“PERSONAL METHODS” OF THE PHYSICAL TREATMENT OF LYMPHEDEMA AND “EVIDENCE BASED MEDICINE”

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Cheville et al. (1) rightly state, that “combined manual therapy”, often referred to as “Complex Decorative Physiotherapy” (CDT) has emerged as the standard in the treatment of lymphedema. One of the four constituents of this technique is “Minimal lymph drainage” (MLD) which has been devised by the Vodder’s in 1932, however by no means for the treatment of lymphedema. In a “Guide for postgraduate education” entitled “On the track of the lymph vessels” the author Rösser (2) states: “The Vodder’s worked in the French Riviera. They had contact with many English people, who, due to the wet and cold climate of their country, have suffered from chronic common cold. Many had swollen cervical lymph nodes… The Vodder’s started to teat them. The result was astounding. By means of careful, turning pumping movements the signs of common cold have vanished forever”. Obviously the Vodder’s can’t be blamed for being, in 1932, unaware of the fact, that the common cold has nothing to do with the climate of the British isles, the author of the post-graduate article, on the other hand should know, that it is a mild, self-limited viral infection. The first physicians, Asdonk, who has tried to treat lymphedema by the massage technique derived by the Vodders, which is highly effective in increasing the lymphangiomotoric activity of healthy lymphatics has observed, that it was inadequate in the treatment of fibrosclerotic lymphedema. It has therefore added what he called “edema-grips”. As a consequence, a vehement “grips dispute” has broken out between the Vodder’s and Asdonk: henceforth the latter designated his “edema grips” as “Vodder-Asdonk-method”. This term is not to mention of elephantiastic lymphedema. This term is therefore coined by the Vodder’s in 1932, however by no means for the treatment of lymphedema and CDT: not only the patients in the trial should to disappear on the other. According to them, the test gives the light of their own findings, “somewhat modified and upgraded” (3) which they have designated as “Foldi-Method of CDT”. In our “Textbook of Lymphology” (4) I have declared: “I stress that we did not develop any personal method of CDT. This means that there is no Foldi method of CDT. What we do in our clinic is to integrate CDT with the broad field of physical medicine and with comprehensive, individualized treatment of the patient.”

What concerns the contended “modification and upgrading” of the non-existing “Foldi-Method” attention has to be called to the fact, that neither in their lecture given in Washington, nor in their booklet entitled: “Lymphedema: A guide for therapists and patients” (5) did the Casley-Smith’s explain, in which respect they have “modified and upgraded” the “Foldi-Method” which Judith Casley-Smith had the chance to have a look at in our Clinic in the course of a morning. In addition, they have omitted to perform a prospective – randomised study aiming to compare the method which they designated as “the Foldi’s” with that they henceforth designated as the “Casley-Smith-method”.

It is a nonsense to train lymphedema therapists by limiting oneself to the technique, to the work to be done by hand; an exclusive medical knowledge has to be imparted, too! (A conductor has to understand music, it is not enough, if he knows how to stickly fidget with a baton!)

In the native country of CDT, in Germany, a law has been passed which has authorized the federation of the statutory sick-funds to prescribe the members of which occupational groups are allowed to be trained in CDT. The federation has specified the requirements the physicians who give lessons have to fulfill and how the training of lymphedema therapists who act as instructors has to be accomplished. The duration (170 forty-five-minutes lessons), the curriculum and the order of the exams are also specified. Unfortunately, the subjects of the medical curriculum are specified, but not the messages to be imparted. As a consequence, unfortunately at times nonsensical matters are taught.

For example there is a passage in the paper of Rösser, entitled “The impression test as an indicator”. Rösser has been informed by lymphedema therapists working as instructors in one of the accredited CDT-colleges, that there is a correlation between the protein concentration of the edema fluid on the one hand and the period of time it takes for the impression, caused by the pressure of the thumb into the extaneous area to disappear on the other. According to them, the test gives...
consequences concerning treatment: the higher the protein concentration, the more delayed the therapeutic result! As a consequence, "both therapists and patients have to muster much patience!" The lymphologist-instructor of the same CDT-college has published a book which contains serious professional mistakes. Although it is textbook knowledge, that the essence of chronic venous insufficiency (CVI) in the leg is ambulatory venous hypertension, according to this author venous pressure in CVI is elevated while standing and sitting! He regards MLD to be indicated in cases of cardiac edema refractory to treatment. There is not a single textbook of Medicine or Cardiology which shares this opinion! In reality, cardiac edema represents an absolute contraindication for MLD, because, by the elevated myocardial lymphatic preload and afterload the left chamber is also effected: the increase of the blood volume brought about by the uptake of edematous fluid into the circulation could trigger a congestive left heart failure. Taking the fact into consideration, that even the reputed "Cecil Textbook of Medicine"(6) contains serious mistakes where it deals with questions of Lymphology (for example the nonsense, that "chronic lymphedemas may be caused by... renal or cardiac failure") (1), one should strike for an international consensus concerning the subject matter and the relevant message which has to be imparted to students of CDT.

REFERENCES
CONCENTRATION OF TNF- AND IL-1- IN WISTAR RATS SERUM AND LYMPH UNDER PHYSIOLOGICAL CONDITIONS

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ABSTRACT

TNF- and IL-1- levels both in the lymph collected from thoracic duct and in serum in Wistar rats were determined using immunoenzymatic methods (Bender Med Systems and Endogen, respectively). TNF- concentrations both in the serum and lymph were below sensitivity threshold of the method (<17 pg/ml). Serum IL-1- concentration was statistically significantly higher (p<0.005) – 35.89±3.23 pg/ml compared to lymph concentration (22.50±2.45 pg/ml).

The lymph is an excellent carrier of information about any changes in tissues, whereas the blood delivers only substances which are necessary for the functioning of the organism. It is possible that cytokines are "conserved" during their flow through lymphatic organs and vessels. As a result, the concentration of cytokines in thoracic duct may be lower than in peripheral lymphatics. This may explain a higher IL-1- concentration in blood serum obtained in our study.

KEY WORDS: TNF- and IL-1- - serum - lymph

INTRODUCTION

The lymphatic system, after the nervous and endocrine systems plays a crucial role in maintaining homeostasis. In the last decades an increasing attention has been devoted to the role of lymphatic system in pathomechanism.

The lymphatic system comprises the lymphatic organs, lymphatics and lymphocytes which produce immunoglobulins and cytokines [1, 2, 3].

The cytokines, a group of micromolecular signalling proteins play an important role in immunological responses, acute phase reaction, hematopoiesis and antiinflammatory defense. However, cytokines can sometimes cause life - threatening complications [3, 4].

In literature there are only a few reports on cytokines concentration in lymph. The aim of the present study was to answer the question whether there are any differences between the serum – and lymph concentrations of TNF- (Tumor Necrosis Factor-alfa) and IL-1- (Interleukin 1-beta) in Wistar rats in normal conditions.

MATERIAL AND METHODS

The studies were performed on 20 adult male Wistar rats weighing 180-200 grams each. All the animals were kept in an air conditioned room in 12/12 hour light/dark cycle. They were on a standard diet and were supplied with water ad libitum.

Under pentobarbital anaesthesia the thoracic duct was exposed below the diaphragm and cannulated with 1.2 F hydrophilic elastic catheter (Balton). The abdominal walls were closed and lymph was collected into heparinized test-tube. After an appropriate amount of lymph had been obtained, the blood was collected from the heart. After coagulation the blood was centrifuged. Both in the lymph and in serum the TNF- and IL-1- levels were determined using immunoenzymatic methods (Bender Med Systems and Endogen, respectively).

RESULTS

INTRODUCTION

The TNF- concentrations both in the serum and lymph were lower than 17 pg/ml i.e. below sensitiveness threshold of the method. Serum IL-1- concentration was statistically significantly higher (p<0.005) – 35.89±3.23 pg/ml compared to lymph concentration (22.50±2.45 pg/ml).

DISCUSSION

TNF- is one of the main cytokines in involved in inflammatory and immunological responses [5, 6, 7]. In 1975 Cawell identified the factor responsible for tumor necrosis factor (TNF-). In 1984 a gene encoding the TNF- synthesis was cloned [8, 9]. TNF- co-operating with other cytokines such as IL-1, IL-2, IL-7.
enhances thymocytes' proliferation, while with IL-6 it may cause a decrease in proliferation and differentiation of B lymphocytes. Together with IL-2 it stimulates the proliferation and cytotoxicity of NK cells and formation of LAK cells. By endo-, para-, and autocrine activity TNF- influences monocytes and macrophages. It also considerably increases cytotoxicity of monocytes, macrophages and NK cells. TNF- increases phagocytic capability of neutrophils and accelerates their release from bone marrow. It may also activate the eosinophils' cytotoxicity in protozoa infection response [5, 10, 11].

TNF- affects the immune system directly and indirectly through release of many cytokines. (e.g. from macrophages are released IL-1, IL-6, INF- (Interferon-beta), NGF (Nerve Growth Factor), EGF (Epidermal Growth Factor) and from lymphocytes INF-.) [2, 13, 14]. TNF- is capable of inducing the expression of MHC (Major Histocompatibility Complex) class I molecules, but together with INF- the expression of MHC class II is induced [14]. IL-1 possesses a wide variety of biological activities and is one of the main regulators of immune and inflammatory responses. It is mainly secreted by monocytes and macrophages from various tissues. Lipopolysaccharides, the main constituents of the Gram-negative bacteria cell wall, are one of the most effective factors which induce the release of IL-1. The inducers of IL-1 are also viruses, saccharomyces, eutoxins, IL-2, IL-3, IL-12, TNF- complement fragment C5a, lectins, and IL-2 alone. Besides monocytes and macrophages IL-1 can also be secreted by keratinocytes, chondrocytes, Langerhans' cells, glia cells, mesangium cells, endothelial cells, and even by T and B lymphocytes [3, 4]. IL-1 stimulates INF- production by thymocytes, and IL-6 by macrophages, fibroblasts and endothelial cells. It also influences the proliferation and differentiation of B lymphocytes. IL-1 induces enhanced production of neoptalin and monocytes, mainly by stimulating release of colony activating factors. It also affects proliferation of fibroblasts and monocytes which is partly the result of the stimulated release of platelet - derived growth factor (PDGF) which acts on these cells both auto- and paracriytically.

IL-1 facilitates the evolution of inflammatory reaction not only as a result of hemotactic attraction of neutrophils and monocytes. It increases histamine release from basophils, degranulation of eosinophils and production of prostaglandins by stimulating phospholipase A2 synthesis. The latter releases arachidonic acid from cell membrane phospholipids. Acting on endothelium IL-1 increases its permeability, induces its procoagulatory activity, stimulates the production of platelet activating factor (PAF) and intensifies adhesion of lymphocytes and neutrophils to endothelial cells [3, 4, 13]. There are two types of IL-1: IL-1α and IL-1β. They are products of two different genes, IL-1α and IL-1β, and are in 25% homologic. They are synthesized intracellularly from precursors as aals its precursor. Stimulated by LPS monocytes produce mainly IL-1α, whereas IL-1β dominates in keratinocytes [2]. The lymph contains proteins which originate from circulating blood, reaching the intestinal fluid through small vessel wall from where they are exclusively transported to blood circulation by lymphatics [1, 16]. Thoracic duct lymph concentration constitutes about 60% of that in plasma. In the human being about 50% of plasma proteins content (100 g) are transported daily through the thoracic duct lymph. In some laboratory animals (such as dogs, cats, rabbits) the total amount of daily transported proteins ranges from 60% to 80% of their plasma concentration.

The concentrations of proteins in lymph are lower than in serum. There are also differences between proportional composition of particular protein fractions in blood and lymph. It is caused by limited transport ability of proteins through the blood vessel walls to tissues and then to lymph. As a result, the lymph concentration of proteins or higher molecular weight is lower than the lymph concentration of lower molecular weight. Moreover, the biological activity of some proteins can be in a considerable degree determined by their occurrence either in blood or in tissue fluid [17]. In normal conditions no active cells and biochemical processes in blood were noted. Contrary to this the active processes in lymph are continuously taking place (e.g. autotransformation of lymphocytes, which begin production of cytokines). The cells which are present in lymph differ functionally and phenotypically from those present in blood. Lymph contains more lymphocytes and monocytes. There are no granulocytes, whereas the Langerhan's cells, absent in blood, in lymph constitute from 6 to 8%. The lymph is a fluid in which the morphological equivalents of cell cooperation are found. IL-1β is produced by monocytes, T- and B- lymphocytes and Langerhan's cells [12, 14]. Although greater number of these cells is to be found in lymph as compared to blood, in our study we found surprisingly lower IL-1 concentration in lymph than in blood. It must be emphasized that lymph is an excellent carrier of information about any changes in tissues, whereas the blood delivers only substances which are necessary for the functioning of the organism. The role of blood as a carrier of information has been progressively supplemented by the lymphatic system an evolutionary process [13]. The blood concentration of cytokines is a sum of amounts of cytokines produced by cells present in blood and in lymphatic system as well. Taking into account a dynamic nature of lymph, it is possible to state that cytokines are "consumed" during their flow through lymphatic organs and vessels. As a result, the concentration of cytokines in thoracic duct lymph may be lower than in peripheral lymphatics. This, in turn, may explain a higher IL-1 concentration in blood serum obtained in our study. What is more the cytokines were determined in the lymph from thoracic duct, i.e. in lymph taken only from a part of the body, which could have additionally influenced lower IL-1 concentration in lymph, as compared to blood.

REFERENCES


CHRONIC Lymphedema, NO MORE STEPCHILD TO MODERN MEDICINE!

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ABSTRACT

The new concept of total care management based on multidisciplinary approach to accommodate various nosological and surgical therapies has brought substantial progress in the management of chronic lymphedema. The new knowledge to lymphodynamics of lymphedema is the functional unit of lymphatic circulation was provided logical ground to develop more physiologic approach to the chronic lymphedema. Various surgical, reconstructive or excisional, therapies were implemented as adjunct therapy to enhance over-all effectiveness of the CDP (complex decongestive physiotherapy) and/or compressotherapy-based main therapy. New additional role of surgical therapy was improve overall management to deliver better quality of life as the ultimate goal of the management of chronic lymphedema. After all, lymphedema, either primary or secondary, is no more “insurmountable” disease but manageable if not preventable, when the ignorance and poor compliance should be further overcome.

KEY WORDS: lymphedema management, Global therapeutic approach.

CHANGING CONCEPT

The lymphedema has remained one of obscure condition of limb swelling for so many decades, and did not get enough attention it deserved as one of serious disease entity to need the treatment, remaining as a stepchild in modern medicine(1). It has been simply known as the condition related to the lymphatic dysfunction of various etiologies and benignly neglected as relatively harmless condition only to need to learn to live with. Lymphatic circulation system was also vaguely understood as supplemental role to the essential arterial and venous circulation system, even though it has been well documented from earlier centuries(2-4).

However, new hemodynamic knowledge in circulatory system have been rapidly accumulated through earlier decades of 20th century, and once neglected and relatively unknown lymphatic system was finally recognized as crucial last piece of puzzles to be able to answer various important questions on the circulation properly(5,6).

New discovery of “lymphangion”, for example, as a functional unit of lymph transport system through early ‘60, has served for proper recognition of major differences between normal lymphatics and venodynamics, and corrected previous misconceptions on this system as identical one to the venous system with same hemodynamics(5,6).

Lymphatic circulation is based on active autonomous peristaltic movement to transport lymph from the low pressure to high pressure environment for more than 60mmHg, while venous circulation is based on passive movement from high to low pressure in contrast(7).

Such major discovery in anatomy and physiology of lymphatic system(8) gave new momentum for more rational challenge to the chronic lymphedema to clear its ill reputation as one of last enigma in modern medicine. Many mysteries in the lymphatic dysfunction (eg. latent edema) have been successfully explained with this new knowledge, and new concept and principle of the lymphedema management have been accordingly well established.

The relationship between the primary and secondary lymphedema became much clear to give proper guide to the each with different etiology for more effective management(9-11), and modified clinical/laboratory staging of lymphedema also gave more room to implement various surgical therapies together with conservative treatment(12,13). This changing concept was fully implemented to the contemporary management of the chronic lymphedema(9), not only through medical/physical therapy but also through surgical therapy either as an independent or mutually complimentary therapies during the last decades, and whole aspect of chronic lymphedema has made substantial change, resulting in new prospect in its future management. Old concept of chronic lymphedema as a simple phenomenon of lymph stagnation following obstruction of lymph transport system, has been completely replaced by new concept which accepts the chronic lymphedema not only as a regional (local) problem involving tissue soft tissue (e.g. cellulitis) in addition to lymphatic system itself (e.g. lymphangitis), but also as a systemic problem (e.g. sepsis) involving immune system as well(14-16).

The chronic lymphedema is no longer considered as a simple lymph fluid collection within the soft tissue by the lymphatic obstruction, but is now viewed as a steadily progressing degenerative disease affecting from skin to entire soft tissue, named as “phenomenon of dermato-lipo-fibrosclerosis”(15). Therefore, critical role of subclinical infection with serious potential to accelerate the progress of tissue damage from reversible acute condition to the irreversible chronic status, drew new attention lately, especially on prevention point of view.

In view of limited ability of the presently available treatment, medical or surgical, modalities with limited success, the
MANAGEMENT

The reconstructive surgery in particular remains one of the last resort to provide chance of "cure" so that it keeps unique position as most ideal form of therapy if applicable. Reconstruction of lymphatic transportation system with various microsurgical techniques(39-46) has been well established, successfully bypassing the obstruction sites of interrupted collecting vessels to restore lymphatic circulation. Lymphovenous anastomoses with/without lymphatic or venous graft interposition(40), and free transfer of tissue containing lymph vessels and lymphnodes(51-54), have brought excellent long term results, although limited to a few dedicated teams of expert microvascular surgeons. Eventually surgical reconstruction can deliver such ideal results of cure, its proper indication warrants earlier stage of lymphatic obstruction/lymphedema while intrinsic contractility of the lymph channels remains to be intact which also respond very well to the conservative therapy with MLD-based CDP.

Hence, the selection of surgical indication from earlier stage of lymphedema becomes difficult, if not, controversial especially in ethical point of view, since conservative treatment alone is also very effective, although not curative, in same early stage while the peristaltic function of lymphangion is still preserved(55-57). The proper document/evidence to ease this concern over the potential harm of long term failure by the surgical therapy resulting in unnecessary sacrifice of previously healthy lymphatic channels is warranted. Exceptional surgery to remove grotesquely disfigured lymphangiocutaneous tissue, resistant to all available conservative regimens also gained new attention lately to improve the management of late stage to improve efficacy of the CDP/compressotherapy(58,59). But the compliance of the patient to maintain postoperative CDP/compressotherapy remains crucial for the long term outcome, and it warrants careful selection of the candidate through scrutinizing evaluation of mental, psychological and physical condition before the final decision.

We at the Lymphedema Clinic, Sinsil Chung Medical Center, Seoul, Korea, therefore, limited the indication for reconstructive surgery to the patients in early stage of lymphedema which has progressed in spite of adequate management with all available conventional conservative therapies at least for 12 months periods(9). The treatment failure of conservative therapy has been carefully documented by the multidisciplinary team of the Clinic before the selection/decision for the candidates, and additional efforts were made to obtain good compliance from the patient throughout the process.

Same rationale was also implemented to limit the selection of the candidate for the excisional surgery only to the patients who have progressed to the end stage from latter stage of lymphedema with further deterioration of quality of life and increased episodes of sepsis in spite of maximum treatment(9). Excisional surgery was mostly provided to the patient with end stage (clinical stage IV, modified from the I.S.L. staging) to pre-end stage (stage III), in order to change grotesquely disfigured contour of the limb to the normal so that the CDP/MDL compression therapy can be implemented more effectively. Once lymphedema should reach the end-stage, effectiveness and efficiency of CDP is strongly substantiated mainly due to the continuation of the lymphatic drainage and excisional surgery(47-50) for the palliation to improve the current lymphedematous condition before the final decision.

Venous surgical therapies, either independent or supplemental, have been also evolved as essential component of total care management: reconstructive surgery(39-46) to restore lymphatic function, mostly in earlier stage of lymphedema, and excisional surgery(47-50) for the palliation to improve the management and subsequent quality of life, mostly in latter stage toward end stage of lymphedema.
difficultly to wrap the swollen extremity properly with non-
elastic bandage for the exercise therapy.

High cost of advanced medical care of lymphedema became
significant burdening to the patient, family and society, so that the
maintenance care following initial physician-initiative in-hospital care
has to be based on patient-initiative home-based care to reduce the
cost involved. The role of self-help club, organized voluntarily by the patients and their
families, to enhance motivation out of ignorance by chronic nature of the disease and subsequently
to improve compliance, has been increased, providing necessary
supplemental boost (financial and psychological, etc.) with good
maintenance of non-decreasing compliance(9).

The new role of self-help club as self-imposed surveillance system for the patient-initiative home-care for the maintenance
care is increasingly important for the adequate management of
lymphedema without extra cost.

CLINICAL EXPERIENCES - DEMOGRAPHIC DATA

Among total of 761 patients, registered in Lymphedema Clinic,
Samsung Medical Center and Sungkyunkwan University, Seoul,
Korea (1994 September through February 2001), 182(26 males
and 116 females with age range from 2 months through 81 years -
mean 31.3 years) belonged to primary lymphedema (23.9%); 33
congenital type (18.1%), 110 procox type (60.4%), and 32 tarda
type (21.4%), and 579(26 males and 553 females with age range
from 21 through 82 years - mean 53.3 year) to secondary
lymphedema (76.1%); mostly postgstrual (536/579) and also
combined with radiation therapy postoperatively (458/579).

Among total of 761 patients, 327 had lesions in lower extremity
(177 on the right and 222 on the left and 130 on both sides), and
227 patients in upper extremity (99 on the right, 126 on the left
and 2 on both sides) and 7 patients with multiple lesions.

Among 182 primary lymphedema, 161 had lesion in lower extremity
(46 in the right and 54 in the left, and 28 in both limbs), 14 in upper extremity (4 in the right, 7 in the left, 1 in
the both sides), and 7 in multiple sites; head and neck, upper
and lower extremities, and abdomen.

Out of total 579 secondary lymphedema patients, 366 had
lesions in lower extremity (113 in the right and 156 in the left
and 97 in both sides), 213 in upper extremity(93 in the right
and 119 in the left and 1 in both sides).

The clinical staging, based on modified I.S.L. staging (clinical
stage I through IV) of 761 patients, confirmed 99 at the clinical
stage I, 354 at stage II, 224 at stage III and 40 at stage IV.

Another 44 patients were deferred for the proper staging due to
significant discrepancy with laboratory (image) staging based on
lymphoscintigraphic findings of chronic lymphedema although it would belong to the stage III of I.S.L. staging.

CLINICAL EXPERIENCES - RESULTS

Following full investigation of lymphedema status per protocol,
518 out of total 761 patients remained on follow-up protocol
with reasonable compliance and 243 patients were excluded due to
various reasons, mainly related to the poor compliances.

However, among 518 patients are able to meet the various
criteria to fulfill the condition of then ongoing project.

Among 220 patients (clinical stage I-77, II-98, III-29 & IV-16),
more effective management results were achieved in earlier
clinical stages: 70/77 of Stage I, 84/98 of Stage II, 16/29 of Stage
III, and 7/16 of Stage IV during average 4.0 year follow up period.

Progress/deterioration of clinical(C) stage of the lymphedema
despite adequate treatment was more frequently noticed among
the group accompanying higher lab+atory(L) stage based on
lymphoscintigraphic evaluation: Among 7 out of 77 in C stage I,
which progressed to C stage II or higher, 5 accompanied L stage
II or III on initial evaluation. 10 among 14 in C stage II, advanced

to C stage III, accompanied higher I stage, III or higher;
another 11 among 13 in C stage III, deteriorated to C stage IV,
also accompanied I stage IV or higher before the
CDP-based treatment was instituted.

Among treatment resistant/failure patients deteriorating from
the earlier stage in spite of adequate treatment, 19 patients (19 limbs: 18 females & 1 male: primary-4 & secondary-15: a mean age of
49.0 years) were selected for the venoymphatic reconstructive
surgery(VLRS) at clinical stage II (9/19) and early III (10/19).

Sixteen of 19 responded with satisfactory outcome (excellent-
8, good-6, and fair-2) on initial evaluation at 6 months
following the surgery, but only 8 with good compliance to
keep postoperative CDP, were able to maintain initial success to the follow-up assessment on 24 months.

All others with unsatisfactory outcome (3 initial failure and 8
subsequent failure) were mostly (8/11) related to the poor
to inadequate compliance for the postoperative CDP
maintenance.

Postoperative lymphoscintigraphic evaluation have shown
correlatable improvement with decreased dermal backflow
and/or increased clearance, etc. on 5 among 8 patients with good clinical response.

Among 6 of 7 patients (7 limbs: 5 females & 2 males: primary-5 &
secondary-2) clinical stage I-II-6: mean age - 34 years) with
initial success of free lymphodes transplant surgery(VLTS), only 3
out of 5 available for the first interim assessment (12 months), have
shown satisfactory response to the surgery clinically. All 3 have
shown viable lymphodes ultrasonographically and/or functioning
status of lymphodes lymphoscintigraphically to support clinical
evidence of improvement.

The results of palliative excisional surgery with modified
Homan's operation on 33 limbs of 22 patients (9 females & 3
males: primary-17 secondary-6: mean age of 43.2 years,
clinical stage III-6 & IV-16), were more striking with closer
relationship with the compliance: 28 out of total 33 limbs (22 patients with good initial (6 months and 12 months)
responses, were reduced to 16 during the interim(24 months)
follow up assessment period, and further to 6 with good
compliance to the final (48 months) assessment.

There has been no evidence of lymphatic function improvement
lymphoscintigraphically even to the clinically successful
patients with the excisional surgery.
**DISCUSSION**

The limited experiences of multidisciplinary approach to combine the CDP, SIPC, and various surgical therapies, on the basis of new concept of total care management, gave us various preliminary informations to improve future management as following:

1. CDP-based total care management appears to be the most effective and physiologic treatment of chronic lymphedema available today. It appears to provide consistently better responses only on its earlier stage (Stage I to II), but more effective when combined with SIPC on the latter to the end-stage (Stage III to IV) of the lymphedema.

2. SIPC seems to have more powerful and faster effect of decongestion of the lower (distal) part of the extremity but with limited success due to tendency to push up the fluid mechanically toward torso (proximally) leaving the edema ring. SIPC, therefore, seems to need sequential and/or simultaneous MLD for the further central mobilization of proximally shifted and retained fluid as edema ring out of the extremity to the torso. SIPC is more effective to improve and maintain overall results of treatment especially to the advanced stage and it can enhance its effect with complementary support by MLD-based CDP.

3. MLD seems to be more efficient on earlier stage (Stage I to II) than later stage (Stage II to III) and more efficient on proximal part than distal part of the extremity.

4. The compliance of the patient and/or the family can not be overemphasized for its critical value since the long-term results of the treatment, either surgical or non-surgical seem to depend on this compliance.

5. Home maintenance care is as important as initial hospital care, to maintain the stabilized results following the in-hospital care, and it will depend on self-initiating motivation with proper commitment by the patients themselves. Therefore, CDP-based treatment should not be started until thorough education convinces the patients of the necessity of life-time commitment to the treatment of this incurable disease to maintain maximum control.

6. To convince them to achieve good compliance, sufficient information about this disease should be provided to the patient and family first, prior to friendly persuasion to improve patient compliance and motivation. Further encouragement of the patient through self-help organization seems to be very effective to maintain the necessary support to each other psychologically and socioeconomically.

7. Multidisciplinary team of our Clinic has set a strict policy against early implementation of the venolymphatic reconstructive surgery at the clinical stage I, in contrast to other leading groups in this field with different indication. We rather limited its indication only to the unequivocal progression of disease from stage I to II despite all the available therapy implemented and declared as the "failure" by the multidisciplinary team. Therefore, most of our candidates already advanced to the clinical stage II with significant progress of the lymphatic failure/paralysis, particularly resistant to the MLD-based CDP distally along the lower leg to foot.

Local condition among our candidates in general was relatively too advanced to find suitable healthy lymph vessels at the femoral level preoperatively, for the standard approach of microsurgical anastomoses (G. Campisi et al. Genova, Italy). Instead, the reconstruction was made at the popliteal/below-knee level with more healthy vessels, advocated by Professor V. Krylov (Moscow, Russia).

Our experiences on the venolymphatic reconstructive surgery are however, very limited with less ideal candidates to restore normal lymphatic function, comparing to those by Campisi's, and its role has been strictly limited as an auxiliary method to supplement the CDP-centered therapy to already damaged lymphatic system in significant degree(s). The FLT was originally adopted for the primary lymphedema but extended also to the secondary lymphedema recently as one of reconstructive surgery when the patients should fail to become candidate for the VLRS. Our preliminary results are quite promising, but we are not yet ready to draw a reliable conclusion on the long term outcome of FLT at this moment(9), and further final evaluation at least up to the second interim follow-up assessment on 24 months and preferably to the final assessment on 48 months to all the FLT patients, including subsequently performed another 2 patients, is warranted.

The new role of FLT as potential substitute of VLRS especially to the patients with relatively advanced stage, and/or with lymphangioglophia involving lymphnodes and lymph vessels among primary lymphedema remains to be confirmed through future multicenter studies.

Our results of excisional surgery to the end stage of chronic lymphedema are much better than those of earlier experiences by others, although our indication was strict, remaining in supplemental role to improve the efficacy of CDP+compressotherapy during the limited period of follow up for no more than 4 years(9). However, it seems to be able to provide easier control of end stage of lymphedema with subsequently better quality of life postoperatively with reduced infective rate.

The reconstructive surgery or excisional surgery should be considered as a part of total care management only when sufficient postoperative CDP can be guaranteed with good compliance to enhance and maintain its complimentary effect on over-all total care.

Preventive and/or control of the infection (local/systemic) is utmost important to delay the progress of the disease, and therefore, liberal commitment to the prophylactic antibiotics should be encouraged even indefinitely when the infection should recur frequently or even on the latent sub-clinical status if indicated(14,15).

It was best way to convince the patient and family that the healthcare provider is able to provide only limited role through super supervision and patients have to learn to take initiative for its own daily home maintenance care.

Therapy regimen should be flexible to accommodate the best-suit treatment to each patient although the MLD-based CDP is...
most effective treatment strategy but only to the fully committed patients in earlier stage. The SPC should be included together with CDP especially to the advanced stage since MLD and SPC seems to hold the mutually complimentary effect as total care.

PROSPECT – PRIMARY LYMPHEDEMA

Although the primary and secondary lymphedema have been treated successfully together in same category of chronic lymphedema, the potential for the future treatment prospect for the primary lymphedema became much clear lately. Therefore, better understanding of these differences in etiology is mandatory for the contemporary management of chronic lymphedema as a whole(9-11,60).

The primary lymphedema represents a clinical manifestation of one of two types of lymphatic malformation (LM). LM is one of various congenital vascular malformation, as the result of developmental arrest occurred in the lymphatic system(10,11). When it should occur in the later stage of lymphangiogenesis, it is classified as the truncular(T) form (Modified Hamburg Classification)(10) and clinically manifested as primary lymphedema. Other form of LM, developed in earlier stage of embryonal life, is classified as the extratruncular(ET) form (e.g. cystic/cavernous lymphangioma) and often combined with other kinds of vascular malformation (e.g. venous malformation)(61-66). Both forms of LM have entirely different characteristics with different clinical behavior so that clear understanding of the relationship between this primary lymphedema as the T form, and other as ET form is essential, since it may exist either alone or together to make the condition more complicated(10).

However, the new prospect of primary lymphedema management is now much bright. Much increased feasibility for the gene manipulation to correct/compensate the genetic defect of lymphangiogenesis as the cause of primary lymphedema will give new opportunity to make fundamental change on our concept to the chronic lymphedema(67-69). And it is also going to give new vision to us for how to lead the management of chronic lymphedema not only for the primary lymphedema but also for the secondary lymphedema (e.g. venolymphangiogenetic manipulation) as well for the future(70,71).

CONCLUSION

The progress of chronic lymphedema, either primary or secondary is no more “incurable” disease but manageable if not preventable, when the ignorance and poor compliance should be overcome together. The new concept of total care management based on multidisciplinary approach to accommodate the new additional role of surgical therapy as adjunct therapy to enhance over-all effectiveness of the CDP-based main therapy, can deliver improved quality of life as the ultimate goal of the management of chronic lymphedema.

REFERENCE


HOW CAN LYMPHEDEMA OF THE UPPER LIMB AFTER AXILLARY DISSECTION DUE TO BREAST CANCER BE MEASURED? REVIEW OF LITERATURE AND A PROPOSAL OF CLINICAL PAPER

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ABSTRACT

BACKGROUND AND PURPOSE: The lymphedema of the upper extremity is a pathology which can give a severe and permanent physical disability. From the clinical picture and the functional assessment we choose the specific rehabilitation plan. The aim of this study is to propose a Lymphological Medical Record and a Measurement Card. An easy and useful method that could help clinical lymphologist and physical therapist to cure these patients.

MATERIALS AND METHODS: Height, body weight and circumference measurements of both upper extremities are taken by physical therapist at the first treatment. The different size of the affected limb and the unaffected limb at various point along the arm are compared. With computer technology (Microsoft Excel) you can have: the centimetric difference between oedematous limb and non-oedematous limb and its average increase%, the difference after treatment and its average reduction% and from the analyses of these data the lymphedema value % after treatment PARTECNST. The study included 10 women with lymphedema of upper extremity after axillary dissection due to breast cancer treated as outpatients.

RESULTS: Before treatment oedematous limb of all patients showed average increase of 15.5% compared with non-oedematous limb. At final treatment oedematous limb of all patients showed average reduction of 40.9% compared with their own initial measurement. At final treatment oedematous limb of all patients showed average value of 10.9% compared with non-oedematous limb.

CONCLUSION: Standard measurement criteria and data collection are lacking. They could be an useful method to assess lymphedema in clinical practice.

KEY WORDS: lymphedema – measurement – breast cancer

Lymphedema of the upper limb is one of the most feared side effects of breast surgery due to tumour.

INTRODUCTION

Thanks to the progress made in surgery, chemotherapy and radiation therapy, women who suffer of breast cancer are able to prolong their life and in many cases to defeat their disease. The axillary dissection as a key surgical act for staging, assessment and subsequent treatment, however, causes a remarkable unbalance in lymph vessels of the upper limb, the remaining part of breast and the thoracic wall, between the quantity of lymph produced and the transportation capacity of the lymph system. In conditions of hypoplasia of the compensation collateral vessels, the lymph system is unable to carry out its task thus causing the lymphedema of the arm.

The incidence of lymphedema is reported variably in the various studies as it can develop either early, i.e. soon after surgical intervention, directly connected to the intervention and the radiation therapy, or after some time, often “triggered” by an infection, an acute lymphangitis, or by an even slight trauma.

In other cases, after a period of stationary conditions, lymphedema develops rapidly: this worsening in health conditions should lead to a diagnosis of the so-called malignant lymphedema.

Most lymphedemas are assessed and treated without hospitalization; this is the reason why they aren’t recorded at national and international level.

Out of the 140 million lymphedemas recorded by the World Health Organization (WHO) in 1994 (latest recorded data), 20 million were post-surgery lymphedemas (caused by the removal of lymph nodes at the root of the limb according to criteria of the surgical treatment), with a greater incidence in the most developed Countries [1].

In a national epidemiological study, carried out by the Italian Society of Lymphangiology between 1997 and 1998 (a year of data recorded by 34 specialist centres located on the national territory), secondary lymphedemas were over 65% and, among this percentage, the post-surgery cases amounted, alone, to about 35%.

According to statistics of the various groups, the incidence of “arm big size” due to post-breast removal or post-quadrantectomy with axillary lympho-adenectomy oscillates around 20-25% (with extreme from 5 to 45%) [2].

If surgery is added to the complementary radiotherapy, the average incidence rises to 35% of cases.
A greater incidence is recorded in patients who underwent quadrantectomy with axillary lymph-node dissection compared to patients who underwent mastectomy. No significant variations due to seasonal or geographical factors connected to climate were recorded.

The variable incidence depends on an early or late diagnosis is made, on the patient being informed on the possible future problems she might have to face, and on health practitioners who often, in the past, did not care of this pathology. Standard measurement criteria and data collection are lacking. Determination of lymphedema starts in the pre-surgery phase, with the assessment of functional conditions of the shoulder girdle and neck, muscle tropism, by the measuring of the upper limb size and with special attention to the unilateral extremity of the tumour loci.

A lymphoedematherapy should be made already in this stage to evaluate lymphatic circulation and drainage through lymph nodes. The co-morbid conditions should be considered, such as: obesity, familiarity to lymphatic disease, metabolic disease, venous insufficiency.

These data allow to define the rehabilitation program tailored to the patient in the post-surgery phase to obtain a rapid functional recovery of the upper extremity. Added to health information on the movement allowed and measures to be taken, these figures represent the essential information that a woman should receive to start her social and/or working life again.

In particular, the arm measurement is essential to recognize and make a diagnosis of lymphedema at its early stage, follow its development and treat the possible side effects. When an early diagnosis is not made and lymphedema has already developed, measurement is usually carried out by comparing the two upper extremities, taking into account the difference in size that the two arms have in normal conditions.

The latter situation is what a physical therapist has often to face with outpatients.

Women who underwent a surgical intervention and realize that their arm has increased in size often turn to the Operative Unit of Rehabilitation Medicine. It is therefore essential to find a valid measurement method in order to have an accurate diagnosis, to decide the appropriate therapy (Complex Decongestive Physiotherapy), as well as to monitor the disease development to prevent severe and recurring lymphangiitic complications.

A study with database ( PubMed/ MEDLINE, SCIRUS and PEDMs) was carried out to find review of literature, consensus conference, guidelines and congress literature which would help to define a valid measurement method for lymphedema. By using key words, i.e. lymphedema-measurement- volumetry-breast cancer, a good number of scientific articles were sorted out, thus proving the great interest that this issue is arousing at international level.

A survey at national level was also made on vascular and lymphatic rehabilitation. A unique, validated and acknowledged method to measure lymphedema is not available yet.

Two primary methods of measuring lymphedema are water displacement volumetric measurements and girth measurement. The water displacement is based on Archimedes' Principle, which states that the water volume displaced is equal to the volume of the object immersed in the water. Water displacement has been considered to be the "gold standard" for its accuracy, with an error of less that 1%, but many researchers chose not to use it because this method is time consuming, expensive and can be unhygienic.

Additionally, the use of water displacement is unsuitable for patients with skin ulcers, in the immediate post-surgery period and doesn't identify the locations of ulcers on the arm. Girth measurements, by taking measurements at fixed points, are simple and clinically useful. This method, however should be avoided avoiding any causes of error: the tension of the tape on the skin, the accuracy in choosing the reference point and the position of the tape with respect to the limb. This method records girth measurements on the oedematous limb, not its volume. A few years ago the interest of many researchers turn to the calculations of volume on the bases of girth measurements at pre-defined points. Various geometrical formulas were tested to measure limb volume and the results obtained are than compared with water displacement results to prove the reliability of measurements. Researchers wish to find an accurate, reliable and time-efficient method and which could be used both hospital and with outpatients.

AM Megens et al. (2001) [1] find to determine if two methods of measuring upper extremity volume, the single truncated cone calculations and the summed truncated cone calculation (using arm circumferences), can substitute for water displacement volumetry. The results of their investigation show that the truncated cone calculation of lymphedema from circumferential measurements cannot be used interchangeably with volume measurements. Both calculated volumes, by the single or summed truncated cone methods, overestimate the volume of the upper extremity by more than 100mL.

The water-displacement volumetry is the only method that will provide an accurate estimate of the volume of the upper extremity. Therefore, as the volume of an upper extremity increases, both volumetry and calculated volume measurements will also increase. Volumetry and calculated volume will change in the same direction wish one another.

This provides researchers with an alternative method for monitoring upper extremity volume. Circumferential measurements can be used in other methods of size determination of upper extremity. Direct comparison of the circumference at varying sides on the arm has been used, as well as alternative calculations that have shown agreement with volume measurements in the lower extremity. Again, water displacement and circumferential measurements do not capture the change of quality of edema. Health care professionals who work with women with lymphedema are attempting not only to decrease the amount of swelling, but also to reduce pain and decrease the hardness in the Jobh issues. It is very important to document change in these features.

Sander et al. (2002) [4] did not find, in literature, any reports in which geometric volume of the hand was included in the total arm volume measurement.
The purpose of their study was to compare geometric methods of determining upper extremity volumes with water displacement.

Geometric volume formulas for a cylinder, frustum, rectangular solid, and trapezoidal solid were used to calculate volumes of the arm and hand at different measurement intervals (3, 6, and 9 cm). They wanted to determine an optimal length of segments for use in clinical practice.

They studied only women with lymphedema. Measuring limbs with edema is different from measuring limbs without edema because of the tissue texture change that accompanies swelling, such as pitting and fibrosis. Both pitting and Ehlers can respond to external pressure on the skin that may alter the accuracy of girth measurements.

They recommended that the frustum formula be used to calculate volume in both the arm and the hand because the geometric frustum volume had the smallest standard error of measurement. They recommended using a frustum volume calculation with measurements in 3-cm segments for the hand and either 6-cm or 9-cm segments for the arm. Although strongly correlated, the measurements obtained by the two methods did not agree.

Karges et al (2003) [5] considered water displacement volume the gold standard to determine limb volume. Therefore, the purpose of their study was to determine the concurrent validity of calculated volume derived from circumference measurements and water displacement volume in lymphedematous and non edematous upper extremities. In their opinion, circumference measurements may be used frequently in the clinic because they are simple and time-efficient.

They calculated the volume using the frustum formula mentioned by Casley-Smith [6]:

\[ V = \frac{1}{3} \pi (C + C + c) l \]

where \( V \) is the volume, \( C \) is the upper extremity circumference, \( c \) is the finger circumference, and \( l \) is the distance between the finger and the elbow. First, they calculated volume of upper extremities with girth measurements in regular intervals from the finger metacarpophalangeal (MCP) joints proximal to the upper arm between the mid-humerus and the axilla.

Second, they determined the upper extremity minus fingers volume by subtracting finger volume from the upper-extremity volume and compared these two kinds of measurements. Third, they compared calculated volume side-to-side differences and water displacement volume side-to-side differences. However, the differences between the measures indicated that they were highly associated but not interchangeable.

Clinicians or researchers should feel confident in using either the calculated volume or the water displacement volume for clinical and research purposes, but they should not mix or substitute methods with a single patient or in a single study.

Lymphovenous Canada (2002) [7] stated that without scientific protocol and standardized measurements, we cannot truly evaluate the effectiveness of treatments for persons with lymphatic disorders.

Lymphovenous Canada looks at the efforts of two researchers: A. Megen (we just know her study) and N. Piller. Neil Piller was charged by Australasian Lymphology Association to reach a consensus on standards of measurement.

"You can’t force people to use standards, but the bair to encourage people to use the standard is that you can talk to someone else about how what they are doing compares with what you are doing. Most importantly, you can get a much better quality of result for your patients, you can collaborate in a research sense to try and get a better understanding and better outcomes for the patient".

Through extensive group discussions, what they came with is hereunder indicated:

- Tape measurements should start from the tip of the middle finger. Measurements should be taken using the narrow tape.
- There should be so minimal pressure in using that tape that there is no indent mark.
- Only take one measurement should be taken unless therapists feel unsure about the measurement in which case we should take two and then average them.
- Measurements should be taken at 10-centimeter measurement intervals.
- Calculation of volume was considered to be very important for scientific study. Most respondents thought volume should be calculated from tape measurements of circumference. Some persons thought it should be calculated from immersion in water and perometry if available for the high level or accuracy and repeatability it gives.

Agreeing to these standards in Australia represented a major accomplishment in getting better outcomes for patients.

MC Kenzie DC and Kalda AL (2003) [7] examined the effect of a progressive upper body exercise program on lymphedema secondary to breast cancer treatment. Lymphedema was assessed by arm circumference and measurement of arm volume by water displacement. They also measured quality of life before and after intervention by the Medical Outcomes Trust Short-Form 36 Survey.

No changes were found in arm circumference or arm volume as a result of the exercise program, but they found an increase in quality of life in the exercise group (SF-36).

Percentage difference of arm volume calculated from the two measurements techniques were also correlated, although the means were significantly different. However, it is impossible with these measurement techniques to know what tissue changes occurred within the upper extremity. Regular exercise is associated with muscle hypertrophy and a loss of adipose tissue. Although arm circumference did not change, we do not know if the level of lymphedema was influenced by the exercise; other tissue changes may have masked any positive effects on lymph accumulation.

Mrfida and Odman (1989) [9] at home years ago told how volumetry and the surface measurements determined only the degree of swelling in the limb and therefore indicated nothing about the complex changes in the mechanical properties of the tissue due to oedema. The aim of their study was to study the changes in the viscoelastic properties of oedematous tissues with treatment. Oedematous tissues was compressed for 20 sec by a cylindrical head 15 mm in diameter to a depth of 4 mm. After withdrawal of the compression head a depression remained due to the translocation of oedematous limb.
Many techniques are available for lymphedema assessment: the vothmetry and other investigation techniques give high level girth measurements are one alternative to water displacement. From the analysis of international paper, the measurement of the circumferential measurement technique has limitation as well as in determining the viscoelastic properties of the oedematous tissues. With the tonometer, the viscoelastic properties of the tissue in compression can be assessed, and the level of tissue tonicity and ultrasound described the characteristic of tissue involvement with filariasis or in those who are evaluated pre- and post-lymphatic-venous-lymphatic anastomoses. Developing good measures will help in determining the incidence of the problem, its response to treatments and the impact of lymphedema on function. This type of measurement should be easy to use, accessible, no expensive, reliable and quantifiable. Quantitative imaging technique are more sensitive but also less accessible and expensive. Measurement of fluid translocation was useful in selecting and evaluating the effectiveness of lymphedema treatment, as well as in determining the viscoelastic properties of the oedematous tissues. Recently Aloisio (2003) [10] assessed the tissue fluid translocation under the action of deformation with an impression tonometer. A very important parameter to evaluate lymphedema is its tissue fibrosis. Subcutaneous pitting edema can be subjectively expressed using the classical clinical test, in which the tissue is indented with the tip of the physicians finger. When the tonometer, the viscoelastic properties of the tissue in compression can be assessed, and the level of tissue tonicity and its changes can be measured in an accurate and repetitive way. Therefore, interesting information about lymphedema can be taken to determine the changes of lymphedema and its reduction after treatment.

Gerber LH (1998) [11] undertaken a review of literature about measurement of lymphedema. Many techniques are available for lymphedema assessment: circumferential measures of limbs at various points, volumetric measures with water displacement, skin tonometry in which soft tissue compression is quantified, magnetic resonance imaging, computerized tomography and ultrasound described the characteristic of tissue involvement - lymphoscintigraphy and Doppler venous to evaluate patients with filariasis or in those who are evaluated pre- and post-lymphatic-venous-lymphatic anastomoses. In the initial assessment is important to observe the skin of the partially operated breast for the risk of complications, such as shoulder girdle and cervical rachis. The clinical examination values the range of motion and the clinical progression of disease. Failure to control lymphedema may lead repeated infections (dermato-lymphangio-adenitis), progressive elephantine tropic changes in the skin and on rare occasions even to the development of a highly lethal angiosarcoma (Stewart-Treves Syndrome).

**MATERIALS AND METHODS**

The lymphedema of the upper extremity is a pathology which can give a severe and permanent physical disability; for this reason in rehabilitation medicine it have to be considered the whole clinical picture. It’s important to know the clinical history of the lymphedema, its possible reason, how and in which way it has come out. We have also to consider the co-morbid conditions such as obesity, metabolic disease, venous insufficiency and familiarity to lymphatic disease. The Lymphangiography is a modern investigation technique which is essential to evaluate lymphatic circulation and drainage through alternative lymphatic vessels to second level lymph nodes. The study of both deep and superficial lymph circulation is useful for therapeutic and prognostic considerations. Physical examination evaluate the extension of disease, the staging of lymphedema and its fibro sclerotic tissue component. When it’s possible it will be interesting to value the fibro sclerotic tissue component with tonometry. In the Measurement Card is considered the all body area with lymphedema. The clinical examination values the range of motion and muscular tropism of shoulder girdle and cervical rachis. Joint limitation associated with muscle hypotrophy don’t allow the functional recovery of the upper limb and produce negative effects in lymphedema. In women underwent to a quadrantectomy is important to assess the partially operated breast for the risk of complications, such as mastitis, and the breast skin changes after radiotherapy. In the initial assessment is important to observe the skin of the
hand, its hydration and if there are some micro injuries or microtraumas that could start lymphangitis disease. The cure of the hand is index of the cure women have by herself and the kind of her activity daily living. We also assess the arm sensibility and if there are paresthesias produced by lymphedema. From description of patient pain and disability, we can know her way of life, her knowledge about lymphedema and its impact in daily activity. Height, body weight and circumference measurements of both upper extremities are taken by physical therapist at the first treatment. The different size of the affected limb and the unaffected limb at various point along the arm are compared. From the clinical picture and the functional assessment we choose the specific rehabilitation plan.

With computer technology (Microsoft Excel) you can have:
- the centimetric difference between oedematous limb and non-oedematous limb and its average increase in %,
- the difference after treatment and its average reduction in %
- and from the analyses of these data the lymphedema value in % after treatment

Body weight and circumference measurements are taken by the same physical therapist at the last treatment.

Body weight is controlled every follow-up to avoid false assess of lymphedema.
Rehabilitation Plan

<table>
<thead>
<tr>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manual lymph drainage</td>
<td>Pneumatic compression</td>
</tr>
<tr>
<td>Compressive bandage</td>
<td>Low-stretch elastic garment</td>
</tr>
<tr>
<td>Range of motion exercise</td>
<td>Health care education</td>
</tr>
</tbody>
</table>

The Combined Physical Therapy is considered the better therapy of peripheral lymphedema by the International Society of Lymphology. This methodology generally involves a two-stages treatment program: the first phase consists of skin care, manual lymph drainage, range of motion exercise and compression, typically applied with multi-layered bandage-wrapping. The second phase (initiated promptly after phase one for maintain and optimize the results obtained) consists of skin care, compression by a low-stretch elastic stocking or sleeve and continued "remedial" exercise. A prescription for low stretch elastic garments (custom made with specific measurement if needed) to maintain lymphatic reduction after CPT is essential for long-term care.

The physical therapist teach the patients about their pathology, how they can care their limb. Every patient may be the protagonist of her clinical improvement. Great adhesion of patient to the therapeutic protocol allow to obtain the better reduction of arm oedema.

The prevention of lymph stasis is very important to prevent severe and recurring lymphangitis complications and it can be considered a long-term objective. Self-lymph drainage technique are taught to woman that demonstrate attention at their therapeutic protocol. The study was done on 10 outpatient women with lymphedema of upper extremity after axillary dissection due to breast cancer. The patients had a mean age of 68 years (range 57 to 88). The patients had undergone different breast cancer treatment, but all of them had axillary node dissection (tab 1).

Table 1: Kind of breast cancer treatment and patient population

<table>
<thead>
<tr>
<th>KIND OF BREAST CANCER TREATMENT</th>
<th>NUMBER PATIENT</th>
<th>PATIENT POPULATION %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mastectomy</td>
<td>3</td>
<td>30%</td>
</tr>
<tr>
<td>Quadrantectomy</td>
<td>7</td>
<td>70%</td>
</tr>
<tr>
<td>Axillary dissection</td>
<td>10</td>
<td>100%</td>
</tr>
</tbody>
</table>

The study was done on 10 outpatient women with lymphedema of upper extremity after axillary dissection due to breast cancer. The patients had a mean age of 68 years (range 57 to 88). The patients had undergone different breast cancer treatment, but all of them had axillary node dissection (tab 1).

Table 1: Kind of breast cancer treatment and patient population
Eight patients had undergone post-surgical therapy, two patients had no additional treatment.

**Table 2: Post-surgical therapy and patient population.**

The time of edema beginning since the surgery treatment was 2.3 years (ranged from 1 month to 7 years).

**Table 3: Time edema beginning and patient population.**

Patients showed lymphedema at different clinical stage (Table 4). (Clinical staging by the Italian Society of Lymphangiology guidelines[13])

**PROCEDURE**

Before treatment all patients underwent measurements of both upper limb and body weight. At the end of the treatment the measurements of oedematous limb and body weight are repeated. If from the beginning to the end of the treatment there are differences about the weight, also the not oedematous limb have to be measured again.

That’s an important parameter because body weight changes don’t allow to value the result.

The initial and the final measurement was carried out by the same physical-therapist. It’s important that each physical therapist finds to standardize his own measurement method to reduce errors.

All measurements are performed under identical conditions: the therapist uses a narrow tape calibrated in centimetres there should be so minimal pressure in using the narrow tape circumference measurements are taken at fixed point on the subject in the supine position with arms resting comfortably at the sides circumference measurements are taken by the same therapist at the first and the last treatment.

By using this particular method is especially important to have an adequate number of points to be measured.

Sides for measuring upper extremity circumference: 1° level - metacarpophalangeal joint 2° level - ulnar styloid process 3° level - 15 cm down from elbow 4° level - 10 cm down from elbow 5° level - 5 cm down from elbow 6° level - elbow 7° level - 5 cm above elbow 8° level - 10 cm above elbow 9° level - 15 cm above elbow

**DATA ANALYSES**

Each patient received 17 treatments (range from 10 to 30) of manual lymph drainage, compression bandaging and upper extremities exercises. Four patients received also cervical exercises.

Clinical evaluation of the outcome of therapy showed a decrease in the circumference of the oedematous limb in all the patients.

All the patients received health care education about lymphedema.

For every measurement level have been calculated:

- **Difference before treatment** = oedematous limb - non-oedematous limb
- **Increase %** = \( \frac{\text{Difference before treatment}}{\text{Non oedematous limb}} \) \times 100
- **Difference after treatment** = final edema - initial edema

**Table 4: Clinical stage and patient population**

**Table 5: Post-surgical therapy and patient population.**

**Table 6: Time edema beginning and patient population.**

**Table 7: Clinical stage and patient population.**

**Table 8: Data analyses.**
For all these dates have been calculated the average:

\[
\text{Average Increase} \% \ = \ \text{addition increase} \% \\
\text{Average Reduction} \% \ = \ \text{addition reduction} \%
\]

\[
\text{Average Lymphedema value after treatment} \% \ = \ \text{Medium increase} \% \ \text{less Medium reduction} \%
\]

This is the measure of lymphedema after treatment compared with non-oedematous limb

<table>
<thead>
<tr>
<th>Table 5: patients dates</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PATIENT</strong></td>
</tr>
<tr>
<td>M.E.</td>
</tr>
<tr>
<td>D.C.</td>
</tr>
<tr>
<td>G.P.</td>
</tr>
<tr>
<td>B.A.</td>
</tr>
<tr>
<td>C.M.P</td>
</tr>
<tr>
<td>C.M.L</td>
</tr>
<tr>
<td>C.C.</td>
</tr>
<tr>
<td>L.F.</td>
</tr>
<tr>
<td>P.I.</td>
</tr>
<tr>
<td>S.M.C.</td>
</tr>
<tr>
<td><strong>AVG. OF ALL PATIENTS</strong></td>
</tr>
</tbody>
</table>

Before treatment oedematous limb of all patients showed average increase of 15.5% compared with non-oedematous limb (ranged from 3.8 to 29.2).

At final treatment oedematous limb of all patients showed average reduction of 40.9% compared with their own initial measurement (ranged from 5.1 to 96.9).

At final treatment oedematous limb of all patients showed average value of 10.9% compared with non-oedematous limb (ranged from 0.1 to 29.3).

Patients dates are compared with their clinical stage.:

| Table 6: Patients Lymphedema modification and clinical stage |
|-----------------|-----------------|-----------------|
| **CLINICAL STAGE** | **NUMBER PATIENTS** | **AVG. INCREASE** | **AVG. REDUCTION** | **AVG. LYMPHEDEMA VALUE AFTER TREATMENT** |
| I* | 2 | 5.9% | 11.0% | 2.8% |
| II* | 5 | 12.1% | 47.2% | 3.2% |
| III* | 2 | 25.4% | 22.1% | 19.3% |
| IV* | 1 | 29.2% | 17/0% | 26.3% |

Patients with lymphedema at second and third stage have obtained best reduction of girth measurements.

Patients with lymphedema at fourth and fifth stage have obtained less reduction of girth measurements. In spite of these patients felt reduction of heaviness and tension sensation referred before treatment.

The patient with post-trauma lymphedema had tolerated bandage only few hours every day, obtained the smaller average reduction (5.1%).

The patient who obtained the best reduction showed lymphedema in second stage beginning one month after breast treatment. She was treated early and at the final treatment there was no differences between the upper limbs size.

Before treatment the patient at the fifth clinical stage showed the worst average increase (29.2%) and at final treatment her average lymphedema value was 26.3%. She was at her first lymphedema treatment!!!! I take also a photo of the upper-extremities of this patient.

**DISCUSSION**

The Lymphological Medical Record and the Measurement Card, together with imaging technique, could help the clinician and the physical therapist to care women with lymphedema. They could be an useful method to assess lymphedema in clinical practice.

Girth measurements don’t give the arm volume but manage to make evident the lymphedema changes.

However is possible to obtain the “calculated volume” by use of mathematical formulas.

The clinical examination values the range of motion and muscular tropism of shoulder girdle and cervical rachis. Height, body weight and circumference measurements of upper extremities are taken at the first treatment. From the analysis of these dates you can define the specific rehabilitation plan.

A photo of the upper limb can help to show the lymphedema changes after treatment.

**CONCLUSION**

Prevention of lymphedema starts in the pre-surgery phase, with the assessment of functional conditions of the shoulder girdle and neck, muscle tropism, and with measuring of the upper limb size, with special attention to the unilateral extremity of the tumour location.

To fight lymphedema it is important an early diagnosis and an early Combined Physical Therapy. The measurement of upper extremities is still open to questions.

Without a valid and reliable method of measurement, accurate comparisons of treatment effectiveness, of therapeutic modalities remain impossible.

It is desirable that the International Society of Lymphology gives standard indications about how to take circumference measurements, at which fixed point and in which position is placed the subject.
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FACIAL LYMPHEDEMA IN MELKERSSON-ROSENTHAL SYNDROME.

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ABSTRACT:
The Melkersson-Rosenthal syndrome is a rare disorder characterized by the triad: recurrent facial edema, facial nerve paralysis and lingua plicata. We present the case of a woman diagnosed of Melkersson-Rosenthal syndrome that started at six years of age with recurrent swelling of the face and lip that has developed a facial lymphedema after several outbreaks. She was treated with metronidazol, estanozolol and systemic corticosteroids with lack of response. Physical therapies for lymphedema will try to reduce the swelling and fibrosis.

KEY WORDS: Melkersson-Rosenthal syndrome; Miescher’s cheilitis granulomatosa; Facial edema; Lymphedema.

The Melkersson-Rosenthal syndrome is a rare disorder that was first described in 1928 as a facial edema and paralysis and in 1931 Rosenthal reported the additional feature of lingua plicata, or fissured tongue. The complete triad: recurrent facial edema, facial nerve paralysis and lingua plicata is very rare, and monosymptomatic and oligosymptomatic variants are more common, that’s why the diagnosis may be difficult.

CASE REPORT:
We present the case of a woman diagnosed of Melkerson-Rosenthal syndrome that has developed a facial lymphedema. A 25-year-old woman presented a right-sided lymphedema of the face and upper lip to the Lymphedema Unit. Her medical history was a recurrent angioedema of the face and lip that started at six years of age, with multiples outbreaks that were irregular and othas related with herpes simplex virus infection. She also presented with the asymmetric right-sided facial swelling an erytematous eruption that was painless and nonpruritic accompanied with nonpitting edema, as well as right-sided cervical adenopathy (Figure 1). Facial palsy was absent. In the last times, the attacks have become more and more frequent, and now she is having one recurrence per month that stays for 7 to 10 days. After several attacks, facial edema became chronic with a consistence similar to lymphedema that did not reduce after the outbreak. Oral examination revealed a fissured tongue. We were unable to identify evidence to support an allergic or a hereditary cause for the syndrome, the last because she was adopted in childhood and doesn’t have any relationship with her biological parents.

The laboratory findings were normal and all the allergy lest results were negative. In the dematology service, the magnetic resonance showed a non hemorrhagic, non ischaemic, non malformative process. Only the edema in the right cheek with a trabeculated fat tissue and cervical adenopathies were identified. The biopsy specimen of the upper lip showed a small non necrotizing granuloma between salivary acini (Figures 3 and 4).

She was treated with metronidazol, estanozolol and systemic corticosteroids with lack of response. Physical therapy was prescribed to try to reduce the swelling and fibrosis, not to prevent a new attack. It consisted in self-drainage, exercises and a compression mask during the night. We find it difficult to assess the results during the remission phase (Figure 2).

DISCUSSION:
The prevalence of the syndrome is low and there are near 300 cases reported in the literature. But the incidence must be higher, and many cases lacking the complete triad are misdiagnosed. The syndrome is more frequent in women being the ratio 2: 1, according to Zimmer. The age at onset of the disease varies widely with a mean age of 33 years according to the studies of Greene and Zimmer. The Melkersson-Rosenthal syndrome is rarely seen in childhood. The syndrome is generally thought to be more common in Europe than in North America.
Clinical Manifestations

Orofacial swelling is the most common presentation of Melkersson-Rosenthal Syndrome affecting between 80 to 100% of the patients, and it is the first symptom in 40% of the cases. In some patients the upper lip was affected with episodic and recurrent swelling and in others it was a permanent edema. The swelling can affect only the lip causing dysesthesias of the tongue, or the face have involvement as dysesthesias of the tongue, or the face have been described. The facial nerve is affected in 33% to 47% of the patients in Zimmer' study and palatal involvement in 10% of the cases. Few cases have been described with eyelid edema. This recurrent episodic edema presents as an attack of erythematous eruption that last some days or weeks without systemic involvement and is always painless, nonpitting, and does not reduce after the bout, during the intermittent phase. After many attacks, facial edema becomes chronic, and does not reduce after the bouts during the intermittent periods of remission. The skin has a peau d'orange texture due to systemic and intralesional corticosteroids, antibiotics, radiotherapy and reduction cheiloplasty have been tried to reduce the swelling and control the recurrent episodes, with partial results. The association with Crohn's disease has been well documented in the past, but no evidence of Crohn disease was found in our case. The Physical Therapy was performed not to prevent the recurrence but to reduce the lymphedema and the fibrosis. It constitutes Melkersson-Rosenthal syndrome, and it is not patognomonic. It has been reported to be the first symptom of the syndrome in just one case, while 60% of the cases present it with the time in different degrees. Such a nonspecific and frequent complaint is supposed to remain unnoticed to the medical team, and it is probably diagnosed only when other features of the syndrome appear.

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consisted in training the patient in self-drainage following Földi’s indications**, exercises and a compression mask during the night. We did not find in the literature any reported case of Melkersson-Rosenthal syndrome treated with Complex Physical Therapy for the lymphedema.

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LYMPHOLOGY IN MEDICAL AND SURGICAL PRACTICE
ITALIAN GUIDELINES LOOKING TOWARDS EUROPE AND THE WORLD

C. Campisi, S. Michelini, F. Boccardo
Italian Society of Lymphangiology (SIL)

Friday, October 29, 2004, by the Department of Surgery of the University of Genoa, a meeting on "Lymphatic Microsurgery" was organized and coordinated by Prof. C. Campisi, in the ambit of the so called "lveve Project", which aims at creating a real scientific network among distinguished international experts in different surgical fields (Fig. 1). During the meeting, two surgical operations were carried out of derivative lymphatic-venous microsurgery for the treatment of lower and upper limb lymphedemas. Prof. W. Okazewski, from the Medical Research Center of the Polish Academy of Science of Warsaw, Poland, took part in the first operation, upon the lower limb, together with the Italian surgical team, Prof. C. Campisi and Prof. F. Boccardo. The operation was transmitted to the Auditorium and to the University of Arizona, Tucson (AZ, USA) by "interactive" teleconference between the two scientific centres.

In the Auditorium, the Session was chaired by Prof. M. H. Witte, from the Department of Surgery of the University of Arizona College of Medicine of Tucson, Prof. E. Falchieri, from the Institute of Pathological Anatomy of the University of Genoa (Italy), and Prof. S. Michelini, from the Neuro-Vascular Rehabilitation Center of S. Giovanni Battista Hospital of Rome (Italy). Among the foreign experts, there were also the President of the International Society of Lymphology, Prof. M. O. Okumura, from Kinki University, Saki (Japan), Professors Etelka and Michael Foldi, from the FoldiKlinik, Hinterzarten (Germany), Prof. G. Thibaut, from the University Henri Poincaré, Nancy (France), and the therapist J. P. Belgrado, from the Free University of Brussels (Belgium). Prof. A. Passas, from the Department of Surgery of the Hospital Bagnolet, sur-Cite (France), participated in the second operation, upon the upper limb, together with the same Italian surgical team. From the surgical point of view, it was pointed out that with the advent of Microsurgery, functional and causal therapeutic solutions for lymphedemas were investigated and implemented, aiming at draining the lymph flow or reconstructing the lymphatic pathways where they had been obstructed or were missing. Microsurgery techniques have yielded positive and long-lasting results in the treatment of primary lymphedemas - including those in children - as well as in secondary lymphedemas following cancer treatment. Among derivative microsurgery techniques, aiming to restore lymph flow at the obstruction site, through a lympho-venous drainage, multiple end-to-end and end-to-side lymphatic-venous anastomoses are most commonly employed. Conversely, with reconstructive microsurgery techniques, the lymphatic flow is restored by overcoming the obstruction site through the implant of autologous vein segments between collectors down and upstream the obstruction: lymphatic-venous-lymphatic plasty (LYLA).

Indications for the various microsurgical techniques depend on the presence of a viable lymphatic-venous pressure gradient in the affected limb. Should lymphostatic deficiency be associated with venous insufficiency (a condition mostly found in the lower extremities: varices, venous hypertension, valvular incompetence), derivative microsurgery is not recommended, while only reconstruction techniques can be applied. Another important item was discussed during the meeting concerning immunohistochemical investigations. Interesting immunohistochemical investigations have recently been conducted on lymphatics-lymph node material taken during the same lymphatic microsurgical operations and on the intimal matrix. These studies have yielded valuable information on lymphedema pathophysiology. In particular, dysfunctions of lymphatic vessel walls and of lymph nodes have been identified and classified. They progressively develop and evolve as parallel with lymphedema progression and, more specifically proportionally with lymphedema duration. These observations have confirmed that, for a proper treatment of this disorder, whenever lymphatic drainage is lacking or obstructed, it is essential to restore its good functioning, as soon as possible. In this way, successful and long-lasting results will be obtained, through the preservation of a good autonomous lymphatic pump performance linked with smooth muscle fibrocellular tissues that are normally present in lymphatic pre-collectors and collectors, as well as in lymph node capsules. With disease progression, smooth muscle cells are gradually lost and replaced by non-dynamic fibrosclerotic tissue.

Moreover, on Saturday 30 October 2004, a meeting on the Italian Guidelines on "Diagnosis and Treatment of Lymphedema" was organized and coordinated by Prof. C. Campisi, with the participation of distinguished experts in the field of Lymphology coming from all over Europe, the United States, and Japan. It was a good occasion to update and integrate the guidelines upon different items such as: classification and staging, diagnosis, non operative and operative treatment, prevention, angiodysplasia-lymphedema syndromes, immunohistochemical findings (Fig. 2). Furthermore, the clinical and research activities of various lymphological centers throughout the world were also reported. The Italian Guidelines, like the Consensus Document of the International Society of Lymphology, include different diagnostic and therapeutic protocols carried out worldwide and adapted to the socio-economic and sanitary situation of our Country. With those considerations, these guidelines represent an evidenced based tool to approach patients affected from peripheral lymphoedema and at the same time is continuously updated on the basis of wide discussions at local, national and international meetings in Lymphology and related disciplines.
ULYMPHOLOGY IN MEDICAL AND SURGICAL PRACTICE: ITALIAN GUIDE-LINES LOOKING TOWARDS EUROPE AND THE WORLD

I.ymphologic Research and Clinical Activity:
- A. D'Alberto (Department of Hematology, University of Bari, Italy)
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- C. Trabucchi (Department of Surgery, University of Padua, Italy)
- D. Ceribelli (Department of Surgery, University of Milan, Italy)
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- H. F. Taveras (Department of Surgery, University of Genoa, Italy)

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Final Remarks
A. Costa and A. Debarba (Department of Surgery, University Hospital San Martino, Genova, Italy)

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