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Review Article

Factors Associated with Immediate Complications After Mastectomy with Axillary Lymph Node Dissection for Breast Cancer: A Systematic Review from 2016 to 2025

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Abstract

Mastectomy with axillary lymph node dissection (ALND) remains the standard operation for breast cancer in many low-resource settings, but it carries substantial early morbidity. This systematic review aimed to identify the frequency of immediate (30-day) complications after mastectomy with ALND and the factors associated with their occurrence. Following the PRISMA 2020 statement, PubMed, Google Scholar and Research Rabbit were searched for studies published between 1 January 2016 and 31 December 2025 (last search on 18 May 2026). Cohort, case-control, cross-sectional and randomized studies of women with breast cancer undergoing mastectomy with ALND, published in English or French and reporting immediate complications and associated factors, were eligible. After removal of duplicates, records were screened on title and abstract and then on full text; risk of bias was assessed with the Newcastle-Ottawa Scale, the Joanna Briggs Institute checklist and the Cochrane RoB 2 tool, and, because of marked heterogeneity, results were synthesized narratively. Of 2,251 records identified, 27 studies from 15 countries were included (19 cohort studies, 6 randomized controlled trials and 2 cross-sectional studies), only 4 of which were conducted in Africa. Seroma was the most frequent complication: in the 18 studies that reported an overall incidence, it ranged from 19.5% to 71.1% (median 29.4%). It was followed by surgical site infection (3.9–30%), haematoma (2.7–8.6%), wound dehiscence (2.9–5.5%) and skin flap necrosis (3.0–6.7%). Four factors were consistently associated with complications and confirmed in multivariable analyses: older age, high body mass index, extent of axillary dissection and prolonged operative time. Diabetes, smoking and hypertension were mainly associated with infection, whereas early drain removal and high early drainage volume were associated with seroma. Dead-space obliteration (quilting), advanced haemostatic devices, axillary exclusion and lymphatic-sparing techniques reduced seroma in individual studies. Seroma and surgical site infection therefore dominate the early morbidity of mastectomy with ALND. Distinguishing non-modifiable factors (age, tumour burden), which identify high-risk patients, from modifiable ones (obesity, glycaemic control, smoking, surgical technique and drain management) provides concrete targets for prevention in resource-limited settings, where prospective African studies with harmonized definitions are now needed.

Keywords

Breast Cancer, Mastectomy, Axillary Lymph Node Dissection, Seroma, Surgical Site Infection, Postoperative Complications, Risk Factors, Systematic Review

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1. Introduction

Breast cancer is the most frequently diagnosed cancer in women worldwide. According to the Global Cancer Observatory (GLOBOCAN) 2022 estimates, it accounted for an estimated 2.30 million new cases and about 670,000 deaths, making it also the leading cause of cancer death among women [1]. Incidence is highest in countries with a very high human development index, whereas mortality is highest in low-development settings [2]. In Burkina Faso, 1,372 new cases and 818 deaths were estimated in 2022, accounting for 15.3% of cancers in women and giving a mortality-to-incidence ratio of about 0.60 [1]. As in other sub-Saharan African countries, most patients are diagnosed at a locally advanced stage, because of the absence of organized screening, socio-cultural barriers and limited treatment resources [3, 4].

The management of breast cancer is multidisciplinary and combines locoregional treatment (surgery and radiotherapy) with systemic treatment (chemotherapy, endocrine therapy, targeted therapy and immunotherapy) [5]. While breast-conserving surgery followed by radiotherapy has become the standard in high-income countries, modified radical mastectomy with level I–II axillary lymph node dissection (ALND) remains the most frequent operation in low- and middle-income countries, because of late diagnosis and limited access to radiotherapy [6, 7]. This operation provides oncological safety but carries substantial morbidity. Early complications include seroma, haematoma, surgical site infection (SSI), skin flap necrosis, wound dehiscence and sensory disturbances due to nerve injury; reported frequencies range from 15% to 52% for seroma, 5% to 25% for wound infection, 2% to 10% for haematoma and 2% to 15% for flap necrosis [7].

Seroma is a sterile collection of serous fluid under the skin flaps or in the axilla. The division of lymphatic vessels during dissection, the large dead space left after surgery and early mobilization of the shoulder all promote fluid accumulation [8]. Its origin, lymphatic or inflammatory, is still debated [9]. Seroma increases the risk of infection, delays healing, promotes flap necrosis and dehiscence, prolongs convalescence and may delay adjuvant treatment [10]. It is also associated with a higher risk of later lymphoedema (odds ratio, OR 1.46) [11]. Suction drains are widely used, but their optimal duration remains debated, and several techniques have been proposed to reduce seroma, including flap fixation, advanced energy devices, fibrin sealants and shoulder immobilization [8, 9].

To our knowledge, no recent systematic review has specifically synthesized the factors associated with immediate complications after mastectomy combined with ALND. This gap limits the surgeon's ability to identify high-risk patients and to target preventive measures, particularly in low-resource settings where this operation remains the standard of care and where many risk factors may be modifiable before or during surgery.

The aim of this systematic review was therefore to identify, in studies published between 1 January 2016 and 31 December 2025, the frequency of immediate complications after mastectomy with ALND for breast cancer and the factors associated with them, to assess the quality of the available evidence, and to derive practical recommendations for surgical practice.

2. Methodology

2.1. Protocol and Reporting

This systematic review was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement [12]. It was carried out as part of a specialist diploma (Diplôme d'Études Spécialisées, DES) dissertation in Obstetrics and Gynaecology at Joseph KI-ZERBO University, Ouagadougou. The protocol was not registered in a public register such as the International Prospective Register of Systematic Reviews (PROSPERO).

2.2. Eligibility Criteria

Eligibility was defined with the PICO (Population, Intervention, Comparator, Outcome) framework. Population: women with breast cancer. Intervention/exposure: mastectomy with ALND. Comparator: mastectomy without ALND, or another surgical technique, when available. Outcome: occurrence of immediate postoperative complications and their associated factors. Cohort studies, case-control studies, cross-sectional studies and clinical trials published between 1 January 2016 and 31 December 2025, in English or French and conducted in an appropriate clinical setting, were included.

Studies were excluded if they dealt exclusively with sentinel lymph node biopsy or breast-conserving surgery, did not report ALND separately from other axillary procedures, were conducted in animals, or were not available in full text.

2.3. Information Sources and Search Strategy

PubMed, Google Scholar and Research Rabbit were searched. The last search was run on 18 May 2026. Search equations combined, with the Boolean operator AND, four conceptual blocks: the surgical procedure (mastectomy, modified radical mastectomy), the axillary procedure (axillary lymph node dissection, axillary clearance, ALND), the complications (complications, morbidity, seroma, haematoma, surgical site infection, nerve injury) and the risk factors (risk factors, predictors, comorbidities, age, body mass index (BMI), smoking, tumour stage, neoadjuvant therapy), together with the disease (breast cancer, breast neoplasms). Two equations were used in Google Scholar and two in PubMed, one of them restricted to the [Title/Abstract] field. The Research

Rabbit equation, written in English and French, extended the search to tumour characteristics, adjuvant treatment and operative parameters. The PubMed equation was: (mastectomy [Title/Abstract] OR "modified radical mastectomy") AND ("axillary lymph node dissection"[Title/Abstract] OR "axillary dissection" OR ALND) AND (complications OR morbidity) AND ("risk factors" OR predictors OR age OR BMI OR comorbidities OR smoking OR "tumor stage" OR "neoadjuvant therapy") AND "breast neoplasms". The full equations for each source are available as supplementary material.

2.4. Selection Process

All records retrieved from the three sources were exported to Zotero version 8 and pooled, and duplicates were removed. Selection then proceeded in two stages. First, titles and abstracts were screened against the eligibility criteria, and clearly irrelevant records were excluded. Second, the full texts of potentially eligible reports were read, and the reason for each exclusion was recorded; the numbers of records at each stage are reported in the PRISMA flow diagram (Figure 1). Screening was performed by one reviewer (Yaogo Kiswendsida Gaetan Raoul).

2.5. Data Extraction

Data were extracted by the same reviewer with a standardized form, piloted on the first included studies, that recorded: first author, year of publication, country, study design, sample size, mean age, definition and frequency of each immediate complication, factors examined with their measures of association (odds ratio [OR], risk ratio or p value), whether each association came from a univariable or a multivariable analysis, and the authors' conclusions. When a sample size or an incidence was not reported directly, it was derived from the published percentages and flagged as such (Table 1). Factors were classified into three groups: patient-related, tumour-related, and treatment- and surgery-related.

2.6. Risk of Bias Assessment

The methodological quality of each study was assessed with a tool adapted to its design: the Newcastle-Ottawa Scale (NOS) for cohort studies (maximum 9 stars; good 7–9, fair 6, moderate 5, high risk of bias ≤ 4) [13]; the Joanna Briggs Institute (JBI) 8-item checklist for analytical cross-sectional studies (good ≥ 7 "yes", moderate 4–6, poor ≤ 3) [14]; and the Cochrane Risk of Bias 2 (RoB 2) tool for randomized controlled trials [15].

2.7. Synthesis

Heterogeneity was assessed qualitatively at three levels: clinical (definitions of complications, in particular clinical versus ultrasound diagnosis of seroma, populations and types of surgery), methodological (study designs, follow-up periods and adjustment for confounders) and statistical (thresholds, effect measures and outcome reporting). Because this heterogeneity was marked and many studies did not report comparable effect estimates, no meta-analysis was performed and no pooled estimate or statistical test of heterogeneity was computed. Results were synthesized narratively and summarized in tables, grouped by complication and by category of factor. For each complication, the range and median of the reported incidences were described. For each factor, we report the number of studies that evaluated it, the number that found a statistically significant association (vote counting based on the direction and significance of the reported effect), and the reported OR. Associations confirmed by multivariable analysis were distinguished from simple (univariable) associations, and the risk-of-bias assessment was considered when judging the consistency of the evidence.

2.8. Operational Definitions

Immediate (early) complication: any complication occurring during hospital stay or within 30 days of surgery. *Seroma:* accumulation of serous fluid under the skin flaps or in the axilla, detected clinically (fluctuant swelling) and/or by ultrasound, in the absence of bleeding or infection. *Surgical site infection:* superficial or deep incisional, or organ/space infection occurring within 30 days of surgery. *Haematoma:* collection of blood at the operative site, detected clinically and/or by ultrasound, which may require surgical evacuation or transfusion. *Associated factor:* a characteristic whose presence is statistically associated with the occurrence of the outcome, without necessarily implying causality.

2.9. Ethical Considerations

This review was based exclusively on published, aggregated data, without contact with patients or access to identifiable individual data; it therefore did not require ethics committee approval.

3. Results

3.1. Study Selection

The search identified 2,251 records. After removal of 1,069 duplicates, 1,182 records were screened on title and abstract, and 1,095 were excluded. Of the 87 full-text reports assessed, 60 were excluded and 27 studies were included in the review (Figure 1).

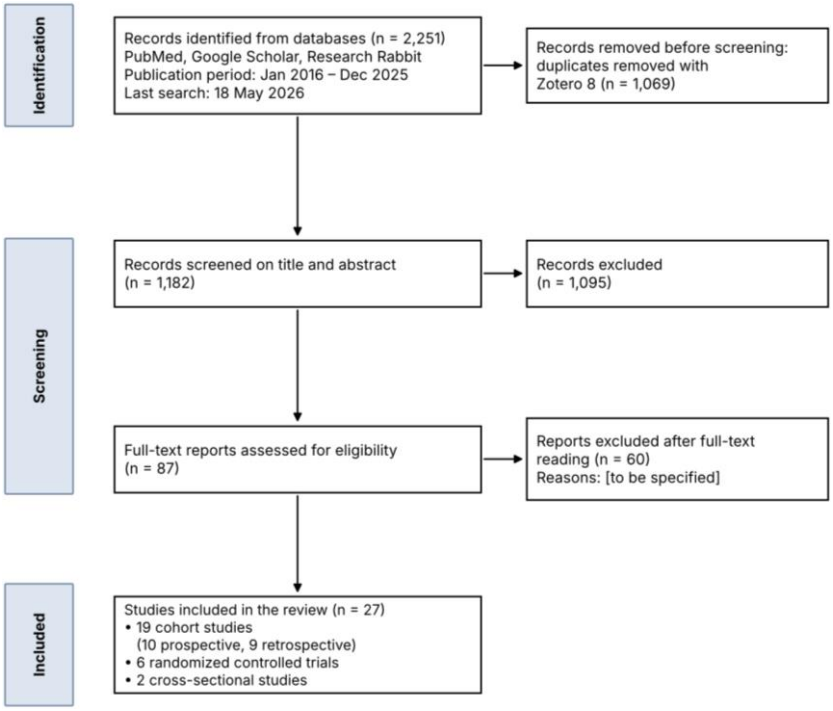

Figure 1. *PRISMA 2020 flow diagram of study selection.*

3.2. Characteristics of the Included Studies

The 27 included studies comprised 19 cohort studies (10 prospective and 9 retrospective), 6 randomized controlled trials and 2 cross-sectional studies (Table 1). They were conducted in 15 countries: 14 studies (51.9%) came from Asia (India 3, Pakistan 3, China 2, Iraq 2, Bangladesh, Iran, Japan and Thailand 1 each), 5 (18.5%) from the Americas (United States 4, Brazil 1), 4 (14.8%) from Africa (Egypt 3, Tanzania 1) and 4 (14.8%) from Europe (Italy 2, Germany 1, Finland 1). Sample sizes ranged from 40 to 226,899 patients. The total reported in the dissertation was 263,672 patients, but more than 90% of them came from two analyses of the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) registry, which provide coded rather than clinically measured outcomes [16, 17].

Table 1. *Characteristics of the 27 included studies.*

Study (year), country	Design	n	Main immediate complications (%)	Associated factors / main finding
Naz (2017), Pakistan [18]	Cross-sectional	271	Seroma 21.4	No association with age, BMI or tumour size
Nedooshan/Jafari (2022), Iran [19]	RCT, drain 1 vs 5 days	88[a]	Seroma 31.8; SSI 12.5	Early drain removal: seroma 52.3% vs 13.6%
Njile (2024), Tanzania [20]	Prospective cohort	106	Seroma 49.1	Age ≥ 50 years; drainage ≥ 150 mL in first 24 h
Agarwal (2022), India [21]	Prospective cohort	72	Seroma 37.5; SSI 8.3; dehiscence 5.5; haematoma 2.7; paraesthesia 11.1	Descriptive: higher seroma with age > 50, diabetes, NACT
Abdulnabi (2019), Iraq [22]	Prospective cohort	170	Seroma 23.5; SSI 12.4	Seroma 36.3% when ≥ 10 nodes involved
Ali (2022), Pakistan [23]	Cross-sectional	62	Seroma 25.8; SSI 8.1	Infection more frequent at stage II
Ashok (2025), India [24]	Prospective cohort	88	Seroma 44; SSI 30; pain/paraesthesia 28; flap necrosis 3;	Smoking, hypertension, NACT, stage III

Study (year), country	Design	n	Main immediate complications (%)	Associated factors / main finding
			haematoma 3	
Köpke (2023), Germany [25]	Prospective cohort	100	Seroma 52	Age (OR 1.095/year), specimen weight
Faisal (2016), Egypt [26]	RCT, axillary exclusion vs conventional	64	SSI 5.9 vs 11.7; dehiscence 2.9	Axillary exclusion reduced drainage and seroma
Rana (2023), Bangladesh [8]	Prospective cohort	46	Seroma 21.7	Age, BMI, electrocautery, early drain removal (OR 2.89)
Gaber (2017), Egypt [27]	RCT, axillary reverse mapping vs control	72	Seroma 6.5 vs 25; SSI 6.5 vs 11.1; dehiscence 3.2 vs 5.6	Reverse mapping reduced seroma
Gambardella (2019), Italy [28]	Retrospective, 4 haemostatic devices	100	Seroma 16–64 by device; SSI 4	Advanced devices (ThunderBeat 16% vs electrocautery 64%)
Jonczyk (2019), USA [16]	Retrospective (NSQIP)	226,899	All 30-day complications 6.56 (mastectomy alone)	Operative time, ASA class, BMI, smoking, comorbidities
Kuntaraksa (2018), Thailand [29]	RCT, lymphatic ligation vs conventional	68	Seroma 26.1	Age (OR 1.09), BMI (OR 1.23); ligation ineffective
Leppäpuska (2021), Finland [30]	Prospective cohort	47	SSI 17; prolonged seroma 87; haematoma 4.3	Low TGF-β1 in day-1 exudate predicted SSI
De Luca (2020), Italy [31]	Retrospective, 3 groups	41	Seroma 6–14 by group	Glues: no effect on seroma; shorter drainage
Nadeem (2023), Pakistan [7]	Prospective cohort	105	Sensory loss 38.1; seroma 32.4; SSI 17.1; haematoma 8.6; flap necrosis 6.7; dehiscence 4.8; axillary vein thrombosis 1.9	Diabetes (OR 2.5), BMI > 30 (OR 2.8), surgery > 120 min
Obaid (2024), Iraq [32]	Prospective cohort	100	Seroma 24; SSI 24	Seroma rose with nodal involvement (8%, 27%, 44%)
Isozaki (2019), Japan [33]	Retrospective	202	Seroma 19.5 (ALND), 18.2 (SLNB)	BMI ≥ 25 (OR 2.54), level of dissection, specimen weight
Suresh (2019), India [10]	Retrospective	83	Seroma 27	Age > 40, tumour > 3 cm, nodes, BMI > 30, MRM (35.8% vs 13.8%)
Wu (2020), China [34]	Retrospective, quilting vs conventional	235	Seroma 26.1–27.6; SSI 3.4–4.3; haematoma 4.2–4.3	Age ≥ 60, BMI ≥ 25; quilting reduced grade 2–3 seroma
Abouelsoued (2024), Egypt [35]	RCT, quilting vs conventional	40	Seroma 55 (35 vs 75)	Quilting reduced seroma and drained volume
Li (2025), China [36]	Retrospective, minimally invasive vs conventional ALND	147	No difference in complications	Less blood loss, better shoulder mobility
Baker (2020), USA [37]	Retrospective, immediate reconstruction	986	Breast complications 35.9 vs 25.6	Nodal surgery (OR 1.62); access through mastectomy incision (seroma OR 3.60)
Bogach (2022), USA [17]	Retrospective	18,232	30-day morbidity 4.9 (ALND)	BMI (OR 1.06), operative time

Study (year), country	Design	n	Main immediate complications (%)	Associated factors / main finding
	(NSQIP)		vs 4.3 (SLNB)	(OR 1.003/min)
Brown (2025), USA [38]	Trial-based comparison, ILR vs none	214	Seroma 3.5 vs 12.1	Immediate lymphatic reconstruction reduced seroma
Fabro (2024), Brazil [39]	Prospective cohort	249	Seroma 71.1	BMI ≥ 25 (OR 1.92), ALND (OR 2.06)

ALND: axillary lymph node dissection; BMI: body mass index; ILR: immediate lymphatic reconstruction; MRM: modified radical mastectomy; NACT: neoadjuvant chemotherapy; NSQIP: National Surgical Quality Improvement Program; RCT: randomized controlled trial; SLNB: sentinel lymph node biopsy; SSI: surgical site infection. [a] Sample size not reported in the dissertation; 88 assumed from the reported percentages.

3.3. Risk of Bias

Among the 19 cohort studies, 11 were of good quality (NOS 7–8), 4 of fair quality (6), 2 of moderate quality (5) and 2 at high risk of bias (4): the registry analysis of Jonczyk et al. and the univariable study of Isozaki et al. [16, 33]. The most frequent deficiencies were incomplete reporting of losses to follow-up and absent or partial adjustment for confounders. Both cross-sectional studies were of moderate quality (5/8 on the JBI checklist), mainly because confounders were neither identified nor controlled [18, 23]. All six randomized trials had an overall moderate risk of bias, driven by the impossibility of blinding the surgeon to the technique (domain 2) and, in two trials, by insufficient reporting of randomization or of prespecified outcomes [26, 35, 38] (Table 2).

Table 2. *Summary of risk-of-bias assessment.*

Tool and judgement	Studies
NOS – good (7–9 stars)	Abdulnabi, Ashok, Baker, Rana, Köpke, Leppäpuska, Li, Nadeem, Njile, Obaid, Wu (n = 11)
NOS – fair (6 stars)	Agarwal, De Luca, Gambardella, Suresh (n = 4)
NOS – moderate (5 stars)	Bogach, Fabro (n = 2)
NOS – high risk of bias (≤ 4 stars)	Isozaki, Jonczyk (n = 2)
JBI – moderate (5/8)	Naz, Ali (n = 2)
RoB 2 – some concerns (moderate)	Nedooshan/Jafari, Faisal, Gaber, Kuntaraksa, Abouelsoued, Brown (n = 6)

NOS: Newcastle-Ottawa Scale; JBI: Joanna Briggs Institute; RoB 2: Cochrane Risk of Bias 2.

3.4. Frequency of Immediate Complications

Seroma was the most frequent immediate complication and was reported in 22 studies. In the 18 studies that reported an overall incidence for the whole cohort, seroma occurred in 19.5% to 71.1% of patients (median 29.4%), the lowest rate being reported by Isozaki et al. and the highest by Fabro et al. [33, 39]. Much lower rates (3.5–14%) were observed in the intervention arms of comparative studies, and much higher rates (87%) when prolonged seroma or ultrasound-detected collections were counted [30, 31, 38]. SSI was the second most frequent complication (13 studies), ranging from 3.9% to 30% [24, 34]. Haematoma, wound dehiscence and skin flap necrosis were less frequent. Sensory disturbances, pain and thromboembolic events were rarely reported (Table 3).

Table 3. *Incidence of immediate complications in the included studies.*

Complication	Studies (n)	Incidence range (%)	Studies at the lower and upper bounds
Seroma (overall cohort incidence)	18[a]	19.5–71.1 (median 29.4)	Isozaki; Fabro
Surgical site infection	13	3.9–30	Wu; Ashok
Haematoma	5	2.7–8.6	Agarwal; Nadeem
Wound dehiscence	4	2.9–5.5	Faisal; Agarwal
Skin flap necrosis	2	3.0–6.7	Ashok; Nadeem
Pain, paraesthesia or sensory loss	3	11.1–38.1	Agarwal; Nadeem
Axillary vein thrombosis	1	1.9	Nadeem

[a] Seroma was reported in 22 studies; four reported it only by arm or as an odds ratio (Gaber, Brown, Baker, Leppäpuska) and are not included in the range.

3.5. Patient-Related Factors

Patient-related factors are summarized in Table 4.

Table 4. *Patient-related factors associated with immediate complications.*

Factor	Studies evaluating it (n)	Studies with a significant association	Reported OR
Older age	9	7/9	1.09–29
High BMI or obesity	12	9/12	1.06–3.31
Undernutrition or weight loss	2	½	2.7–3.5
Specimen weight / breast volume	2	2/2	–
Diabetes mellitus	5	4/5	2.5
Smoking	3	2/3	1.2
Hypertension	3	2/3	1.2
High ASA score	2	2/2	1.2–5.2

ASA: American Society of Anesthesiologists; BMI: body mass index; OR: odds ratio.

Age. Older age was the most frequently reported patient factor for seroma. In the study of Njile et al., mastectomy after the age of 50 years was associated with a 20% higher frequency of seroma (60% vs 39%; p = 0.03) [20]. Köpke et al. found a median age of 73 years in patients with seroma versus 52 years in those without (p < 0.001; OR 1.095 per year) [25]. Age remained an independent factor in the randomized trial of Kuntaraksa et al. (OR 1.09; p = 0.008) [29] and in the study of Wu et al. (≥ 60 years) [34]. Thresholds of 40 years (Suresh et al.) and 50 years (Agarwal et al.) were also reported [10, 21], and Rana et al. reported a strong association between increasing age, drainage volume and seroma (OR 29; p = 0.026) [8]. In the NSQIP analysis of Jonczyk et al., age below 60 years was protective [16]. Naz et al. found no association [18].

Body mass index. High BMI was associated with both seroma and infection. It was an independent risk factor in the studies of Fabro et al. (BMI ≥ 25 kg/m^2; OR 1.92; 95% confidence interval [CI] 1.02–3.61; p = 0.042), Bogach et al. (OR 1.06 per unit; 95% CI 1.04–1.08), Nadeem et al. (BMI > 30 kg/m^2; OR 2.8) and Kuntaraksa et al. (OR 1.23; p = 0.025) [7, 17, 29, 39]. Overweight and obese patients had more seromas in the studies of Rana et al. (p = 0.002), Suresh et al., Wu et al. and Isozaki et al. (OR 2.54) [8, 10, 33, 34]. In the registry study of Jonczyk et al., obesity increased the risk of infection 1.68-fold and of thromboembolic events 1.66-fold [16]. In the study of Köpke et al., BMI was associated with seroma in univariable analysis (p = 0.005) but not after adjustment (OR

0.987; p = 0.828), whereas specimen weight remained significant (median 580 g vs 330 g; p < 0.001) [25]. Naz et al. and Njile et al. found no association [18, 20].

Diabetes, smoking and hypertension. These factors were mainly associated with infection. Diabetes was significantly associated with wound infection in the study of Ashok et al. and was an independent predictor of major complications in the study of Nadeem et al. (OR 2.5) [7, 24]. Comorbidities (diabetes and hypertension) were associated with seroma in the study of Rana et al. (p < 0.001) [8]. Smoking was associated with seroma and wound infection in the study of Ashok et al. (p = 0.008 and p = 0.009) and increased infectious complications 1.2-fold in the study of Jonczyk et al., but was not an independent predictor in the study of Nadeem et al. (OR 1.6) [7, 16, 24]. Hypertension was associated with seroma (p = 0.001) in the study of Ashok et al. and with infection (risk multiplied by 1.2; p = 0.005) in the study of Jonczyk et al., but not with seroma in the study of Njile et al. [16, 20, 24].

3.6. Tumour-Related Factors

Tumour-related factors are summarized in Table 5. Tumour size was associated with seroma in the studies of Suresh et al. (> 3 cm) and Köpke et al. (univariable analysis; p = 0.036), but not in that of Naz et al. [10, 18, 25]. Stage III disease was associated with seroma and wound infection in the study of Ashok et al. [24], while differences across stages were small and descriptive in the studies of Ali et al. and Agarwal et al. (seroma 36.6%, 32.6% and 40% at stages I, II and III) and absent in that of Njile et al. [20-23]. A higher histological grade was associated with seroma in univariable analysis in the study of Köpke et al. (p = 0.015), but not in that of Njile et al. [20, 25]. Nodal involvement showed a dose–response relationship with seroma: 8%, 27% and 44% according to the degree of involvement in the study of Obaid et al., and 24.4%, 21.9% and 36.3% for 1–3, 4–9 and ≥ 10 involved nodes in the study of Abdulnabi et al. [22, 32]. The number of positive and retrieved nodes was also associated with seroma in the study of Suresh et al., but not in that of Köpke et al. [10, 25].

Table 5. *Tumour-related factors associated with immediate complications.*

Factor	Studies evaluating it (n)	Studies with a significant association
Tumour size	3	2/3
Tumour stage (stage III)	4	1/4 (2 descriptive only)
Histological grade	2	1/2 (univariable)
Nodal involvement / number of nodes	4	3/4

3.7. Treatment- and Surgery-Related Factors

These factors are summarized in Table 6.

Table 6. *Treatment- and surgery-related factors associated with immediate complications.*

Factor	Studies evaluating it (n)	Studies with a significant association	Reported OR
Type of surgery (MRM vs conservative) / route of nodal access	4	3/4	1.62–3.60
Extent or level of axillary dissection	4	4/4	2.06
Prolonged operative time	3	3/3	1.003 per min to 7.16[a]
Early drain removal	5	2/5	2.89
High drainage volume	3	3/3	–
Early shoulder mobilization	1	0/1	–
Neoadjuvant chemotherapy	3	1/3	–
Radiotherapy, surgeon experience	0	–	–

[a] Upper value: risk ratio for bleeding complications with the longest operative times in the NSQIP analysis of Jonczyk et al. MRM: modified radical mastectomy.

Type of surgery and route of nodal access. In the NSQIP analysis of Jonczyk et al., mastectomy procedures carried an almost two-fold risk of wound, infectious, bleeding, thromboembolic and neurological complications ($p < 0.002$) [16]. Seroma was more frequent after modified radical mastectomy (MRM) than after breast-conserving surgery (35.8% vs 13.8%) [10]. In patients undergoing immediate reconstruction, nodal surgery increased the risk of any complication (OR 1.62; $p = 0.001$), and accessing the nodes through the mastectomy incision rather than a separate incision was an independent risk factor for seroma (OR 3.60; $p = 0.002$) [37]. In contrast, Bogach et al. found no increase in 30-day morbidity with ALND compared with sentinel node biopsy (4.9% vs 4.3%) [17].

Extent of axillary dissection. ALND was an independent risk factor for seroma in the study of Fabro et al. (OR 2.06) [39]. The level of dissection was associated with prolonged fluid drainage in the study of Isozaki et al., and seroma increased with the extent of dissection in the studies of Obaid et al. and Abdulnabi et al. [22, 32, 33].

Operative time. Prolonged surgery was an independent predictor in the studies of Nadeem et al. (> 120 minutes) and Bogach et al. (OR 1.003 per minute; 95% CI 1.001–1.005) [7, 17]. In the analysis of Jonczyk et al., longer operative times increased wound complications 1.32- to 2.79-fold, infections 1.34- to 2.55-fold, bleeding complications 2.9- to 7.16-fold and thromboembolic complications 1.95- to 6.36-fold [16].

Drain management. Early drain removal was associated with seroma. In the randomized trial of Nedooshan (Jafari) et al., seroma at one week was found by ultrasound in 52.3% of patients drained for one day versus 13.6% of those drained for five days ($p < 0.0001$), and at three weeks in 20.5% versus 0% ($p = 0.002$) [19]. In the study of Rana et al., drain removal before day 7 almost tripled the risk of seroma (OR 2.89; 95% CI 1.74–4.82; $p < 0.001$) [8]. Drain duration was not associated with seroma in the studies of Njile et al., Kuntaraksa et al. and Ashok et al. [20, 24, 29]. A drainage volume above 150 mL in the first 24 hours was associated with seroma in the study of Njile et al. (59% vs 26%; $p = 0.002$), and high early or total drainage volumes were associated with prolonged drainage or seroma in the studies of Isozaki et al. and Rana et al. [8, 20, 33].

Other factors. Early shoulder mobilization (from day 1) was followed by a seroma incidence 13.6 percentage points higher than late mobilization in the study of Njile et al., without statistical significance [20]. Neoadjuvant chemotherapy was associated with seroma and wound infection in the study of Ashok et al. ($p = 0.001$), and seroma was more frequent after chemotherapy in the study of Agarwal et al. (42.9% vs 32.8%) [21, 24]. A low concentration of transforming growth factor beta 1 (TGF-β1) in day-1 wound exudate predicted SSI in the study of Lepp äpuska et al. [30]. No included study specifically evaluated radiotherapy or surgeon experience.

3.8. Surgical Techniques Evaluated for Seroma Prevention

Nine techniques were evaluated in the included studies (Table 7). Dead-space obliteration by quilting, axillary exclusion, axillary reverse mapping, advanced haemostatic devices and immediate lymphatic reconstruction reduced seroma, whereas lymphatic ligation, surgical glues and minimally invasive dissection did not.

Table 7. *Surgical techniques evaluated for the prevention of seroma.*

Technique (vs comparator)	Study	Effect on seroma	Other effects
Quilting / flap fixation	Abouelsoued; Wu	Significant reduction (35% vs 75%; grade 2–3 seroma 9.5% vs 19.3%)	Less drained volume; suturing about 7 min longer
Axillary exclusion	Faisal	Significant reduction	Total drainage 1,476 vs 4,526 mL; drain removed earlier (11.3 vs 17.8 days)
Axillary reverse mapping	Gaber	Reduction (6.5% vs 25%)	Fewer healing complications; drains removed earlier
Electrocautery vs sharp dissection	Rana	Electrocautery associated with more seroma	–
Advanced haemostatic devices (ThunderBeat)	Gambardella	Reduction (16% vs 64% with electrocautery)	Less drained volume
Lymphatic ligation	Kuntaraksa	No effect (23.5% vs 28.6%)	Longer operative time
Immediate lymphatic reconstruction	Brown	Reduction (3.5% vs 12.1%)	No reduction in drain days

Technique (vs comparator)	Study	Effect on seroma	Other effects
Surgical glues (Glubran® 2, fibrin sealant)	De Luca	No effect	Shorter drainage
Minimally invasive axillary dissection	Li	No effect	Less blood loss; better shoulder mobility

4. Discussion

This systematic review of 27 studies published between 2016 and 2025 confirms that seroma is by far the most frequent immediate complication after mastectomy with ALND, followed by SSI and, much less often, by haematoma, wound dehiscence and flap necrosis. Three groups of determinants emerged: patient-related factors (older age, high BMI, diabetes, smoking, hypertension), tumour-related factors (size, stage, grade, nodal involvement) and treatment- and surgery-related factors (type and extent of the axillary procedure, operative time and drain management). Four factors stood out for the consistency of their association and its confirmation in multivariable analyses: older age, high BMI, extent of axillary dissection and prolonged operative time.

4.1. Frequency of Complications and Heterogeneity of Definitions

The incidence of seroma in our review overlaps that of the literature but exceeds it at its upper bound. In the meta-analysis of randomized trials by Crestani et al., the pooled incidence of seroma or lymphocele was 24.2%, close to the lower part of our range [9]. The wide range of 19.5–71.1% is mainly explained by heterogeneous definitions. Studies that used ultrasound, and therefore included subclinical collections, reported higher rates than those that counted only clinically significant seromas requiring aspiration. This heterogeneity was the main reason for choosing a narrative synthesis rather than a meta-analysis. The SSI range (3.9–30%) is consistent with series of mastectomy without reconstruction; its upper bound comes from settings with late diagnosis and advanced stages, similar to ours [24, 32].

4.2. Patient-Related Factors

Older age was one of the most frequently reported associations. Ageing reduces tissue elasticity and slows lymphatic regeneration and wound healing, which favours exudation and persistence of the collection. The association was found by Köpke et al., Rana et al., Kuntaraksa et al. and Wu et al. [8, 25, 29, 34]. The absence of association in the study of Naz et al. and the different age thresholds used (40, 50 or 60 years) suggest that age should be considered a continuous risk factor [18]. As a non-modifiable factor, age is mainly useful to identify patients who need closer surveillance.

High BMI was one of the most robust factors, associated with both seroma and infectious complications. Abundant adipose tissue leaves, after resection, a large dead space and a wide, poorly vascularized dissection surface, the site of an inflammatory reaction that sustains fluid production. Our findings (OR 1.06–3.31 across studies) agree with the NSQIP cohort of Sousa et al., in which high BMI independently predicted surgical morbidity, and with the meta-analysis of Xue et al., which identified obesity as a risk factor for SSI after breast surgery [40, 41]. However, as illustrated by Köpke et al., BMI, breast volume and specimen weight are collinear and partly capture the same mechanism, which calls for caution in interpreting their independent effects [25].

Diabetes, smoking and hypertension weighed more on healing and infection than on seroma. Hyperglycaemia impairs neutrophil function, tissue perfusion and collagen synthesis, and nicotine causes vasoconstriction and tissue hypoxia that favour necrosis and infection. These mechanisms explain the associations reported by Ashok et al., Rana et al. and Jonczyk et al., and are consistent with the determinants of SSI identified by Xue et al. and Sousa et al. [8, 16, 24, 40, 41].

4.3. Tumour-Related Factors

Tumour size, stage, grade and nodal involvement were frequently associated with complications but rarely independently. Their effect appears to be largely mediated by the extent of surgery they require. The dose–response relationship between nodal burden and seroma observed by Obaid et al. and Abdulnabi et al. supports this mechanism: heavier nodal involvement leads to a more extensive dissection, more divided lymphatics and a larger residual cavity [22, 32]. Tumour-related factors thus behave as markers of the extent of axillary dissection, which explains why their association weakens when models are adjusted for the extent of surgery.

4.4. Treatment- and Surgery-Related Factors

The type of breast surgery and the extent of the axillary procedure were major determinants. Seroma was more frequent after modified radical mastectomy than after breast-conserving surgery, and the extent or level of dissection was an independent risk factor [10, 22, 32, 33, 39]. Baker et al. also showed that accessing the nodes through the mastectomy incision more than tripled the risk of seroma (OR 3.60) [37]. Prolonged operative time was a reproducible independent predictor, reflecting both the complexity of the procedure and longer tissue exposure [7, 16, 17].

Drain management plays a central role. Early drain removal

was followed by fluid re-accumulation in the trial of Nedooshan (Jafari) et al. and in the study of Rana et al. [8, 19]. This agrees with the meta-analysis of Crestani et al., in which shortening drainage significantly increased seroma (risk ratio [RR] 1.88; 95% CI 1.43–2.48) [9]. Prolonged drainage, however, may increase the risk of infection. These data favour drain removal guided by daily output rather than by a fixed duration. Early shoulder mobilization, neoadjuvant chemotherapy and biological markers of wound exudate such as TGF-β1 are additional leads that deserve further study [20, 21, 24, 30].

4.5. Effectiveness of Preventive Techniques: Comparison with Meta-Analyses

Comparing the preventive techniques evaluated in the included studies with recent meta-analyses helps rank the options. Dead-space obliteration by quilting appears to be the best-supported measure: the meta-analysis of Velotti et al. reported a reduction in seroma of about 73% (OR 0.267; 95% CI 0.153–0.464), consistent with the results of Wu et al. and Abouelsoued et al. [34, 35, 42]. This conclusion should be qualified, because surgical technique modifications as a whole did not significantly reduce seroma in the meta-analysis of Crestani et al. (RR 0.86; 95% CI 0.72–1.03) [9]. The effect of quilting should therefore be confirmed by high-quality trials.

Advanced energy devices are the second option. In the network meta-analysis of Watanabe et al., ultrasonic coagulating shears reduced seroma (RR 0.61; 95% credible interval 0.49–0.73), drained volume (−313 mL) and drainage duration (−1.79 days) compared with conventional techniques, with low to moderate confidence in the evidence [43]. These data support the observations of Gambardella et al. and suggest that limiting thermal spread contributes to seroma prevention [28].

Lymphatic-sparing techniques, such as axillary reverse mapping and immediate lymphatic reconstruction, mainly target lymphoedema, a late complication, rather than early seroma. The meta-analysis of Guo et al. confirmed the effectiveness of axillary reverse mapping on lymphoedema (OR 0.20; 95% CI 0.13–0.29; 4.71% vs 18.79%), which supports the techniques evaluated by Gaber et al. and Brown et al. [27, 38]. Conversely, fibrin sealant is not supported: Crestani et al. found no benefit (RR 1.36; 95% CI 0.77–2.38), which calls for caution in interpreting the results of De Luca et al. [9, 31].

4.6. Modifiable and Non-Modifiable Factors: Clinical Contribution

The distinction between modifiable and non-modifiable factors is the main practical contribution of this review. Non-modifiable factors (age, tumour stage and grade, nodal involvement, breast volume) do not offer direct preventive leverage but allow high-risk patients to be identified before surgery and monitored more closely. Modifiable factors (obesity, glycaemic control, smoking, choice of surgical technique and drain management) are concrete targets for action. This framework is particularly useful in resource-limited settings, where mastectomy with ALND remains the reference operation and where perioperative optimization is an accessible way to reduce morbidity.

4.7. Strengths and Limitations

This review followed the PRISMA 2020 statement, assessed the risk of bias with design-specific tools, and distinguished simple associations from predictors confirmed by multivariable analysis. It also has limitations. First, definitions of seroma varied widely, from a clinically significant collection requiring aspiration to an ultrasound image, which precluded a meta-analysis. Second, the evidence was dominated by observational studies, often small and retrospective; only six trials were included, all with some concerns about bias. Third, the apparently large cumulative sample was driven by two registry analyses that provide coded rather than clinically measured outcomes. Fourth, the search was limited to three sources, two of which (Google Scholar and Research Rabbit) are not standard bibliographic databases; Embase, Scopus, Web of Science and African databases were not searched, grey literature was not systematically sought, only English and French publications were considered, the protocol was not registered, and publication bias could not be excluded. Fifth, screening, data extraction and risk-of-bias assessment were performed by a single reviewer, which increases the risk of selection and extraction errors. Sixth, the narrative synthesis relied on vote counting, which does not take into account the size or precision of the effects reported by each study, and some sample sizes and incidences had to be derived from published percentages. Seventh, the follow-up of complications was limited to 30 days in most studies, so late events such as lymphoedema or chronic pain were not captured. Finally, Africa was poorly represented (4 of 27 studies, only one from sub-Saharan Africa), which limits the transferability of the results to our setting [4].

4.8. Implications for Research

Prospective studies are needed in sub-Saharan Africa, which is almost absent from this literature. Definitions should be harmonized, starting with seroma, to make studies comparable and allow meta-analyses. Adequately powered randomized trials are needed to confirm the effectiveness of preventive techniques. Finally, a simple risk score based on age, BMI, extent of dissection and operative time could help target prevention in resource-limited settings.

5. Conclusion

This systematic review of 27 studies published between 2016 and 2025 confirms that seroma is the most frequent immediate complication after mastectomy with ALND, followed

by SSI. Older age, obesity, the extent of axillary dissection related to nodal involvement and prolonged operative time are the factors most consistently associated with these complications and confirmed in multivariable analyses. Age, nodal involvement and tumour stage cannot be modified, but glycaemic control, smoking cessation, weight optimization, the choice of surgical technique and drain management guided by daily output are levers to reduce postoperative morbidity. Dead-space obliteration, advanced haemostatic devices and lymphatic-sparing techniques are promising. These results should be interpreted with caution given the heterogeneity of definitions, the predominance of observational studies and the under-representation of Africa. They call for prospective studies adapted to African populations, harmonized definitions and the validation of a simple risk score.

Abbreviations

ALND	Axillary Lymph Node Dissection
ASA	American Society of Anesthesiologists
BMI	Body Mass Index
CI	Confidence Interval
DES	Diplôme d'Études Spécialisées (specialist diploma)
GLOBOCAN	Global Cancer Observatory
ILR	Immediate Lymphatic Reconstruction
JBI	Joanna Briggs Institute
MRM	Modified Radical Mastectomy
NACT	Neoadjuvant Chemotherapy
NOS	Newcastle-Ottawa Scale
NSQIP	National Surgical Quality Improvement Program
OR	Odds Ratio
PICO	Population, Intervention, Comparator, Outcome
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPERO	International Prospective Register of Systematic Reviews
RCT	Randomized Controlled Trial
RoB 2	Cochrane Risk of Bias 2 tool
RR	Risk Ratio
SLNB	Sentinel Lymph Node Biopsy
SSI	Surgical Site Infection
TGF-β1	Transforming Growth Factor beta 1

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Conflicts of Interest

The authors declare no conflicts of interest.

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