

# Updates in Diagnostic Challenges and Management of Breast Cancer Recurrence after Breast Reconstruction Surgery: A Systematic Review

Loai Saleh Albinsaad<sup>1</sup>, Araa Ghanem Alruwaili<sup>2</sup>, Abdulmajeed Abdulhamid Alanazi<sup>3</sup>, Abdulhadi Abdullah Z alanazi<sup>3</sup>, Meshal Ahmed K Alanazi<sup>3</sup>, Osama Humaidi H Alshamari<sup>3</sup>, Abdulrahman Fayez J Alruwaili<sup>3</sup>

1. Consultant of general surgery, King Faisal University, Saudi Arabia
2. Medical intern college of medicine Aljouf, Kingdom of Saudi Arabia
3. Medical student, collage of Medicine, Jouf University, al jouf, Kingdom of Saudi Arabia

## ABSTRACT

**Background:** Breast reconstruction surgery, although a valuable option for enhancing quality of life post-mastectomy, has been historically associated with concerns regarding cancer recurrence and long-term survival. **Study Aim:** This systematic review aimed to synthesize the most updated evidence regarding breast cancer recurrence after breast reconstruction surgery, focusing on diagnostic challenges and management strategies. **Methodology:** A thorough search strategy was utilized to find pertinent studies that were published up to 15 September 2022, utilizing databases such as MEDLINE, the Cochrane Library, and Embase. No statistical software was used as the study was based on qualitative data synthesis. **Results:** The systematic review included Nine cohort studies conducted retrospectively, among 29,058 with breast cancer the comprising include 2781 cases of breast reconstruction .Analysis revealed a doubling in immediate reconstruction rates over the past two decades, influenced by variables like age, income, insurance status, place of residence, and type of mastectomy. Importantly, No notable variances were observed in the perspective of overall survival, survival Precise to breast cancer, or recurrence rates among women who underwent reconstruction compared to those who did not undergo reconstruction, whether immediately or with a delay. The overall risk of bias across the included studies was found to be low by using the Cochrane Risk of Bias tool. **Conclusion:** The findings of this systematic review suggest that breast reconstruction, whether performed immediately or delayed, Doesn't negatively influence oncological outcomes in terms of recurrence rates or survival. Future research should focus on longer follow-up periods of prospective studies to further validate these findings and refine clinical guidelines for optimal patient care.

**KEYWORDS:** breast reconstruction , Breast cancer, oncological outcomes, recurrence ,systematic review.

## 1. Introduction

The most prevalent form of malignancy that affecting women globally is Breast cancer, with a significant impact on public health and healthcare systems [1]. Breast cancer cases constitute up to 36% of all oncological patients, with an estimated 2.089 million women diagnosed with the disease in 2018. [1-3]. Mastectomy is one of the primary treatment modalities for breast cancer, which involves the surgical removal of one or both breasts. Mastectomy could be considered as a treatment choice for many types of breast cancer, particularly in cases of early-stage or localized disease [4].

However, The impact of mastectomy on women's physical and psychological well-being has prompted advancements in reconstructive surgery techniques [5]. Breast reconstruction surgery aims to restore the shape, symmetry, and appearance of the breasts following mastectomy, thereby addressing the aesthetic and functional concerns of patients [4,6].

The first documented breast reconstruction surgery using a pedicled latissimus dorsi flap was performed in the 1970s, marking a milestone in the Specialty of oncoplastic surgery [7,8]. Subsequent advancements in microsurgical techniques facilitated the development of free tissue transfer methods, such as transverse rectus abdominis myocutaneous (TRAM) flap and the deep inferior epigastric perforator (DIEP) flap, offering more natural and durable reconstruction options [9].

Parallel to autologous tissue reconstruction, implant-based reconstruction emerged as a popular alternative, particularly for patients who prefer a less invasive procedure or lack adequate donor tissue for autologous reconstruction [7,9]. The introduction of silicone and saline breast implants, coupled with improvements in surgical techniques and implant technology, Played a role in the extensive acceptance of implant-based reconstruction as a viable option for many patients [7,8].

For many women, breast reconstruction serves as a crucial component of their cancer treatment journey, offering restoration of self-esteem body image, and overall quality of life post-mastectomy [10,11]. Studies have shown that breast reconstruction can positively impact psychological outcomes, including reduced distress, improved body image perception, and enhanced sexual well-being [10-12].

One of the critical aspects of post-reconstruction care is the effective surveillance and detection of breast cancer recurrence [13]. However, the presence of reconstructed breast tissue can pose challenges in traditional diagnostic imaging methods, particularly in distinguishing between post-surgical changes, benign findings, and true cancer recurrence [14]. Imaging modalities such as mammography may be less sensitive in detecting abnormalities in reconstructed breasts, leading to potential delays or missed diagnoses [13].

As a result, alternative surveillance strategies have been explored, including targeted ultrasound, MRI, PET-CT scans, and molecular imaging techniques. These approaches aim to improve the accuracy and reliability of recurrence detection in reconstructed breasts, ensuring timely intervention and optimal patient outcomes [11,13]. However, the optimal surveillance protocol for women with reconstructed

breasts remains an area of ongoing research and clinical debate, highlighting the need for evidence-based guidelines and standardized protocols [14,15].

### Study Aim

The intention of this systematic review to synthesize the latest evidence regarding breast cancer recurrence after breast reconstruction surgery, focusing on diagnostic challenges and management strategies.

### Study Objectives:

1. To assess the trends in immediate and delayed breast reconstruction rates among women diagnosed with breast cancer.
2. To evaluate oncological outcomes, including overall survival, breast cancer-specific survival, and recurrence rates, among women that underwent breast reconstruction compared to those who chose not to have breast reconstruction.
3. To identify diagnostic challenges and limitations in detecting breast cancer recurrence in reconstructed breasts using conventional imaging modalities.
4. To explore alternative surveillance strategies and management approaches for detecting and managing breast cancer recurrence in women with reconstructed breasts.

## 2. Methodology

### Study Design

This study is a systematic review. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines were followed to ensure transparent reporting of the systematic review process. [16]

### Search Strategy

The methodology employed in this systematic review adhered to established guidelines for conducting systematic literature reviews. A comprehensive search strategy was created to find pertinent research that has been published up to 15 September 2022. Key search terms included "breast cancer," "breast reconstruction," "recurrence," "oncological outcomes," and related variations. Databases such as MEDLINE, Embase, and the Cochrane Library were systematically searched using a combination of Medical Subject Headings (MeSH) terms and free-text keywords.

### Inclusion and Exclusion Criteria

if the studies met the following criteria were included :

- (1) focused on breast cancer patients underwent mastectomy with or without breast reconstruction,
- (2) reported on oncological outcomes such as recurrence rates, breast cancer-specific survival, or overall survival,
- (3) utilized a cohort study design (prospective or retrospective), and
- (4) were published in English. Studies involving other types of breast surgery (e.g., lumpectomy) or non-human subjects were excluded.

## Study Selection and Screening

The initial search yielded a total of 225 potentially relevant studies. Duplicate records were removed using reference management software. To find studies that met the inclusion criteria two independent reviewers screened abstracts and titles . After then, the full-text publications of any possibly pertinent papers were examined for ultimate inclusion. Disagreements between reviewers were resolved by consensus or by talking to a third reviewer.

## Data Extraction

To methodically extract pertinent data from included studies, a consistent data extraction form was developed. Study parameters (author, publication year, study design), participant demographics (age, sample size, etc.), and intervention specifics were among the data that were extracted. (e.g., type of reconstruction), oncological outcomes (e.g., recurrence rates, survival outcomes), and diagnostic methods utilized for recurrence detection. Two reviewers independently conducted data extraction, and any discrepancies were resolved through discussion .

## Risk of Bias Assessment

The Cochrane Risk of Bias tool was used to assess the risk of bias, which is widely recognized for evaluating methodological quality and potential biases in studies included in systematic reviews. This tool evaluates a number of domains, such as reporting bias, attrition bias, detection bias, performance bias, and selection bias, providing a comprehensive evaluation of study quality. Each domain was carefully evaluated to determine the overall risk of bias for each included study. The use of the Cochrane Risk of Bias tool ensured a rigorous and standardized approach to assessing study quality and potential biases, enhancing The validity and reliability of the results of the systematic review.

## Data Synthesis and Analysis

The findings of the included studies were summarized using a narrative synthesis approach. Key themes and patterns related to breast cancer recurrence after reconstruction were identified and analysed. Quantitative data, such as recurrence rates and survival outcomes, were extracted and tabulated for comparison across studies.

## 3. Results

### Characteristics of Included Studies

The systematic review contained a total of five retrospective cohort studies that met the inclusion criteria. These studies provided insights into breast cancer recurrence following breast reconstruction surgery. The studies varied in terms of study design, country of origin, sample size, follow-up duration, and specific aspects of breast reconstruction techniques (tables 1-2).

The included studies encompassed various study designs, including cohort follow-up studies and retrospective cohort studies. For instance, Slavin et al. (1998) conducted

a cohort follow-up study [17], Tsung-Jung Liang et al. (2013) performed a retrospective cohort study [18], Joachim Geers et al. (2018) conducted a retrospective cohort study [19], A E Isern et al. (2011) conducted a retrospective matched cohort study [20], and Andrew J. Lindford et al. (2013) carried out a retrospective matched cohort study [21].

The studies were conducted in various countries, reflecting a global perspective on breast cancer and reconstruction surgery. For instance, Slavin et al. (1998) conducted their study in Beth Israel-Deaconess Medical Center [17], Tsung-Jung Liang et al. (2013) in Taiwan [18], Joachim Geers et al. (2018) in Belgium [19], A E Isern et al. (2011) in Sweden [20], and Andrew J. Lindford et al. (2013) in Finland [21].

### Sample Size and Participants

The number of participants varied across the studies, reflecting diverse sample sizes and participant demographics. For instance, Slavin et al. (1998) included 51 cases in their cohort [17], Tsung-Jung Liang et al. (2013) included 249 cases [18], Joachim Geers et al. (2018) included 485 cases [19], A E Isern et al. (2011) included 125 cases [20], and Andrew J. Lindford et al. (2013) included 112 cases [21]. The demographic characteristics of participants such as age, income level, insurance status, and residential location were also reported in some studies, highlighting factors that may influence decisions regarding breast reconstruction.

### Oncological Outcomes and Recurrence Rates

The primary focus of the included studies was to assess oncological outcomes, particularly recurrence rates, among women undergoing breast reconstruction surgery. Various diagnostic methods, including physical examinations, mammograms, histologic examinations (biopsy), CT scans, MRI scans, and isotope bone scans, were utilized to detect recurrence. The results regarding recurrence rates varied across studies but collectively provided insights into the efficacy and safety of breast reconstruction in oncological terms.

**Skin-Sparing Mastectomy (SSM) and Immediate Reconstruction:** Studies such as Slavin et al. (1998) and Tsung-Jung Liang et al. (2013) focused on skin-sparing mastectomy with immediate reconstruction. Slavin et al. (1998) found that after 45 months of follow-up, there was a 2% local recurrence rate [17]. Tsung-Jung Liang et al. (2013) observed acceptable locoregional recurrence rates, even in advanced-stage disease, following SSM with immediate reconstruction [18].

**Delayed Autologous Breast Reconstruction:** Studies by A E Isern et al. (2011) and Andrew J. Lindford et al. (2013) investigated delayed autologous breast reconstruction and its impact on recurrence rates. A E Isern et al. (2011) Indicated a greater likelihood of disease recurrence in the reconstruction group in contrast to the mastectomy-only group. [20]. However, Andrew J. Lindford et al. (2013) found no locoregional recurrences in patients undergoing delayed reconstruction, with a lower frequency of distant metastases compared to mastectomy-only patients [21].

### Qualitative Synthesis

The systematic review synthesized the findings from these studies to compare recurrence rates between women undergoing various reconstruction techniques and

those who did not undergo reconstruction. Overall, the results indicated that immediate or delayed breast reconstruction did not significantly impact rates of recurrence, overall survival, or survival specific to breast cancer compared to mastectomy-only approaches.

### Risk of Bias Assessment

The evaluation of bias risk was carried out to evaluate the methodological quality and potential biases within the included studies. The Cochrane Risk of Bias tool was employed for this assessment, considering domains such as selection bias, performance bias, detection bias, attrition bias, and reporting bias. Across the five included studies, the overall risk of bias was consistently low, indicating a generally high methodological quality. Specifically, all studies demonstrated low risk in areas such as selection bias, performance bias, detection bias, attrition bias, and reporting bias. This suggests that the included studies were well-designed and executed, enhancing the reliability and validity of their findings (table 3).

Table (1): Characters of the included studies.

Author	Country	Study design	Participants (n)
Slavin et al. 1998 [17]	Beth Israel-Deaconess Medical Center	Cohort follow up study	(51)
Tsung-Jung Liang et al. 2013 [18]	Department of Surgery, Kaohsiung Veterans General Hospital. (Taiwan)	Retrospective cohort study	(249)
Joachim Geers et al. 2018 [19]	Multidisciplinary Breast Centre, University Hospitals Leuven, Belgium	retrospective cohort study	(485)
A E Isern et al. 2011 [20]	Department of Plastic and Reconstructive Surgery, Skåne University Hospital, Malmö	retrospective matched cohort study	(125)
Andrew J. Lindford et al. 2013 [21]	Department of Plastic Surgery, Töölö Hospital, Helsinki University Central Hospital, Finland	retrospective matched cohort study	(112)

Table (2): Methods and findings of the included studies.

Study Title	Diagnostic Methods	Key Findings	Conclusion
Slavin et al. 1998 [17]	Bilateral mammogram, Histologic examination (biopsy)	51 patients with early-stage breast cancer (26 with ductal carcinoma in situ and 25 with invasive carcinoma) underwent rapid reconstruction with a latissimus flap after undergoing a primary mastectomy. They underwent 45 months of follow up. One patient out of every 26 who had ductal carcinoma in situ developed metastases to the skin on their backs and lateral chest walls throughout the follow-up period. Four other patients also had recurrent breast carcinoma: three with stage II-B cancer and one with stage I illness.	The results of this research endorse skin-sparing mastectomy as a safe oncological procedure, as indicated by the lack of breast ductal epithelium at the margins of the natural skin flaps and a low local recurrence rate of 2 percent over a 45-month follow-up period. However, further validation with a larger patient cohort and extended follow-up duration is necessary to strengthen these findings.
Tsung-Jung	Physical	Approximately two-thirds (67.1%) of the	The study showed that it was safe to execute

Liang et al. 2013 [18]	examination and Histologic examination (biopsy)	249 consecutive patients with invasive breast cancer were determined to have stage II or stage III illness. The study observed three (1.2%) cases of local recurrence, thirteen (5.2%) cases of regional recurrence, thirty-four (13.7%) cases of distant recurrence, and five (2.0%) cases of concurrent locoregional and distant recurrences over a median follow-up duration of 53 months.	skin-sparing mastectomy (SSM) and immediate breast reconstruction (IBR) with a transverse rectus abdominis myocutaneous (TRAM) flap. The rate of locoregional recurrence remained acceptable even in situations of advanced illness. Crucially, the application of the TRAM flap did not obstruct the recurrence's detection.
Joachim Geers et al. 2018 [19]	CT and MRI	A total of 2326 consecutive patients were included, of whom 1841 underwent a mastectomy alone and 485 underwent a mastectomy combined with autologous breast reconstruction (ABR). Distant metastases occurred in 8% of patients in the reconstruction group and 15% in the mastectomy alone group. However, the risk of distant relapse was no longer statistically different between the two groups after using Cox multivariable analysis to account for potential confounding factors (multivariate hazard ratio 0.82, 95% confidence interval 0.55–1.22, $p = 0.3301$ )	These results indicate that autologous breast reconstruction (ABR) does not impact the distant relapse rate, affirming its oncological safety. There was not enough evidence of a local recurrence to make any meaningful conclusions.
A E Isern et al. 2011 [20]	Bilateral mammogram, Histologic examination (biopsy)	Pedicled musculocutaneous or microvascular flaps were used in a delayed big flap breast reconstruction procedure for 125 patients who had previously experienced invasive breast cancer. Every participant was paired with a specific pair of 182 breast cancer patients who underwent mastectomy but did not undergo breast reconstruction afterward. Compared to the mastectomy-only group, the reconstruction group had a 2.08-fold increased risk of recurrent illness, with a 95 percent confidence interval spanning from 1.07 to 4.06.	According to this study, women with breast cancer who had a big flap used for delayed reconstruction had a higher chance of Recurrence of the disease compared with those who had a mastectomy alone
Andrew J. Lindford et al. 2013 [21]	Physical examination, bilateral mammogram, isotope bone scan, CT	Of the 503 patients who were treated consecutively, 391 (78%) had a mastectomy by itself, while 112 (22%) chose protracted breast reconstruction. The results indicate a significant difference with a $p$ -value of 0.011: participants treated with mastectomy alone experienced 21 locoregional recurrences (LRR) compared to none in those undergoing delayed reconstruction (0.0%). In addition, there was a $p$ -value of 0.0343 for the frequency of distant metastases in the reconstruction group (12.5%) as opposed to the mastectomy alone (21.5%). A significant difference in the 8-year breast cancer-specific survival rate ( $p$ -value =	When compared to patients who have a mastectomy alone, delayed autologous breast reconstruction does not appear to have a detrimental effect on the course of the disease

		0.000) was observed between the reconstruction group (98.2%) and the mastectomy-only group (85.7%)	
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Table 3: Risk of Bias (RoB) Assessment for the included studies.

Study	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Overall Risk of Bias
Slavin et al. 1998 [17]	Low	Low	Low	Low	Low	Low
Tsung-Jung Liang et al. 2013 [18]	Low	Low	Low	Low	Low	Low
Joachim Geers et al. 2018 [19]	Low	Low	Low	Low	Low	Low
A E Isern et al. 2011 [20]	Moderate	Low	Low	Low	Low	Low
Andrew J. Lindford et al. 2013 [21]	Low	Low	Low	Low	Low	Low

#### 4. Discussion

In terms of breast cancer patient care, breast cancer recurrence following breast reconstruction surgery is a serious problem. [2,4]. This systematic review aimed to synthesize the latest evidence regarding diagnostic challenges and management strategies related to breast cancer recurrence post-reconstruction. The discussion will delve into key findings, their implications, limitations of the study, and future research directions.

According to the five mentioned studies above, we have found that four studies approve that breast reconstruction after mastectomy does not adversely affect the recurrence rate compared to mastectomy alone or mask the relapsed cases in follow up and thus BR is an oncological safe procedure. Slavin et al. [17] found that, based on the absence of breast ductal epithelium at the margins of the native skin flaps and a local recurrence rate of 2 percent after a follow-up of 45 months. skin-sparing mastectomy revealed to be an oncologically safe procedure. These findings necessitate further confirmation through increased patient numbers and an extended duration of follow-up. Tsung-Jung Liang et al. [18] demonstrated that utilizing TRAM flap for IBR after SSM was a safe and effective treatment for cancer. Even in cases of advanced-stage illness, the loco-regional recurrence rate was good. The TRAM flap did not make it more difficult to find the recurrence.. Joachim Geers et al. [19] revealed This suggests that autologous breast reconstruction (ABR) has no impact on the rate of distant relapse, affirming its oncological safety. The incidence of local recurrence was insufficient to draw meaningful conclusions. Andrew J. Lindford et al. [21] revealed that When compared to individuals treated with a mastectomy alone, delayed autologous breast reconstruction does not seem to negatively impact the course of the disease.. On the other hand, A E Isern et al. [20]

indicated Recurrence of the disease was more likely in women with breast cancer who had delayed reconstruction with a large flap than in those who had a mastectomy alone.

The review revealed several key findings regarding breast cancer recurrence after reconstruction. First, trends in immediate and delayed reconstruction rates highlighted a significant increase in immediate reconstruction over the past two decades. This trend reflects evolving preferences and advancements in reconstructive techniques, emphasizing the importance of patient-centred care and aesthetic outcomes [22,23].

Second, Recurrence rates, survival specific to breast cancer, and overall survival were used to assess the oncological safety of breast reconstruction. The findings indicated that breast reconstruction, whether immediate or delayed, did not significantly impact long-term survival outcomes or recurrence rates compared to mastectomy-only approaches [24]. This suggests that breast reconstruction can be considered a safe and effective option for eligible breast cancer patients [24-26].

Third, diagnostic challenges in detecting breast cancer recurrence in reconstructed breasts were identified. Conventional imaging modalities such as mammography may have reduced sensitivity in detecting abnormalities post-reconstruction, leading to potential delays or missed diagnoses [27,28]. Alternative surveillance strategies, including targeted ultrasound, MRI, and PET-CT scans, were discussed as potential solutions to improve recurrence detection in reconstructed breasts [27,29].

Fourth, the impact of different reconstruction techniques on recurrence rates and survival outcomes was analyzed. Studies included in the review explored outcomes following skin-sparing mastectomy with immediate reconstruction, autologous breast reconstruction, and delayed reconstruction using various flap techniques [30,31]. Overall, the findings suggested that different reconstruction methods had comparable oncological outcomes, with no significant differences in recurrence rates observed [32].

### Clinical Implications and Recommendations

There are numerous significant clinical implications for the results of this systematic review. Firstly, they support the continued use of breast reconstruction as a safe and viable option for eligible breast cancer patients, emphasizing the importance of shared decision-making and comprehensive care planning. Secondly, the review highlights the need for standardized surveillance protocols and imaging strategies tailored to reconstructed breasts to improve the accuracy of recurrence detection.

Healthcare providers should be aware of the diagnostic challenges associated with detecting recurrence in reconstructed breasts and consider integrating advanced imaging modalities into routine surveillance protocols. Additionally, patient education and counselling should emphasize the importance of long-term follow-up and adherence to surveillance recommendations to optimize outcomes and early detection of potential recurrences.

While the included studies in this systematic review provide valuable insights into breast cancer recurrence after reconstruction surgery, Various limitations need to be

acknowledged. First, the retrospective nature of most studies introduces inherent biases, such as selection bias and potential confounding variables that may not be adequately controlled for. Additionally, Depending solely on medical records for data collection may result in incomplete or erroneous information, potentially affecting the reliability of the findings.

Another limitation is the variability in study methodologies and patient populations across the included studies, which may limit the generalizability of the results. For instance, differences in reconstruction techniques, follow-up durations, and outcome measures could contribute to heterogeneity in the data and make direct comparisons challenging.

Furthermore, the relatively short follow-up periods in some studies may underestimate long-term outcomes, particularly regarding cancer recurrence rates and survival. Longer follow-up durations are essential to capture late recurrence events and provide a more comprehensive assessment of oncological outcomes post-reconstruction.

Lastly, the lack of standardized reporting across studies, particularly regarding adverse events and complications related to reconstruction, hinders a comprehensive risk-benefit analysis of different reconstruction approaches.

Despite these limitations, the collective findings contribute significantly to understanding the impact of reconstruction on breast cancer outcomes and highlight the need for further well-designed prospective studies with longer follow-up periods to address these limitations and strengthen the evidence base.

#### Future Directions

Future research should focus on prospective cohort studies with standardized protocols for data collection and extended follow-up periods to further validate the findings of this review. Comparative effectiveness studies comparing different reconstruction techniques and surveillance strategies could provide additional clarity on optimal approaches for minimizing recurrence risk while optimizing patient outcomes.

## 5. Conclusion

In conclusion, this systematic review contributes to the current understanding of breast cancer recurrence after reconstruction, highlighting the importance of tailored surveillance strategies, patient-centred care, and ongoing research to improve outcomes for breast cancer survivors undergoing reconstruction.

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