

Original Research Article

IMPACT OF TUMOR BIOLOGY ON LOCAL RECURRENCE AFTER BREAST-CONSERVING SURGERY

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ABSTRACT

Background: Breast-conserving surgery is a proven treatment option for the right patient with breast cancer. **Objective:** To assess the role of tumor biology on local recurrence after breast conserving surgery and to determine pathological and molecular factors associated with a higher risk of local recurrence.

Materials and Methods: This was a retrospective observational cohort study carried out from October 2025 to March 2026 at Surgery Department, Naseerullah Khan Babar Memorial Hospital, Peshawar. A total of 120 patients who were undergoing breast-conserving surgery were assessed. Data are gathered on demographic, clinical, pathological, receptor, HER2, treatment, and follow-up parameters. Postoperative follow-up was used to evaluate for local recurrence.

Results: The number of patients with local recurrence was 15 (12.5%). The percentage of recurrence was higher in patients with ER-negative, PR-negative, HER2-positive, and high-grade tumors, and high Ki-67 expression. The recurrence rate was 28.2% for high Ki-67 tumors and 4.9% for low Ki-67 tumors.

Conclusion: Local recurrence after breast conservation surgery is highly dependent on tumor biology. Biological factors should therefore be considered in the planning of postoperative risk assessment and surveillance.

Keywords: Breast cancer; local recurrence; tumor biology; HER2; Ki-67; hormone receptors.

INTRODUCTION

For the right patients with breast cancer, breast conservation surgery is a proven surgical option that allows patients to have their breast preserved while keeping their cancer safe. Although there has been progress in surgery, radiotherapy, systemic therapy, and pathological assessment, local recurrence is a significant clinical issue after breast-conserving surgery.^[1] Ipsilateral breast tumor recurrence can either be a recurrence of residual disease or a new primary tumor in the treated breast, and this distinction is clinically important as there may be

different biological activities between the two that can have different prognoses and therapeutic responses. Local recurrence is not only dependent on surgical margins and treatment technique, but also influenced by the intrinsic biology of the tumor, as more and more evidence accumulates. Several clinical and pathological factors interact to affect the risk of recurrence following breast-conserving surgery.^[2] The biology of the primary tumor is important, since tumors with aggressive molecular features could have a higher ability to invade and spread to other parts of the body, to resist treatment, and to regrow after treatment.

Multiple ipsilateral breast tumors are a particularly complex case of tumor biology. In certain patients with multiple lesions on the same breast, breast-conserving surgery may be an option if adequate surgical removal and cosmetic results can be obtained. The ACOSOG Z11102 study results showed that patients with multiple ipsilateral breast cancers who have been carefully selected for breast conservation can achieve acceptable local recurrence rates, which underscores the importance of disease distribution alone not necessarily being an absolute contraindication to breast conservation.^[3] However, multifocal or multicentric disease can be an indicator of a larger field of biological abnormality in the breast, and knowledge of tumor characteristics is important when assessing the risk of local failure. Another factor that can interact with tumor biology to influence recurrence risk is age. Young women with breast cancer may have more aggressive pathological characteristics of their tumors, and the issue of local recurrence has historically played a role in surgical decisions in this group.

While both breast-conserving therapy and mastectomy can achieve similar oncological results in appropriately selected women, the different patterns of recurrence in younger women underscore the need to take into account biological risk, rather than age alone, when choosing treatment.^[4] Therefore, the concept of breast conservation must be considered in the context of a personalized treatment plan where tumor biology plays a role in the evaluation of recurrence, in addition to surgical preference. If ipsilateral breast tumor recurrence occurs, it can be treated with breast salvage surgery in carefully selected cases or with salvage mastectomy. As more and more patients receive repeat breast conservation, it is clear that local recurrence is not always a failure of treatment. But a second breast-conserving operation is not feasible if the recurrence is in a different location, if the recurrence is larger, if the patient has been previously treated with radiotherapy, if there has been a long disease-free period, or if the recurrent tumor is different.

Studies comparing repeat breast conservation surgery highlight the need for patient selection and oncological risk stratification when considering breast conservation after recurrence.^[5] In addition, real-world data show that recurrence after breast-conserving surgery remains a problem, even with modern, multidisciplinary treatment. Measurable recurrence rates have been reported in retrospective cohort studies after breast conservation, further highlighting the importance of identifying factors that distinguish those patients who are at low and high risk for local failure.^[6] Most importantly, recurrence risk is not a direct impact of breast preservation. Instead, the nature of the underlying tumor and the sensitivity of the patient to the treatment may account for significant differences between patients. This distinction is important

because for many patients, breast-conserving surgery is an oncologically sound treatment when done appropriately and when combined with the indicated adjuvant therapy.

Another view on tumor biology is the link between neoadjuvant chemotherapy, treatment response, and subsequent breast conservation. If neoadjuvant therapy is followed by surgery, to be eligible for breast-conserving surgery, there may be significant tumor downstaging. The assumption that downstaging necessarily leads to higher local recurrence rates has not been supported by studies that have evaluated the question, and treatment response and biological behavior of the residual disease should be considered when evaluating risk.^[7] Likewise, long-term real-world comparisons of breast-conserving therapy versus mastectomy have highlighted the need to assess oncologic outcomes over a longer follow-up period, and the rate of recurrence is not just a function of the local surgery performed.^[8]

Surgical margins continue to play an important role in local control, as some microscopic disease may be left behind to allow for subsequent recurrence. Re-excision is typically performed when margins are involved or deemed to be too close, but its correlation with a decrease in local recurrence is not consistent in all patients. Based on contemporary evidence, the benefit of re-excision should be considered in the context of tumor characteristics, margin definitions, pathological assessment, and adjuvant treatment, and not as a standalone factor for recurrence.^[9] These observations further reinforce the need for a multi-dimensional approach that takes into account biological characteristics and surgical considerations. With increasing focus on tumor biology, there have been attempts to create risk models that include molecular and pathological features to predict local recurrence.

Biologically informed risk stratification suggests that not all tumors should be treated in the same way, even when they are in the same location, if they have significantly different biological behaviors. The connection between tumor biology and local recurrence is complex, and a single molecular marker or simplified risk category may not take into account interactions between molecular subtype, treatment response, patient characteristics, and local therapy.^[10]

However, local recurrence is still dependent on the nature and response to systemic therapy of the primary tumor. Recurrence patterns are also not understood by the extent of surgery, as is demonstrated further by comparing early-stage breast cancer with locally advanced breast cancer following neoadjuvant chemotherapy.^[11] The variation in local recurrence rates between these patient groups may be due to different levels of tumor burden, biological aggressiveness, response to treatment, lymph node status, and other pathological factors. These results highlight the need to take into account the biological characteristics and the disease

stage when evaluating recurrence following breast conserving surgery (BCS).^[12]

Postoperative outcome and wound-related complications from various types of breast cancer surgeries are also important factors to consider when choosing a treatment, but these surgical outcomes are not related to the biological mechanisms of tumor recurrence.^[13] Another big part of breast conserving treatment is radiotherapy, and modern treatment strategies increasingly take into account the biological characteristics of the cancer when deciding whether a patient might be able to receive a de-escalation of treatment. In some patients with early-stage disease, radiotherapy has been studied and may be avoided, especially in those with a low risk of recurrence based on biological characteristics. On the other hand, patients with biologically aggressive tumors might need full local therapy due to a higher base risk of recurrence.^[14] This emphasizes the overall concept that local therapy should be customized to the biological behavior of the tumor and not given as a blanket treatment to all patients.

The risk of residual disease may also be affected by technical improvements in breast-conserving surgery. For instance, cavity shaving has been studied as a means of locating and resecting more tissue at the margins of the cavity.^[15] But good surgical clearance is not enough to prevent recurrence because there are other factors contributing to local failure, one of which is microscopic residual disease. The biology of the tumor can affect whether there are any cells left behind that are dormant, that are sensitive to adjuvant therapy, or that will become clinically detectable recurrent disease. The oncoplastic breast-conserving surgery has given the opportunity to achieve wider resections with acceptable breast shape and appearance, even in high-risk breast cancer patients. Multicenter evidence has been used to compare the conventional and oncoplastic techniques, proving the feasibility of oncoplastic approaches with an evaluation of both oncologic and surgical outcomes.^[16]

With these advances, surgeons can perform an adequate tumor resection while retaining the breast's shape. However, the surgical technique alone is not a substitute for a careful evaluation of tumor biology, and this is still very important in understanding why some patients suffer local recurrence after apparently satisfactory surgery. If ipsilateral breast tumor recurrence occurs, further treatment options include repeat breast-conserving surgery or salvage mastectomy with various surgical and oncologic considerations. The evidence from multiple centers in recent years that has been used to assess postoperative complications following these salvage procedures demonstrates the complexity of treating those who have received a breast-conserving surgery and have experienced recurrence.^[17] The evidence available overall suggests that local recurrence is a complex

phenomenon that reflects the interplay of tumor biology, tumor burden, surgical factors, adjuvant therapy, and patient factors. Therefore, the role of tumor biology in local recurrence after breast-conserving surgery is clinically relevant for better risk stratification, personalized approach, and identification of patients who might benefit from more intensive local and systemic therapy or closer surveillance.

Objective: To investigate how the biological features of the tumor affect the local recurrence rate after breast-conserving surgery, and to determine which pathological and molecular features are linked to a higher risk of local recurrence in breast cancer patients.

MATERIALS AND METHODS

Study Design: Retrospective Observational Cohort study.

Study Setting: Surgery Department, Naseerullah Khan Babar Memorial Hospital, Peshawar.

Duration of the Study: October 2025 to March 2026.

Inclusion Criteria: Patients included were women 18 years of age or older with a diagnosis of breast cancer made by histology and who had been treated with breast-conserving surgery. Patients were eligible if full pathological data on tumor characteristics were available, such as tumor size, histological type, grade, lymph node status, hormone receptor, and HER2 status if applicable. Patients with documented postoperative follow-up adequate to evaluate local recurrence were also included.

Exclusion Criteria: This study excluded patients who had a primary mastectomy. Patients with incomplete pathological records, inadequate postoperative follow-up, or insufficient information on the biological characteristics of the tumor were also excluded. To minimize the potential for local recurrence outcome to be confounded, patients with distant metastatic disease at initial breast-conserving surgery and those with a prior history of breast cancer or prior breast-conserving surgery were excluded.

Methods: A structured data collection proforma was used to review patients' records. Demographic data (age) and clinical and pathological data relevant to tumor biology were obtained. When available, the Ki-67 proliferation index was also noted. Tumor biological characteristics were used to classify patients, and the postoperative follow-up records were checked for ipsilateral local recurrence. Recurrence was considered local if there was a recurrence of breast cancer in the ipsilateral breast or surgical bed, either histologically or clinically, after the completion of initial treatment. The main outcome was the development of local recurrence. The data were entered in a statistical database and analyzed to see if there were associations between

the tumor biological characteristics and local recurrence. Descriptive and inferential statistical tests were used, and statistical significance was defined as $p < 0.0$.

RESULTS

120 breast cancer patients undergoing breast-conserving surgery were included in the analysis. The average age of the study population was 48.6 ± 10.7 years, ranging from 29 to 72 years

Table 1. Demographic and clinicopathological characteristics of the study population

Characteristic	Number (n=120)	Percentage
Age ≤ 50 years	68	56.7%
Age > 50 years	52	43.3%
Invasive ductal carcinoma	94	78.3%
Invasive lobular carcinoma	15	12.5%
Other histological types	11	9.2%
Tumor size ≤ 2 cm	76	63.3%
Tumor size > 2 cm	44	36.7%
Grade I	24	20.0%
Grade II	67	55.8%
Grade III	29	24.2%
Node negative	72	60.0%
Node positive	48	40.0%

Biological heterogeneity within the cohort was significant with regard to hormone receptor and HER2 status. 84 (70.0%) patients were found to have ER positivity, 75 (62.5%) PR positivity, and 25 (20.8%) HER2 overexpression. Thirty-nine (32.5%)

patients had a high Ki-67 proliferation index. Local recurrence was more common in patients with high-grade tumors, HER2-positive disease, and high proliferative index.

Table 2. Tumor biological characteristics according to local recurrence

Tumor characteristic	No recurrence (n=105)	Local recurrence (n=15)	p-value
ER positive	77 (73.3%)	7 (46.7%)	0.041
ER negative	28 (26.7%)	8 (53.3%)	
PR positive	70 (66.7%)	5 (33.3%)	0.018
PR negative	35 (33.3%)	10 (66.7%)	
HER2 positive	18 (17.1%)	7 (46.7%)	0.012
HER2 negative	87 (82.9%)	8 (53.3%)	
Grade I-II	83 (79.0%)	8 (53.3%)	0.038
Grade III	22 (21.0%)	7 (46.7%)	
Low Ki-67	77 (73.3%)	4 (26.7%)	0.006
High Ki-67	28 (26.7%)	11 (73.3%)	

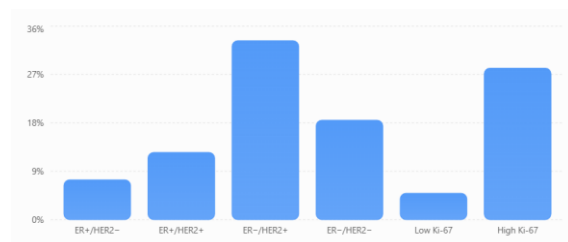
There was a greater percentage of local recurrence in patients with biologically aggressive tumors. The recurrence rate was especially high in patients with high Ki-67 expression, HER2-positive, and hormone receptor-negative disease. Patients with high-grade

tumors also had a higher rate of recurrence. The results show that the biological features of the tumor were more unfavorable in those patients who went on to develop local recurrence.

Table 3. Local recurrence according to major tumor biological profiles

Biological profile	Total patients	Local recurrence	Recurrence rate
ER+/HER2-	68	5	7.4%
ER+/HER2+	16	2	12.5%
ER-/HER2+	9	3	33.3%
ER-/HER2-	27	5	18.5%
Low Ki-67	81	4	4.9%
High Ki-67	39	11	28.2%

The highest recurrence rate was seen in patients with ER-negative/HER2-positive disease, followed by those with ER-negative/HER2-negative disease. Recurrence rates were significantly higher for patients with a high Ki-67 proliferation index compared with those who had a low Ki-67 index.



DISCUSSION

The present study aimed to assess the correlation between local recurrence after conservative breast surgery and tumor biological features. In 120 patients, local recurrence was observed in 12.5% during the follow-up period. These results further validate the idea that local recurrence after BCS is a multifactorial event in which tumor biology is an important factor, as well as surgical, pathological, and treatment-related factors. Qu et al. pointed out that ipsilateral breast tumor recurrence after breast-conserving surgery is a clinical phenomenon that should be viewed in the context of tumor biology; it can be the regrowth of the primary tumor or the appearance of a new primary tumor that is biologically different from the first.^[1]

The association between tumor biology and recurrence is clinically important because breast cancer is not a single disease entity. Tumor growth, response to therapy, and the possibility of residual disease are influenced by differences in receptor expression, proliferative activity, histological grade, and molecular subtype. While perioperative factors have also been explored, Gu et al. concluded that the decision for local versus general anesthesia in breast-conserving surgery was not a straightforward explanation for recurrence because it has to be looked at in the context of oncological care.^[2]

The present findings are also applicable to patients with more complicated patterns of breast disease. In the study of Boughhey et al. (ACOSOG Z11102), the authors stated that in appropriately selected patients with multiple ipsilateral breast cancers, breast-conserving surgery is an acceptable option with regard to local recurrence outcomes.^[3] This evidence suggests that having more than one lesion is not a reason to automatically have a mastectomy. But multifocality, tumor grade, receptor status, and other pathological characteristics should be considered together, as they may all have an impact on local control. In this regard, individual assessment is still necessary when considering breast conservation.

In a systematic review and meta-analysis, Sun et al. found that breast-conserving therapy and mastectomy may be equally effective for local recurrence in young women who are carefully selected, but that younger women may have clinical and biological factors that contribute to their inherent risk.^[4] Our study findings support this concept, as there is evidence that biological parameters are more valuable than the surgical procedure alone in identifying patients at a higher risk. However, younger age should not necessarily be considered a contraindication to breast-conserving surgery. Local recurrence also emphasizes the need to know about the biology of the tumor.^[5]

But there is no uniformity in the recurrence of the disease, and factors such as disease-free interval,

biological features, and previous treatment must be taken into account when deciding whether to repeat surgery. The overall recurrence rate for our study was relatively low, which further supports the continued use of breast-conserving surgery, and the clustering of recurrence in the biologically unfavorable tumors indicates that follow-up options should be customized based on individual risk. The recurrence rate of 12.5% in our cohort falls within the range that can be seen in modern breast conserving surgery cohorts, but there are differences in the follow-up time, patient selection, tumor stage, any additional treatment administered, and definitions of local recurrence between studies.

In a retrospective cohort, Wang et al. reported recurrence outcomes after BC and emphasized the ongoing need to monitor patients after surgery.^[6] Recurrence was not evenly distributed across the population in our study, since there was a higher proportion of recurrence events among patients with high-risk biological characteristics. The overall recurrence rates in this observation may mask clinically relevant differences among the biological subgroups. Another context for the interpretation of recurrence risk is the use of neoadjuvant chemotherapy.^[7] They also found that there was no automatic association between systemic treatment and conversion to breast conservation with increased local failure. Rather, the response to treatment and the nature of the remaining tumor should be included in the risk assessment.

The notion that a mastectomy offers a complete eradication of the risk of recurrence has also been challenged by long-term comparisons of breast conserving therapy and mastectomy.^[8] Our study findings add to this evidence, indicating that the biological characteristics of the tumor may be more important than the amount of the breast removed in determining the risk of recurrence. Therefore, breast-conserving surgery should not be considered a less desirable option from an oncological point of view. Surgical margins continue to be a critical factor in local control. Weiner et al. showed that the utility of re-excision for involved or close margins must be evaluated in the context of the overall clinical situation.^[9] Biological characteristics were strongly correlated with recurrence in the present study, suggesting that proper margins are important but may not be enough to prevent local failure.

Recurrence is possible in a patient with apparently adequate excision in the event that the primary tumor has aggressive biological features. This further emphasizes the need for the use of pathological and biological data in the postoperative risk assessment. Torres called attention to the growing interest in using tumor biology as a guide to stratify the risk of local recurrence, but warned against simplifying this relationship.^[10] This caution is supported by our results. While high Ki-67, HER2 positivity, and hormone receptor negativity were linked to higher recurrence rates, none of these characteristics alone can fully account for the

biological behavior of breast cancer. Tumor biology is a complex and integrated set of molecular, pathological, and clinical parameters. Therefore, future risk models should ideally use multiple biological variables instead of a single biomarker. These results are important because they show that the choice of surgery must be combined with tumor burden and biological behavior and cannot be used alone. Local control may be influenced by other factors related to treatment. In a study by Yang et al., the surgeons looked at wound complications after various breast cancer surgical procedures, revealing that surgical outcomes are not limited to recurrence.^[13] Allen et al. also pointed out that the biology of the tumor is becoming more important in the context of radiotherapy omission in certain early-stage breast cancer patients.^[14] This is especially relevant as radiotherapy is still a crucial part of breast-conserving therapy, and biologically aggressive tumors are not likely to be good candidates for treatment escalation. Meticulous surgical clearance is also important, as Fernández-Pacheco et al. have shown the potential value of cavity shaving in reducing residual tumor rates.^[15] Lastly, the advent of oncoplastic surgery has broadened the range of acceptable oncological resections with maintenance of breast aesthetics. Oncoplastic breast conserving surgery has been shown to be an acceptable oncological and surgical treatment even among women with high-risk breast cancer by Fitzal et al.^[16] But, as with all surgical advances, tumor biology still plays a role. If recurrence does happen, treatment is more complicated and may involve repeat breast-conserving surgery or salvage mastectomy. However, both may be linked to postoperative complications, as shown by Tiels et al., which further highlights the importance of preventing recurrence wherever possible, through appropriate initial treatment and risk-based follow-up.^[17] In summary, the current results suggest that tumor biology plays an important role in determining local recurrence following breast conservation surgery. The inclusion of receptor status, HER2 expression, tumor grade, proliferative activity, and other biological parameters in the postoperative risk assessment could enhance patient selection, surveillance strategies, and individual treatment planning.

CONCLUSION

The biology of the tumor is a significant factor in deciding the risk of local recurrence after breast-conserving surgery for breast cancer. In this study, patients with biologically aggressive tumors were more likely to experience local recurrence, including those with hormone receptor-negative disease, HER2 positivity, high histological grade, and elevated Ki-67 proliferation. These results suggest that the use of breast-conserving surgery must be

included in a broader oncological context, not as a standalone surgical procedure. Local control is still crucial, and biological characteristics offer extra information for identifying patients at higher risk of recurrence after adequate tumor removal and appropriate adjuvant treatment. The use of tumor biological markers in postoperative risk stratification can be useful to customize surveillance and treatment strategies. Careful systemic and local treatment and close follow-up may be warranted for patients with a poor biological profile.

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