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REVIEW

Spatial location of local recurrences after mastectomy: a systematic review

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Abstract

Purpose We performed a systematic review to document the spatial location of local recurrences (LR) after mastectomy.
Methods A PubMed search was conducted in August 2019 for the following terms: breast [Title/Abstract] AND cancer [Title/Abstract] AND recurrence [Title/Abstract] AND mastectomy [Title/Abstract]. The search was filtered for English language. Exclusion criteria included studies that did not specify the LR location or studies reporting LR associated with inflammatory breast cancer, or other breast cancers such as phyllodes tumours, lymphoma or associated with sarcoma/angiosarcoma.
Results A total of 3922 titles were identified, of which 21 publications were eligible for inclusion in the final analysis. A total of 6901 mastectomy patients were included (range 25–1694). The mean LR proportion was 3.5%. Among the total of 351 LR lesions, 81.8% were in the subcutaneous tissue and the skin, while 16% were pectoral muscle recurrences.
Conclusion Local recurrences are mostly located within the subcutaneous tissue and the skin, assumed to result from unrecognized/subclinical tumour foci left behind after mastectomy, surgical implantation of tumour cells in the wound/scar and/or tumour emboli within the subcutaneous lymphatics. Pectoral muscle recurrences are less frequent and may be attributed to residual disease along the posterior surgical margin and/or lymphatic involvement.

Keywords Breast cancer · Mastectomy · Breast reconstruction · Nipple sparing · Skin sparing · Local recurrence

Introduction

The surgical treatment of breast cancer aims to remove the in-breast neoplasia with/without lymphatic drainage and to reduce the risk of local recurrence (LR), regional recurrence (RR) or a new primary breast tumour [1]. It has evolved significantly over the years, as a result of better understanding of disease spread and improvements in surgical techniques, post-surgical management, imaging and preoperative systemic therapy [1]. Breast-conserving therapy (BCT,

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lumpectomy and radiation) is considered to be the preferred procedure for the surgical treatment of most breast cancer patients [2–4]. In some patients with extensive disease, including ductal carcinoma in situ (DCIS), hereditary breast cancer, or upon patient's preference, mastectomy may still be indicated.

There are several types of mastectomy, which differ by the surgical extent of the procedure [1, 5, 6]. The common types of procedures that are currently used include total/simple mastectomy (removal of breast tissue and skin) and skin-sparing mastectomy (SSM) with/without resection of the nipple–areola complex (NAC) (i.e. nipple-sparing mastectomy, NSM) [1]. The remaining breast skin is preserved to facilitate immediate breast reconstruction (IBR) [1]. Depending on the indication, sentinel lymph node biopsy and/or axillary lymph node dissection can be performed in each of the procedures [1].

Residual breast tissue can be noticed in most types of mastectomy [7, 8], mainly in NSM or SSM [9, 10]. Nonetheless, despite the extensive resection of breast and lymphatic tissue (selective or full axillary dissection), locoregional recurrences (LRRs) after mastectomy (in the skin or subcutaneous tissue of the ipsilateral chest wall and/or regional lymph nodes) may occur [11]. Early trials (more extensive mastectomies) reported post-mastectomy LRR rates of 10–20% at 10 years in patients with breast cancer stage I–IIIA [6, 12–16]. Systemic therapies [17, 18] and post-mastectomy radiation therapy (PMRT) [19] reduce the rates of any recurrences including LRR, resulting in a chest wall recurrence as a first event of disease recurrence at 10 years with a cumulative incidence between 2% and 5% (depending on the treatment arm). However, most trials report the rate of LRR (local recurrence, LR and/or regional recurrence, RR) and not LR, and these two are different entities.

The aim of this work is to evaluate and document the spatial location of post-mastectomy LRs reported in literature and to investigate whether there is a relation between the spatial location and the different types of mastectomy.

Methods

The current study is part of a PhD project and an international project of a multidisciplinary breast cancer experts' team to generate treatment guidelines for PMRT [20]. The research was planned as stepwise sub-projects eventually aiming to develop guidelines based on in-depth understanding of LR and RR. All projects were agreed upon after discussions within the team and approved by the PhD supervisors (L.B., B.V.O.. P.H.P., and D.d.R.). All projects were pre-planned and supervised. This review was designed to provide data about the location of LR according to published literature. The review strategy was not conducted according to the whole Cochrane Guideline for systematic reviews and meta-analyses: we did not perform an assessment of risk of bias of the included studies since our initial 'scoping review' prior to initiation of the formal search and data collection indicated a lack of data to perform meta-analyses.

For the purpose of this review, LR was defined according to the Maastricht Delphi consensus of recurrence in breast cancer research [11]. Post-mastectomy LR was defined as any epithelial breast cancer or DCIS in the skin and subcutaneous tissue on the ipsilateral thoracic wall. RRs were defined as breast cancer in ipsilateral lymph nodes. A distant recurrence is breast cancer in any other location including metastasis in contralateral lymph nodes and breast cancer involving the sternal bone [11].

The search strategy included the Cochrane Breast Cancer Group's Specialized Register, the Cochrane Centre Register of Controlled Trials (CENTRAL) and MEDLINE/PubMed search of the following Medical Subject Headings (MeSH) terms: breast [Title/Abstract] AND cancer [Title/Abstract] AND recurrence [Title/Abstract] AND mastectomy [Title/Abstract].

We searched the WHO International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp/en/) and ClinicalTrials.gov (www.clinicaltrials.gov/) for prospectively registered studies to identify potential registered studies that were completed. The search was conducted in August 2019. An EMBASE search was not conducted due to limited access.

The search was filtered for 'English language' and 'Human' studies only. No limitations were set for the year of publication or type of study (retrospective or prospective).

A systematic review was conducted to identify studies that reported post-mastectomy LR without limitations for the method of LR detection (i.e. imaging) or follow-up time.

Only studies with full text available for further evaluation were included.

Inclusion criteria included studies reporting LR after mastectomy for epithelial breast carcinoma or ductal carcinoma in situ (DCIS); LR location was indicated within the chest wall tissues, such as skin/subcutaneous/chest wall/pectoralis muscle, and the type of surgical procedure was reported.

Exclusion criteria included studies that did not specify the exact LR location within the chest wall structures as indicated above, studies reporting RR or LRR without clear specification of spatial location or studies reporting LR associated with non-carcinoma breast cancer such as phyllodes tumours, lymphoma or associated with sarcoma/angiosarcoma, or reports that included only-inflammatory breast cancer. Case reports, review papers, unpublished studies or abstracts and meta-analyses were excluded. Reference lists of selected publications were further searched for relevancy.

Data were extracted and recorded in an Excel file which was created for this review, including a division into 'relevant–analysed', 'relevant–for citation only', and 'non-relevant', and the inclusion and exclusion criteria for each entry to support the decision. Additional report forms were created for data extraction from 'relevant–analysed' studies. In publications that were categorised as 'non-relevant' or 'citation only', the reason for exclusion was indicated. We included the following information from individual studies on data extraction forms: publication details; study design, study setting and inclusion/exclusion criteria; patient population (e.g. age); disease-related factors (e.g., histology); type of mastectomy; type of reconstruction; follow-up; time of LR; location of LR. To reduce the risk of false analysis, the location of the LR lesions was recorded as reported in the publications (e.g. some studies defined skin recurrence or subcutaneous tissue or scar separately, compared with studies reporting skin and subcutaneous tissues as a single entity; other studies reported 'chest wall' as any musculoskeletal recurrence, while others clearly indicated pectoralis recurrence versus other components of the chest wall). The term 'skin envelope' is used to describe a recurrence at the site of residual native breast/chest wall skin, whereas the term 'skin flap' is used to describe a recurrence at the area of autologously transplanted skin flap.

All titles were initially reviewed by a single author (O.K.P.), who reported to the project supervisors (L.B., B.V.O., P.H.P., D.d.R.) at pre-defined stages for additional consultation in cases of uncertainty. Data are presented using descriptive statistics.

Results

A total of 3922 titles were identified using the key words, of which 22 publications were eligible for inclusion in the final analysis [21–42]. One additional study was excluded since full text was not available for review. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) are presented in Fig. 1 [42]. Figure 2 schematically illustrates the location of LR according to topographical incidence. Figure 3 illustrates magnetic resonance imaging (MRI) of LR to serve as a visual aid to understand the spatial location of LR reported in our study after different types of reconstruction. LR at the 'skin envelope' and 'skin flap' in cases of autologously transplanted skin flap are shown in Fig. 3d.

A total of 6901 mastectomy patients were included (range 25–1694) [21–41]. Nineteen were retrospective studies [21–24, 26–30, 32–41]. One was a retrospective review of a prospective study [25], and one was a prospective study [31].

Analysis of the location of LR in relation to the treatment intervention (type of mastectomy, perioperative treatment) was not possible. Moreover, the studies included in this review display heterogeneity in the primary study aim, clinical factors (disease stage, treatment intervention, follow-up) and data analysis, but all of them indicated the spatial location of LR after mastectomy. Consequently, we report the results of this study using descriptive statistics.

Of the 6901 patients, 241 (3.5%) had a LR, comprising 351 lesions at the mastectomy site (i.e. the various components mentioned above). The range of follow-up was 0.5–192 months [22, 25–37, 39–41], and LR occurred at a range of 1–169 months [21, 23, 24, 38]. A summary of the included studies is presented in Table 1. One study [33] did not indicate the site of 11 lesions, thus these were not analysed further.

Out of 340 lesions, 278 (81.8%) were in the skin and/or subcutaneous tissue and 62 (18.2%) were at the musculoskeletal part of the chest wall (i.e. pectoralis muscles, intercostal muscles, ribs).

In the studies indicating that the LR was within the skin or subcutaneous tissue [21, 23, 25, 27, 29, 32, 37, 41], 56 of 85 lesions (66%) were within the subcutaneous tissue and 29 (34%) lesions were within the skin (recurrences within the nipple–areola complex were not included for this purpose). Two studies indicated that 58% and 86% of the LRs, respectively, were near the primary tumour site [23, 24].

The location of skin-flap recurrences was described by three studies at the flap margins near the skin envelope (i.e. near the native chest wall skin that was not removed at the time of mastectomy) [22, 36, 40] (Fig. 3d). Five cases were in the core biopsy site that was not excised at the time of mastectomy [26, 32]. In studies that reported LR within the mastectomy scar, 25% (10 out of 40 lesions) of LRs occurred in the mastectomy scar [27, 41, 43].

Seventeen lesions (16%) involved the pectoral muscle [23, 24, 41]. Non-pectoralis musculoskeletal chest wall lesions included only one case of rib and five cases of intercostal muscle involvement [24].

Only 13 studies were further analysed for LR according to the type of mastectomy. We divided the studies into LR after mastectomy (neither SSM nor NSM procedures) with/without autologous reconstruction (M group) [21, 22, 36, 37, 39], compared with SSM with/without NSM (SSM/NSM group) [25–27, 29–32, 35]. A total of 74 LR lesions were included in the M group (1582 patients) compared with 75 lesions in the SSM/NSM group (1799 patients). In the M group, skin/subcutaneous LRs accounted for 80–86% of the lesions, and chest wall (non-skin/subcutaneous) accounted for 14–20% of the lesions, compared with 96–100% of the lesions within the subcutaneous/skin in the SSM/NSM group. The follow-up time or time to LR was not clearly reported: in the M group it was up to 15.5 years, and recurrences were reported at a median of 4.4 years [22] and a mean of 5.9 years (range of 2 weeks–16 years) [21, 36, 37, 39]. The follow-up time in

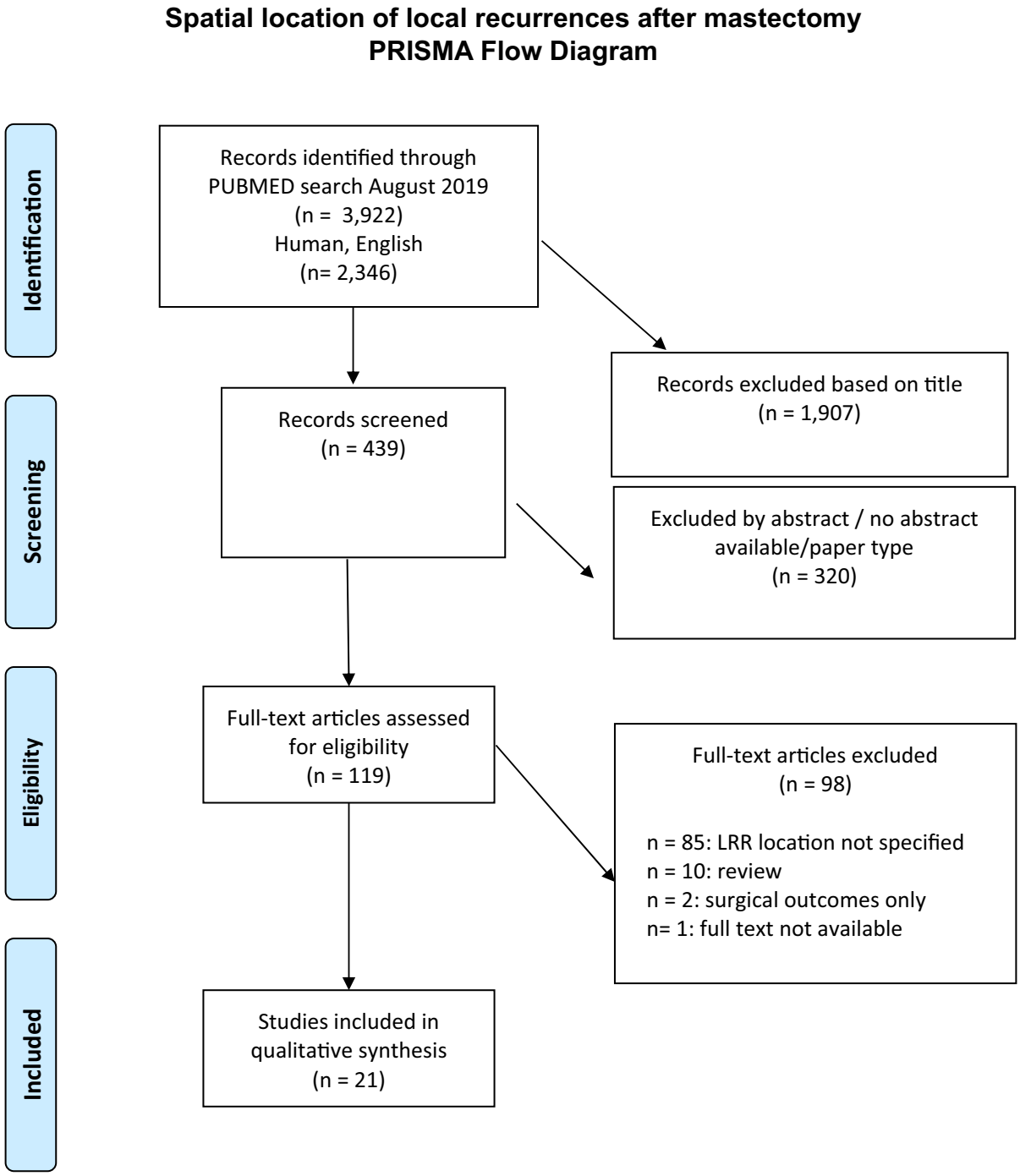

Fig. 1 Spatial location of local recurrences after mastectomy: PRISMA flow diagram

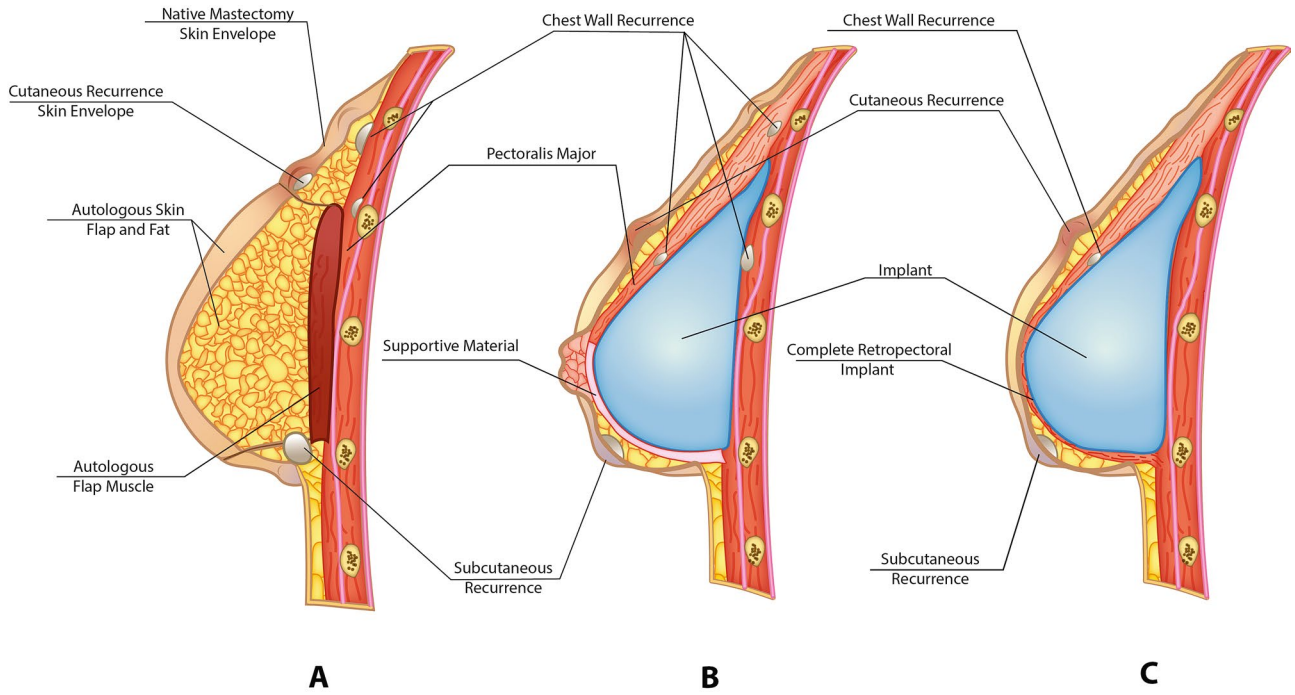

Fig. 2 Sagittal view of tumour recurrence at different locations (subcutaneous, skin, pre-pectoral, inter-pectoral; the size of the lesions is proportional to the proportion of occurrence at that specific site). **a** Autologous-based reconstruction, showing the native breast skin envelope and the autologous skin flap, areas of native breast subcutaneous and autologous subcutaneous skin. **b** Retro-pectoral implant-based reconstruction in a skin-sparing mastectomy, showing the pectoralis major covering the superior part of the implant, native breast nipple, residual breast subcutaneous, supportive material in the inferior part. **c** Retro-pectoral implant-based reconstruction, a result of a two-stage procedure with a tissue expander, showing the pectoralis major covering the whole implant

the SSM/NSM group was up to 13.2 years [25–27, 29–32, 35], and recurrences were reported at a mean of 2 years [25, 26] and median of 2 years [35].

Discussion

The proportion of patients with LR after mastectomy was 3.5%, with a total of 351 lesions at the mastectomy site. In this review, 82% of the LRs were in the skin/subcutaneous tissue (of which two-thirds were within the subcutaneous tissue), while 18% were at the pectoralis muscle. Rib, sternal and intercostal muscle involvement was rather rare.

In studies that reported the LR in relation to the tumour bed location, recurrences occurred often in proximity to the primary tumour bed (~80%) and possibly result from a focus that was not excised at the time of surgery [21–41, 44]. They may also occur at the site of the biopsy track if not excised at the time of mastectomy [21–41]. Interestingly, when analysing according to type of mastectomy (mastectomy versus SSM/NSM), in the latter, LRs were reported exclusively in the skin/subcutaneous tissue and at a shorter time of occurrence. In the M group, skin/subcutaneous LR was reported mostly in the native skin of the chest wall [22, 36, 39].

Note that these data should be analysed vary cautiously. The studies had several methodological flaws and poor reporting, which meant that not all of them reported the timing of LR, and whether the timing was calculated from the mastectomy or from the reconstruction (if a delayed procedure was performed). Moreover, differences between surgery groups in tumour stage and margin status (e.g. recurrence within 2 weeks is most probably due to residual disease) may account for the timing of LR [22, 36], and mortality is a competing factor for (any) recurrence. Furthermore, mastectomy with/without autologous reconstruction was suggested in these studies to be the surgical approach in more advanced breast cancer cases (compared with SSM/NSM), which also might influence the LR patterns [27, 36]. Nevertheless, the timing to LR was shorter in the SSM/NSM group and the location was exclusively in the skin/subcutaneous tissue, which might imply that there was residual disease at the time of the primary procedure because of a larger amount of residual glandular breast tissue after these procedures [9, 45]. However, due to a lack of data, we cannot draw any conclusions as to whether this was a result of residual disease, residual glandular tissue, type of procedure and/or (most probably) other unaccounted-for confounding factors. Similarly, a Cochrane meta-analysis of NSM in the treatment

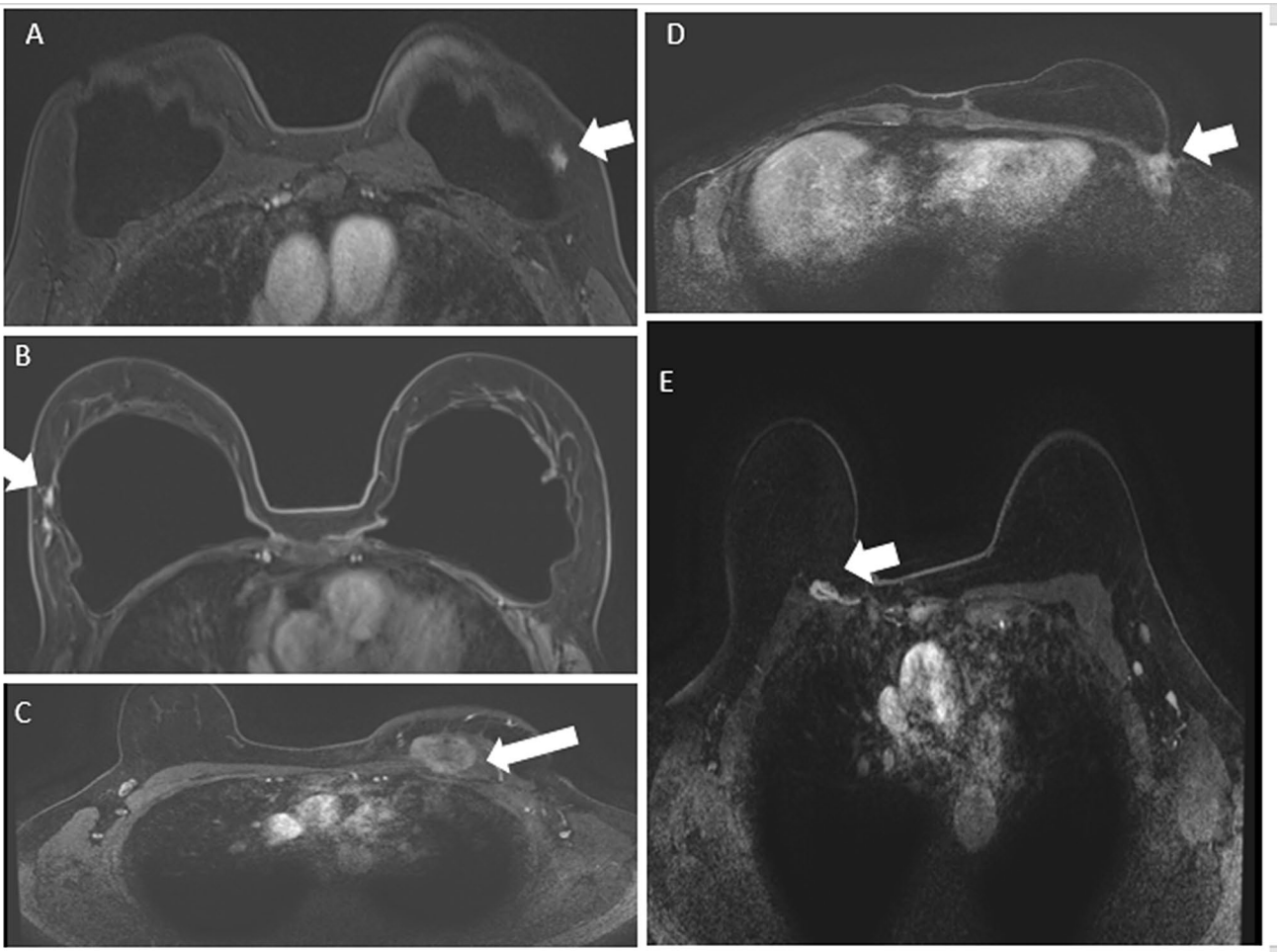

Fig. 3 Magnetic resonance imaging showing local recurrences (LR) after breast reconstruction. **a**–**c** LR after retro-pectoral implant reconstruction. **a**, **b** LR at subcutaneous location, **c** LR at the anterior border of and invading the pectoralis major, at the superior portion of the reconstructed breast (defined as chest wall or subcutaneous LR). **d**, **e** LR in cases of autologous-based reconstruction. **d** LR and the lateral edge of deep inferior epigastric perforators (DIEP)-based reconstruction at site of the skin-flap (skin envelope recurrence/subcutaneous). **e** LR at the anterior surface of the pectoralis major in case of transverse rectus abdominis myocutaneous (TRAM)-based reconstruction (chest wall recurrence)

of breast cancer indicated that the oncological safety of these procedures cannot be determined due to the poor quality of reported studies [46].

Similar to the Cochrane meta-analysis [46], the studies included in this review were mostly retrospective, thus preventing the performance of a robust statistical analysis to investigate more deeply the association of LR with the procedure type, perioperative treatment, follow-up duration and other factors that may influence LR occurrence, location and timing. Considering the limits of the retrospective nature of the included studies and the heterogeneity of the disease stage, treatment and follow-up time, our results are consistent with the results published by Vargo et al., showing that most recurrences were isolated to tissues anterior to the pectoralis muscle. Additionally, Vargo et al. reported that up to 23.5% of LRs are located both anterior to and between the pectoralis muscles, while only 11.8% were isolated to the tissue between the pectoralis major and minor (most probably a result of interpectoral nodal recurrence and not 'true' LR) [47, 48]. Further studies are needed to analyse the location and timing according to the different types of mastectomy, reconstruction procedures and perioperative treatment.

The finding that most LRs occur anterior to the pectoral muscles might be explained by the location of the lymphatics from the mammary region, which drain via the dermal plexus located within the subcutaneous tissues [56]. This coincides with the route of tumour spread from the primary tumour to the (axillary) lymph nodes. Scar recurrences were reported by a limited number of studies. Other case reports that were not included in our analysis reported scar recurrences at the site of the neo-areola and the area of the filling

Table 1 Sites of local recurrences after mastectomy

Author, year	No. of patients	No. of breasts	Type of surgery	Treatment indication for mastectomy	No. of patients with LR	No. of lesions	Location of LR (% lesions)[a]
Noroozian, 2018 [22]	515	618	M + AMF	Therapeutic RRS	20[c]	20	Skin (10%) Chest wall (20)[b] Flap margins (70%)
Chang, 2018 [23]	25	N/A	M ± reconstruction	Therapeutic	25	29	Skin (24%) Subcutaneous (52%) Pectoralis (24%) Rib and intercostal (0)
Cont, 2017 [25]	518	N/A	NSM + implant IBR	Therapeutic	14	14	Subcutaneous (100%)
Chang, 2016 [24]	129	N/A	M	Therapeutic	23?	11	Major pectoralis (45%) Intercostal (45%) Rib (9%)
Farras Roca, 2016 [21]	247	N/A	M + DIEP	Therapeutic	10	10	Subcutaneous tissue (80%) Chest wall (20%)
Sood, 2014 [26]	87	118	NSM + implant IBR	Therapeutic RRS Other±	6[c]	6	Skin envelope (50%) NAC (50%)
Stanec, 2014 [27]	361	421	NSM SSM Different types of reconstructions	Therapeutic RRS	15	15	Skin scar (27%) Superficial subcutaneous (53%) NAC (20%)
Freyvogel, 2014 [39]	541	N/A	M + autologous	Therapeutic RRS	20	20	Skin envelope (80%) Chest wall (20%)
McCarthy, 2008 [28]	618	618	M M + IBR implant	Therapeutic	14	12	Skin/subcutaneous (75%) Chest wall muscle (25%)
Meretoja, 2007 [29]	207	207	SSM + IBR Different types of reconstructions	Therapeutic RRS	8	8	Skin envelope, surgical scar (87.5%) Subcutaneous (12.5%)
Meretoja, 2007 [29]	146	146	SSM + IBR	Therapeutic	4	4	Skin envelope (100%)
Caruso, 2006 [31]	50	50	NSM + IBR	Therapeutic	1	1	NAC (100%)
Uriburu, 2006 [32]	58	58	SSM + IBR	Therapeutic	3	4	Core biopsy site Skin (75%) Subcutaneous (25%)
Howard, 2006[38]	419	N/A	M + autologous SSM + autologous	Therapeutic RRS	16	16	Skin envelope (50%) Chest wall (50%)
Gerber, 2003 [33]	246	246	NAC SSM M	Therapeutic	17	6	Skin/subcutaneous (50%) NAC (17%) Chest wall (33%)
Langstein, 2002 [34]	1694	1694	M + IBR autologous or implant	Therapeutic	39	39	Skin/subcutaneous (71%) Chest wall, muscle or skeletal (28%)
Newman, 1998 [35]	372	372	SSM + IBR	Therapeutic	23	23	Skin envelope (96%) Chest wall (4%)

Table 1 (continued)

Author, year	No. of patients	No. of breasts	Type of surgery	Treatment indication for mastectomy	No. of patients with LR	No. of lesions	Location of LR (% lesions)[a]
Noone, 1998 [41]	329	306	M ± Reconstruction	Therapeutic	16	18	Skin (11%) Subcutaneous (28%) Scar (22%) NAC (11%) Pectoralis muscle (superficial to implant) (28%)
Slavin, 1994 [36]	161	161	M + autologous	Therapeutic	17	17	Skin envelope/subcutaneous (100%)
Johnson, 1989 [37]	118	139	M	Therapeutic RRS	7	7	Subcutaneous (57%) Skin scar (29%) Superficial muscular chest wall (14%)
Gilliland, 1983 [40]	60	N/A	M ± reconstruction	Therapeutic	60	60	Scar/skin graft (65%) Skin/subcutaneous (28%) Skin supraclavicular (~2%) Chest wall diffuse (5%)

Therapeutic mastectomy (i.e. not risk-reducing mastectomy, RRS) may include ductal carcinoma in situ (DCIS); ±Other, including symmetry or patient request

AMF autologous myocutaneous flap, *M* mastectomy, *NSM* nipple-sparing mastectomy, *SSM* skin-sparing mastectomy, *NAC* nipple–areola complex, *IBR* immediate breast reconstruction, *LR* local recurrence, *skin flap* skin from the autologous flap, *skin envelope* native breast skin, *reconstruction* includes various types including autologous and/or implant

[a]As indicated by the publication (thus 'skin' may indicate skin and subcutis), includes only local recurrence, not regional

[b]Chest wall recurrences, including those involving the pectoral muscle and/or underlying thoracic wall structures

[c]Therapeutic indication patients only. Some studies did not indicate the timing of the reconstruction (immediate, immediate-delayed, delayed)

port (dome) for the prosthesis (tissue expander) [27, 29, 37, 40, 41, 49, 50]. Additionally, in cases of autologous flaps, recurrences were reported at the edge between the flap skin and the skin envelope (Figs. 2, 3d) [22, 49]. Therefore, these recurrences might be a result of undiagnosed preoperative involved skin, or tumour cell grafting/seeding at the time of surgery [51]. The frequency of residual cancer tissue in the wall of the biopsy tract of the mastectomy specimen was previously described in up to 46% of biopsy tracks [52]. It might be that the risk of residual disease at the biopsy track is different according to the type of biopsy performed [32, 52]. This phenomenon is less frequent in patients who are undergoing BCT, most probably because of the anti-tumour effect of postoperative radiation therapy.

Pectoral muscle recurrences may be a result of a tumour bed adjacent to or invading the muscle, incomplete resection of pre-pectoralis glandular tissue (Figs. 2, 3e) or inter-pectoral lymph node recurrence (Fig. 2) [53, 54]. The importance of close surgical margins and pectoralis fascia involvement requires further research, as there is no consensus regarding whether additional resection of a cuff of muscle reduces the LR rate [55]. In cases with close deep margins, we recommend that the surgeon position surgical clips for localization and inform the radiation oncologist that an area of potential close/involved margins was marked at the time of surgery (if complete resection/clear margins are not possible). This will allow the radiation oncologist to ensure dose coverage or additional radiation boost.

The high incidence of LR within the skin and subcutaneous tissue indicates that the subcutaneous tissue is without a doubt the higher-risk volume for LR. In recent years, the rates of immediate reconstruction after mastectomy for breast cancer have been increasing, mostly being implant based [56]. In previous years, the implant was generally inserted in a retro-pectoral position (after the expander was removed, Fig. 2c). Early attempts at subcutaneous implants resulted in poor aesthetic outcomes and a high risk of surgical complications [57, 58]. A two-stage procedure, using tissue expanders and permanent implants, was considered standard of care for many years. This procedure provided a complete submuscular pocket (Fig. 2c) of the implant with excellent soft tissue coverage. In the past few years, use of

SSM and NSM with new supportive materials for implant coverage has allowed for a single-stage procedure, avoiding the phase of expansion of muscle and skin tissue. In these procedures, only the upper part of the implant is covered by the pectoralis major muscle, while the lower pole is supported by a mesh, an acellular matrix or autologous flap to create a pocket (Fig. 2c) [57, 58]. With the increasing experience with SSM and NSM and the experience with the new materials for implant coverage, the pre-pectoral approach was re-introduced [58]. Since soft tissue coverage of the implant is important to avoid complications, surgeons tend to leave behind thicker skin flaps (thicker subcutaneous layer) (personal communication, author T.K.). Therefore, pre-pectoral implants might be associated with higher rates of local failures when the operation is not performed correctly. Another issue might be the rate of capsular contractures, especially in patients with little subcutaneous fat tissue and where radiation therapy to the chest wall is required. So far, there are no long-term prospective data to support the oncological safety of pre-pectoralis implants, which are located at the higher-risk volume for LR (the subcutaneous tissue of the native breast) [57].

Importantly, the higher-risk volume (subcutaneous/skin) should be covered by a sufficient radiation dose in case of PMRT. The studies included in our review are relatively old, thus if PMRT was utilized, treatment planning was likely not computed tomography (CT) based as is done nowadays. Additionally, treatment planning systems (TPS) (if any) were not as accurate as today in estimating dose coverage. Therefore, the surgical procedure (pre-pectoral/retro-pectoral) might change the location of the high-risk region and the radiation dose coverage. This should be taken into consideration at the time of PMRT treatment planning, especially if the high-risk volume might be within the 'build-up' dose region, thus potentially being subjected to insufficient radiation dose coverage and poor estimation of coverage by the TPS [20]. There is no consensus on the use or extent of bolus (e.g. scar or entire chest wall skin) after mastectomy without reconstruction, which is even more controversial for cases of immediate breast reconstruction. This should be determined per case according to dosimetry and high-risk volumes to allow for better coverage of high-risk areas of subcutaneous tissues, scar etc. [20, 59].

The median time to recurrence was 26 months (range 1–169 months) [21, 23, 24, 38]. It is unclear from the literature if/how reconstruction and other factors associated with the surgical procedure (SSM, NSM, pre/retro-pectoral, timing, autologous versus implant, lipofilling) influence the LR patterns (location and time of recurrence) [34, 60]. Dillekås et al. [60] noted in their study that timing of LR was not associated with the extent of surgery (extensive reconstructive surgery and simple implant surgery). Advanced disease stage (i.e. tumour and nodal stage) and previous breast cancer (i.e. mastectomy as salvage) have been reported independently as significant risk factors for LR within 12–24 months [16, 38, 60].

Patients who recur within 24 months tend to have poor outcomes [16]. It cannot be excluded that a late LR may represent a second primary at a site of residual glandular tissue (Fig. 3a–c, represented by the native breast subcutaneous tissue anterior to the implant) [61], while a very early recurrence (within a few months from surgery) most probably represents residual disease. Local recurrence should be confirmed by histology. The molecular features of LR should be evaluated. In a study evaluating the molecular features of LRs, in four out of seven (58%) mastectomy scar LRs, the molecular subtype was different from the primary tumour [60]. The distinction between LR and a new primary tumour can be difficult and should be discussed at a multidisciplinary team meeting, as it may change the treatment approach. It should be kept in mind that one-third of patients with LRR will be diagnosed with distant recurrence in < 6 years, leaving a large fraction of patients who can be treated with curative intent [62].

Importantly, at the time a LR occurs, recurrences at the skin/subcutaneous tissue can be discovered clinically in up to 96% of cases [22, 35, 41, 63]. Studies indicate that clinical presentation includes a palpable mass, skin changes and nipple discharge (in case of NSM) [22, 35, 41, 63]. Hence, clinical follow-up with appropriate physical examination and patient education for self-examination could assist in early detection (Fig. 2) [22, 35, 41, 63]. As shown in Fig. 3, imaging can also aid in viewing LR, including subcutaneous and deeply located recurrences (Fig. 3). Further research is needed to validate the role of supplementary screening/surveillance by imaging (mammography, ultrasound and/or MRI) in this population.

Conclusions

Notwithstanding the limitations of our work, this review showed that local recurrences following mastectomy occurred mostly within the subcutaneous tissue and the skin. Pectoral muscle recurrences are less frequent and may be attributed to residual disease along the posterior surgical margin and/or lymphatic involvement.

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