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INFLUENCE OF ICG-TECHNOLOGY ON THE RESULTS OF SURGICAL TREATMENT OF EARLY FORMS OF BREAST CANCER

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Kew word: breast cancer, surgical tactics, intraoperative ICG-technology

Abstract. Influence of ICG-technology on the results of surgical treatment of early forms of breast cancer. Masia J., Savenkov O.Y. Breast cancer (BC) is one of the most common causes of death in women under 50 years old. For today the choice of adequate methods of surgical intervention and the need for an adequate surgical adjuvant therapy, quality of life of patients after surgery are important. The aim of our study was to select the volume of surgery for breast cancer using the technique of intraoperative identification of the sentinel lymph node (intraoperative ICG technology) and to evaluate the results of its urgent histological examination. It was shown that the most common method of surgery in patients who underwent intraoperative ICG technology was quadrantectomy, which was performed in 27 cases (54%), rarely subcutaneous mastectomy was performed (30%) and radical mastectomy (by Madden) – 16%. In the control group, priority was given to radical removal of the breast (63.2% of cases); partial resection (by U. Veronesi) was performed in 33.3% of patients, and subcutaneous mastectomy – in 3.5%. Pathomorphological examination of the sentinel lymph node during its intraoperative imaging using ICG-technology established metastatic lesion in 10 of 50 cases (20%) in the main group. The obtained results of the assessment of the regional lymph dissection size in the main group indicate its adequate nature to ensure the radicality of surgical treatment. In our opinion, it is one of the important preliminary conclusions of this study, as to assess the clinical significance of signal lymph node (SLN) analysis as a marker of regional tumor spread, firstly it is necessary to be sure that existing surgical techniques provide radical tumor removal.

Реферат. Влияние ICG-технологии на результаты хирургического лечения ранних форм рака молочной железы. Масия Хайме, Савенков О.Ю. Рак молочной железы (РМЖ) входит в пятерку наиболее распространённых в мире онкологических заболеваний и лидирует среди причин смерти женщин в возрасте до 50 лет. На сегодня актуальными остаются вопросы выбора адекватного объема хирургического вмешательства, необходимости назначения послеоперационной адъювантной терапии и качества жизни пациенток после операции. Целью нашего исследования стали выбор объема хирургической операции при раке молочной железы при применении методики интраоперационной идентификации сторожевого лимфоузла (интраоперационная ICG-технология) и оценка результатов срочного его гистологического исследования. Нами показано, что наиболее частым методом хирургического вмешательства у пациенток, у которых использовалась интраоперационная ICG-технология, была квадрантэктомия, которая была проведена в 27 случаев (54%), реже проводилась подкожная мастэктомия (30%) и у 16% радикальная мастэктомия (по Маддену). При этом в группе контроля приоритет отдавался радикальному удалению молочной железы (63,2% случаев); частичная резекция (по U. Veronesi) выполнена у 33,3% пациенток, а подкожная мастэктомия – у 3,5%. Патоморфологическими исследованиями сторожевого лимфоузла, во время его интраоперационной визуализации с использованием ICG-технологии, метастатическое поражение установлено в 10 из 50 случаев (20%) в основной группе. Полученные результаты оценки объема регионарной лимфодиссекции в основной группе указали на ее адекватный характер обеспечения радикальности хирургического лечения. Это, на наш взгляд, является одним из важных предварительных выводов данной работы, так как для оценки клинического значения анализа сигнального лимфоузла как маркера регионарного распространения опухоли необходимо в первую очередь удостовериться, что существующая хирургическая техника обеспечивает радикальное удаление опухоли.

Breast cancer (BC) is one of the main medical and social problems of modern oncology, which is explained by the prevalence of this pathology and psychological aspects associated with the problems of social adaptation of patients after surgery [3, 6, 7]. This form of cancer belongs to those malignant neoplasms, the characteristic features of which are high growth rate, territorial and geographical uneven distribution of morbidity levels [1, 4, 10], which is primarily mediated by a variety of socio-demographic, ethnic and individual risk factors [5, 9].

Breast cancer is one of the five most common cancers in the world and the leading cause of death for women under the age of 50. In 25% of cases, it is diagnosed during the reproductive period. Every year, more than 1 million new cases of breast cancer are registered in the world: the highest incidence is in the United States, Canada, France, Israel, Switzerland, Spain, Finland, the Baltic States, Australia and Hawaii. Low rates of breast cancer are observed in Japan, China, Mexico and Venezuela. According to the World Health Organization, the occurrence and development of malignant neoplasms in the population are largely due to the state of anti-cancer measures, as evidenced by the wide range of fluctuations in morbidity in different countries, especially in breast cancer.

Currently, the widespread introduction of modern diagnostic techniques and a fuller coverage of the female population with preventive examinations contribute to the effective and timely detection of minimal forms of breast cancer. However, the issues of choosing an adequate amount of surgery and the need for postoperative adjuvant treatment remain relevant, primarily to prevent the development of local recurrences and complications and improve the quality of life of this group of patients.

The aim of our study was to substantiate the use of the method of intraoperative identification of sentinel lymph nodes (intraoperative ICG-technology) in the surgical treatment of breast cancer.

MATERIALS AND METHODS OF RESEARCH

Our study is based on the analysis of data from a comprehensive examination and treatment of 107 patients with early resectable forms of infiltrative breast cancer (T1-2aN0M0). The work was performed during 2016-2020 on the basis of Dnipropetrovsk Regional Oncology Center and MC Clinic "Garvis" (Dnipro). The planning and implementation of the work took into account the practical recommendations of the European Society of Medical Oncologists (ESMO) and the International Practical Recommendations (NCCN) 2016-2019.

The mean age of the observed patients was 56.5 ± 1.9 years (from 27 to 83 years).

Criteria for inclusion of patients in this study were:

- early forms of breast cancer (tumor size – T1, T2);
 - morphological (histological, immunohistochemical) verification of the diagnosis of breast cancer;
 - absence of clinical, radiological and morphological signs of metastatic lesions of regional lymph nodes (N0);
 - absence of preoperative treatment (neoadjuvant therapy) and previous breast surgery.
- Patients excluded from the study:
- previous treatment of breast cancer (neoadjuvant radiation or polychemotherapy) was performed;
 - multicentric tumor growth;
 - diagnosis of edematous breast cancer;
 - presence of scars on the breast and/or axillary area due to surgeries, injuries, inflammatory processes;
 - comorbidities in the stage of decompensation [7].

The results were processed by the methods of variation statistics (M.Yu. Antomonov, 2018) [2] using the licensed statistical program STATISTICA v.6.1 (Statsoft Inc., USA), (serial number AGAR909E415822FA).

RESULTS AND DISCUSSION

According to the results, the maximum proportion of patients in the group of those after radical surgery with full regional lymph dissection and in patients who underwent intraoperative ICG-technology, were middle-aged and at the age of maturity in conditions for compliance of the observed sample with the normal general population (Shapiro-Wilk's W test: $SW-W=0.9883$; $p=0.2365$) (Table 1).

The average body mass index (BMI, Kettle index) in the examined patients of the main group was 25.7 ± 1.8 , the control group – 27.9 ± 1.2 : the number and percentage of women taking into account BMI ($W=0.9829$; $p=0.1058$).

The results of the distribution of patients in the main and control groups depending on the volume of surgery are shown in table 2.

It was shown that the most common method of surgery in patients who underwent intraoperative ICG technology was quadrantectomy, which was performed in 27 cases (54%), subcutaneous mastectomy (30%) and radical mastectomy (according to Madden) (16%) were performed rarely. In the

control group, priority was given to radical removal of the breast (63.2% of cases); partial resection (according to U. Veronesi) was performed in 33.3% of patients and subcutaneous mastectomy – in 3.5%.

Table 1

Distribution of patients by age in the main and control group

Age, years	Number of patients	
	main group	control group
27 – 45	13	10
46 – 60	27	28
61 – 75	8	14
76 – 83	2	5
Total	50	57

We noted that neither in the main nor in the control group patterns of tumor localization in the left or right breast ($p=0.805$) were found. Thus, in the group where intraoperative ICG technology was used, in 26 out of 50 cases (52%) the tumor was found in the right breast, in 24 (48%) – in the left (in

the control group – 54.4% and 45), 6% respectively). In the main group, in most cases (42%) the tumor was localized in the upper outer quadrant, less often – in the lower outer (18%), inner quadrants (4%) and central sector (24%) (Table 3).

Table 2

Distribution of patients by volume of surgical treatment in the main and the control group

The nature of the intervention	Number of patients, n (%)		Statistical indicators
	main group	control group	
Quadrantectomy	27 (54%)	19 (33.3%)	$\chi^2=28.8$; $p<0.001$
Radical mastectomy (according to Madden)	8 (16%)	36 (63.2%)	
Subcutaneous mastectomy	15 (30%)	2 (3.5%)	
Total	50 (100%)	57 (100%)	

Note. p – level of statistical significance of differences between groups (according to Pearson's criterion χ^2).

It was found that in patients who underwent intraoperative ICG technology, the size of the primary tumor averaged 20.8 ± 1.3 mm (T2). In general, in the main group in 27 patients (54%) the size of the tumor ranged from 5 to 20 mm, in 23 (46%) - from 21 to 50 mm (in the control group – 54.4% and 45.6%, respectively) (Table 3). Patients with tumor growth in the skin or anterior thoracic

wall, as well as edematous infiltrative forms of the tumor were excluded from the study.

It is important to note that in patients who showed signs of metastatic lesions of regional lymph nodes at the preoperative stage and the presence of metastases confirmed by histological analysis were excluded from this study.

Table 3

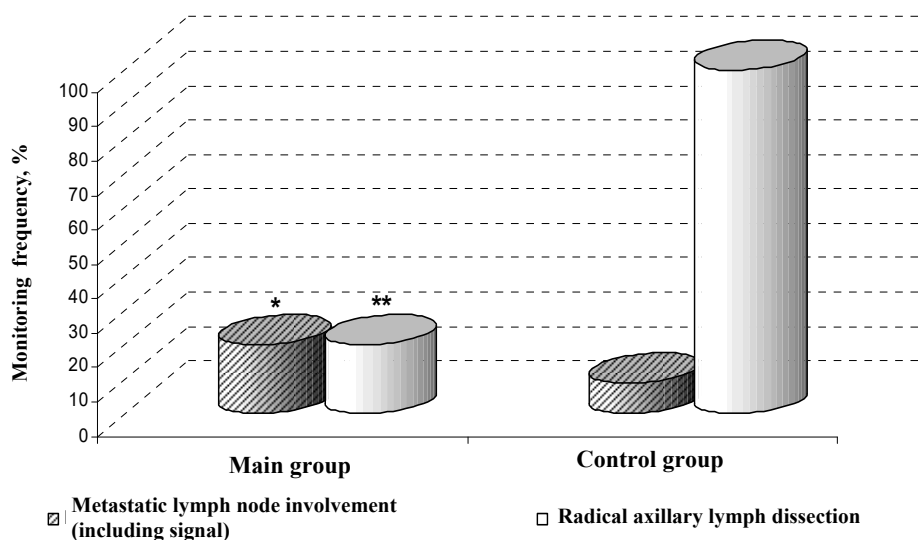
Distribution of patients by tumor location and size in the main and the control group

Parameters		Number of patients, n (%)		Statistical indicators
		main group	control group	
Side of lesion	Left (S)	24 (48%)	26 (45.6%)	$\chi^2=0.061$; $p>0.05$
	Rights (D)	26 (52%)	31 (54.4%)	
Tumor localization (quadrant)	Upper outer	22 (44%)	26 (45.6%)	$\chi^2=2.15$; $p>0.05$
	Lower outer	10 (20%)	8 (14.0%)	
	Upper inner	3 (6%)	4 (7.0%)	
	Lower inner	0	2 (3.6%)	
	Central	12 (24%)	11 (19.3%)	
	Multifocal	3 (6%)	6 (10.5%)	
Tumor size	T1 (less than 20 mm)	27 (54%)	23 (40.4%)	$\chi^2=1.99$; $p>0.05$
	T2 (20 - 50 mm)	23 (46%)	34 (59.6%)	
	Average, mm, M ± m	20.8±1.3	22.6±1.7	

Note. p – level of statistical significance of differences between groups (according to Pearson's criterion χ^2 and Student's t-test for unrelated samples).

Pathomorphological examination of the sentinel lymph node during its intraoperative imaging using ICG technology showed metastatic lesions in 10 out of 50 cases (20%) in the main group. In such

patients, complete regional lymph dissection (LD) must be performed simultaneously with breast surgery; in 80% of cases the patient's lymphatic collector was preserved (Fig.).



Note. * – $p<0.05$ (differences are statistically significant for control), ** – $p<0.001$ (differences are statistically significant for control).

Distribution of patients by metastatic lymph node involvement in the main and control group

According to the Unified Clinical Protocol of primary, secondary (Specialized), tertiary (highly specialized) medical care "Breast Cancer", in the control group, which consisted of 57 patients with early forms of breast cancer, along with radical surgery a complete volume of regional lymph dissection of I-III level was performed. According to the results of the pathomorphological study, metastases in the axillary lymph nodes were absent in 53 patients (93.0%), and metastatic lesions of regional lymph nodes were found in 4 patients (7.0%) of the control group. The absence of signs of metastatic lesions of regional lymph nodes in these patients at the stage of examination is probably due to the presence of micrometastases in the affected lymph nodes, single tumor cells and the small size of the lymph nodes.

The obtained results of the assessment of the volume of regional lymph dissection in the main group indicate its adequate nature to ensure the radicality of surgery. In our opinion, this is one of

the important conclusions of this work, because to assess the clinical significance of signal lymph node (SLN) as a marker of regional tumor spread, first it is necessary to make sure that existing surgical techniques provide radical removal of tumors.

CONCLUSIONS

1. Intraoperative use of ICG technology proved its effectiveness in removal of sentinel lymph node in surgical treatment of BC

2. Evaluation of clinical and pathomorphological importance of signaling lymph node as a marker of the regional spread of the tumor is necessary primarily for the confidence that the existing surgical technique provides a radical excretion of the tumor.

3. Analysis of the volume of regional lymphodissection indicates its adequate nature in providing radicality of surgical treatment of BC.

Conflict of interest. The authors declare no conflict of interest.

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