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Reconstructive

Liposuction and Controlled Compression Therapy Reduce the Erysipelas Incidence in Primary and Secondary Lymphedema

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Background: Skin infections are a recurring problem for people with lymphedema, and lymphedema has been proven to be the single most important risk factor for developing erysipelas in the leg. This study aimed to determine whether liposuction for late-stage lymphedema reduces the rate of erysipelas in lower extremity lymphedema.

Methods: One-hundred twenty-four patients with a median age of 49 years who had liposuction and controlled compression therapy for lower extremity lymphedema were included. Excess volumes were calculated before and after surgery. Median preoperative and postoperative patient years at risk were 11 and 5 years, respectively.

Results: With a total of 1680 preoperative person years at risk and 335 bouts of erysipelas experienced in 64 patients, the preoperative incidence rate was 0.20 bouts per person per year, and the period prevalence was 52%. Postoperatively, the patients were followed over a total of 763 person years at risk, and 28 patients experienced a total of 53 bouts of erysipelas, resulting in a postoperative incidence rate of 0.07 bouts per person per year, and a period prevalence of 23%. This represents a 65% decrease in the erysipelas incidence rate ($P < 0.001$). The preoperative median excess volume of 3158 ml was reduced with a median of 100% ($P < 0.0001$).

Conclusions: Liposuction and controlled compression therapy significantly reduce the risk for erysipelas in lower extremity lymphedema and completely reduces the excess volume. This finding is similar to our previous research including patients with upper extremity lymphedema. *(Plast Reconstr Surg Glob Open 2022;10:e4314; doi: 10.1097/GOX.0000000000004314; Published online 6 May 2022.)*

INTRODUCTION

Causes of lower extremity lymphedema (LEL) include oncological surgery to the genital/inguinal area, trauma, endemic filariasis, and genetic variations resulting in abnormalities in the lymphatic system.[1] Lymphedema results in an inflammatory process leading to adipose tissue deposition, predominantly subcutaneous in the lymphedematous tissue, but to a small extent also subfascial in the muscle.[2–10] At this stage (corresponding to the International Society of Lymphology grading system stages II & III[11]), the excess volume cannot be reduced solely using conservative measures or microsurgical procedures because these treatment modalities aim to remove the fluid component of the lymphedema, not the adipose tissue. Therefore, liposuction has been introduced as a method of treatment in late-stage lymphedema, with excellent long-term results.[12–15]

Erysipelas is a skin infection involving the dermis and part of the hypodermis, and is normally a result of a streptococcal infection.[16] The condition is categorized within the group of cellulitis infections, which also include

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infections reaching deeper into the hypodermis.[16] There is some confusion about the terms "cellulitis" and "erysipelas" in the literature because the words are sometimes used interchangeably, particularly in Europe.[17] We do not address infections in the deeper subcutaneous layer, such as necrotizing dermo-hypodermitis and necrotizing fasciitis. The lower extremities are the areas most affected by erysipelas, and up to 85% of cases occur in lower extremities.[18] Both the superficial erysipelas infection and the deeper infections present with similar symptoms: redness, tenderness, heat of the affected area, and fever. Differences are normally seen in the erythematous area, where erysipelas normally has a clear distinction between infected and healthy tissue and the red skin is elevated, whereas the borders of cellulitis are less defined due to its deeper location.[19]

The incidence of erysipelas in LEL ranges between 36% and 48%.[20–22] In a case-control study by Dupuy et al,[23] it was shown that lymphedema was the greatest risk factor for developing erysipelas of the leg, with an OR of 58 (95% CI: 17–197). Another study by Inghammar et al[24] has shown that lymphedema is the greatest risk factor for erysipelas recurrence, which is in accordance with results from more recent research.[25] It has also been shown that late-stage lymphedema correlates with a higher incidence of erysipelas[26] and that lymphedema is a risk factor for developing bacteremia in the presence of cellulitis.[27] In a study by Deng et al,[20] patients with LEL had an increased OR of 2.53 (95% CI: 1.77–3.62) for developing skin infections compared with patients with upper extremity lymphedema (UEL).

In a majority of patients with erysipelas in the upper and lower extremities without a prior history of lymphedema, decreased lymphatic transport can be found on lymphoscintigraphy in both the affected and nonaffected extremities, indicating a previously impaired lymphatic system.[28] Thus, it has been speculated that a substantial amount of erysipelas infections may be caused by subclinical lymphatic impairment.[28,29] The infection in itself has also been indicated to further impair the lymphatic system.[30] The current study aimed to determine whether liposuction and controlled compression therapy (CCT) for LEL reduce the incidence of erysipelas.

Takeaways

Question: Does liposuction reduce erysipelas in patients with leg lymphedema?

Findings: One-hundred twenty-four patients were operated on followed by controlled compression therapy. Excess volumes were calculated before and after surgery. The preoperative erysipelas incidence was 0.20 bouts per person per year with a period prevalence of 52%. Postoperatively the incidence was reduced to 0.07 bouts per person per year, and a period prevalence of 23%. This represents a 65% decrease in the erysipelas incidence ($P < 0.001$). The preoperative median excess volume of 3158 ml was reduced with a median of 100% ($P < 0.0001$).

Meaning: Liposuction significantly reduces erysipelas incidence and normalizes the leg volume.

MATERIALS AND METHODS

Patients

Patients with LEL who were treated with liposuction in combination with CCT at Skåne University Hospital in Malmö, Sweden, between 1993 and 2020 were included in this study. Eligibility criteria for liposuction included a 10% volume increase in the affected extremity, no or marginal pitting on pressure (<6–7 mm) indicating adipose tissue deposition,[31–33] no active cancer, no current infections, and a positive attitude toward the continuous use of compression garments. Patients with bilateral lymphedemas were excluded from the study. Our criteria for erysipelas are an erythematous area on the affected leg in combination with fever (body temperature > 38.0°C), which may or may not be accompanied by nausea and often warmth and pain in the affected area. All patients get compression garments as soon as the lymphedema is diagnosed. Fifty-four of 61 patients with secondary lymphedema had removal of lymph nodes, 29 were irradiated and 23 received chemotherapy.

Volume Measurements

All preoperative measurements and measurements up to around 2 years postoperatively were conducted using plethysmography, where the extremity is lowered into a container of water and the overflow of water is measured to the nearest 5 g, corresponding to 5 ml.[34–36]

Data Collection

On their first visit, all patients were asked in detail about previous episodes of erysipelas in the affected extremity, including what year they occurred and what treatment they received. Data were also complemented with information from hospital charts. The occurrence of postoperative episodes of erysipelas was checked at follow-up appointments as well as using data received from patients' home clinics.

Treatment Protocol

The surgical procedure and the subsequent protocol for CCT have been described in detail in previous studies.[13,14,36–38] In short, power-assisted liposuction (Lipomatic, Nutational Infrasonic Liposculpture, Euromi, Andrimont, Belgium) is performed, first by using a tourniquet placed in the most proximal part of the thigh. Before releasing the tourniquet, a sterilized flat-knit compression garment (panty with a leg, Jobst Elvarex, compression class 3, compression range 33–46 mm Hg) is put on up to the tourniquet to stem any bleeding.[39] Compression garments are ordered 2 weeks before surgery based on measurements of the unaffected leg. The proximal part of the thigh is then treated using the tumescence technique, after which the rest of the compression garment is applied. During 1993–1996, the "dry technique" with no tourniquet nor tumescence was used (n = 2). From 1997 to the end of the study, the combination of tourniquet and tumescence

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was used for all patients except when only tourniquet liposuction was necessary due to distal lymphedema (n = 1). Postoperative antibiotics (isoxazolyl penicillin) are given intravenously for the first postoperative day and then orally for 10 days. The compression garment is changed on the second postoperative day after showering and lubrication of the skin and a new garment (panty with a leg) is put on. On top of this, a leg-long compression garment (Jobst Elvarex, compression class 2, compression range 23–32 mm Hg) is put on.

The patient receives two sets of garments; one set contains one panty with a leg, and the one leg-long compression garment. The leg-long garment is removed at night, and the patient sleeps with the panty with a leg. Subsequently, garments are changed every second day during the first week and thereafter they are changed every day. The used set is washed and dried to be used for the next change. Compression is used continuously. Postoperative follow-ups are conducted at 2 weeks, 1, 3, 6, 9, and 12 months, and thereafter every 12 months unless complete reduction is not achieved, which would lead to continued follow-ups at three-month intervals. Garments are ordered every third month during the first year and if complete reduction is achieved after the first year, garments for a whole year are ordered. Normally a patient needs six to eight sets of garments per year. When complete reduction is accomplished, patients are referred back to their ordinary lymph therapist for further follow-up.

When patients were referred back to their home clinic, measurements were taken every 4 cm along the extremity once a year, and the excess volume was calculated using the formula of the truncated cone, which correlates well with plethysmography.[40] All measurements were reported back to us and inserted into our quality register.

Statistics

The incidence rate of erysipelas for each patient was calculated with the following formula: total number of bouts of erysipelas for all patients divided by total number of person years at risk, where preoperative person years at risk included the time of lymphedema debut until liposuction, and postoperative person years at risk was the date of liposuction until the latest follow-up. The period prevalence was defined as the percentage of patients who experienced at least one bout of erysipelas during the observation period. The data are presented as median and interquartile range (IQR) due to the data's nonparametric characteristics. For statistical analysis, preoperative and postoperative incidence rates were divided into clusters, where a cluster represents a patient, and the data were summarized into incidence rates for each patient. This was done because there might be an explanation for why some patients experience many bouts of erysipelas (risk factors), and thus, bouts experienced by one patient (a cluster) are more correlated to each other than bouts of a number of patients are. These clusters did not follow a normal distribution and were compared using a Wilcoxon matched-pair signed-rank test for preoperative and postoperative incidence rate. The occurrence of preoperative bouts of erysipelas (yes/no) was compared with the occurrence of postoperative bouts of erysipelas (yes/no) using MacNemar's exact test. Demographics were analyzed for correlation to the preoperative erysipelas incidence rate using a Mann-Whitney U test. Also, age was analyzed for correlation to preoperative incidence rate of erysipelas, and the ratio (volume affected leg/volume nonaffected leg) at the last follow-up was analyzed for correlation to the clustered postoperative decrease in the erysipelas incidence rate using a Spearman correlation test. All calculations were performed using IBM SPSS Statistics for MacOS 10.14.2, version 26.0. (Armonk, N.Y.: IBM Corp, released 2019). A *P*-value less than 0.05 was used to indicate a statistically significant result.

Ethics

The study was approved by the Swedish Ethical Review Authority (2020-03102). Participants have given their consent to be included in a local lymphedema register and an "opt out" method has been used for participation in this study.

RESULTS

In total,130 patients underwent liposuction due to LEL between 1993 and 2020. Of these, two patients had bilateral lymphedema and four did not want to participate and were excluded. Thus, 124 patients were included in this study, with a median age of 49 years (IQR 37–60) at the time liposuction was performed. The demographics are presented in Table 1. Three patients had lympho-venous anastomoses performed before liposuction and of these,

Table 1. Demographics of the Studied Population

Demographics	Years (median, IQR)	Range
Age at liposuction	49 (37–60)	15–77
Onset of lymphedema after cancer surgery	1 (1–3)	0–33
Duration of lymphedema	11 (6–18)	1–63
Follow-up after liposuction	5 (2–90	0–26
Demographics	**No.**	**Percent**
Primary lymphedema	63	51
Secondary lymphedema	61	49
Male and primary lymphedema	9	7
Male and secondary lymphedema	5	4
Female and primary lymphedema	54	44
Female and secondary lymphedema	56	45
Cause (secondary lymphedemas)		
Cervical cancer	34	56
Endometrial cancer	9	15
Malignant melanoma	6	10
Penile cancer	2	3
Hodgkin's lymphoma	2	3
Trauma	2	3
Ovarian cancer	2	3
Sarcoma	1	2
Non-Hodgkin lymphoma	1	2
Seminoma	1	2
Snakebite	1	2
Irradiation	29	23
Chemotherapy	23	19
Removal of lymph nodes	54	89
Conservative treatment (other than compression garments)	118	95
Compression garments	121	98
Erysipelas preoperatively	64	52
Erysipelas postoperatively	28	23
Total number of erysipelas bouts preoperatively	335	86
Total number of erysipelas bouts postoperatively	53	14

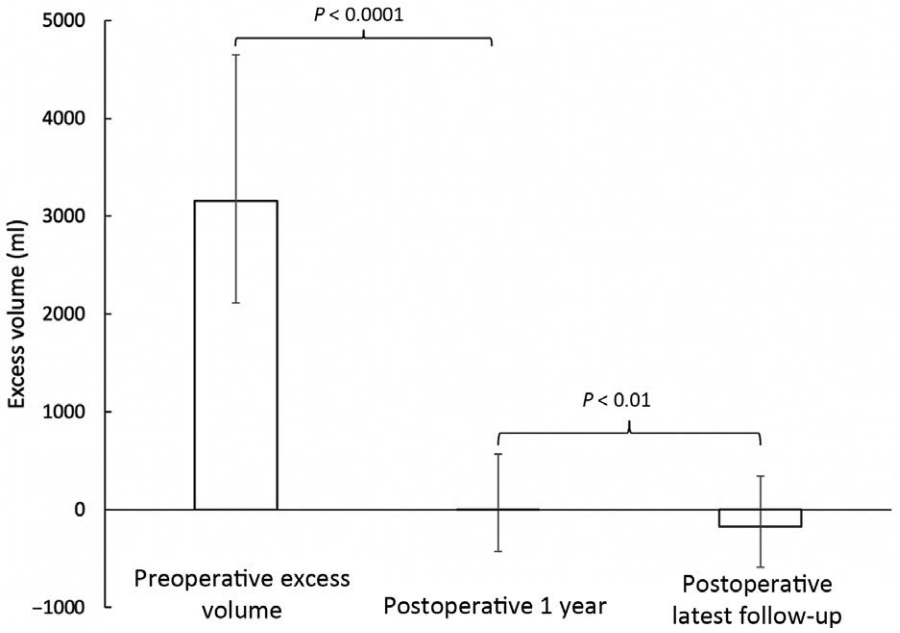

Fig. 1. Pre- and postoperative excess volume reduction (median, IQR). Following surgery, a significant reduction was seen after 1 year, which was maintained at the most recent follow-up.

none experienced erysipelas before liposuction and one experienced it after surgery. None of the patients have had any physiologic lymphatic surgery after liposuction. In total, 110 patients were women (89%) and 63 patients (51%) had primary lymphedema. The median duration of lymphedema until liposuction was 11 years (IQR 6–18).

An estimated 121 patients used compression garments before liposuction where two of the remaining three patients used bandaging. The remaining patient had a temporary lymphatic blockage in childhood due to a fracture of the femur with hemorrhage that led to lymphedema and adipose tissue deposition, but because the preoperative lymphoscintigraphy was normal after clearance of the hemorrhage, no compression was necessary. There

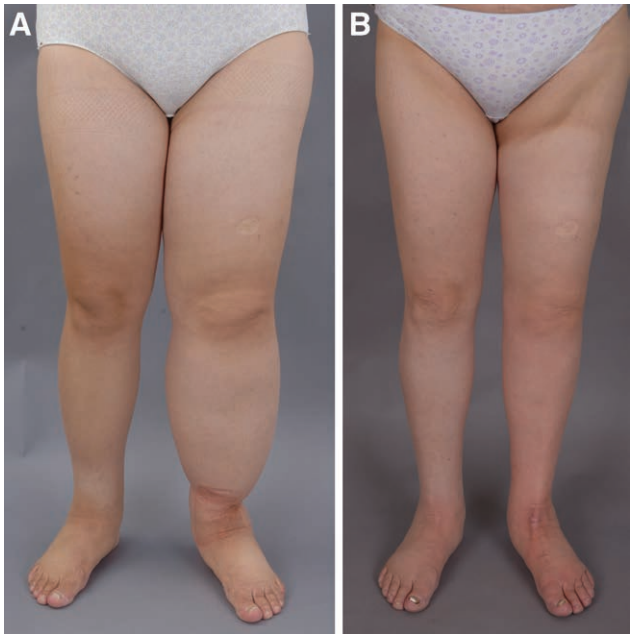

Fig. 2. Liposuction completely reduces the excess volume. A, A 50-year-old woman with a preoperative excess volume of 4415 ml in the left leg following treatment of uterine cancer 12 years before liposuction. At surgery 4470 ml adipose tissue was removed. B, At 8 years after liposuction, the excess volume was −180 ml, a slight overcorrection.

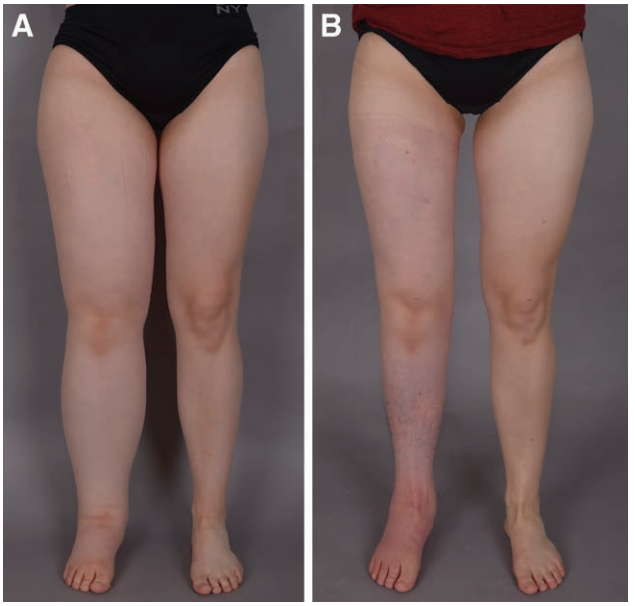

Fig. 3. Liposuction completely reduces the excess volume. A, A 31-year-old woman with primary lymphedema for 6 years and a preoperative excess volume of 4565 ml in the right leg. At surgery 4420 ml was removed. B, At 2 years after liposuction the excess volume is −45 ml, a slight overcorrection.

was no need for skin excision in any patient. The median follow-up time after liposuction was 5 years (IQR 2–9), and four patients were followed for less than 1 year.

The preoperative median excess volume was 3158 ml (IQR 2114–4650 ml) with a median ratio to the nonaffected leg of 1.34 (IQR 1.24–1.44). At the 1-year follow-up after liposuction (n = 120), the excess median volume was –5 ml (IQR –430 to 568) ($P < 0.0001$), representing a median reduction of 100% (IQR 83–116) (Fig. 1). Figures 2 and 3 show typical outcomes following liposuction.

Sixty-four patients experienced at least one bout of erysipelas preoperatively, and in total 335 bouts of erysipelas were counted preoperatively during 1680 person years at risk, resulting in a preoperative incidence rate of 0.20 bouts per person per year. The preoperative period prevalence was 52%.

Postoperatively, 28 patients experienced erysipelas, with a total of 53 bouts in 763 person years at risk, an incidence rate of 0.07 bouts per person per year, which is a 65% decrease from the preoperative incidence rate ($P < 0.001$). The postoperative period prevalence was 23%. No significant difference was found in preoperative incidence rate in men compared with women ($P = 0.11$). Age did not show a significant correlation to the preoperative incidence rate of erysipelas, with a Spearman correlation coefficient of $\rho = 0.17$ ($P = 0.07$).

The number of patients experiencing erysipelas preoperatively (n = 64) was significantly different from the number of patients experiencing erysipelas postoperatively (n = 28) ($P < 0.001$). Of the 64 patients who had erysipelas preoperatively, 18 patients experienced bouts of erysipelas after liposuction and 46 patients experienced no erysipelas (Fig. 4). Ten patients who had no erysipelas preoperatively experienced bouts of erysipelas postoperatively, and 50 patients experienced no erysipelas at all. The incidence for the patients who experienced erysipelas both pre- and postoperatively (n = 18) was 0.41 and 0.23 respectively (<0.025), representing a reduction of 45%. Table 2 illustrates the rates of erysipelas along with the median observation time. No significant correlation was found between the volume ratio (affected leg to nonaffected leg, representing postoperative results) at the last follow-up and the postoperative incidence rate reduction (bouts per year) (Spearman correlation coefficient ρ = -0.14 (P = 0.14) as shown in Fig. 5). Comparing the preoperative incidence of erysipelas in primary and secondary lymphedemas, the incidence was 0.17 bouts per person per year and 0.24 bouts per person per year, respectively, with no difference between them ($P = 0.095$). Postoperatively, the incidences decreased to 0.04 bouts per person per year ($P = 0.01$) and 0.10 bouts per person per year ($P = 0.002$), respectively. There was no statistical difference between the postoperative incidence reduction between primary and secondary lymphedemas ($P < 0.10$), nor any difference in postoperative incidence ($P < 0.47$).

DISCUSSION

Few reports are available that include the total number of bouts per patient, the period prevalence of erysipelas/cellulitis, in combination with the number of patient-years included in the study, as well as an adequate follow-up time and a statement of what type of skin infection is included.

A previous study conducted by Lee et al[41] showed that liposuction in combination with CCT reduces the incidence of erysipelas by 87% from 0.47 to 0.06 bouts per person per year in patients with UEL. Similar results have been shown in other studies with an incidence reduction of 45%–92% in patients treated with LVA[42–46] and a reduction of 64%–95% in patients treated with vascularized lymph node transfer.[47–50] Complete decongestive therapy has been shown to reduce the incidence of erysipelas by 41%–63%.[51,52]

The reduction in erysipelas incidence probably leads to financial savings due to fewer admissions to hospital care and fewer prescriptions of antibiotics with less physical suffering for lymphedema patients.

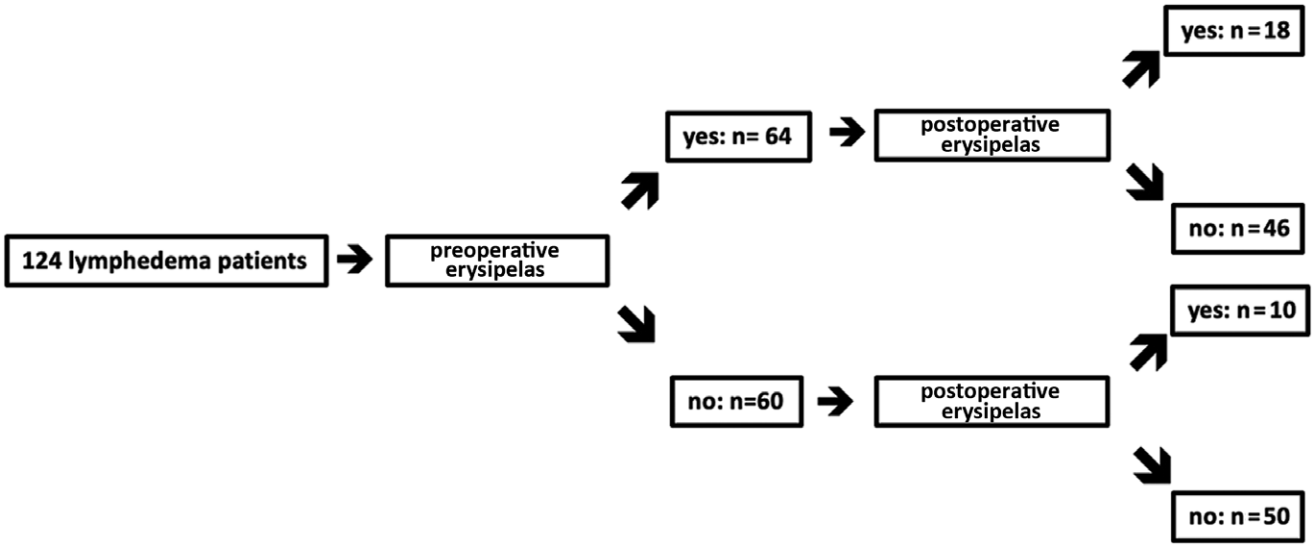

Fig. 4. Flowchart illustrating the number of patients included in the study who experienced at least one bout of erysipelas before and after liposuction. n = number of patients.

Table 2. The Median (IQR) Observation Time in Years for all Patients, Divided into Groups Based on the Occurrence of Erysipelas before and after Surgery

Observation Time (y)	EB Before: Yes EB After: Yes	EB Before: Yes EB After: No	EB Before: No EB After: Yes	EB Before: No EB After: No	Total
n	18	46	10	50	124
Before	9.5 (6.3–20)	14 (9.0–21)	4.5 (3.0–12)	11 (6.0–15)	
After	7.5 (4.0–12)	5.0 (2.0–9.0)	3.0 (2.0–7.5)	4.0 (2.0–7.0)	

EB, erysipelas bouts; n, number of patients.

The underlying reason for the reduction in erysipelas can be speculated to be a result of better skin blood flow and skin management, continuous wearing of garments in combination with a reduction in the amount of adipose tissue that could enhance bacterial overgrowth.[7–9,41,53]

In general, our results show a lower incidence rate of erysipelas compared with the existing literature.[20,21,50,54] The difference observed in this study compared with previous studies could reflect the fact that our observation started at lymphedema debut. However, most studies do not report the observed number of years preoperatively, and if not all years since the first lymphedema debut are included, those studies may not reflect the general incidence but a more specific incidence in the period before the intervention. For example, Aljaaly et al[49] have reported an incidence of 6 bouts per year per patient of cellulitis in 15 patients with UEL before vascularized lymph node transfer treatment, which is an incidence 30 times higher than the preoperative incidence in this material. A shorter observation period and the lower number of recruited patients might result in the observed difference in the general cellulitis/erysipelas incidence. Other factors might also affect the risk for erysipelas, such as socioeconomic status, water quality, climate, and access to healthcare.

No correlation could be seen between the last volume ratio and the postoperative reduction of erysipelas bouts, which are in accordance with previously reported results showing no evident correlation between lymphedema size and the risk of recurrence of cellulitis.[55] It has been shown that skin condition has an influence on the risk of developing skin infections because leg wounds and interdigital intertrigo leads to increased risk of erysipelas.[23]

For patients to be compliant to the postoperative protocol, they should follow the instructions on compression garments, considering usage and changes as well as to adhere to follow-up appointments so garments can be renewed regularly. If patients think that they cannot be

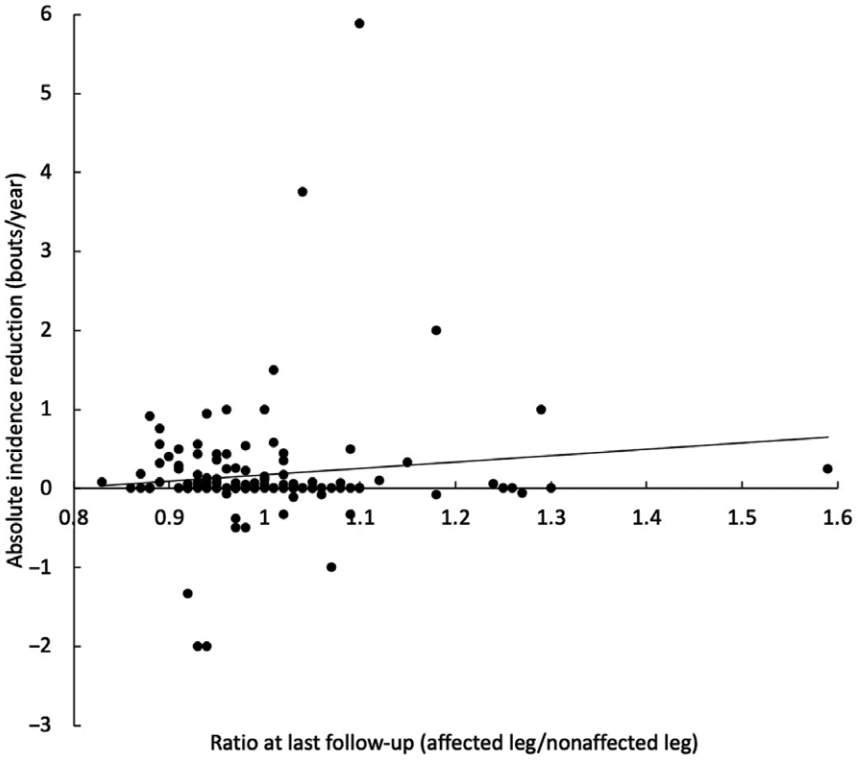

Fig. 5. Correlation between the absolute postoperative reduction in erysipelas incidence rate and the latest volume ratio (volume affected leg/volume nonaffected leg). No significant correlation could be found, Spearman correlation coefficient $\rho = -0.14$ ($P = 0.14$).

compliant with compression after surgery, they will not be operated on. If the excess volume increase at any point after liposuction, there is always a discussion with the patient about usage of compression garments. In these few cases, patients are not excluded from the study because compliance is not measured objectively.

One weakness of the study is the retrospective nature of data collection when patients are considered for liposuction and patients provide information about previous bouts of erysipelas. Some patients had lymphedema for many years, and it might have been difficult to remember the precise number of bouts during this time span. Also, because admission to hospital was not a mandatory criterion for erysipelas in this study, bouts of erysipelas treated on an out-patient basis by their general practitioners are also included, thus relying on the recognition of symptoms by the patient. Naturally, some bouts may be missed, but due to our thorough investigation of patients' records, we believe recall bias is small. It cannot be determined how much of the decrease is attributed to liposuction or to the strict compliance to postoperative CCT, but because all patients wore compression before liposuction, liposuction may play a major part in the reduction of bouts of erysipelas. One patient used continuous prophylactic antibiotics before surgery and no one after. The long observation time and the large study cohort are major strengths of this study. Also, the precise follow-up program and the concrete CCT management make the results easy to interpret, compare and reproduce.

CONCLUSIONS

Liposuction in combination with CCT for nonpitting LEL significantly reduces the incidence rate of erysipelas and leads to complete reduction of the excess volume. When studying erysipelas incidence, we encourage the presentation of the total number of observational years before (from lymphedema debut) and after treatment, the total number of bouts of infection, and the period prevalence along with the diagnostic criteria for the skin infection to achieve comparable outcomes.

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