Current Evidence on Surgical Approach to Local Recurrence After Nipple-Sparing Mastectomy: Is It Time to Classify in Order to Decide Better?

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AIM: Nipple-sparing mastectomy has become an increasingly preferred surgical option for selected breast cancer patients, enabling immediate breast reconstruction with either prosthetic implants or autologous tissues while ensuring oncologic safety alongside favorable aesthetic and psychosocial outcomes. Despite its benefits, managing local recurrence remains a clinical concern. Current guidelines recommend complete excision when feasible, following the principles of conservative surgery. However, a standardized classification of local recurrence after conservative mastectomy is still lacking. This review aims to gather current evidence on the incidence, characteristics, and treatment of local recurrence following nipple-sparing mastectomy with immediate breast reconstruction. Additionally, it seeks to propose the development of a standardized classification system to support treatment decision-making and future research.
METHODS: A targeted literature search was conducted in PubMed/MEDLINE, Scopus, and EMBASE to identify relevant articles published in English between 1 January 2013 and 31 December 2024. The search string used for PubMed was: *("nipple-sparing mastectomy" OR "skin-sparing mastectomy") AND ("local recurrence" OR "nipple recurrence" OR "chest wall recurrence") AND ("immediate reconstruction" OR "implant-based reconstruction")*. For Scopus, the adapted string was: (TITLE-ABS-KEY ("nipple-sparing mastectomy" OR "skin-sparing mastectomy") AND TITLE-ABS-KEY ("local recurrence" OR "nipple recurrence" OR "chest wall recurrence") AND TITLE-ABS-KEY ("immediate reconstruction" OR "implant-based reconstruction")). For EMBASE, the adapted strategy was: ('nipple-sparing mastectomy'/exp OR 'skin-sparing mastectomy'/exp) AND ('local recurrence'/exp OR 'nipple recurrence' OR 'chest wall recurrence') AND ('immediate reconstruction' OR 'implant-based reconstruction'). We included only English-language publications and excluded conference abstracts, letters, and case reports. Given the narrative nature of this review, the process did not follow Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) guidelines, and no formal records of deduplication or structured screening flow diagrams were maintained.
RESULTS: The reviewed literature reveals significant variability in defining and classifying local recurrence after nipple-sparing mastectomy with immediate reconstruction. This lack of consensus highlights the need for a clear and standardized classification system centered specifically on local recurrences, which could enhance risk stratification and guide personalized treatment strategies, thereby supporting the design of prospective studies and evidence-based guidelines.
CONCLUSIONS: The absence of a standardized approach to local recurrence after nipple-sparing mastectomy represents a critical gap in current breast cancer care. Establishing a dedicated classification could streamline clinical decision-making and lay the groundwork for large-scale prospective studies to inform future guidelines.

Keywords: breast cancer; local recurrence; nipple-sparing mastectomy; surgery; classification system

Introduction

The surgical approach to breast cancer (BC) treatment has undergone a significant shift over the past three decades, moving away from radical procedures toward breast conserving techniques, especially with the introduction of oncoplastic surgery [1,2]. Despite recent advances in adjunct treatments that have led to high rates of conversion from mastectomy to breast conserving surgery (BCS), reported mastectomy rates still range from 25% to 35% [3,4]. These percentages are related to factors such as the unfavorable ratio between tumor and breast size, multicentric disease, contraindications to radiotherapy (RT), and even patient preferences [5,6]. Conservative mastectomies, specifically skin-sparing mastectomy (SSM) and nipple-sparing mastectomy (NSM), represent direct developments of the BC

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paradigm shift, encapsulated by Umberto Veronesi's maxim "from maximum tolerable treatment to minimum effective treatment" [7]. As with any mastectomy, there is a risk of local recurrence (LR), and evidence suggests that SSM or NSM may be equivalent to total mastectomy in this regard [8]. However, concerns about the oncological safety of NSM persist, particularly due to the potential increased risk of LR associated with preserving a small amount of retro-areolar glandular tissue and the skin envelope [9–11]. Preserving the cutaneous and subcutaneous tissues allows for immediate breast reconstruction (IBR) using either implant-based or tissue-transfer techniques [12], which improves both aesthetic and psychological satisfaction. Oncological factors, including a history of RT or the need for adjuvant RT, mainly influence the choice of IBR technique. Additionally, patient-related factors such as smoking habits, body mass index, and breast size also significantly impact this decision [8].

Among implant-based IBRs, the pre-pectoral approach has gained widespread recognition and adoption due to advances in safe and effective placement of implants on the pectoralis fascia [13]. This shift toward pre-pectoral reconstruction marks a significant innovation in reconstructive breast surgery: moving from submuscular to pre-pectoral techniques has become the new standard in many centers, offering benefits in postoperative recovery and aesthetic results, including a reduced complication rate in women undergoing post-mastectomy radiotherapy, but also presenting new challenges in managing local recurrence [14–16].

In this evolving landscape, with increasing breast cancer survival and IBR rates, the surgical management of LR is becoming a growing concern. There is no established consensus on this issue, and either randomized controlled trials or prospective studies are necessary to establish clear and uniform guidelines. Evidence on how to handle local recurrence in patients with prior implant-based reconstruction—especially in pre-pectoral settings—remains limited and inconsistent across the literature, reflecting the absence of standardized protocols. This gap causes significant variation in clinical practice, where treatment decisions often depend on individual surgeon experience or institutional preference rather than evidence-based criteria.

Therefore, this review aims to compile current evidence on the surgical management of LR after NSM with IBR, highlighting existing controversies and emphasizing the critical need for a structured classification system for LR that could support personalized management strategies.

Conservative Mastectomies

Conservative mastectomies aim to improve cosmetic outcomes while following established aesthetic standards and ensuring oncological safety, even for patients who might otherwise require more invasive procedures [17]. The most commonly used techniques include SSM and NSM. By creating a pocket while preserving the skin envelope, these techniques facilitate IBR through the placement of a prosthetic implant or an autologous graft, in accordance with the latest guidelines [8]. SSM removes the entire breast gland via a lozenge-shaped incision that includes the nipple-areola complex (NAC), whereas NSM preserves the NAC, representing a significant conservative advancement. Compared to traditional total mastectomy, both SSM and NSM offer better cosmetic results. They are associated with higher satisfaction and improved quality of life, especially when combined with IBR, as shown by various studies [7,18–20].

When applicable [8], NSM has become the preferred technique because of the aesthetic results and the psychological importance of preserving NAC [21–23]. Despite the growing use of NSM, its oncological safety is still debated. This is mainly due to the small amount of retro-areolar glandular tissue intentionally left to maintain the NAC's viability. This concern is even more relevant in pre-pectoral immediate breast reconstruction (PP-IBR), where a 1 cm thick flap must be preserved, highlighting the potential risks of residual breast tissue [24].

Local Recurrence

There is no universally accepted classification for LR after NSM with prosthetic IBR.

Yamaguchi and colleagues [25] describe two patterns of LR with distinct biological features: nipple-areolar recurrence (NAR) and recurrence involving all other ipsilateral sites (such as the chest wall and subcutaneous tissue), collectively called other local recurrence (oLR).

The potential flaw lies in treating all non-NAR as the same, even though chest wall and skin involvement could require T4a and T4b staging, respectively [26]. Conversely, isolated subcutaneous tissue involvement does not change the initial disease stage. This does not eliminate the need for surgical removal of LR when possible; however, it can influence subsequent treatment decisions through RT or systemic therapy [8].

Other researchers also consider chest wall recurrence (CWR) as a pattern of locoregional recurrence (LRR), including involvement of clavicular or internal mammary lymph nodes [27,28]. Multiple studies report LR rates ranging from 0% to 11.7%, with NAR rates of 0–4.7% (Table 1) [24,29–35].

These findings should be correlated with the tumor's biological behavior and size, its proximity to the NAC, contact with the pectoralis fascia, and the patient's oncological history, such as prior neoadjuvant chemotherapy.

Similar to Yamaguchi, some authors have identified different biological characteristics based on recurrence location [22]. Therefore, all these factors must be incorporated into a multidisciplinary evaluation of the surgical approach.

The implant location is another essential consideration when discussing LR after NSM with prosthetic IBR. With more widespread use of PP-IBR, LR may involve the implant itself, necessitating en bloc removal of the periprost-

Table 1. Evidence table on local recurrence (LR) and nipple-areolar recurrence (NAR) after NSM.

Study	Study type	Sample size	Follow-up	LR rate (%)	NAR rate (%)	Key outcomes
De La Cruz *et al*. (2015) [24]	Meta-analysis	N/A (meta-analysis)	Varied	0–11.7	0–4.7	OS, DFS, LR, NAR; NSM comparable to other mastectomy types in oncologic safety.
Gerber *et al*. (2009) [29]	Prospective study	122	Mean 101.7 months	3.3	2.5	Low recurrence with NAC preservation and autologous reconstruction.
Galimberti *et al*. (2018) [30]	Retrospective cohort	1989	Median 69 months	3.6	1.2	Favorable oncological safety profile of NSM in a large population.
Wu *et al*. (2019) [31]	Retrospective cohort	829	Median 55.1 months	2.8	1.1	Low NAR with good oncologic outcomes post-NSM with IBR.
Sakurai *et al*. (2013) [32]	Single-center cohort	200	Median 80 months	4.5	1.5	Long-term safety of NSM without radiotherapy in selected patients.
Adam *et al*. (2014) [33]	Matched cohort study	337 (NSM group)	Median 53 months	2.7	0.6	NSM is safe in terms of recurrence, matched comparison to traditional mastectomy.
Agresti *et al*. (2017) [34]	Propensity-matched cohort	162	Median 43 months	5.6	2.5	NAC-sparing after chemotherapy feasible and safe in selected cases.
Wadasadawala *et al*. (2017) [35]	Narrative review	N/A	N/A	Varies	Varies	Summary of local/systemic treatment strategies for LR; includes radiotherapy guidance.

Table notes: Inclusion period: Studies published between 1 January 2013 and 31 December 2024. Inclusion criteria: Original research articles in English reporting outcomes of nipple-sparing mastectomy (NSM) with or without immediate breast reconstruction, with available data on local recurrence and nipple–areola complex recurrence rates, sample size, and follow-up duration. Conference abstracts, letters, case reports, and non-English publications were excluded. Abbreviations: N/A, not applicable; OS, overalla survival; DFS, disease free survival; NAC, nipple-areola complex; IBR, immediate breast reconstruction.

Table 2. Diagnostic performance of imaging modalities for detecting local recurrence after conservative mastectomy with immediate breast reconstruction.

Imaging modality	Sensitivity (%)	Specificity (%)	Key notes/indications	Cost-benefit/resource implications
Standard mammography (MG)	55–68%	57–75%	Limited sensitivity and specificity, need for ultrasound integration [37]	Low cost, limited added benefit in reconstructed breasts [37]
Ultrasound (US)	86% (80–90)	96% (95–97)	High specificity and good sensitivity for detecting recurrences [37,43]	Low cost, widely available, operator-dependent, efficient as first-line tool [37,43]
Contrast-enhanced magnetic resonance imaging (MRI)	95% (92–97)	93% (90–95)	Most reliable diagnostic exam; high negative predictive value [37,39,43,46]	High cost, limited availability; excellent in high-risk cases [37,39,43,46]
Positron emission tomography-computed tomography (PET-CT) with 18-Fludeoxyglucose (FDG)	95% (94–97)	86% (82–90)	Indicated for systemic stadiation; lower specificity than US/MRI [43,46,47]	High cost; integrates metabolic and anatomical assessment [43,46,47]

hetic capsule along with the recurrence, and possibly implant removal and replacement [8].
Currently, limited evidence—and especially the lack of extensive prospective studies—has hindered the development of classification systems to aid clinical decision-making regarding LR management after NSM with IBR. Consequently, creating a standardized system is essential to establish more precise variables for future research, which may lead to the development of tailored clinical guidelines.
In this context, a multidisciplinary approach is crucial to ensure that all potential treatment options are thoroughly evaluated and tailored to the patient's specific clinical situation. Each specialist offers unique yet complementary expertise: the breast surgical oncologist assesses resecability, surgical margins, and reconstructive possibilities; the medical oncologist evaluates systemic therapy options, including neoadjuvant and adjuvant treatments, especially for aggressive or recurrent disease; the radiation oncologist determines the need for post-mastectomy or re-irradiation protocols, considering previous radiation and reconstruction factors; the radiologist plays a key role in detecting recurrence and guiding diagnosis through specialized imaging (such as ultrasound, magnetic resonance imaging (MRI), positron emission tomography-computed tomography (PET-CT)); the pathologist provides the definitive diagnosis and insights into tumor biology, informing treatment based on receptor status, grade, and margins; and finally, the plastic and reconstructive surgeon assesses whether implant retention or replacement is feasible or if autologous reconstruction is necessary, balancing aesthetic outcomes with oncological safety. This collaborative approach improves both cancer control and quality of life, supporting truly personalized care.
Building on this rationale, the evidence reviewed in this paper suggests that any future standardized classification system for LR after NSM with IBR should, at a minimum, incorporate the following dimensions:

1. **Anatomical location** – differentiating between nipple–areola complex recurrence, other skin/subcutaneous recurrences, and chest wall invasion;
2. **Relationship to the implant** – particularly whether the recurrence involves the implant capsule, with special consideration in prepectoral implant-based reconstruction;
3. **Tumor biology and prior treatment history** – including hormone receptor/human epidermal growth factor receptor 2 (HER2) status, tumor grade, and prior treatments such as radiotherapy and systemic therapy.

Such a framework could form the basis of a clinically relevant and pragmatic classification, providing a common language for reporting, facilitating comparison between studies, and guiding personalized management strategies in both clinical and research settings.

Diagnosis

The diagnosis of breast cancer recurrence after mastectomy with reconstruction presents unique challenges due to altered anatomy and surgical modifications.
Detection mainly depends on clinical examination, imaging, and, when necessary, tissue biopsy [35].
Historically, the physical examination has been considered the primary method for detecting local recurrence after mastectomy. However, recent advances in breast reconstruction—particularly the use of pre-pectoral implant placement—have raised concerns about how IBR may affect recurrence detection [36].
Clinical surveillance, including physical exams, has proven essential for patients undergoing total mastectomy without reconstruction, and earlier studies have confirmed the reliability of physical exams in managing this patient group [37,38]. Kanavou and colleagues [38] have also proposed physical examination as a surveillance method for reconstructed breasts. The benefit of physical examination lies in the fact that most local recurrences in reconstructed breasts occur in subcutaneous areas or on the skin, making them detectable clinically. However, not all recurrences present clinically, and relying solely on physical examination may limit detection capabilities [39]. Nonetheless, physical exams of reconstructed breasts tend to be less sensitive than those of non-reconstructed breasts because of variable post-operative changes resulting from reconstruction [37,40].
Regarding imaging surveillance, specific guidelines for women who have undergone breast reconstruction are lacking, and the role of mammography in surveillance remains debated [40]. Mammography is generally less effective in this group, especially when implants are used, due to post-surgical distortion [37], although a study suggest that retropectoral implants might help lift the mastectomy flap off the chest wall, improving visualization of underlying tissue [41]. Ultrasonography is frequently used to evaluate suspicious areas because of its effectiveness in detecting locoregional recurrences in reconstructed breasts. Screening ultrasound can identify non-palpable recurrences before they are detectable through physical exams, thus supporting routine ultrasound in early detection of these lesions [42,43]. Breast MRI, known as the most sensitive imaging modality for detecting breast cancers, has been shown to be useful for surveillance after breast conserving surgery in several studies [42,44,45]. However, limited data exist on its utility after mastectomy and reconstruction. Lee *et al*. [39] demonstrated that MRI effectively identifies small ($<$1 cm), asymptomatic recurrent lesions and can detect lesions that ultrasound might underestimate, especially in patients with silicone implants, as it can distinguish scar tissue from recurrent tumors. PET-CT with 18-Fludeoxyglucose (FDG) shows high diagnostic accuracy in detecting recurrent breast cancer, with a sensitivity of 90% and a specificity of 81%, making it a reliable tool for confirming or ruling out recurrence, though its local specificity may be lower than ultrasound or MRI [46,47]. Regardless of the imaging

modality, any suspicious findings or radiological abnormalities should be biopsied [48]. However, concerns remain about whether breast reconstruction complicates the diagnosis of recurrent disease. Chagpar *et al*. [49] studied 155 breast cancer patients with contralateral breast reconstruction after mastectomy, including 27 patients with reconstruction. They found that patients with reconstruction generally had their CWR diagnosed later (median 27.1 versus 22.4 months after mastectomy); however, this difference was not statistically significant ($p = 0.202$) [49]. This suggests that breast reconstruction does not significantly delay recurrence detection or affect prognosis [48,50]. Overall, regular follow-up and patient self-awareness are key to early detection of recurrence. Early diagnosis improves outcomes, and combining advanced imaging with histological analysis offers a comprehensive approach to managing recurrence. The data on the sensitivity, specificity, and cost-effectiveness of each imaging modality are summarized in Table 2 (Ref. [37,39,43,46,47]).

Treatment

The recurrence of breast cancer after IBR poses a complex challenge requiring personalized treatment strategies.

For post-mastectomy patients experiencing recurrences on the chest wall, there are no universally accepted guidelines for subsequent surgical interventions, nor are there established treatment protocols [48,51,52].

Furthermore, the role of breast prostheses in managing patients with recurrent disease has not been thoroughly studied, and its potential impact remains underreported in the literature [48].

Surgical treatment often needs a complex approach and involves a multidisciplinary effort, including collaboration with a plastic surgery team to ensure the best oncologic and reconstructive results [49].

Treatment decisions depend on several factors, such as the location, size, and depth of the recurrent lesion, the condition of residual skin flaps, and whether the patient has previously received radiation therapy [51,53].

It is recommended to achieve a safe oncological resection, regardless of any concurrent muscular involvement [8,35,51,54].

In most cases, chest wall coverage can be obtained with primary closure and the use of local advancement flaps [49].

Therefore, completing a radical mastectomy with concurrent implant removal is not necessary to achieve negative margins, and chest wall coverage can be achieved by reconfiguring the inset of the previously reconstructed breast, as confirmed by McCarthy and colleagues [48].

Alternatively, various myocutaneous flaps, including rectus abdominis flaps, pectoralis major flaps, latissimus dorsi flaps, and external oblique myocutaneous flaps, have been described to obtain chest wall coverage after a CWR [55,56].

The concurrent role of RT in CWR is debated, even on indications and irradiation volumes [57].

Postoperative radiotherapy should be considered for unirradiated locoregional sites and [55] in patients who have undergone post mastectomy radiotherapy (PMRT). In these cases, electron beams or hyperfractionated RT may be used to reduce late side effects on critical structures such as the ribs, heart, and lungs [51].

In a comprehensive review, Ho *et al*. [58] questioned whether the combination of IBR and PMRT could minimize the incidence of complications without compromising oncological or cosmetic outcomes. These findings suggested a potential compatibility between IBR and PMRT. Whereas autologous reconstructions show better tolerance to radiotherapy [58].

PMRT remains a key component of treatment for selected patients after NSM and IBR, especially in cases with high-risk features like positive lymph nodes or close/positive margins. Incorporating PMRT in patients with implant-based reconstruction presents a significant challenge because it can increase the risk of reconstructive complications and cosmetic dissatisfaction.

Recent ESTRO-ACROP consensus guideline offers specific recommendations for target volume delineation in patients receiving PMRT after implant-based IBR. These guidelines promote reducing radiation exposure to reconstructed tissues and using refined contouring techniques, which may help lower complication rates without affecting oncologic outcomes [57].

New data suggest that the updated ESTRO-ACROP criteria could significantly influence complication rates based on the reconstructive technique used. For instance, a 2024 prospective study showed a statistically significant decrease in breast-related complications when PMRT was delivered following the updated ESTRO-ACROP delineation protocols, compared to older contouring standards [59]. Notably, prepectoral reconstructions—which keep the pectoralis major muscle intact—may have a different profile of PMRT-related complications compared to subpectoral techniques, though this remains under investigation.

On the oncologic front, a recent study continues to confirm that PMRT effectively reduces locoregional recurrence and improves disease-free survival in patients with positive lymph nodes or high-risk node-negative disease [60]. However, there is still no consensus on the best timing and sequencing of PMRT in relation to reconstruction, especially when newer systemic therapies such as cyclin-dependent kinase 4/6 (CDK4/6) inhibitors, PARP (poly (ADP-ribose) polymerase) inhibitors, or immune checkpoint inhibitors are used. As emphasized in the latest ESTRO-endorsed consensus [60], multidisciplinary evaluation is crucial to customize PMRT indications and techniques based on each patient's oncologic and reconstructive profile.

Overall, the combination of updated radiotherapy guidelines, reconstruction-specific planning, and emerging systemic therapies highlights the importance of personalized treatment strategies. Effective communication among oncologic surgeons, radiation oncologists, and plastic surgeons is vital to optimize both cancer control and reconstructive results in this continually evolving treatment landscape.

Conclusions

NSM, combined with IBR, has become a key part of modern breast cancer surgery, offering an optimal balance between cancer control and aesthetic preservation.

Although relatively rare, local recurrence remains an ongoing clinical challenge. This review summarizes current knowledge on local recurrence after NSM with IBR, emphasizing the potential benefits of a structured, multidimensional classification system that could support personalized treatment planning, enhance consistency in clinical practice, and facilitate future research efforts.

The unique contribution of this work lies not only in collecting and integrating the available evidence, but also in proposing, for the first time, three key dimensions—anatomical location, relationship to the implant, and tumor biology/prior treatment history—that should form the foundation of a future classification system.

Recognizing the value of this approach may enhance communication among multidisciplinary teams, standardize reporting in clinical studies, and ultimately contribute to the development of evidence-based guidelines.

Nevertheless, prospective validation remains essential to assess its clinical significance and to improve recurrence management strategies in this specific surgical setting. In this context, a multidisciplinary approach is vital to ensure all treatment options are considered for optimal patient outcomes.

Abbreviations

BC, breast cancer; BCS, breast conserving surgery; RT, radiotherapy; SSM, skin-sparing mastectomy; LR, local recurrence; IBR, immediate breast reconstruction; NAC, nipple-areola complex; NAR, nipple-areolar recurrence; oLR, other local recurrence; CWR, chest wall recurrence; MRI, magnetic resonance imaging; PET-CT, positron emission tomography-computed tomography; PMRT, post mastectomy radiotherapy.

Availability of Data and Materials

Not applicable.

Author Contributions

Conceptualization: AMS, FDL. Methodology: VC, AM, SDA. Validation: AMS, GF. Investigation: EP, ADP, EDG. Resources: ES, AB, CVP, GDA, LS, SDA. Data curation: EDG, ES. Writing—original draft preparation: FDL, AB, CVP. Writing—review and editing: AMS, FDL, LS. Visualization: FDL, NB, LS. Supervision: GF, AMS, LS. Project administration: AMS, FDL. Conception and design of the study: ES, AB, CVP, GDA. All authors have been involved in revising it critically for important intellectual content. All authors gave final approval of the version to be published. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

Alejandro Martin Sanchez and Gianluca Franceschini are serving as the Editorial Board members of this journal. We declare that Alejandro Martin Sanchez and Gianluca Franceschini had no involvement in the peer review of this article and has no access to information regarding its peer review. Other authors declare no conflict of interest.

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