

Management of secondary lymphoedema

TW Chiu *

ABSTRACT

Lymphoedema is a chronic, progressive condition. There is no cure but it is most easily managed with early recognition and therapy; those who do not have treatment tend to worsen rapidly and advanced disease is more difficult to treat than early disease. Surgery for lymphoedema is often regarded as a last resort but traditional excisional techniques that have been slightly modified for modern practice have shown good results, whilst newer microsurgical reconstruction techniques show promise although

long-term results are lacking. This report provides an update on the therapy of lymphoedema.

Hong Kong Med J 2014;20:519–28

DOI: 10.12809/hkmj134116

TW Chiu *, FHKAM (Surgery)

Division of Plastic Aesthetic and Reconstructive Surgery, Prince of Wales Hospital, Shatin, New Territories, Hong Kong

* Corresponding author: torchiu@surgery.cuhk.edu.hk

This article was published on 29 Aug 2014 at www.hkmj.org.

Introduction

Lymphoedema is characterised by an imbalance of lymphatic flow leading to accumulation of protein-rich fluid in the interstitium of subcutaneous tissues. The consequent swelling may cause cosmetic and functional impairment, with significant physical and psychological morbidity. There is progressive damage to the lymphatics with inflammation, fibrosis and more swelling, eventually leading to elephantiasis. Recurrent infection is a common complication whilst lymphangiosarcomas are rare, occurring in 0.03% of patients surviving more than 10 years after mastectomy.¹

It is traditional to classify lymphoedema into primary or secondary forms—in the former there is congenital lymphatic dysfunction related to dysplasia/malformation whilst in the latter there is disruption of lymphatic outflow related to another disease process or due to iatrogenic mechanisms.

Primary lymphoedema

The traditional subdivision of primary lymphoedema according to the time of onset has little clinical significance. There is confusion in the literature regarding the terms used, particularly, the various eponymous syndromes that have been described; most cases of primary lymphoedema are not associated with specific syndromes.

- Congenita (10% of cases): the swelling is often present at birth (any swelling that begins before the age of 2 years is included in this group).
- Praecox (80% of cases): patients present with swelling before the age of 35 years.
- Tarda (10% of cases): patients present after the age of 35 years with swelling that is usually bilateral. Lymphatic vessels tend to be hyperplastic.

It is important to appreciate that primary lymphoedema is a heterogeneous group with many subtypes occurring due to many different causes which are generally poorly understood. The term Milroy's disease is often used interchangeably with lymphoedema congenita—it should only be applied to the group of inherited congenital lymphoedemas that demonstrates autosomal dominant inheritance; it is linked to vascular endothelial growth factor (VEGF) receptor-3 mutations (*FLT4* gene on locus 5q35.3)^{2,3} and some evidence reveals that there is a functional defect of absorption rather than a gross structural defect.

Lymphoedema praecox is the commonest type (80% of cases) and the swelling may be unilateral and limited to the foot/calf region. Patients lack distal lymphatics (hypoplasia) and often have a strong family history, some demonstrating autosomal dominant inheritance with different mutations in *FOXC2* gene on chromosome 16.⁴ Some patients with praecox have distichiasis (double row of eyelashes) and form a distinct syndromic entity—lymphoedema distichiasis (mutation on 16q24.3).⁵ Patients with Meige's disease, which is a subset of lymphoedema, usually present at puberty and the term should be reserved for those with the familial form of the disease (with as-yet unknown mutation).

Secondary lymphoedema

Worldwide, the commonest cause of secondary lymphoedema is filariasis, caused by infection with *Wuchereria bancrofti*. However, this condition is rare in developed countries such as Hong Kong where lymphoedema is most commonly related to malignant disease and, particularly, its treatment with surgery and/or irradiation.⁶ Upper limb

繼發性淋巴水腫的治理

趙多和

淋巴水腫是一種慢性、進行性的疾病。如果未能及時接受治療，疾病惡化的速度會很快，而晚期淋巴水腫會較早期的情況更難醫治。目前，淋巴水腫不能治愈，但及早識別和醫治會令此病較為容易管理。以手術治療淋巴水腫往往被視為最後的方法，但採用改良了的傳統手術切除技術有良好效果。採用較新穎的顯微外科重建術，儘管有關其長期臨床效果的研究甚少，但也總算開啟了治療淋巴水腫的可能性。本文概覽有關治理淋巴水腫的最新情況。

lymphoedema most often follows the treatment of breast cancer, typically after a latent period of variable duration—77% of cases present within 3 years of surgery⁷ but the condition can arise at any time.

Although the exact mechanism of the response of lymphatic channels to trauma is unknown, in general, the more extensive the surgery the greater is the damage. Thus, a formal axillary node dissection carries a risk of up to 20% compared to 4% to 10% following sentinel node biopsy.⁸⁻¹¹ Irradiation causes fibrosis and inhibits lymphangiogenesis and, approximately, doubles the risk of developing lymphoedema after nodal surgery. Lymph vessels do have some regenerative capacity¹² and not all patients undergoing surgery and/or radiotherapy develop lymphoedema; it may be related to some underlying susceptibility that is as yet undefined, and may be, possibly, genetic.¹³ Patients with lymphoedema often have subtle lymphatic anomalies in the contralateral

limb.¹⁴

Staging

The International Society of Lymphology staging is the most commonly used system (Table 1¹⁵), but it is somewhat flawed in that it is based only on physical findings. Some experts suggest incorporating measures of quality of life (QOL) to improve its usefulness.¹⁶ The classification offered by Campisi et al¹⁷ shows congruence with indocyanine green (ICG) dermal backflow patterns, which provides an indication of lymphatic function (Table 2).¹⁷⁻¹⁹ Bioimpedance spectroscopy uses electric current to measure the degree of tissue fluid retention and is useful in detecting early-stage lymphoedema including stage 0 disease.

The most commonly used method of objectively assessing the swelling is some form of conal measurement, such as measuring the circumference at 4 cm intervals, which is more practical than water displacement methods^{20,21} but is, supposedly, similar in accuracy.²² A perometer uses infrared rays to measure limb cross-sections at multiple intervals and, thus, determine the volume of the limb.²³ The author has been exploring the idea of using Kinect (part of the Microsoft Xbox game system) as a three-dimensional scanner to gauge volume in collaboration with the Department of Computer Science and Engineering at The Chinese University of Hong Kong.

Imaging

In most cases, diagnosis can be made from the

TABLE 1. International Society of Lymphology (ISL) staging 2003 with ratification in 2009 consensus document; stage 0 (latent lymphoedema) is a recent addition¹⁵

ISL stage	Features
0/la	No oedema but presence of lymphatic impairment
I	Mild oedema that is reversible with appropriate limb position. May pit
II	Moderate oedema that is not reversible with limb elevation. Pitting present, except in late stage II when more fibrosis occurs
III	Lymphostatic elephantiasis with trophic skin changes such as acanthosis, deposition of fat and fibrosis, warty overgrowth

TABLE 2. Campisi staging 2010¹⁷

Campisi stage	Features
1A	No oedema but presence of lymphatic impairment; no difference in volume/consistency of oedema between limbs
1B	Mild oedema that is reversible with appropriate limb position
2	Persistent oedema that is partially reversible with appropriate limb position
3	Persistent oedema that continually becomes more severe; recurrent acute lymphangitis
4	Fibrotic lymphoedema with lymphostatic warts, column-shaped limbs
5	Elephantiasis with severe limb deformation, scleroindurative pachydermatitis, widespread lymphostatic warts

clinical history and examination, although some co-morbidities may confound the clinical picture. Lymphoedema can be assessed by common imaging techniques including computed tomography, magnetic resonance imaging, and duplex ultrasonography that can reliably show volume differences between the affected and normal limbs, the presence of subcutaneous fatty fibrosis, and help exclude proximal obstruction in late-onset unilateral lymphoedema which may be due to an occult visceral tumour.

Lymphangiography involves direct cannulation of a lymphatic vessel on the dorsum of the foot or hand (under magnification). An oil-based contrast material is then injected through this vessel and serial plain radiographs of the limb are taken, allowing the lymphatics to be precisely delineated. Due to the potential of damage to the lymphatic vessels, it can theoretically worsen lymphoedema and, thus, is not commonly used.

Radionuclide lymphoscintigraphy is the current standard investigation for evaluation of lymphatic function. Technetium-labelled colloid is injected into the web spaces of the toes or fingers, and drainage of the colloid from the injection site and the time taken to move proximally are recorded using a gamma camera. It is minimally invasive and enables making both qualitative and quantitative analyses. It does not require dye injection, a method that has been occasionally complicated by allergic skin reactions or anaphylaxis.

Magnetic resonance lymphangiography may replace lymphoscintigraphy as it does not require direct injection of contrast and avoids the use of ionising radiation using a magnetic contrast medium to provide a sharp image of lymphatic vessels. In our early experience with this investigation, reproducibility has been a potential issue and needs further evaluation.

Near-infrared fluorescence imaging with ICG is a promising emerging imaging modality that allows dynamic study of even small lymphatics in the skin.

Treatment

There is no cure for lymphoedema but it is easily managed with early recognition and therapy. Those who do not have treatment tend to worsen rapidly and advanced disease tends to be more difficult to treat than early disease. Patients are best treated in a specialised clinic²⁴; inexperienced staff may delay treatment, or worse, advocate inappropriate treatments.

The standard of care for lymphoedema is, what is commonly referred as, complex (or combined or complete) physical therapy (CPT, sometimes called complex decongestive therapy [CDT]), which is a staged combination of various components in two phases. The actual treatment regimen varies

significantly by locality but, in general, 60% to 70% of compliant patients will respond to CPT when administered by specially trained therapists, with an average volume reduction of 50%.^{25,26} However, the time and effort involved, as well as the associated moderate discomfort, lead to decreased patient compliance, particularly in the long term.

(1) Phase 1, also known as the 'decongestive phase', often requires the patient to be admitted as an in-patient as the regimen is intensive. Treated 5 days a week, it may take 4 to 6 weeks or more to have an effect on the limb volume, depending on the severity of the disease. A lack of effect may be due to improper technique, non-compliance, or incorrect diagnosis.

- Manual lymph drainage (MLD) is not the same as massage; it is a much lighter, slow and specific action that aims to promote lymph movement in the superficial tissues away from the swelling.
- Compression bandage is applied to reduce limb size but the bandages used are not of the standard variety—they are short and non-stretch, and applied with more pressure distally than proximally. This aims to move fluid out of the limb (hence the proximal portions need to be emptied with MLD first). It is only really effective within a CPT programme; the efficacy is reduced considerably in advanced disease.
- Nail/skin care and exercises with bandaging/pressure garments as tight as tolerated to oppose the filtration pressure and provide counterforce to muscle contractions. Concerns that exercise may exacerbate or trigger lymphoedema have not been proven in studies.

(2) Phase 2, or the maintenance phase, can be out-patient-based or as self-care in selected trained patients. Patients should wear pressure garments during the day and compression bandages at night (alternatives include specifically designed garments such as Reid sleeves). Intermittent pneumatic compression machines are sometimes used but care needs to be taken to ensure that they have appropriate design, action, and pressures (usually 30-60 mm Hg though pressures of >45 mm Hg can cause lymphatics to rupture). Pneumatic compression is to be avoided in those with chronic non-pitting disease or those with active infection.

Systematic reviews support the use of CDT and MLD. Conservative therapy can give good results but the effects are temporary without the maintenance and continued compression. In Hong Kong, the climate may reduce patient compliance with pressure garments. General care is also important; patients are advised to avoid even minor degrees of trauma

such as venepuncture, insect bites, and acupuncture. The evidence for some of the following preventive practices is low but they are simple to follow.

- Air travel: maintain hydration and mobilisation, whilst some experts suggest wearing pressure garments.
- Avoid overuse of the affected limb.
- Avoid trauma; take care when cutting nails, avoid needlestick/venepuncture, and blood pressure measurement. Patients can wear medical alert bracelets to inform others of the condition.
- Avoid extremes of heat/cold and overtight clothing.

Medications such as benzopyrenes and diuretics are not useful and will not be discussed any further. Oral penicillins such as amoxicillin and dicloxacillin should be started early when there is evidence of infection in a lymphoedematous limb and continued until the signs of inflammation resolve. There is borderline support for the use of prophylactic antibiotics in those who have more than two to three episodes of infection a year. Many modalities have been promoted for the non-surgical treatment of lymphoedema but at present only low-level laser therapy has approval from the US Food and Drug Administration (FDA), although evidence of its long-term effects is lacking—it generates low-intensity light (650-1000 nm) that is believed to promote lymph vessel regeneration and increase lymph pumping. The typical response is moderate and slow, and requires repeated treatments. Near-infrared light therapy aims to increase nitric oxide in the tissues to improve tissue repair and lymph regeneration but has not received FDA approval, whilst electrical stimulation is not recommended based on current evidence.²⁷

Surgery

For reasons such as concerns of scarring or perceived lack of effect, surgery has often been regarded as a 'last resort', meaning that there is often a delay before patients are referred²⁸ by which time they may only be suited for 'salvage' procedures. Whilst initial attempts at 'physiological' reconstruction were met with disappointing late results, improved understanding of the pathophysiology accompanied by improved microsurgical techniques have seen the development of newer techniques that seem to potentially offer better outcomes.

Physiological/reconstructive techniques

Physiological techniques aim to repair the damage and increase the return of lymph to the circulation, by reconnecting the lymphatic pathways above and beyond the obstruction, either directly (lymphatic to lymphatic) or indirectly via another segment such as

veins/venules. Campisi et al^{17,29,30} have been a pioneer of these microsurgical techniques and classified them into 'derivative' techniques (essentially a lymphovenous bypass) and 'reconstructive' techniques (lymphatic-to-lymphatic connections).

Lymphovenous anastomosis or bypass

When interpreting the literature describing lymphovenous bypass, it is important to note the fundamental difference between early (lymphovenous) and newer (lymphaticovenular) techniques. The bypass concept was first described in 1963 in a rat model³¹ whilst Yamada³² and O'Brien et al³³ were the first to use it in patients. O'Brien et al³³ anastomosed lymphatics to veins measuring approximately 1 to 3 mm diameter and reported an average volume reduction of 44% in this series with 14 years' follow-up. Campisi et al³⁰ reported an average of 67% reduction in volume and 87% reduction in cellulitis in this large long-term series. Overall, 85% of patients were able to stop conservative management. However, one criticism of these retrospective studies was patient heterogeneity.

However, Damstra et al³⁴ found no improvement in patients with postmastectomy lymphoedema who were treated with lymphovenous anastomosis/bypass; a prospective study of 10 patients demonstrated only a 4.8% volume reduction at 3 months that was further reduced to 2% after 1 year, with minimal improvement in reported QOL. Boccardo et al^{35,36} performed lymphovenous bypass at the time of breast surgery with the aim of preventing lymphoedema—they anastomosed tributaries of the axillary vein to lymphatics with a patency rate of 95.6% but found no difference in limb volume compared with controls at up to 18 months' follow-up.

Lymphaticovenular anastomoses

In Koshima et al's opinion,³⁷⁻³⁹ there were inherent problems in lymphovenous anastomoses: (1) it is difficult to find larger lymphatic trunks, most are 0.8 mm or under in diameter; (2) reduced lymphatic pumping function; and (3) increased venous pressure and high rate of thrombosis due to blood at anastomotic site. According to these authors, lymphaticovenular anastomosis (LVA) offered better vessel size match compared with lymphovenous anastomoses. In 52 patients with an average of 2.1 LVAs per patient, there was a mean reduction of 41.8% in leg circumference at a mean follow-up of 14.5 months. Benefit could be demonstrated even in patients with stage III/IV disease, with recurrent lymphangitis and fibrosis. Koshima et al³⁷⁻³⁹ have also applied the technique in early disease for prophylaxis against development of fibrotic disease.

The Tokyo group uses ICG fluorescent lymphography to stage the disease severity based on the amount of dermal backflow, and thus, select patients for surgery.^{40,41} Subdermal vessels are explored through small (<3 cm) skin incisions, aiming to use lymphatic vessels of approximately 0.2 mm in diameter with venules sized 0.5 mm or less on the basis that smaller veins will have lower pressures. Some call this 'supermicrosurgery' although the use of the term is rather arbitrary. The procedure can be performed under local anaesthesia with short hospital stay, which, in the author's opinion, is one of the biggest advantages of this technique.

The studies from Koshima et al's unit³⁷⁻³⁹ have demonstrated an average volume reduction of 82.5% in those not responding to CPT. Chang's series⁴² demonstrated a 35% reduction of lymphoedema in breast cancer patients 1 year after LVA. Cormier et al⁴³ reviewed eight studies and calculated a mean volume reduction of 54.0%. It is generally accepted that microsurgery will offer better results in early disease when patients have some healthy lymphatics before progressing to the fibrotic stage when damage is irreversible.

Lymph node transfer

Wongtrungkapun⁴⁴ performed lymph node transfer in patients with filariasis; one to two groin nodes were partially decapsulated and anastomosed to the saphenous vein. Becker et al^{45,46} described the transfer of lymph nodes from the groin to the axilla in 24 patients with postmastectomy lymphoedema; 62.5% of the patients were said to be 'cured' and able to discontinue physiotherapy. Overall, in Becker et al's experience,^{45,46} 98% of the patients had some improvement; only 2% had repeat infections. Whilst 40% of patients with stage 1 or 2 lymphoedema had complete normalisation and did not require additional conservative therapy, those with stage 3 lymphoedema needed conservative therapy. Lin et al⁴⁷ anastomosed superficial circumflex iliac nodes at the wrist to treat upper limb lymphoedema and reported a 55% reduction in volume at 56 months, with fewer episodes of cellulitis.

Proponents of node surgery say that LVA or lymphatic-lymphatic anastomosis eventually become occluded (possibly due to the effect of interstitial pressure on low-pressure thin vessels) whilst lymph nodes are supposedly less susceptible. The lymphatic vessels are not actually anastomosed; it seems that the transplanted nodes develop new drainage pathways—proposed theories for this drainage include nodes acting as suction pumps whilst others suggest they are a source of VEGF-C that promotes lymphangiogenesis.

Some experts have developed a procedure to transfer lymph nodes as part of a breast recon-

struction procedure⁴⁸; there may be several other benefits of such a procedure including release of scar tissue in the axilla and the provision of vascularised tissue as a lymphatic bridge.⁴⁹ Isotope scans at 3 and 6 months demonstrated improved function in all but one patient.⁴⁸ With this type of surgery, it is important to only harvest nodes of lower abdomen and not the leg; axillary reverse mapping may help to spare limb lymphatics.⁵⁰

Overall, good long-term functional data are lacking and some authors have had difficulty reproducing published results,²⁵ possibly, due to the significant learning curve. Some have found 38% risk of complications, although mostly transient (eg lymphocele and hydrocele); however, some complications such as iatrogenic lymphoedema and chronic pain may be more persistent.⁵¹ They also found no volume difference after a median follow-up of 40 months with interval CDT and pressure garments. Viitanen et al⁵² found reduced lymphatic flow in the donor site/limb with lymphoscintigraphy without overt clinical lymphoedema in a small group of 10 patients.

Preliminary results suggest that node transfer is more successful if performed sooner after nodal dissection surgery.^{45,53} Saaristo et al⁴⁸ regard it as largely experimental but can be justified if performed at the time of breast reconstruction. Some surgeons have looked at animal models, combining node transfer with additional VEGF-C and -D,^{54,55} and this may offer a new type of treatment; however, the effect on lymphatic metastasis is unknown and deserves attention.

Lymphatic grafting/transplantation

Other less commonly used procedures include lymphatic grafting. Baumeister et al⁵⁶⁻⁵⁹ have significant experience in using this technique to treat secondary lymphoedema with an average volume reduction of 65%.^{60,61} In the lower limb, a long segment of lymphatic vessel is dissected out from the upper inner thigh and tunnelled over to affected contralateral leg for a lymphatic-lymphatic anastomosis. The efficacy in the upper limb where the lymphatic tissue is used as a free graft has also been demonstrated with significant improvement in over 90% of patients, with a mean volume reduction of 22% to 31% whilst scintigraphy shows continued graft function.⁶²⁻⁶⁴ The dissection of lymphatics is technically challenging; Campisi⁶⁵ used veins instead of lymphatic vessels to bridge lymphatics.

Some experts have used flaps for lymphatic bridging; for instance, the inclusion of random lymphatics in tissues such as the omentum⁶⁶ or an axial flap such as the deltopectoral.⁶⁷ The use of omentum has largely been abandoned as there is no evidence that it actually promotes lymph drainage,

and the surgery is associated with high rates of morbidity. Similarly, enteromesenteric bridge operations and tube/thread implants should be avoided, based on current evidence.

Debulking or excision

Early attempts at treating lymphoedema involved techniques that were mainly based on debulking, that is, removing the oedematous tissue to restore form. The underlying lymphatic dysfunction is not addressed and may actually lead to further deterioration of the condition.

Charles procedure

The Charles procedure used in 1912 has been wrongly attributed to Sir Richard Charles for the treatment of leg lymphoedema by McIndoe.⁶⁸ The surgeon had primarily treated scrotal swelling⁶⁹ and had only described one unsuccessful case involving the lower limb. In simple terms, the lymphoedematous tissue is excised down to the fascial level and the defect is covered with skin grafts. The grafts can be taken from the excised tissue if it is not grossly abnormal⁷⁰; otherwise, it has to be harvested from another site. Complications include graft breakdown/ulceration, scarring, and recurrence. The aesthetic results are rather poor and, thus, usually reserved for cases with severe skin changes.

Homans-Miller procedure

The Homans-Miller procedure, first used in 1936, is based on a multistage procedure initially described by Sistrunk⁷¹—skin flaps are elevated along one border of the limb, and after the deeper swollen tissue has been excised along with the fascia, the skin flaps are replaced.^{72,73} It is a traditional practice to avoid surgery at or below ankle, taking care to avoid damage to the common peroneal and sural nerves. A study with 14 years' follow-up showed that this type of surgery was capable of long-lasting reduction in size in 80% of the treated patients, and associated with improved function and reduced cellulitis.⁷³ It is the most common excisional surgery for lymphoedema. Others have refined this further by preserving the perforator vessels during flap elevation, allowing the flaps to be thinner (5 mm) and, potentially, for both sides to be treated in one stage.⁷⁴

The Thompson technique used in 1962 involves similar tissue resection whilst also harvesting a dermal flap⁷⁵ that is buried into the muscle next to the neurovascular bundle, with the aim of creating a bridge for lymphatic return. However, long-term results were similar to excision alone and did not support the theoretical aim of a physiological effect and, thus, has largely been abandoned.

The proven benefits of excisional surgery are often ignored, in part due to misconceptions of morbidity and complications; these were mostly related to early aggressive use of the technique leading to almost total abandonment of procedures in the mid-20th century. Recently Karri et al⁷⁶ demonstrated that good results are possible with modern application of the Charles procedure that may also be combined with negative-pressure wound therapy.⁷⁷ Similarly, surgeons have modified the Homans-Miller procedure²⁵ and combined this with postoperative pressure garments to achieve good results.

Liposuction

Liposuction is a relatively recently described debulking technique based on the observation that there is adipose hypertrophy in lymphoedema. The fat accumulation may be related to altered lipid transport^{78,79} and corresponds to a non-pitting type of swelling that is not responsive to compression.

O'Brien et al⁸⁰ were one of the first surgeons to use liposuction to treat lymphoedema, and reported a volume reduction of 23%. Brorson et al⁸¹ used liposuction to treat patients with post-breast cancer lymphoedema that had been resistant to conservative therapy with reasonable effects that were confirmed with volume measurements, computed tomographic scans, and plethysmography. Liposuction for lymphoedema is similar but not the same as cosmetic liposuction. The technique has evolved in several ways, particularly, with the adoption of a tumescent technique with injection of adrenaline combined with use of a tourniquet that causes less bleeding—13% versus 25% without tourniquet.⁸² More recently, Schaverien et al⁸³ used the Brorson technique (1997) and demonstrated a 101% reduction compared to normal limb at 1 year, and that was maintained at 5 years.

The technique seems to be straightforward and safe, and produces consistent results⁸⁴⁻⁸⁶ with treated patients reporting improved QOL and suffering from decreased episodes of cellulitis. Preliminary results with laser Doppler scanning seem to support the theory that liposuction can reduce the lymphatic load⁸⁷ without damaging lymph function.⁸⁸ The National Institute for Health and Care Excellence⁸⁹ suggests that liposuction may be considered in those patients with severe disease (massive incapacitating disease, unresponsive to conservative therapy). The morbidity may be less than traditional debulking surgeries and, thus, it can be regarded as the first choice of a debulking operation, if the skin is normal. Its main disadvantage is that patients are required to wear lifelong compression garments⁹⁰; otherwise, the treated limb enlarges again; this may make the modality less suited in regions such as Hong Kong.

Lymphoedema surgery in Hong Kong

Since 1993, breast cancer has become the most common cancer in women in Hong Kong with an incidence of 79.4/100 000 in 2009.⁹¹ A local study presented at the 2010 Hospital Authority Convention found that 11.3% of patients had lymphoedema at 3 months after breast cancer surgery with axillary dissection.⁹² Mak et al⁹³ found that previous infection-inflammation (odds ratio [OR]=4.49), surgery on the side of the dominant hand (OR=2.97), increased body mass index, and older age at the time of axillary dissection were significant risk factors for the development of moderate-to-severe lymphoedema in our local population.

Despite the significant number of patients liable to suffer from breast cancer-related lymphoedema (BCRL), the general awareness of lymphoedema in Hong Kong is low among both health care professionals and patients. It is a common misconception that nothing can be done for the condition; thus, patients tend to be diagnosed late with symptomatic moderate-to-severe disease, and salvage-type surgical procedures are often the only therapeutic option.

Medical costs for women with BCRL are substantially higher than for those without,⁹⁴ with the difference mostly accounted for by the costs of treating infections. A local study⁹⁵ found that instituting effective and standardised primary intervention for BCRL in the form of CDT/MLD would be beneficial to both patients and the health care institute, with savings of as much as HK\$444 200 per year in a local hospital.

Improvements in care for lymphoedema patients in Hong Kong require establishment of integrated treatment protocols which may include the following:

- (1) Education for caregivers and patients is important. Public/teaching hospitals should take the lead; in addition, support groups such as the Hong Kong Breast Cancer Foundation have a particularly important role. Medical staff with an interest in treating lymphoedema should keep themselves updated.
- (2) Establishment of multidisciplinary care units focusing around nurse-led clinics with formalised protocols following proven MLD/CDT programmes such as Foldi or Vodder that should be offered as a first option for lymphoedema patients. These clinics should be supported by medical staff who would offer medical advice, discuss surgical options, as well as treat complications when they occur.
- (3) Although CDT/MLD remains the mainstay of treatment for patients with lymphoedema, surgery may be considered in those patients who

do not respond to conservative therapy. Newer microsurgical techniques (LVA and lymph node transfer) may be useful in early-stage disease though they have a significant learning curve and, therefore, should be undertaken only by experienced microsurgeons.

- (a) The author prefers offering LVA under local anaesthesia as a first option in stage I/II lymphoedema, with lymph node transfer for stage II/III disease.
- (b) Debulking surgery (Homans-Miller procedure with perforator preservation or Charles procedure with negative pressure dressings) may be considered in those with severe disabling swelling; the role of liposuction is likely to be minor in Hong Kong but can be offered to those willing to wear pressure garments continuously.

A number of local surgeons have travelled to regional centres of excellence for training and our



FIG 1. A patient undergoing lymphaticovenular anastomosis procedure under local anaesthesia



FIG 2. A completed lymphaticovenular anastomosis

unit has organised courses in supermicrosurgery and lymph node transfer to encourage the uptake of these techniques among other surgeons. Lymphatic venous anastomosis has been performed in Hong Kong since 2012 (Figs 1 and 2) and the preliminary results are encouraging, with patients often describing early relief, particularly from symptoms of 'tightness'. Given the short period of experience and small number of patients, it is too early to comment on local results; however, there is no reason to suggest that the results would not be comparable with international findings in the long term.

References

- de Jong MA, Oldenburg S, Bing Oei S, et al. Reirradiation and hyperthermia for radiation-associated sarcoma. *Cancer* 2012;118:180-7.
- Karkkainen MJ, Ferrell RE, Lawrence EC, et al. Missense mutations interfere with *VEGFR-3* signalling in primary lymphoedema. *Nat Genet* 2000;25:153-9.
- Irrthum A, Karkkainen MJ, Devriendt K, Alitalo K, Vikkula M. Congenital hereditary lymphoedema caused by a mutation that inactivates *VEGFR3* tyrosine kinase. *Am J Hum Genet* 2000;67:295-301.
- Cederberg A, Grønning LM, Ahrén B, Taskén K, Carlsson P, Enerbäck S. *FOXC2* is a winged helix gene that counteracts obesity, hypertriglyceridemia, and diet-induced insulin resistance. *Cell* 2001;106:563-73.
- Yildirim-Toruner C, Subramanian K, El Manjra L, Chen E, Goldstein S, Vitale E. A novel frameshift mutation of *FOXC2* gene in a family with hereditary lymphoedema-distichiasis syndrome associated with renal disease and diabetes mellitus. *Am J Med Genet A* 2004;131:281-6.
- Warren AG, Borson H, Borud LJ, Slavin SA. Lymphedema: a comprehensive review. *Ann Plast Surg* 2007;59:464-72.
- Petrek JA, Senie RT, Peters M, Rosen PP. Lymphedema in a cohort of breast carcinoma survivors 20 years after diagnosis. *Cancer* 2001;92:1368-77.
- Langer I, Guller U, Berclaz G, et al. Morbidity of sentinel lymph node biopsy (SLN) alone versus SLN and completion axillary lymph node dissection after breast cancer surgery: a prospective Swiss multicenter study on 659 patients. *Ann Surg* 2007;245:452-61.
- Lucci A, McCall LM, Beitsch PD, et al. Surgical complications associated with sentinel lymph node dissection (SLND) plus axillary lymph node dissection compared with SLND alone in the American College of Surgeons Oncology Group Trial Z0011. *J Clin Oncol* 2007;25:3657-63.
- Veronesi U, Paganelli G, Viale G, et al. A randomized comparison of sentinel-node biopsy with routine axillary dissection in breast cancer. *N Engl J Med* 2003;349:546-53.
- Wilke LG, McCall LM, Posther KE, et al. Surgical complications associated with sentinel lymph node biopsy: results from a prospective international cooperative group trial. *Ann Surg Oncol* 2006;13:491-500.
- Tammela T, Alitalo K. Lymphangiogenesis: molecular mechanisms and future promise. *Cell* 2010;140:460-76.
- Newman B, Lose F, Kedda MA, et al. Possible genetic predisposition to lymphedema after breast cancer. *Lymphat Res Biol* 2012;10:2-13.
- Aldrich MB, Guillod R, Fife CE, et al. Lymphatic abnormalities in the normal contralateral arms of subjects with breast cancer-related lymphedema as assessed by near-infrared fluorescent imaging. *Biomed Opt Express* 2012;3:1256-65.
- International Society of Lymphology. The diagnosis and treatment of peripheral lymphedema. 2009 Consensus Document of the International Society of Lymphology. *Lymphology* 2009;42:51-60.
- Lee BB, Laredo J, Neville RF. Combined clinical and laboratory (lymphoscintigraphic) staging. In: Lee B, Bergan J, Rockson SG, editors. *Lymphedema: a concise compendium of theory and practice*. London: Springer; 2011: 97-104.
- Campisi C, Bellini C, Campisi C, Accogli S, Bonioli E, Boccardo F. Microsurgery for lymphoedema: clinical research and long-term results. *Microsurgery* 2010;30:256-60.
- Yamamoto T, Narushima M, Doi K, et al. Characteristic indocyanine green lymphography findings in lower extremity lymphedema: the generation of a novel lymphedema severity staging system using dermal backflow patterns. *Plast Reconstr Surg* 2011;127:1979-86.
- Yamamoto T, Matsuda N, Doi K, et al. The earliest finding of indocyanine green lymphography in asymptomatic limbs of lower extremity lymphedema patients secondary to cancer treatment: the modified dermal backflow stage and concept of subclinical lymphedema. *Plast Reconstr Surg* 2011;128:314e-321e.
- Stanton A, Modi S, Mellor R, Levick R, Mortimer P. Diagnosing breast cancer-related lymphoedema in the arm. *J Lymphoedema* 2006;1:12-5.
- Sander AP, Hajer NM, Hemenway K, Miller AC. Upper-extremity volume measurements in women with lymphedema: a comparison of measurements obtained via water displacement with geometrically determined volume. *Phys Ther* 2002;82:1201-12.
- Taylor R, Jayasinghe UW, Koelmeyer L, Ung O, Boyages J. Reliability and validity of arm volume measurements for assessment of lymphedema. *Phys Ther* 2006;86:205-14.
- Stanton AW, Northfield JW, Holroyd B, Mortimer PS, Levick JR. Validation of an optoelectronic limb volumeter (Perometer). *Lymphology* 1997;30:77-97.
- Garfein ES, Borud LJ, Warren AG, Slavin SA. Learning from a lymphedema clinic: an algorithm for the management of localized swelling. *Plast Reconstr Surg* 2008;121:521-8.
- Lee BB, Kim YW, Kim DI, Hwang JH, Laredo J, Neville R. Supplemental surgical treatment to end stage (stage IV-V) of chronic lymphedema. *Int Angiol* 2008;27:389-95.
- Ko DS, Lerner R, Klose G, Cosimi AB. Effective treatment of lymphedema of the extremities. *Arch Surg* 1998;133:452-8.
- Moseley AL, Carati CJ, Piller NB. A systematic review of common conservative therapies for arm lymphoedema secondary to breast cancer treatment. *Ann Oncol* 2007;18:639-46.
- Lee BB. Contemporary issues in management of chronic lymphedema: personal reflection on an experience with 1065 patients. *Lymphology* 2005;38:28-31.
- Campisi C, Davini D, Bellini C, et al. Lymphatic microsurgery for the treatment of lymphoedema. *Microsurgery* 2006;26:65-9.
- Campisi C, Boccardo F, Zilli A, Macciò A, Napoli F. Long-

- term results after lymphatic-venous anastomoses for the treatment of obstructive lymphoedema. *Microsurgery* 2001;21:135-9.
31. Laine JB, Howard JM. Experimental lymphatico-venous anastomosis. *Surg Forum* 1963;14:111-2.
 32. Yamada Y. The studies on lymphatic venous anastomosis in lymphoedema. *Nagoya J Med Sci* 1969;32:1-21.
 33. O'Brien BM, Sykes P, Threlfall GN, Browning FS. Microlymphaticovenous anastomoses for obstructive lymphoedema. *Plast Reconstr Surg* 1977;60:197-211.
 34. Damstra RJ, Voesten HG, van Schelven WD, van der Lei B. Lymphatic venous anastomosis (LVA) for treatment of secondary arm lymphedema. A prospective study of 11 LVA procedures in 10 patients with breast cancer related lymphedema and a critical review of the literature. *Breast Cancer Res Treat* 2009;113:199-206.
 35. Boccardo F, Casabona F, De Cian F, et al. Lymphedema microsurgical preventive healing approach: a new technique for primary prevention of arm lymphedema after mastectomy. *Ann Surg Oncol* 2009;16:703-8.
 36. Boccardo FM, Casabona F, Friedman D, et al. Surgical prevention of arm lymphedema after breast cancer treatment. *Ann Surg Oncol* 2011;18:2500-5.
 37. Koshima I, Nanba Y, Tsutsui T, Takahashi Y, Itoh S. Long-term follow-up after lymphaticovenular anastomosis for lymphoedema in the leg. *J Reconstr Microsurg* 2003;19:209-15.
 38. Koshima I, Nanba Y, Tsutsui T, Tahahashi Y, Itoh S, Fujitsu M. Minimal invasive lymphaticovenular anastomosis under local anesthesia for leg lymphedema: is it effective for stage III and IV? *Ann Plast Surg* 2004;53:261-6.
 39. Koshima I, Kawada S, Moriguchi T, Kajiwaraya Y. Ultrastructural observations of lymphatic vessels in lymphedema in human extremities. *Plast Reconstr Surg* 1996;97:397-405; discussion 406-7.
 40. Mihara M, Uchida G, Hara H, et al. Lymphaticovenous anastomosis for facial lymphoedema after multiple courses of therapy for head-and-neck cancer. *J Plast Reconstr Aesthet Surg* 2011;64:1221-5.
 41. Furukawa H, Osawa M, Saito A, et al. Microsurgical lymphaticovenous implantation targeting dermal lymphatic backflow using indocyanine green fluorescence lymphography in the treatment of postmastectomy lymphedema. *Plast Reconstr Surg* 2011;127:1804-11.
 42. Chang DW. Lymphaticovenular bypass for lymphedema management in breast cancer patients: a prospective study. *Plast Reconstr Surg* 2010;126:752-8.
 43. Cormier JN, Rourke L, Crosby M, Chang D, Armer J. The surgical treatment of lymphedema: a systematic review of the contemporary literature (2004-2010). *Ann Surg Oncol* 2012;19:642-51.
 44. Wongtrungkapun R. Microsurgical lymphonodovenous implantation for chronic lymphedema. *J Med Assoc Thai* 2004;87:877-82.
 45. Becker C, Assouad J, Riquet M, Hidden G. Postmastectomy lymphedema: long-term results following microsurgical lymph node transplantation. *Ann Sur* 2006;243:313-5.
 46. Becker C, Vasile JV, Levine JL, et al. Microlymphatic surgery for the treatment of iatrogenic lymphedema. *Clin Plast Surg* 2012;39:385-98.
 47. Lin CH, Ali R, Chen SC, et al. Vascularized groin lymph node transfer using the wrist as a recipient site for management of postmastectomy upper extremity lymphedema. *Plast Reconstr Surg* 2009;123:1265-75.
 48. Saaristo AM, Niemi TS, Viitanen TP, Tervala TV, Hartiala P, Suominen EA. Microvascular breast reconstruction and lymph node transfer for postmastectomy lymphedema patients. *Ann Surg* 2012;255:468-73.
 49. Card A, Crosby MA, Liu J, Lindstrom WA, Lucci A, Chang DW. Reduced incidence of breast cancer-related lymphedema following mastectomy and breast reconstruction versus mastectomy alone. *Plast Reconstr Surg* 2012;130:1169-78.
 50. Klimberg VS. A new concept toward the prevention of lymphedema: axillary reverse mapping. *J Surg Oncol* 2008;97:563-4.
 51. Vignes S, Blanchard M, Yannoutsos A, Arrault M. Complications of autologous lymph-node transplantation for limb lymphoedema. *Eur J Vasc Endovasc Surg* 2013;45:516-20.
 52. Viitanen TP, Mäki MT, Seppänen MP, Suominen EA, Saaristo AM. Donor-site lymphatic function after microvascular lymph node transfer. *Plast Reconstr Surg* 2012;130:1246-53.
 53. Slavin SA, Van den Abbeele AD, Losken A, Swartz MA, Jain RK. Return of lymphatic function after flap transfer for acute lymphedema. *Ann Surg* 1999;229:421-7.
 54. Tammela T, Saaristo A, Holopainen T, et al. Therapeutic differentiation and maturation of lymphatic vessels after lymph node dissection and transplantation. *Nat Med* 2007;13:1458-66.
 55. Lähteenvuo M, Honkonen K, Tervala T, et al. Growth factor therapy and autologous lymph node transfer in lymphedema. *Circulation* 2011;123:613-20.
 56. Baumeister RG, Seifert J, Hahn D. Autotransplantation of lymphatic vessels. *Lancet* 1981;1:147.
 57. Baumeister RG, Seifert J, Wiebecke B, Hahn D. Experimental basis and first application of clinical lymph vessel transplantation of secondary lymphedema. *World J Surg* 1981;5:401-7.
 58. Baumeister RG. Microsurgery of the lymphatic system [in German]. *Chirurg* 1983;54:374-8.
 59. Baumeister RG, Siuda S. Treatment of lymphedemas by microsurgical lymphatic grafting: what is proved? *Plast Reconstr Surg* 1990;85:64-74; discussion 75-6.
 60. Baumeister RG, Siuda H, Bohmert H, Moser E. A microsurgical method for reconstruction of interrupted lymphatic pathways: autologous lymph-vessel transplantation for treatment of lymphedemas. *Scand J Plast Reconstr Surg* 1986;20:141-6.
 61. Kleinhans E, Baumeister RG, Hahn D, Siuda S, Büll U, Moser E. Evaluation of transport kinetics in lymphoscintigraphy: follow-up study in patients with transplanted lymphatic vessels. *Eur J Nucl Med* 1985;10:349-52.
 62. Weiss M, Baumeister RG, Hahn K. Post-therapeutic lymphedema: scintigraphy before and after autologous lymph vessel transplantation: 8 years of long-term follow-up. *Clin Nucl Med* 2002;27:788-92.
 63. Weiss M, Baumeister RG, Hahn K. Dynamic lymph flow imaging in patients with oedema of the lower limb for evaluation of the functional outcome after autologous lymph vessel transplantation: an 8-year follow-up study. *Eur J Nucl Med Mol Imaging* 2003;30:202-6.
 64. Baumeister RG, Frick A. The microsurgical lymph vessel transplantation [in German]. *Handchir Mikrochir Plast Chir* 2003;35:202-9.

65. Campisi C. Use of autologous interposition vein graft in management of lymphedema: preliminary experimental and clinical observations. *Lymphology* 1991;24:71-6.
66. Goldsmith HS, De los Santos R. Omental transposition in primary lymphoedema. *Surg Gynecol Obstet* 1967;125:607-10.
67. Withey S, Pracy P, Wood S, Rhys-Evans P. The use of a lymphatic bridge in the management of head and neck lymphoedema. *Br J Plast Surg* 2001;54:716-9.
68. Dumanian GA, Futrell JW. The Charles procedure: misquoted and misunderstood since 1950. *Plast Reconstr Surg* 1996;98:1258-63.
69. Charles R. Elephantiasis scroti. In: Latham A, English TC, editors. *A system of treatment*. London: Churchill; 1912.
70. Gibson T, Tough JS. A simplified one-stage operation for the correction of lymphedema of the leg. *AMA Arch Surg* 1955;71:809-17.
71. Sistrunk WE. Further experience with the Kondoleon operation for elephantiasis. *JAMA* 1918;71:800-6.
72. Homans J. The treatment of elephantiasis of the legs. A preliminary report. *N Engl J Med* 1936;215:1099-104.
73. Miller TA, Wyatt LE, Rudkin GH. Staged skin and subcutaneous excision for lymphedema: a favorable report of long-term results. *Plast Reconstr Surg* 1998;102:1486-98; discussion 1499-501.
74. Salgado CJ, Mardini S, Spanio S, Tang WR, Sassu P, Chen HC. Radical reduction of lymphedema with preservation of perforators. *Ann Plast Surg* 2007;59:173-9.
75. Thompson N. Surgical treatment of chronic lymphoedema of the lower limb. With preliminary report of new operation. *Br Med J* 1962;2:1566-73.
76. Karri V, Yang MC, Lee JJ, et al. Optimizing outcome of Charles procedure for chronic lower extremity lymphoedema. *Ann Plast Surg* 2011;66:393-402.
77. van der Walt JC, Perks TJ, Zeeman BJ, Bruce-Chwatt AJ, Graewe FR. Modified Charles procedure using negative pressure dressings for primary lymphedema: a functional assessment. *Ann Plast Surg* 2009;62:669-75.
78. Brorson H. Surgical treatment of postmastectomy lymphedema—liposuction. In: Lee BB, Bergan J, Rockson SG, editors. *Lymphedema: a concise compendium of theory and practice*. London: Springer; 2011: 409-18.
79. Dixon JB. Lymphatic lipid transport: sewer or subway? *Trends Endocrinol Metab* 2010;21:480-7.
80. O'Brien BM, Khazanchi RK, Kumar PA, Dvir E, Pederson WC. Liposuction in the treatment of lymphoedema; a preliminary report. *Br J Plast Surg* 1989;42:530-3.
81. Brorson H, Ohlin K, Svensso B. The facts about liposuction as a treatment for lymphoedema. *J Lymphoedema* 2008;3:38-47.
82. Wojnikow S, Malm J, Brorson H. Use of tourniquet with and without adrenaline reduces blood loss during liposuction for lymphoedema of the arm. *Scand J Plast Reconstr Surg Hand Surg* 2007;41:243-9.
83. Schaverien MV, Munro KJ, Baker PA, Munnoch DA. Liposuction for chronic lymphoedema of the upper limb: 5 years of experience. *J Plast Reconstr Aesthet Surg* 2012;65:935-42.
84. Brorson H. Liposuction in arm lymphoedema treatment. *Scand J Surg* 2003;92:287-95.
85. Brorson H, Svensson H. Complete reduction of lymphoedema of the arm by liposuction after breast cancer. *Scand J Plast Reconstr Surg Hand Surg* 1997;31:137-43.
86. Brorson H, Svensson H. Liposuction combined with controlled compression therapy reduces arm lymphoedema more effectively than controlled compression therapy alone. *Plast Reconstr Surg* 1998;102:1058-67; discussion 1068.
87. Brorson H. Liposuction gives complete reduction of chronic large arm lymphedema after breast cancer. *Acta Oncol* 2000;39:407-20.
88. Brorson H, Svensson H, Norrgren K, Thorsson O. Liposuction reduces arm lymphoedema without significantly altering the already impaired lymph transport. *Lymphology* 1998;31:156-72.
89. National Institute for Health and Clinical Excellence. *Liposuction for chronic lymphoedema*, February 2008. Available from: <http://www.nice.org.uk/guidance/ipg251/resources/guidance-liposuction-for-chronic-lymphoedema-pdf>. Accessed Jan 2014.
90. Brorson H, Ohlin K, Olsson G, Långström G, Wiklund I, Svensson H. Quality of life following liposuction and conservative treatment of arm lymphoedema. *Lymphology* 2006;39:8-25.
91. Hong Kong Cancer Registry. Available from: <http://www3.ha.org.hk/cancereg/statistics.html>. Accessed Jan 2014.
92. Leung SY. A prospective cohort study on physiotherapy service to identify service gaps for post-operative breast cancer patients. *Proceedings of the Hospital Authority Convention 2010*; 2010 May 10-11; Hong Kong.
93. Mak SS, Yeo W, Lee YM, et al. Predictors of lymphedema in patients with breast cancer undergoing axillary lymph node dissection in Hong Kong. *Nurs Res* 2008;57:416-25.
94. Shih YC, Xu Y, Cormier JN, et al. Incidence, treatment costs, and complications of lymphedema after breast cancer among women of working age: a 2-year follow-up study. *J Clin Oncol* 2009;27:2007-14.
95. Tang KS. *A clinical guideline for management of lymphoedema using nurse-led manual lymphatic drainage therapy*. Hong Kong: The University of Hong Kong; 2013.