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REVIEW

D2, D3 LYMPH NODE DISSECTION IMPORTANCE IN COLON CANCER SURGERY

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ABSTRACT

Colorectal cancer (CRC) is a relevant issue of modern oncology and ranks the third place among most common malignancies. Every year, more than 1 million new cases of CRC are diagnosed worldwide, with approximately the same frequency of prevalence among the male and female population. Colon cancer (CC) amounts for more than half of all cases of CRC, and it's incidence and mortality remain rather high.

Surgery remains the main method of CRC treatment, and determining the extent of surgery and lymph node dissection remains an urgent problem.

For the first time in Japan, a classification of groups of lymph nodes (l.n.) was proposed depending on the level of lymph outflow and location in relation to the main vessels. According to the numbering of l.n. groups by the Japanese Society for Cancer of the Colon and Rectum (JSCCR), all lymph nodes are numbered with three digits.

As a rule, lymphogenic metastasis occurs in one direction, bilateral spread is possible if the tumor is located at the same distance from two feeding vessels. With tumors of the right-sided localization, all groups of l.n. located along the branches of the superior mesenteric artery are removed, and with tumors of the left half of the colon, all l.n. located along the trunk of the inferior mesenteric artery are removed. The presence of affected l.n. is important for assessing the prognosis and further determining the need for adjuvant therapy. Some literature data demonstrate good results of surgical interventions performed in accordance with the concept of embryonic planes and complete mesocolonic excision. D3 lymph node dissection is not performed in daily practice in some European countries and North America, unlike a number of Eastern countries. However, the level of vessel ligation remains the subject of scientific discussion.

The purpose of this review was to analyze the available literature on the problem of choosing the level of lymph node dissection in CC surgery.

Keywords:
colorectal cancer, colon cancer, surgical treatment D2/D3 lymph node dissection

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ОБЗОР

РОЛЬ D2, D3 ЛИМФОДИССЕКЦИЙ В ХИРУРГИИ РАКА ОБОДОЧНОЙ КИШКИ

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РЕЗЮМЕ

Колоректальный рак (КРР) является актуальной проблемой современной онкологии и занимает третье место в структуре общей онкологической заболеваемости. Ежегодно во всем мире диагностируются более 1 млн. новых случаев заболевания КРР, приблизительно с одинаковой частотой распространенности среди мужского и женского населения. Более половины всех случаев КРР приходятся на рак ободочной кишки (РОК), заболеваемость и смертность от которого остается на достаточно высоком уровне, несмотря на современные диагностические возможности и принципы терапии. Основным методом лечения пациентов с опухолями ободочной кишки остается хирургический, а определение объема оперативного вмешательства и уровня лимфодиссекции остается актуальной проблемой современной онкопроктологии. Впервые в Японии была предложена классификация групп лимфатических узлов (л.у.) в зависимости от уровня лимфооттока и расположения по отношению к магистральным сосудам. Согласно нумерации групп л.у. по Japanese Society for Cancer of the Colon and Rectum (JSCCR) все лимфатические узлы пронумерованы трехзначными цифрами. Как правило, лимфогенное метастазирование происходит в одном направлении, билатеральное распространение возможно в случае, если опухоль расположена на одинаковом расстоянии от двух питающих сосудов. При опухолях правосторонней локализации удаляются все группы л.у., располагающиеся вдоль ветвей верхней брыжеечной артерии, а при опухолях левой половины ободочной кишки – все л.у., находящиеся вдоль ствола нижней брыжеечной артерии. Наличие пораженных л.у. важно для оценки прогноза и дальнейшего определения необходимости проведения адъювантной терапии. В литературе имеется данные, которые свидетельствуют о хороших результатах оперативных вмешательств, которые выполнены с использованием принципов эмбрионально-ориентированной хирургии и тотальной мезоколонэктомии. В некоторых европейских странах и Северной Америке D3 лимфодиссекция (расширенная лимфодиссекция) не выполняется в повседневной практике, в отличие от ряда восточных стран. Однако, уровень перевязки сосудов остается предметом научных споров.

Цель данного обзора: провести анализ имеющейся литературы, посвященной проблеме выбора уровня лимфодиссекции в хирургии РОК.

Ключевые слова:
колоректальный рак, рак ободочной кишки, хирургическое лечение, D2/D3 лимфодиссекция

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RELEVANCE

Colorectal cancer (CRC) is an urgent problem of modern oncology and ranks third in the structure of general oncological morbidity both in Russia and in foreign countries [1; 2]. More than half of all cases of CRC occur in colon cancer (CC), the morbidity and mortality from which remains at a fairly high level [3]. The main method of treatment of CRC remains surgical, and determining the volume of surgery and the level of lymph dissection remains an urgent problem of oncosurgery.

There are data in the literature that indicate good results of surgical interventions performed using the principles of embryonic-oriented surgery and total mesocolonectomy (complete mesocolon excision, CME). In some European countries and North America, D3 lymph dissection is not performed in everyday practice, unlike in a number of Eastern countries. However, the level of vascular ligation remains a subject of scientific debate [4].

The purpose of the study: to analyze the available literature on the issue of choosing the level of lymphodissection in CC surgery.

Japanese classification of lymph node groups

For the first time in Japan (1977), a classification of groups of lymph nodes was proposed depending on the level of lymph outflow and location in relation to the main vessels [5; 6]. According to the numbering of the l.n. groups by the Japanese Society for Cancer of the Colon and Rectum (JSCCR), all lymph nodes are numbered with three digits [6] (Fig. 1).

L.ns. are divided into 3 levels:

- N1 – paracolitic,
- N2 – mesocoliic,
- N3 – central l.n.

Usually, lymphogenic metastasis occurs in one direction, bilateral spread is possible if the tumor is located at the same distance from two feeding vessels. With tumors of the right-sided localization, all groups of LV located along the branches of the upper mesenteric artery are removed, and with tumors of the left half of the colon, all l.n. located along the trunk of the lower mesenteric artery are removed [9].

D2, D3 lymphodissection in colon cancer surgery: meta-analysis

The presence of affected l.ns. is important for assessing the prognosis and further determining the need for adjuvant therapy.

The aim of the Tsai H. L. et al. study was to determine whether the number of removed l.ns. can affect the prognosis of the clinical course of patients who underwent surgery for CRC. The authors noted that the amount of tumor invasion and the number of removed lymph nodes are independent prognostic factors for the development of postoperative relapse ($p < 0.05$). The 5th overall survival of patients who had 18 or more lymph nodes examined was significantly higher than those who had less than 18 nodes examined ($p = 0.015$). The results of this work show that the removal and examination of at least 18 HP can be taken into account for more reliable and correct postoperative staging [10].

According to Willaert W. et al. the described method of total mesocolonectomy (complete mesocolon excision, CME) with complete removal of l.n. should be subjected to a prospective randomized study. However, there is undoubtedly a proven relationship between the number of removed l.ns. and survival in CRC [11].

The question of whether extended lymphadenectomy in CC leads to an increase in postoperative complications or improves survival is still controversial. In some European countries and North America, D3 lymph dissection is not performed in everyday practice, unlike in a number of Eastern countries. However, the level of vascular ligation remains a subject of scientific debate. There are data in the literature that indicate good results of surgical interventions that are performed using the principles of embryonic-oriented surgery and CME.

In a randomized RELARC phase 3 trial, the hypothesis is considered that survival after D2 lymphodissection is better than after CME. The primary endpoint is 3-year relapse-free survival. To date, researchers have presented the results of comparing the following criteria: intra- and postoperative complications within 30 days after surgery (according to the Clavien-Dindo classification), mortality (death from any cause within 30 days after surgery) and the frequency of metastasis to the central l.ns. only in the CME group. The frequency of postoperative surgical complications was 20 % (97 out of 495 patients) in the CME group compared with 22 % (109 out of 500 patients) in the D2 group ($p = 0.39$). The frequency of Clavien-Dindo grade I–II complications was the same between the groups and amounted to 18 %, and grade III–IV complications They were significantly less common in the CME group than in the D2 group (1 % and 3 %, respec-

tively, $p = 0.022$). There were no fatal outcomes in the compared groups. In the structure of intraoperative complications, vascular damage was significantly more common in the CME group than in the D2 group (15 (3 %) vs. 6 (1 %), $p = 0.045$). Metastases in the central l.n. were detected in 13 (3 %) of 394 patients, but none of the patients had their isolated metastatic lesion. Thus, the authors concluded that CME can increase the risk of intraoperative vascular damage, but in general it seems safe and feasible for experienced surgeons [12].

A number of papers have been published indicating a significant decrease in the frequency of local relapses and an increase in the overall 5-year survival after surgical intervention using the CME technique.

So in the work of Bertelsen C. A. et al. It was proved that 4-year relapse-free survival was 85.8 % (95 % CI 81.4–90.1) after CME and 75.9 % (72.2–79.7) after surgery without using the CME technique ($p = 0.0010$), and Cox regression showed that CME was a significant independent prognostic factor for higher relapse-free survival for patients. Thus, according to the authors, CME can improve the results of treatment of patients with CRC [13].

A prospective study by Galizia G. et. al. showed that the number of removed l.n. and the length of vascular ligation were significantly better in the CME group ($p < 0.01$). A larger number of affected l.n. were removed, which allowed for an adequate selection of adjuvant treatment. The authors proved that CME with CVL is a safe and effective surgical approach for right colon cancer, reduces local recurrences and improves survival, especially in patients with N+ [14]. However, no increase in the frequency of postoperative complications was found in these studies.

In a retrospective study by K. Kotake et al. The advantages of D2 and D3 lymph node dissection in CC surgery were studied. In all groups of patients, there was a statistically significant difference in overall survival between patients who underwent dissection of lymph nodes D3 and D2 ($p = 0.00003$). It was found that dissection of D3 lymph nodes in pT3 and pT4 colon cancer is associated with a significant advantage in improving patient survival, which can serve as a basis for dissection of D3 lymph nodes in radical surgery of pT3 and pT4 colon cancer [15].

The aim of the Hwang D. Y. et al. study was the assessment of the safety and oncological results of

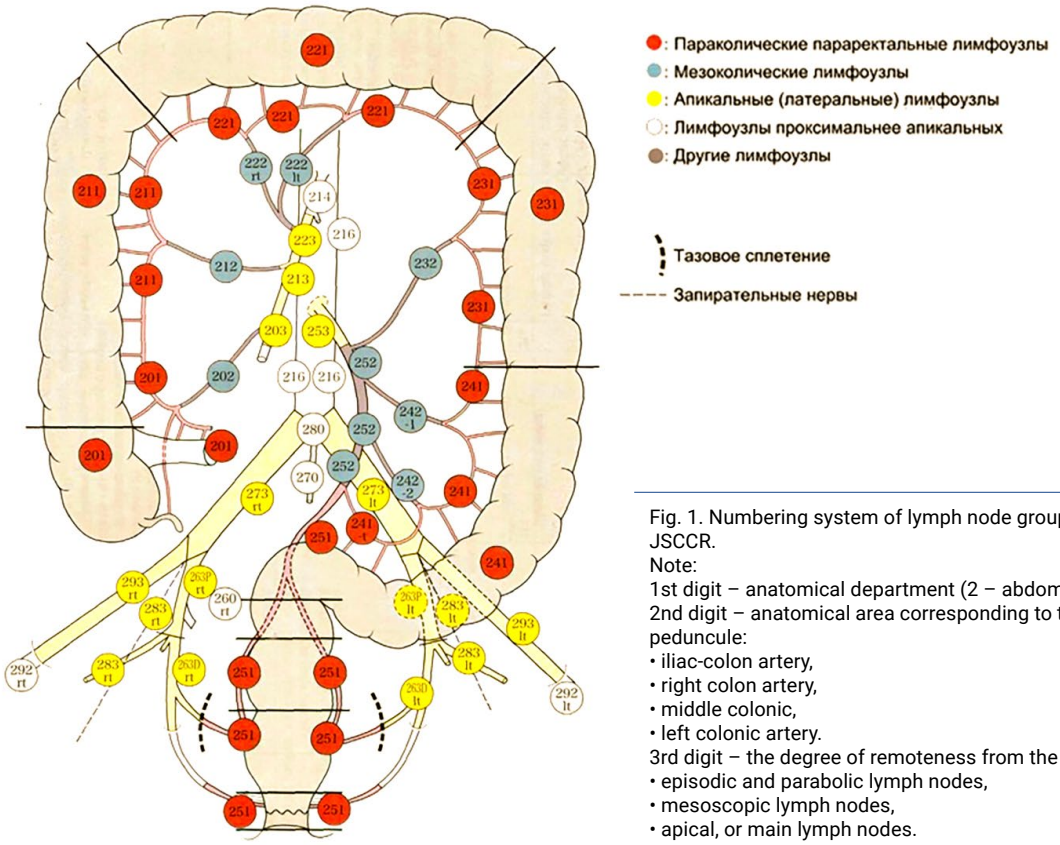

Fig. 1. Numbering system of lymph node groups according to JSCCR.
Note:
1st digit – anatomical department (2 – abdominal cavity, pelvis).
2nd digit – anatomical area corresponding to the lymphovascular peduncule:
• iliac-colon artery,
• right colon artery,
• middle colonic,
• left colonic artery.
3rd digit – the degree of remoteness from the intestine:
• episodic and parabolic lymph nodes,
• mesoscopic lymph nodes,
• apical, or main lymph nodes.

laparoscopic CME with D3 in cancer of the right colon in elderly patients. Patients who underwent right-sided hemicolectomy were divided into groups A (age ≥ 70 years, *n* = 80) and B (age < 70 years, *n* = 127). Short-term and long-term results were analyzed. It was found that the overall and relapse-free survival rates were the same between the compared groups, and laparoscopic CME with D3 lymphodissection is a safe and feasible surgical option for cancer of the right half of the colon in the elderly [16].

In our country, an international multicenter randomized COLD Trial was launched in 2017, the main purpose of which is to evaluate and compare the overall 5-year survival after D2- and D3-lymphodissection performed in CC [4]. Patients with resectable CC were randomized for D2 or D3 dissection in a 1:1 ratio.

The data obtained were analyzed to assess the safety of D3 lymph dissection

In the work of Karachun A. et al. the results for the first 100 patients are presented. There were no fatalities. The 30-day postoperative morbidity rate was 47 % in group D2 and 48 % in group D3 with a RR1.04 (95 % CI from 0.68 to 1.58) (p = 0.867). There were two anastomosis failures (5 %) in group D2 and none in group D3. Postoperative recovery, the frequency of complications and repeated hospitalizations did not differ between the groups. N-positive status was more common in group D3 (46 % vs. 26 % in group D2) with RR 1.81 (95 % CI from 1.01 to 3.24) (p = 0.044). The authors concluded that D3 lymph node dissection is possible and may be associated with a better staging of the process [17].

CONCLUSION

After the carried out analysis of the available up to date literature, the following conclusions can be drawn. On one hand, the relationship between the number of removed HP and a more accurate determination of the N status has been proven, which is important for assessing the clinical prognosis and further determining the need for adjuvant therapy. On the other hand, it is indisputable that D3 lymph dissection can increase the risk of intraoperative vascular damage. Thus, due to the lack of a convincing evidence base, it is difficult to talk about the advantages and long-term results of performing D2 and D3 lymphodissections in CC surgery. The recruitment of patients in some large studies continues to this day, and the publication of the results of others is expected in the near future.

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