

A Clinical Study of Liposuction combined with Lymphovenous Anastomosis for Treatment of Breast Cancer-Related Lymphedema

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Abstract

Objective: In this work, we studied the clinical effect of liposuction combined with lymphovenous Anastomosis (LVAs) for treatment of breast cancer-related lymphedema (BCRL).

Methods: We studied 158 patients with unilateral upper limb BCRL underwent liposuction combined with LVAs. Arm circumferences before and 7 days after the combined treatments were prospectively recorded. Circumferences of different upper extremities were measured before the procedure, 7 days after LVAs and during the follow-ups. Volumes were calculated with the frustum method. During the follow-ups, the conditions of patients' treated arms, i.e. the frequency of erysipelas episodes and dependence on compression garments, were recorded.

Results: The mean circumference difference between two upper limbs decreased significantly from M (P25, P75) 5.3 (4.1, 6.9) preoperatively to 0.5 (-0.8, 1.0) 7 days after treatments, while at follow-up 0.3 (-0.4,1.0). The mean volume difference decreased significantly from M (P25, P75) 838.3 (662.4, 1129.0) preoperatively to 7.8 (-120.3, 151.4) 7 days after treatments, while at follow-up 43.7 (-59.4,161.1). The incidence of erysipelas also significantly decreased. 6.3% patients were already independent of compression garments during the past six months or even more.

Conclusion: Liposuction combined with LVAs is an effective method for the treatment of BCRL.

Introduction

Lymphedema is a chronic condition which is usually not life-threatening, but can cause quite a deleterious impact on the quality of life. Insufficiency or obstruction of lymph backflow caused by lymphatic vascular malformations or secondary factors such as trauma, infection or mostly oncologic therapy leads to fluid accumulation of extremities. The condition of excess infiltration of interstitial fluid rich of protein then causes fibrosis and sclerosis of skin and adipose tissues, which finally ends up with the increase of fluid and tissue volume of limbs (Kerchner et al., 2008; Maclellan and Greene, 2014; Shaitelman et al., 2015; Zhang et al., 2017). Breast cancer-related lymphedema (BCRL) is currently the leading cause of secondary lymphedema in the upper limbs. Lymphedema in BCRL usually happens at the ipsilateral upper limb. It is reported that the incidence of BCRL in breast cancer patients is 3%-65% depending on the factors such as surgical options, wound healing of the surgical area, radiation therapy, invasive manipulation of the ipsilateral limb, body mass index (BMI), delayed recovery of the affected limb function and repeated infection of the affected limb (2016; Gillespie et al., 2018; Hayes et al., 2008; Michelotti et al., 2019; Sagen et al., 2009; Shaitelman et al., 2017). The survival rate of breast cancer has been continuously improved with the development of the diagnosis and treatment. As a consequence, more and more attentions are paid to the complications, for instance, BCRL. Besides, the risk of erysipelas occurred on the lymphedema limb is especially higher than the normal occasions, which makes BCRL one of the complications that impairs the long-term life quality most seriously.

Lymphatic obstruction leads to the increase of lymphatic hydrostatic pressure, which causes progressively damage of lymphatic structures manifesting as dilated lymphatic vessel, impaired valve function, and distal lymph stasis. Long-term stasis of lymph rich of nutrient leads to tissue deposition of fat, fibrosis, repeated erysipelas, and thickening of extremities eventually. It is a vicious cycle that the increase of cutaneous and subcutaneous lesions produces more lymph which in turn increases lymph pressure (Ridner, 2013; Tashiro et al., 2017).

The treatment of BCRL includes non-surgical and surgical treatments. Patients with BCRL at the early-stage of lymphedema mostly get relieved with conservative therapies (Executive Committee of the International Society of, 2020). Those refractory to conservative treatments and more severe will receive surgical treatments. At present, the most common surgical methods for limb lymphedema are debulking procedures (including excisional surgery and liposuction, etc.) and lymphatic reconstructions (including lymphovenous Anastomosis (LVAs), vascularized lymph node transfer/transplantation (VLNT), lymphatic grafting, etc.) (Chang and Cormier, 2013; Gallagher et al., 2018). When the excess volume is dominated by dermato-lipo-fibrosclerosis tissue instead of accumulated lymph, conservative treatment is limited. Liposuction enables the removal of the adipose tissue besides accumulated lymph, which microsurgical reconstructions cannot achieve. Compared with the traditional excisional surgery, liposuction is safer and lesser invasive, and is able to perform twice (Boyages et al., 2015; Brorson, 2016). While liposuction can effectively reduce limb volume and is aimed at the process from hyperplasia to lymph stasis in the pathophysiological cycle of lymphedema, the lymph flow is still obstructed without effective lymphatic flow pathways. As a result, lymphedema recurs and aggravates gradually with the accumulation of lymph fluid. When the pressure in lymphatic vessel is higher than in vein, lymph fluid smoothly flows from lymphatic vessels to the vein. In this aspect, lymphatic reconstructions can effectively improve the lymphatic flow and reduce the lymphatic stasis of the affected limb.

For the first time, the combination of liposuction and LVAs in the treatment of BCRL was carried out widely in department of lymphatic surgery, Beijing Shijitan Hospital, and the outcome was quite satisfactory in this study.

Patients And Methods

This study was approved by the Medical Ethics Committee of Beijing Shijitan Hospital. Patients with unilateral upper limb BCRL admitted in department of lymphatic surgery, Beijing Shijitan Hospital from November 2015 to February 2018 and underwent liposuction combined with LVAs were included in this study. Any patients who were discovered recurrence of malignant tumor or comorbidities of venous reflux disorders as well as those who had edema of contralateral limb were excluded from this study.

The circumferences at the lower and upper third of the forearm and upper arm, and elbow as well of both upper extremities were measured before the procedure of liposuction as the control for the response to therapy. Patients included underwent liposuction and followed by LVAs 2–4 months later. The circumferences at the same points were measured 7 days after LVAs and during the follow-ups. The

volumes of the extremities were calculated with frustum method (Sitzia, 1995). Finally, the circumferential and volume difference, and the reduction rate after treatments and during the follow-ups were compared.

The patients' demographics, breast cancer surgical approach, chemical and radiation therapy, operative notes, episodes of erysipelas, circumferences of affected arm before and 7 days after the combined treatments were prospectively recorded. During the follow-ups, the patients' conditions of treated arms, including frequency of erysipelas episodes and dependence on compression garments were recorded.

Indications

The International Society of Lymphology reported four clinical stages of lymphedema. The latent or subclinical stage, defined as stage 0, refers to the impaired lymph transport without extremity lymphedema. Stage I represents an early fluid accumulation presented as pitting edema that subsides with limb elevation. Stage II signifies pitting and fibrosis, which manifests that limb elevation alone rarely reduces tissue swelling. Stage III encompasses lymphostatic elephantiasis where pitting is absent and trophic skin changes, such as acanthosis, fat deposits, and warty overgrowths. The severity within each stage is based on the volume differences between two upper limbs: minimal (< 20% increase), moderate (20–40% increase), and severe (> 40% increase). In this study, stages II and III of BCRL with the severity of moderate and severe (≥20% increase of volume) within the forearm or upper arm underwent the combination of surgical treatments.

Surgical Techniques

Liposuction

The patient was in the supine position under general anesthesia, and transverse skin incisions 3–5 mm in length are made on the ulnar side of the wrist, the ulnar and radial side of the forearm, and the radial side of the upper arm. To minimize the blood loss, tumescence (containing 1 mg adrenaline, 0.2 g lidocaine and 0.5 g sodium bicarbonate per 1L of saline) was infiltrated according to the degree of the swelling of the affected limb. Next, Power-Assisted Pneumatic Liposuction Machine (PAPLM) with a negative atmospheric pressure of approximately 0.8–0.9 atm was used to perform liposuction with 15–25 cm-long cannulas. The cannulas should be as parallel as possible to the longitudinal axis of the upper limbs. After all the target subcutaneous adipose tissue and lymph fluid were absorbed, and subcutaneous drainage tubes were placed, sterilized compression (crushed gauze, cotton pad and elastic bandage) is applied to stem the bleeding and reduce the postoperative edema. The drainage tubes and compression were removed 3 days later, and a sleeve with finger-cut glove was put instead.

Lymphovenous Anastomosis

A 5 cm-long skin incision at the middle third of the upper arm was performed along the medial bicipital sulcus under general anesthesia. The humeral artery, vein and the median nerve was exposed, among which the deep lymphatics were found using of microscope with magnification (12.5×4-6X). One or more humeral vein branches without reflux that matched the number and diameter of lymphatic were chosen.

The branch vein was cut leaving the distal end ligated, and the proximal part was flushed thoroughly with heparinized saline (6250 U/500 mL) in case of any thrombus left. If there was reflux at the proximal end, the vessel wall will be narrowed circularly with the method of femoral vein valve repair. Then all these lymphatic vessels were cut off and anastomosed into one (or more if necessary) venous lumen with 10 – 0 or 11 – 0 Prolene sutures, and the venous lumen would be narrowed in general (Fig. 1). Nonoperative compression treatment was applied postoperatively and an elastic sleeve was replaced one month later.

Statistical analysis

The statistical analysis was performed using SPSS 24.0 statistical software. The measurement data did not conform to the normal distribution after Shapiro-Wilk test, so it was represented by M (P25, P75). The differences among the data before and after treatment were assessed using Friedman test and then the multiple comparisons were carried out with Wilcoxon test.

Results

Patient characteristics

From November 2015 to February 2018, a total of 179 patients with BCRL received treatments in our department. All the patients underwent the same preoperative evaluation, including lymphoscintigraphy for confirmed diagnosis (Fig. 2) and doppler ultrasound for the venous system to rule out venous reflux disorders. 3 cases with bilateral BCRL and 3 cases with upper limb venous reflux disorder as well as 5 cases who did not choose combined treatments were ruled out. 10 of the remaining 168 patients lost contact or died of other disease. Finally, 158 patients with BCRL in total were retrospectively included and were followed up one by one.

All the 158 patients included in this study were females, with the age of 57.0 ± 8.3 years old. 86 (54.4%) patients had left-sided breast cancer and 72 (45.6) right-sided. All of the 158 patients underwent axillary lymph node dissection and 133 (84.2%) patients received concurrent radiation therapy.

The median (P25, P75) duration of onsets of lymphedema symptoms since breast cancer surgery was 1.0 year, ranged from 0 to 23.0 years during which some patients chose variety of conservative therapies while others did not experience formal conservative therapies (Table 1). 34 (21.5%) patients had recurrent episodes in one year before the visit to hospital and our treatments.

Table 1
Conservative therapies before the visit to hospital

Conservative therapy	none#	elastic sleeve	medication	traditional Chinese medicine	acupuncture*	cupping	circulation driving therapy
N	131	11	7	4	3	2	1
#none, no formal conservative therapies							
*acupuncture is forbidden in the treatment of lymph edema							

Before the treatment, the circumferential difference of the affected and unaffected arms varied from - 3.0 to 23.9cm, and the volume increase rate varied from 6.56–190.4%. All of our 158 patients were at stage II and III of whom 32 (20.3%) suffered 20%-40% volume increase and 120 (75.9%) suffered >40% volume increase. The rest 6 (3.8%) patients' arms were swelled unevenly, with the severity of moderate (20%-40% increase of volume) within the forearm or upper arm separately. In view of this, the combination of surgical treatments was chosen in all of these patients with no satisfactory expectation using conservative therapy.

Response to the combined treatments

All the 158 patients completed the combination treatments of liposuction and LVAs successfully without severe complications. The median (P25, P75) follow-up period was 30 (28, 32) months, ranging from 23 to 36 months. The median circumferential difference reduced significantly ($P < 0.01$) from 5.3 cm before treatments to 0.5 cm seven days after treatments, and the median volume difference (volume increase rate) reduced significantly ($P < 0.01$) from 838.3 mL (50.7%) to 7.8 mL (0.6%). The median circumferential difference, volume difference and volume increase rate went on reducing ($P < 0.05$) surprisingly from 7 days after the surgery to the follow-ups (median 30 months after combined treatments) (Fig. 3, Table 2, Table 3, Table 4).

Table 2
Circumferential difference of the affected and unaffected arms before and after the combined treatments of liposuction and lymphatico-venous Anastomosis

Time point	N	Circumferential difference (cm)			Z1/P1	Z2/P2
		Min	Max	M (P25, P75)		
Before treatments	158	0.7	15.9	5.3 (4.1, 6.9)	-	-
7days after treatments	158	-3.4	6.2	0.5 (-0.8, 1.0)	-10.903/0.000*	-
30months Follow up	158	-2.6	4.9	0.3 (-0.4, 1.0)	-10.903/0.000*	-1.982/0.048

M, median; Z1/P1, consequences compared with before treatments; Z2/P2, consequences compared with 7 days after treatments; *Statistically significant (p value < 0.05).

Table 3

Volume difference of the affected and unaffected arms before and after the combined treatments of liposuction and lymphovenous Anastomosis

Time point	N	Volume difference (mL)			Z1/P1	Z2/P2
		Min	Max	M (P25, P75)		
Before treatments	158	111.0	3600.0	838.3 (662.4, 1129.0)	-	-
7days after treatments	158	-448.6	1096.1	7.8 (-120.3, 151.4)	-10.903/0.000*	-
30months Follow up	158	-344.4	809.7	43.7 (-59.4, 161.1)	-10.903/0.000*	-2.173/0.030

M, median; Z1/P1, consequences compared with Before treatments; Z2/P2, consequences compared with 7 days after treatments; *Statistically significant (p value < 0.05).

Table 4

Volume increase rate of the affected arm and unaffected arm before and after combined treatments of liposuction and lymphovenous Anastomosis

Time point	N	Volume increase rate (%)			Z1/P1	Z2/P2
		Min	Max	M (P25, P75)		
Before treatments	158	6.6	190.4	50.7 (40.1, 71.1)	-	-
7days after treatments	158	-26.3	55.5	0.6 (-7.8, 9.4)	-10.903/0.000*	-
30months Follow up	158	-20.6	56.60	2.5 (-3.5, 10.2)	-10.903/0.000*	-2.108/0.035

M, median; Z1/P1, consequences compared with Before treatments; Z2/P2, consequences compared with 7 days after treatments; *Statistically significant (p value < 0.05).

The frequency of erysipelas episodes also decreased significantly ($P < 0.05$) after combined treatments. Originally before our treatments, 33 (20.9%) patients had no more than three episodes every year and 1 (0.6%) patient had six times of episodes every year. While during our 30-month follow-ups, 134 (84.8%) patients had no erysipelas episodes at all and only 19 (12%) had one-time episode and 5 (3.2%) twice (Table 5).

Table 5

Frequency of erysipelas episodes between before the treatments and during the follow-ups

Time point	N	Min	Max	M(P25, P75)	Z Value	P Value
Before treatments	158	0	6	0.00 (0.00,0.00)		
30months Follow up	158	0	2	0.00 (0.00,0.00)	-5.011	0.000*

M, median; *Statistically significant (p value < 0.05).

Dependence on the compression therapy

Compression therapy is the corner stone of conservative therapy as well as a supplementary therapy to help shape the arm after liposuction and help lymph flow after LVAs. Usually, lifelong sustained compression is essential to maintain the edema reduction. However, 10 (6.3%) patients in our study were already independent of compression garments during the past six months or more. Most patients (144, 91.1%) only wore compression garments during daytime activities. Only 4 (2.5%) needed compression all day long.

Discussion

Our interest in solving lymphedema started 30 years ago. In the development of lymphedema, thickening and sclerosis of the skin and adipose tissue contains large amount of fibrotic tissue, which makes the subcutaneous tissue denser than usual (Ghanta et al., 2015). The traditional liposuction with negative atmosphere could hardly remove the dense fibrotic tissue. Therefore, we used a PAPLM which can effectively destroy fibrotic and adipose tissue with cannula vibration, and shorten the operation time. Additionally, we made the cannulas parallel to the longitudinal axis of the upper limbs during the procedure to reduce damage to lymphatic and blood vessels and prepare for the next LVAs according to Fricks' theory (Frick et al., 1999).

Lymphatic channels were anastomosed end-to-end or end-to-side to subdermal venules above deep fascia at multiple points traditionally, which was on the traditional anatomic basis that there are no wide connections between the superficial and deep lymphatic vessels, and hypertrophic and proliferative tissue changes in lymphedema occur mainly in the tissue above the deep fascia (Suami and Scaglioni, 2018). However, recently single or multiple deep collecting lymph vessels have been found along neurovascular bundles in the forearm and upper arm (Ma et al., 2019). All the 158 LVAs procedures were performed using deep lymphatics and humeral vein branch beneath deep fascia, which were proved to be effective in improving lymph flow. At the same time, LVAs using deeper lymphatic and blood vessels instead of superficial ones reduced the chance of anastomotic closure from infection or trauma, and LVAs procedure beneath the deep fascia would also not be affected by liposuction performed months before. After LVAs procedure, lymph fluid flow into veins and lymphatic stasis was ameliorated gradually. Then the pressure of lymphatic vessel declined little by little and finally blood reflux occurred at the anastomosis. As a result, thrombus formed and blocked the anastomosis (Campisi et al., 2010; Ito et al., 2016). Considering this problem, we improved the LVAs procedure by selecting the vein with better valve function to avoid or reduce blood reflux, and reduce the venous pressure at the anastomosis. In terms of lymphatic vessel, we chose those with thinner wall with less fibrotic and more obvious contractive function to ensure the flow of lymph fluid. With all these efforts, long-term results after our combined treatments were gratifying.

Based on above data, we concluded that all the 158 patients' swelling limb got relieved after the combined treatments and the condition of treated arms remained stable from after the treatments to the follow-ups. Therefore, the combination of liposuction and LVAs for BCRL not only reduced the volume of affected arms and the amount of lymph fluid production, but also rebuilt the lymph flow. In this way, the vicious cycle of

lymph stasis, fat hyperplasia, and more lymph stasis is broke. After all these systematic surgical treatments and compression therapy, there were patients who already got rid of compression garments. How many of them would be independent of compression therapy at last and return to normal life completely remained to be investigated further.

Conclusion

Our combined treatments of liposuction and lymphovenous Anastomosis for breast cancer related lymphedema received satisfactory results without worrying complications. After the systematic treatments, patients got rid of compression garments and returned to normal life again, and there were no recurrences during the follow-ups.

Statements And Declarations

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Author Contributions All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Kun Chang, Song Xia and Wenbin Shen. The first draft of the manuscript was written by Chen Liang and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Data Availability The datasets generated during and analysed during the current study are not publicly available due to privacy but are available from the corresponding author upon request.

Ethics approval This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of of Beijing Shijitan Hospital (sjtkyll-ix-2020(50))

Consent to participate Informed consent was obtained from all individual participants included in the study.

Consent to publish The authors affirm that human research participants provided informed consent for publication of the images in Figure 1a, 1b, Figure 2 and Figure 3a, 3b

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Figures



Figure 1

(A) The humeral artery was marked with blue tape and humeral vein with orange tape; the lymphatics were anastomosed into humeral branch vein. (B) The vein was flushed with lymph fluid and then turned white

Figure 2

Lymphoscintigraphy in a BCRL patient at 10 minutes (left), 1 hour (middle) and 3 hours (right). Neither lymphatic vessels of left upper limb nor the left axillary lymph nodes were visualized. Imaging agents were distributed diffusely in the left arm subcutaneously, and a supraclavicular lymph node was visualized. Lymphatic vessels of right upper limb and the right axillary and subclavian lymph nodes were clearly visible and imaging agents flowed back smoothly



Figure 3

Female, 49 years old, right-sided BCRL (A) before treatments (i.e. combination of liposuction and lymphovenous Anastomosis), with the volume increase rate of 45.5%, and (B) 32 months after treatments, with the volume increase rate of -11.7%