



## Recurrence of Breast Cancer in the Locoregional Area Following Mastectomy: Analysis of Diagnostic and Treatment Process

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### ABSTRACT

. Locoregional recurrence of breast cancer (LRB) is the reappearance of a tumor in the same or opposite breast or in regional lymph nodes after mastectomy. LRB can occur within several years after the primary operation, but it is most commonly observed within the first 5 years. Examining the incidence rate, clinicomorphological manifestations, accessible treatment options, and prognostic variables associated with local recurrences in initially treatable breast cancer is the aim of this study. In order to accomplish the stated research goals, a retrospective examination of the disease development was carried out on 149 patients with breast cancer that was initially treatable and who received radical treatment at the Republican Scientific and Practical Center of Oncology and Radiology's Samarkand branch between 2021 and 2023. After conducting a univariate analysis, we were able to identify several factors that were statistically significant in relation to an early onset of LR. The occurrence rate of isolated local recurrences in primary operable breast cancer following radical treatment is as follows: 3.5%, with 3.3% after radical mastectomies (with or without radiation therapy), 7.4% after organ-preserving surgeries without radiation therapy, and 3.3% with adjuvant radiation therapy. The peak risk of local recurrence is observed in the second year post-surgery, affecting 29.3% of patients.

Keywords: *radical mastectomy, LRB, adjuvant radiation therapy, TNM classification, clinimorphological manifestations.*

### Introduction

Currently, in the world, approximately 70,000 new cases of breast cancer are registered annually, with around 30,000 women undergoing mastectomy. Locoregional recurrence of breast cancer (LRB) is the reappearance of a tumor in the same or opposite breast or in regional lymph nodes after mastectomy. LRB can occur within several years after the primary operation, but it is most commonly observed within the first 5 years. In contemporary literature, the terms "local" and "locoregional" recurrence differ. Local recurrence, as defined by Torsten U. (1993) and Cowen D. (1998), is a tumor that arises after radical surgery within the area bounded by the lower margin of the clavicle, rib arc, midclavicular, and posterior axillary lines. In this anatomical area, local, regional, and locoregional recurrences can occur. Local recurrence is a tumor similar in morphological structure to the primary one, arising in the remaining part of the breast (after organ-preserving treatment), in the area of the postoperative scar, or in soft tissues beyond the scar on the corresponding surface of the chest. Locoregional recurrences refer to local recurrences associated with regional lymph node involvement.

According to the 6th international edition of the TNM classification of malignant tumors, the following types of locoregional recurrences are distinguished in scientific literature: axillary, infraclavicular lymph nodes, supraclavicular fossa lymph nodes, and internal mammary lymph nodes recurrences. However, most domestic and foreign authors imply that "local recurrence" includes all recurrences occurring in the operative zone. This creates difficulties not only in determining the frequency and clinicomorphological characteristics of recurrences but also in assessing treatment possibilities and prognosis. According to global statistics, the frequency of local recurrences of breast cancer ranges from 10 to 30%, and not all authors note that local recurrences constitute no more than one-third of these cases, with two-thirds of patients having locoregional recurrences.

Various treatment modalities for local recurrences have been studied, including surgical, pharmacological, and radiation methods, as well as their combinations. However, data on the significance of individual treatment modalities are quite contradictory: some authors consider a local approach to the treatment of local recurrences (surgical tactics, radiation therapy) sufficient, while others emphasize the necessity of applying comprehensive treatment for local recurrences. The choice of the extent of repeat surgical intervention in patients with local recurrences after organ-preserving treatment is an important issue for both the patient and the clinician. Despite this, the possibility of performing repeat organ-preserving treatment and the impact of the extent of the repeat operation on the course of the disease are not well studied.

The role of local recurrence in the prognosis of breast cancer is debatable. According to Fisher, local recurrences occur in no more than 20% of patients who have undergone radical surgery and do not affect the further fate of the patients. In contrast, data from the Gustave Roussy Institute suggest that the survival of patients with isolated local recurrences is 80% lower than that of patients without recurrences.

Thus, local recurrence (LR) not only affects the quality of life of patients but also serves as the first sign of disease progression. Studying the frequency and timing of isolated local recurrences, clinicomorphological characteristics, modern treatment options, and disease prognosis is a relevant task in contemporary oncology.

### **Research Objective:**

Examining the incidence rate, clinicomorphological manifestations, accessible treatment options, and prognostic variables associated with local recurrences in initially treatable breast cancer is the aim of this study.

### **Materials and Methods:**

In order to accomplish the stated research goals, a retrospective examination of the disease development was carried out on 149 patients with breast cancer that was initially treatable and who received radical treatment at the Republican Scientific and Practical Center of Oncology and Radiology's Samarkand branch between 2021 and 2023. All patients received radical operations during the first phase of treatment; 40.9% chose organ-preserving surgeries, while 59.1% had mastectomies (using the Holsted, Peit, or Madden techniques). T1N0M0 (30.6%), T1N1M0 (12.7%), T2N0M0 (28.9%), T2N1M0 (23.3%), and T3N0-N1M0 (4.5%) were the patient distribution across phases. Of the patients, 27.6% received adjuvant radiotherapy; these patients primarily received it following organ-preserving procedures (67.3%) and mastectomy (32.7%). In addition, adjuvant medication therapy (hormone therapy, chemotherapy) was administered to 42.6% of patients; this occurred 28.9% after radical breast resection and 71.1% after mastectomy. In 12.1% of cases, a comprehensive treatment strategy (including radiation therapy and adjuvant medication) was used.

34 patients had isolated LR recurrences, which are the only sign of disease progression, across a span of 4 months to 10 years. LR was identified by clinical and radiological exams as a tumor node on the surface of the chest, either in the soft tissues of the chest wall, the surgical scar area, or the remaining portion of the breast. Morphological verification using histology or cytology techniques verified LR in every patient. 3.5% of initially operable breast cancer cases had LR, and rates rose to 3.31% following mastectomy without radiation. Between LR occurrence and disease stage, a significant correlation was found, with LR occurrence ranging from 3.04-3.9% in T1-2M0-1 stages to 8.3% in T3N0-1 stages.

The average age of the patient at the time of primary tumor treatment was 50.3 years; the patient population was divided into three age groups: 8.6% under 35, 43.1% between 36 and 50, and 48.3% over 51. 52.6% of patients were postmenopausal, and 47.4% still had menstrual function. The majority of tumors had external localization (57.7%), internal localization (20.7%), and central localization (21.6%). Tumor localization on the left and right sides happened equally frequently at 50%. The morphological characteristics of primary tumors included an average size of 2.8 cm; 44.8% of patients had tumors less than 2 cm, 53.4% had tumors between 2 and 5 cm, and 1.8% had tumors larger than 5 cm. Of those with tumors, 81% had a non-proliferative background, 14.7% had fibrocystic disease, and 4.3% had proliferation of mammary gland epithelial cells.

The distribution of disease stages was as follows: 1.8% was at stage III (T3N0-1), 32.8% was at stage I (T1N0), and 65.4% was at stage II (T1N1, T2N0-N1).

As part of the main tumor treatment plan, all patients underwent radical surgery in the first stage; 42.2% had mastectomy (Madden modification) and 57.8% had organ-preserving surgery (radical resections).

### **Research results.**

After conducting a univariate analysis, we were able to identify several factors that were statistically significant in relation to an early onset of LR. These factors included age under 35 and over 51 years old ( $p < 0.05$ ), menopause ( $p < 0.05$ ), tumor size larger than 2 cm ( $p < 0.02$ ), stage IIA of the disease ( $p < 0.05$ ), the primary tumor's ER (-) PR (-) status ( $p = 0.01$ ), and the treatment of the primary tumor solely through surgery, regardless of its volume ( $p = 0.03$ ). Patients with early recurrences had higher rates of rare histological forms of breast cancer (medullary, mucinous, and tubular; 6 out of 8 patients), however the statistical significance of this feature cannot be determined due to the small number of observations. These factors occur independently of each other. In a multifactorial analysis (using the Bayesian method with the analysis of 60 features), risk factors for the early onset of LR were identified: ER (-) PR (-) status of the primary tumor ( $p = 0.006$ ); performing only surgical treatment of the primary tumor, regardless of its volume ( $p = 0.002$ ). Based on the multifactorial analysis, we created a mathematical table for calculating the risk prognosis of early LR. The table presents factors with plus and minus signs in points, depending on their statistical significance. To determine the risk of early LR, it is sufficient to calculate the sum of factors in points: if the sum is positive, the patient belongs to the risk group for early LR, if the sum is negative, the risk of early LR recurrence is minimal. The statistical accuracy of the method is 77.3%, which allows recommending the method for practical use.

**Clinical Example I:** Patient M, 30, underwent a radical mastectomy without further treatment for breast cancer. Her medical history included menstrual cycles and 11360/29001. The tumor had ER(-) PR(-) status and showed signs of mucinous carcinoma. Beyond the tumor, the breast background was non-proliferative. Finding the cumulative points for the following factors: Age thirty years plus or minus thirty-one; menstruation preserved twenty-one; primary tumor size up to twenty-one centimeters twenty-one; disease stage IA one; non-proliferative background of the breast outside the tumor twelve; mucinous carcinoma plus or minus eighteen; radical mastectomy plus or minus forty-six; exclusive surgical treatment of the tumor plus or minus eighteen; irreversible radiation therapy plus or minus fifty; no adjuvant hormone therapy plus or minus (5); tumor receptor status ER(-)PR(-) +56. The total sum is +345, with a statistical likelihood of 77.3%, indicating the patient is anticipated to experience early LR (LR manifested 22 months post-surgery).

**Clinical Example II:** Patient A, a 47-year-old with a medical history of 96/7681, continued to have menstruation. underwent radical excision of the breast due to T1M0 breast cancer. The tumor showed an ER (+) PR(+) infiltrating ductal carcinoma structure, and the surrounding breast tissue was non-proliferative. The patient underwent extensive tumor treatment, which included radiation castration, adjuvant radiation therapy (50 Gy), chemotherapy with the CMF regimen for six courses, and tamoxifen hormone therapy for two years. Finding the cumulative points Menstruation preserved -21, age 47 years -21, tumor size T1 -21, Stage IIA -6, non-proliferative breast background outside the tumor -12, infiltrating ductal carcinoma -12, surgery volume: breast resection -33, primary tumor treatment scheme: surgery + adjuvant treatment -31, adjuvant radiation therapy applied -61; Adjuvant hormone therapy applied -70; Adjuvant chemotherapy applied -8; Receptor status of the tumor ER (+) PR (+) -33. The total sum is -329. The patient is not classified in the high-risk group for early LR (LR occurred 7 years post-surgery).

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## Conclusions:

The occurrence rate of isolated local recurrences in primary operable breast cancer following radical treatment is as follows: 3.5%, with 3.3% after radical mastectomies (with or without radiation therapy), 7.4% after organ-preserving surgeries without radiation therapy, and 3.3% with adjuvant radiation therapy. There is a distinct correlation between the recurrence frequency and the disease stage, ranging from 3.04% to 3.9% for stages T1-2M0-1 and reaching 8.3% for stages T2N0-1. Local recurrences manifested at varying intervals after surgery, with the majority occurring within the initial 5 years (79.4%). The peak risk of local recurrence is observed in the second year post-surgery, affecting 29.3% of patients.

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