MICROSURGERY FOR LYMPHEDEMA: A REAL POSSIBILITY OF CURE.

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CLINICAL BACKGROUND

Lymphedema, refractory to non-operative methods, may be managed by surgical treatment. Indications include insufficient lymphedema reduction by well performed medical and physical therapy (less than 50%), recurrent episodes of lymphangitis, intractable pain, worsening limb function, patient unsatisfied of the result obtained by non-operative methods and willing to proceed with surgical options.

The first microsurgical derivative operations were those using lymphnodal-venous shunts. These have been largely abandoned, except in endemic areas of lymphatic filariasis such as India where thousands of these procedures have been performed. Lymphatic channels in lymphnodal-venous anastomoses are often widely dilated due to the high rate of anastomotic closures caused by the thrombogenic effect of lymph nodal pulp on the venous blood and the frequent re-endothelization of the lymph nodal surface (1). Because of the difficulties encountered with lymphnodal-venous shunts by surgeons worldwide, the next approach was to use lymphatic vessels directly anastomosed to veins (2).

The technique consists in anastomosing lymphatic vessels to a collateral branch of the main vein, checking the perfect function of the valvular apparatus, in order to be sure of the correct continence of the vein segment used for the anastomosis. This way, inside the venous tract there flows only lymph and not blood, avoiding any risk of thrombosis of anastomosis (3).

METHODS AND SURGICAL EXPERIENCE

The operations consist in performing microsurgical multiple lymphatic-venous anastomoses. Healthy appearing lymphatics found at the site of surgical operation are directly introduced together into the vein by a U-shaped stitch and then fixed to the vein cut-end by means of additional stitches between the vein border and the perilymphatic adipose tissue. With the use of Patent Blue dye, properly functioning lymphatics appear blue, and the passage of blue lymph into the vein branch verifies the patency of the lymphatic-venous anastomosis under the operating microscope when the anastomosis is completed (Fig.1).

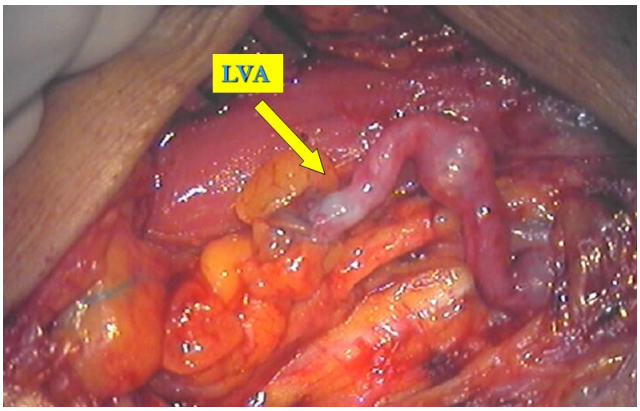

Fig.1: Lymphatic-venous multiple anastomosis: several lymphatics are introduced inside a valved vein. The blue dye flowing into the vein demonstrates the patency of the vein. The well functioning valve assures the continence of the vein avoiding blood reflux towards the lymphatics. This technical trick is important for the long term patency of the anastomosis.

For patients with lower limb lymphedema, anastomoses are performed at the sub-inguinal region. Lymphatic-lymph nodal superficial structures are isolated, and all afferent lymphatics are used for the operation. Lymph nodes are subjected to histopathologic examination. The usual finding in primary lower limb lymphedemas is a varying grade of nodal fibrosclerosis and thickening of the nodal capsule but with normal afferent lymphatic vessels.

For upper limb lymphedema, lymphatic-venous anastomoses are performed at the medium third of the volar surface of the arm, using both superficial and deep lymphatic collectors, evidenced by the blue dye. Deep lymphatics are found in between humeral artery, vein and the median nerve. The vein used for anastomoses is a patent branch of one of the humeral veins, and the technique most performed is the microsurgical one (Fig.2).

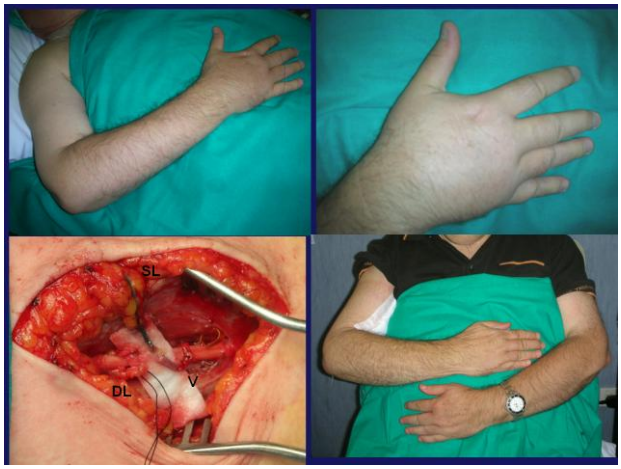

Fig.2: Primary right upper limb lymphedema in a man treated with derivative lymphatic-venous anastomosis at the volar surface of the upper third of the arm. Superficial (SL) and deep (DL) lymphatics are prepared together with a vein (V) branch of one of the brachial veins with well functioning valves. The result of the operation is immediate and the technique allowed to obtained stable results at long term follow-up.

Primary lymphedemas largely include lymph nodal dysplasias (LAD II, according to Papendieck's classification (4)) consisting of hypoplastic lymph nodes with sinus histiocytosis and a thick and fibrous capsule with microlymphangioadenomyomatosis. In these cases, lymph flow obstruction was apparent as seen by alterations of the afferent lymphatics which appeared dilated and swollen with thickened walls and where smooth muscle cells are reduced in number and appear fragmented by associated fibrous elements. Secondary lymphedemas are largely due to lymphadenectomy and radiotherapy performed for oncological reasons (carcinoma of the breast, uterus, penis, bladder, prostatic gland, rectum, and seminoma of epididymis), as well as for complications of minor operations for varicose veins, crural and inguinal hernias, lipomas, tendinous cysts, or axillary and inguinal lymph node biopsies. Most of the lymphedemas treated by microsurgery in our experience were at stages II (39%) and III (52%), while 3% of the patients were stage Ib and 6% were stages IV and V.

Lymphoscintigraphy, performed with 99mTc-labeled antimony sulfur colloid, is employed in the diagnostic work-up of patients with lymphedema and as a test for selecting patients for derivative microsurgical operations. Lymphoscintigraphy clearly discriminates whether or not edema was of lymphatic origin and also provides important data about the etiologic and pathophysiologic aspects of the Lymphedema.

Echo Doppler is performed in all patients to identify any venous disorders possibly associated with lymphedema. In most patients, venous dysfunctions is corrected at the same time of microlymphatico-venous anastomoses (i.e., valvular plasty in case of venous insufficiency). In other cases, finding venous dysfunction contraindicates derivative lympho-venous shunts but at the same time facilitates referral of the patient for reconstructive microsurgical operations.

In those cases involving the lower limbs, where surgically uncorrectable venous disease exists, it is not advisable to use derivative lymphatic-venous techniques, and accordingly, reconstructive methods are used. The most commonly used technique is the interposition of an autologous vein graft between lymphatics above and below the obstacle to lymph flow. The venous segment can be obtained from the same operative site or from the forearm (mostly the cephalic vein). The length of the graft is variable from 7 to 15 cm, and it is important to collect several lymphatics at the distal cut end of the vein so as to maintain the segment filled with lymph and avoid closure due to fibrosis. The valves of the veins are useful for the correct direction of the lymphatic flow and to avoid gravitational backflow. The technique of anastomosis is the microsurgical one with introduction of lymphatics inside the vein cut ends by a U-shaped stitch, which is then fixed by some peripheral stitches (Fig.3).

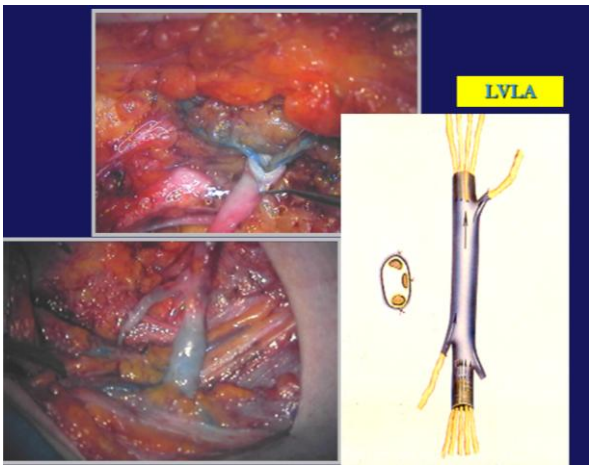

Fig.3: Lymphatic-venous-lymphatic anastomoses used in those cases in which, owing to venous dysfunction, derivative technique are contraindicated. The technique consists in interposing a vein segment inbetween lymphatics above and below the obstacle to lymph flow (Campisi, 1982).

RESULTS AND CLINICAL CONSIDERATIONS

Clinical outcome improves the earlier microsurgery is performed owing to absent or minimal fibrosclerotic alterations of the lymphatic walls and surrounding tissues. Subjective improvement in our experience was noted in 87% of patients. Objectively, volume changes showed a significant improvement in 83%, with an average reduction of 67% of the excess volume. Of those patients followed-up, 85% have been able to discontinue the use of conservative measures, with an average follow-up of more than 10 years and average reduction in excess volume of 69% (Figs.4-8). There was a 87% reduction in the incidence of cellulitis after microsurgery.

Fig.4: Right upper limb lymphedema due to breast cancer treatment managed by derivative lymphatic-venous microsurgical anastomoses at the arm (long term follow-up).

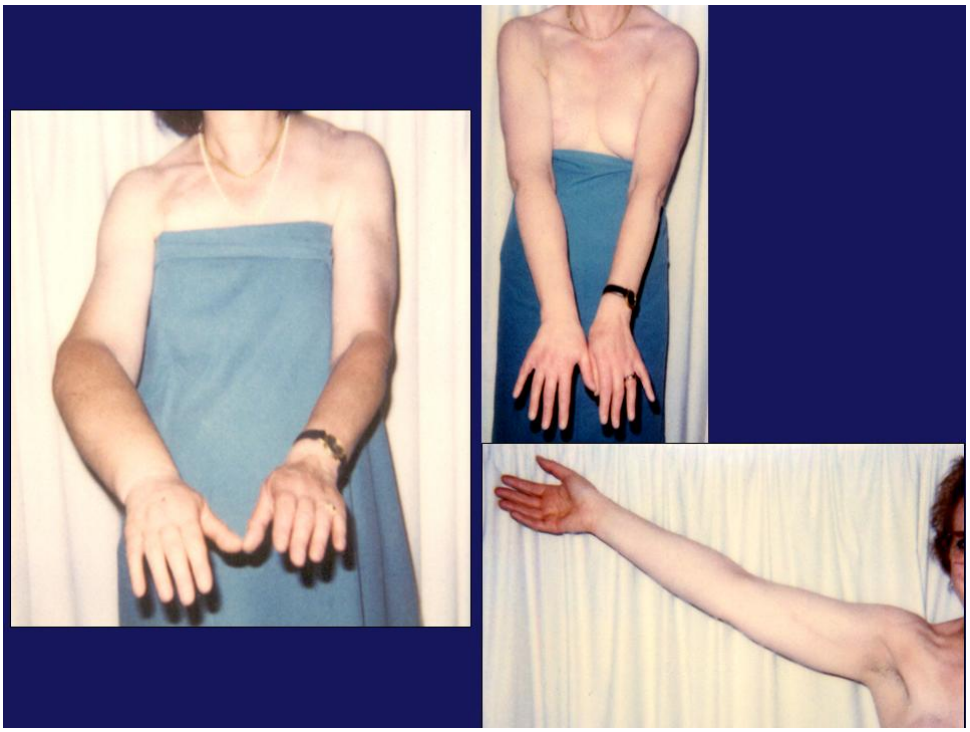

Fig.5: Another case of secondary upper limb lymphedema. Of note the good result also at the hand and the nice result also from the cosmetic point of view.

Fig.6: Bilateral lower limb primary lymphedema before and after 15 years from microsurgical derivative operation at the groin. The technique of lymphatic-venous anastomoses, if performed in a proper way, represents a physiologic long lasting repair of the lymphatic drainage of the extremity

Fig.7: Right lower limb lymphedema treated with derivative lymphatic-venous anastomoses at the inguino-crural region. These techniques allow to use the compression garments irregularly thanks to the formation of preferential lymphatic pathways and to the positive lymphatic-venous pressure gradient.

Fig.8: Bilateral primary lower limb lymphedema with associated important venous dysfunction. In this case, reconstructive lymphatic-venous-lymphatic anastomoses was used bilaterally with good long term result. This technique can be used also in bilateral lymphedemas and does not determine any risk of secondary lymphedema at the harvesting site.

Lymphoscintigraphy helped in verifying the patency of microanastomoses long term after operation by direct and indirect findings: reduction of dermal backflow together with the appearance of preferential lymphatic pathways not visible before microsurgery; disappearance of the tracer at the site of lymphatic-venous anastomoses due to direct tracer passage into the blood stream; and earlier liver uptake compared to pre-operative parameters (indirect patency test) (Figs.9,10).

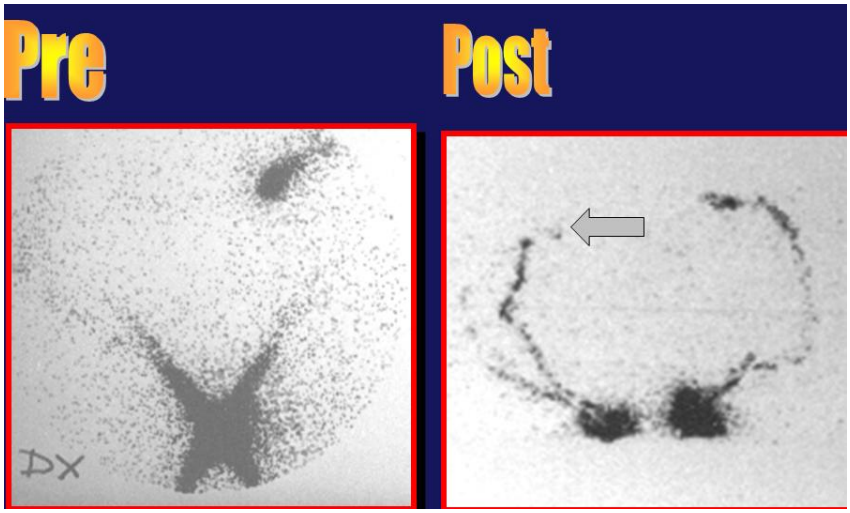

Fig.9: Lymphoscintigraphic follow-up of an upper limb secondary lymphedema treated by derivative lymphatic microsurgery. Post-operatively, preferential lymphatic ways are evident and the tracer disappears at the site of anastomosis due to the passage into the blood stream.

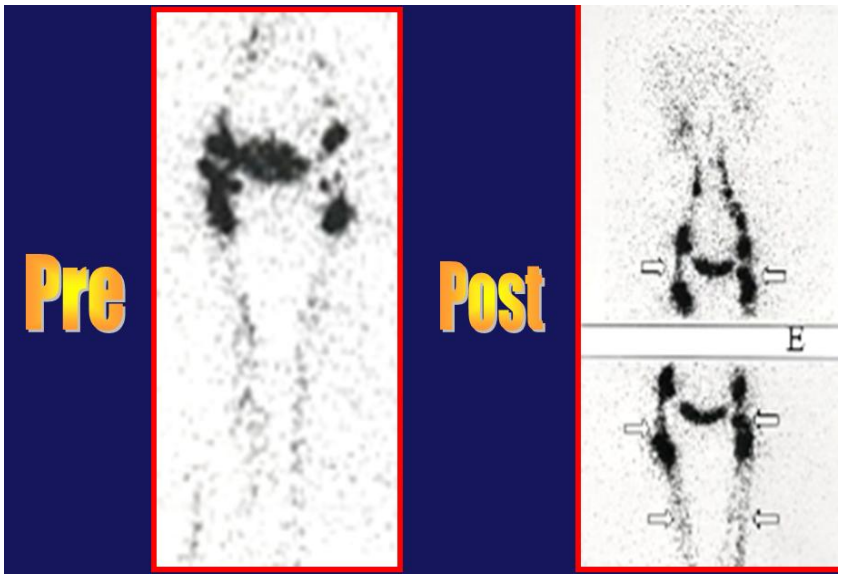

Fig.10: Lymphoscintigraphy before and after reconstructive microsurgical lymphatic-venous-lymphatic technique performed in a bilateral lower limb lymphedema. Post-operatively, venous grafts are visualized inbetween lymphatic pathways below and above the inguinal region.

Lymphatic microsurgery represents a means to bypass the obstacle to lymph flow through lymphatic-venous drainage (lymphatic-venous anastomoses) or by using venous grafts between lymphatic collectors below and above the obstruction (lymphatic-venous-lymphatic plasty). Combined physical therapy nonetheless represents the initial treatment of patients affected by peripheral lymphedema and it is best performed in specialized centers. The surgical timing follows completion of conservative treatment when further clinical improvement can no longer be achieved and/or recurrent lymphangitic attacks are not further reduced (5). Microsurgical operations can then be performed and provide further improvement in the condition (6,7).

The optimal indications for lymphatic microsurgery are represented by: early stages (Ib, II, early III); lymphoscintigraphy showing a low inguinal or axillary lymph nodal uptake and minimal or absent passage of the tracer beyond this proximal nodal area; excellent patient compliance; and a lymphological center where the patient can easily refer for any needs in addition to a Center of Lymphatic Surgery where the patient undergoes this specialized surgery.

At later stages (advanced III, IV, and V), with absent visualization of lymphatic channels and regional lymph nodes, it is necessary to reduce the stage of the lymphedema by non-operative methods before microsurgery. After operation, it is particualrly important for these patients to be followed closely to improve the clinical outcome and maintain the short-term operative results for the long term (so called Complete Lymphedema Functional Therapy - CLyFT 8) (Fig.11).

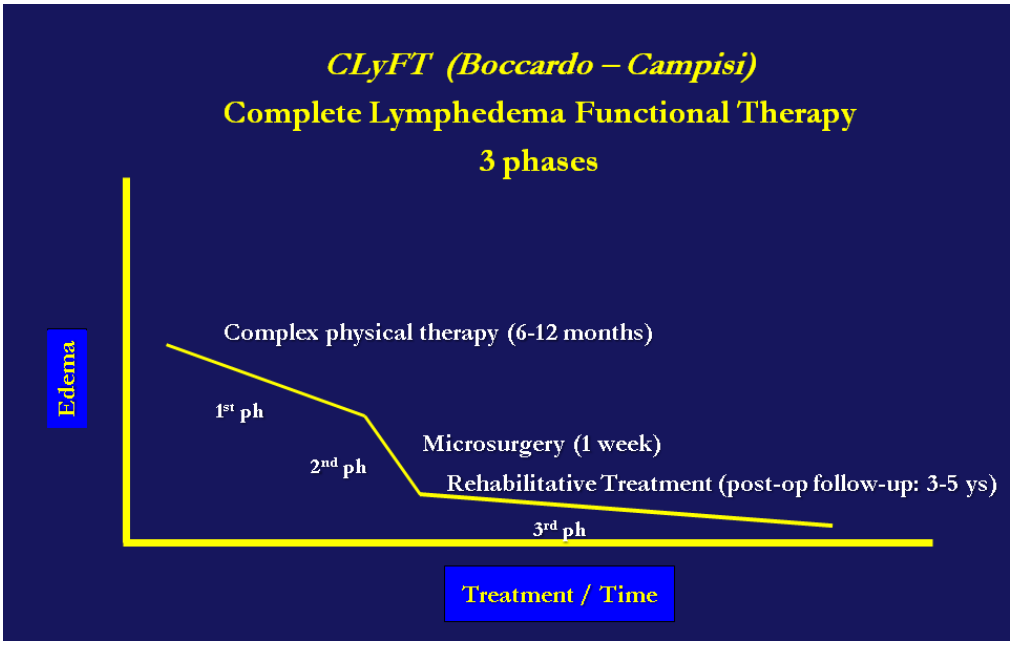

Fig.11: Scheme of the complete lymphedema fuctional therapy (CLyFT) proposed for the combined non-operative and microsurgical treatment of lymphedema. This therapeutical association proved to supply the best and long lasting results combining the efficacy of non-operative methods with the results of microsurgical procedures and giving the patient the possibility to wear compression garments irregularly at the beginning and also to avoid the use of stockings and sleeves in the long run.

In case of poor patient compliance, the results may be unsatisfactory. Relative contraindications to lymphatic microsurgery are represented by cases of lymphatic-lymph nodal aplasia (extremely rare), diffuse metastatic disease, and advanced stage (V) not responsive to conservative therapy. Traditional debulking operations are presently less utilized to treat lymphedema except in cases of late stage lymphedema to reduce skin folds after marked edema reduction obtained by conservative physical and microsurgical methods; in body regions relatively inaccessible to effective compression such as the genitalia; in advanced lymphatic filariasis at times combined with lymphatic-venous or nodal-venous anastomosis in the setting of widely dilated lymphatic channels; and in localized lipolymphedema associated with massive obesity and forced immobility.

In recent years, both primary and secondary peripheral lymphedemas are becoming better understood and more manageable problems with increased awareness and early detection (9-13). Nonetheless, apparent non-operative measures are aimed at minimizing morbidity without removing the cause of the underlying disturbance (14,15). Microsurgical derivative and reconstructive operations can restore lymphatic drainage, both in the short and long term, and the best results are obtained when these surgical procedures are combined with physical rehabilitative methods.

Finally, we recently proposed the use of lymphatic-venous anastomoses for primary prevention of arm lymphedema, performing anastomoses at the same time of axillary lymphnodal dissection for breast cancer treatment (Lymphatic Microsurgical Preventive Healing Approach – LyMPHA) (16). This technique was used also for preventing lower limb secondary lymphedema for vulvar carcinoma and melanoma of the trunk.

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