

THE DIAGNOSIS AND TREATMENT OF PERIPHERAL LYMPHEDEMA

Consensus Document of the International Society of Lymphology Executive Committee

The following document attempts to amalgamate the broad array of protocols advocated for the diagnosis and treatment of peripheral lymphedema into a coordinated proclamation representing a "Consensus" of the international community. The document is not meant to override individual clinical considerations for problematic patients nor is it meant to be a legal formulation that if varied from signifies medical malpractice. Rather it represents the best judgment of the International Society of Lymphology (ISL) Executive Committee members on how to approach patients with peripheral lymphedema as of 1995. We anticipate that the document will be challenged, debated in the pages of Lymphology (e.g., as Letters to the Editor), and ideally become a focal point for robust discussion at local, national and international lymphologic conferences. We further anticipate as experience evolves and new ideas emerge that this "living document" will undergo periodic revision and refinement. (The Editors and Secretary-General of the ISL)

GENERAL CONSIDERATIONS

Articles about lymphedema are often introduced with the misleading statement that the pathophysiology of the disease is unclear and treatment is unsatisfactory. Yet, the general principles of the pathophysiology

of lymphedema are known, although the exact pathogenesis is still open to investigation. In its purest form, the principal disturbance is a *low output failure* of the lymph circulatory system, that is, overall lymphatic transport is reduced. This derangement arises either from congenital lymphatic dysplasia (primary lymphedema) or anatomical obliteration, such as after radical operative dissection (e.g., axillary or retroperitoneal nodal sampling), from repeated lymphangitis with lymphangiosclerosis or as a consequence of functional deficiency (e.g., lymphangiospasm, paralysis, and valvular insufficiency) (secondary lymphedema). The common denominator, nonetheless, is that lymphatic transport has fallen below that needed to handle the load of microvascular filtrate including plasma protein and cells that normally leaks from the bloodstream into the interstitium. *High output failure* of the lymph circulation, on the other hand, occurs when a normal or increased transport capacity of intact lymphatics is overwhelmed by an excessive burden of capillary filtrate. Examples include hepatic cirrhosis (ascites), nephrotic syndrome (anasarca), and deep venous insufficiency of the leg (peripheral edema). Although the final pathway may be tissue edema whenever lymph formation exceeds lymph absorption, the latter entities should properly be distinguished from lymphedema, which is characterized by decreased lymphatic transport. In some syndromes

where high output lymphatic circulatory failure is longstanding, a gradual functional deterioration of the draining lymphatics may supervene and thereby reduce overall transport capacity. Reduced lymphatic circulatory capacity may then develop in the face of increased capillary filtration. Examples include recurring infection, burns, and repeated allergic reactions. These latter conditions—safety valve insufficiency—be considered a mixed form of lymphedema and are particularly troublesome to treat.

In the treatment of "classical" lymphedema of the limbs (that is, peripheral lymphedema), highly satisfactory therapeutic results can usually be achieved. On the other hand, treatment of lymphedema of the genitalia and of the head and neck is much less successful. Because lymphedema is a chronic generally incurable ailment, it requires, as do other chronic diseases, lifelong care and attention along with psychosocial support as appropriate. The continued need for therapy does not mean a priori that treatment is unsatisfactory, although it may be less than ideal. For example, patients with diabetes mellitus continue to need drugs (insulin) or special diet (low calorie, low sugar) in order to maintain metabolic homeostasis. Similarly, patients with chronic venous insufficiency require a lifelong need for external compression therapy to minimize edema, lipodermatosclerosis and skin ulceration. The compliance and commitment of the patient is also essential to successful therapy. For example, in the patient with diabetes, poor compliance can result in acute loss of weight, polyuria, and even coma and, in the long-term, blindness, renal failure, and stroke. With chronic venous insufficiency, poor patient cooperation may be associated with progressive skin ulceration, hyperpigmentation, and other trophic changes in the lower leg. Similarly, failure to control lymphedema may lead to progressive elephantine changes, sometimes crippling invalidism and on rare occasions, the development of a highly lethal angiosarcoma

(Stewart-Treves syndrome).

DIAGNOSIS

An accurate diagnosis of lymphedema is essential for proper therapy. In most patients, the diagnosis can be readily distinguished from the history and physical examination alone. In considering the etiology of lymphedema especially in adults, a latent tumor obstructing or invading proximal lymphatics must be considered. Accordingly, a thorough medical evaluation is indispensable. Moreover, coexistent diseases such as congestive heart failure, hypertension, and cerebrovascular disease including stroke may influence the therapeutic approach undertaken.

If the diagnosis is unclear or in need of further documentation, consultation with a clinical lymphologist or referral to a lymphologic center should be undertaken if either is available. The simple diagnostic tool of isotope lymphography (lymphoscintigraphy or lymphangioscintigraphy) should become universally adopted and has proved exceedingly useful as a screening test. In most centers where specialists in nuclear medicine are available, lymphoscintigraphy, has largely replaced conventional oil contrast lymphography for visualization of peripheral lymphatics. Although lymphoscintigraphy is not universally standardized (different tracers, different injected volumes and radioactivity, intracutaneous versus subcutaneous injection, epi- or subfascial injection, one or more injections, carried out at rest or under different protocols of physical activity, varied imaging times), the results, which are easily repeated for verification, offer remarkable insight into the underlying anatomic and functional lymphatic derangement.

Lymphoscintigraphy provides both images of lymphatics and lymph nodes as well as quantitative data on tracer (lymph) transport. Since its introduction, dermal injections of blue-dye are rarely indicated. Dye studies are occasionally complicated by

allergic reactions or serious anaphylaxis. Misleading interpretations of lymphatic function are also common with intradermal dye injections. Direct oil contrast lymphography, which entails some morbidity, should now be reserved for complicated lymphedemas such as those associated with chylous reflux syndromes. Non-invasive duplex-Doppler studies and on occasion phlebography may be appropriate in selected patients to examine the deep venous system and supplement the clinical impression of peripheral lymphedema. Other diagnostic and investigative tools of lymphologists and lymphological centers include magnetic resonance imaging, computed tomography, ultrasonography, indirect (water soluble) lymphography and fluorescent microlymphangiography.

Regarding lymph node biopsy, great care should be exercised before removing regional lymph nodes in the setting of longstanding lymphedema as the histologic information is seldom helpful and the operation may aggravate lymphatic dysfunction. Fine needle aspiration biopsy with cytological examination by a skilled pathologist may be a useful alternative when malignancy is suspected.

TREATMENT

Therapy of peripheral lymphedema is divided into conservative (non-operative) and operative methods.

Non-operative Treatment

1. Physical therapy

a. Combination of physical therapies (CPT). This approach has a long experience and generally involves a two-stage treatment program. The first phase consists of skin care, manual lymphedema treatment (MLT), remedial exercises and compression applied with multi-layered bandage wrapping. Phase 2 (initiated immediately after Phase 1) aims to conserve and optimize the results obtained

in Phase 1. It consists of compression by low-stretch elastic stockings or sleeves, skin care, remedial exercises, and repeated MLT as necessary. The basic principle of MLT is that the therapist initiates manual manipulation in the area free of edema bordering proximal to the lymphostatic region, which is treated subsequently in a centrifugal fashion (i.e., most proximal first and distal thereafter).

Indispensable prerequisites of successful combined physiotherapy are the availability of clinical lymphologists, physicians, nurses, and physiotherapists trained specially in this method, acceptance of health insurers to underwrite the cost of treatment, and a biomaterials industry willing to provide high quality products. Compressive bandages can be harmful and/or useless if applied incorrectly. Accordingly, such bandaging should be carried out only by professionally trained personnel.

CPT may also be used for palliation as, for example, to control lymphedema caused by tumor blockage of lymphatics. The treatment is performed in conjunction with chemo- or radiotherapy directed specifically at the tumor. Rare reports suggest that MLT may promote metastatic disease, although theoretically, only diffuse carcinomatous infiltrates which have already spread to lymph collectors as tumor thrombi could be mobilized by mechanical compression. In these instances, the long-term prognosis for the patient is already poor, and some reduction of morbid swelling may be decidedly palliative. Mobilization of dormant tumor cells by arm compression in patients after treatment of carcinoma of the breast remains speculative and thus far unconvincing or unfounded.

A prescription for low stretch garments (custom made with specific measurement as needed) to preserve the results of CPT is essential. It is preferable that a physician be responsible for such garments to avoid inappropriate prescriptions for patients with arterial or deep venous disease. In principle,

the highest compression level (usually 40-0 mmHg) tolerated by the patient is likely to be the most beneficial.

Failure of CPT prevails only when intensive treatment in a clinic specializing in management of lymphedema and directed by an experienced clinical lymphologist has been unsuccessful.

b. Intermittent pneumatic compression. Pneumomassage is usually a two-phase program. After external compression therapy is applied, preferably a sequential pump, form-fitting elastic stockings or sleeves are necessary to maintain edema reduction. Displacement of edema more proximally in the limb and genitalia and the development of a fibrosclerotic ring at the root of the extremity with further obstruction of lymph flow must be assiduously avoided.

c. Massage alone. Performed as an isolated technique, classical massage or effleurage usually has minimal benefit. Moreover, if performed overly vigorously, massage may actually injure lymphatic collectors.

d. Wringing out. "Tuyautage" or wringing out performed with bandages or rubber tubes is now regarded as potentially dangerous and thus obsolete.

e. Thermal therapy. This technique involves a combination of heat, skin care, and external compression. Although the effectiveness of thermo-therapy has been acclaimed by practitioners in Europe and Japan, as well as China, it should still be considered as under investigation.

f. Elevation. Simple elevation of a lymphedematous limb reduces swelling primarily in the early stage of lymphedema. If swelling has been reduced by antigravimetric means, the effect should be maintained by low-stretch stockings.

2. Drug therapy

a. Diuretics. Diuretic agents may occasionally be useful, but by no means indispensable, during the initial phase of

physiotherapy. Long-term administration of diuretics is discouraged as being of marginal benefit and potentially complicated by fluid and electrolyte disturbances. It may be helpful in lymphedema complicated by effusions in body cavities (e.g. ascites, hydrothorax) and with protein-losing enteropathy. Patients with peripheral lymphedema from malignant obstruction may derive some benefit from a short course of diuretic drug treatment.

b. Benzopyrones. Oral benzopyrones, which are thought to activate extralymphatic absorption of tissue proteins and stimulate the remaining lymphatic collectors, are neither an alternative nor substitute for CPT. The exact role for benzopyrones as an adjunct in primary and secondary lymphedema including filariasis is still to be definitively determined including appropriate formulations and dose regimens. Rarely coumarin, one such benzopyrone, causes idiosyncratic hepatitis.

c. Antimicrobials. Antibiotics should be administered for the complication of superimposed acute inflammation (cellulitis or erysipelas). If repeated attacks of limb "sepsis" are not prevented by CPT, the administration of prophylactic antibiotics is imperative. Fungal infection, a common complication of lymphedema, should be treated with antimycotic drugs. In filarial lymphedema, washing with an alkaline pH and clean water, along with a mild disinfectant or antibiotic-antifungal cream is helpful. To eliminate microfilariae from the bloodstream in patients with lymphatic filariasis, the drugs Ivermectin or diethylcarbamazine are recommended.

d. Mesotherapy. The injection of hyaluronidase or similar agents to loosen the extracellular matrix is of doubtful therapeutic benefit.

e. Immunological therapy. An attempt to boost immunity by the intraarterial injection of lymphocytes is still deemed experimental.

f. Diet. No special diet is useful for peripheral lymphedema. In an obese patient,

a reducing diet in combination with an exercise program are of some value in decreasing limb bulk. Fluid intake should not be restricted. In the case of chylous reflux syndrome, a diet low in long chain triglycerides and high in short and medium chain triglycerides may be beneficial.

1. Psychosocial rehabilitation.

Psychosocial support and quality of life assessment-improvement program is an integral component of any treatment of lymphedema.

Operative Treatment

Most operations designed to alleviate peripheral lymphedema have not as yet been perfected or usually are still inferior to combined physiotherapy where the latter is available as an intensive treatment course. In selected patients, they may be used as an adjunct to CPT or appropriately when CPT has clearly been unsuccessful.

1. Resection

The simplest operation is "debulking" that is, removal of the excess skin and subcutaneous tissue of the lymphedematous limb. Its major disadvantage is that superficial skin lymphatic collaterals are removed or scarred, which interferes with later CPT. Liposuction or operations which entail extensive resection or dermal inversion are discouraged in treatment of peripheral lymphedema. Lymphedema of the genitalia may require reduction (i.e., debulking) surgery. After aggressive CPT, redundant skin folds may require excision. Debulking may also be necessary in the treatment of advanced elephantiasis. Extreme caution should be exercised in removing lymph nodes or masses (e.g., lymphangiomas) in the affected extremity as lymphedema often worsens thereafter. Omental transposition, enteromesenteric bridge operations, and the implantation of

tubes or threads to promote perilymphatic spaces (substitute lymphatics) have not shown long-term value. Chylous and other reflux syndromes are special considerations which may require computed tomographic guided sclerosis, operative ligation of ectatic and dysplastic lymphatic collectors, or lymph diversion.

2. Microsurgical procedures

The goal of this operative therapy is to augment the rate of return of lymph to the blood circulation. The surgeon should be well-schooled in both microsurgery and lymphology.

a. Reconstructive methods. These sophisticated techniques involve the use of a lymphatic collector or an interposition vein segment to restore lymphatic congruity. Autologous lymph vessel transplantation has been restricted to unilateral peripheral lymphedema.

b. Derivative methods. Although lymph-venous and lymph-nodal venous shunt are promising, these procedure still require confirmation of long-term patency (e.g., imaging by lymphoscintigraphy) and demonstration of improved lymphatic tracer transport (objective measurements of long-term efficacy). Clinical experience with these procedures over the last 20 years suggest that better and more lasting beneficial results are forthcoming if performed early in the course of lymphedema before irreversible fibrosclerosis supervenes.

CONCLUSION

Lymphedema may be simple or complex but should not be neglected. Accurate diagnosis and effective therapy is now available, and lymphology itself is recognized as a bona fide speciality in which clinicians are specially educated in the intricacies of the lymphatic circulation and its disorders.