those patients that need regional lymph node dissection. In this study, 8 out of 40 patients had lymph node metastasis, the detection rate of SLN was 92.50%, the accuracy rate 94.59%, the diagnostic specificity 87.50%, the false negative rate 12.50% and the negative predictive value 21.88 %, suggesting that SLN evaluation has high accuracy and specificity, which can guide patients' surgical treatment. In elderly patients with colorectal cancer, SLN detection and evaluation helps improve the accuracy of pathological staging, timely detect the abnormal lymph node drainage pathways, guide the kind of surgical resection, help reduce the work for the pathology department, and reduce the economic burden of patients.

In this study, there were no statistically significant differences in the metastasis rates of black-stained and non-black-stained lymph nodes in the observation group ($p>0.05$). The black-stained rate of micrometastatic lymph nodes was higher than the total black-stained rate ($p<0.05$). The rate of micrometastatic lymph node metastasis was lower than that of lymph node metastasis > 5mm ($p<0.05$), suggesting that the preoperative SLN detection in elderly patients with colorectal cancer can evaluate the abdominal lymph nodes, guide the treatment and improve the prognosis. However, in the SLN identification using carbon nanoparticles for elderly patients with colorectal cancer, the indications must be strictly followed. Thus, the surgical treatment can be more targeted, contributing to more early recovery [22].

In summary, the preoperative SLN detection in elderly patients with colorectal cancer can be used to assess the abdominal lymph nodes status, which is simple and accurate and can guide the treatment, so it is worthy of popularization and application.

Conflict of interests

The authors declare no conflict of interests.

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