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Liposuction for Advanced Lymphedema in a Multidisciplinary Team Setting in Australia – Five-Year Follow-Up

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Statement of Financial Disclosures, Conflicts of Interest, and Products

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Abstract

Background

Liposuction for International Society of Lymphology (ISL) late stage II or III limb lymphedema is an established surgical option to remove excessive adipose tissue deposition and has been performed in Australia since 2012 at the Australian Lymphoedema Education, Research and Treatment (ALERT) Program, Macquarie University.

Patients and methods

Between May 2012 and May 2017, 72 patients with unilateral primary or secondary lymphedema of the arm or leg underwent suction-assisted lipectomy using the Brorson protocol. This prospective study presents 59 of these patients who had consented to research with a five-year follow-up.

Results

Of the 59 patients, 54 (92%) were women, 30 (51%) had leg lymphedema and 29 (49%) had arm lymphedema. For arm patients, the median preoperative volume difference between the lymphedematous and the contralateral arm was 1061 mL, which reduced to 79 mL one year after surgery and to 22 mL five years after surgery. For leg patients, the median preoperative volume difference was 3447 mL, which reduced to 263 mL one year after surgery but increased to 669 mL five years after surgery.

Conclusions

Suction-assisted lipectomy is a long-term option for the management of selected patients with ISL late stage II or III limb lymphedema when conservative management can offer no further improvement.

Introduction

Lymphedema is a condition of persistent swelling with associated skin and tissue changes that can be of either primary and secondary origin.(1) Secondary extremity lymphedema in the Western world is often a result of lymph node dissection and radiation therapy for breast and gynecological cancer leading to arm and leg lymphedema, with a postoperative incidence of around 20% in both conditions.(2,3) Currently, the mainstay for conservative lymphedema treatment is Complex (or Complete) Decongestive Therapy, which includes education, skin care, exercise, compression therapy and manual lymphatic drainage.(4) It has been shown that chronic inflammation leads to adipose tissue deposition in lymphedema, which is unresponsive to conservative treatment.(5-8) The International Society of Lymphology (ISL) classifies lymphedema into three stages, where stage I is defined as 'an early accumulation of fluid relatively high in protein content which subsides with limb elevation' and stage II as 'more changes in solid structures'.(4) Later in stage II 'the limb may not pit as excess subcutaneous fat and fibrosis develop'. Stage III 'encompasses lymphostatic elephantiasis where pitting can be absent and trophic skin changes such as acanthosis, alterations in skin character and thickness, further deposition of fat and fibrosis, and warty overgrowths have developed'. In these later stages, liposuction has become useful and enables complete long-term limb excess volume reductions by liposuction and controlled compression therapy (9-12).

Liposuction for lymphedema is not new to Australia. In 1989, O'Brien and colleagues from Melbourne (13) published a preliminary report of 19 patients who underwent liposuction for lymphedema. They reported 'objective improvement in 10 of the 11 patients with unilateral lymphedema, with an average reduction of 23% of the excess volume'. Around the same time,

Sando and Nahai from the US (14) reported a similar experience in 15 lymphedema patients, with average volume reductions of 8%.

Not long thereafter, Brorson and Svensson from Sweden published their results of complete reduction of lymphedema of the arm through liposuction after breast cancer in 1997, with an average reduction in limb excess volume of 106% in 28 patients.(15) Their follow-up report revealed that liposuction needed to be combined with controlled compression therapy to be effective, and without compression the lymphatic fluid will reaccumulate.(16) Subsequent long-term follow-up reports did not show any recurrence of the swelling .(9, 17) Liposuction does not affect the already impaired lymph transport (18), and quality of life was found to be improved after reduction of limb volumes with liposuction.(19) Also, the incidence of cellulitis was reduced by 87 percent in patients with arm lymphedema (20) as well with 65 percent in patients treated for leg lymphedema (21).

Other teams have been trained in this technique and the results were reproduced by Damstra in the Netherlands (22), by Munnoch in the United Kingdom (23, 24), by Singhal (25, 26) and Greene (27) in USA, and by Boyages et al. in Australia (28) At Macquarie University, Sydney, Australia, we established a multi-disciplinary ALERT Surgical Clinic in 2012 and carried out our first liposuction surgery for a patient with lymphedema of her right arm after treatment for breast cancer.(28) To date, we have performed over 100 cases of liposuction for arm and leg lymphedema. The aim of this study was to evaluate the effectiveness and outcomes of liposuction for lymphedema over a five-year period.

Patients and Methods

Patients and Study Design

Between May 2012 and May 2017, 72 patients underwent liposuction for lymphedema. The study period was chosen to include patients with a five-year follow-up. Within this group, nine patients did not consent to their data being used for research purposes and were excluded from this study. In addition, three patients did not return for follow-up more than once and were also excluded. Another patient was excluded as she had bilateral lower limb lymphedema from multiple soft tissue excisions after massive weight loss. As a result, 59 patients with unilateral limb lymphedema treated with liposuction were included. Liposuction for arm lymphedema commenced in May 2012, followed by leg lymphedema 12 months later. Approval for the use of this data has been obtained under Macquarie University Human Research Ethics Application (reference numbers: 5201300315 and 52020613914268) and patients gave their written, informed consent to participate with their data.

A detailed description of our multidisciplinary setting and team approach has previously been published.(28) Our selection criteria for liposuction were: 1) advanced primary or secondary lymphedema (ISL late stage II or III) (4) resulting in significant functional, physical and psychological morbidity; 2) no evidence of active cancer in patients with lymphedema secondary to cancer treatment; 3) limb volume difference greater than 20% for whole limb or limb section; 4) increased amount of adipose tissue in the affected limb with minimal fluid component, measured with magnetic resonance imaging (MRI) (29); 5) previous conservative lymphedema management had resulted in a stable limb volume difference where the pitting-test showed no or minimal pitting; 6) willingness to wear compression garments continuously and to attend the outpatient clinic at approximately two to six weeks, and then at three, six, nine, 12, 18 and 24

months and, 7) agreement to continue longer-term management with the ALERT program or with their local lymphedema therapist, supported by ALERT therapists. The final decision for surgery was made within a multidisciplinary team discussion where selection criteria and MRI results were considered along with patient's goals.

Limb volume and Bioimpedance Spectroscopy measurements

Limb volumes were calculated based on circumferential limb measurements taken with a tape measure and measuring board at 4 cm intervals starting at the ulnar styloid for arms and the lateral malleolus for legs continuing as far proximally as possible. Volumes were then calculated using the truncated cone formula.(30, 31) Both extremities were always measured at each visit, and the difference was defined as the excess volume.

Bioimpedance spectroscopy (BIS) was used to measure extracellular fluid in the affected limb as a ratio compared to the unaffected limb. BIS measurements were recorded in L-Dex units (normal range is -10 to +10) with the L-Dex® U400 (ImpediMed, Brisbane, Australia) following standard operating procedures. The device has been validated for use in patients with lymphedema.(32)

Liposuction and follow-up

We followed the Brorson protocol (9, 10, 15-17, 33) and members of our ALERT multidisciplinary team were trained by Professor Brorson in Sweden. Liposuction of the affected limb was performed under general anaesthesia via multiple small stab incisions. Before liposuction was started a tourniquet was applied as proximal as possible on the extremity after exsanguination using Esmarch bandages (34). Whereas Brorson used his own specially made cannulas, we used the commercially available Microaire power-assisted liposuction (PAL®) system (Microaire, Charlottesville, VA, USA) with 'spiral' cannulas. The orientation of cannula

movement should always be longitudinal to the limb, as this has been found to reduce the risk of lymphatic injuries.(35, 36) Once liposuction was completed, with the affected limb measurements checked against the unaffected limb, and the aspirated fat volume equivalent to the calculated volume difference, the surgical stab incisions were left open to drain with dressings applied. Compression was applied prior to tourniquet release. For the arm a flat-knit compression sleeve from wrist to axilla (JOBST Elvarex, compression class 2) and a flat-knit, standard, ready-to-wear glove (Medi) was applied. For the leg an adjustable Velcro wrap (Haddenham Easy-wrap for the foot and Lohmann and Rauscher Ready-wrap from the ankle to the proximal thigh) with foam padding at the ankle, shin and back of the knee was used. These garments and wraps were ordered from preoperative measurements of the unaffected limb but using the actual measurements of the affected limb for the hand to the wrist and the foot to the ankle. After the tourniquet was released, tumescent liposuction was performed to the proximal part of the limb that was previously under and above the tourniquet. Once liposuction was completed, the compression sleeve or Velcro wrap was adjusted to cover these areas. Postoperatively, patients were given intravenous antibiotics for two days and then oral antibiotics for a further two weeks, as a number of these patients preoperatively suffered from recurrent and potentially life-threatening cellulitis in the affected limb. For arms, compression garments were changed after two days, and again every other two days until the patient was comfortable to return to the usual daily alternate wash and wear regimen. For legs, the wraps were exchanged for compression garments within the next week with a preoperatively measured JOBST Elvarex Class 3 one-legged pant style. If patients with arm lymphedema could manage the garment change by themselves on day four postoperatively, they were discharged with skin care and hygiene instructions. Interstate or international patients (37%) and most lower limb patients were

usually transferred to a rehabilitation hospital for a further five to seven days to ensure independent management before returning home. Typically, garments were replaced every three to six months for the first year, and then every six months once limb volume reduction was stable and equivalent to the unaffected limb. Two sets of garments were always supplied so one could be washed when the other one was used. After 24 months, patients either continued to attend the outpatient clinic for ongoing six-monthly follow-up or were transferred to their local lymphedema therapist with support and advice concerning garments from the ALERT team. At the time of this study, there was a dropout of available postoperative data beyond 24 months due to transfer of ongoing care to local lymphedema therapist, in some cases overseas (New Zealand), along with Covid-19 travel restrictions and lock down policies.

Statistics

Statistical analysis was performed using IBM SPSS Statistics for Macintosh, Version 27.0. Armonk, NY: IBM Corp, released 2020. The dataset was divided into arm and leg lymphedemas and statistical analyses were performed separately for each group. Normality of the variables was tested by the Shapiro-Wilk test but could not be confirmed. Therefore, non-parametric tests were applied, and the results presented as median and interquartile range (IQR). The significance of outcome measures (limb volume and BIS) was tested with the Wilcoxon signed-rank test and differences among groups were tested with the Mann-Whitney U test or chi-squared test for binary variables. For correlation analysis, the Spearman correlation coefficient was used, and baseline demographics was also tested in a multiple linear regression model. A p-value <0.005 was considered statistically significant.

Results

Among the 59 patients, there were 29 lymphedema arms and 30 legs [**Table 1**]. All arm patients had secondary cancer-related lymphedema (27 breast cancer and two melanoma). Twelve of the 30 leg patients had primary lymphedema. Approximately 37% of the patients came from interstate or from New Zealand. Twenty-two patients (76%) with arm lymphedema and 21 patients (70%) with leg lymphedema completed two years follow-up and loss to follow-up increased as patients were transferred to local lymphedema therapist. Twelve patients (41%) with arm lymphedema and six patients (20%) with leg lymphedema completed five years follow-up.

Limb volume reduction

The median preoperative arm excess volume was 1061 mL (IQR: 763-1599). After one year (n=27) it was 79 mL (IQR: -106 to 170), after two years (n=22) it was -22 mL (IQR: -258 to 133) and after five years (n=12), it was 22 mL (IQR: -303 to 355). Before surgery, the percentage excess arm volume was 42% (IQR: 31-53), which reduced to 3% (IQR: -5 to 8) after one year, and to 1% (IQR: -9 to 14) after five years. The reduction corresponds to a 95% (IQR: 81-119) decrease in excess volume after one year ($p<0.001$) and 98% (IQR: 74-120) after five years ($p=0.002$).

The corresponding median preoperative leg excess volume was 3447 mL (IQR: 2065-5656). After one year (n=29) it was 263 mL (IQR: -105 to 893), after two years (n=21) it was 261 mL (IQR: -195 to 696) and after five years (n=6) it was 669 mL (IQR: 282-1711). The percentage excess leg volume was 37% (IQR: 25-63) before surgery and reduced to 3% (IQR: -1 to 10) after one year, and 9% (IQR: 4-24) after five years. This corresponds to a 90% (IQR: 71-104) reduction in excess volume after one year ($p<0.001$) and 72% (IQR: 55-91) after five years ($p=0.028$) [**Table 2**, **Figures 1** and **2**]. No significant difference in outcome after one and two

years was observed in primary and secondary leg lymphedemas. Additionally, no correlation between excess volume reduction in percent after one and two years and age, body mass index (BMI), duration of lymphedema or preoperative excess volume was found for arm or leg lymphedemas, analyzed separately or in the model-based analysis. The only variable indicating close to significant correlation in the model-based analysis was preoperative excess volume with excess volume reduction in percent after one year for leg lymphedemas (β=-0.004, p=0.065). **Table 3** presents baseline demographics for the patients followed for five years and no statistical difference could be found compared with the patients lost to follow-up. Examples of postoperative results for arm and leg lymphedemas are illustrated in **figures 3-5**.

Bioimpedance spectroscopy measurements

The median preoperative L-Dex score for lymphedematous arms (n=27) was 41 (IQR: 32-60). This decreased to 27 (IQR: 21-38) after one year (n=24) and to 20 (IQR: 14-28) after five years (n=11). There was both a significant difference from preoperative to one year after surgery (p<0.001), and from preoperative to five years after surgery (p=0.009). This finding represents a reduced amount of fluid in the arm after liposuction. For legs, the median L-Dex score was 41 (IQR: 20-73) preoperatively (n=25) and this decreased to 36 (IQR: 22-56) after one year (n=26) and to 34 (IQR: 14-66) after five years (n=6). None of the L-Dex changes were significant for lymphedematous legs (p=0.11 and p=0.50, respectively) [**Table 2 and Figure 6**].

Surgical complications

No major complications were reported. Minor complications experienced were compression garment-related, usually superficial pressure wounds behind the knee or in front of the ankle, of which there were five cases. All healed by secondary intention within a few weeks.

Discussion

This series of patients from the first five years of liposuction for limb lymphedema indicates, in accordance with previous published research, that this treatment is a safe and effective method to reduce the excess volume of advanced lymphedemas. The results show a significant near total reduction in the excess volume in arm lymphedemas, both at one and five years after surgery. For leg lymphedemas, a near complete reduction in excess volume was also seen one year after liposuction with a slightly lower reduction for the patients at five years. L-Dex showed significant better values for arms at 1 year and thereafter. The postoperative increase at 2-6 weeks is due to postsurgical swelling, that has subsided at 1 year.

There may be some obstacles to overcome to achieve excellent long-term results with liposuction for lymphedema treatment in Australia. Verbal reports from the leg lymphedema patients with five-year data indicate that problems with fitting of garments, challenges with warm climate and sleep, and the cost of compression garments in some regions, led to changes in compression garment wear. The L-Dex for leg lymphedema patients after five years indicated higher values than after four years, highlighting the importance of appropriate compression to reduce oedema formation. However, most of these patients had relatively stable measurements during their five-years' follow-up, indicating that loss to follow-up had an influence on the long-term results presented in this study. Comparing these results with postoperative liposuction results elsewhere, for example five-year reductions in arm lymphedema from Brorson in Sweden (117%) (12) and two-year reductions in arm and leg lymphedema from Munnoch in the United Kingdom (109% and 94%, respectively) (23, 24), the reductions in excess volume are comparable. Physiologic surgery for lymphedema aims at improving fluid outflow from the affected limb and are most likely most effective in early-stage lymphedema and therefore, not comparable to debulking

procedures like liposuction. Compliance to compression garments has not been measured objectively, and this would be an interesting aspect for future research. One aspect for Brorson's outcomes is that in Sweden compression garments are covered by the National Health Care and there is no restriction on the number of garments ordered.

The only significant surgical complications in this first group of patients were minor skin wounds from garment use. Using tourniquet, we have aspirated up to 10 litres in a leg without the need for a blood transfusion. With the immediate application of a compression garment, the excess skin shrinks without the need of surgical excision.(10, 12). While our patients indicate a reduction in cellulitis frequency after surgery, loss to follow-up hindered any statistical analysis. From 2012 – 2016, functional and emotional impairment was assessed, and positive results were previously reported (28). The 'quality of life' data was incomplete for the duration of this study and with the adoption of new, validated quality of life assessments, results will be published in future studies.

Other centers are advocating to combine liposuction with physiological procedures for lymphedema (such as vascularized lymph node transfer or lymphovenous anastomoses) to reduce the need for compression garments(37, 38). Although an interesting approach, to our knowledge no longitudinal randomized controlled trials or other structured comparisons are done to evaluate this combination. Reducing the need for compression garments is especially beneficial in regions, such as Australia, where patients often pay for compression garments and the climate challenges garment wear.

Limitations of this study include loss to follow-up, which has reduced the statistical significance of the long-term data. Strengths include a large number of patients and a clear treatment and follow-up program, which is easy to compare to previous research. Future research can include more patients with long-term follow-up and incorporate data on cellulitis and quality of life.

Conclusions

The results indicate that liposuction as a debulking procedure at a multidisciplinary team setting in Australia is a safe and effective option for appropriately selected patients with advanced lymphedema. In addition, liposuction has previously been found to have a considerable positive impact on the quality of life and function of patients. However, it is critical to inform patients preoperatively that postoperative, continuous use of compression garments is required to achieve and maintain a complete excess volume reduction.

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Legends

Table 1. Study population characteristics. All values are presented as median or number (%). IQR= interquartile range.

Table 2. Limb volume characteristics. All values are presented as median or number. IQR= interquartile range.

Table 3. Study population characteristics at baseline for the patients followed for five years. All values are presented as median or number (%). IQR= interquartile range.

*Statistical test for difference in baseline demographics for patients followed for five years compared to patients lost to follow-up.

Figure 1. Median arm excess volume during the study period. The *line within the box* represents the median value, the *borders of the box* represent IQR and the *whiskers* represents the lowest and highest values without outliers (*circles*) and extreme outliers (*stars*).

Figure 2. Median leg excess volume during the study period. The *line within the box* represents the median value, the *borders of the box* represent IQR and the *whiskers* represents the lowest and highest values without outliers (*circles*) and extreme outliers (*stars*).

Figure 3. A 55-year-old woman with secondary right arm lymphedema since one year with a preoperative excess volume of 1,478 ml (*top*). Postoperative result after one year with an excess volume of –182 ml, a reduction of 112% (*bottom*).

Figure 4. A 64-year-old woman with primary left leg lymphedema since 24 years with a preoperative excess volume of 4,236 ml (*left*). Postoperative result after one year with an excess volume of –528 ml, a reduction of 112% (*right*).

Figure 5. An 82-year-old woman with secondary left leg lymphedema since 50 years with a preoperative excess volume of 6,192 ml (*left*). Postoperative result after one year with an excess volume of –755 ml, a reduction of 112% (*right*).

Figure 6. L-Dex value at each follow up which is measured as a ratio of the affected to the unaffected limb. Normal values range between -10 to +10. The *line within the box* represents the median value, the *borders of the box* represent IQR and the *whiskers* represents the lowest and highest values without outliers (*circles*) and extreme outliers (*stars*).

Table 1

	Arms (n=29)	**Legs (n=30)**	**Total (n=59)**
Age (years, median)	57	57	57
IQR	53-67	48-65	50-65
Range	39-73	21-82	21-82
BMI (kg/m2, median)	29	28	29
IQR	27-31	25-30	26-31
Range	22-43	19-41	19-43
Lymphedema Type:			
- Primary	0 (0%)	12 (40%)	12 (20%)
- Secondary	29 (100%)	18 (60%)	47 (80%)
Lymphedema duration prior to liposuction (years, median)	7	14	11
IQR	4-13	10-22	5-16
Range	1-29	2-51	1-51
Gender Male:Female	1:28	4:26	5:54

	Preoperative	**Postoperative**						
		2-6 weeks	*6 months*	*1 year*	*2 years*	*3 years*	*4 years*	*5 years*
Arms (n)	29	29	29	27	22	13	10	12
Excess volume (mL) (IQR) Reduction in %	1061 (763-1599)	114 (3-406) 89	69 (7-211) 95	79 (-106 to 170) 95	-22 (-258 to 133) 102	27 (-245 to 114) 98	1 (-204 to 246) 100	22 (-303 to 355) 98
Significance (to preop)		***p<0.001***	***p<0.001***	***p<0.001***	***p<0.001***	***p=0.001***	***p=0.005***	***p=0.002***
L-Dex (IQR)	41 (32-60)	54 (39-62)	39 (29-47)	27 (21-38)	26 (13-38)	23 (19-29)	21 (18-27)	20 (14-28)
Significance		*p=0.078*	*p=0.11*	***p<0.001***	***p=0.005***	***p=0.004***	***p=0.022***	***p=0.009***
Legs (n)	30	29	29	29	21	17	12	6
Excess volume (mL) (IQR) Reduction in %	3447 (2065-5656)	1147 (618-1706) 70	358 (-112 to 1009) 89	263 (-105 to 893) 90	261 (-195 to 696) 93	410 (-232 to 719) 89	266 (-83 to 730) 93	669 (282-1711) 72
Significance(to preop)		***p<0.001***	***p<0.001***	***p<0.001***	***p<0.001***	***p<0.001***	***p=0.002***	***p=0.028***
L-Dex (IQR)	41 (20-73)	54 (36-73)	38 (23-48)	36 (22-56)	29 (11-40)	26 (13-41)	25 (10-41)	34 (14-66)
Significance		*p=0.072*	*p=0.27*	*p=0.11*	*p=0.33*	*p=0.33*	*p=0.40*	*p=0.50*

Table 3

	Arms (n=29)	**Legs (n=30)**	**Total (n=59)**
Age (years, median) IQR Range	57 53-67 39-73	57 48-65 21-82	57 50-65 21-82
BMI (kg/m2, median) IQR Range	29 27-31 22-43	28 25-30 19-41	29 26-31 19-43
Lymphedema Type: - Primary - Secondary	 0 (0%) 29 (100%)	 12 (40%) 18 (60%)	 12 (20%) 47 (80%)
Lymphedema duration prior to liposuction (years, median) IQR Range	7 4-13 1-29	14 10-22 2-51	11 5-16 1-51
Gender Male:Female	1:28	4:26	5:54

Figure 1

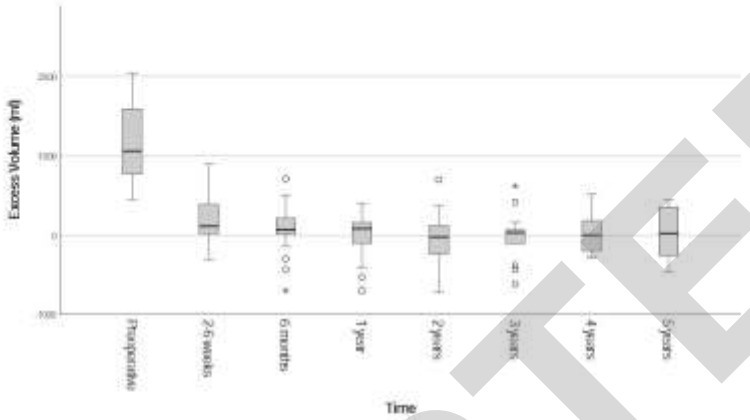

Figure 2

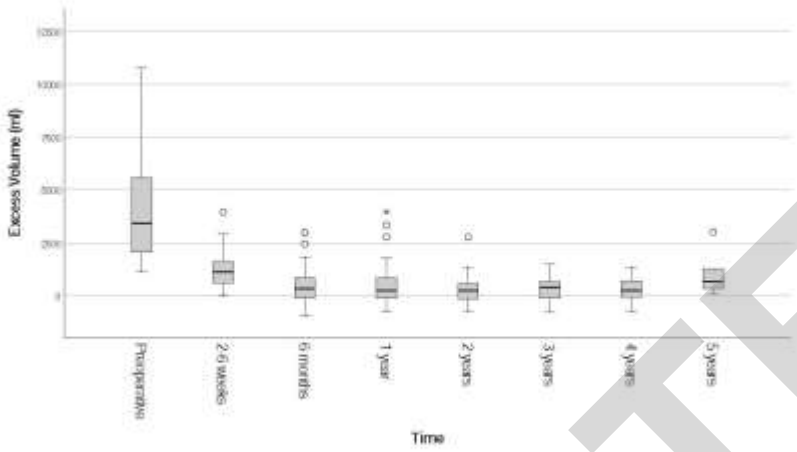

Figure 3

Figure 4

Figure 5

Figure 6