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OPTIMIZING THE EXTENT OF SURGERY AFTER NEOADJUVANT THERAPY IN LOCALLY ADVANCED BREAST CANCER: CLINICAL OUTCOMES AND EVIDENCE-BASED SURGICAL DECISION-MAKING

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ABSTRACT

Background: Optimizing surgical extent after neoadjuvant systemic therapy (NST) in locally advanced breast cancer requires balancing adequate locoregional control against treatment-related morbidity and functional outcomes. Objective: To critically examine surgical de-escalation and oncological endpoints using a supplied regional clinical report alongside evidence from major randomized trials and meta-analyses. Methods: A descriptive appraisal of an author-supplied retrospective/prospective cohort summary (84 women, 2023–2025) was integrated with a focused narrative synthesis of published evidence. The cohort's aggregated values were not independently verified; no patient-level reanalysis was possible. Results: The source report described 44 patients managed with neoadjuvant multimodality therapy and 40 comparison patients; reported local recurrence proportions were 9.1% and 22.5%, respectively, and reported three-year overall survival was 68.2% and 47.5%. These unadjusted findings cannot establish a treatment effect because stage, molecular subtype, follow-up, and treatment selection were not controlled. Published evidence supports increased breast conservation after NST, but also underscores the importance of localization, margin assessment, radiation, and systemic therapy tailored to tumor biology. Conclusions: Surgical extent should be determined by residual disease distribution, feasibility of negative margins, nodal response, and multidisciplinary planning rather than tumor shrinkage alone. Prospective standardized outcome assessment is required to validate regional findings.

Keywords: locally advanced breast cancer; neoadjuvant therapy; breast-conserving surgery; mastectomy; axillary surgery; pathological response; locoregional recurrence; overall survival.

INTRODUCTION

Locally advanced breast cancer encompasses a clinically heterogeneous spectrum of non-metastatic presentations characterized by extensive primary tumor involvement and/or advanced regional nodal disease. Unlike stage IV disease, which includes distant metastasis and requires a distinct therapeutic framework, stage III disease is commonly approached with curative intent using coordinated systemic therapy, surgery, and radiotherapy [1–3]. The precise choice of surgery after NST is increasingly guided by pretreatment disease distribution, radiological and clinical response, molecular phenotype, patient preferences, and expected radiation requirements. Thus, surgical optimization is not synonymous with minimizing resection in every patient; it refers to achieving adequate cancer control with the least necessary morbidity.

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Neoadjuvant therapy may convert some patients initially considered unsuitable for breast-conserving surgery into candidates for conservation. However, a clinical or radiological complete response does not reliably exclude microscopic residual disease. Multicentric residual involvement, extensive malignant calcifications, inflammatory breast cancer, persistent skin involvement, or inability to achieve negative margins may preclude conservation despite measurable tumor regression. In the axilla, downstaging creates opportunities for selected less extensive staging procedures, although these depend on the initial nodal status, response documentation, operative technique, and local standards [2–5].

An individual-patient meta-analysis by the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) found greater use of breast conservation after neoadjuvant rather than adjuvant chemotherapy (65% versus 49%). Nevertheless, historical trials showed higher 15-year local recurrence in the neoadjuvant groups (21.4% versus 15.9%), while breast cancer mortality did not significantly differ [4]. These findings should not be interpreted as evidence against contemporary NST; rather, they emphasize careful localization, pathology, radiotherapy, and selection when reducing surgical extent. The objective of this article is to expand the regional report through critical comparison with externally published evidence and to define an auditable framework for surgical decision-making.

MATERIALS AND METHODS

The regional source manuscript reports a retrospective and prospective assessment conducted at a Bukhara oncology service during 2023–2025, involving 84 women with breast cancer classified in the original document as stage III–IV (T3–4N1–3M0–1). Patients were allocated descriptively to a multimodality group (n=44) receiving neoadjuvant polychemotherapy followed by surgery and indicated postoperative treatment, and a comparator group (n=40) receiving heterogeneous conventional management. The source reports a mean age of 52.4 ± 8.1 years and aggregate outcome percentages. These statements are transcribed from the author-provided report, not independently audited data. Because the source combines M0 and M1 disease, stage-specific conclusions about non-metastatic locally advanced cancer cannot be derived without separating patients by distant-metastatic status.

The analytical component is a focused narrative synthesis of established surgical and neoadjuvant evidence, including an individual-patient meta-analysis and randomized studies addressing molecularly selected systemic treatment [4–8]. Published trial estimates are reported separately from regional cohort figures. No new database extraction, pooled statistical analysis, Kaplan–Meier reconstruction, significance testing, or causal effect estimate was performed. Clinical variables needed for a publishable comparative cohort include clinical and pathological TNM stage, ER/PR/HER2 status, grade, neoadjuvant regimen, surgical procedure, pathological response, margin status, radiotherapy, recurrence dates, and censoring information.

RESULTS

The source report describes tumor size reduction of approximately 45–60% following neoadjuvant treatment, without specifying the measurement method, timing, or denominator. Its aggregate comparison suggests lower observed local recurrence and

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higher reported three-year survival in the multimodality group; however, the report does not state event counts with dates, observation duration, censoring, baseline stage balance, or a reproducible survival-analysis method. Table 1 therefore presents the source figures strictly as descriptive values, not verified comparative efficacy estimates.

Table 1. Descriptive outcomes reproduced from the author-supplied regional manuscript (not independently validated).

Measure	Multimodality group	Comparator group	Interpretation
Patients	44	40	Non-randomized groups
Treatment	NST → surgery → indicated adjuvant therapy	Mixed conventional approaches	Substantial treatment heterogeneity
Reported local recurrence	9.1%	22.5%	Follow-up interval and event definitions unclear
Reported 3-year overall survival	68.2%	47.5%	No Kaplan–Meier curves or censoring data
Reported tumor reduction	45–60% (overall statement)	Not specified	Response measurement not documented

Numerically, the reported recurrence proportions correspond approximately to 4/44 and 9/40 patients, and the survival percentages to approximately 30/44 and 19/40 patients. These back-calculations are illustrative arithmetic only; they cannot substitute for verified event-level records or survival probabilities. A between-group percentage difference should not be described as statistically significant without appropriate analyses and control for confounding.

Table 2 summarizes selected external clinical evidence. Its populations, endpoints, and treatment comparisons differ from those in the regional report; the published estimates must not be presented as additional observations from the 84-patient cohort.

Table 2. Selected published evidence relevant to response-adapted surgery and postoperative outcomes.

Study / population	Comparison	Selected published finding	Relevance / limitation
EBCTCG meta-analysis (2018), 4,756 women [4]	Neoadjuvant vs adjuvant chemotherapy	Breast conservation 65% vs 49%; 15-year local recurrence 21.4% vs 15.9%	Historical regimens; underscores need for safe surgical selection
KEYNOTE-522,	Perioperative	60-month overall	Systemic treatment

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stage II–III TNBC [6]	pembrolizumab + chemotherapy vs chemotherapy	survival 86.6% vs 81.7%	benefit; not a trial of surgical extent
KATHERINE, residual HER2-positive disease [7]	Adjuvant T-DM1 vs trastuzumab	7-year invasive disease-free survival 80.8% vs 67.1%	Residual pathology guides adjuvant treatment, not automatic surgical reduction
DESTINY-Breast05, selected residual HER2-positive disease [8]	T-DXd vs T-DM1	3-year invasive disease-free survival 92.4% vs 83.7%	Evolving post-neoadjuvant evidence; toxicity and eligibility matter

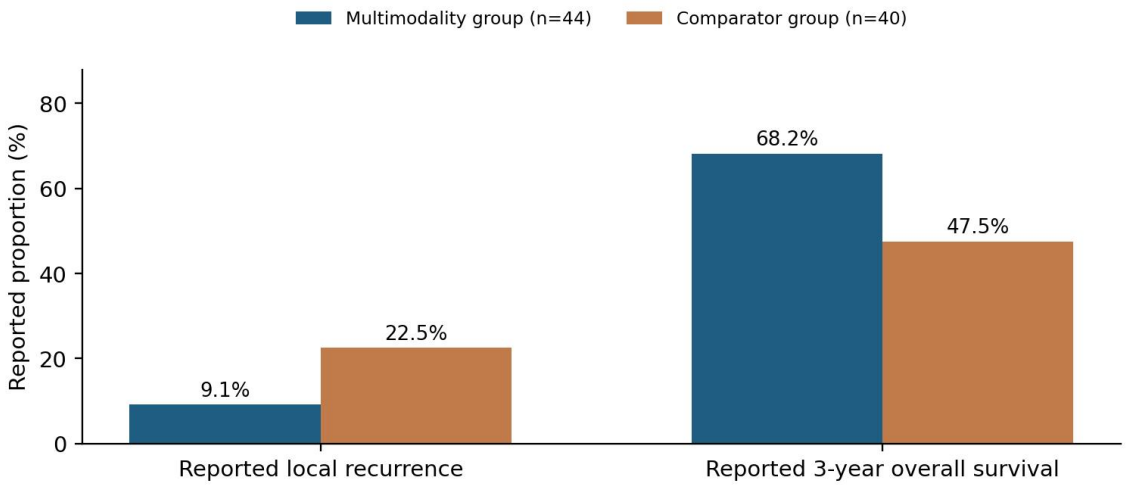


Figure 1. Reported group-level outcomes from the author-supplied regional manuscript. Descriptive, unverified percentages; groups were non-randomized, and no causal or statistically significant effect is inferred.

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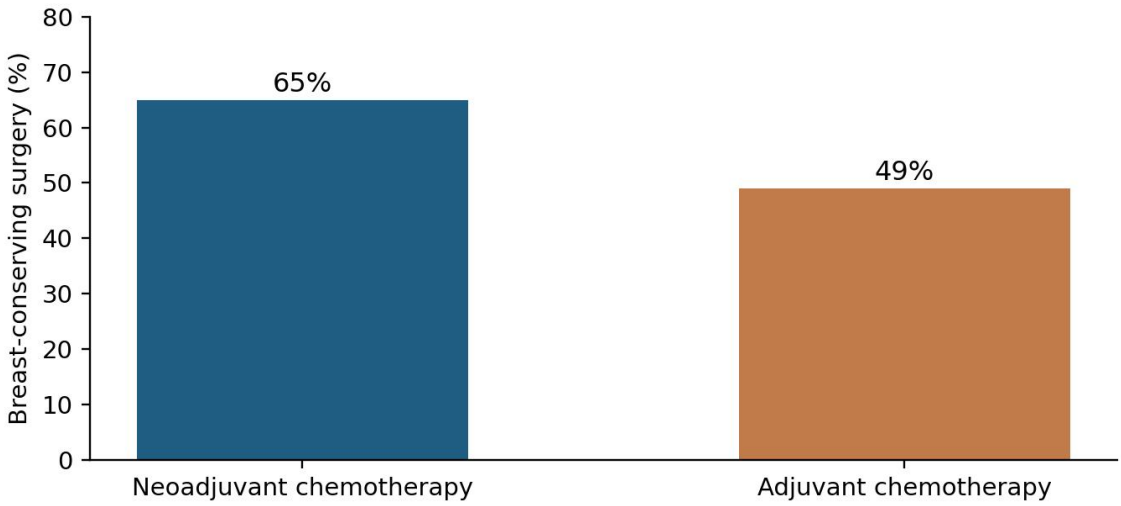


Figure 2. Breast-conserving surgery proportions in the EBCTCG individual-patient meta-analysis of neoadjuvant versus adjuvant chemotherapy [4]. External published evidence; not derived from the regional 84-patient sample.

DISCUSSION

A central clinical principle is that the magnitude of tumor regression and the safety of breast conservation are related but not interchangeable. Surgical decisions require documentation of the original tumor bed, the spatial pattern of residual disease, and the anticipated ability to obtain clear margins. Localization clips placed before NST, repeat targeted imaging, specimen orientation, and comprehensive histopathological assessment can help prevent incomplete excision. In appropriately selected patients, breast-conserving surgery with indicated radiotherapy is a reasonable alternative to mastectomy; in other patients, extensive residual disease or anatomic constraints justify a wider operation. The EBCTCG findings highlight why increasing conservation rates alone is an insufficient quality indicator [4].

Biological subtype influences both response probability and the significance of residual disease. Triple-negative and HER2-positive tumors often show substantial pathological responses to effective NST, but their subsequent risk is also affected by response-adapted systemic treatment. KEYNOTE-522 demonstrated an overall-survival advantage with a pembrolizumab-containing perioperative regimen in stage II–III triple-negative disease, while KATHERINE demonstrated durable benefits of T-DM1 for HER2-positive residual invasive disease [6,7]. More recent randomized evidence from DESTINY-Breast05 suggests additional benefit of trastuzumab deruxtecan in a defined high-risk residual HER2-positive population [8]. These trials are not direct comparisons of lumpectomy versus mastectomy; they illustrate that postoperative oncological outcomes depend on multimodality treatment and tumor biology, not merely resection volume.

Axillary management presents a related opportunity and challenge. Following NST, axillary staging may be tailored to pretreatment nodal involvement and treatment response, with attention to retrieval of a previously marked positive node where appropriate,

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sentinel-node mapping performance, residual nodal burden, and planned regional nodal irradiation. Broadly applying de-escalated axillary surgery to all patients initially presenting with advanced nodal disease would be unsupported. Multidisciplinary assessment is essential, particularly for patients with extensive N2–N3 disease or residual nodal metastases.

The original regional dataset has several methodological limitations that substantially constrain interpretation. The inclusion of both M0 and M1 disease creates clinical heterogeneity; stage IV patients should be analyzed separately because primary-tumor surgery in metastatic disease has different indications and cannot be equated with curative surgery for stage III disease. The comparator group includes diverse treatment strategies rather than a clearly defined standard-of-care regimen. There is no reported distribution of ER/PR/HER2 status, initial tumor size, performance status, operative type, margin positivity, radiation completion, or duration of follow-up. Consequently, confounding by indication, immortal-time effects, unequal surveillance, and missing-data bias cannot be excluded.

For future clinical validation, the principal endpoint should be explicitly defined—for example, ipsilateral locoregional recurrence from a prespecified time origin—alongside overall survival, disease-free survival, distant recurrence, and surgical morbidity. Time-to-event endpoints require Kaplan–Meier or competing-risk methods as appropriate, confidence intervals, and multivariable adjustment for stage and molecular subtype. A prospectively documented decision pathway would allow a more informative comparison of surgical extent than an unadjusted contrast between heterogeneous treatment packages.

Table 3. Proposed variables and clinical decision criteria for a reproducible prospective evaluation.

Domain	Minimum documentation	Why it matters
Disease at baseline	cT/cN/cM, imaging, tumor location, skin involvement	Separates non-metastatic from metastatic disease
Tumor biology	ER, PR, HER2, grade, histology, Ki-67 when available	Determines NST selection and response interpretation
Neoadjuvant treatment	Agents, doses, cycles, completion, response imaging	Allows regimen-specific analyses
Surgical management	BCS vs mastectomy, localization, margins, axillary procedure	Measures actual extent and adequacy of surgery
Pathological response	ypT/ypN, pCR definition, residual cancer burden if available	Links response to post-treatment risk
Adjuvant treatment	Radiotherapy fields; subtype-specific systemic	Controls major prognostic co-interventions

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	therapy	
Outcomes and follow-up	Dates of recurrence, death, last contact; complications	Enables valid survival and morbidity analyses

These recommendations also have practical relevance to resource-constrained oncology systems. Standardized documentation of stage, receptor status, neoadjuvant response, and surgical margins may improve both clinical consistency and research quality. However, the apparent advantage in the supplied cohort should be considered hypothesis-generating until primary records are verified, M0/M1 patients are separated, and adjusted time-to-event comparisons are completed.

Additional randomized evidence informs the balance between local treatment and systemic disease control. NSABP B-18/B-27 established the feasibility of preoperative chemotherapy as a means of increasing surgical options [9], whereas NeoSphere demonstrated the biological importance of HER2-directed neoadjuvant regimens [10]. For residual invasive disease, postoperative escalation with trastuzumab emtansine in HER2-positive cancer and capecitabine in selected HER2-negative populations has demonstrated benefits in randomized trials [11,12]. The ACOSOG Z1071 trial underscored the technical limitations of sentinel node surgery after neoadjuvant treatment in initially node-positive patients [13]; the AMAROS trial provides evidence on axillary radiotherapy versus dissection in a different, predominantly upfront-surgery population and should not be directly extrapolated to all locally advanced cases [14]. The OlympiA trial further illustrates how germline BRCA status can influence adjuvant systemic management of high-risk HER2-negative disease [15]. These studies support individualized multidisciplinary planning but do not validate the regional cohort estimates without patient-level verification.

CONCLUSION

Optimization of surgical extent after neoadjuvant therapy in non-metastatic locally advanced breast cancer is a response-adapted, multidisciplinary process rather than routine surgical minimization. Evidence supports improved opportunities for breast conservation in selected patients, while long-term local control requires appropriate localization, complete pathological assessment, radiotherapy, and subtype-specific systemic treatment. The author-supplied 84-patient report suggests potentially favorable outcomes after multimodality care, but its aggregate data are insufficient to establish a causal or statistically verified survival advantage. A standardized prospective evaluation with explicit stage stratification and validated oncological endpoints is required before clinical generalization.

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