Chapter 40
General Principles and Indications

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Chronic lymphedema continues to be a challenge in both diagnosis and management. The diagnostic dilemma remains about how to best define detailed anatomy and lymphatic function, Whereas the problem with treatment remains our inability to cure chronic lymphedema. Still, both evaluation and treatment have greatly improved in recent years. Progress in genetics, imaging studies, physical therapy, and microsurgical techniques have sparked interest in chronic lymphedema, a disease long considered to be the stepchild of medicine. This textbook is testimony to the increasing interest in the investigation and treatment of lymphatic disorders.

The introduction of vascular microsurgery in the early 1960s by Jacobson established the possibility of surgical reconstruction of lymph vessels and lymph nodes.[1] The observations of Edwards and Kinmonth,[2] that, in lymphedema, spontaneous lymphovenous shunts in lymph nodes developed, and were likely to decompress the high pressure lymphatic system distal to an obstruction, led to early attempts to perform microsurgical lymphovenous anastomoses in patients with lymphedema. Lymph-vessel-to-vein[3-26] and lymph-node-to-vein anastomoses[27-30] were soon followed by lymphatic grafting to bypass the lymphatic obstructions.[31-36] In patients with lymphangiectasia, vein grafts with competent valves were used to drain the lymph and to prevent reflux of blood into the lymphatic system.[35,37,38] The free flap technique of lymph node transplantations was also developed.[39] Interest and enthusiasm for lymphatic microsurgery has waxed and waned during the last five decades, mostly because only a few centers around the world have had the expertise to perform these most difficult and challenging procedures (Fig. 40.1). In this section of the book we review the principles and indications, and briefly discuss the microsurgical techniques, results, and problems of the different types of lymphatic reconstructions.

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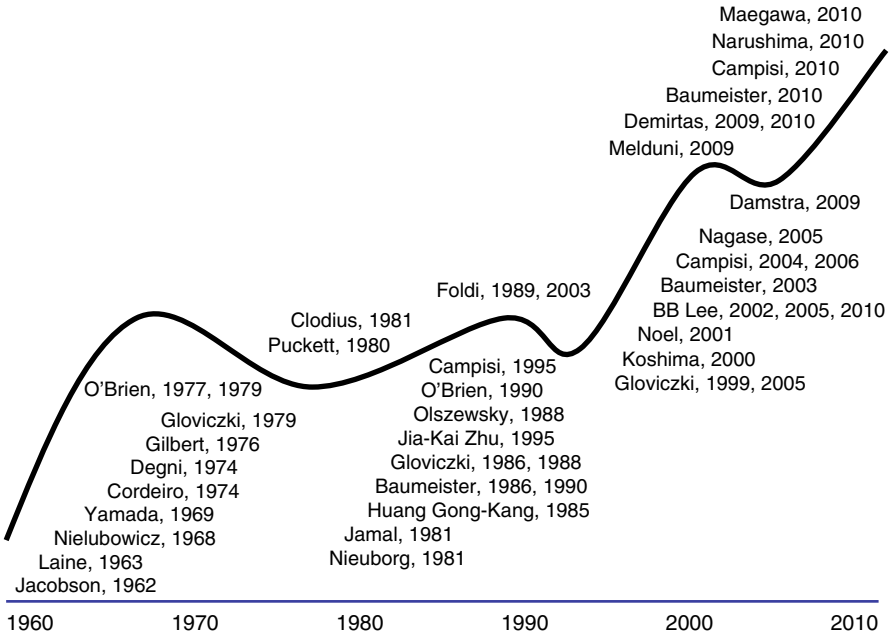

Fig. 40.1 Publications (first author, year) on microsurgical lymphatic reconstructions between 1962 and 2010 (By permission of Mayo Foundation for Medical Education and Reasearch)

Principles

In most patients chronic lymphedema is the result of acquired or congenital obstruction of the lymph vessels and the lymph–conducting elements of the lymph nodes. In some, valve incompetence of lymph vessels is the cause of poor lymph transport. The condition becomes clinically significant when the lymphatic collateral circulation is inadequate for draining lymph from the affected part of the body and lymph production exceeds the transport capacity of the lymphatic system. Other compensatory mechanisms, such as the tissue macrophage activity and drainage through spontaneous lymphovenous anastomosis, also are exhausted. The condition is aggravated by higher lymph production due to venous obstruction, venous valve incompetence, dependency of the limb, infection, or inflammation.

Surgical treatment of lymphedema includes excisional operations and lymphatic reconstructions.[40,41] Excisional surgery involves reduction of the volume of the limb by excision of the excess lymphatic tissue. This can be performed alone or with lymphatic reconstructions. Liposuction also has been used as an effective technique to decrease the excess volume of the affected limb.[42,43]

The goal of microsurgical lymphatic reconstructions is to restore or improve lymph transport in patients with chronic lymphedema. The ultimate goal is reduction of chronic swelling, decrease of the episodes of infection, and improvement of the quality of life of these patients.[44]

Indications

As discussed in ample detail in this book, multimodal complex decongestive physical therapy currently is recommended as first-line treatment for chronic lymphedema.[41,45] Successful therapy results in decreased volume, improved function, and improved quality of life. Considerations for surgery include no response to medical management after at least 6 months of therapy in surgically fit patients without recent episodes of cellulitis or lymphangitis and the availability of a center with an expert in lymphatic microvascular reconstructions. Severe pain is rare and it is a relative indication for surgery, whereas aesthetics alone is seldom an indication, although some patients are unwilling to undergo more conservative treatment, but are willing to proceed with experimental operations. The most suitable anatomy for lymphatic reconstructions is an acquired proximal (pelvic, axillary) lymphatic obstruction, with documented distal lymphatics on lymphoscintigraphy,[46,47] magnetic resonance lymphangiography,[48] or using the technique of indocyanine green injection and infrared scope imaging.[26]

Intrinsic contractility of the lymph vessels is one of the main factors responsible for normal lymphatic flow. Preserved contractility is ideal to assure good lymphatic flow against the higher pressure venous system. Activity and muscular contractions of the limb are also helpful and can generate intermittent pressures as high as 50 mmHg in the normal lymphatic system.[49] Unfortunately, compliance of the lymph vessels deteriorates in chronic lymphedema, and loss of contractility, especially when coupled with lymphatic obstructions or valvular incompetence, is an important reason why the response to lymphatic reconstructions in advanced stages of chronic lymphedema is so poor. Also, patients with lymphatic fibrosis, congenital hypoplasia, or even aplasia of the lymph vessels, as seen in those with primary lymphedema, are frequently poor candidates for lymphatic reconstructions.

Microsurgical Reconstructions

Three main techniques of lymphatic reconstructions have been developed. These include lymphovenous anastomosis, lymphatic grafting, and lymph node transplantations.

Lymphovenous Anastomosis

Lymphovenous anastomoses have been performed to drain lymph into the venous system in an area distal to the lymphatic obstruction.[3-30] Most patients have acquired or primary iliac lymphatic obstruction. Occasionally the operation is performed for congenital lymphangiectasia[37] or filariasis.[28,29] Two techniques have been introduced, lymph node-to-vein and lymph vessel-to-vein anastomoses (Fig. 40.2a, b).

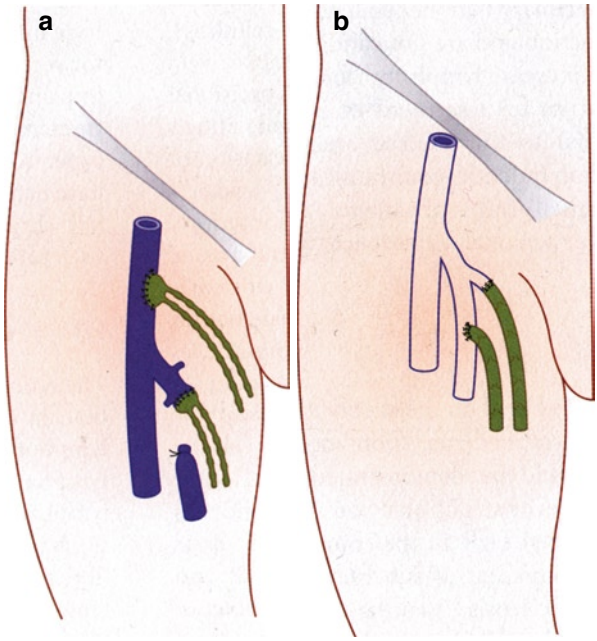

Fig. 40.2 (**a**) End-to-end and end-to-side lymph node-to-vein anastomosis at the groin. (**b**) End-to-end and end-to-side microsurgical lymph vessel-to-vein anastomosis. (By permission of Mayo Foundation for Medical Education and Reasearch)

Lymph Node-to-Vein Anastomosis

Technique

Lymph node-to-vein anastomoses were first performed by Nielubowicz and Olszewski in Poland in 1968.[27,50] During the operation transected inguinal lymph nodes are anastomosed end-to-end or end-to-side to the saphenous or the femoral veins (Fig. 40.2a).

Results

Clinical improvement after lymph-node-to-vein anastomoses has been reported in a few uncontrolled studies,[27,30,50] but concerns about scarring over the cut surface of the lymph nodes leading to failure prevented widespread application of this technique in most types of secondary lymphedema. In filariasis, however, lymphatics are frequently enlarged even within the lymph nodes and lymph flow is high. Jamal from India reported good results in 90% of patients with parasitic lymphatic infections.[28] Jamal also found that patients with congenital lymphangiectasia who underwent lymph node venous shunts constructed in the inguinal area, improved after the procedure.[28,29]

Lymph Vessel-to-Vein Anastomosis

Microsurgical Technique

Earlier techniques of lymph vessel to vein anastomosis involved simple invagination of transected lymph vessels into large veins, like the saphenous, femoral, basilic, or brachial veins. This technique was popularized first in Brazil by Degni[51] and Cordeiro, and was used in a large number of patients by Campisi's group in Italy[16,18,52] (Fig. 40.3a, b). The same method of lymphatic reconstruction was also used in a recent prospective study by Damstra.[53] Variations of the invagination technique include pulling of the lymphatics into a vein graft and fixing with one or two sutures. Additional lymphatics distal to the obstruction can be pulled into the vein graft in an attempt to improve lymphatic drainage, and using the vein graft as a large lymphatic conduit to bypass the obstruction (Fig. 40.3b).

Most microsurgeons perform direct end-to-end or end-to-side lymphovenous anastomoses, using high power magnification and 8-10/0 microsutures (Fig. 40.2b).[3,7,12,54] The latest techniques of supermicroscopic surgery use very high power magnification. The introduction of intravascular stents and multiple configuration anastomosis, using both the proximal and distal ends of the transected lymph vessel (Figs. 40.4 and 40.5), enables better anastomosis of smaller (<1 mm) lymph vessels and likely contributes to improved patency rates and durable efficacy.[24-26,35,36,55] Reconstruction of larger lymph collectors and of the thoracic duct has also been reported.[23,56]

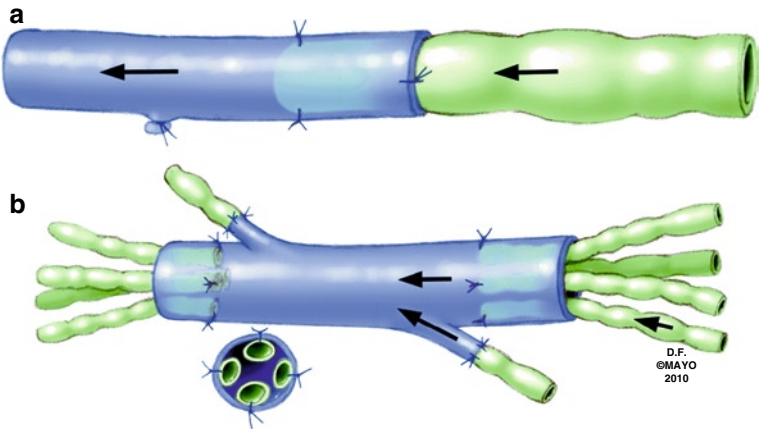

Fig. 40.3 Invagination techniques of Campisi. (**a**) Lymphovenous anastomosis, (**b**) lymphatic–venous–lymphatic anastomoses, performed using invagination of multiple lymphatics into an interposition vein graft. (By permission of Mayo Foundation for Medical Education and Reasearch)

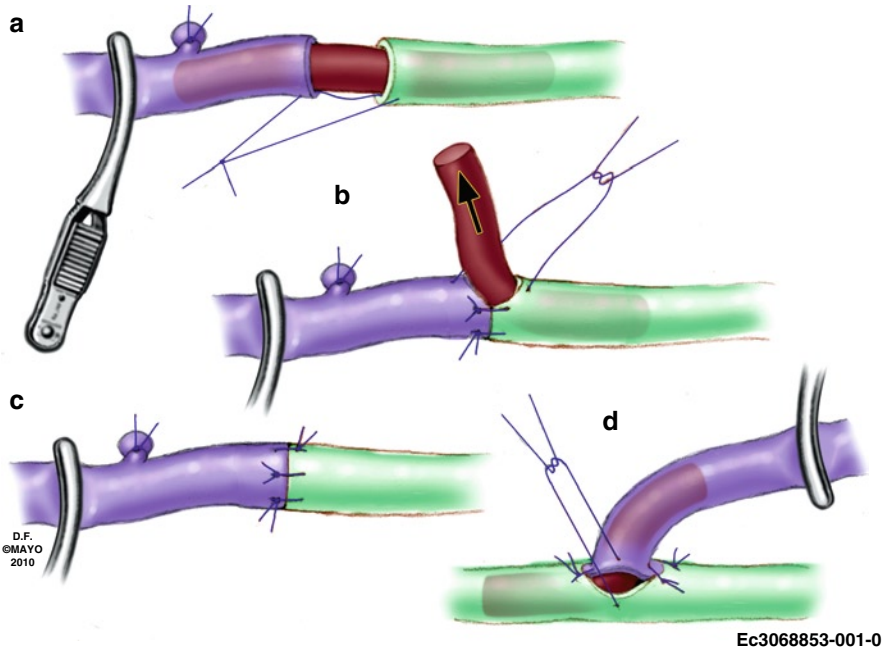

Fig. 40.4 Lymphovenous anastomoses performed with supermicroscopic technique, high-power magnification, and intravascular stents, according to Narushima. (**a**, **b**, **c**) Steps in performing end-to-end anastomosis with a stent. (**d**) End-to-side anastomosis. Stent is removed before completion of the anastomosis. (By permission of Mayo Foundation for Medical Education and Reasearch)

Results

Technically, lymphovenous anastomosis can be performed by experienced microsurgeons, and in experiments anastomoses between normal femoral lymph vessels and a tributary of the femoral vein yielded a patency rate of 50% at 3–8 months after surgery.[7] The clinical effectiveness of this operation is more difficult to prove in humans, because almost all studies were uncontrolled and adjuvant compression therapy was used in most published series. In only five patients out of 14 on whom we operated in an earlier series maintained the initial improvement at an average of 46 months after surgery.[8] Patients with secondary lymphedema did better than those with primary lymphedema. In a group of 13 patients, 10 with primary and three with secondary lymphedema, Vignes et al.[57] failed to prove clinically significant long-term efficacy of the procedure. Damstra et al.,[53] in a similar, small cohort of 10 operated breast cancer patients with 11 procedures did not find a durable benefit of the invagination technique of lymphovenous anastomosis as described by Degni.

Experiences with large numbers of operated patients, however, suggest that clinical improvement can be achieved with lymphatic drainage procedures.[7-9,11-16] In O'Brien's series from Australia, 73% of the patients had subjective improvement

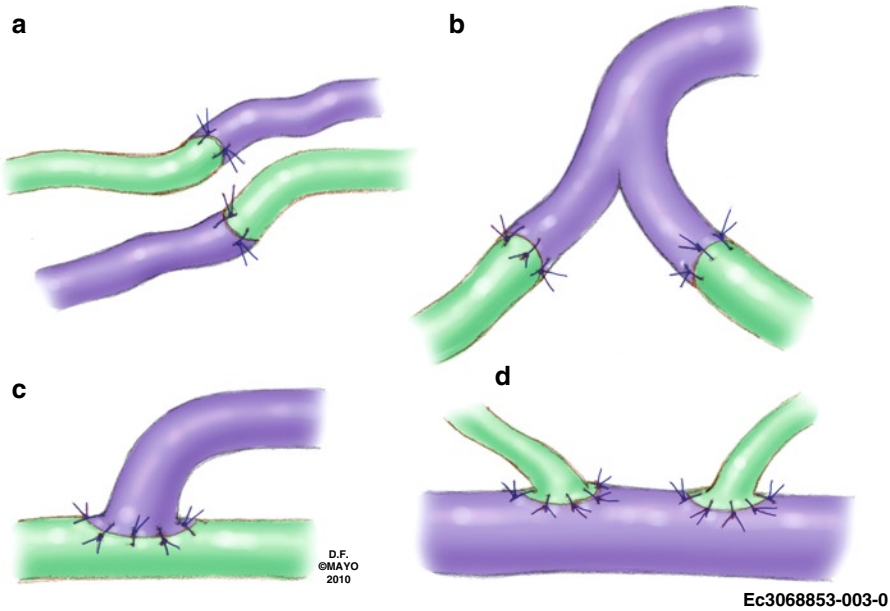

Fig. 40.5 Techniques of Narushima for multiconfigurational lymphovenous anastomoses, with reconstruction of both the proximal and the distal ends of the transected lymph channels. (**a**) lymphovenous anastomosis with using both ends of the transected vessels. (**b**) anastomosis of two lymphatics with a bifurcated vein, end-to-end. (**c**) end-to-side vein – to-lymphatic anastomisis. (**d**) End-to-side anastomosis of two lymphatics into the same vein. (By permission of Mayo Foundation for Medical Education and Reasearch)

and 42% experienced long-term efficacy.[6] Campisi in Italy currently has the most experience with lymphatic microsurgery.[13-18,58,59] His team reported results in 665 patients with obstructive lymphedema using microsurgical lymphovenous anastomoses, with subjective improvement in 87% of the patients.[58,59] Four-hundred and forty-six patients were available for long-term follow-up: volume of the limb was reduced in 69%, conservative treatment was discontinued in a surprisingly high number of patients (85%). In 1,500 operated patients, using a variety of microsurgical reconstructions (Fig. 40.3), Campisi reported diminished volume of the operated limbs in 83% of the patients and decreased cellulitis in 87%.[60]

Significant recent progress in supermicroscopic surgical techniques has been documented in the past decade in publications by Koshima,[55] Demirtas,[24,25] and Narishima.[26] These authors have used high-power magnifications for direct lymphovenous anastomosis and lymphovenous implantations. Takeishi[61] suggested that lymphovenous anastomosis will prevent lymphedema in patients who undergo pelvic lymphadenectomy for cancer.

Narashima et al.[26] recently reported the use of temporary intravascular stents in 14 patients to ensure the patency of 39 multiconfiguration lymphaticovenous

anastomoses capable of decompressing proximal, refluxing, and distal, antegrade lymphatic systems. These authors observed significant reduction in limb girth at a mean follow-up of 8.9 months, and found a greater decrease in the cross-sectional area with an increasing number of lymphaticovenous anastomoses per limb. Demirtas et al.[24,25] performed microlymphatic surgery in 80 lower extremities with primary and 21 with secondary lymphedema. Reduction of the edema occurred earlier in the secondary lymphedema group, but the mean change in the edema volume was comparable between the two groups. Although these results need confirmation by other investigators, this is the first promising study on using microsurgery with good results in patients with primary lymphedema.

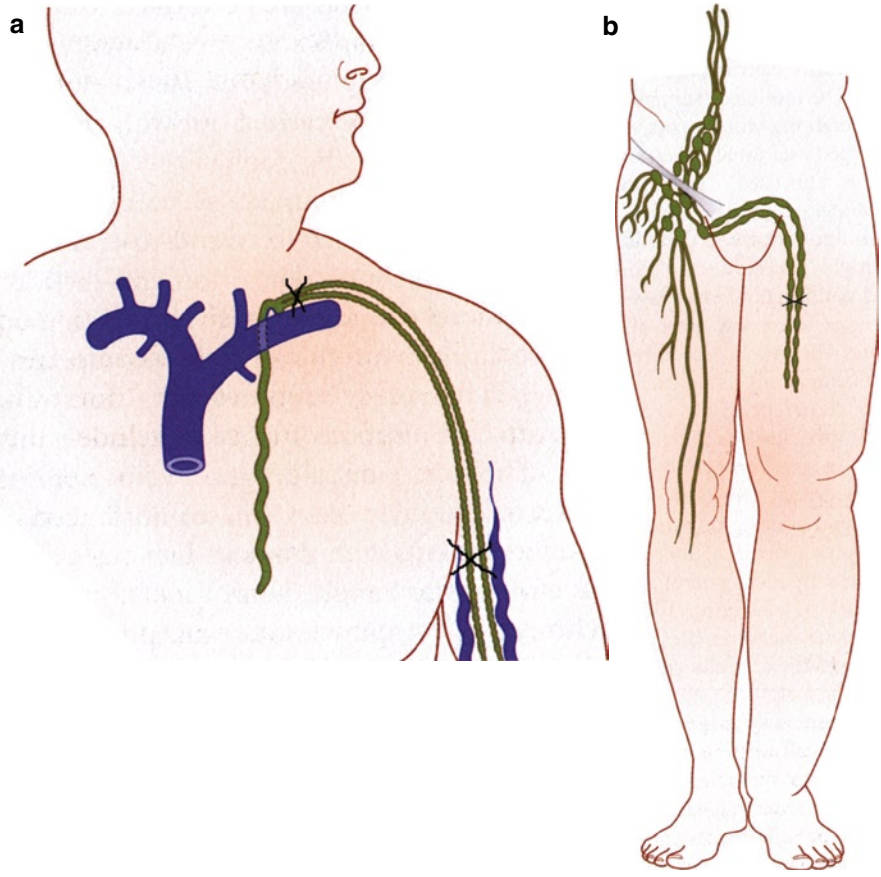

Fig. 40.6 Techniques of Baumeister: (**a**) Treatment of postmastectomy lymphedema with transplantation of two lymph channels from the lower to the upper extremity to by-pass the axillary lymphatic obstruction. (**b**) Cross-femoral lymph vessel transposition for unilateral lower extremity lymphedema. (By permission of Mayo Foundation for Medical Education and Reasearch)

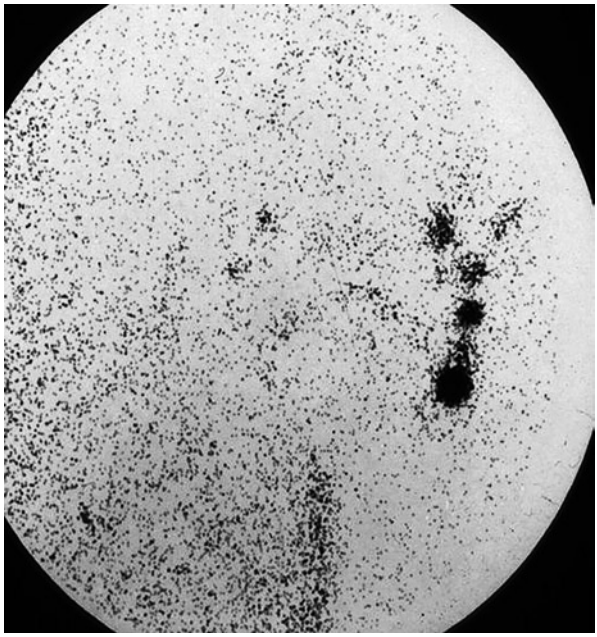

Fig. 40.7 Lymphoscintigraphy 3 months after cross-femoral lymphatic transposition. Note visualization of the left inguinal nodes following injection of isotope into the right edematous foot. There was no uptake prior to operation. (By permission of Mayo Foundation for Medical Education and Reasearch)

Lymphatic Grafting

Technique

Baumeister developed the technique of bypass with lymphatic grafts, harvested from the unaffected lower limb. Two to three lymph vessels of the perisaphenous superficial lymphatic bundle are harvested under magnification and used either as a free graft for postmastectomy lymphedema to by-pass the axillary lymphatic obstruction (Fig. 40.6a), or as a suprapubic cross-femoral transposition graft to treat unilateral lower limb lymphedema in patients with iliac or iliofemoral lymphatic obstruction (Fig. 40.6b).

Results

In a recent comprehensive review[34] of the subject, Baumeister, an experienced lymphatic microsurgeon, detailed the long-term results of these tedious operations. In a group of 55 patients undergoing lymphatic grafting, improvement in limb volume after a mean follow-up of 3 years was documented in 80% of the patients.[33] Patency of transposed suprapubic lymph vessels can be documented with lymphoscintigraphy (Fig. 40.7). Using semiquantitative lymphoscintigraphy, significant improvement in lymphatic function could be demonstrated in 17 out of 20 patients at 8 years after the operation.[34,62] In a series of 127 patients suffering from arm edema,

a significant volume reduction was achieved with this technique, both at 8 days and at a mean of 2.6 years after surgery. In 81 patients with unilateral lower limb edema volume reduction after suprapubic transposition was significant, both early after surgery and at 1.7 years.[32]

Lymph Node Transplantation

Technique

Becker et al.[39,63] reported on the technique of lymph node transplantation, harvested from the groin as a free flap, to bridge the lymphatic obstruction in patients with postmastectomy lymphedema. The feeding artery and the draining vein of the flap are anastomosed to the appropriate vessels in the axillary fossa using a standard microsurgical technique.

Results

In 22 out of 24 patients the volume of the limb either decreased or returned to normal at 5 years or more after lymph node transplantation.[39,63] However, in only 5 out of 16 (31%), isotopic lymphoscintigraphy demonstrated activity of the transplanted nodes. Still, physiotherapy was discontinued in 15 patients (62.5%) and cure was demonstrated in 10 (41.6%).[39] The authors noted most improvement in patients with early stages of lymphedema. The use of this technique for lymphedema is appealing, but it needs independent confirmation by other microsurgical groups.

Problems with Microvascular Lymphatic Reconstructions

During the past few decades concerns and comments on the reasons for failures of lymphatic reconstructions have been voiced by Puckett,[64] Clodius,[65] and Foldi,[66,67] among others, and most recently by Damstra.[53] A thorough review of these publications by all experts who embark on the always challenging and sometimes unrewarding field of lymphatic microsurgery is strongly recommended.

One concern raised by critiques of lymphovenous anastomosis has been the lack of documented late patency. While lymphoscintigraphy is suitable to show patent lymphatic grafts[62,68] or transplanted lymph nodes,[39] this test can provide only indirect evidence of patency of lymphovenous anastomosis by showing improved lymph transport of the limb. Such improvement, however, can also be achieved by conservative measures. Observing contrast material during lymphangiography as it passes through the anastomosis is the only current way to document patency of lymphovenous shunts. Also, the droplets of the lipid-soluble contrast material are taken

Table 40.1 Guidelines of the American Venous Forum on surgical treatment of chronic lymphedema[40]

Number of guideline	Guideline	Grade of recommendation	Grade of evidence
6.4.1	All interventions for chronic lymphedema should be preceded by at least 6 months of non-operative compression treatment.	1	C
6.4.2	We suggest excisional operations or liposuction only to patients with late stage non-pitting lymphedema, who fail conservative measures	2	C
6.4.3	We suggest microsurgical lymphatic reconstructions in centers of excellence for selected patients with secondary lymphedema, if performed early in the course of the disease.	2	C

1 strong, *2* weak, *A* high quality, *B* moderate quality, *C* low or very low quality

away immediately by the venous blood stream; thus, the technique of cinelymphangiography is essential for documenting patency. In experiments, our group could demonstrate this,[6,7] but in patients, no firm data are available. In addition, assessment of the efficacy of microsurgical reconstructions is also hampered by the fact that the reported studies are uncontrolled, almost all are retrospective and, as pointed out by Damstra,[53] they lack a validated method of outcome evaluation. Damstra, disappointed by the negative results of his prospective study of 10 patients who underwent the Degni technique of lymphatic invagination, concluded that there was no convincing evidence of the success of lymphovenous anastomosis.[53] Another recent review of the literature[40] was somewhat more optimistic: it considered that evidence of the efficacy of surgery was there, but that it was of low or very low quality. Based on the available literature and consensus of experts, the American Venous Forum recently formulated recommendations for surgical treatment of lymphedema (Table 40.1).[40]

Finally, an observation on the clinical ineffectiveness of lymphovenous shunts in some patients deserves attention, as emphasized by Clodius, Piller, and Casley-Smith.[65] As these authors pointed out, some lymphatic microsurgeons consider the lymphatic system to be a canalicular system of drainage tubes and expect complete resolution of the edema by reestablishing lymph circulation using perfect microsurgical techniques. Unfortunately, in chronic lymphedema, inflammatory tissue changes occur that frequently will not reverse to even complete reconstruction of the lymph vessels or the lymph-conducting elements of the lymph nodes.

Conclusions

Conservative management with compression garments, decongestive lymphatic therapy, manual lymphatic drainage, bandaging, life-style modification, skin care, and treatment of infectious complications continues to be the mainstay of therapy for chronic lymphedema. Scientific evidence for the efficacy of lymphatic reconstructions to decrease limb swelling and improve the quality of life of patients with chronic lymphedema remains of very low quality. Most studies are uncontrolled and retrospective. Current recommendations for lymphatic microsurgery in patients with chronic lymphedema, non-responding to at least 6 months of intensive physical therapy, are weak. We suggest performing lymphatic reconstructions only in microsurgical centers of excellence in selected patients with obstructive, secondary lymphedema, early in the course of the disease.[40] Progress in the field of lymphatic microsurgery, however, has been noticeable and improvement in technique has been substantial. Interest in lymphatic microsurgery is increasing and supermicroscopic surgical techniques permit more reliable reconstructions of lymph vessels <1 mm in size. As non-invasive imaging techniques of the lymphatic system has also progressed, patient selection will likely be better and clinical improvement attributed solely to surgery can be documented in larger number of patients, in multiple centers. These are good reasons for being optimistic about treating chronic lymphedema effectively. However, until controlled prospective trials prove the clinical efficacy and durable function of lymphatic reconstructions, lymphatic microsurgery continues to remain an unfulfilled promise.

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