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Degree of Malignancy of the Tumor Process and Assessment of Therapeutic Pathomorphosis in Breast Cancer

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Summary: Pathomorphosis is one of the most important prognostic factors in breast cancer. The significance of determining the histological grade of malignancy (Grade, G) and the results of neoadjuvant treatment depending on pathomorphosis are considered. This allows for specifying the degree of tumor progression in each case, selecting appropriate treatment methods, and accurately assessing the prognosis.

Keywords: breast cancer, histological grade of malignancy (G-grading), neoadjuvant chemotherapy, therapeutic pathomorphosis.

Resume: Pathomorphosis is one of the key prognostic factors in breast cancer. This study examines the significance of determining the histological grade of malignancy (Grade, G) and the outcomes of neoadjuvant treatment depending on pathomorphosis. This approach enables a more precise assessment of tumor progression, facilitates the selection of appropriate treatment methods, and improves prognosis evaluation.

Introduction: Breast cancer (BC) remains one of the most pressing issues in oncology due to its high incidence, continuous growth, and increasing prevalence among younger populations. The development and implementation of new treatment methods—including various types of conservative therapy, surgical interventions, and combinations of surgery with adjuvant and neoadjuvant chemotherapy and radiotherapy—require a comprehensive evaluation of these approaches (Dumansky Yu.V. et al., 2004; Bondar G.V. et al., 2005). Research on the morphological and pathomorphological changes in BC is ongoing.

Tumor pathomorphosis assessment is actively utilized as it serves as a crucial indicator of treatment effectiveness (Akramov A.R. et al., 2014; Akramov A.R. et al., 2015; Akramov A.R., 2025). Complete morphological regression of the tumor following neoadjuvant drug therapy is a key prognostic factor for breast cancer patients. It has been reliably proven that achieving full pathomorphosis in both the tumor and lymph nodes significantly increases overall and relapse-free survival rates while reducing mortality risk. Compared to radiotherapy, preoperative polychemotherapy (PCT) results in a higher rate of complete morphological regression and better long-term treatment outcomes in breast cancer patients (Roshin E.M. et al., 2010; Picci P. et al., 1997).

Different neoadjuvant therapy regimens yield varying degrees of pathomorphosis, depending on the histological grade of tumor cells (G-grading), histological subtype, and stage of the tumor process (Lushnikov E.F. et al., 2021; Rubbia-Brandt L. et al., 2007). Achieving a complete clinical response in 30-60% of patients does not always correlate with full tumor pathomorphosis (Kraevsky N.A. et al., 1980; Semiglazov V.F., Semiglazov V.V., 2008; Mandard A.M. et al., 1994). Nevertheless, the analysis of pathomorphological changes, alongside overall survival assessment, remains a key criterion for evaluating therapy effectiveness (Yonemura Y. et al., 1996).

Up to 60% of primary breast cancer cases are diagnosed at a stage where surgical treatment is no longer an option. This group mainly consists of patients with locally advanced breast cancer, for whom

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preoperative polychemotherapy (neoadjuvant PCT) is particularly relevant (Bondar G.V. et al., 2005; Roshin E.M. et al., 2010).

Objective: To assess the histological grade of malignancy (G-grading) and therapeutic pathomorphosis in breast cancer when using polychemotherapy in a neoadjuvant setting.

Materials and Methods: The study is based on data from medical histories and outpatient records of 60 patients who received treatment at the Samarkand Regional Oncology Dispensary from 2015 to 2020. All patients underwent core needle biopsy of the tumor, morphological verification, and assessment of malignancy differentiation (G-grading). The patients were women aged 30 to 70 years, with an average age of 52 years.

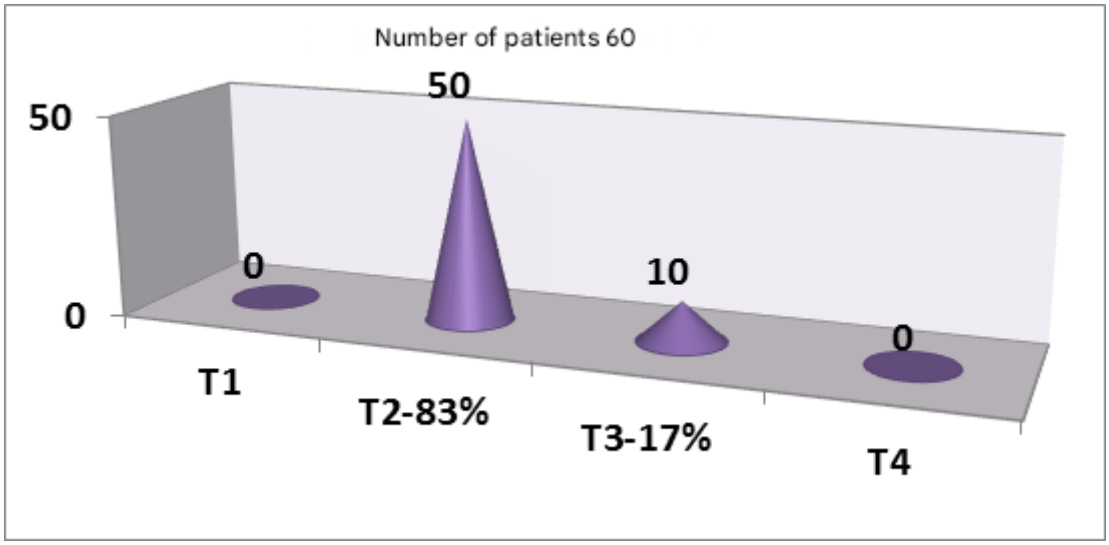
During the examination period, all patients underwent core needle biopsy of the breast tumor using a **BARD** device (manufactured in Mexico). The obtained material was morphologically analyzed to determine the histological grade of tumor malignancy (G-grading).

After staging and evaluation, all patients received neoadjuvant polychemotherapy (neo-PCT) consisting of four sequential courses according to the **CAF, FAC, and CAF+FAC** regimens. The chemotherapy dosage was calculated according to standard protocols, with intervals of **three weeks** between courses. In cases of side effects or complications, such as local or systemic toxicity, the drug dosage was reduced or temporarily suspended.

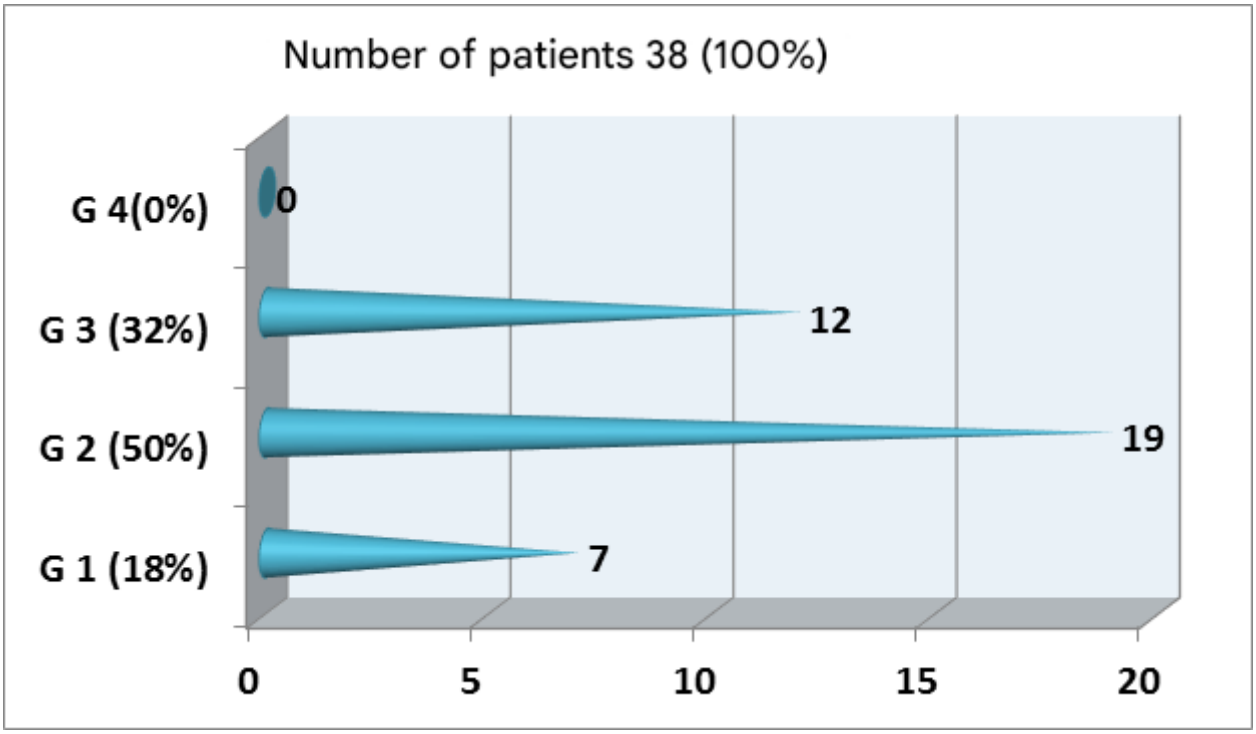
Treatment effectiveness was assessed after each neoadjuvant PCT course through **clinical examination, ultrasound (US), and mammography**. After achieving partial or complete tumor regression, all patients underwent **radical mastectomy using Madden's technique (RME)**. The degree of drug-induced pathomorphosis was determined by histopathological examination of the surgical specimen according to the classification proposed by **Lavnikova G.A. (1979)**.

Study Results: When classifying patients according to the **TNM criteria**, it was found that **83%** of cases were in **stage II (T2N0-1M0)**. In **10 cases (17%)**, stage **III** was recorded. See **Diagram No. 1** for details.

Distribution of patients according to the T criterion of the international classification TNM (2011) Diagram No. 1



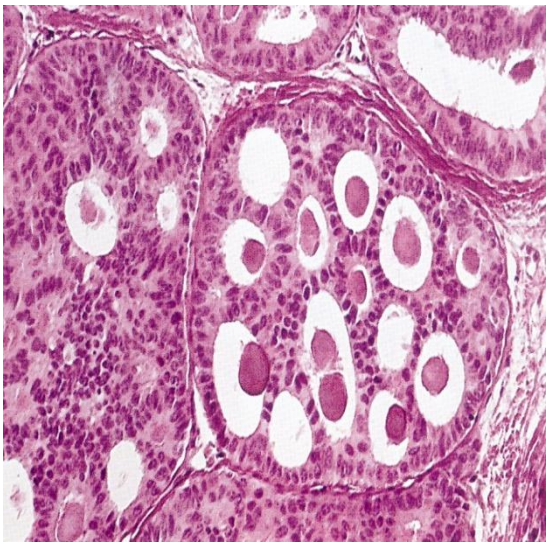
Histologically confirmed grade of tumor cell malignancy (G-gradation) before neoadjuvant chemotherapy. Diagram No. 2



As can be seen from diagram No. 2, before neoadjuvant polychemotherapy, the histologically confirmed degree of malignancy of tumor cells (G-gradation) was in the second and third degree in 31 patients out of 38 patients, which is 81.5%.

Below are the microscopic pictures of the degree of malignancy of tumor cells (G-gradation): G-1, G-2, G-3 of our patients photographed:

Fig. 1 Ductal cancer G-1



Full name Khalmurodova M. 1975

D-z: Cancer of the left mammary gland T2N0M0 Outpatient card No. 13737

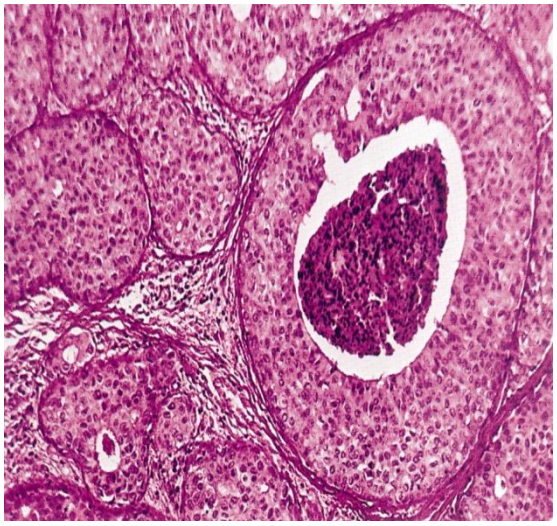


Fig. 2 Ductal cancer G-2

Full name: Ulugova S. 1966

Doctor of health: Cancer of the right mammary gland T2N0M0 Outpatient card No. 12711

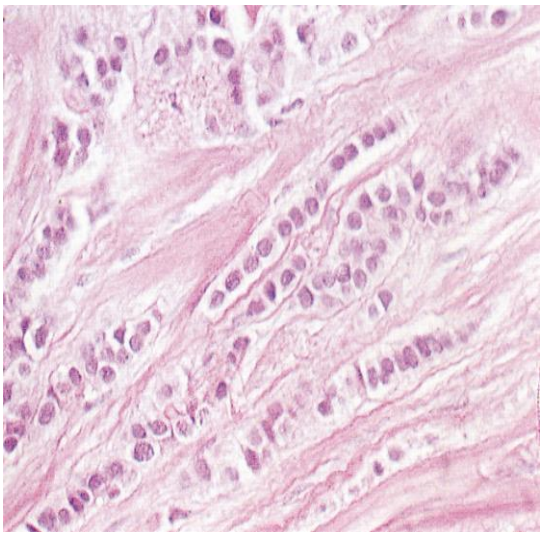


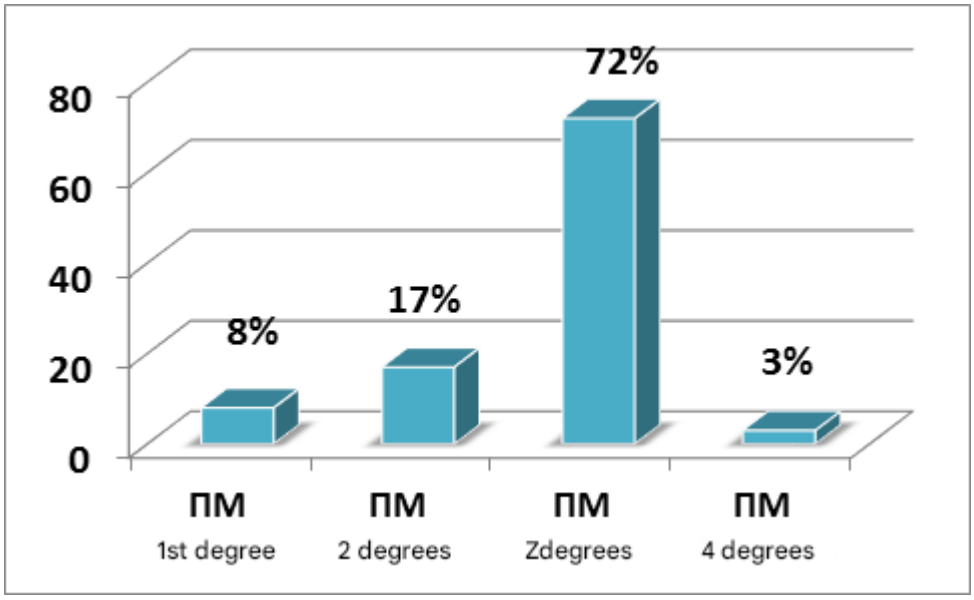
Fig. 3 Ductal cancer G-3

Full name: Uzakova G. 1958. D-z: Cancer of the left mammary gland T2N0M0 chart No. 2714

Characteristics of pathomorphological changes after neoadjuvant polychemotherapy.

Distribution of patients by the degree of pathomorphosis after neoadjuvant polychemotherapy for breast cancer (%) ratio.

Total number of patients – 60. Therapeutic pathomorphosis of stage III after neoadjuvant polychemotherapy was assessed in 43 (72%) patients with stage II (T2N0-1M0) and in 10 (17%) patients with stage III (T3N0-3M0) breast cancer. See diagram №3



Degrees of Pathomorphosis Diagrams No. 3

Below in the figures - examples are shown and given characteristics of the degrees of therapeutic pathomorphosis after neoadjuvant polychemotherapy of patients with breast cancer, who were and received treatment in the Samarkand Regional Oncology Dispensary. See Fig. 4,5,6,7.

Ductal cancer. Pathomorphosis of the 1st degree

Full name Dolieva Gulnoza 1975

Doctor of health: Cancer of the right mammary gland T2N0M0 card No. 7625

Pathomorphosis of the 1st degree in 5 (8%) patients, more than 50% of the tumor parenchyma is preserved, the structure of the tumor did not change, polymorphism and dystrophy of individual cells appeared in the cells, mitotic activity decreased.

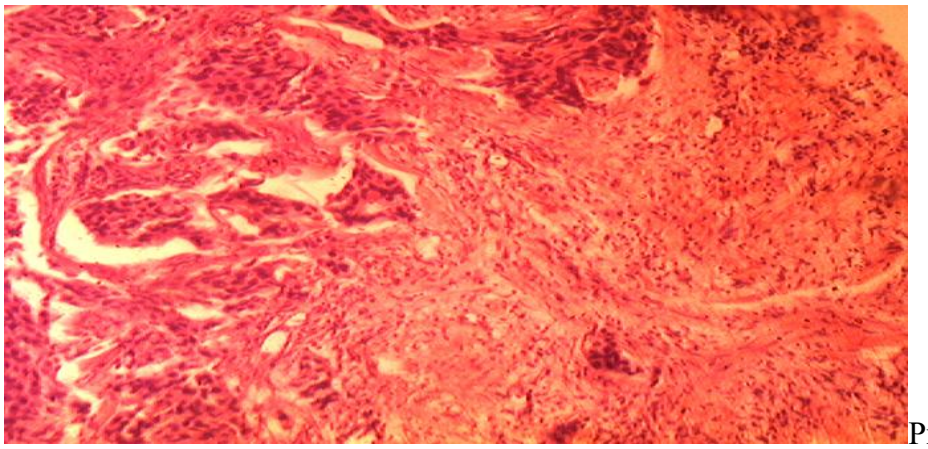


Рис.4

Ductal cancer. Pathomorphism of the II degree.

Full name: Boymurodova D. Born in 1979

D-z: Cancer of the right mammary gland T2N1M0 card No. 9192

Pathomorphism of the II degree in 10 patients (17%) - 20-50% of the tumor parenchyma is preserved. The main mass of the tumor was preserved. Foci of regression in the form of dystrophic changes in cells, areas of necrosis and the presence of pyknotic nuclei were observed. Ugly giant therapeutic cells appeared.

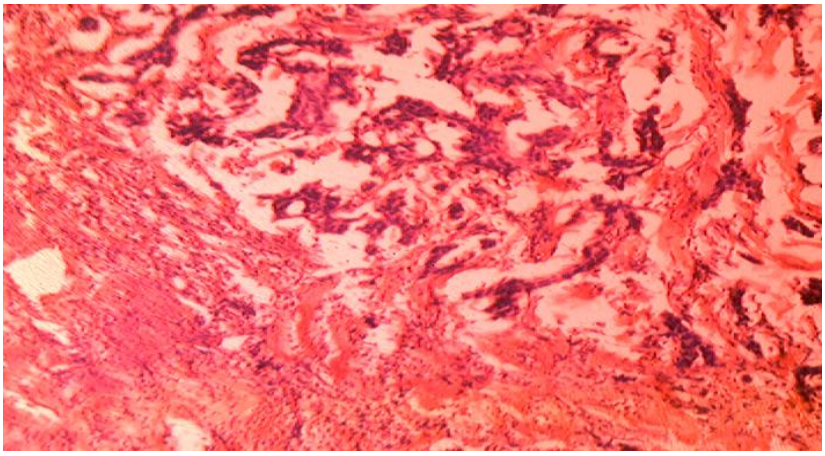


Fig.5 Ductal carcinoma. Pathomorphism of grade III.

Full name Eshonkulova Sh. Born in 1976

D-z: Cancer of the left mammary gland T2N1M0 card No. 8786

Pathomorphism of grade III was detected in 43 (72.0%) - up to 20% of the tumor parenchyma remained in the form of separate foci. The structure of the tumor is disrupted due to fibrous replacement or necrosis. The remains of the tumor remained in the form of scattered groups of cells with pronounced dystrophic changes.

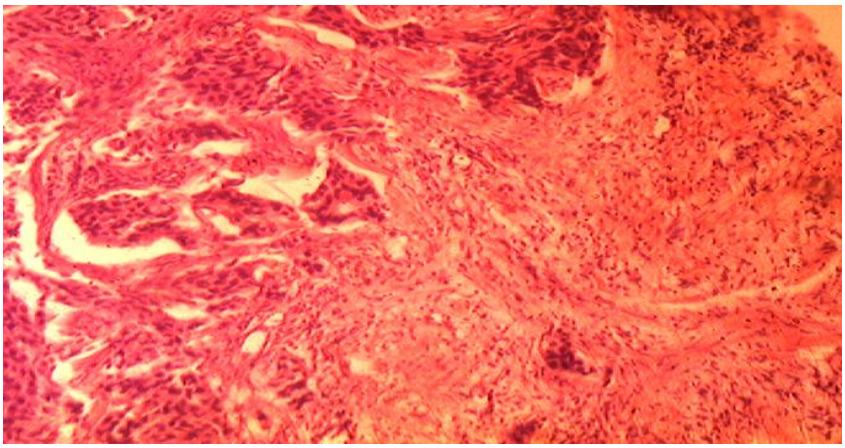


Fig.6. Ductal cancer. Pathomorphosis of the IV degree.

Full name: Murodova H. Born in 1963. D-z: Cancer of the left mammary gland T2N1M0 card No. 5789

Therapeutic pathomorphosis of the IV degree was detected in 2 (3.0%) women - complete disappearance of tumor cells, extensive fields of fibrosis with single giant multinuclear ugly cells are observed. A trace of the former tumor was determined in the form of granulomas around horny masses and foci of necrosis, devoid of cellular elements.

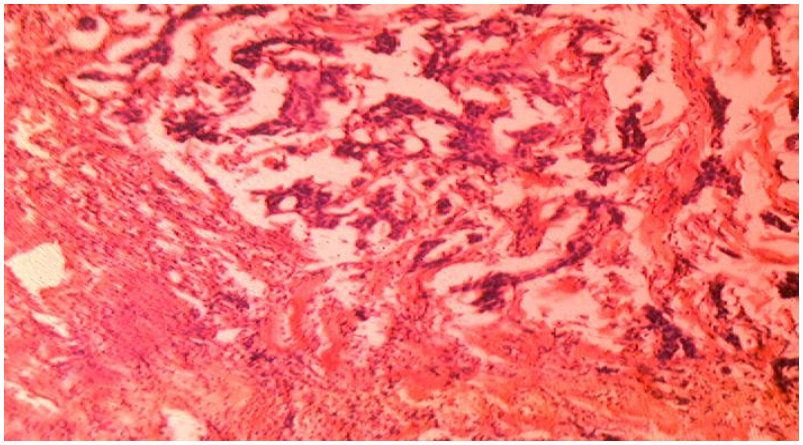


Fig. 7.

The obtained quantitative and qualitative morphological characteristics of infiltrating breast carcinomas, under conditions of therapeutic impact on them, show characteristic changes in certain tumor structures, inherent in a certain type of preoperative treatment. Neoadjuvant polychemotherapy has a systemic effect on the entire tumor clone, which, in turn, reduces the risk of developing distant metastases.

When studying the therapeutic pathomorphosis in patients with breast cancer at stage T2N0-1M0. See diagram No. 4, which indicates the (%) ratio and the total number of patients - 50.

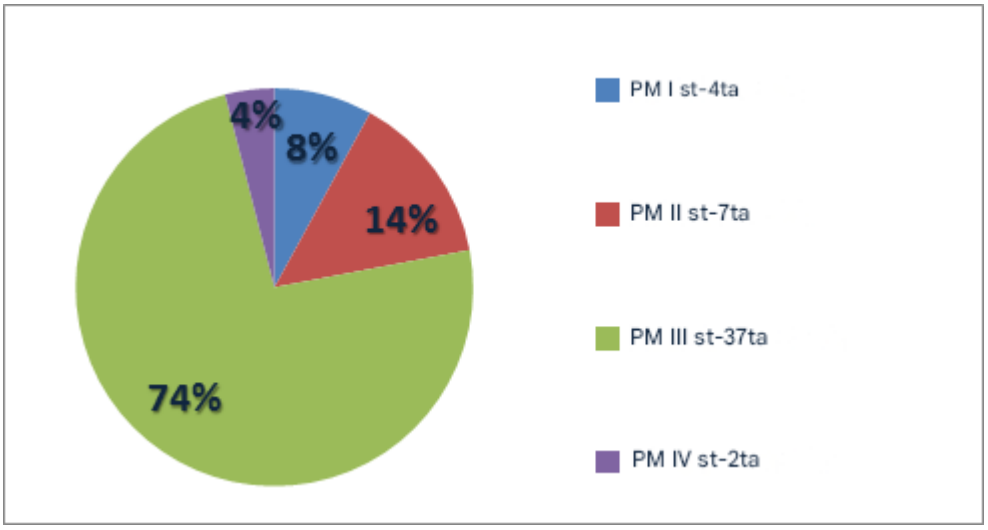


Diagram №4

Assessment of the therapeutic pathomorphosis of patients with breast cancer stage II T2N0-1M0 in 37 (74%) was found pathomorphosis of the III degree, which is shown in diagram №4.

Study of the therapeutic pathomorphosis in patients with breast cancer at stage T3N0-3M0. Assessment of the therapeutic pathomorphosis in patients with breast cancer at stage T3N0-3M0 III pathomorphosis of the III degree was found in 6 (60%) patients. See diagram №5.

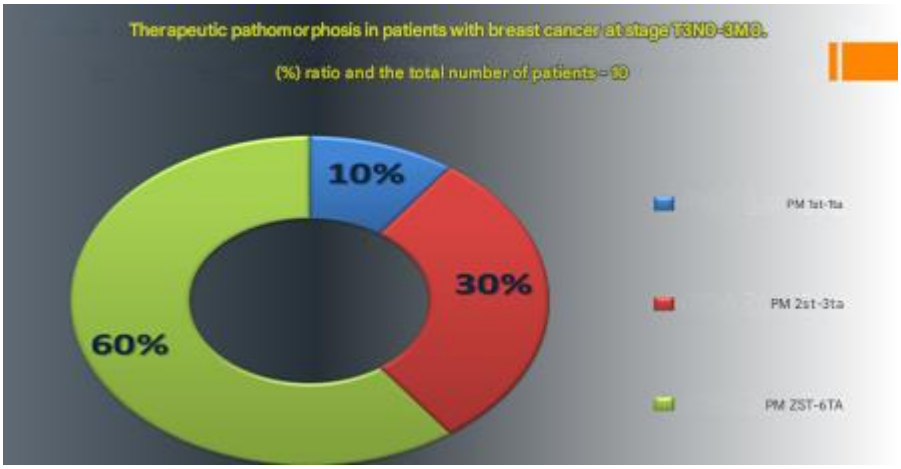


Diagram №5

When studying the distribution of patients T2N0-1M0 in the second stage who received neoadjuvant chemotherapy according to the schemes, it was shown that the distribution of patients according to the CAF, FAC, CAF+FAC schemes was almost the same. See diagram №6

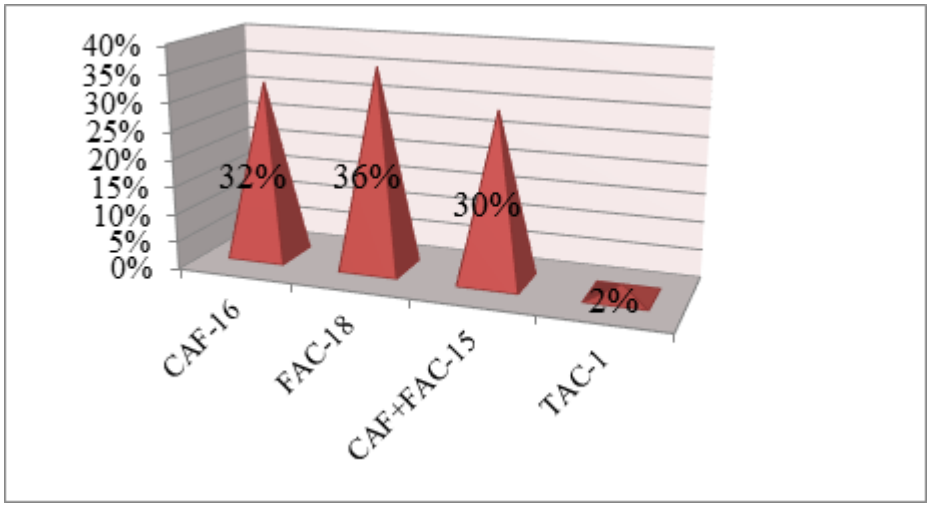


Diagram №6

Evaluation of neoadjuvant polychemotherapy used according to standard schemes CAF, FAC, CAF+FAC showed that the FAC scheme exhibits the best efficiency. At the same time, NeoPCT using the CAF scheme out of 16 patients in 11 (69%) had pathomorphosis of grade III, see diagram №7

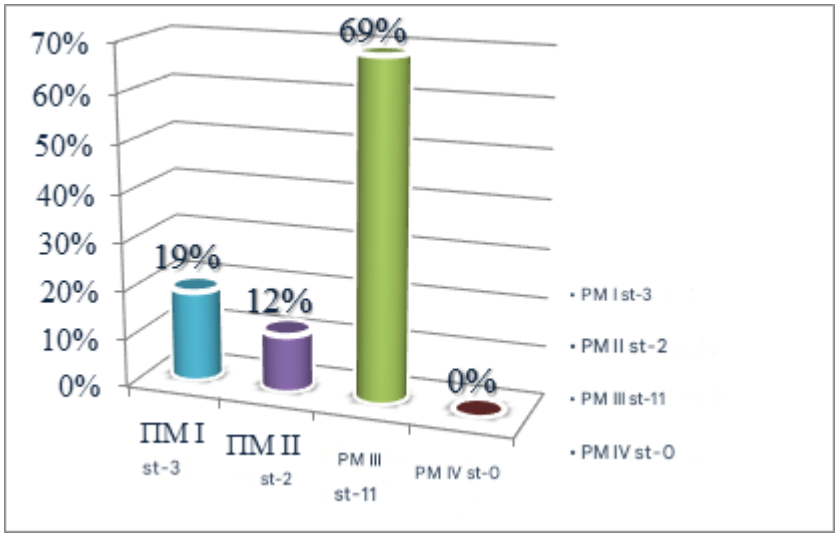


Diagram № 7

Indicators of therapeutic pathomorphosis in patients

T2N0-1M0 in the second stage receiving NeoPCT according to the scheme

FAC corresponded to 88% (16) of patients. See diagram № 8

Indicators of therapeutic pathomorphosis in patients of stage T2N0-1M0 receiving NeoPCT according to the scheme FAC
Number of patients - 18

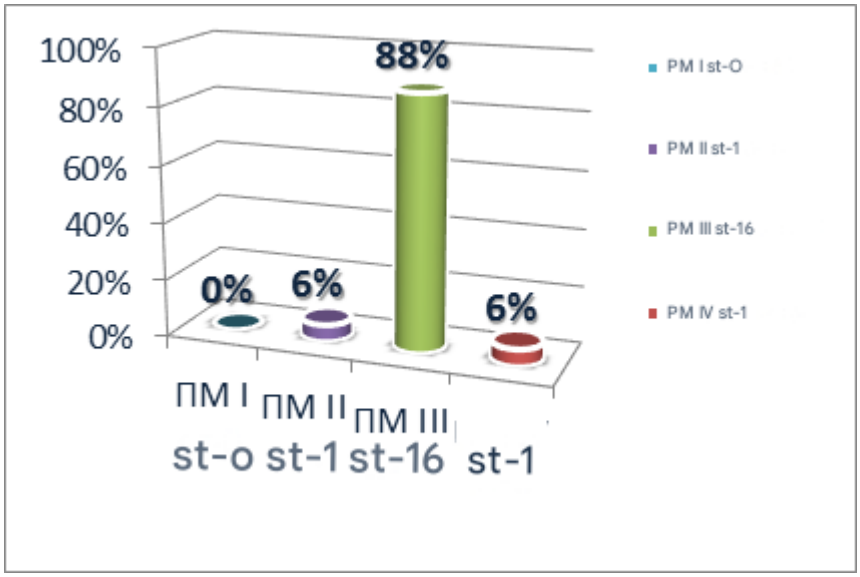


Diagram №8

Indicators of therapeutic pathomorphosis in patients

stage T2N0-1M0 receiving NeoPCT according to the scheme

CAF+FAC. Number of patients - 15. Corresponded - 67% (10) of patients. See diagram №9

Indicators of therapeutic pathomorphosis in patients

stage T2N0-1M0 receiving NeoPCT according to the scheme CAF+FAC

Number of patients - 15

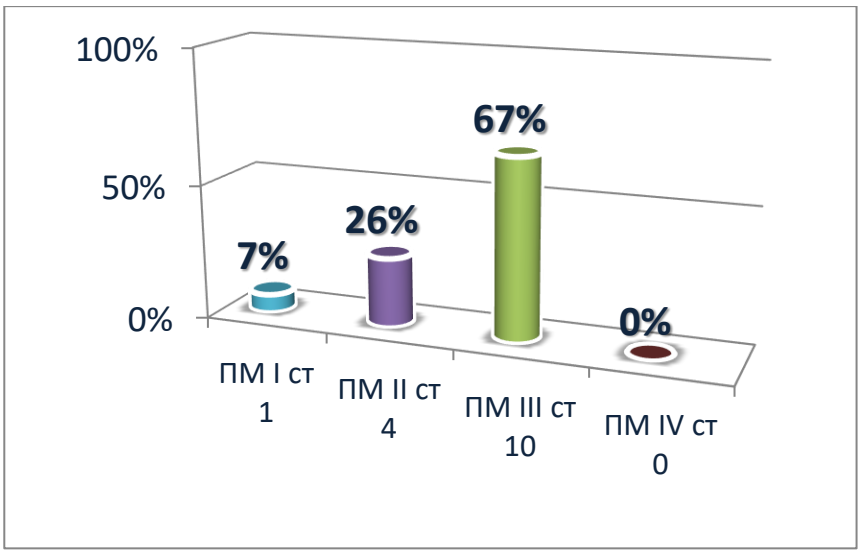


Diagram №9

When studying the dependence of therapeutic pathomorphosis on the degree of malignancy of tumor cells (G-gradation), in breast cancer stage II, it was shown that G2, G3 are more prone to therapeutic pathomorphosis of stage III, and in breast cancer stage III, due to an insufficient number of patients, the data were unreliable. See diagram №10.

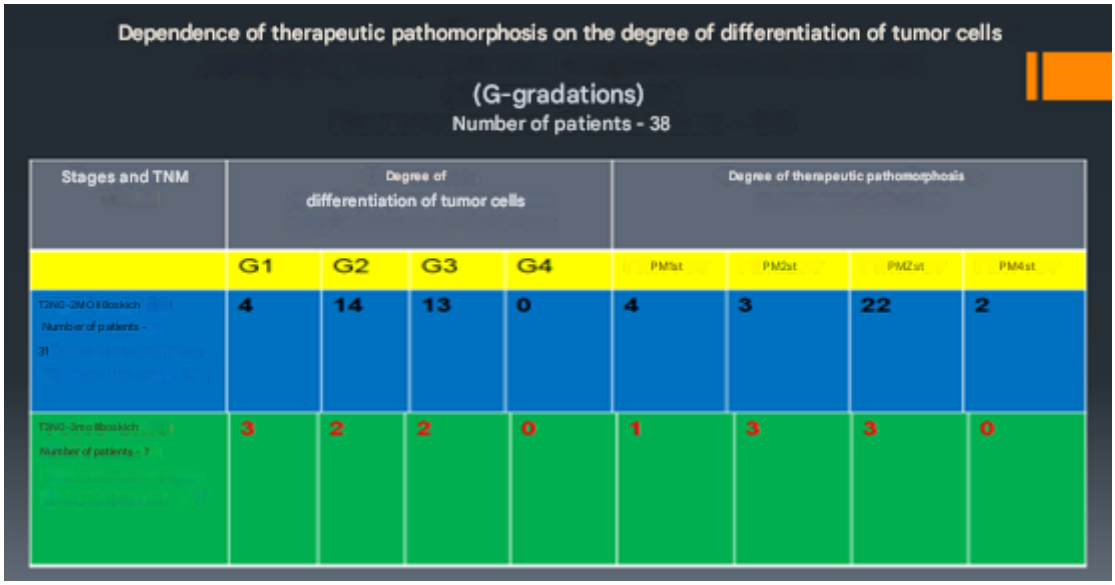


Diagram #10

Discussion of the obtained data

Currently, neoadjuvant polychemotherapy is one of the most important components of complex treatment of breast cancer, the main tasks are to reduce the volume of the primary lesion in order to improve the conditions for performing organ-preserving surgical interventions, to determine the sensitivity of the tumor in vivo and to plan adjuvant therapy based on the severity of therapeutic pathomorphosis.

The study of morphological and pathomorphological changes in breast cancer has been going on for over 50 years. Evaluation of drug-induced tumor pathomorphosis is still actively used today as it is an important indicator of therapy effectiveness. When using various neoadjuvant polychemotherapy regimens, a different effect on pathomorphosis is achieved, which depends on the degree of tumor malignancy and its histological variant (Lushnikov E.F. 2021; Moisenko V.M. 2002).

In this work, we analyzed biopsy and surgical material from 60 patients with breast cancer who received preoperative neoadjuvant chemotherapy. Before the start of treatment, a tumor biopsy was performed using the "BARD" device. The biopsy determined: the histological structure of the tumor, the degree of its malignancy. The therapeutic pathomorphosis was studied in the surgical material.

The degree of tumor malignancy (G-gradation) is not only an important prognostic factor in relation to the course of the disease, but also a factor predicting the probability of obtaining a complete morphological response in the tumor. The frequency of morphological effects is directly proportional to the degree of G-gradation: at the 1st and 2nd degree of tumor malignancy, the frequency of therapeutic pathomorphosis is only 10%, and at the 3rd, 4th degree of malignancy it is up to 90%. (Archer C.D. et all. 2003; Janjan N.A. et all.1999). It is known that the proliferating pool of cells is most sensitive to the effects of cytostatics, as well as in the S-phase. When studying the G-gradation of tumor cells, we determined the G3 degree of malignancy in 19 (50%) patients with G2 and in 12 (31.6%) patients.

In the work (Janjan N.A. et al.1999) it was shown that the maximum life expectancy is observed with complete pathomorphosis, the minimum - with weak or absent pathomorphosis. Complete tumor regression (IV degree according to Lavnikova) is accompanied by the highest overall survival rates: 3-, 5-, 10-year survival rates in patients of this group are 100%, 92.3%, 83.1%, respectively. On the contrary, with weak pathomorphism, the overall survival rates at similar periods were 57.8%, 42.3%,

28.7%, respectively. When we assessed the pathomorphism after neoadjuvant polychemotherapy for breast cancer, 43 patients, which is 72%, had grade III therapeutic pathomorphism. In stage II breast cancer (T2N0-1Mo), these rates were 74% (37) of patients. In stage III cancer T3N0-3M0, 60% (6) of patients.

Thus, the degree of morphological regression is the most important factor of a favorable prognosis, allowing to improve the remote results of treatment in patients with breast cancer. Pathomorphosis is affected by the use of various schemes of neoadjuvant polychemotherapy. We studied the effectiveness of standard schemes of CAF, FAC, CAF + FAC neoadjuvant polychemotherapy, while the distribution of patients was almost the same. In breast cancer stage II T2N0-1M0, the therapeutic pathomorphosis of grade III was assessed in 69% of patients with the CAF scheme, in 88% with the FAC scheme and in 67% with the CAF + FAC scheme. In breast cancer stage III T3N0-3M0, pathomorphosis of grade III was assessed in all schemes, but due to an insufficient number of patients, the data were unreliable.

When assessing the therapeutic pathomorphosis depending on the degree of malignancy of tumor cells (G-gradation), it was shown that breast cancer stage II, G2, G3 are more prone to therapeutic pathomorphosis of stage III. This can be explained by the cellular polymorphism of tumor tissue, since in tumor tissue the cells are at different phases of cell division and differentiation.

Thus, the assessment of the degree of malignancy of tumor cells (G-gradation) and tumor pathomorphism in breast cancer is the most important criterion for the direct assessment of the effectiveness of preoperative polychemotherapy, which allows increasing the radicality.

Conclusions

1. Evaluation of the effectiveness of neoadjuvant chemotherapy depends on the degree of cancer malignancy - gradation G, as well as on the degree of therapeutic pathomorphosis in patients with breast cancer.
2. Evaluation of the effectiveness of neoadjuvant polychemotherapy in breast cancer showed that the standard CAF, FAC and CAF + FAC schemes are almost equally effective, but the FAC scheme showed the best results.
3. These indicators allow us to determine the radicality of treatment, is important for planning postoperative adjuvant therapy based on the severity of therapeutic pathomorphosis in breast cancer.
4. Also important for prognosis and drawing up an individual treatment program after surgery.

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