Medical science of Uzbekistan
published: 28 June 2025
Received: 11 April 2025
Accepted: 23 May 2025
Published: 28 June 2025
doi.org/10.56121/2181-3612-2025-3-09-13

Article/Original paper

LOCOREGIONAL RECURRENCE OF BREAST CANCER AFTER RADICAL MASTECTOMY: RISK FACTORS, DIAGNOSIS, AND REGIONAL MANAGEMENT STRATEGIES

M.D.Djurayev[1] **P.I.Zaripova**[2]

1. Republican scientific-practical medical center of oncology and radiology, Tashkent, Uzbekistan.
2. Samarkand State Medical University, Samarkand, Uzbekistan.

Abstract.

Relevance. Locoregional recurrence (LRR) of breast cancer (BC) following radical mastectomy presents a significant clinical challenge and is associated with reduced survival. **Objective.** To assess the risk factors for LRR and develop regional recommendations for effective surveillance and treatment strategies. **Materials and methods of the study.** A retrospective-prospective analysis of 206 breast cancer patients treated between 2017 and 2024 in the Samarkand region was conducted. The study focused on tumor characteristics, molecular profiles, treatment modalities, recurrence localization, and survival outcomes. **Research results.** The LRR rate was 5.4%. Most recurrences occurred in women aged 31–50 and in patients with stage IIB–IIIA tumors. Hormone receptor status, HER2 expression, Ki-67 index, and completeness of adjuvant therapy were significant predictors of recurrence. The proposed management algorithm, based on molecular stratification and regional resources, demonstrated potential for improving long-term outcomes. **Conclusion.** Personalized follow-up and therapy plans based on tumor biology and regional guidelines are essential for reducing recurrence and improving survival in postmastectomy breast cancer patients.

Key words: Breast cancer, locoregional recurrence, mastectomy, risk factors, immunohistochemistry, personalized medicine.

Introduction

Breast cancer remains the leading oncologic pathology among women worldwide. According to the World Health Organization, over 2.3 million new cases of breast cancer were diagnosed globally in 2020, making it the most common cancer worldwide, accounting for approximately 11.7% of all cancer diagnoses [1]. It is also the leading cause of cancer-related mortality in women, with more than 685,000 deaths reported annually. In Uzbekistan and Central Asia, the incidence of breast cancer has been steadily rising, attributed to both improved diagnostics and changes in reproductive and lifestyle factors [2].

Despite the widespread adoption of radical mastectomy as a standard of care, a significant number of patients experience locoregional recurrence (LRR). These recurrences are associated with higher risks of distant metastases and reduced survival. In developing regions such as Uzbekistan, delayed diagnosis and uneven application of modern treatment protocols contribute to the burden of LRR [3,4].

The clinical manifestations of LRR include nodules in the chest wall, scar area, axillary and supraclavicular lymph nodes, often diagnosed late. Risk factors for recurrence include young age, advanced tumor stage, triple-negative or HER2-positive subtypes, and suboptimal adjuvant therapy. Thus, defining a regional algorithm based on local patient profiles and resources becomes essential [5].

Materials and Methods

This study was conducted at the Samarkand Branch of the Republican Scientific-Practical Center for Oncology and Radiology. A total of 206 female patients treated between January 2017 and July 2024 were included. The study design was retrospective-prospective.

Cohort A (n=120): Women with newly diagnosed stage I–IIIA BC who received standard multimodal treatment including radical mastectomy (Madden technique), chemotherapy, radiotherapy, and hormone therapy where indicated.

Cohort B (n=86): Patients who developed clinically confirmed LRR during follow-up.

Inclusion criteria: Female patients aged 18–75 years, stage I–IIIA, treated per national guidelines, with at least 6 months of follow-up.

Collected data:

- Age
- Tumor stage and histologic type
- IHC profile (ER, PR, HER2, Ki-67)
- Recurrence location
- Type and completeness of therapy
- 7-year overall survival

Statistical analysis:

- Kaplan-Meier survival estimates
- Chi-square and t-tests for group comparisons
- Relative risk (RR) and 95% confidence intervals
- $p < 0.05$ considered significant

Table-1. Baseline Characteristics of Study Cohorts

Parameter	Cohort A (n=120)	Cohort B (n=86)
Mean Age (years)	51.6 ± 8.1	44.3 ± 6.8
Stage I	18 (15%)	0 (0%)
Stage IIA	32 (26.7%)	4 (4.6%)
Stage IIB	46 (38.3%)	38 (44.2%)
Stage IIIA	24 (20%)	44 (51.2%)

Table-2. IHC Profiles of Recurrent vs. Non-Recurrent Tumors

Marker	Cohort A (n=120)	Cohort B (n=86)
ER+/PR+	58 (48.3%)	22 (25.6%)
HER2+	34 (28.3%)	42 (48.8%)
Triple Negative	14 (11.7%)	18 (20.9%)
Ki-67 > 20%	36 (30%)	62 (71.6%)

Figure-1. Age Distribution of LRR Cases [Insert bar graph: X-axis = Age Groups (≤30, 31–40, 41–50, 51–60, >60); Y-axis = % of patients in Cohort B]

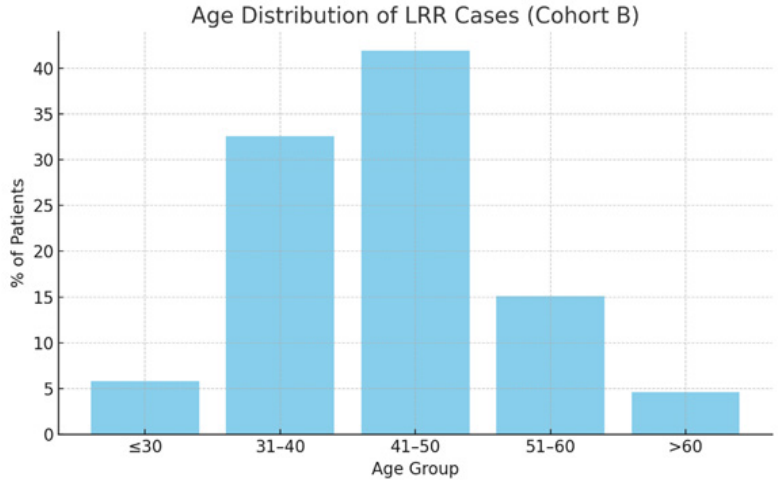
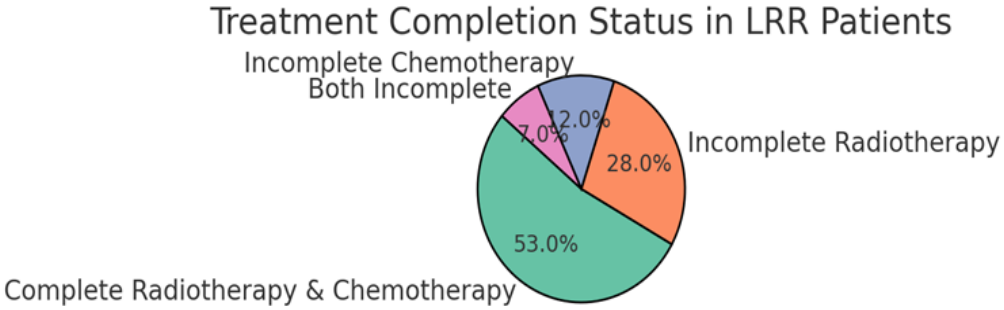


Figure-2. Treatment Completion Status in LRR Patients [Insert pie chart: % patients receiving complete vs. incomplete radiotherapy and chemotherapy]



Results

Recurrence Rate and Demographics Out of a total of 206 patients who underwent radical mastectomy during the studied period, 86 individuals developed locoregional recurrence (LRR), yielding a cumulative recurrence rate of 5.4%. Stratification of the LRR cohort revealed that the predominant age category was between 31 and 50 years, with a statistically significant younger mean age of 44.3 ± 6.8 years ($p < 0.05$) compared to the non-recurrence cohort (mean age: 51.6 ± 8.1 years). This trend underscores the prognostic importance of younger age as a potential marker for recurrence risk.

Tumor Stage and Molecular Subtypes Histopathological reassessment of tumors showed that the majority of LRR cases were initially staged at IIB (44.2%) and IIIA (51.2%), cumulatively accounting for over 95% of recurrences. There were no cases of recurrence among stage I tumors, and only a small fraction of stage IIA tumors progressed to LRR.

Immunohistochemical (IHC) analysis further elucidated the biological aggressiveness of tumors prone to recurrence. High proliferative index (Ki-67 >20%) was recorded in 71.6% of LRR cases versus only 30% in the primary treatment cohort. HER2 overexpression was also significantly more prevalent among recurrent tumors (48.8%) compared to non-recurrent cases (28.3%), while hormone receptor positivity (ER+/PR+) was less frequent (25.6% vs. 48.3%), suggesting a predominance of more aggressive, less-differentiated molecular phenotypes among recurrences.

Treatment Completeness and Monitoring Deficits Evaluation of treatment modalities revealed several therapeutic insufficiencies within the LRR cohort:

- 28% of patients had not received postoperative radiotherapy despite indications.
- 19% were treated with incomplete or suboptimal chemotherapy regimens.
- Only 35% of patients underwent repeat biopsy and IHC reassessment at the time of recurrence, highlighting a critical gap in the application of precision oncology principles.

These findings strongly correlate with current oncologic literature identifying insufficient adjuvant therapy and lack of biomarker re-evaluation as independent predictors of poor prognosis.

Survival Outcomes Kaplan–Meier survival analysis showed a statistically significant difference in 7-year cumulative survival between patients with and without recurrence. The survival rate in the LRR group was 53.7%, while non-recurrent patients demonstrated a substantially higher survival rate of 78.4% ($p < 0.01$).

Moreover, among the LRR cohort, early recurrence (defined as occurring within 24 months post-surgery) was observed to be associated with the poorest outcomes, indicating the need for intensified surveillance in the early postoperative years. These results reinforce the prognostic value of recurrence timing as an indicator of tumor aggressiveness and treatment resistance.

The summarized data in Tables 1 and 2, as well as Figures 1 and 2, further illustrate the differential distribution of clinical and molecular features and highlight specific gaps in treatment implementation across cohorts.

Discussion

The results of the present study corroborate and expand upon existing data regarding the multifactorial etiology of locoregional recurrence (LRR) in breast cancer patients following radical

mastectomy. The observed 5.4% recurrence rate aligns with previously reported figures from regional cancer registries and confirms that despite adherence to standard surgical techniques, a non-negligible proportion of patients remain at elevated risk.

A key finding was the significant association between younger patient age and higher recurrence risk. This observation has been consistently validated in international studies and may be attributed to the biological aggressiveness of tumors in younger women, as well as potential variations in treatment response and hormonal milieu. The high prevalence of LRR among patients with stage IIB–IIIA disease and elevated Ki-67 index underscores the prognostic value of these parameters in clinical practice. Ki-67, as a marker of proliferative activity, remains a cornerstone of molecular risk assessment and its incorporation into therapeutic decision-making should be standardized.

HER2-positive and triple-negative subtypes were overrepresented in the LRR cohort, confirming that molecular classification significantly influences recurrence dynamics. The relatively low ER/PR positivity among recurrent cases suggests the limited efficacy of endocrine therapy in preventing LRR in these subgroups, thereby warranting consideration for more intensive adjuvant strategies, including targeted agents and chemotherapy intensification.

Equally concerning were the identified deficiencies in the application of adjuvant therapy. The omission of radiotherapy in over a quarter of eligible patients, and incomplete chemotherapy in nearly one-fifth, reflect systemic barriers to comprehensive oncologic care [6]. The infrequent use of repeat IHC profiling at the time of recurrence further illustrates a missed opportunity to refine treatment in the setting of biological tumor evolution.

Our findings advocate for the integration of precision medicine principles into routine oncology workflows. Implementing individualized follow-up regimens based on molecular risk, ensuring completion of adjuvant therapy, and performing molecular reassessment at recurrence could collectively enhance long-term outcomes [7].

Furthermore, the markedly reduced 7-year survival among the recurrence group (53.7%) compared to non-recurrent patients (78.4%) highlights the prognostic significance of LRR as a surrogate for systemic disease progression. Early recurrences (<24 months post-surgery) in particular denote biologically aggressive disease requiring close monitoring and possibly novel systemic interventions.

In summary, the study affirms that LRR after mastectomy is not merely a localized event but a reflection of intrinsic tumor biology and treatment adequacy. Regional oncology systems must prioritize risk-adapted care pathways, improve adherence to adjuvant protocols, and establish platforms for multidisciplinary decision-making. Such efforts will be vital in closing the survival gap and reducing recurrence burdens in breast cancer populations.

Conclusion

LRR of BC remains a pressing clinical issue despite surgical advances. This study underlines the prognostic value of molecular markers and highlights the need for individualized surveillance strategies in regional oncology settings. Implementation of risk-stratified follow-up protocols can improve outcomes and reduce recurrence rates.

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