Liposuction and Controlled Compression Therapy in the Treatment of Arm Lymphedema following Breast Cancer

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by

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To Karin, Erik, Oskar, Axel,
and in memory of my parents

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Håkan Brorson

leg. läkare, Bl

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Title and subtitle
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Abstract
About one-third of all women treated for breast cancer develop arm lymphedema. The cancer itself is a worry, but the swollen and heavy arm is an additional handicap for the patients, both physical and psychosocial. Previous surgical and conservative treatments have not always given satisfactory and permanent results, conceivably because lymphedema causes hypertrophy of the subcutaneous adipose tissue. From this point of view, liposuction (LS) combined with Controlled Compression Therapy (CCT) is an interesting approach as the hypertrophied adipose tissue is effectively removed and the outcome sustained by wearing a compression garment.

Altogether 51 women participated in the present investigations. All, except one had received radiotherapy after the breast cancer operation which included the excision of axillary lymphnodes in all cases. Thirty-six patients were treated with LS and postoperative CCT, whereas 15 received CCT only.

Pre- and postoperative arm edema volumes were measured using water displacement technique. Skin blood flow was recorded using laser Doppler imaging. Lymph transport in the arm was assessed with indirect lymphoscintigraphy. Rage of motion in the shoulder joint was measured using a protractor. Effects on quality of life were estimated using the Visual Analogue Scale, Nottingham Health Profile, Psychological General Well-Being index, and the Hospital Anxiety Depression scale. Results were monitored for up to one year after treatment.

LS+CCT reduced the arm edema volume completely, compared with a 50% decrease following CCT alone. The use of a compression garment after liposuction is necessary to maintain the normalized arm volume. LS+CCT did not affect the already impaired lymph transport; it merely increased skin microcirculation. A reduced incidence of cellulitis was noted. The treatment improved range of motion in the shoulder joint and patients' quality of life, particularly qualities directly related to the volume reduction and thereby qualities associated with everyday activities. As could be expected from the volume measurements, the more favorable outcomes were recorded mostly in the LS+CCT group.

Key words: arm lymphedema, breast cancer, liposuction, controlled compression therapy, skin blood flow, laser Doppler imaging, lymphoscintigraphy, VAS, shoulder mobility, Nottingham Health Profile, Psychological General Well-Being index, Hospital Anxiety and Depression Scale, quality of life

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ABSTRACT

About one-third of all women treated for breast cancer develop arm lymphedema. The cancer itself is a worry, but the swollen and heavy arm is an additional handicap for the patients, both physical and psychosocial. Previous surgical and conservative treatments have not always given satisfactory and permanent results, conceivably because lymphedema causes hypertrophy of the subcutaneous adipose tissue. From this point of view, liposuction (LS) combined with Controlled Compression Therapy (CCT) is an interesting approach as the hypertrophied adipose tissue is effectively removed and the outcome sustained by wearing a compression garment.

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LIST OF PAPERS

The thesis is based on the following papers which will be referred to in the text by their roman numerals:

I. Brorson H, Svensson H.
Complete reduction of lymphoedema of the arm by liposuction after breast cancer.
Scand J Plast Rec Surg Hand Surg 1997; 31: 137-143.

II. Brorson H, Svensson H.
Skin blood flow of the lymphedematous arm before and after liposuction.
Lymphology 1997; 30: 165-172.

III. Brorson H, Svensson H, Norrgren K, Thorsson O.
Liposuction reduces arm lymphedema without significantly altering the already impaired lymph transport.
Lymphology. [In press]

IV. Brorson H, Svensson H.
Liposuction combined with controlled compression therapy reduces arm lymphedema more effectively than controlled compression therapy alone.
Plast Reconst Surg 1998;102: 1058-1067.

V. Brorson H, Svensson H, Wiklund I.
Quality of life following liposuction and conservative treatment of arm lymphedema. [Submitted for publication]

BREAST CANCER

Breast cancer incidence

Breast cancer is the most common type of cancer among Swedish women (27%). According to the Swedish National Board of Health and Welfare the incidence of breast cancer has increased by about 1% per year over recent decades (Cancer incidence in Sweden, 1995). The registered increase in breast carcinoma incidence can partly be attributed to the introduction of mammography screening, and increased longevity. The occurrence of axillary metastases has, on the other hand, decreased. In the city of Malmö, for example, 52% were node positive 1961-70, whereas 36% were node positive in 1981-88 (Garne et al. 1994).

Breast cancer treatment

Modified radical mastectomy is recommended for patients with large tumors, multifocal tumors, or microcalcifications extending more than one quadrant, when there are clinical signs of obvious axillary node involvement, in elderly patients or patients with concomitant disease where postoperative radiotherapy should be avoided.

Breast conserving therapy, including partial mastectomy and postoperative radiotherapy directed at the remaining breast tissue, is recommended for smaller tumors and when the relation between tumor size and breast size is such that a cosmetically acceptable result can be achieved, which is usually not the case when the resection must extend over more than a quadrant. The patient must not have any additional disease which makes postoperative radiotherapy unsuitable (Cedermark et al. 1984, Aspegren et al. 1988, Veronesi et al. 1993, Rydén 1996).

When there is extensive axillary node involvement, adjuvant radiotherapy is usually given to the remaining breast or the thoracic wall and to the axillary and supraclavicular lymph nodes (Wallgren 1977, Auquier et al. 1992)

Arm lymphedema following breast cancer treatment

The incidence of lymphedema of the arm following mastectomy ranges between 8% and 38%, depending mainly on whether axillary lymph nodes are excised and radiation is given. Other factors such as recurrent infections may increase the incidence still further, but differences in the definition of edema may also contribute to the differing figures (Swedborg & Wallgren 1981, Kissin et al. 1986, Borup-Christensen &

Lundgren 1989, Segerström et al. 1992). In an attempt to minimize surgery of the axilla in node negative patients lymphatic mapping and the sentinel node technique has started to be applied in breast cancer treatment (Veronesi et al. 1997).

Due to increased breast cancer incidence, reduced mortality due to breast cancer (Garne et al. 1997), and prolonged mean length of life, more women will face the risk of developing lymphedema. Lymphedema negatively affects activities of daily living, work capacity and leisure activities. Consequently it is important to avoid overtreatment which can lead to a high incidence of treatment-induced morbidity.

Mainly for therapeutic reasons, attempts have been made to classify arm edema. Such classification can be based either on circumferential or volumetric measurement, or on functional disabilities or symptomatic syndromes.

Treves (1957) used the following definitions of the degree of swelling: temporary or slight, up to 3 cm in circumference larger than the normal arm; moderate, between 3 and 6 cm; and severe, more than 6 cm. Lobb and Harkins (1949) distinguished: slight, less than 1.5 cm; moderate, between 1.6 and 2.9 cm; and severe, more than 3 cm. Tracy et al. (1961) defined edema as a difference in volume: slight, 150–400 ml; moderate, 400–700 ml; and severe, >750 ml. The definition used by Stillwell (1977) was based on the volume of the edema in relation to the volume of the contralateral limb expressed as a percentage: insignificant, <10% difference; slight, 10–20%; moderate, 20-40%; marked, 40-80%; and severe arm edema, >80%.

The lymphedema can also be classified according to clinical signs as proposed by ISL (International Society of Lymphology 1985). Grade I edema is characterized by pits left after pressure, it is largely reduced or completely restored by arm elevation, and clinically there are no or only slight signs of fibrosis. Grade II edema is characterized by moderate to severe fibrosis and it does not respond to either pressure or arm elevation. The patients in the present studies all had Grade II edema. Elephantiasis is a severe form of Grade II edema.

LYMPHATICS

Anatomy

Herophilos discovered the lymph vessels as long as ca. 300 BC (Herophilos, cited by Hirsch 1886). However, it was not until 1627 that Gasparo Asellio delineated the "mesenteric lacteal vessels" (Asellius 1627). In 1647, Pecquet described the cisterna chyli and the thoracic duct (Pecquet 1651). The discovery of the lymphatic system is ascribed to Olof Rudbeck of Sweden, who in 1652 at the age of 22, submitted his medical thesis *De Circulatione Sanguinis* and the following year published his discoveries concerning the "vasa serosa" (Rudbeck 1653). In 1653, Bartholin, described the "vasa lymphatica" (Bartholin 1653).

Modern technology has given us a detailed insight into the structure of the lymphatic system. The initial lymph vessels, the lymphatic capillaries of the soft tissues, consist of a single endothelial layer. They start 'blind', are valveless, branch abundantly, and anastomose freely. The prelymphatic tissue channels, located distal to the lymphatic capillaries, do not possess an endothelial lining and are not considered to be lymphatic vessels. The lymph capillaries communicate with larger vessels, the precollectors, which in addition also contain an accessory membrane, few muscle cells, and valves. Next, the lymph collectors consist of three layers corresponding to the inner, medial, and adventitial coats of arteries and veins, although the boundaries are often indistinct. They also contain valves. The lymphatic ducts form the main parts of the transporting vessels. The walls are supplied by blood from the vasa vasorum originating from the adventitia.

The superficial lymphatic system consists of a minute dermal network that drains into the subdermal and subcutaneous lymphatic systems that merely follow the superficial veins. The deep lymphatic system is located beneath the deep fascia and follows the main blood vessels. The superficial and deep systems are considered to be anatomically distinct from one another. However, connections between the two systems have been demonstrated, particularly under pathological conditions (Malek et al. 1964). In addition to these inter-lymphatic anastomoses, lymphovenous communications have also been found, some of which seem to function constantly whereas others do so under pathological conditions only (Aboul-Enein et al. 1984).

The superficial and deep lymphatics unite distinctly in regional lymph nodes. Such nodes are located along the course of lymphatic vessels, whose contents pass through the nodes on their way to the main lymphatic ducts. The ducts finally carry the lymph to the central venous system.

Normal turnover of tissue fluid

The rate of filtration along a capillary depends upon the filtration pressure gradient, i.e. the hydrostatic pressure in the capillary minus the hydrostatic pressure of the interstitial fluid. The filtration pressure is counteracted by the inwardly directed protein osmotic gradient, due to the presence of large amounts of proteins in the blood plasma, viz. oncotic pressure. Normally, fluid moves into the interstitial space at the arteriolar end of the capillary, and back into the capillary at the venular end. Fluid efflux, however, slightly exceeds influx across the capillary membrane and the net filtrate enters the lymphatics and drains back to the bloodstream. This steady-state maintains a stable interstitial pressure.

Normal molecular exchange

Exchange of molecules between plasma and interstitial fluid is determined by passive diffusion. Circulating plasmaproteins and lipids leave the bloodstream through the wall of the arterial capillaries. Most of them are recycled to the blood circulation via the venous capillaries. However, larger molecules cannot readily re-enter venous capillary walls. Some are lysed by macrophages and can thereafter enter the venous capillaries. This is called the extra-lymphatic mastering of plasma proteins. Others leave the interstices by entering openings between the endothelial cells of the initial lymph vessels (Clodius 1990).

Lymph transport following breast cancer treatment

Various states of abnormality have been characterized by Földi (Földi et al. 1989). Lymphatic load is defined as the amount of plasma proteins and the volume of capillary filtrate not cleared from the interstices by venous outflow and extralymphatic mastering. The "lymphatic safety factor" implies that the normal lymph vascular system is able for a time to handle an increased lymphatic protein and water load and thus prevent edema. "Dynamic insufficiency" or "high output failure" arises if the lymphatic load exceeds the lymphatic transport capacity. This is typically caused by venous obstruction, simply leading to an excess of tissue fluid. Another form of insufficiency, "mechanical insufficiency" or "low output failure" is caused by a reduction in transport capacity by some pathological process affecting the lymph vessels or nodes. Conceivably, this situation occurs after breast cancer treatment. Indeed, this situation is taken as the definition of lymphedema, namely a high protein edema caused by reduced lymph transport capacity with insufficient tissue proteolytic activity in the face of a normal lymphatic load (Witte et al. 1977, Földi 1983). If lymphatics with a reduced transport capacity are additionally subjected to an increased load, a severe form of insufficiency develops, called "safety valve insufficiency". Surprisingly, resection of the axillary vein in connection with the primary cancer operation did not provoke a serious situation (Neuhof 1938, MacDonald 1948).

Breast cancer treatment typically includes excision of regional axillary lymph nodes as staging and often radiotherapy for eradication of regional tumor spread. Both measures interfere with normal lymph drainage from the arm, and subcutaneous arm lymphedema commonly ensues. Accumulation of interstitial fluid gradually increases tissue pressure and thereby reduces (counterbalances) the filtration pressure gradient. Excess tissue fluid also reduces the protein osmotic gradient by virtue of an increased content of osmotically active macromolecules in the interstices. Both effects interfere with the normal turnover of tissue fluid.

The interrelationship between microvascular blood flow and subcutaneous fat is not completely understood, and the pathophysiological state of the lymphedematous arm does not make matters easier. In normal subjects, however, Larsen (Larsen et al. 1966) found that the thicker the subcutaneous fat layer, the smaller the blood flow per unit weight, and a slow flow rate is considered one condition for lipogenesis and further deposition of fat (Vague & Fenasse 1965, Smahel 1986, Ryan & Curri 1989, Ryan 1995). This may explain the marked hypertrophy of the adipose tissue seen in our patients. Subsequently subcutaneous lymphedema becomes firm and more dense. Probably pinocytosis of white blood cells, in combination with activation of fibrocytes, increases the connective tissue component of the primordial loose subcutaneous fat (Casley-Smith & Gaffney 1981, Gaffney & Casley-Smith 1981). Although it is not exactly known how these phenomena alter the microcirculation, or how microcirculatory changes themselves influence the lymphedema, the aforementioned sequence of events leading to lymphedema and subcutaneous tissue hypertrophy becomes a vicious circle.

TREATMENT OF ARM LYMPHEDEMA

Conservative treatment

Non-surgical ways to treat lymphedema were first used by von Winiwarter, who introduced physical therapy (von Winiwarter 1892). He applied the classical massage techniques, such as pétrissage, effleurage, frictionement and tapotement, which had been introduced by the founder of physiotherapy, Pehr Henrik Ling of Sweden, in 1813 (Asdonk 1995). Winiwarter also emphasized the complex decongestive treatment, consisting of meticulous cleanliness, bedrest, elevation of the swollen arm, exercises and compression bandages (Földi & Földi 1981). His massage technique was rather crude compared with that introduced by Vodder in 1932; Vodder used a specific light massage technique, manual lymph drainage, to improve lymph flow, especially in patients with primary lymphedema (Vodder 1936, Vodder 1965). The edema reduction achieved by these methods could not be maintained, however, because suitable compression garments were not available at that time (Casley-Smith & Casley-Smith 1992, Morgan et al. 1992). In 1969, Stillwell developed a variant of complex decongestive treatment, quite unaware of von Winiwarter's published work. He advocated mainly firm massage and pneumatic compression (Stillwell 1969, Földi & Földi 1981, Földi et al. 1985). Vodder's technique was further refined by Asdonk in 1963 (Hutzschenreuter et al. 1991, Asdonk 1995). He called the improved technique *manuelle Lymphdrainagetherapie* (manual lymph drainage therapy, MLD). In 1978, Földi, after collaborating with Asdonk, further developed Vodder's original technique, combining it with Winiwarter's complex decongestive treatment, and introduced *komplexe physikalische Entstauungstherapie* (complex decongestive physiotherapy) (Földi & Földi 1981a, Földi & Földi 1981b, Földi et al. 1985, Földi et al. 1989). This technique combines manual lymph drainage, skin care, remedial exercises, and compression bandaging complemented by compression garments. Földi also defined two treatment phases: stage I, the primary intervention, and stage II, repeated follow-up treatments. The technique is also known as combined physiotherapy (Földi 1994). In Australia, the Caseley-Smiths adopted the concept and called it complex physical therapy (CPT) (Casley-Smith & Casley-Smith 1992, Morgan et al. 1992). The various methods described above (MLD and CPT) are generally called manual lymph therapy. Pneumatic compression therapy (PCT), combining various pumps and different compression devices, has also gained widespread acceptance (Stillwell 1969, Zelikovski et al. 1980, Alexander et al 1983, Swedborg 1984, Zanolla et al. 1984, Kim-Sing & Basco 1987, Klein et al. 1988, Yamazaki et al. 1988, Pappas & O'Donnell 1992).

Active prevention of arm lymphedema is important and can also be achieved by the use of compression garments only (Bertelli et al. 1992). Indeed, Mackenzie suggested the use of elastic bandaging already in 1883 (Mackenzie 1880). Several varieties of elastic supports have been described to be used in combination with manual lymph therapy or pneumatic compression (Brush et al. 1958, Tinkham & Stillwell 1965, Beninson 1975). The quality and performance of garments have steadily improved and nowadays effective garments with acceptable design and colors are widely available. This has facilitated the institution of compression therapy and probably helped the patient.

Besides simple elevation of the arm (Foley 1951, Hughes & Patel 1966, Stillwell 1977, Swedborg 1993), there is wide variety of alternative, more or less effective methods. Mann reported in 1874 the use of local galvanization (Mann 1874). The use of laser therapy is an interesting contemporary technical approach (Piller & Thelander 1995). Medical treatment includes nitric acid (Cooke 1807), diuretics (Bedell 1960), fibrinloytic inhibitors (Smedal & Evans 1960), benzopyrones (Casley-Smith et al. 1993, Casley-Smith & Casley-Smith 1994a, Casley-Smith & Casley-Smith 1996), and antibiotics (Olszewski 1996). Sympathetic nerveblock (Hanelin et al. 1947), heat (Zhang et al 1984, Gan et al. 1996) as well as microwaves (Chang et al. 1989, Ohkuma 1992) have been tried. However, it was considered beyond the scope of this thesis to go into further details regarding these measures.

Surgical treatment

Despite prophylaxis the lymphedema will often progress slowly but steadily, necessitating a surgical approach. Surgical treatment becomes indicated in patients who fail to respond to conservative treatment because of hypertrophy of the subcutaneous adipose tissue, and later fibrosis (Vague & Fenasse 1965, Casley-Smith & Gaffney 1981, Gaffney & Casley-Smith 1981, Smahel 1986, Ryan & Curri 1989, Ryan 1995). Various surgical procedures have therefore been proposed to reduce the arm lymphedema.

Elephantiasis with ulceration and leakage of lymph was common in India 1500 BC and was proscribed as an obstacle to a priest's marriage according to the Laws of Manu. Hippocrates (460-377 BC) practiced scarification for various swellings of the extremities (Hippocrates, cited by Zieman 1962). Surgical treatment of breast cancer was practiced already in 100 AD. Celsus (ca. 100 AD) maintained that surgical intervention in advanced cases should not be performed, and the edema complication could have contributed to this opinion (Celsus, cited by Zieman 1962). Galen (138-201 AD) actually classified both cancer and edema in advanced cases as an inflammatory disease (Galen, cited by Zieman 1962).

Modern treatment methods of lymphedema date back to Lisfranc who in 1841 simply needled or made superficial incisions in the skin (Lisfranc, cited by Keysser 1927). In 1851 Carnochan proposed ligation of the femoral or external iliac artery in an attempt to reduce the blood volume flow and thereby decrease the tendency to develop lymphedema (Carnochan 1852). Although results varied (Alcock 1866, Hueter 1868, Sondén 1868), such a measure unfortunately sometimes led to ischaemic necrosis of the extremity, ending up in an amputation (Fayrer 1865). Eves actually proposed primary amputation as a treatment of pronounced edemas (Eves 1859). Decompression of the axillary vein has also been suggested for lowering lymph load (Hughes & Patel 1966, Larson & Cramton 1973, Segerström et al. 1991).

Dieffenbach (1792-1847) practiced multiple cuneiform excision of the dermis and underlying fibrous tissues and reported a beneficial effect (Dieffenbach, cited by Hirsch 1885). Quite another approach was outlined by Morton in 1879, who proposed "nerve section" (Morton 1879).

In 1908, Handley placed silk threads subcutaneously in an attempt to reduce the lymphedema by capillary forces, but the method failed (Handley 1908, Handley 1910a, Handley 1910b). Neither have successful long-term results followed substitution of the silk threads by rubber tubes (Walther 1918), strips of fascia (Lexer 1919), nylon (Ransohoff 1945, Zieman 1951), celloidin/cellophane (Beck 1942), Gelfoam rolls (Treves 1952a), polythene (Hogeman 1955), or polyvinylchloride (Portex) (Jantet et al. 1961). Failure was occasionally due to infection or extrusion. But the operative techniques could simply not counteract the force of gravity (Stone & Hugo 1972). The concept that tunnels around implanted materials might substitute the complicated function of interstices and lymphatics must be considered far-fetched (Clodius 1990).

Various interventions in the subcutaneous tissue and deep fascia have been made to create functional lymphatic communications from the superficial to the deeper tissues. Lanz (1911) inserted pedicled strips of fascia lata into the underlying muscle layer, and even into the medullary canal. Rosanow buried pedicled flaps of subcutaneous fat and deep fascia into the muscle (Rosanow 1912). Kondoléon (1912) simplified the technique and excised long strips of deep fascia and muscle aponeurosis. With increasing observation, the results were disappointing and led to modification of the technique by Sistrunk (Sistrunk 1918, Sistrunk 1927), Auchincloss (1930), Ghormly and Overton (1935) and Homans (1936), who made wide excision of the deep fascia together with the skin and various amounts of subcutaneous tissue to reduce the bulk of the limb. Henry (1921) and Ghormly and Overton (1935) disagreed with the opinion that lymph was absorbed not by the deep lymphatics but rather by the rich vascular bed of the muscle. The same principle lay behind the idea of implanting shaved dermal flaps, proposed by Thompson as late as in 1962 (Thompson 1962).

Bridging procedures using various rotational flaps from the trunk to the affected limb have been described by several authors (Kimura 1925, Gillies & Fraser 1935, Clodius et al. 1982). Even suturing of the arm to the thoracic wall has been proposed (Standard 1943). Omental transposition combines excision and a bridging operation in transferring the omental lymphatics to the affected limb (Dick 1935, Goldsmith & De Los Santos 1967). Muscle transposition (Murphy 1906, Peck & White 1922, Reinhoff 1937, Treves 1952b) was used to minimize the dead space in the axilla and to protect the axillary nerve and vessels after exaeresis, but the muscle tissue was also considered to provide a pathway for lymphatic regeneration. Transposition of the saphenous vein with its adjacent adipose tissue and lymphatics from the healthy limb has been tried in the lower extremity (Pho et al. 1989, Tanaka et al. 1996).

Wide excision with split skin grafting remains an option in serious cases (Charles 1912, Macey 1940, Poth at al. 1947), but these patients often develop troublesome skin conditions, such as papillomatosis, eczema, lymph fistulas, keloids, ulceration, and cellulitis. From this point of view it is better to use the excised skin as full thickness grafts than to carry out split skin grafting (Gibson & Tough 1954, Barinka 1977).

The breakthrough in reconstructive microsurgery has also led to application of the technique in the lymphatic system. Anastomoses have been established between lymph nodes and the venous system (Olszewski, Nielubowicz 1966, Nielubowicz and Olszewski 1968, Jamal 1981), between lymph collectors and the venous system (Laine & Howard 1963, Degni 1974, Huang et al. 1985, O'Brien et al. 1990). Promising results have recently been reported after transplantation of lymph collectors (Baumeister et al. 1981, Ho et al. 1983, Baumeister 1986, Baumeister & Siuda 1990, Baumeister 1995), as well as after the creation of various forms of lymphatic venous anastomoses (Mandl

1981, Campisi et al. 1995a, Campisi et al. 1995b). Although attractive in concept, these methods do not give consistently satisfactory results.

Reduction of the volume of the lymphedema by using the less traumatic liposuction constitutes an interesting new approach, and preliminary clinical reports, although not impressive, warranted further refinement and evaluation of the procedure (Teimourian 1987, Nava & Lawrence 1988, Illouz 1989, Louton & Terranova 1989, O'Brien et al. 1989, Sando & Nahai 1989). Our first liposuction of arm lymphedema was undertaken in 1987, but it was not until 1993 that a more detailed treatment protocol was established and our lymphedema team was founded.

OBJECTIVES OF THE STUDY

In view of the limitations of previous treatment techniques and the promising preliminary results of liposuction, the aims of the present investigation were:

- to develop a standardized technique for liposuction of arm lymphedema in combination with CCT (I),
- to investigate the effects of treatment on the skin blood flow in the arm (II),
- to investigate the effects of treatment on the lymph transport in the arm (III),
- to compare the effects of liposuction+CCT versus CCT alone (IV),
- to elucidate the importance of CCT after liposuction (IV), and
- to elucidate the effects of treatment regarding the general quality of life (V).

MATERIAL AND METHODS

Patients

Altogether 51 women participated in the present investigation. The patients were recruited consecutively after having been referred by general surgeons, oncologists, and general practitioners. All patients, except one, had undergone radiotherapy immediately after the breast cancer operation, which included the excision of lymph nodes in all cases. No patient had an ongoing local wound complication or systemic disease when entering the study. Indications for treatment intervention included the subjective discomfort of a heavy arm, and the fact that treatment with pneumatic compression therapy and/or manual lymph therapy had not yielded satisfactory edema reduction. No patient was refused treatment on the grounds of age. The lymphedema was firm in all cases and showed clinical signs of grade II fibrosis with adipose tissue hypertrophy, conceivably as no intensive treatment had immediately preceded enrollment in the study.

Whether they were treated with liposuctiom+CCT, or with CCT alone, is shown in Table I (page 33), which also shows their participation in the different studies. All had been informed about the performance and the purposes of the investigations, and had given their consent to participate. Study III had received approval from the Isotope Committee at Malmö University Hospital.

Liposuction - surgical technique

General anesthesia was used in most cases but some patients preferred nerve blockade. Neither local anesthetic nor epinephrine was injected locally, hence the "dry technique" was used. Through numerous 3 mm incisions, the shoulder, arm, hand — and even proximal phalanges when indicated — were treated. Normally, 20–30 incisions were needed. Cannulas were connected to a vacuum pump giving a negative atmospheric pressure of 0.9. One cannula had an outer diameter of 3 mm (length 15 cm, three openings at the tip); another had a diameter of 4 mm (16 cm, two openings). The finer cannula was used mainly for the hand, fingers, and distal part of the forearm and also when irregularities were remedied. Liposuction was executed circumferentially, step-by-step from hand to shoulder, and the hypertrophied and edematous fat was removed with vacuum aspiration as completely as possible. The incisions were left open to drain. Treated areas were subsequently compressed firmly to stem bleeding and postoperative edema. Rolls of clean bandage were eventually applied and retained for 2 days. Elastic bandages were used on the arm, and non-elastic ones on the fingers. In more recent patients we have used a standard arm and glove for compression (Jobst-Elvarex, compression class 2, Beiersdorf AB, Sweden) instead. Operating time was 2 hours on average. An isoxazolylpenicillin or a cephalosporin was given intravenously for the first 24 hours, and then in tablet form for 2 weeks.

Postoperative care

The arm was held raised during the hospital stay, usually for 5–7 days. Two days postoperatively, measurements were taken for a custom-made compression garment, a sleeve and glove, that gave a compression in the range 32–40 mmHg (Jobst-Elvarex, compression classes 2 and 3, Beiersdorf AB, Sweden) For temporary use, an interim dressing was worn for 2 weeks to maintain compression. In later patients we have simply continued with the standard arm and glove until the 2-week control. Thereafter the new custom-made compression garment was applied, and during the subsequent course, this rigorous compression regime, referred to as Controlled Compression Therapy (CCT), was maintained exactly as described below.

Controlled Compression Therapy (CCT)

The compression therapy is crucial, and its application was therefore thoroughly described and discussed at the first clinical evaluation. If the patient had any doubts about continued controlled compression therapy, she was not accepted for treatment. After institution of the compression therapy, the custom-made garment (Jobst-Elvarex, compression classes 2 and 3, Beiersdorf AB, Sweden) was taken in at each visit, using a sewing machine, to compensate for reduced elasticity and reduced arm volume. This was most important during the first 3 months when the most notable changes in volume occurred, particularly in the surgery group. At the 3-month visit, the arms were measured for new custom-made compression garments. This procedure was repeated at 6 and 12 months. It was important however, to take in the garment repeatedly to compensate for wear and tear. This required additional visits in some instances, although such adjustments could often be made by the patient herself. When the edema volume had decreased as much as possible and a steady state was achieved, new garments could be prescribed, using the latest measurements. In this way, the garments were renewed three or four times during the first year. Two sets of sleeve-and-glove garments were always at the patients' disposal, one being worn while the other was being washed. Thus, a garment was worn permanently, and treatment was interrupted only briefly when showering and, possibly, for formal social occasions. The patient was informed about the importance of hygienic measures and skin care.

Arm volume measurements

Arm volumes were recorded for each patient using the water displacement technique. The displaced water was weighed on a balance to the nearest 5 g, corresponding to 5 ml. Both arms were always measured at each visit, and the difference in arm volumes was designated as the edema volume (Swedborg 1977, Casley-Smith 1994b, Bernas et al. 1996, Brorson & Svensson 1997). The decrease in the edema volume was also calculated in percent, thus:

$$\frac{(EA_{pre} - HA_{pre}) - (EA_{post} - HA_{post})}{EA_{pre} - HA_{pre}} \times 100,$$

where

EA_{pre} = edematous arm before treatment

HA_{pre} = healthy arm before treament

EA_{post} = edematous arm after treatment

HA_{post} = healthy arm after treatment

Laser Doppler imaging (LDI)

In study II, skin blood flow of the arm was measured using LDI (Lisca Development AB, Linköping, Sweden). In this technique, light is directed onto the tissue by means of a scanner system consisting of two stepping motors and mirrors. The backscattered light is detected by a remote photodiode. Each step takes approximately 50 milliseconds to perform. The Doppler signal from the detector unit is amplified and fed through a filter with a power amplification factor proportional to frequency. The energy of the output is, after noise compensation, taken as a measure of perfusion and read in volts (V). The LDI value can roughly be considered to be proportional to the number of photons being changed and their average frequency shift. The data are stored in a computer and the images produced using a color printer on a scale ranging from dark blue to red, related to increasing flow. The total amount of backscattered light is also measured in order to distinguish the background (low light intensity) from no-flow areas (high light intensity), which both generate backscattered light without any Doppler shifts. LDI value is expressed in perfusion units (P.U.), where 1 P.U. equals 1 V.

Skin blood flow was determined in both arms by using LDI. Measurements were performed in a room at a constant temperature of 23.4 ± 0.8°C. The patients were seated comfortably in a chair with the forearm resting on a table. A 15 min period was allowed for acclimatization. During measurements after operation, the compression garment was removed. Measurements began with the non-edematous contralateral arm, which served as a control. The dorsal aspect of the hand and forearm and the lateral aspect of the upper arm were measured. The device was positioned 17 cm above the skin surface. Measurements were obtained from about 4,096 points, corresponding to an area of 12 x 12 cm. Each image took 4 min to record. The recordings from the operated arm were made approximately 20 min after removal of the compression garment. LDI ratios between the normal and the healthy arm were calculated.

Indirect lymphoscintigraphy (ILS)

In study III, lymph flow of the arm was assessed using ILS. The radiopharmaceutical was prepared from a lyophilized kit (Solco, Nanocoll, Sorin Biomedica S.p.A, Italy) containing 0.5 mg of human albumin as a nanocolloid (=HSA nanocolloid). The particle size was less than 80 nm for more than 95% of the labeled colloid. The patient rested comfortably in the supine position beneath the gamma camera with arms abducted about 15°. Injections were made subcutaneously into the second and third digital webspaces of each hand. Tuberculin syringes and 27 gauge needles (diameter 0.4 mm) were used; each injection emitted an activity of approximately 5 MBq and a volume of about 0.1 ml. The injection sites were gently massaged for 20 sec. Images were recorded with a gamma camera (Toshiba GCA-901A) equipped with a LEGP (Low Energy General Purpose) collimator.

Immediately following the injection and again at 180 min, an image of the injection site was generated, lasting 15 sec. After the initial imaging of the injection site the patient made pumping movements with the hand for 2 min while the arm was kept still and imaging of the arm began. Five-minute posterior images of the arm were obtained at 0, 5, 10, 15, 20, 25, 75 and 180 min after injection. Regions of interest (ROI) were drawn on the images to allow determination of the washout of the tracer from the injection site, as well as tracer uptake in the arm. Correction for background activity was made, as well as for decay of ^{99m}Tc.

The injection site, the proximal part of the forearm, the upper arm, and the axillary lymph node region were the ROIs studied separately in each arm. Uptake curves were approximated using linear regression and the constants were calculated and used for the statistical analyses. Uptake activity at 180 min was recorded as a percentage both of the injected activity, and of the cleared activity. Analyses were made both to elucidate differences between the healthy and the lymphedematous arm, and also to reveal any scintigraphic changes in response to treatment. In the latter respect, we considered the comparisons between pretreatment recordings without compression, and those recorded at 3 and 12 months with compression garments as the more relevant, as they represented the clinical situation during the normal treatment regimen.

Both arms were studied. Two ILS were performed on each occasion with an interval of 2 days between studies (with and without the garment). For the initial studies, each patient wore a temporary compression garment that was adjusted to fit the arm as well as possible. After these initial studies, liposuction was performed without delay in the operated group, whereas in the CCT group the patients simply continued with external garment compression (see above).

Range of motion of the shoulder joint (ROM)

In study V, ROM was measured in degrees with a standard protractor. The tests were performed in the standing position, and care was taken to prevent compensatory movements of the torso. Without passive movements, ROM was determined for the following six active movements of the arm: elevation, abduction, outward rotation, inward rotation, and extension.

Visual Analogue Scale (VAS)

VAS (study V) is widely used as an easy, reliable and sensitive test instrument to evaluate patients' subjective opinion of the outcome of various treatments in clinical studies (Aitken 1969). In paper V, we studied the following parameters: pain, difficulties with activities of daily living (ADL), and swelling of the back of the hand. The ADL protocol was supplemented with the following five questions to be answered with "yes" or "no":

- Is there a reduced mobility in the shoulder joint?
- Do you feel that the arm is swollen ?
- Does the arm feel heavy?
- Do you feel any fatigue or weakness in the arm?
- Do you feel numbness or pricking sensation in the arm?

The scale is a straight line (100 mm) upon which the patient makes an appropriate mark corresponding to the appraisal of the specific question. The scale is graded from 0 (no difficulty) to 100 (extreme difficulty). There are no established normal values, but a patient without edema would conceivably rate "0" in all instances.

Nottingham Health Profile (NHP)

NHP (study V) is a two-part, self-administered questionnaire designed to provide a standardized measure of perceived health problems (Hunt et al. 1980, Hunt et al. 1981). Both reliability and validity of the test have been confirmed for Swedish circumstances (Wiklund et al. 1988). The 38 "yes" or "no" items of part I reflect degrees of distress within the domains of emotions, sleep, lack of energy, pain, physical mobility, and social isolation. Weights in each section total 100, indicating the presence of all possible problems, whereas 0 denotes no problems whatsoever (McKenna et al. 1981, Hunt & Wiklund 1987). Part II has 7 "yes" or "no" statements about the frequency of health-related problems such as gainful employment, housework, social life, family life, sex life, hobbies, and holidays. Findings in NHP were related to mean values of a normal female Swedish population, taking age and sex into consideration (Halling 1998).

The Psychological General Well-Being index (PGWB)

PGWB (study V) is a psychometrically well documented test which can be used to detect differences in clinical studies (Dupuy 1984). The PGWB index has been translated to Swedish and psychometrically documented following standard principles (Wiklund & Karlberg 1991). The test consists of 22 questions which in addition to providing a total score covering six subscales depicting anxiety, depressed mood, well-being, self-control, general health, and vitality. Patients rate each question on a six-point scale with 1 as the most negative and 6 as the most positive option. Findings in PGWB were related to mean values of a normal Swedish population (Dimenäs et al. 1996).

The Hospital Anxiety Depression Scale (HAD)

The HAD scale (study V) is a reliable instrument for screening of anxiety and depression among patients attending a health unit for regular medical care (Zigmond & Snaith 1983). The test has been shown to provide a regular valid measure of the severity of disorders related to mood, and repeat application of the test gives the physician useful information concerning any emotional alterations. The original HAD scale is available in Swedish. The test comprises of 14 questions, 7 representing anxiety and 7 depression. Patients rate each question on a four-point scale, graded 0-3, corresponding to increasing degree of anxiety or depression, giving a maximum of 21, respectively.

Statistical analysis

Standard methods were used to test statistical significance. Changes in various parameters were analyzed using Student's paired *t*-test and Wilcoxon's signed-rank test. When differences between groups were analyzed, the Student's unpaired *t*-test and Wilcoxon's rank sum test were used. The paired *t*-test was used, however, when observations were matched (paper IV). In paper V, with "yes" or "no" questions in VAS and NHP part II, McNemar's test and the Cochran-Mantel-Haenszel test were used. A p-value <0.05 was considered to indicate statistical significance. In paper V, however, a p-value <0.01 was required in order to avoid the occurrence of statistical significance due to multiple testing.

Methods of linear regression were used to show relationships between variables.

REVIEW OF THE PRESENT INVESTIGATIONS

Table I shows the distribution of the participating patients in Papers I-V (page 33).

I. Complete reduction of lymphoedema of the arm by liposuction after breast cancer.

Twenty-eight women with lymphedema of the arm following breast cancer were consecutively treated with liposuction+CCT. All patients had undergone radiotherapy after the mastectomy. Limb compression with a garment was instituted immediately after operation. Mean preoperative volume of edema was 1,845 ml (range, 570 to 3,915 ml).

There were no major surgical complications, but blood transfusion was necessary in 8 patients whose aspirate volumes exceeded 2,000 ml. The mean volume of aspirate was 2,250 ml (range, 1,000 to 3,850 ml), and the proportion of fat in the aspirate was 63% (range, 41 to 82%). The volume of aspirate correlated linearly with the volume of preoperative edema; the coefficient of regression was 0.7 and the coefficient of correlation 0.73.

The effect of operation was obvious, and during the postoperative course a further reduction was seen in mean volume of edema. At 12 months (n=24), it was 30 ml (range, –655 to 1,135 ml) corresponding to an average relative reduction of 106% (range, 66 to 179%). The percentage reduction in the volume of edema was linearly related to the preoperative volume of edema (slope = –0.02, $p<0.01$) and the operation serial number (slope = 1.33, $p<0.05$), but showed no linearity with the duration of lymphedema. These figures show that the volume actually removed sometimes exceeded the volume of edema. In 15 patients, a normalization or even overcorrection of the lymphedematous condition could thus be demonstrated after one year. Such a normalization can be expected in patients with edema amounting to about 2,500 ml. Although the edema cannot be completely removed in more severe cases, substantial reduction ought to be beneficial from both functional and cosmetic aspects.

Liposuction is safe and effective for reducing arm lymphedema after an operation for breast cancer. In a one-stage procedure, edematous and hypertrophic fat tissue can be removed with a very satisfactory clinical outcome being maintained with CCT.

II. Skin blood flow of the lymphedematous arm before and after liposuction

Twelve patients participated in this study in which edema volume and skin blood flow (LDI) were measured before and after liposuction+CCT. Episodes of cellulitis, defined as a marked reddening of the arm skin requiring antibiotics, were also recorded.

The median preoperative edema volume was 1,745 ml (range, 810 to 3,915 ml). The median aspirate volume was 2,060 ml (range, 1,000–3,850 ml). The edema volume at 3 months was 230 ml (range, –185 to 1,960 ml), and at 12 months it had further declined to 60 ml (range, –445 to 1,135 ml), corresponding to relative edema reductions of 87% and 97%, respectively.

Median LDI values before liposuction from the lymphedematous arm were 1.64 in the hand, 0.91 in the forearm, and 0.93 in the upper arm. Corresponding values from the control limb were 1.80, 1.09, and 0.99. The preoperative median LDI ratios were 1.01, 0.90 and 0.92, respectively. Significantly increased skin blood flow was measured in the lymphedematous arm after liposuction, but not in the hand. Median LDI ratios were 1.03, 1.01 and 1.15 at 3 months, and 1.06, 1.05 and 1.07 at 12 months.

Whereas previous investigations have indicated an increased total blood flow in the lymphedematous arm, we found reduced superficial skin blood flow preoperatively. Both in the forearm and in the upper arm, skin blood flow increased significantly after liposuction and values were similar to those of the non-edematous (control) arm. Along with increased skin blood flow, the frequency of cellulitis also decreased. The annual incidence of cellulitis was 0.4 (40/97) before liposuction, and 0.1 (3/30) afterwards.

In this series of patients, liposuction produced a median edema reduction of 97% after 12 months. Treatment also improved skin microcirculatory blood flow, which might explain the reduced incidence of cellulitis.

III. Liposuction reduces arm lymphedema without significantly altering the already impaired lymph transport

Twenty patients participated in this study in which indirect lymphoscintigraphy (ILS) was used to study lymph kinetics before and after liposuction+CCT (n=11), and before and after CCT alone (n=9).

In the operated group, there were no major surgical complications. The median edema volume before liposuction was 1,610 ml (range, 570 to 2,950 ml). The immediate effect of liposuction followed by CCT was a sharp reduction in arm volume and over the subsequent postoperative course a gradual reduction was seen in the median edema volume. After 12 months it was –230 ml (–655 to 235 ml).

In the group that received CCT alone, the median edema volume before treatment was 1,415 ml (range, 670 to 3,245 ml). After CCT, a gradual but substantial reduction was seen. At 12 months, the median volume of edema had decreased to 625 ml (range, 340 to 1,955 ml).

The images of the non-edematous healthy arm showed a normal truncal pattern of lymph vessels with little or no uptake of the radiotracer in the soft tissues. Thus, the radiopharmaceutical was transported directly to the axillary lymph nodes and radioactivity registered in the arm represented tracer in transit within the lymphatics. In the lymph nodes, a marked normal uptake was recorded.

In the lymphedematous arm, the clearance rate from the injection site was similar among the patients. Lymph trunks were absent or barely detectable, and the tracer rarely reached the axilla where lymph nodes had been resected and in all but one case also irradiated. Tracer transport was slow and marked dermal back flow was common with prominent accumulation of radiotracer in the soft tissues. Compared with the normal contralateral arm, uptake activity and uptake constants were significantly "depressed" as described by Ketterings and Zeddeman (1997).

The depressed lymph flow profile remained essentially unchanged after liposuction and CCT. With wearing of a compression garment at 12 months there was slightly increased uptake activity in the upper arm as a percentage of cleared activity. Otherwise, there was no difference in ILS findings between with and without compression at 3 and 12 months.

The depressed lymph flow profile remained after treatment with CCT alone. With a compression garment, there was a slightly greater uptake in the arm at 3 months, but at 12 months, tracer uptake in the upper arm was slightly reduced. Without a compression garment, there was also slightly greater tracer uptake in the arm at 3 months.

No effect of wearing the compression garment for 2 days before definitive treatment was detected (n=20). Nor was there any effect of not wearing the compression garment for 2 days at 3 or 12 months in either the operated or non-operated group.

Liposuction combined with CCT reduced the edema volume by a median of 115% (p=0.005), whereas CCT alone achieved only a 54% volume decrease (p=0.008). Liposuction combined with CCT proved better than CCT alone for reducing arm edema (p=0.0002).

Lymphoscintigrams from the normal arm were characterized by transit of the isotope to the axillary lymph nodes, whereas accumulation due to dermal backflow was visualized in the lymphedematous arm. Neither liposuction, nor CCT alone, could alter this flow profile. Liposuction therefore does not appear to further reduce the already compromised lymphatic transport.

IV. Liposuction combined with controlled compression therapy reduces arm lymphedema more effectively than controlled compression therapy alone

In this study with matched pairs, 28 patients were randomly selected for either liposuction+CCT (n=14), or for CCT alone (n=14). Additionally, the CCT group was compared with our complete group of patients treated thus far with liposuction+CCT (n=30). To further clarify the importance of CCT, 6 patients temporarily removed their compression garment for 1 week, 1 year postoperatively.

In the CCT group, the mean volume of edema before treatment was 1,680 ml (range, 670 to 3,320 ml). After compression therapy, a gradual but substantial reduction was observed. After 12 months, the mean volume of edema had decreased to 873 ml (range, 340–2,275 ml) corresponding to an average relative reduction of 47% (range, –2 to 80%).

In the liposuction+CCT group, there were no major surgical complications. The mean volume of edema before liposuction was 1,745 ml (range, 570 to 2,950 ml). The immediate effect of liposuction followed by CCT was obvious, and during the postoperative course, a further reduction was seen in the mean volume of edema. After 12 months, it was –122 ml (range, –655 to 820 ml), corresponding to an average relative reduction of 113% (range, 66 to 179%). The statistical analysis of the paired groups showed that liposuction is more effective than CCT alone (p<0.0001).

In the group of all patients who have undergone surgery thus far (n=30), the mean volume of edema was 1,790 ml (range, 570 to 3915 ml) preoperatively, and 52 ml (range, –655 to 1,135 ml) after 12 months, corresponding to a relative reduction of 104% (range, 66 to 179%).

Removing the compression garment for 1 week after 1 year, showed a mean increase in the arm volume difference of 370 ml (range, 135 to 775 ml; n=6). The increase in the edema was completely reversed by reinstituting compression.

Liposuction+CCT reduces lymphedema significantly more effectively than CCT alone. Continued use of compression garments is important, however, to maintain the primary surgical outcome.

V. Quality of life following liposuction and conservative treatment of arm lymphedema.

Forty-nine patients participated in this study in which parameters related to quality of life were recorded before and after liposuction+CCT (*n*=35), and before and after CCT alone (*n*=14). Effects were assessed using the Visual Analogue Scale (VAS), Nottingham Health Profile (NHP), Psychological General Well-Being index (PGWB), and the Hospital Anxiety Depression scale (HAD). Arm edema volume and range of motion in the shoulder joint (ROM) were also recorded. Results were monitored on five different occasions up to one year after treatment commenced.

In this series of patients, liposuction+CCT reduced arm lymphedema by 102%. CCT was beneficial as well, but the effect was less than when combined with surgery 49%. The reduction in arm lymphedema volume had significant consequences for the patients. As could be expected from the volume measurements, the more beneficial effects were recorded mostly in the liposuction+CCT group.

The subjective sensation of swelling of the hand and arm subsided accompanied by a decrease in heaviness, fatigue and weakness. The mobility of the shoulder joint was considered better, which was confirmed by the ROM measurements. The subjective sensation of pain and numbness or pricking sensation decreased in the liposuction+CCT group, whereas this effect was not so obvious in the CCT group. The VAS score for pain in the CCT group actually increased.

Even regarding more global parameters related to ADL (VAS, NHP total score, part I) some beneficial effects were recorded, particularly in the liposuction+CCT group. Some important subscale parameters in NHP actually indicated an improvement, such as physical mobility, social isolation, and house work. Other subscale parameters were fairly constant, however, such as qualities related to emotions, sleep, energy, social life, family life, hobbies, and holidays. Starting values for these parameters were in most instances compatible with or even better than those obtained from the normal age-matched population indicating that the lymphedema situation hardly limits these functions (Halling 1998). Consequently, no improvement after treatment could be expected.

Although parameters related to the PGWB index showed high values when compared with the normal population (Dimenäs et al. 1996), the women obtained even higher scores after treatment with liposuction+CCT. The magnitude of this improvement has previously been reported to be of clinical relevance in a population with well-being scores in the normal range (Wiklund et al. 1997). The increase in total score could not be attributed to any individual subscale parameter, as these showed only minor changes. The findings in the HAD subscales similarly supported that the women were compatible with the normal population without evidence of anxiety or depressive disorders.

Hence, liposuction+CCT removed arm lymphedema completely, whereas CCT alone reduced it by only half. The treatment improved patients' quality of life, particularly in domains directly related to the volume reduction, such as activities associated with everyday life . The effects were less obvious with regard to social life and psychological well-being and warrant further investigation. As could be expected from the volume measurements, the more favorable outcomes were recorded mostly in the liposuction+CCT group.

Patient no.	Liposuction+CCT	CCT alone	Paper I Liposuction+CCT	Paper II LDI	Paper III Scintigraphy	Paper IV Liposuction+CCT vs. CCT alone	Paper V QoL
1	•		•	•		•	•
2	•		•			•	•
3	•		•	•		•	•
4	•		•	•		•	•
5	•		•	•		•	•
6	•		•	•		•	•
7	•		•	•		•	•
8	•		•	•		•	•
9	•		•	•		•	•
10	•		•	•		•	•
11	•		•	•		•	•
12	•		•	•		•	•
13	•		•	•		•	•
14	•		•			•	•
15	•		•		•	• *	•
16	•		•		•	• *	•
17		•			•	•	•
18	•		•		•	• *	•
19		•			•	•	•
20	•		•		•	• *	•
21	•		•		•	• *	•
22		•			•	•	•
23		•			•	•	•
24	•		•		•	• *	•
25	•		•		•	• *	•
26		•				•	•
27		•			•	•	•
28		•			•	•	•
29	•		•		•	• *	•
30		•			•	•	•
31		•			•	•	•
32		•			•		
33	•		•		•	• *	•
34	•		•		•		
35	•		•		•	• *	•
36	•		•			• *	•
37	•		•			• *	•
38		•				•	•
39		•				•	•
40	•		•			• *	•
41		•				•	•
42	•					• *	•
43		•				•	•
44	•					•	•
45	•					•	•
46		•				•	•
47	•						•
48	•						•
49	•						•
50	•						•
51	•						•

Table I. Participating patients in Papers I-V.

* indicates patients in the liposuction+CCT group being matched with all patients in the CCT group, but no. 32.

GENERAL DISCUSSION

Volume measurements

Estimation of the edema volume in the arm can be accomplished by measuring arm circumference, or girth. Many reports of postmastectomy edema are indeed based on such measurements. The method is simple, and consequently it is widely used. Its accuracy depends on the number of measuring points used (Kettle al. 1958). Measurements made at 10-cm intervals have been proposed (Casley-Smith & Casley-Smith 1992, Morgan & Casley-Smith 1992, Boris et al. 1994, Boris et al. 1997), but give a rather crude approximation of the arm edema volume. A more accurate estimate can be obtained by reducing the measuring intervals, for instance, to 4 cm, as described by Kuhnke (Kuhnke 1976, Kuhnke 1978). However, measurements are highly biased by variations in the degree of firmness and the contour of the limb, by the tension placed on it by the tape measure, or by the fact that the swelling of the soft tissue is not uniform (Stillwell 1977). The water displacement method of assessing arm volume is far more reliable (Swedborg 1977, Bernas et al. 1996, Brorson & Svensson 1997) as it measures the arm edema volume directly in ml. As in this study, both arms should be measured simultaneously so that the arm edema volume can be monitored, with the contralateral arm serving as a control, thus avoiding the effect of casual variations in the general body mass.

Manual lymph therapy and pneumatic compression therapy

Manual lymph therapy and pneumatic compression therapy are primary methods of prevention of arm lymphedema. Their direct beneficial effects on longstanding edema with fibrosis and adipose tissue hypertrophy are uncertain. Hutzschenreuter et al., for instance, monitored a series of 62 patients with an initial volume of edema of 550 ml (Hutzschenreuter et al. 1991). Despite intensive treatment in hospital for 3 weeks, only a 20% decrease in the edema volume was achieved. Furthermore, relapses occurred periodically within one year, necessitating repeated sequences of treatment.

The effects of conservative treatment are also detailed in a study by Boris et al. (1994). This was is a 1-year follow-up with a fairly detailed presentation of the study material, and non-responders were not excluded from the analysis of the results. The effects of complex physical therapy given 4 hours a day for 30 days followed by the application of compression garments were analyzed. The study participants were 16 women with postmastectomy arm lymphedema; judged to be fibrotic in 13 cases. It was not reported whether the patients had undergone axillary node dissection or had received postoperative irradiation. Moreover, the lymphedemas were rather small, with a mean volume of 690 ml, and the healthy control arm was measured only on commencing the study. However, an overall initial edema reduction of 73% was achieved upon treatment. After 1 year, the relative edema reduction was 86%; however, this latter figure is ambiguous, as it also included a group of 17 patients treated for lower leg lymphedema. In a recent survey of 56 patients with arm lymphedemas, a mean initial reduction of 63% was found immediately after treatment. This figure was the same at the 3-year follow-up. The study shows the percentage reduction achieved by a single treatment episode, as no additional courses of complex physical therapy were administered. However, no information was given regarding the quantitative edema volumes before and after treatment (Boris et al. 1997). Furthermore, 12 patients had only grade I lymphedema, and 9 patients were lost to follow-up.

Manual lymph therapy may be considered the preferred method for treatment of lymphedema, but its direct beneficial effect on long-standing, pronounced edema with fibrosis and adipose tissue hypertrophy is uncertain, because complete and convincing reports of long-term follow-up studies are sparse. This same qualification applies to pneumatic compression therapy. A recently published randomized study in women with postmastectomy arm edema showed that 2 weeks of manual lymph therapy reduced the arm edema by 75 ml (15% reduction). Two weeks of pneumatic compression by a sequential pump reduced the edema by 28 ml (7% reduction) and there was no significant difference between the two treatment methods (Johansson et al. 1998). Patients treated with these methods all seem to be prone to recurrence, necessitating repeat treatment or additional measures. Another important issue is that when hypertropic adipose tissue is present, as in grade 2 edema, it cannot be removed by massage or compression. This limits conservative treatment. Consequently, these treatment regimes seem to produce only moderately good long-term results, despite considerable efforts.

Controlled Compression Therapy (CCT)

The results of the present studies clearly show that the use of simple compression garments remains an interesting alternative to manual lymph therapy and pneumatic compression therapy. Following CCT, a gradual reduction in the mean volume of edema is seen, and after 12 months the reduction is about 50%. This outcome is very good, particularly considering that all the patients had heavy edema with marked signs of adipose tissue hyperthrophy and fibrosis (grade 2). Although our therapy requires careful follow-up, preferably by a lymphedema team, it appears to be a cost effective method. It is performed on a purely outpatient basis, and does not require protracted intervention by therapists. Furthermore, no expensive technical devices of any kind are used. We consider CCT worthwhile as the use of a standard elastic sleeve without adjustments reduces the edema by only 15% (Bertelli et al. 1992).

Contemporary surgical techniques: microsurgery and liposuction

A surgical approach intended either simply to remove the edematous tissue, or to create favorable conditions for alternative drainage, nevertheless seems logical. This is particularly true in cases of long-standing, massive, and fibrotic edema with adipose tissue hypertrophy. Lymphangiosarcoma might develop in severe lymphedema (Stewart & Treves 1948) and, if the duration exceeds more than 10 years, the risk is 10% (Woodward et al. 1972). By removing edematous tissue, the risk may be reduced (McConnel & Haslam 1959).

Modern microsurgical techniques seem to be an advance regarding surgical treatment of arm lymphedema, but reported results are partly contradictory and therefore still not entirely successful. For instance, in a series of 52 patients treated with lymphatic-venous anastomoses and postoperative compression garments reported by O'Brien et al. et al. 30 patients had not responded at all after a 3-year follow-up, whereas in 22 the mean decrease in volume of edema was 44% (596 ml) after 4.3 years (O'Brien et al. 1990). Baumeister and Siuda used lymphatic grafting combined with compression garment and obtained an 80% reduction in the volume of edema (about a liter) after 3 years in 11 patients (Baumeister and Siuda, 1990). Long-term follow-up of a larger group of patients showed less favorable results, however (Baumeister 1995). Campisi et al. undertook lymphatic anastomoses using interpositional vein grafts, mainly in the lower limbs, and recorded variable results when the operation was combined with postoperative compression (Campisi et al. 1995a). The volume of edema was reduced by at least 75% in 40 patients, between 50 and 75% in 18, and between 25 and 50% in 6 patients. In a larger series of patients treated by various forms of lymphatic-venous anastomoses, clinical outcomes also showed pronounced intersubject variability (Campisi et al. 1995b). Corresponding figures were 289 (>75%), 271 (50–75%), and 119 (25–50%), but 30 patients did not respond at all.

In the light of these experiences, the concept of combining the more recent liposuction technique with CCT is clearly an interesting new approach that is potentially capable of effecting predictable and reliable improvements in cases of lymphedema. An early investigation by Sando and Nahai (1989) reported modest results, but better results were obtained when using liposuction combined with a garment. Slightly better results were reported by O'Brien et al. (1989) with a mean decrease in edema volume of 23% in combination with compression garments. Our results with liposuction combined with CCT show that further methodological improvements are possible, as we have, on average, managed to remove the edema volume completely. The tissue volume removed is sometimes greater than the initial edema volume. Consequently, not only a normalization, but even an overcorrection of the lymphedematous condition can be achieved after 1 year. Because only normalization is intended, Bernas et al. have suggested using 100% as an upper limit for reporting results, in order to make the interpretation of results more comprehensible (Bernas et al. 1996). Taking this into consideration, the mean relative reduction in our series was about 93%.

The volume of aspirate was found to be linearly related to the preoperative volume of edema. Regression analysis showed that there was an inverse correlation between the percentage reduction in the volume of edema and the volume of preoperative edema after one year. This means that normalization is easier to achieve when the edema is less pronounced. Despite subject variations in responsiveness, we found that complete reduction of the edema volume is possible up to 2,500 ml. Substantial reductions can be achieved in even more severe cases. For example, an edema of 3,915 ml was reduced by 72%. In some cases, though, results are not so good, possibly as a result of fibrosis, although multiple regression analysis did not indicate that duration of the edema was a significant factor.

Other factors to consider are variations in surgical technique and improvements in the method of liposuction over time. Although our early patients came through with satisfactory clinical results, there was a significant relationship between operation serial number and percentage reduction of edema. It is therefore conceivable that increasing personal familiarity with the operative technique on the part of the surgeon will improve the outcome still further.

Few complications arose and these were easily remedied. The need for blood transfusion in cases of pronounced edema may be considered a drawback, however. An interesting refinement is therefore to execute the operation after exsanguination and application of a temporary arterial occlusion, as introduced by O'Brien et al. (O'Brien et al. 1989).

Liposuction and CCT vs. CCT alone

Our wish to ascertain how much liposuction contributes to our favorable results indicated the need for a prospective study (IV), with patients receiving CCT alone serving as matched controls based on the volume of edema. Although the matching procedure could not be done in an optimal way, for clinical and ethical reasons, the paired patients seemed to match one another very closely. Coincidentally, other parameters of interest showed only slight differences.

The results clearly show that liposuction gives an instant and significant reduction of the edema volume, compared with CCT alone. The unequivocal effect of surgery is due to removal of the lymphatic load, consisting of both edematous and hypertrophied fatty tissue and accumulated proteins. Although CCT may afford complete relief during prolonged treatment, the accelerated postoperative course achieved by liposuction is important when considering quality of life, particularly in view of the patients' malignant underlying disease and their age. On the other hand, our findings also show that CCT becomes an important complement in the treatment to maintain the primary surgical outcome. In 6 patients who underwent surgery and a complete removal of the edema, the compression garments were removed for 1 week, 1 year postoperatively. A sudden marked increase in the arm volume was observed, which was immediately remedied by reapplying the garments. The importance of maintaining compression is also indicated by our observation of the one patient in the CCT group who showed poor compliance, probably because of diminished intellectual capacity caused by an operation for two brain aneurysms 9 years before compression therapy.

Liposuction and skin blood flow

LDI measures linearly the "blood cell flux", i.e., the movements of blood cells within the microvascular network of the skin (Nilsson et al. 1980, Nilsson 1984). Although LDI cannot be used to measure skin blood flow quantitatively, it has proved useful for monitoring relative changes in various physiological and pathophysiological conditions (Bornmyr et al. 1994, Ljung et al. 1995). Flow completely obstructed by arterial occlusion gives a remaining signal which, though weak, does not fall to electrical zero, as the instrument is equipped with an electrical zero offset to prevent negative values from occurring in the images. Another contributory factor is a "biological zero", most likely produced by randomized cell and tissue movements (Caspary et al. 1988). It is uncertain, however, whether the phenomenon responsible for the biological zero occurs with normal perfusion. It may simply reflect an obstructed bloodstream. Furthermore, arterial occlusion is impractical in the present clinical experimental set-up. Taking these considerations into account, we opted to study changes in skin blood flow by LDI without calibrating to an arterial occlusion value.

Compared with single-site measurements using the original laser Doppler flowmetry method, LDI provides a new and broader dimension. By using several measuring sites, a more reliable recording is obtained when the mean flow is estimated in a defined tissue, such as the arm or hand skin as in our study (II). One potential drawback (not directly applicable to this study) is that scanning is time consuming, and rapid changes in blood flow over larger skin areas cannot be monitored.

The measuring depth of LDI depends on particular instrumental factors, such as the wavelength. Recent investigations using Monte Carlo simulation suggest a rather shallow average median sampling depth of about 0.3 mm in the scattering volume, which corresponds to the superficial capillaries only (Jakobsson & Nilsson 1992). Although the measuring depth is influenced by scattering properties in various tissues, the most important tissue-related factor that must be taken into account is the vascular geometry. Arteriovenous shunts and vascular plexi in the deep dermis, for instance, may contribute appreciably to the LDI signal due to the high blood volume flow, even though they are seemingly located below the average sampling depth. This methodological aspect is an important consideration when interpreting the findings of our study.

In the lymphedematous arm, previous reports have found increased blood flow (Jacobsson 1967a, Jacobsson 1967b, Svensson et al. 1994). In our study, however, skin blood flow in the lymphedematous arm was significantly lower than that in the non-edematous control arm preoperatively. There are various possible explanations for these differences, the most obvious being that both Jacobsson (Jacobsson 1967a, Jacobsson 1967b) using venous occlusion plethysmography, and Svensson et al. (Svensson et al. 1994) using Doppler ultrasound, measured total arm blood flow, whereas methodologically, LDI measures blood flow only to the skin. Jacobsson also found increased skin blood flow when using isotope clearance methods, but mainly during body heating (Jacobsson 1967a, Jacobsson 1967b).

Thick edematous skin alters the vascular geometry, thereby focusing the LDI measurements on the most superficial capillary level. Lowered blood flow values were recorded from the lymphedematous arm before treatment. A decreased capillary density seem an unlikely explanation for impaired perfusion, as neovascularization in lymphedema has been described (Roberts et al. 1994). An increased number of capillary elements, in combination with condensation of blood vessels in the skin after volume reduction, may explain the higher LDI values from liposuction. According to the Starling hypothesis, removal of trapped macromolecules from the interstice should increase the transcapillary protein osmotic pressure gradient and thereby promote resorption of tissue fluid into the bloodstream. Liposuction increased skin blood flow in the arm with LDI ratios exceeding 1.0. Postoperative reactive hyperemia could be a contributory phenomenon and perhaps explain the elevated values at 3 months. It seems less likely, however, that this explanation is sufficient to account for the persistently elevated skin blood flow 12 months after liposuction.

In the hand, the preoperative LDI ratio was 1.0 and liposuction caused no significant change. Whereas the explanation for this finding is unclear, our clinical impression is that lymphedema of the hand is generally less prominent than that of the arm, thus necessitating less extensive liposuction. Indeed, 3 patients required no liposuction of the hand whatsoever. Accordingly, both the effect of lymphedema itself and the effect of liposuction on local skin blood flow may be less evident in the hand.

Whereas preoperative LDI measurements were made before instituting compression therapy with garments, postoperative measurements had to be made after removing such a garment. These differing circumstances led us to study the immediate LDI response upon removal of the garments in 5 additional patients at their 3-month scheduled check-up. Three patients had undergone liposuction, whereas 2 were treated with compression only. LDI recordings were made promptly after garment removal and then after 20, 40 and 60 min. The LDI values from the hand did not change, whereas slight increases in LDI values from the forearm and upper arm were noted. These changes were not statistically significant, however. The effect of the compression garment on the local skin blood flow thus seems to be limited. The direction of the blood flow changes noted in these 5 patients suggests that increased skin blood flow after liposuction cannot be ascribed to external compression therapy.

Lymphatic transport after liposuction

Although the procedure of liposuction is less traumatic than previous surgical methods there is still serious concern about its potential deleterious effects on the microcirculation and especially lymphatic drainage of the soft tissues and skin of the lymphedematous arm (Ketterings & Zeddeman 1997). Thus, on the one hand, lymphatic transport capacity may further decrease in response to operative trauma to the subcutaneous lymph vessels. On the other hand, the early removal of hypertrophied fatty tissue may create a more optimal balance between lymphatic load and residual lymph flow competence. Furthermore, skin capillary blood flow tends to increase after liposuction, a phenomenon which may augment the turnover of tissue fluid (Brorson & Svensson 1997).

The lymphatic system has for many years been depicted primarily by direct lymphography. This method is useful for morphology but functional assessment of lymph dynamics is less precise (Weissleder & Weissleder 1988). Injection is also often difficult and oily contrast media can cause local infection (Koehler 1968) or incite inflammation and fibrosis with damage to the endothelial lining of the lymphatics (Weissleder & Weissleder 1989). Besides local complications, hypersensitivity reactions and pulmonary embolism can also ensue (Steckel & Furmanski 1975).

Indirect lymphoscintigraphy (ILS) using intradermal or subcutaneous injection of ^{99m}Tc-labeled microcolloid has nowadays replaced direct contrast lymphography as the preferred imaging tool for peripheral lymphedema (Weissleder & Weissleder 1988, Gloviczki et al. 1989). The technique is safe, minimally invasive and seemingly harmless to the lymph vessels, and is therefore particularly suited for studying patients with lymphedema where microcirculatory dynamics are already suboptimal. Another advantage is that repeated injection — and therefore serial examination — is feasible. Various radiopharmaceuticals have been proposed for lymphoscintigraphy but in our facility we routinely use ^{99m}Tc-human serum albumin (HSA) nanocolloid.

Although ILS evaluation of lymph transport can be done in several ways, measurement of colloid retention at the injection site is straightforward (Vaqueiro et al. 1986, Göltner et al. 1988), as is measuring the time to appearance of tracer in the regional lymph nodes (Gloviczki et al. 1989). A more detailed evaluation is possible by examining the distribution of the radioactivity in a scintigraphic image (Koehler 1968, Stewart et al. 1985, Ohtake & Matsui 1986, Gloviczki et al. 1989, McNeill et al. 1989). In our study, repeated recordings allowed dynamic evaluation by using tracer isotope uptake curves related to regions of interest representing different parts of the limb (Pecking et al. 1984, Mostbeck et al. 1985, Stewart et al. 1985, Weissleder & Weissleder 1988, Gloviczki et al. 1989). A more refined yet simple analysis is calculation of a transport index taking the various characteristic findings in the scintigram into consideration (Kleinhans et al. 1985, Cambria et al. 1993, Williams et al 1996).

Interpretation of ILS is not always simple. There are multiple anatomical and physiological variations between individuals, and pathophysiological changes may vary widely, depending on the chronicity of the disease process. Technical factors relating to injection site, choice of radiotracer and imaging technique also need to be taken into account (Weissleder & Thrall 1989). Although visual interpretation is paramount, additional quantitative analysis of radiotracer uptake is desirable (Stewart et al. 1985, Ohtake & Matsui 1986, Carena et al. 1988, Rijke et al. 1990).

ILS was performed according to our established departmental protocol, utilizing subcutaneous injection of the radiopharmaceutical. Opinions differ as to whether the tracer should be injected subcutaneously or intradermally. The advantage of an intradermal injection is a more reliable uptake and better proximal transport, because lymphatics are more abundant within the dermis than in the subcutaneous tissue (McNeill et al. 1989). This procedure has, however, an inherent risk of concomitant puncture of cutaneous microvessels in the deep dermis, with rapid bloodstream uptake that may render findings difficult to interpret (Weissleder & Weissleder 1988, Weissleder & Thrall 1989). Radioactive uptake over the liver may detect such unintended premature uptake by the bloodstream (Ketterings & Zeddeman 1997). Nonetheless, this drawback can be circumvented by subcutaneous injection of the tracer, which may be particularly important for dynamic and quantitative studies. The slower uptake, combined with a possible partial elimination via the venous system means, however, that tracer clearance from the hand may not reflect lymph dynamics (Göltner et al. 1988, Vaqueiro et al. 1986). This limitation was in fact observed in our study, where the clearance of the tracer from the injection site was very similar in both arms (i.e., lymphedematous and non-edematous). However, nodal uptake and transport constants were decidedly different with much slower tracer migration on the lymphedematous arm.

With CCT alone, there was a significant reduction in arm edema volume. Compression by the external garment allows gradual mobilization of the lymph fluid component, while the tissue matrix remains constant. Like a squeezed sponge, the lymph capillaries are able to better absorb edema fluid. This pathophysiological reasoning is supported by our experience in patients in whom compression therapy was temporarily interrupted and which resulted in a significant increase in arm edema volume over a one-week period (Brorson & Svensson 1998). This situation also favors increased radiotracer uptake (Ketterings & Zeddeman 1997), which was documented at 3 months.

Further compression by an external garment, however, is also associated with decreased lymph formation as heightened interstitial hydrostatic pressure restricts blood capillary filtration and further collapses the lymph capillaries. These effects are supported by radioactivity dynamics at 12 months, which had returned to the initial levels and uptake constants were unchanged.

Liposuction before CCT promptly reduces arm edema volume. Not only is fluid removed by liposuction but, equally importantly, a notable amount of fat and tissue matrix is also removed. This phenomenon may explain (compared with the CCT group) why no increased radioactivity is detected at 3 months. Nor are notable differences in radioactive uptake values or constants evident at 12 months, consistent with the response to CCT alone. Accordingly, it seems likely that limb compression determined lymph dynamics at this stage. Theoretically, liposuction exerts two effects: one is to decrease lymph fluid formation with a consequent decrease in tissue load, while the other is to directly damage and obliterate remaining lymphatics. Either way, the outcome appears to be incidental to the underlying pathophysiological derangement of impaired lymph return. In other words, liposuction does not appear to further reduce the already impaired lymph transport. In view of the beneficial effect, with markedly reduced arm edema volume, liposuction combined with CCT remains an attractive therapeutic option.

Liposuction and cellulitis

Removal of the hypertrophic adipose tissue and the unaltered lymph flow together with an improved skin circulation is a plausible explanation for the beneficial effect of liposuction also on the incidence of arm cellulitis, a common clinical complication in patients with chronic lymphedema. The point of bacterial entry may be a minor injury to the edematous skin, and impaired skin blood flow may respond inadequately to counteract impending infection. Other circumstances may also provide a more favorable environment after liposuction. First, the wearing of a protective compression garment probably renders a patient less prone to injury or other skin lesions. Second, reducing the edema volume by liposuction probably decreases the reservoir of proteinaceous fluid, which may potentiate bacterial overgrowth. Moreover, already colonized tissue may also be removed.

Effects on the general health profile

The reduction in arm lymphedema volume following both liposuction + CCT and CCT alone has significant consequences for the patient. As could be expected from the volume measurements, the more favorable effects are mostly recorded with liposuction+CCT. Swelling, heaviness, fatigue or weakness, and pain all decreased, while mobility of the arm increased. ADL improved as well as some important health parameters in NHP, whereas others remained fairly stable. Findings in HAD showed no evidence of anxiety or depressive disorders. PGWB index even showed high starting values, and after treatment they were even higher. The magnitude of this improvement has previously been reported to be of clinical relevance in a population with well-being scores in the normal range (Wiklund et al. 1997).

It may be thought surprising that qualities related to social life and psychological well-being were undisturbed, as qualities related to everyday activities were clearly impaired by the lymphedema. One explanation for the high scores might be that the emotional consequences of the stigma are gradually alleviated once the breast cancer turned out to be properly treated. Another explanation is that women treated for breast cancer are prone to develop a high degree of physical adaptation to the disease and its consequences. Since the baseline or "before treatment" values were compatible with or better than values observed in a normal healthy population, there was little scope for improvement. Hence, no major changes after treatment, or differences between the groups, were likely to appear. Furthermore, groups were comparatively small and the tests used may be too blunt to detect small alterations in this particular patient group. From this point of view, complementary investigations using a larger material and alternative tests seem interesting.

Our findings thus show that the arm lymphedema implies subjective discomfort in terms of pain, swelling, heaviness, fatigue/weakness, and restricted mobility of the arm. These impairments are reflected primarily by difficulties in carrying out activities related to everyday life. Treatment with CCT alleviates these problems, but combined with liposuction, the effect is even more obvious. The consequences of the arm lymphedema for more psychologically oriented qualities seem so far to be less serious.

The lymphedema team

An integral part of our lymphedema project was the establishment of a lymphedema team comprising a plastic surgeon, an occupational therapist, a physiotherapist and a social welfare officer. A 60-minute period is reserved for each scheduled visit to the team, when arm volumes are measured, garments are adjusted or renewed, the social circumstances are assessed, and other matters of concern are discussed.

The patient is also encouraged to contact the team whenever any unexpected problems arise, so that these can be tackled without delay. In retrospect, a working group such as this one seems to be a prerequisite both for thorough preoperative consideration and informing patients, and for successful maintenance of immediate postoperative improvements. The long-term outcome is also monitored by the team, and our experiences so far indicate that a visit twice a year is necessary to maintain a good functional and cosmetic result in most cases. It is beyond the scope of this study to establish definite standards regarding indications for surgery by liposuction in lymphedema of the arm, but preliminary findings suggest that the most impressive improvements from a general point of view are achieved in patients with a preoperative volume of edema exceeding one liter.

Long-term results (4 years)

The thesis presents the one-year results. Regarding the surgical results, continuous follow-up now extends over 4 years. Presently 48 women have been treated with liposuction+CCT. Their mean age at treatment start was 65 years (range, 46 to 89 years) with a mean disease duration of 9 years (range, 1 to 27 years).

Aspirate mean volume was 2,140 ml (range, 1,000 to 3,850 ml). The mean preoperative oedema volume was 1,890 ml (range, 570 to 3,915 ml). As shown in Fig. 1, postoperative mean edema reduction was 83% at 1 month (n=48), 92% at 3 months (n=44), 98% at 6 months (n=41), 104% at 1 year (n=35), 108% at 2 years (n=29), 110% at 3 years (n=22), and 106% at 4 years (n=12).

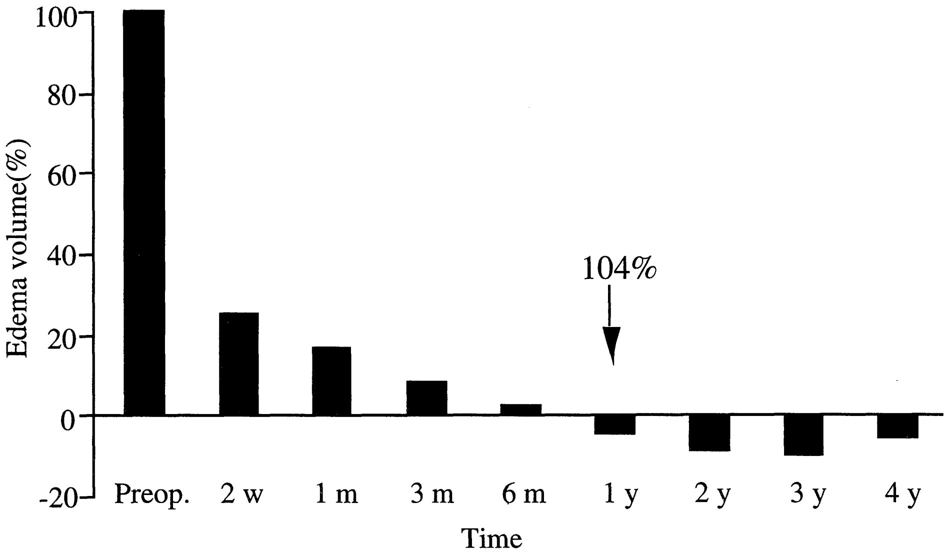

Figure 1. Mean percentage edema reduction after treatment. The preoperative 100% corresponds to the mean initial edema volume of 1,890 ml.

These long-term results show that liposuction+CCT produces a consistent and stable reduction of chronic arm lymphedema.

CONCLUSIONS

A standardized technique for liposuction of arm lymphedema in combination with CCT was established.

The treatment does not jeopardize the skin blood flow in the arm; rather, an improved skin microcirculation is obtained.

The treatment does not further impair the remaining lymphatic transport capacity in the arm.

Liposuction combined with CCT reduces arm lymphedema significantly better than does CCT alone.

The use of a compression garment after liposuction is necessary to maintain the normalized arm volume.

Liposuction combined with CCT improved the quality of life, particularly qualities directly related to the volume reduction and thereby qualities associated with everyday activities.

SUMMARY IN SWEDISH

Liposuction av armlymfödem efter bröstcancerbehandling

Behandlingen av bröstcancer är kirurgisk. Förutom att bröstet avlägsnas innefattar behandlingen ofta borttagning av lymfkörtlar i armhålan samt strålbehandling. Detta leder till att flödet av lymfa från armen kraftigt försämras med svullnad som följd (lymfödem). Detta inträffar i c:a 25% av fallen. Cancern i sig utgör ett orosmoment, men den svullna och tunga armen adderar ytterligare handikapp både ur fysisk och psykosocial synpunkt. Tidigare kirurgiska och icke-kirurgiska (konservativa) behandlingsmetoder har inte alltid givit tillfredsställande och varaktiga resultat, sannolikt p.g.a. att lymfödemet orsakar en tillväxt av underhudsfettet och på sikt en förhårdnad av vävnaden (fibros). I detta perspektiv är operation med fettsugning (liposuction, LS) kombinerad med kontrollerad kompressionsbehandling med en elastisk armstrumpa (Controlled Compression Therapy, CCT) en intressant ny metod. Därigenom avlägsnas den förtjockade fettvävnaden effektivt, och resultatet vidmakthålls med kompressionsstrumpan.

Totalt har 51 kvinnor deltagit i studierna. Samtliga patienter utom en hade strålbehandlats efter bröstcanceroperationen, som också omfattade borttagning av lymfkörtlar i armhålan i samtliga fall. 36 patienter behandlades med LS följd av CCT, och 15 med enbart CCT. Hos 6 opererade patienter avlägsnades kompressionsstrumpan under en vecka efter ett år.

Mätning av ödemvolymen skedde genom att den svullna respektive friska armen sänktes ned i en behållare med vatten. Skillnaden mellan de undanträngda vätskevolymerna blir därigenom ett mått på ödemvolymen. Hudblodflödet registrerades med laser Doppler bildanalys (laser Doppler imaging, LDI). Metoden bygger på att ljus av en våglängd får ett breddat spektrum om det reflekteras av hudkärlens blodkroppar i rörelse. Lymfflödet registrerades med s.k. indirekt lymfscintigrafi (ILS). Metoden innebär att en radioaktiv substans sprutas in under huden i handen och dess transport längs armens lymfsystem följes genom substansens spontana strålavgivning. Rörligheten i axelleden mättes med gradskiva. Effekter på livskvalitén uppskattades med väl etablerade metoder. "Visuell analogskala" användes för att avspegla grad av smärta, handsvullnad och problem med vardagliga aktiviteter. "Nottingham Health Profile" och "Psychological General Well-Being index" utnyttjades för mätning av upplevelser av olika hälsorelaterade problem. "Hospital Anxiety Depression Scale" användes som ett mått på graden av oro och nedstämdhet. Samtliga parametrar registrerades före behandling och upp till ett år därefter.

LS+CCT avlägsnade armlymfödemet fullständigt, jämfört med en reduktion på 50% med enbart CCT. Användande av kompressionsstrumpa är en förutsättning för att vidmakthålla behandlingseffekten. LS+CCT försämrade inte den redan nedsatta lymftransporten och förbättrade snarast hudcirkulationen. Sannolikt som en följd av detta registrerades en minskad förekomst av rosfeber i armen. Behandling med LS+CCT samt enbart CCT förbättrade axelrörlighet och livskvalité, speciellt i sådana avseenden som direkt kunde hänföras till ödemminskningen såsom smärta, svullnad, tyngdkänsla och trötthet/svaghet, varigenom vardagliga aktiviteter underlättades. Som kunde förväntas av ödemreduktionerna sågs de bästa resultaten i LS+CCT gruppen.

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