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THE PLACE OF LYMPH DISSECTION IN THE TREATMENT OF CANCER AND THE CHOICE OF SURGICAL TACTICS (REVIEW ARTICLE)

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Abstract

Over the past years, due to increase of detection of patients with early-stage stomach cancer and colorectal cancer, and improvement of survival rate, the efforts have been made to gradually develop the concept of sentinel lymph nodes detection in order to improve postoperative quality of life. The article presents the review of the literature on the feasibility of sentinel lymph nodes intraoperative diagnosis the choice of surgical treatment of patients with tumors of the stomach and colon. Analytical work demonstrates that the real time intraoperative visualization of lymph sinases using fluorescent imaging of indocyanine green during laparoscopic surgery for stomach or colorectal cancer is possible and it is a useful method of the lymph nodes mapping, therefore it can lead to intraoperative changes at lymphadenectomy as well as to reduce the surgical injury. It indicates the need in further research and improvement of approach.

Key words: stomach cancer; colon cancer; colorectal cancer; sentinel lymph node; lymph dissection; indocyanine green.

Despite great intensive achievements and development of modern medicine, the number of colorectal and stomach cancer is growing every year around the world [1-4]. One of the main factors influencing the quality of life of patients, the number of relapses and survival rate of patients with colorectal and stomach cancer is the regional lymph nodes (LN) involvement [5-7]. Imaging techniques, such as contrast-enhanced MRI and PET-CT, have significantly improved the resolution of LN involvement at the preoperative stage, but still require histological examination of LN, which remains the “gold standard” for cancer diagnosis [8-10]. Intraoperative examination of sentinel lymph nodes (SLN) in colon, rectal and stomach cancer determines not only the stage of the disease and the extent of operation, but also improves the quality of life of patients, reduce recurrence and mortality [11].

Colorectal cancer is a serious problem for human health [1, 11]. Worldwide, about 500,000 patients die each year from colorectal cancer [1, 12], in the United States 5-year survival of patients with this diagnosis is 60–65% [11]. In Ukraine, 24 new cases of colorectal cancer are detected annually per 100 thousand of the population [4]. Colon and rectal cancer is diagnosed by endoscopic polyp biopsy or intestinal tumor formation [5]. In patients with tumor invasion, radical resection of the intestine with LN as a single unit, which in some cases is quite aggressive and traumatic techniques, and is associated with a great number of intraoperative, postoperative complications and disability of patients [12].

Although submucosal resection of colon and rectal neoplasms is suggested as a sufficient volume of surgical treatment, in some cases, uncertainty about possible undetected concomitant LN metastases remains a serious drawback of this surgical approach [11, 12].

The standard therapy for colorectal cancer is an adequate radical resection of the colon or rectum as a single unit with regional LN [12]. This surgery can be performed both by standard open methods and laparoscopic methods, due to the development of modern surgical equipment. At resection of a gut with a tumor removal of not less than 12 LN is necessary, though removed in practice much less [12]. So, due to the non-radical nature of surgery, postoperative recurrences take place in 30% of cases [13].

Lymph node status is the most important prognostic factor in colorectal bowel, but the role of SLN biopsy as a tool to detect micrometastatic disease and extra-anatomical LN for adjuvant strategies and an adapted approach remains unclear [12, 13].

Depending on the stage of the disease in patients with colorectal cancer, the appropriate amount of surgery is performed [12]. According to the recommendations of the American Joint Cancer Committee (AJCC), patients with stage I and II colorectal cancer have been indicated to perform only surgical resection of the tumor and lymphadenectomy, without

adjuvant chemotherapy [2, 6, 12]. At the same time, according to the AJCC recommendations, at the stage III, radical surgical treatment is indicated with the next standard adjuvant chemotherapy [6]. The most important criterion for classification between stage II and stage III is the SLN metastatic involvement [2, 6].

Detection of indocyanine green (ICG) fluorescence is a new method for SLN biopsy, which allows the real-time lymphography and intraoperative detection of LN involvement [4, 13].

The essence of the technique is that during the operation with the help of a colonoscope 1–2 mm of the ICG dye is introduced in the submucosal layer of the tumor. Then, in 15 minutes, laparoscopy is performed in the ultraviolet illumination mode, which allows to see the colored regional LN. Then the SLN is removed and its urgent histological examination is performed. If there are no cancer micrometastases in the SLN, local removal of the tumor is performed. In the presence of the SLN metastatic involvement, laparoscopic or open resection of the intestine with lymph dissection is performed.

Every year more than 1 million people in the world suffer from stomach cancer [1, 14]. According to consolidated epidemiological data, this disease occupies the fourth place in the world after lung cancer and breast cancer [6, 9]. More than 930 thousand new cases of the disease are diagnosed annually, and the annual mortality is more than 700 thousand [14, 15].

Ukraine is one of the countries where stomach cancer is considered one of the most common malignant pathologies [1, 4]. In terms of mortality up to one year, this oncopathology is at the 2nd place in men and women [1]. The main link in the relevance of the problem of stomach cancer are neglected cases of the disease — 75–85% in the overall structure [1, 5]. High incidence of stomach cancer, lack of real improvement in the diagnosis of the disease necessitate the search for new ways to provide timely detection [8].

Stomach cancer is difficult to diagnose and treat [16]. Subtotal resections (distal or proximal) and gastrectomy can be used as radical operations in stomach cancer surgery [8].

The concept of the SLN made a revolution in the surgical staging of both melanoma and breast cancer over the past two decades [3, 17]. The application of this concept can benefit patients by preventing various complications associated with unnecessary prophylactic dissection of regional LN in patients with negative SLN [18, 19, 20]. The clinical application of SLN mapping in patients with early stomach cancer has been a controversial issue for many years [6].

Ever since Morton and co-authors [17] demonstrated the validity of this concept in melanoma, and the subsequent identification of SLN by lymphatic mapping of breast cancer

by Krag [19] and Giuliano [7], the use of SLN in therapeutic strategy essentially changed treatment of these types of cancer [8, 20].

The sentinel lymph node or nodes are the first LN in the regional lymphatic basin which receives lymph flow from the primary tumor [7, 11]. Assuming the orderly spread of metastases in the lymphatic system, SLN will be the first nodes to contain metastases, and their biopsy will accurately predict the status of a regional node [2]. SLN biopsy provides low morbidity and for many patients with malignancies such as breast cancer and melanoma, complete regional lymphadenectomy has been replaced by SLN biopsy [3, 15, 20].

Currently, the most accurate method of detecting LN involvement is intraoperative diagnosis using the SLN biopsy [9]. SLN biopsy is a multi-stage technique consisting of six main elements: indications, choice of indicator, correct method of indicator introduction, objective detection of SLN, reliable biopsy technique and accurate detection of nodular metastases [6].

The concept of lymphatic mapping in oncology is based on the fact that the lymph vessels from the tumor flow into a specific regional LN or LNs, the so-called SLNs [5, 16, 19]. From these nodes, the lymph passes through the efferent lymph vessels into the secondary LNs [11]. In the case of the lymphogenic spreading, tumor cells will first accumulate in SLN [6].

Laparoscopic gastrectomy with lymphadenectomy is increasingly performed for treatment of early stages of stomach cancer due to the minimally invasive character of this method compared to a conventional open resection [2, 9, 14, 20].

As far back as in 2003, Bilchyk et al. [12] reported a possibility of laparoscopic intraoperative lymphatic mapping with blue dye in patients, but unfortunately the method was not widely used at that time.

As the incidence of LN involvement is low at the early stages of cancer of the stomach, LN dissection during gastrectomy may be too much invasive for such patients. However, gastrectomy with D1+ or D2 lymphadenectomy has become the standard surgical procedure because the sensitivity of the current preoperative imaging is low to detect LN involvement. To overcome the ambiguity of preoperative examinations for the detection of LN metastases, the SLN concept was used [8, 17].

However, a number of multicenter studies on SLN biopsy in stomach cancer using the staining method with ICG intraoperative administration led to an unexpectedly high rate of false-negative results [3].

SLN biopsy by ICG fluorescence during laparoscopic gastrectomy has contributed to the development of laparoscopic ICG fluorescence imaging systems [10], which allows after the creation of pneumoperitoneum and the necessary site preparation, to enter ICG with a puncture needle at 4 points around the tumor. Within 20 minutes after the injection, the lymph nodes are evaluated using a laparoscope and a fluorescent system ICG and the fluorescent-positive lymph nodes are removed, followed by the main stage. In case of confirmation by rapid histological examination of the SLN lesion, standard subtotal gastrectomy or gastrectomy with lymph dissection in the amount of D2 is performed. If cancer cells are not detected in SLN, a functional-preserving operation on the stomach is performed: segmental pyloro-sparing gastrectomy, proximal gastrectomy, excision of the gastric wall or combined endoscopic excision of the gastric tumor with adjacent lymph nodes [4, 16].

The experience of such organ-sparing operations at the early stages of stomach cancer showed that a 5-year survival rate was the same like in gastrectomy with radical lymph dissection [3, 7], while the quality of life of these patients had almost no difference from healthy people.

Lymph node involvement remains the single most important prognostic sign in cancer management.

So, the proposed review of numerous studies proves that the concept of intraoperative detection of SLN is correct for different localizations of cancer and is important for the choice of further treatment strategy. Intraoperative mapping of SLN may play a significant role in the future in colorectal and stomach cancer surgery by increasing the incidence of early-stage disease, which will reduce the negative consequences and complications of lymphadenectomy and improve patients' quality of life at the postoperative period.

With the improvement of methods for detecting SLN in patients with early stages of the disease, it will be possible to avoid of superradical, traumatic and disabling operations [6].

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