THE GUARD LYMPH NODES WHEN CHOOSING TACTICS OF OPERATIONAL TREATMENT OF COLORECTAL CANCER

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ABSTRACT
In this article, we analyzed the studies, that were conducted over the past 10 years to study the role of the "guard lymph node" in colorectal cancer. Researches were studied prospectively as well as retrospectively, in which "guard lymph nodes" were defined and was studied the lesion of lymph nodes 1, 2 and 3 orders. The purpose of this work is to evaluate and compare the results of operations used in collorectal cancer. Results and conclusions are presented on the basis of developed and developing countries.

Introduction. The wide spread of colorectal cancer, which ranks third, as the cause of deaths among all malignant neoplasms, makes the problem of improving the quality of treatment of this disease very urgent [1]. The main method of treating colorectal cancer remains surgical, with the removal of the colon segment with the tumor and enlarged regional lymphadenectomy. The study of the removed lymph nodes has a great practical importance for determining the adequacy of the surgical operation and the conduct of adjuvant chemotherapy [2]. The protocols developed by the American Ioint Committee on Cancer (AICC) recommend removing at least 12 lymph nodes, but in practice half the cases remove less than 12 lymph nodes [3].

Because of insufficiently radical surgery, recurrences are required in 30 % of cases, requiring repeated interventions [4]. Incomplete and inadequate lymphadenectomy leads to incorrect staging, and thus to the choice of inadequate treatment of colorectal cancer. The accuracy of the diagnosis of the cancer stage also depends on the quality of the histological examination. The use of immunohistochemistry methods increases the accuracy of diagnosis [5].

Ideally, all deleleted lymph nodes should be examined using the immunohistochemistry technique, but this leads to additional time and cost.

The concept of the defining role of the "guard lymph node" can fundamentally change the approach when choosing the treatment of colorectal cancer [6]. The role of the "guard lymph node" is well studied in breast cancer and melanoma [7,8]. It is believed that if there are no cancer cells in the remote guard lymph node, it is unlikely that they will be in the lymph nodes of 2 and 3 order. Therefore, with early breast cancer, far from always resorting to radical lymphadenectomy [9].

The role of the "guard lymph node" in the spread of the cancer process, with colorectal cancer has not been studied enough.

We have analyzed the searches conducted over the past 10 years to study the role of the "guard lymph node" in colorectal cancer. Researches were studied prospectively as well as retrospectively, in which "guard lymph nodes" were defined and was studied the lesion of lymph nodes 1, 2 and 3 orders. In total were studied 108 publications in which the authors investigated the ways of the cancer process spreading through the lymphatic system.

Unfortunately, only 10 multicentre studies have reported data about a sufficiently large number of patients [10-19]. Remaining studies are presented with a small number of patients. Most

publications are devoted to colon cancer, and only in 33 studies have the searches of lymph node involvement in patients with colorectal cancer.

The number of lymph nodes removed during surgery ranged from 7 to 30, an average is 15 lymph nodes.

Different authors used different methods of "guard lymph nodes". In most studies were used dyes: patented blue (patent blue V), 1 % of isosulfan blue (lymphazurin), 1 % of methylene blue. In 2 studies was used radioactive technetium 99 to represent the guard lymph node. In 11 studies were used both dyes and radioactive technetium. There is a very small number of works about the use of the luminescence method with indiacyanin green [6, 20-26].

In 40 studies "guard lymph nodes" were identified during the operation. In the remaining studies, lymph nodes were studied in remote preparations.

The table shows the results of the study of "guard lymph nodes" in a number of publications. With the help of existing techniques, "guard lymph nodes" were detected in 92.4 % of patients [10-19]. However, not all studies received the same results (Table 1).

It turned out that in studies where comparatively large experience of detection of "guard lymph nodes" the percentage of accurate detection was significantly higher (94.6 %) than in studies where a small number of patients (less than 100) were analyzed (89.5 %) ($p = 0.02$). The existing methods for determining the "guard lymph nodes" are not sensitive enough: the percentage of detection of guard lymph nodes during the operation was significantly lower than their detection in remote preparations (89.2 % vs 93.7 %, $p = 0.04$).

When detecting lymph nodes during surgery, additional aberrant lymphatic drainage pathways were found in 4 % of patients [11-14, 27, 28]. The detection of guard lymph nodes in colon cancer was more effective than in rectal cancer (93.1 % vs 83.1 %, $p = 0.03$).

The sensitivity of the existing methods of detecting cancerous lesions of the guard lymph nodes was only 69.6 % (Table 1), thus, in almost 1/3 of the patients false-negative results were determined. This depended on the quality of the histological examination of distant "guard lymph nodes". In those cases when the immunohistochemistry methods were additionally used, the accuracy of the detection of the cancerous lesion of the guard lymph nodes exceeded 80 % [5, 28, 29-37].

It is interesting to note that when the frequency of detection of cancerous lymph node involvement in the early stages of the cancer process (T1/T2) was compared with the results with advanced cancer (T3/T4), the sensitivity of the techniques was much higher in the early stages (93.4 % vs 58.8 %, $p = 0.01$) [38, 39].

The detection of the lesion of "guard lymph nodes" largely depends on the experience of researchers. With a large experience in the definition of "guard lymph nodes", the incidence of their cancerous lesion was significantly higher than in the authors who did not have much experience (85.6 % vs 66.4 %, $p < 0.01$).

What does give the detection of guard lymph nodes in patients with colorectal cancer? Unfortunately, at present, the detection of the lesion of guard lymph nodes in colorectal cancer does not affect the volume of the operation, in contrast to breast cancer. Standardly for early cancer and for advanced forms of cancer T3/T4 performed approximately the same volume of operations. At the same time, a detailed study of the incidence of cancer of various lymph nodes allows to better understand the spread of cancer cells in colorectal cancer. Recently, Japanese researchers have created a fairly detailed map of the lesion of lymph nodes of various orders in colorectal cancer. The research conducted by English oncologists confirmed the importance of such mapping [6].

At the present time accumulates the actual material that allows to understand which lymph nodes are affected most often and where to look for them. Methods for intraoperative detection of "guard lymph nodes" using indicyanin green (YCG) and luminescence endoscopy are being improved [24-28].

"Guard lymph nodes," as shown by studies conducted by English oncologists [6], can be localized in the first and second order lymph nodes (D1 and D2), which allows to justify the resection of the affected bowel area, with the mesentery site where D2 lymph nodes are located.

The relatively low sensitivity of the existing methods for detecting the early lesion of "guard lymph nodes" is apparently due to the insufficient number of clinical studies. In early T1/T2 cancer, the sensitivity of the techniques for detecting "guard lymph nodes" is significantly higher than with the advanced forms of T3/T4 cancer. A number of researchers proposed a combination of a luminescent method using indicyanin green (YCG) with radioactive technetium (Tc99), which significantly improved the technique of detecting "guard lymph nodes" for cancer head and neck, and urogenital cancer [40].

Table 1. Results of studies of guard lymphatic nodes in patients with colorectal cancer.

Autor	Number of patients	Colon	Rectum	Method of detection	Number of "guard lymph nodes "	There are cancer cells	Cancer cells are not detected	False negative	Frequency of correction of cancer stage, %
Ceranic	45	No data	No data	methylene blue	1,7	14	19	5	22
Finan	58	0	58	isosulfan blue	2,2	15	27	7	0
Sommariva	69	54	15	patented blue	5	12	46	9	12
Dragan	60	60	0	isosulfan blue	4,1	32	26	0	26,9
Ivanov	103	48	55	patented blue	–	48	52	3	20
Nordgard	131	131	0	patented blue	4	29	83	13	21,4
Van der Zaag	132	100	32	patented blue	2	33	11	73	28,8
Park	69	45	24	methylene blue	2,5	26	27	6	18,5
Quadros	52	22	30	patented blue technetium 99	3,5	15	16	8	37,5
Faerden	199	200	0	patented blue	4	32	125	28	29,8
Lim	120	120	0	isosulfan blue technetium 99	4	29	71	20	11,3
Kelder	69	69	0	patented blue	2,3	15	49	3	18,4
Bembenek	315	315	0	patented blue	2	74	156	38	21,3
Stojadinovic	84	84	0	isosulfan blue	2,7	18	56	8	26,8
Matter	52	36	12	patented blue	2,7	8	30	10	19,4
Tiffet	64	49	15	patented blue technetium 99	2,8	12	35	12	5,7
Van schaik	44	27	17	patented blue	5	26	16	0	30,3
Liberale	118	71	47	patented blue	2	22	76	14	9,5
Yagci	47	20	27	patented blue	5,9	16	27	4	14,8
Thomas	69	63	6	isosulfan blue	2,1	12	38	14	5,3
Terwisscha	53	56	0	patented blue technetium 99	2,2	12	35	2	14,8
Saha	500	408	92	isosulfan blue	2,2	186	211	21	26,1
Khafagy	53	0	53	patented blue	–	31	8	8	46
Codignola	56	52	4	patented blue	2	37	13	6	37,5
Braat	91	57	34	patented blue	1,8	23	51	8	10,5
Bell	58	46	12	patented blue	2,9	9	33	14	61
Bertagnolli	72	72	0	isosulfan blue	2,1	10	42	14	0
Demirbas	41	25	16	patented blue	3	18	17	2	11,8
Wong	124	110	12	isosulfan blue	3,8	27	69	24	27,3
Patten	57	57	0	isosulfan blue technetium 99	3,5	14	31	11	14,3
Bembenek	48	0	48	technetium 99	3	7	30	9	0
Bilchik	120	120	18	isosulfan blue technetium 99	1,8	37	73	5	29,5
Broderick-Villa	50	46	5	isosulfan blue	1,5	10	27	10	–
Kitagawa	56	19	37	technetium 99	3,5	18	29	4	0
Paramo	55	55	0	isosulfan blue	1,9	14	30	1	20
Merrie	25	25	0	patented blue technetium 99	3	4	16	3	25
Joosten	50	44	6	patented blue	3	8	15	12	13,3

By now it is unclear whether the concept of guard lymph nodes, which is successfully used in breast cancer and melanoma, can be used in colorectal cancer. More research are needed, but already the experience of using of luminescent laparoscopy with indicyanin green (YCG) shows the advisability of identifying "guard lymph nodes" in the early forms of colorectal cancer. The identification and careful study of "guard lymph nodes" allows to specify the stage of the process in early cancer, which affects the prognosis of the disease and specifies the need for adjuvant chemotherapy.

In our clinic, studies have begun to identify "guard lymph nodes" in case of rectal cancer. In 35 patients with early rectal cancer (T0/T1/T2), we successfully used the surgical technique of transanal local excision of mucosal cancer (TEM). However, in all cases of local cancer resection, the question of possible lesion of lymph nodes naturally arises. In 12 patients with early cancer of the rectum, we used the technique of identifying the guard lymph nodes. For this was injected in a submucosal layer at 4 points around the tumor lesion 1 ml of indiacyanin green (YCG), at a concentration of 5 mg/ml. In 10-15 minutes after the drug was administered, patients underwent laparoscopy. Carefully examined the small pelvis in ordinary and infrared light (Scharz laparoscope). Lymphatic vessels and "guard lymph nodes" were colored green and well identified. Were performed dissection and removal of colored lymph nodes. The removed lymph nodes were subjected to urgent histological examination. In 2 cases of 12 (8 %) in the lymph nodes were found cancer cells. These patients underwent laparoscopic surgery - low rectal resection with removal of mesorectum.

Under observation for 6-24 months in all 12 patients was not detected any recurrence of cancer in all case.

Conclusions. Thereby, the identification of "guard lymph nodes" in colorectal cancer has an important prognostic value. Perhaps later, in improving the methods for detecting "guard lymph nodes," it will be possible to trace more detail the spread of cancer cells through lymphatic vessels and create a more detailed map of lymph node involvement in colorectal cancer.

All this will change the tactics of treating early cancer of the rectum and colon.

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