LIPOSUCTION OF POSTMASTECTOMY ARM LYMPHEDEMA DECREASES THE INCIDENCE OF ERYSIPELAS

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ABSTRACT

The objective of this study was to assess erysipelas incidence before and after liposuction treatment for patients suffering from post-mastectomy lymphedema. A prospective cohort study of 130 patients at Skåne University Hospital in Malmö, Sweden with postmastectomy arm lymphedema, who had poor outcomes from prior conservative treatment and clinical signs of subcutaneous adipose tissue hypertrophy, underwent liposuction between 1993-2012. Pre- and postoperative incident data on erysipelas were available for all of them. Mean duration of lymphedema prior to liposuction was 8.8 years (range 1-38, standard deviation (SD) 7.0 years). Mean age at liposuction was 63 years (range 39-89, SD 10 years). Total pre-liposuction observation years were 1147, and total post-liposuction observation years were 983. Erysipelas incidence dropped significantly (p<0.001) from 0.47 attacks/year (range 0-5.0, SD 0.8 attacks/year) to 0.06 attacks/year (range 0-3.0, SD 0.3 attacks/year) after lipo-suction, a reduction of 87%. Also, compared to 76 patients who experienced at least 1 erysipelas episode preoperatively, only 13 patients experienced erysipelas postoperatively. Of the 54 patients who did not have erysipelas preoperatively, 6 patients had erysipelas postoperatively. The total number of erysipelas attacks observed decreased from 534 to 60 bouts after liposuction. The excess arm volume of 1607 ml (range 570-3950, SD 707) was reduced to -43 ml (range -945 to 1390, SD 379) after 6 months and was maintained during the postoperative follow-up period of, at most, 18 years. Our data suggest that liposuction can significantly reduce incidence of erysipelas in patients with post mastectomy arm lymphedema who prior to the intervention suffered one or more attacks.

Keywords: erysipelas, incidence, lymphedema, post-mastectomy, liposuction

Erysipelas is usually caused by strepto-coccal infection mainly affecting the dermis and to a lesser extent the hypodermis. Classical symptoms are fever, erythema associated with edema and pain, and well demarcated plaque borders (1). Several studies show that there is an increase in erysipelas incidence in patients treated for breast cancer (2-5) as a result of recurrent inflammatory episodes, which begins a vicious cycle of erysipelas increasing the risk of lymphedema as well as its severity (6).

Bartholomeeusen et al's study reveals a yearly incidence of erysipelas ranging from 1.71 to 2.55 per 1000 patient in 160,000 different patients over 740,000 patient years representative of the Flemish population

between 1994-2004 (7). Literature on incidence of erysipelas in lymphedema patients is scarce with risk of developing erysipelas in severe forms of lymphedema suggested to be as high as 50% due to lymph stasis after removal of axillary lymph nodes in post-mastectomy lymphedema patients (8).

Although this study suggests erysipelas in post-mastectomy lymphedema patients, it is imperative to acknowledge the ambiguity among the terms erysipelas, cellulitis, and dermato-lymphangio-adenitis (DLA) (9). Also, due to definitional inaccuracies and conflicting and scarce data currently available, there is much controversy as to which type of skin infection condition the patient is suffering from compounded by the fact that the diagnosis of these skin infections are largely made as a clinical diagnosis (1-8,10). This problem will persist until a general consensus is met regarding the definition, clinical symptoms, and diagnosis.

The imbalance between net capillary filtration and lymph drainage is caused by axillary node removal during mastectomy, which subsequently leads to lymphedema (10). Several reviews of incidence of breast-cancer related lymphedema are available and in Britton and Nelson's analysis, lymphedema incidence ranged between 6.7 to 62.5% (11). In Hughes and Patel's analysis, the range was between 41 to 70% (12) and most recently, Petrek and Heelan reported that lymphedema developed in about 20% (6-30%) of mastectomized patients (13). Such a wide range of lymphedema incidence is in large part due to the type of breast cancer treatment performed and while axillary clearance followed by radiotherapy resulted in a significantly higher risk of lymphedema (38.3%), other types and/or combinations of breast cancer treatment such as radiotherapy alone, axillary sampling plus radiotherapy, and axillary clearance alone (7.4-9.1%) did not yield a significant difference from one another (14). Also, none of the 17 patients in the axillary sampling alone group developed clinical lymphoedema (14). Recently, sentinel lymph node biopsy (SLNB) in lymph node-negative patients reduced the incidence of lymphedema from 16% to 5% compared to the SLNB/axillary lymph node dissection group (15).

In addition, increased incidence and prolonged survival of breast cancer patients accounts for an increase in total disease years and thus a higher risk of complications (16). Therefore, effective chronic management carried out by a lymphedema team, which monitors patients long-term, is necessary to detect and treat early common complications, the initial stages of lymphedema, and associated erysipelas (17).

Liposuction has previously been shown to be effective in controlling lymphedema and associated erysipelas (18-20). This approach is considered when conservative treatments fail to achieve satisfactory limb volume reduction and when a non-pitting edema caused by adipose tissue deposition presents (21,22). In order to control the reduced arm volume after liposuction, the patient must, just as after conservative treatment, use compression garment continuously (23).

The purpose of this study was to demonstrate the effectiveness of liposuction in the reduction of erysipelas in previously mastectomized lymphedema patients suffering from bouts of erysipelas.

MATERIALS AND METHODS

All patients who were treated with liposuction at the Lymphedema Unit, Department of Plastic and Reconstructive Surgery, Skåne University Hospital, Malmö, Sweden between 1993 and 2012 due to lymphedema following breast cancer treatment were included in the study. Patients were normally treated with phenoxymethyl-penicillin when having bouts of erysipelas preoperatively. The patients received isoxazole penicillin pre- and postoperatively, during 7 days. In case of allergy to penicillin, clindamycin was given. No additional antibiotics were given after 7 days. All patients

had been treated conservatively preoperatively without being able to successfully reduce the lymphedema and thus the immediate mean preoperative excess volume was still very large.

In order to estimate the incidence of erysipelas, the number of bouts and their timing prior to and following the liposuction were obtained from the patients' case histories and hospital charts, which both were scrutinized in detail. Patient characteristics such as age at mastectomy, year of mastectomy, irradiation, onset of lymphedema, year of liposuction, and pre- and post-liposuction erysipelas incidence were recorded.

From these data the following were calculated: 1) time interval from mastectomy to lymphedema onset; 2) time interval from lymphedema onset to liposuction (duration of lymphedema) also measured as pre-liposuction total observation years; 3) ongoing follow up after liposuction also measured as post-liposuction total observation years; 4) The number of bouts of erysipelas before and after liposuction. In order to get an overall measurement of the risk of erysipelas it is relevant to account for the number of episodes, not only the existence of "ever/never". Erysipelas incidence was, therefore, calculated as number of attacks divided by observation years. Arm volumes were recorded for each patient using the water displacement technique (20). The displaced water was weighed on a balance to the nearest 5 g (corresponding to 5 ml). Hence, both arms were measured and the difference in arm volumes was designated as the excess volume. The decrease in the excess volume was also calculated in percent using percent reduction of excess volume = (initial excess volume - current excess volume)/initial excess volume and the arm ratio was calculated as swollen arm volume/normal arm volume.

Statistics

The incidence of erysipelas was calculated as the number of bouts of erysipelas divided by the number of observation years.

The preoperative period was defined as the time between the first bout of erysipelas and to the time of liposuction, and the postoperative follow-up as the time between liposuction and to end of the follow-up period. The parametric t-test was used to show any differences between pre- and postoperative outcome of surgery. The number of individuals experiencing an episode of erysipelas pre- vs. postoperatively was calculated and the difference was tested using the non-parametric McNemar test.

RESULTS

130 patients with postmastectomy arm lymphedema following breast cancer were analyzed.

The mean preoperative excess arm volume was 1607 ml (range 570-3950, SD 707) and the ratio of the edematous arm/normal arm was 1.5 (range 1.2-2,4, SD 0.2).

After 6 months (n=130) the mean excess volume was -43 ml (range -945 to 1390, SD 379) corresponding to a reduction of 109% (range 61-198, SD 27) (p<0.001), i.e., the treated arm was somewhat smaller than the normal arm. The ratio was 1.0 (range 0.8-1.4, SD 0.1). This favorable result persisted throughout the follow-up period, which lasted for, at most, 18 years.

Mean age at cancer operation between the years 1952 and 2008 was 51 years old (range 31-86, SD 11). All patients except 8 had irradiation. Lymphedema onset occurred on average 2.9 years (range 0-32, SD 4.8) after mastectomy. The duration of lymphedema until liposuction was performed was on average 8.8 years (range 1-38, SD 7.0). Therefore, the time interval between mastectomy and liposuction was on average 11 years (range 1-44, SD 8.2). The mean age at liposuction was 63 years (range 39-89, SD 10). The maximum pre- and postoperative observation period was 38 and 18 years respectively.

Total pre-liposuction observation years, i.e., time from lymphedema onset to

Observation Time	Ery preop: yes Ery postop: yes	Ery preop: yes Ery postop: no	Ery preop: no Ery postop: yes	Ery preop: no Ery postop no
Number (n)	13	63	6	48
Preop. (years)	**11.1**	**10.7**	5.2	6.2
Postop. (years)	**12.7**	7.0	**13.5**	6.3

TABLE 1
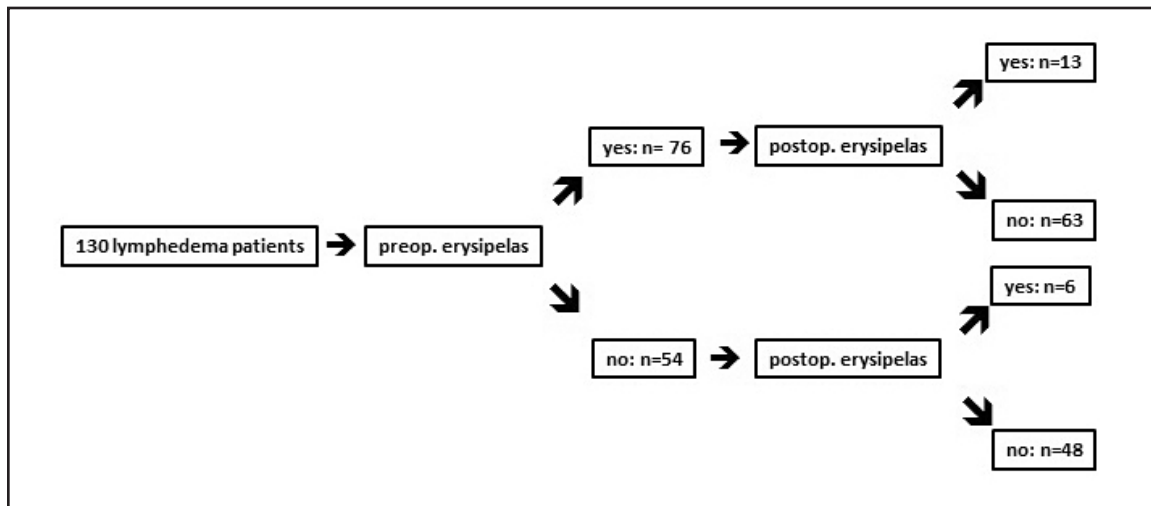**Subgroup Analysis of the Patients Showed in Figure 1**

Fig. 1. Pre- and postoperative number of patients with and without bouts of erysipelas.

liposuction, were 1147 years. During this observation period, erysipelas was clinically diagnosed in 76 patients, the total number of erysipelas attacks was 534 and the erysipelas incidence was 0.47 bouts/year (range 0-5.0, SD 0.8). The post-liposuction total observation years were 983 years. Within this time period, 19 patients were clinically diagnosed with erysipelas, 60 bouts of erysipelas were observed, and the erysipelas incidence was 0.06 bouts/year (range 0-3.0, SD 0.3), corresponding to an incidence reduction of 87% ($p<0.001$). Of the 76 patients who were clinically diagnosed with erysipelas preoperatively, only 13 patients were diagnosed with erysipelas after liposuction ($p<0.001$). Also, of the 54 patients who did not have erysipelas preoperatively, 6 patients were diagnosed

with erysipelas postoperatively. A subgroup analysis showed that the patients who had any bout of erysipelas before or after liposuction had a mean observation time between 10.7 and 13.5 years. On the other hand, no bouts of erysipelas before or after liposuction had a mean observation time between 5.2 and 7.0 years (*Table 1*). Out of 63 patients who had erysipelas preoperatively, none had it after surgery. There were 48 patients who did not have any bouts of erysipelas, either before or after liposuction (*Fig. 1*). There was no correlation between the last recorded excess volume reduction and the reduction in incidence of erysipelas in 119 patients followed for 1 year or more, $p<0.866$ (*Fig. 2*). The remaining 11 patients followed less that 1 year did not have any bouts of erysipelas.
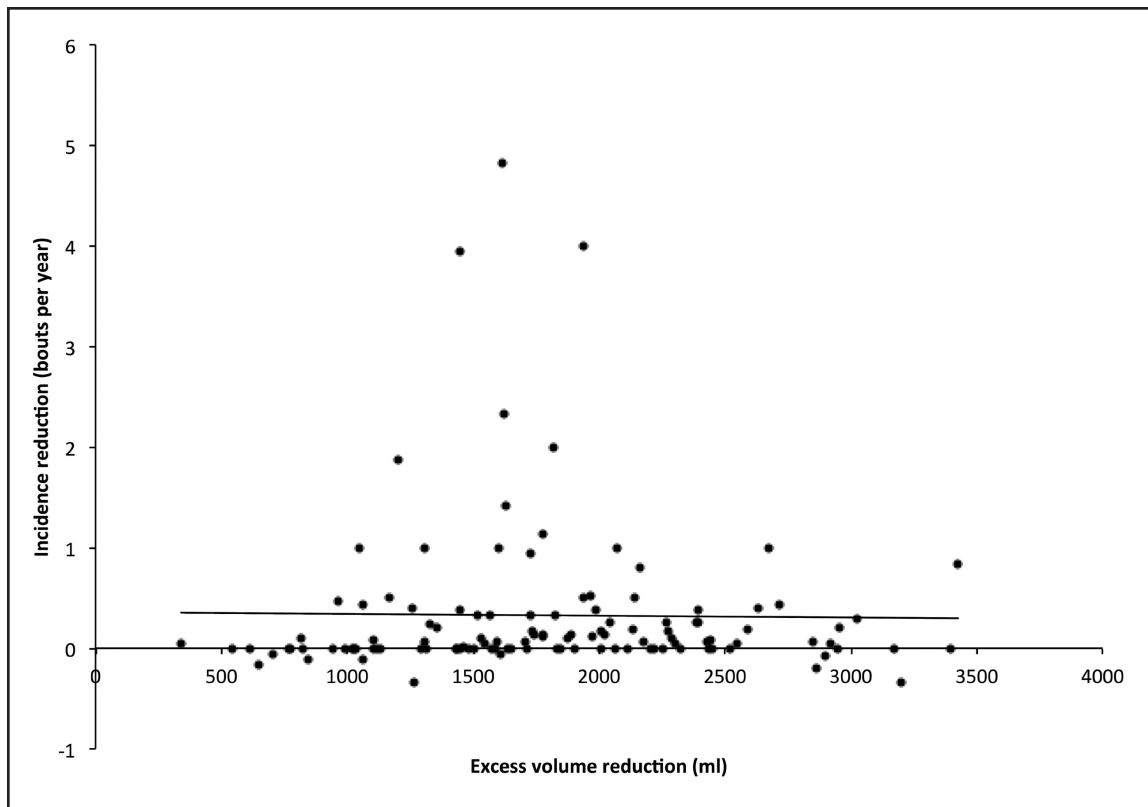
Fig. 2. There was no correlation between the reduction of the incidence of erysipelas and final excess volume reduction.

DISCUSSION

The reduction of erysipelas incidence in breast-cancer related lymphedema patients after liposuction leads to decreased antibiotic usage and hospital visits, and decreased risk of worsening the lymphedema and hence arm volume increase. In turn, this latter may prevent further worsening of quality of life in terms of range of motion of the arm (flexion, extension, abduction, and external/internal rotation) (24) and in various domains such as bodily pain, role-emotional, vitality, mental health, and general health (25). Seventy-six out of 130 patients (58%) suffering from erysipelas clearly indicates that patients with arm lymphedema are at risk of erysipelas. Lymphedema duration for an average of 8.8

years before liposuction suggests that patients suffer from erysipelas for years, which poses physical, social, psychological, and financial burdens on the patients (17). However, only 19 of 130 (14%) patients experienced erysipelas after liposuction. Thus, there was a 75% reduction in lymphedema patients who experienced one or more erysipelas attacks.

According to Jorup-Rönström et al's results, erysipelas provokes a vicious cycle of recurrent episodes in patients with predisposing risk factors such as venous insufficiency and lymphatic congestion. Of the 143 patients admitted primarily with erysipelas, follow-up of 3 years documented in one or more recurrent bouts of erysipelas in 29% of patients and 13% had two or more occurrences (26). To date, although there are

studies on recurrent erysipelas and its risk factors (26,27), there is no reliable data on recurrent erysipelas incidence in breast-cancer related lymphedema patients who were treated with irradiation. Since group A beta-hemolytic Streptococci is the most common cause of erysipelas, antibiotic prophylaxis via narrow spectrum penicillin is administered. Macrolides are used for those who are allergic to penicillin (28). Antibiotic prophylaxis shows effectiveness to prevent recurrent erysipelas to some extent in several studies (9,26,29-31) but does not prevent all episodes, which may be due to patient's non-compliance, incorrect selection/targeting and dosing of antibiotics, and pathogens other than streptococci such as Staphylococcus aureus or Campylobacter species (28).

Conservative treatment or microsurgical reconstructions of the lymphatics cannot remove the excess adipose tissue deposition once it is deposited (21-23). Liposuction however can completely remove this excess tissue thus rapidly normalizing the arm volume (21-23). It reduces recurrent erysipelas incidence from 0.47 to 0.06 attacks/year after liposuction, i.e., an 87% reduction as seen through 18 years of follow up. Possible explanations for this finding include enhanced skin blood flow and a decrease in the accumulation of proteinaceous fluid and adipose tissue (18). Also, wearing of a compression garment and lubricating the arm daily may contribute (18). There were 6 patients who had no erysipelas before surgery but experienced erysipelas after surgery. The explanation is possibly that the preoperative observation time was shorter, 5.3 years as compared to 13.5 years postoperatively (*Table 1*). O'Brian et al reported a reduction in the incidence of recurrent cellulitis by 58% following lymphatic-venous anastomoses (32). Another report on lymphatic-venous anastomoses indicates a reduction of the incidence of erysipelas of 87% (33). In these two studies (32,33), neither bouts of erysipelas (total number of patients who experienced one or more erysipelas attacks and total number of erysipelas attacks diagnosed) nor observation period (total number of years) was presented, which makes the outcome less clear for comparison. A preliminary study with only three years' follow up using lipo-suction combined with myocutaneous flap transfer and lymph-fascia grafting of postmastectomy arm lymphedema showed a reduced frequency of erysipelas after treatment but the preoperative number of observation years and incidence of erysipelas were not presented. Only circumferential measurements, instead of volume measure-ments, were used for postoperative evaluation of the surgical outcome, which showed postoperative increased circumferences, and 7 out of 11 patients were lost to follow-up at 3 years (34).

As discussed earlier, if the lymphedema "pits" on pressure, conservative treatment such as complex decongestive therapy (CDT) must be used in the first place. CDT, just like microsurgery, cannot remove the deposited excess adipose tissue and thus complete and rapid reduction in the limb size cannot be achieved (17). In the literature we found only one paper calculating a reduced incidence of erysipelas after CDT. A 41% reduction was found but here was no description of how the incidence was calculated. The length of the pretreatment observation period was not defined and the follow-up was only 1 year (35). The level of published evidence is as yet insufficient to support the association of microvascular lymphatic reconstruction or CDT and decrease in infection associated with lymphedema.

Since our patients, on average, had complete reduction already after 6 months, we found no correlation between the excess volume reduction and the reduction in incidence of erysipelas. Therefore, it is not possible to postulate whether the reduction in incidence of erysipelas was due to liposuction per se or due to a reduction in lymphedema excess volume (*Fig. 2*). In addition, liposuc-tion removes fat (with some fluid) and treatments such as CDT which result in

volume reduction likely are reducing the "fluid" components.

Accurate and precise analysis on the effectiveness of the different treatment methods of arm lymphedema and registration of incidence of erysipelas is necessary for correctly predicting long-term benefits to the patient. Yet literature on the reduction in erysipelas incidence after lymphedema treatment is scarce. Prospective studies, similar to this one, on erysipelas incidence associated with different treatment methods for lymphedema is recommended as well as long-term track record via systematic approach in the diagnosis of erysipelas and in the collection of data.

CONCLUSION

Our results demonstrate that liposuction as a surgical intervention for lymphedema patients is not only effective in arm volume reduction but is also beneficial in significantly reducing the number of patients who suffer from erysipelas and total bouts of erysipelas.

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