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ORIGINAL ARTICLE

Reconstructive surgery for chronic lymphedema: a viable option, but

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The aim of the paper is to assess the efficacy of reconstructive lymphatic surgery in the treatment of chronic lymphedema via retrospective analysis. Lymphovenous anastomotic surgery (LVAS) or free lymph node transplant surgery (FLTS) was performed on 32 patients who failed to respond to complex decongestive therapy (CDT) alone for a minimum of a one-year period. In LVAS, three patients with good compliance among 19 were able to maintain initial improvement through the four-year follow-up period. All three had secondary lymphedema in clinical stage II. In FLTS, among 13 patients, three compliant patients with the secondary lymphedema in clinical stage II kept initial improvement through the four-year follow-up. In conclusion, reconstructive lymphatic surgery (LVAS and FLTS) appears to be more effective in secondary lymphedema versus primary lymphedema when performed in the early stages. Patient compliance to maintain CDT postoperatively remains the most critical factor in maintaining durable long-term results. FLTS seems to have an additional risk involved to the donor lymph node harvest and a limited role compared to LVAS. Further extended study on FLTS is required to demonstrate its efficacy compared with LVAS.

Key words: *chronic lymphedema; reconstructive surgery; compliance; maintenance CDT*

Introduction

Reconstructive lymphatic surgery has been known for decades as one of the most effective modalities in the treatment of chronic lymphedema.[1,2] Although the majority of patients are managed satisfactorily with manual lymphatic drainage (MLD)-based complex decongestive therapy (CDT),[3,4] many become refractory to the treatment with CDT alone.[5,6]

The aim of reconstructive lymphatic surgery[7–12] is to improve lymphatic function in the lymphedematous limb. In theory, surgical reconstruction may cure lymphedema. In reality, however, reconstructive surgery remains controversial and is still far from being accepted as standard therapy due to various reasons.[1,2,5,6]

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We attempt to answer several questions related to reconstructive surgery based on a retrospective analysis of our limited experience with a selected group of lymphedema patients ($N = 32$).

Materials and methods

As shown in Figure 1, among a total of 1098 patients with various conditions of chronic lymphedema (Samsung Medical Center in Seoul, South Korea [1995–2004] and Georgetown University Hospital, Washington, DC, USA [2005–2008]), the multidisciplinary team selected/approved 44 patients out of 54 potential candidates, who met the criteria/indication to receive reconstructive surgery based on deteriorating clinical stage and/or laboratory stage, and/or increasing frequency of the sepsis despite adequate prevention/treatment of the infection.

Among a total of 44 patients who underwent reconstructive surgery, 32 patients were able to provide sufficient data/records for the current review on a minimum of four years of follow-up assessment during the period from 1994 through 2008. The other 12 patients were unavailable for a minimum 48 months follow-up.

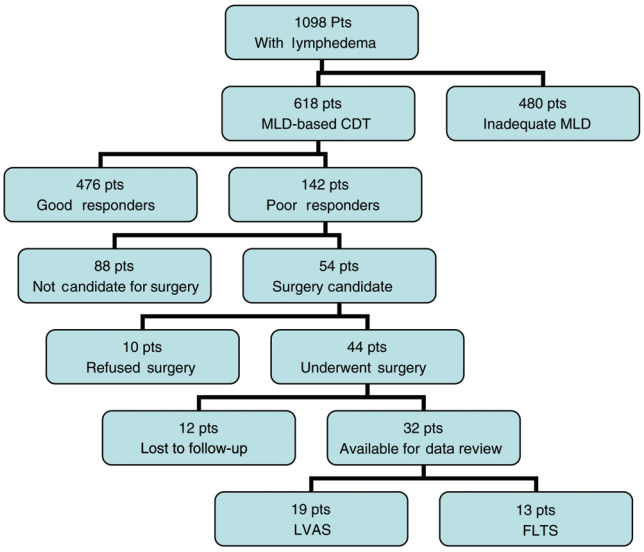

Figure 1 Patient disposition flow chart. MLD, manual lymphatic drainage; LVAS, lymphovenous anastomotic surgery; FLTS, free lymph-node transplant surgery

All 32 patients underwent 'unilateral' reconstructive surgical therapy on a total of 32 limbs before year 2003 and were available for full evaluation until the year 2008.

Based on a detailed history and complete physical examination, combinations of various non-invasive imaging and physiologic studies were performed for diagnosis and lymphedema staging: duplex ultrasonography[13,14] for venous assessment, infrared optometric volumetry for measurement of limb volume, radionuclide lymphoscintigraphy[15,16] to determine lymphatic function status, computed tomography for cancer follow-up and/or standard magnetic resonance imaging to assess patients with primary lymphedema in particular.[17,18]

Lymphoscintigraphic findings remained a gold standard among various laboratory findings to supplement the clinical findings as an additional guideline for assessment of the lymphedema.[5,6,19,20]

We used a new clinical staging system together with laboratory staging[21,22] on clinical assessment of the lymphedema as well as a selection of surgical candidates to compensate a limitation of the International Society of Lymphology (ISL) staging system[23] (Table 1).

As shown in Table 1, the new clinical staging system assessed the clinical condition of the lymphedema in four stages (I through IV) based on five separate criteria: swelling, skin change, sepsis, daily activity limitation and quality of life.

For the laboratory staging, radionuclide lymphosciniti-graphy findings were assessed in four different grades/stages based on five criteria: lymph node uptake (LN), dermal backflow (DB), collateral lymphatics, main lymphatics and clearance of radioisotope from injection site (CR).

All candidates were reviewed by the multidisciplinary team to confirm the progress of the disease for a minimum one-year period despite all the available treatment before referral for reconstructive surgery.[5,6]

The goal of reconstructive surgical therapy is to increase the efficacy of the CDT as a supplemental procedure. Therefore, all candidates met at least three out of four inclusion criteria as below before being offered reconstructive surgery:

(1) Demonstrate clinical evidence of substantial progression of lymphedema, from clinical stage I to stage II, or from stage II to stage III, despite an adequate CDT-based treatment program over a minimum 12-month period;
(2) Demonstrate progressive lymph fluid accumulation, preferably by lymphoscintigraphy to document DB, especially below the knee level;
(3) Demonstrate increasing difficulty of relieving edema by MLD-based CDT, particularly at the below-knee level but less so at the above-knee level;
(4) Document appropriate treatment failure at least twice during a minimum period of a year with six-month interval assessments.

Exclusion criteria included various conditions affecting surgical outcome directly or indirectly: active malignancy, chronic venous insufficiency, status post saphenous vein stripping/endovascular therapy, coagulopathy, primary lymphedema combined with other vascular malformation, morbid obesity and/or lipedema, mental instability and/or poor compliance.

The same inclusion and exclusion criteria were implemented for both lymphovenous anastomotic surgery (LVAS)[9–12] and free lymph node transplant surgery (FLTS).[8,24,25]

In the final selection of the procedure, priority was given to LVAS over FLTS to the secondary lymphedema whenever the anatomic and physiological condition were favorable. But for the primary lymphedema, final decision and selection of FLTS with priority included the patients' choice and preference.[26]

For LVAS, we performed direct end-to-end anastomoses ($N = 13$) between the lymphatic vessels and vein branches or invagination of the lymph vessels into the vein ($N = 6$) for the end-to-end, end-to-side anastomoses. An average of 3.4 pairs of anastomoses was made, and patent blue dye was used to locate the lymph vessels in the majority of cases; the

Table 1 New staging of chronic lymphedema: clinical and laboratory staging

Laboratory (lymphoscintigraphic) staging		*Clinical staging*	
Grade I (stage)	• Lymph node uptake (LN): none to minimally decreased • Dermal backflow (DB): none • Collateral lymphatics (CL): well visualization • Main lymphatics (ML): decreased visualization • Clearance of radioisotope (CR) from injection site: mildly decreased	• Edema – mild and/or easily reversible • Skin change – none without dermatofibrosclerosis (DFS) • Sepsis (systemic and/or local) – none • Daily activity limitation (DAL) – no limitation • Quality of life (QOL) – good with minimal and/or occasional limitation on exercise (e.g. hobby) physically, and no difficulty psychologically and/or socioeconomically	Stage I
Grade II (stage)	• LN: moderately decreased • DB: mild visualization • IIA – extent of DB does not exceed 1/2 of each limb • IIB – exceed 1/2 of each limb • CL: decreased visualization • ML: poor to no visualization • CR: more decreased	• Edema – moderate and/or reversible with effort Skin change – none to minimum without DFS • Sepsis – infrequent (less than 3/y) • DAL – occasional and/or moderate limitation • QOL – fair with moderate limitation physically, psychologically and/or socioeconomically	Stage II
Grade III (stage)	• LN: severely decreased to no uptake • DB: moderate visualization • CL: poor visualization • ML: no visualization • CR: no clearance	• Edema – moderate to severe and/or minimally reversible to irreversible • Skin change – moderate with significant DFS • Sepsis – frequent (more than 3/yr) • DAL – frequent and significant • QOL – poor with significant limitation	Stage III
Grade IV (stage)	• LN: no uptake • DB: intense visualization • CL: no-visualization • ML: no-visualization • CR: no clearance	• Edema – severe and/or irreversible • Skin change – severe with advanced DFS • Sepsis – very frequent (more than 3/y) • DAL – constant and severe • QOL – bad with severe limitation	Stage IV

functional status of candidate lymphatic vessels was evaluated based on the self-peristalsis and propulsion of the lymph vessels before the anastomoses.

The LVAS was performed at the popliteal level ($N = 10$), when significant progression of lymphedema involved the distal leg and foot. Otherwise, anastomoses were made at the inguinal/femoral level ($N = 9$). All patients received the anastomoses between well-functioning lymph vessels and defunctionalized adjacent vein segments with normal valvular function to prevent lymphatic reflux.[1,2,5,6]

Evidence of progressive damage and paralysis of lymph-collecting vessels at the inguinal level was another indication for performing LVAS anastomosis at the popliteal level,[5,6] where it is likely to have better lymph vessels for surgical reconstruction.

MLD-based CDT was continued postoperatively, and assessments were performed every six months for the first 24 months and continued annually until the 48-month follow-up.

The FLTS was performed based on the principle of free flap tissue graft technique.[8,25,26] The lymph-node bearing tissue was harvested from the donor site (e.g. axillary lymph node group) with its feeding arteries and veins intact. The subsequent anastomoses were constructed between the donor artery and recipient artery and between the donor vein and recipient vein using microsurgical techniques. Anastomoses between multiple sets of donor and recipient arteries and veins were made whenever feasible, especially for the venous anastomosis in patients with secondary lymphedema following radical dissection combined with postoperative radiation.

While harvesting an adequate number of lymph nodes with intact vessels from the donor site, special attention was given to the number of remaining lymph nodes at the donor site in order to minimize the risk of developing lymphedema in the donor limb.

The patency of the venous system at the recipient site was thoroughly assessed with duplex ultrasonography and when in doubt, ascending phlebography was performed.

In order to minimize lymphatic congestion along the donor sites, aggressive MLD-based CDT was performed on the donor limb for a minimum of two weeks before and after surgery.

Pre- and postoperative assessments included clinical evaluation with volume measurement of the swollen extremity using infrared optical volume determination, and tape measurement of the circumference of the limb at various levels along the foot, ankle, calf and thigh.[20]

Volume/circumference measurement was interpreted as:

- Fair: 30% reduction of swelling (baseline size/volume difference from normal side);
- Good: 30–60% reduction;
- Excellent: over 60% reduction.

Long-term radionuclide lymphoscintigraphy assessment was made with qualitative, visual evaluation of comparative change on radioisotope tracer clearance between the normal and lymphedematous limb.

Final assessment was made by two independent nuclear medicine specialists based on combined clearance changes in DB and other clearance criteria: groin/inguinal LN, infrainguinal uptake and CR from the injection site as shown in Figures 2b-1 and b-2 .

Lymphoscintigraphic findings were assessed as:

- Fair: mild reduction of DB and no to minimal improvement on other clearance criteria;
- Good: moderate reduction of DB, and noticeable/mild improvement of other clearance criteria;
- Excellent: large or considerable reduction of DB and moderate improvement of other clearance criteria.

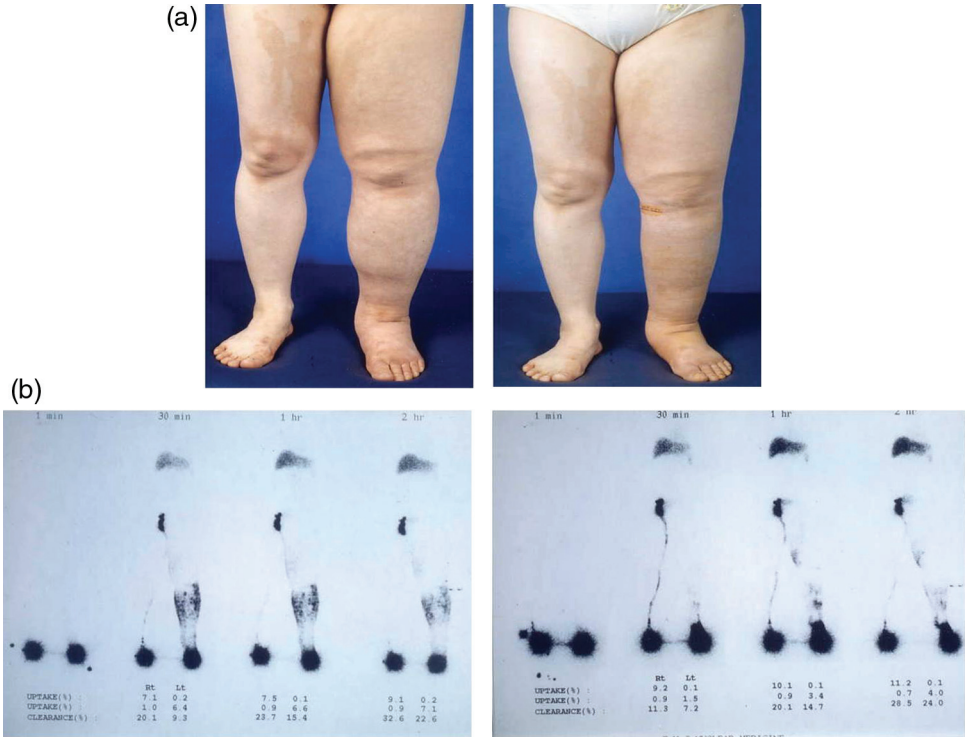

Figure 2 (a-1) Photo shows clinical appearance of the lymphedematous limb (left) before the reconstructive lymphatic surgery is instituted. The lymphedema management with manual lymphatic drainage-based complex decongestive therapy (CDT) has been assessed as a failure with evidence of the progress (clinical stage II), despite maximum therapy for two years, which became the indication of the surgical therapy. (a-2) Photo shows the lymphedematous limb (left) with remarkable response to reconstructive surgery, done three weeks previously. Due to the advanced condition, the lymphatic-venous anastomoses were done at the popliteal level. Two photos depict radionuclide lymphoscintigraphy findings before the surgery (b-1) and after the surgery (b-2) done six months later. Near complete disappearance of dermal backflow along the lower leg shows good evidence of successful surgical relief of lymph stasis

We assessed the patency of the anastomotic sites by indirect methods based on the lymphoscintigraphic and clinical improvement. We did not perform the oil-based contrast lymphangiography to document the patency to avoid a risk of the damage to the lymphatic vessels/anastomoses.

Follow-up assessments were made every six months for a minimum of four years.[5,6] For the FLTS, duplex ultrasonography was performed as an additional surveillance on the viability of transplanted lymph nodes.

Results

LVAS group

As summarized in Table 2, $N = 19$ patients (F = 18, M = 1; mean age = 49.0 years; primary lymphedema = 4, secondary lymphedema = 15) underwent LVAS. These patients belonged to clinical stage II ($N = 9$) and stage III ($N = 10$) while laboratory (L) stage shows extreme variability from L-stage (grade) I ($N = 5$), II ($N = 6$), III ($N = 6$) to IV ($N = 2$).

Table 2 Demographic data on LVAS and FLTS patients

	LVAS	*FLTS*
Total number (patients)	19	13
Age (mean-years)	49.0	34.0
Gender		
Male	1	3
Female	18	10
Clinical stage		
I	0	3
II	9	8
III	10	2
IV	0	0
Etiology		
Primary	4	6
Secondary	15	7
Clinical response		
First (12 months) endpoint		
Excellent to good	14	7
Fair	2	3
Poor	3	3
Second (24 months) endpoint		
Excellent to good	8	5
Fair	3	3
Poor	8	5
Third/final (48 months) endpoint		
Excellent to good	3	3
Fair	0	3
Poor	16	7

LVAS, lymphovenous anastomotic surgery; FLTS, free lymph node transplant surgery

Sixteen patients had clinical improvement (excellent – 8, good – 6 and fair – 2) with up to 75% reduction (average 60%) in limb volume within the initial 12-month period. All 16 patients had good compliance with maintenance CDT postoperatively.

The three patients with poor surgical outcomes with no response had poor to non-compliance and did not receive mandatory postoperative CDT maintenance.

Among the 16 patients with initial clinical improvement, only eight patients had good compliance with maintenance CDT and showed continued clinical improvement at the 24-month follow-up, with an average 60% reduction in limb volume. Follow-up lymphoscintigraphy demonstrated moderate decrease of DB and moderately increased lymphatic clearance in five of the eight patients (Figure 2).

At 48 months, only three patients remained compliant with maintenance CDT and maintained satisfactory clinical and lymphoscintigraphic improvement.

All three underwent surgery for secondary lymphedema in clinical stage II and laboratory stage (grade) II. They have shown excellent ($N = 2$) to good ($N = 1$) clinical response on various criteria: edema, skin change, sepsis, limitation of daily activity as well as overall quality of life. Not a single episode of the local or systemic sepsis occurred in all three patients during the follow-up period.

These three patients have also shown moderate/good ($N = 2$) to excellent ($N = 1$) improvement on follow-up lymphoscintigraphic assessment as well.

Among 16 patients with poor outcome of the LVAS, 11 patients had deterioration of function following an average of 2.2 episodes of moderate to severe cellulitis/erysipelas per year during the four-year follow-up period. Clinically, $N = 6$ patients returned to their preoperative state, while $N = 9$ patients were worse and $N = 1$ patient had mild improvement.

FLTS group

As shown in Table 2, $N = 13$ patients (F = 10, M = 3; mean age = 34.0 y; primary lymphedema = 6, secondary lymphedema = 7) underwent FLTS. These patients belonged to clinical stage I ($N = 3$), stage II ($N = 8$) and stage III ($N = 2$) and all patients were laboratory stage III ($N = 8$) or IV ($N = 4$) due to the lack of lymph node uptake.

All 13 patients underwent technically successful FLTS in 13 limbs (10 lower limbs and 3 upper limbs) with microscopic anastomoses between two and three pairs of donor arteries and veins and recipient arteries and veins on the average ($N = 10$).

The inguinal region was the most common recipient site (10/13) for the FLTS and the donor lymph nodes were harvested mostly from the posterior axillary nodal group (11/13) following the confirmation of normal functional status based on preoperative lymphoscintigrapy.

On initial evaluation of FLTS at 12 months, 10 compliant patients among a total of 13 had shown clinical improvement with a median average of 50% reduction in limb volume: fair ($N = 3$) to good ($N = 5$). All 10 patients demonstrated remarkable clinical improvement with fewer episode of sepsis. However, six patients have shown fair ($N = 4$) to good ($N = 2$) response on lymphoscintigraphy. Duplex follow-up demonstrated a positive evidence of viable lymph nodes at the transplant site in three patients.

Three patients with poor compliance from the outset had steady deterioration to the advanced stage following recurrent sepsis during the same period.

Among these 10 compliant patients, $N = 8$ patients continued to show steady clinical improvement ($N = 5$) with further volume reduction (average 60%) at 24 months with compatible improvement on lymphoscintigraphy. One additional patient had viable lymph nodes on duplex exam.

At 48 months, however, only $N = 3$ patients remained compliant with maintenance CDT and maintained maximum improvement in the range of 60% volume reduction. Follow-up lymphoscintigraphy demonstrated excellent ($N = 1$) to good response ($N = 2$) with equivalent clinical improvement. A duplex scan confirmed viable lymph nodes graft in two patients, which is comparable to lymphoscintigraphic evidence of viable/functioning lymph nodes ($N = 1$) (Figure 3).

These three patients had secondary lymphedema and received the surgery in clinical stage II; all three had clinical improvement, no further episodes of sepsis and improved quality of life.

Six of 10 patients with failed FLTS at 48 months had increased rate of recurrent cellulitis with an average of 1.8 episodes per year before clinical failure was documented as advanced clinical and laboratory stage.

An unexpected complication of FLTS was observed in $N = 3$ patients (out of a total of $N = 13$) where transient lymphedema developed in the limb where the donor lymph nodes were harvested. All patients were managed successfully with CDT and fully recovered during the follow-up period.

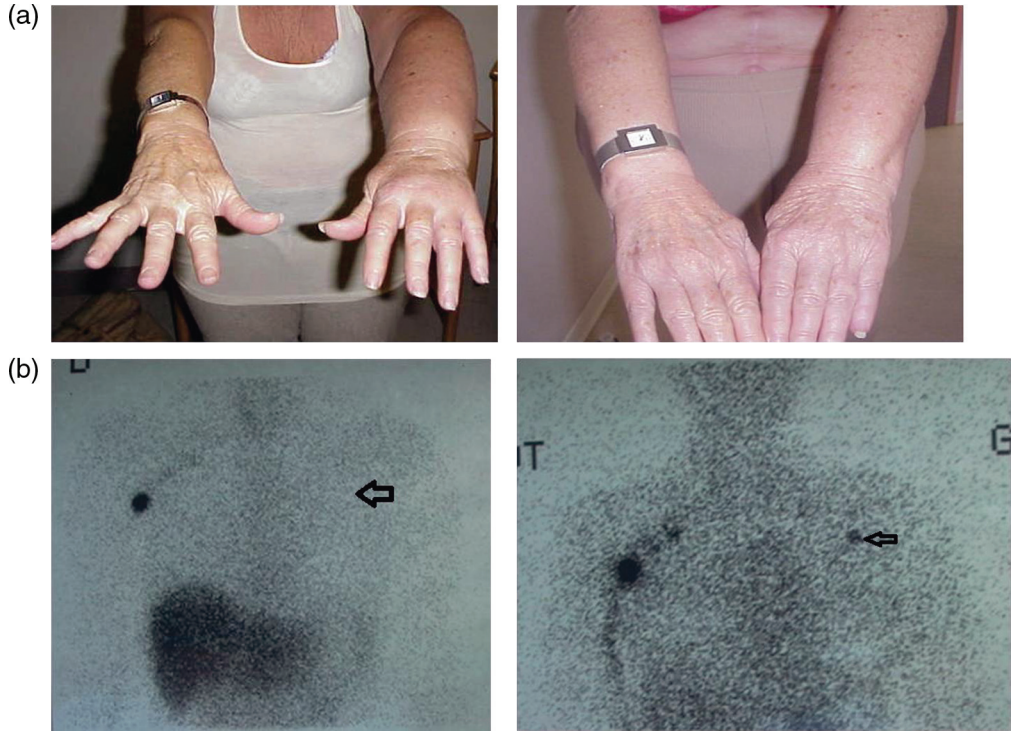

Figure 3 Two photos show a remarkable change/improvement on the lymphedematous limb (left) before (a-1) and after (a-2) the successful free graft/transplantation of the lymph nodes with a two-year interval. Two photos depict radionuclide lymphoscintigraphy findings before (b-1) and after (b-2) the free lymph node graft done 12 months later. Well functioning lymph nodes (b-2: arrow) appeared newly along the left axilla, which did not present in preoperative lymphoscintigraphy (b-1: arrow); it indicates successful outcome of surgical relief of lymph stasis, compatible to the clinical improvement (a-2) (courtesy of Professor C Becker)

Discussion

Preoperative assessment

Appropriate timing of surgical reconstruction in the treatment of lymphedema in patients who have failed to respond to CDT is critical in order to obtain optimal results. Clinical staging is equally important, allowing the earliest possible detection of lymphedema progression and providing accurate information for timely surgical intervention.[19,20]

The ISL staging system[23] does not allow precise evaluation of surgical candidates, although the addition of Stage 0 to previous three stages (stage 1 through 3) has improved the general assessment. We therefore propose a modified clinical staging system.[21,22] This four-stage system based on additional criteria better delineates the level of lymphatic involvement and subsequently allows improved selection of the appropriate surgical procedure.[5,6,19,20]

A two-year observation is often recommended by a CDT-enthusiastic multidisciplinary team[5,6,20] before consideration of lymphatic surgery. However, the two-year observation period often required before declaring the patient a 'treatment failure,' and then considering the patient for surgery is too conservative. Such a delay for more than one year will increase the risk of failure due to irreparable damage to the lymphatic system. This is a major concern held by many experienced lymphatic surgeons.[1,2,20]

Therefore, we believe that one year is sufficient to conclude 'the patient failed to obtain satisfactory control of the lymphedema progression or to prevent disease progression despite vigorous non-surgical treatment' and proceed with surgical reconstruction as indicated.

Appropriate assessment of the anatomic and functional status of the proximal lymph nodes and lymph collecting vessels is extremely important, especially when the reconstructive surgery is planned for patients with primary lymphedema or a relatively advanced stage.

The response to MLD can be an indirect indication of the functional status. Lymphoscintigraphy in both qualitative and semiquantitative assessment (e.g. percentage reduction of the DB and/or improved clearance ratio, etc.) is generally sufficient to assess the response to the MLD.[1,2,20]

Initially, we evaluated the change/improvement on lymphoscintigraphy based on five selected items as an independent criterion for new laboratory staging[21,22] as shown in Figure 1. But due to the change of the tracer material during the follow-up period, from 'antimony sulfur colloid' to 'filtered' sulfur colloid by the US Food and Drug Administration decision, accurate and fair comparison on all five different criteria became impossible due to the two different qualities of the imaging. Therefore, lymphatic clearance assessment was limited with the visual and qualitative measurement of DB and the combined result of other clearance criteria to improve its reliance.

Therefore, we attempted to use currently available imaging technology of magnetic resonance (MR) lymphography and ultrasonographic lymphography to compensate this liability. But, we earned very limited information other than a visualization of 'dilated/non-functioning' lymphatic vessels; their current quality is not capable to provide sufficient data to appropriately plan for lymphatic surgery.

We were mandated to identify normal (functioning) lymphatic vessels more accurately for the LVAS preoperatively. But, lymphoscintigraphy can provide only 'indirect' evidence of improved lymph transport and cannot document the patency of the anastomosis. Direct contrast lymph (angi)ography with oily contrast medium is known to provide the best image as a road map for the operation but it is no longer used for a routine due to the risk involved to the endothelial damage.[1,2,20]

Postoperative contrast lymphangiography was also abandoned long ago for same reason although it would remain the only way to confirm anastomosis patency; the procedure is invasive with the risk of provoking the progression of lymphedema following the study.[1]

Therefore, we relied more on the intraoperative assessment of the lymphatic vessel condition with patent blue dye to identify competent lymph vessels with normal peristalsis/propulsion.[1]

In addition to lymphatic functional assessment, venous function assessment with duplex ultrasonography is also essential for LVAS candidates especially with the secondary lymphedema involved to the postoperative radiation. Vascular injury by radiation is far worse to the vein and a venography should be included whenever indicated.

In FLTS, the selection of appropriate donor lymph-node groups for harvesting is equally important as is the selection of the recipient site.[8,25] Lymphoscintigraphic evaluation of donor sites (e.g. inguinal, cervical or axillary groups) and duplex ultrasonographic evaluation of the lymph nodes are therefore required. Computed tomography can also be useful in the evaluation.

Surgical aspect

Among many different methods of the lymphatic reconstruction with microsurgical technique,[1,2] we chose LVAS as the direct approach and FLTS as the indirect reconstruction/approach. But, both procedures were implied to the

patients with the same condition in order to make a fair comparison later on their results altogether.

Reconstructive surgery,[27–36] regardless of its method, aims at relieving lymphatic hypertension to improve lymphatic function at best, although there is a theoretical chance of a cure when performed under ideal conditions.

But in reality, the lymphatic vessels are often damaged beyond the reversible condition due to prolonged lymphatic hypertension. Subsequently, a delayed relief of lymphatic stasis by the bypass operation often fails to restore/improve lymphatic function adequately. Therefore, it has been a general feeling not to delay for a better chance of surgical success.

Campisi *et al.*[9,11,29–32] of Italy is a leading advocate for microsurgical reconstruction early in the course of lymphedema for the best outcome while intrinsic contractibility of the lymphatics remained intact.

Our limited experiences also suggest that the drainage procedure could provide better long-term results when done in the early stage of the lymphedema, ideally in clinical stage II at the latest, which is roughly compatible to the ISL stage 1.

Although the initial results among our patients were equally satisfactory among the patients with stages II and III, only three patients in clinical stage II remained to maintain the initial improvement till the end of follow-up for four years.

Such impression is compatible with many others' more extensive experiences besides Campisi *et al.*, suggesting better chance by earlier intervention before the significant chronic inflammatory reaction along the subcutaneous tissue would result in fibrotic condition.[1,2]

Campisi *et al.* also reported long-term satisfactory results on 446 patients with continuous volume reduction on 69% after the discontinued conservative measures in 85%. Such findings are quite contrary to our limited experiences showing immediate deterioration of initially improved condition after the surgery whenever postoperative CDT is stopped.

Although their population of the candidates are different from ours, selected with different criteria including the staging of the lymphedema, such critical difference is hardly comprehensible to us. Perhaps their different/better outcome without continuous postoperative maintenance CDT is related to their free accessibility to their candidates to perform the same surgery in a much earlier stage, while we remain with significant limitation by a mandated waiting period, losing the best opportunity for timely surgery.

We, therefore, consider reconstructive surgery is best performed during the early clinical stage, where the residual lymph transporting system remains in salvageable condition and surgical restoration and relief of lymphatic obstruction and stasis can result in revitalization of transiently non-functioning lymphatic vessels to resume normal function.

Another challenge after performing the lymphovenous anastomosis is to document patency of the anastomosis without ruining the recently performed microsurgical procedure. Since the oil-contrast lymphangiography has been abandoned for this reason, we were not able to prove patent anastomosis directly by any currently available tests (e.g. MR lymphangiography; ultrasonographic lymphangiography). Although the lymphoscintigraphy gave 'indirect' evidences of functioning/patent anastomosis, its overall value was not much better than relying on the clinical improvement alone (e.g. reduced recurrence of the sepsis) following the surgery in our experience.

Furthermore, we have very limited ability to give an accurate assessment on the surgery itself versus postoperative CDT comparatively to bring the clinical improvement although both are mutually complementary.

However, our patients were already proved for 'CDT-failed' status for a minimum one-year period with no/poor response to MLD-based CDT including compression stocking and compression bandage before the referral. They were referred as candidates for the reconstructive surgery as a supplemental therapy to improve the efficacy of the CDT on the patients who had already failed with the CDT alone.

Therefore, we consider subsequent clinical improvement should reflect functioning anastomoses to restore the efficacy of previously failed CDT.

Our criteria, hence, to ascertain that the anastomosis is patent and functioning is totally arbitrary based on the clinical improvement, with better response to the CDT-based management following the surgery as well as lymphoscintigraphic improvement because of such unique condition before the surgical therapy was added.

O'Brian *et al.*[7] reported excellent outcome of the surgery with 42% long-term improvement although the improvement among 73% was a subjective one, which is far beyond our reach. The overall outcome on our own 19 patients was disappointingly low with three patients maintaining initial improvement during four-year follow-up.

But, an early report by Gloviczki *et al.*[10] on 14 patients with lymphovenous anastomosis also showed only five patients were able to maintain initial improvement at an average of 46 months after surgery, which is similar to our experience.

However, our results are especially poor on the primary lymphedema while the secondary lymphedema seems to have better outcome; all final three patients of LVAS were

secondary lymphedema although the absolute majority ($N = 15/19$) belonged to the secondary. Our FLTS patients also showed similar poor results among the primary lymphedema while the secondary lymphedema did better.

Gloviczki *et al.* also reported more chance of improvement among the secondary ($N = 4/7$) than the primary ($N = 1/7$), which is also compatible to our data/outcome.

We believe that the patients with secondary lymphedema often have a surgically correctable lesion along the major lymphatics when they develop after cancer surgery or radiation therapy. In this setting, there is a selective damage to the lymph nodes and the distal lymph-collecting vessels remain intact and subsequently more favorable results are obtained. Hence, lymphatic-venous anastomosis has a better chance to restore normal lymphatic function for treating secondary lymphedema.

But, the primary lymphedema involving the lymphatic vessels (e.g. aplasia, hypoplasia and hyperplasia) is well known for its difficulty to manage due to variations in lymphatics and lymph nodes; surgery outcomes are variable and the procedures are generally not as effective as is seen in patients with secondary lymphedema.[19,20]

However, Campisi *et al.* claimed similar/equivalent results in both primary and secondary lymphedema patients,[31,32] although primary lymphedema due to the dysplasia of lymph nodes alone can be exceptional.

FLTS is a relatively unknown indirect approach for a lymphatic reconstruction. But, Becker *et al.*[8,25] of Belgium reported excellent results of FLTS as a new approach for the reconstruction of a damaged lymph-transport system following radical mastectomy/axillary lymph node dissection.

Our limited experience on the FLTS with the same protocol on 13 patients done with full collaboration with C Becker's team was disappointing, especially among the primary lymphedema. We also failed to reproduce similar/excellent results as Becker *et al.* originally reported.

However, all three patients of FLTS, who maintained the initial improvement through the four-year follow-up, belonged to the secondary lymphedema, which is almost equivalent to the results on LVAS. Until the current study is completed with more data added, the conclusion on its relative efficacy to LVAS will be deferred.

We also learned that donor lymph node harvest is not a risk-free procedure to maintain normal lymphatic function of the donor limb after harvest. An 'iatrogenic' lymphedema we experienced in donor limb ($N = 3$), although transient and successfully recovered, is very alarming and may be the result of an unnecessarily aggressive lymph node harvest. Similar risk was also experienced by Baumeister[1] during lymphatic vessel harvest for lymphatic graft. The importance of such precaution cannot be overemphasized.

Postoperative care

Unfortunately, the majority of our patients undergoing surgical reconstruction have significant damage to lymph-transporting vessels caused by long-term lymphatic hypertension. Therefore, postoperative maintenance CDT following successful reconstructive surgery is essential for good long-term outcomes.[5,6,19,20]

However, the majority of our patients had poor compliance with postoperative maintenance CDT.

Lifelong maintenance CDT therapy following surgical reconstruction is, therefore, the single most important factor that determines the long-term outcome of a successful lymphatic reconstruction among our patients. The second most important issue regarding postoperative care is the prevention and treatment of infection. The majority of lymphatic surgery failures observed in our series of patients was due to recurrent infection.[5,6,20]

We support an aggressive surveillance and prevention program in addition to prompt diagnosis and treatment of systemic and local infection such as cellulitis and erysipelas to prevent further injury to an already compromised lymphatic system. Lifelong antibiotic prophylaxis should be considered in patients with a high risk of recurrent cellulitis.[37,38]

There are several reasons why reconstructive lymphatic surgery has failed to gain popularity. It is technically demanding, relatively time consuming and requires a dedicated team with experience in microsurgical techniques. Limited surgical expertise has prevented widespread adoption of lymphatic reconstruction. Therefore, only a handful of institutions throughout the world continue to offer this treatment. Furthermore, indiscriminate use of this delicate and time-consuming procedure has likely resulted in variable results among different institutions.[20]

Conclusion

Reconstructive lymphatic surgery (LVAS and FLTS) appears to be more effective in secondary lymphedema versus primary lymphedema when performed in the early stages. Patient compliance to maintain CDT postoperatively remains the most critical factor in maintaining durable long-term results. FLTS seems to have an additional risk involved to the donor lymph node harvest and a limited role compared with LVAS. Further extended study on FLTS is required to demonstrate its long-term efficacy compared with LVAS.

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