表1　対象症例の内訳

		開存確認(+) n＝9	開存確認(−) n＝12
性差			
	男/女	0/9	1/11
分類			
	続発性/原発性	8/1	10/2
左右			
	みぎ/ひだり/両側	4/4/1	2/8/2
周径差による重症度分類			
	重症	4	4
	中等症	3	4
	軽症	1	2
	分類不能	1	2
術後経過期間		6-36カ月（平均14.7カ月）	6-27カ月（平均18.0カ月）

表2　2群間における体積減少量の比較

	開存確認 あり n=9	開存確認 なし n=12	p値
下腿遠位[ml]	304±345	176±313	0.19
膝周囲[ml]	600±527	324±580	0.13
合計[ml]	905±875	501±875	0.14

$p<0.05$ significant difference　unpaired Student's t-test

減少量が多い傾向を認めたが，統計学的有意差は認めなかった．

続いて，21症例において吻合部ごとに検討を行った．21症例中，総吻合数は121か所で，術後の蛍光赤外線リンパ管造影法で開存/非開存を明確に判断できたのは，おもに下腿遠位部からさらに足背部であり，その数は37吻合箇所であった．その内15吻合では開存が確認され，22吻合では開存が確認されなかった．よって当院での長期開存率は約40.5%程度と算出された（表3）．

評価しえた37吻合の術中所見を記録された動画を元に詳細に評価したのは37吻合中14吻合であった．リンパ流量が多い吻合部や静脈血の逆流が少ない吻合部の長期開存率が高いと期待されたが，静脈逆流を認める吻合部や，吻合後も逆流を認めている吻合部でも長期開存が確認されており，統計学的傾向や有意差は認めなかった（表4）．

表3　吻合部の内訳

部位	評価可能 n＝37 開存	評価可能 n＝37 非開存	評価困難	合計
足背	5	16	10	31
下腿遠位	10	6	25	41
下腿近位	0	0	19	19
大腿	0	0	30	30
合計	15	22	84	121

表4　吻合部毎の詳細な比較検討

		開存確認(+) n＝9	開存確認(−) n＝5
リンパ流量			
	あり	78%（7例）	40%（2例）
	わずかにあり	22%（2例）	60%（3例）
	なし	＿（0例）	＿（0例）
静脈逆流			
	あり	22%（2例）	＿（0例）
	わずかにあり	11%（1例）	＿（0例）
	なし	67%（6例）	100%（5例）
吻合後			
	リンパ液流入	33%（3例）	80%（4例）
	静脈血逆流	22%（2例）	＿（0例）
	なし	11%（1例）	＿（0例）
	判別困難	33%（3例）	20%（1例）

症　例

以下，典型的な吻合部の開存を確認できた症例を提示する．

34歳男性．32歳時に左下肢浮腫を自覚し，近医にて原発性左下肢リンパ浮腫と診断された．同年，当科紹介受診された（図1）．2年間の保存療法を施行したのちにLVAを施行した．

LVA施行後7カ月経過した際，外来においてICG蛍光リンパ管造影を施行した．LVA計5吻合されていたが，評価できたのは下腿遠位部，のみ計2吻合であった．2吻合中長期開存が確認されたのは2箇所であった．特に下腿遠位での吻合部においては，術中記録されていた静脈，リンパ管の走行に一致した造影結果を得た（図3，4）．

現在周径の大きな改善は認めないが，自覚症状が軽減したことや吻合部周囲における保存療法の効きやすさなどを訴えられており，経過良好である（図2）．

図１　術前臨床写真

図２　術後14カ月

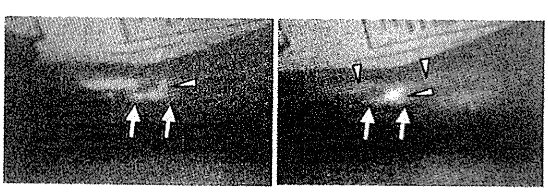

図３
リンパ管静脈側端吻合術術後の造影結果である．造影されたリンパ管（⇨ 矢印）が吻合部を越えて静脈（▷ 矢頭）に流入してH字状に造影されているのが確認された．

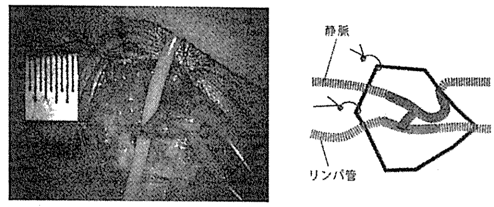

図４
術中写真，およびシェーマを示す．吻合部と静脈合流部が近接しており，H字状になっている．

考　察

LVAの術後長期開存に関する検討は以前より試みられている．1980年代から動物実験においてLVAの吻合部の術後開存と経時的変化に関する報告があった[2),3)]．また，BaumeisterやWeissらはヒトにおけるリンパ管移植術術後のリンパ管吻合部の開存に関する報告をしている[4),5)]．ヒトにおけるLVAに関しては，Campisiらがリンパシンチグラフィ所見の変化を用いて間接的に吻合部の長期開存を評価している[6)]．リンパ管のその他の評価法としてはMRリンパ管造影法[7)]などが挙げられる．しかし，ヒトにおけるLVAの吻合部の術後長期開存を直接証明することは困難であり，それを評価することは長らく克服できなかった臨床的課題の一つであった[8)]．

LVAの外科的治療効果に関する検討は，術後の体積減少量に関する報告が多い[8),9)]．しかし，臨床的には圧迫療法などの複合的理学療法を併用することがほとんどであり，外科治療単独の治療効果の評価は困難であるのが現状である．

今回われわれは，長期開存が確認できた群とできなかった群との比較によりLVAの治療効果の推察を試みた．結果としては長期開存を確認できた群の方が体積減少量の多い傾向はあるものの，統計学的有意差は認めなかった．その理由としては，症例により体積減少量のバラつきが多いことや蛍光リンパ管造影法の観察限界の観点から大腿部などの吻合部の評価はできていないことなどが考察される．そのため，リンパシンチグラフィタイプ分類[10),11)]における同一重症度での比較検討や保存治療のみ施行している症例との比較などが必要と考えている．また，吻合リンパ管の残存機能低下も体積減少量の比較において有意差を得られなかった原因の一つであると考えている．Koshimaらは，慢性リンパ浮腫患者のリンパ管は変性をきたしており，リンパ管機能の廃絶が疑われるということを報告している[12),13)]．実際，われわれが吻合しているリンパ管も肉眼的に変性していることが多く，残存機能の低下が

あると推測している．変性したリンパ管は吻合後も能動的ドレナージ効果は低いため，体積減少や周径の改善を得るためには徒手マッサージや弾性着衣など受動的な外力が必要であると予想される．吻合部が開存しているだけでは体積減少や周径の改善は得られない．いずれにしても，外科的治療効果の評価として周径や体積計測は不十分である．今後は患肢の体積維持に必要な圧迫療法の推移や皮膚硬度の変化，弾性着衣やマッサージの効きやすさなどの解析が必要と考えている．吻合部の長期開存を規定する因子としては，吻合リンパ管のリンパ流や静脈からの逆流の有無，吻合脈管径，リンパ管の変性の程度などが考えられている．今回，吻合後にリンパ液が良好に流入している吻合部の長期開存率が高いと予想し，リンパ液の流入や静脈血の逆流に関して検討した．しかし，実際には静脈逆流を認めた吻合部や，吻合後も静脈血の逆流を認めた吻合部でも長期開存が確認されており，統計学的傾向や有意差をつかむには至っていない．今後は例数を重ね，リンパ管の変性の程度や内腔や壁肥厚の程度，吻合脈管径なども加えた更なる検討が必要である．長期開存を規定する因子を決定し，術中に吻合脈管を取捨選択することで，効率的で新しいリンパ管静脈吻合術が行えると考えている．

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四肢慢性リンパ浮腫に対する外科療法と保存療法による新たな治療戦略

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New strategy for treatment of peripheral lymphedema combined with surgery and conservative therapy

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Key words： combined decongestive physiotherapy, compressive stocking, lymphaticovenous shunt

はじめに

リンパ管静脈吻合術前後の保存療法については詳細な報告が少なく[1)~4)]，われわれは術前理学療法に期間を特に定めず保存治療を行ってから吻合術を適応してきた．しかし，保存療法を続けた症例の中でリンパシンチグラフィー（以下シンチ）の画像上，リンパ機能の悪化が認められた症例を経験した．また，最近では手術時期を設定し，それに合わせて術前保存療法を十分に行うことができれば，その間にシンチの所見上リンパ機能の改善を認め，浮腫改善に良い結果を得られるのではないかと考えるようになった．

また術後の保存療法では，以前は術後１ヶ月経過してから保存療法を行っていたが，一時的に浮腫が戻り，術前と同じ状態に戻すのに時間がかかった症例を経験した．これより術後療法は比較的早期に行うのが良いのではと考えた．さらにこれは患者の目標設定による治療への動機付けと医療費の軽減に繋がる．今回，自験例を供覧し，最近われわれが行っている手術療法と保存療法の関係について報告する．

対象と方法

当施設におけるリンパ浮腫治療のプロトコール（図１）は，はじめにシンチを行い，得られた画像に応じた著者の重症度分類を行う[1),5)]．タイプⅠでは中枢，例えば下肢リンパ浮腫であれば骨盤内や鼠径部，上肢であれば鎖骨下や腋窩部のリンパ節が描出され，タイプⅡでは下肢の場合，大腿で皮膚逆流現象（dermal backflow, 以下DBF）を認めるが，その一部では鼠径のリンパ節が描出される．鼠径や腋窩などの所属リンパ節が描出されないタイプⅢからⅤはリンパ管静脈吻合手術の適応とし，十分な理学療法の後，手術を行った．二重色素造影法とステント法によりリンパ管静脈側端吻合を始めた2006年６月～2010年１月までのリンパ浮腫67症例69肢のうち，術後３から６ヶ月以上で周径計測を行えた65例67肢（下肢54例56肢，上肢11例11肢）を対象とした．

術前後の保存療法の時期の違いから対象症例を２群に分けた．2006年６月～2009年１月までは，特に手術日を意識せず術前の理学療法を行ったため，その期間は６から16ヶ月であり，また術後も退院後初めて外来を受診する約１ヶ月から始め，この群をA群（40肢）とした．2009年２月以降は術前理学療法を短期間に仕上げ，なるべく早く手術を行い，また術後も１週間で圧迫着衣を使用し，マッサージ行うことにし，これをB群（27肢）とした（図２）．両群において術前後の患肢ボリュームの変化を比較検討した．

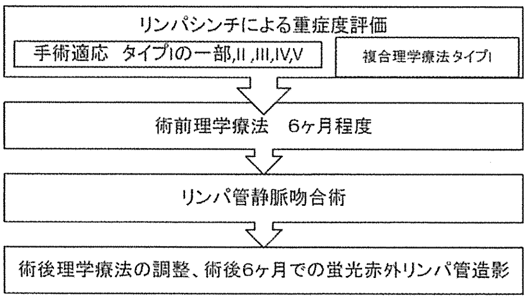

図1　当科における治療プロトコール

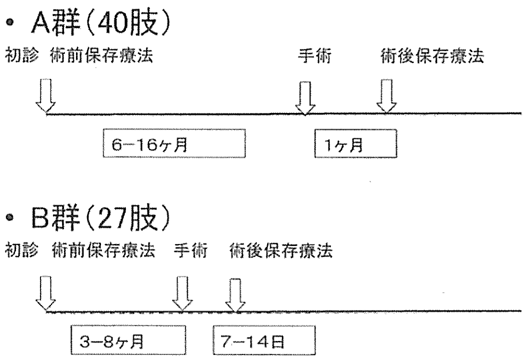

図2　プロトコールの比較

結　果

A群では上下肢（40肢）の平均減少量が592±943ml（平均±標準偏差），下肢（35肢）では672±977ml，上肢（5肢）では31±327ml減少した．B群では上下肢（27肢）で538±798ml減少し，そのうち下肢（21肢）では663±858ml，上肢（6肢）では80±147mlの減少であった．両群間の上下肢のボリュームの平均値に統計的有意差はなかった．症例により圧迫療法の期間に差がでるが，短期例でも以前の長期例のような周径の改善が得られ，シンチでの改善が見られた症例もあった．また，術後の圧迫療法が軽くなった症例や吻合部の長期開存をいくつか経験した．

症　例

A群：58歳女性，2003年に子宮体癌の診断で，子宮広汎切除と所属リンパ節廓清を施行．その後，右下肢と会陰部の浮腫を認めていた．2005年に当科を初診し，下肢周径から患肢体積は5244mlであった．シンチを施行したが，右はタイプⅡであり，理学療法を行い経過観察とした．2008年になり浮腫の悪化に伴い周径が増加したため，再度，シンチを施行したが，タイプⅣと変化し，患肢体積は5907mlと増加した．手術適応と考えて，全麻下にリンパ管静脈吻合術を施行した．足背から大腿にかけて5吻合行った．術後1ヶ月から理学療法を開始し，術後1年8ヶ月，右患肢の体積は術直前と比較して約500ml減少し，5369mlと初診時とほぼ同程度に改善した．術後のシンチもタイプ3に改善した（図3 A－G）．

B群：52歳女性，原発性右下肢リンパ浮腫．1999年に右下肢の浮腫を認め，2008年に某大学病院を受診しリンパ浮腫と診断された．その後，某所で理学療法を受けていたが浮腫が悪化したため，当科を受診した．初診時の右下肢の体積は8144ml，シンチではタイプⅢであり，手術適応であり，今一度，6ヶ月間の理学療法をストッキングの二重履きによる圧迫を中心に行うこととした．術直前に患肢体積は6512mlとなり，初診後6ヶ月でリンパ管静脈吻合術（7吻合）を，9ヶ月後に大腿部で2吻合追加した．術後は約1週間でマッ

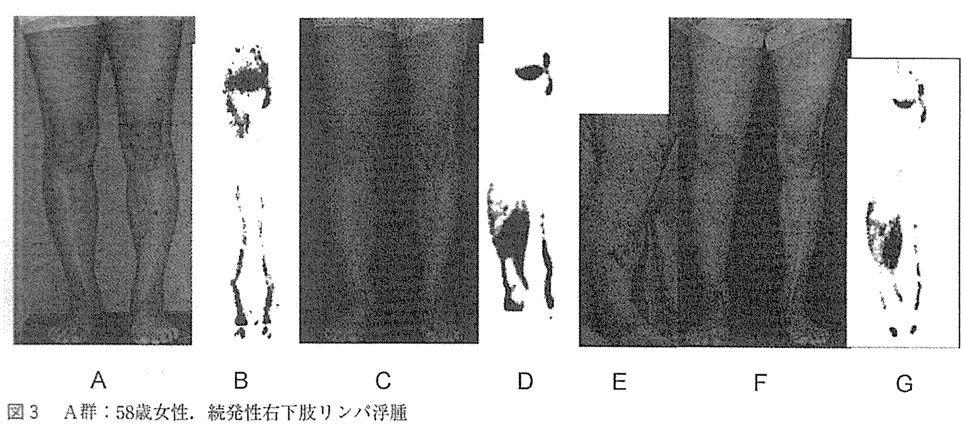

図3　A群：58歳女性．続発性右下肢リンパ浮腫
A, 初診時正面　B, 初診時シンチ　C, 3年後正面　D, 術前シンチ　E, 術中　F, 術後6ヶ月正面　G, 術後シンチ

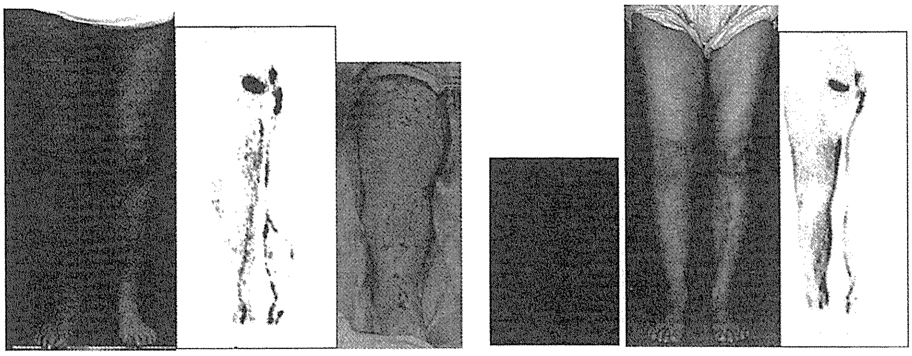

図4　B群：52歳女性．原発性右下肢リンパ浮腫
A，初診時正面　B，術前シンチ　C，初回手術　D，2回目術中のインドシアニングリーンによる蛍光赤外線リンパ管造影　E，2回目術後5ヶ月正面　F，術後シンチ

サージを開始し，その後，ストッキング着用を減らし，2回目術後5ヶ月で右下肢は体積5765mlと改善し，現在，一日を通じてストッキングをほとんど着用していない（図4A－F）．

考　察

リンパ浮腫の圧迫治療を中心とする保存療法にはゴール設定がなく，患者はしばしば長期の治療から離脱する．また，A群の症例で示した如く，理学療法を継続する中で治療に反応せず浮腫が悪化する症例を経験するが，これはシンチの画像変化からリンパ機能の低下によると考えられる．Garfeinら[6]はリンパ浮腫の治療プロトコールとして理学療法の効果を判定し，非効果例に手術適応があるとしているが，リンパ機能が悪化[7]する前にリンパ管内に鬱滞したリンパを静脈にドレナージする手術を行い，残されたリンパ機能を維持することが必要であると思われる．われわれはシンチによって得られる画像を基にリンパ管静脈吻合術の適応を決めているが，リンパ機能障害があまり進んでいないタイプ3がタイプ4，5よりも多くの吻合ができる[1]．B群の症例で示したように，長期のリンパ管静脈吻合の開存を確認しており，吻合開存が多く存在する症例では，浮腫の改善によるADL（activity of daily living）の向上が期待できる．

一方，リンパ管静脈吻合術を中心とする外科療法と保存療法との関係については未だ詳細な報告が少ない[1)~4)]．これは，理学療法や手術療法に一定の基準がなく，また医療効果に明確なエビデンスがないからである．しかし最近の経験から，手術治療を理学療法の短期的なゴールに設定すると，患者は短期間に集中して圧迫療法を受け入れ，効率良い治療が可能となる．また，手術の効果が現れると，圧迫療法の程度が軽くなるなど，さらに患者のADL向上が期待出来る．シンチ所見上で手術適応と思われる症例では，術前理学療法により皮膚や皮下組織を柔らかくし，術中のリンパ管同定を容易にする．理学療法が維持期に入り安定してから手術までの時間が長くなると，前述した如く，リンパ機能の悪化を来す場合もあり，また患者ADLが低下する．今回の報告では術前理学療法の期間を定めていないA群と手術時期に合わせて理学療法を行ったB群と比較して患肢体積を比較したが，有意差を認めなかった．これはADLの観点から見ると，同じ結果を得るのにB群では治療時間と費用の軽減ができる．われわれの治療プロトコールが最善であるという確固たるエビデンスはないが，手術療法と保存療法をうまく組み合わせることで，治療成績をさらに向上させる可能性があり，今後二つの治療方法をどのタイミングで行うか，さらに検討する必要がある．また，理学療法と手術療法をタイミング良く行うために，手術を行う外科医と理学療法を担当する看護師，理学療法士，セラピストとの間で患者さんの情報を交換し，治療方針を決めるために密なコミュニケーションが必要であると考える．

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CLASSIFICATION OF LYMPHOSCINTIGRAPHY AND RELEVANCE TO SURGICAL INDICATION FOR LYMPHATICOVENOUS ANASTOMOSIS IN UPPER LIMB LYMPHEDEMA

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ABSTRACT

Upper limb lymphedema that develops after breast cancer surgery causes physical discomfort and psychological distress, and it can require both conservative and surgical treatment. Lymphaticovenous anastomosis has been reported to be an effective treatment; however the disease severity criteria that define indications for this treatment remain unclear. Here, we examined lymphoscintigraphic findings in 78 patients with secondary upper limb lymphedema and classified them into 5 major types (Type I-V) and 3 subtypes (Subtype E, L, and 0). Results revealed that this classification is related to the clinical stage scale of the International Society of Lymphology. Based on intraoperative examination findings in 20 of the 78 patients, lymphatic pressure is likely to be further elevated in Type II-V cases which are characterized by the presence of dermal back flow. Therefore, lymphaticovenous anastomosis should be considered as a treatment option for lymphedema in Type II-V cases. Furthermore, there are only limited lymph vessel sites usable for lymphaticovenous anastomosis in more severe lymphedema types [Types IV and Type V (which is characterized by dermal back flow only in the hand)]. The findings in Type IV-V cases suggest that therapeutic strategies for severe upper limb lymphedema need further consideration.

Keywords: lymphoscintigraphy, upper limb lymphedema, surgical treatment, lymphaticovenous anastomosis

Regarding malignant tumors, the prevalence rate of breast cancer is relatively high for women in Japan, Europe, and North America (1). Currently, less invasive treatments with limited resection is becoming a preferred surgical option for primary lesions along with advances in chemotherapy and radiotherapy (2-6). Additionally, the use of sentinel lymph node biopsy (SNB) is providing a reduction in axillary lymph node dissection (7-9). Despite these advances, lymphedema is still seen as a common morbidity following breast cancer treatment. According to recent studies, the incidence of lymphedema after breast cancer treatment is in a range of 6-60%, and this appears to increase to 45-60% when patients receive chemotherapy combined with axillary lymph node dissection (1,10,11). In addition, upper limb lymphedema leads to decreases in activities of daily living (ADL) and is often complicated by cellulitis and lymphorrhea (12,13), causing significant distress to patients (14-16).

Treatment options for upper limb lymphedema are similar to those for lower limb lymphedema and include conservative therapy and/or surgical therapy. Conservative therapy includes physical treatment, such as massage and mechanical methods that use elastic compression stockings and bandages (17-19), while the primary surgical options are lymphaticovenous anastomosis (20,21), lymph vessel transplantation (22), and lymph node transplantation (23). In particular, the efficacy of lymphaticovenous anastomosis, which reduces the high pressure of the lymphatics to assist conservative therapy in patients with upper limb lymphedema, has already been demonstrated (24). Few studies, however, have clearly examined the disease severity criteria that define indications for lymphaticovenous anastomosis. In this study, we classified findings from lymphoscintigraphy performed in patients with secondary upper limb lymphedema with their clinical staging and investigated relevance of the classification for use as an indicator for surgical therapy.

PATIENTS AND METHODS

Subjects

Seventy-eight cases of upper limb lymphedema in patients (n=78; 1 male and 77 female; mean age at initial consultation, 55.5 ± 13.2 years; range 22-84 years) who were examined by lymphoscintigraphy at our department between January 2004 and June 2010 were investigated. All patients had a history of previous surgical treatment for breast cancer and had been diagnosed with secondary upper limb lymphedema on the basis of their clinical history and physical findings (edema in the arm on the same side as previous surgery) at initial consultation. Seventy-seven patients previously underwent axillary lymph node dissection, and the remaining one underwent SNB. None of the patients had suspected venous obstruction (e.g., no clinical signs of venous dilation, varicosities, or thrombophlebitis), and they did not undergo an ultrasound examination. None of the patients had a history of previous surgery on the healthy side.

Lymphoscintigraphy

Technetium-99m-labeled human serum albumin was subcutaneously injected (0.2 ml, 40 MBq) between the first and second fingers and between the third and fourth fingers of both hands. Anterior and posterior images were obtained with a gamma camera 30 and 120 min after injection.

The images were first classified into type (Type I-V) on the basis of the sites where dermal back flow (DBF) was observed, in a similar manner to the classification of lymphoscintigraphic findings in patients with lower limb lymphedema (25), and then classified further into subtype (Subtype E, L, or 0) according to the time when supraclavicular or infraclavicular lymph nodes were visualized (Subtype E, detectable on early images taken 30 min after injection; Subtype L, detectable on late images taken 120 min after injection; Subtype 0, not detectable on any images). The clinical stage of each patient was determined according to the clinical stage scale proposed by the International Society of Lymphology (ISL) (26). The criteria for type classification we used were as follows:

Type I–lymphatic flow from the hand to the lymph nodes around the clavicle is depicted as a line. Mild lymphatic obstruction and additional collateral vessels are observed, but signs of DBF are absent in the forearm and upper arm. A typical image of Type I-Subtype E lymphedema is shown in *Fig. 1.*

Type II–mild lymphatic obstruction is observed, and signs of DBF appear in the upper arm on images taken 30 min and/or 120 min after injection. A typical image of Type II-Subtype L is shown in *Fig. 2.*

Type III—significant lymphatic obstruction is observed, and signs of DBF appear in the upper arm and forearm on images taken 30 min and/or 120 min after injection. A typical image of Type III-Subtype L is shown in *Fig. 3.*

Type IV–lymphatic flow from the hand to the lymph nodes around the clavicle

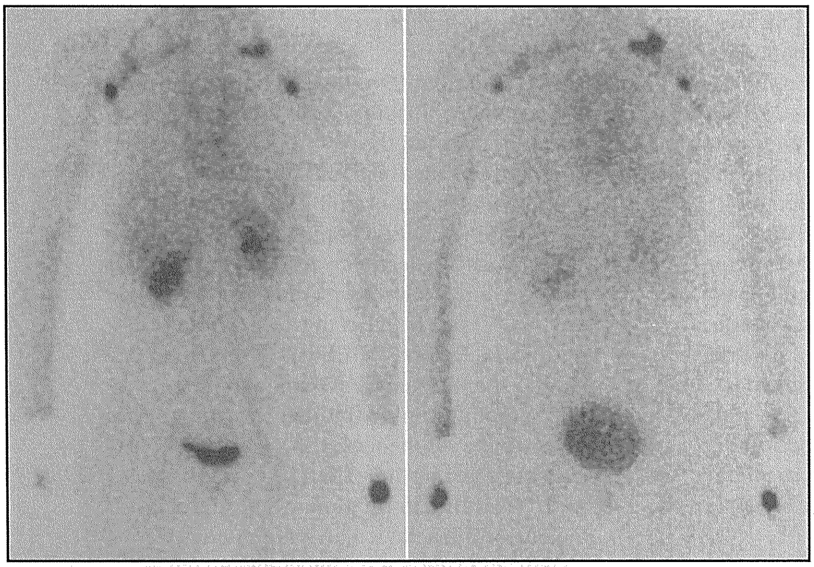

Fig. 1. Lymphoscintigraphy images of a case of Type I-Subtype E lymphedema in the left arm. The left and right panels show images taken 30 and 120 min, respectively, after injection of a contrast medium. Lymph nodes around the clavicle, but not axillary lymph nodes, were observed in the affected left arm. Dermal back flow (DBF) was confirmed to be absent in both arms.

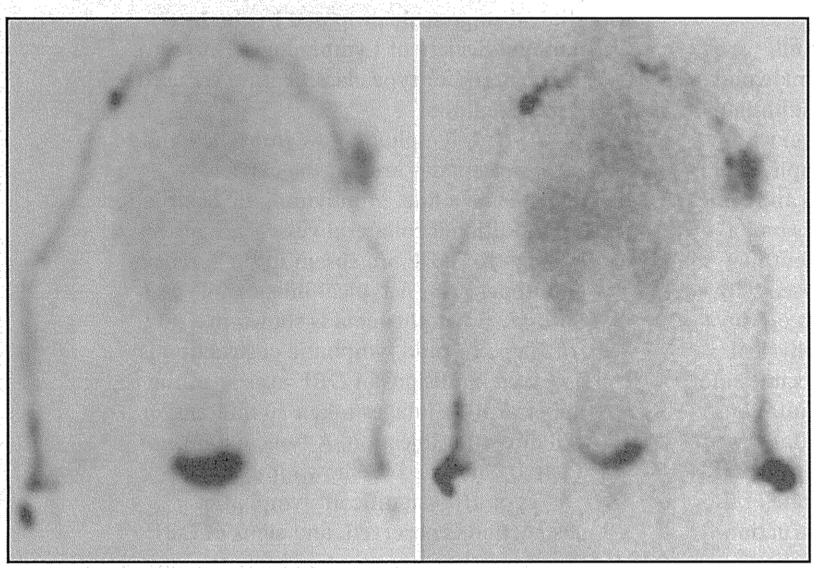

Fig. 2. Lymphoscintigraphy images of a case of Type II-Subtype L lymphedema in the left arm. The left and right panels show images taken 30 and 120 min, respectively, after injection of a contrast medium. Lymph nodes around the clavicle were observed only on the image taken at the later time point. DBF was found only in the left upper arm.

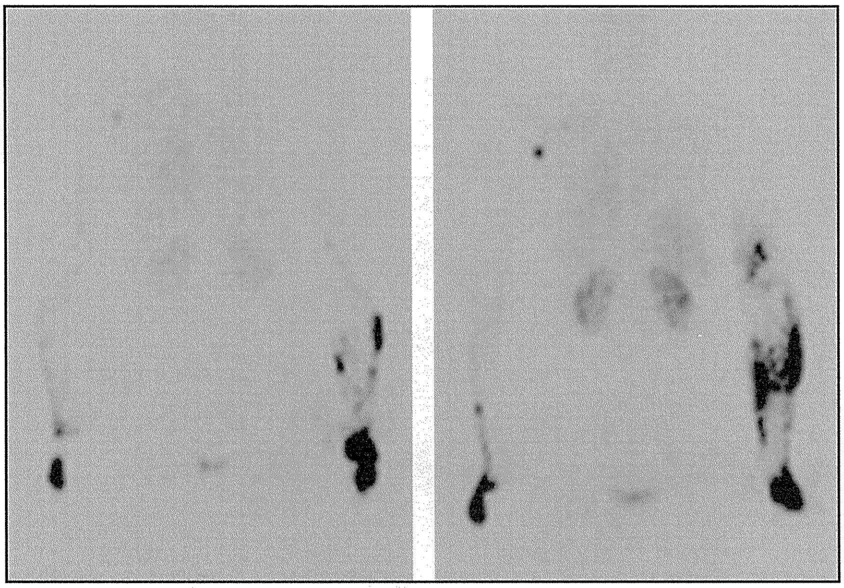

Fig. 3. Lymphoscintigraphy images of a case of Type III-Subtype 0 lymphedema in the left arm. The left and right panels show images taken 30 and 120 min, respectively, after injection of a contrast medium. Lymph nodes around the clavicle were not observed even on the image taken at the later time point. DBF was found in the upper arm and forearm of the affected side on the image taken 120 min after injection.

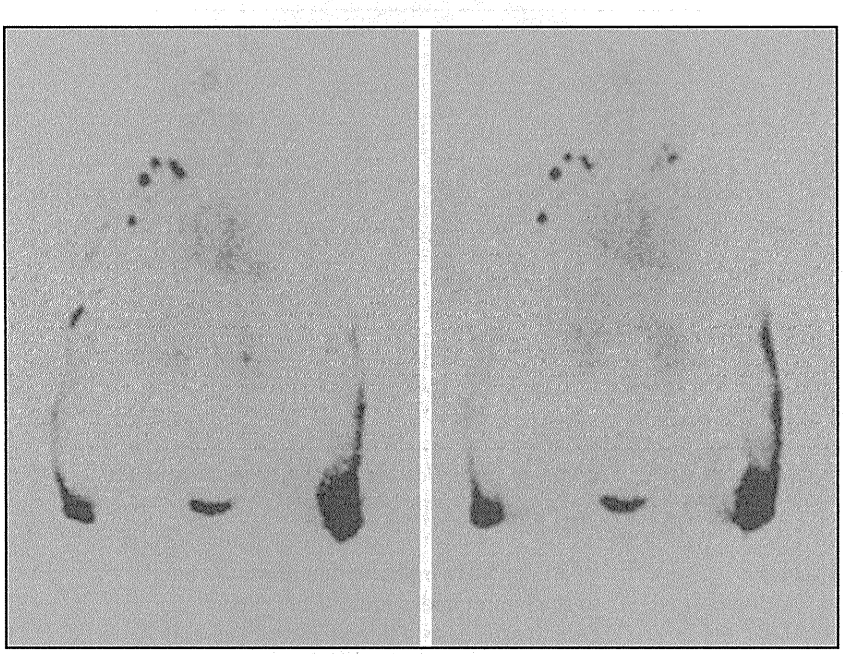

Fig. 4. Lymphoscintigraphy images of a case of Type IV-Subtype L lymphedema in the left arm. The left and right panels show images taken 30 and 120 min, respectively, after injection of a contrast medium. Lymph nodes around the clavicle were observed only on the image taken at the later time point. DBF was found only in the left forearm.

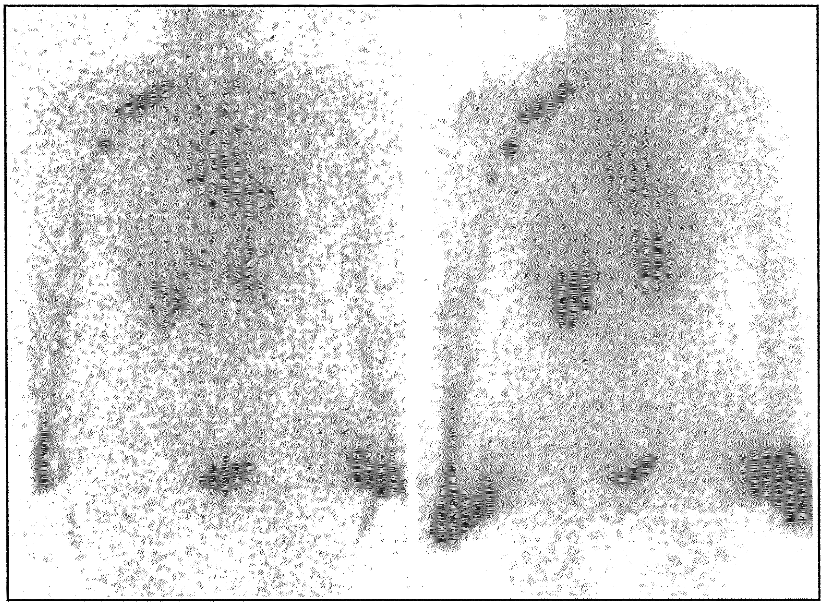

Fig. 5. Lymphoscintigraphy images of a case of Type V-Subtype 0 lymphedema in the left arm. The left and right panels show images taken 30 and 120 min, respectively, after injection of a contrast medium. Lymph nodes around the clavicle were not observed even on the image taken at the later time point. DBF was found only in the hand.

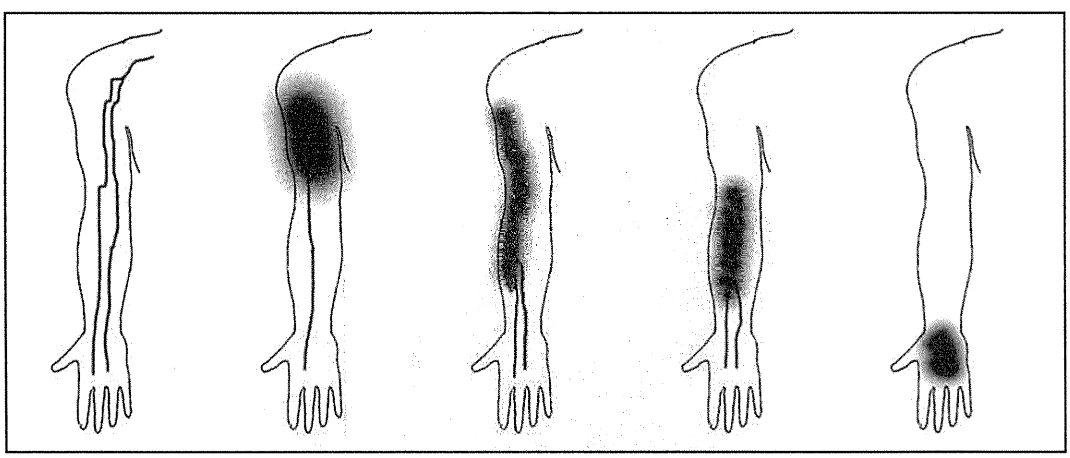

Fig. 6. Schemes of lymphoscintigraphy of Type I to Type V. The lines of lymph-flow are vague in some cases while the location and extent of dermal back flow varies in each case.

(which appear as a line in Type I cases) is almost absent. Instead, significant lymphatic obstruction is observed, and signs of DBF are present only in the forearm. A typical image of Type IV-Subtype L is shown in *Fig. 4.*

Type V–Lymphatic flow from the hand to the lymph nodes around the clavicle (which appear as a line in Type I cases) is absent. Lymphatic obstruction is not observed, and signs of DBF are present only

TABLE 1
Cases of Lymphaticovenous Anastomosis by Type

	Subtype E	Subtype L	Subtype 0	TOTAL
Type I	1	1	0	2
Type II	2	1	2	5
Type III	0	1	2	3
Type IV	0	2	3	5
Type V	0	0	5	5

Subtype E, detectable on early images taken 30 min after injection; Subtype L, detectable on late images taken 120 min after injection; Subtype 0, not detectable on any images

in the hand. A typical image of Type V-Subtype 0 is shown in *Fig. 5.*

Fig. 6 shows schematic illustrations of the images in *Figs. 1-5.*

Surgical Procedures

Lymphaticovenous anastomosis was performed in 20 patients under general or local anesthesia depending on age and underlying diseases (status of cancer and bronchial asthma) (*Table 1*). Prior to making skin incisions, we performed two-color spectral fluorescence lymphangiography using a 5% patent blue dye and indocyanine green (ICG) to identify the anastomosis sites (27,28). ICG infrared fluorescence lymphangiography was performed during surgery to map lymph flow and patent blue was used to indicate the functional superficial lymphatics without the need for special devices. The DBF sites (hand, forearm, and upper arm) were recorded for each classification type.

Several skin incisions were made to reach the superficial lymphatic vessels in the hand, forearm, and upper arm according to the map of lymph flow based on ICG infrared fluorescence lymphangiography. We then identified macroscopically functional lymphatics stained by patent blue. When vessel identification was difficult, skin incisions were made at positions slightly distal from the DBF, and side-to-end (lymphatic-to-vein) anastomosis was performed. This was done in order to preserve the original flow of lymphatics should the anastomosis become obstructed, which is a possibility that should not be ignored in patients with a limited number of functional lymphatic vessels. In addition, further surgery remains possible to other parts of the same lymphatic vessels used for anastomosis if the anastomosis becomes occluded in the future. Usually, the veins were anastomosed just proximal to the venous valve in order to prevent blood reflux into the lymphatics. Venous transplantations were needed in a few sites when a suitable vein was absent. The same surgeon (JM) performed the surgical procedures in all patients.

The circumferences of three points in the arm (point A, wrist; point B, 10 cm distal to the cubital fossa in the forearm; and point C, 10 cm proximal to the cubital fossa in the upper arm) and the distance between points A and B were measured before and after surgery. Arm volume was calculated using a previously reported formula (29) to examine changes in arm volume after surgery. The rates of change in arm volume after surgery were calculated using the following formula:

TABLE 2
Clinical stage scale of the International Society of Lymphology (see Ref. 26)

Stage 0: Subclinical condition
Stage 1: Early accumulation of fluid relatively high in protein content; subsides with limb elevation. Pitting may occur.
Stage 2: Limb elevation alone rarely reduces tissue swelling and pitting. The limb may or may not pit as tissue fibrosis supervenes.
Stage 3: Lymphostatic elephantiasis where pitting is absent, trophic skin changes such as acanthosis, fat deposits, and warty overgrowths develop.

TABLE 3
Results of Type Classification

Subtype	Type I	Type II	Type III	Type IV	Type V	TOTAL
E	12	5	5	0	0	22
L	2	2	4	6	0	14
0	1	6	13	16	6	42
TOTAL	15	13	22	22	6	78

Subtype E, detectable on early images taken 30 min after injection; Subtype L, detectable on late images taken 120 min after injection; Subtype 0, not detectable on any images.

rate of change in arm volume (%) = (postoperative arm volume x preoperative arm volume)/(preoperative arm volume) x 100. An additional calculation of "edema volume" based on a comparison with the non-affected arm was made in each case before and after surgery and the rate of change was calculated.

Statistical Analyses

The type classification results were examined in relation to the clinical stage by ISL (*Table 2*) using Dunn's multiple comparison test. Statistical significance was set at $p<0.05$. The total number of limbs presenting DBF in each site in Group A (Type I-III) and those in Group B (Type IV-V) were compared using the Kruskal Wallis H-test as previously (25). Statistical significance was set at $p<0.05$. STAT MATE III (ATMS Co. Ltd., Tokyo, Japan) was used for all statistical analysis.

The mean rate of change of arm volume and edema volume before and after lymphaticovenous anastomosis (LVA) in Group A was compared to that in Group B using the Student t-test.

RESULTS

Type Classification on the Basis of Lymphoscintigraphy Findings

Abnormal lymphoscintigraphy findings include lymphatic obstruction, appearance of additional collateral vessels and DBF, and poor or no visualization of the supraclavicular

TABLE 4
Type and Clinical Stage Scale

Clinical stage scale	n	1	2	3
Type I	15	14	1	0
Type II	13	6	7	0
Type III	22	5	16	1*
Type IV	22	8	13	1**
Type V	6	1	5	0**
TOTAL	78	34	42	2

n, number of limbs; Type I vs. Types III, IV, and V, *$p < 0.01$, **$p < 0.05$ (Dunn's multiple comparison test)

TABLE 5
Number of Patients Presenting Dermal Back Flow on Intraoperative Indocyanine Green Lymphangiography Images

	n	Hand	Forearm	Upper arm
Type I	2	0	1	0
Type II	5	2	3	4
Type III	3	0	3	3
Type IV	5	2	3	0
Type V	5	4	4	2

n, number of limbs

or infraclavicular lymph nodes. All 78 cases were successfully classified (*Table 3*). There were 15 Type I cases (12 Subtype E, 2 Subtype L, and 1 Subtype 0), 13 Type II cases (5 Subtype E, 2 Subtype L, and 6 Subtype 0), 22 Type III cases (5 Subtype E, 4 Subtype L, and 13 Subtype 0), 22 Type IV cases (6 Subtype L, and 16 Subtype 0), and 6 Type V cases (6 Subtype 0). Lymphoscintigraphy findings of the healthy arm were similarly classified. There were 77 Type I cases (68 Subtype E, 8 Subtype L, and 1 Subtype 0), and 1 Type II-Subtype E case. The clinical stage scale proposed by ISL is shown in *Table 2*. Statistical analysis of the relationship between the type classification and the clinical stage of the ISL revealed significant differences between Type I and III ($p<0.01$), Type I and IV ($p<0.01$), and Type I and V ($p<0.05$) cases (*Table 4*).

Intraoperative Findings

The sites of DBF were identified by two-color lymphangiography. In Group A, DBF was found in 2 sites in the hand, 7 in the forearm, and 7 in the upper arm. In Group B, DBF was found in 6 sites in the hand, 7 in

TABLE 6
Total and Mean Number of Anastomoses per Limb in Each Type

	n	Hand	Forearm	Upper arm	Total
Type I	2	2 (1)	4 (2)	2 (1)	8 (4)
Type II	5	5 (1)	13 (2.6)	5 (1)	23 (4.6)
Type III	3	4 (1.3)	9 (3)	1 (0.3)	14 (4.7)
Type IV	5	5 (1)	14 (2.8)	2 (0.4)	20 (4)
Type V	5	6 (1.2)	12 (2.4)	0 (0)	18 (3.6)

Values are show as total (mean) number

TABLE 7
Volume Change of Limbs

	n	Increased	Decreased	Average percent of change (%)	Average percent of change (%)
Type I	2	1	1	0.67	15.05
Type II	5	0	5	-9.65	-4.18
Type III	3	1	2	-11.5	-2.4
Type IV	5	2	3	-2.47	-10.96
Type V	5	3	2	0.47	1.68
TOTAL	20	7	13	-4.57	-2.22

n, number of limb

the forearm, and 2 in the upper arm. There were no significant differences between the 2 groups (*Table 5*).

Relationship Between Type and Number of Anastomosis Sites

Table 6 shows the total number of anastomosis sites and its mean (per limb) value for each type as determined from the lymphoscintigraphy findings. The mean value was largest for Type III (4.7). There were no significant differences in the mean values of anastomosis sites between Group A (4.30 ±1.16) and Group B (4.00 ± 1.15).

Rates of Changes in Arm Volume after Surgery

Arm volume was decreased after surgery in 13 of 20 patients, but increased in the remaining 7 patients (*Table 7*). The mean rate in 20 patients was −4.57 ± 9.6%, while those in Group A and Group B were −8.15% and −1.0%, respectively. The difference between the two groups was not statistically significant (p=0.067). Arm volume increase was observed in 1 case of Type I (Subtype E), 1 case of Type III (Subtype L), 2 cases of Type IV (Subtype L and Subtype 0), and 3 cases of Type V (Subtype 0). The average change in edema volume in Group A was 0.2% (±12.8) while that in Group B was −4.64% (±16.5). The difference between the two groups was not statistically significant (p=0.483).

DISCUSSION

Type classification of lymphoscintigraphy findings was partially related to the ISL clinical stage (*Table 4*). We presumed that the lymphoscintigraphy images of healthy arms would be classified as Type I-Subtype E, provided the patients had no history of previous surgery, external injury, or exposure to radiation (29). Indeed, our results were generally in agreement with this presumption. However, there were 10 (of 78) exceptional cases in this study, and asymptomatic primary lymphedema or tracer entry into collateral routes is considered a possible reason for these cases.

According to Koshima et al, occlusions of the lymphatic vessels and degeneration of smooth muscle cells start from the proximal ends of the extremities in cases of secondary extremity lymphedema (30), and this is supported by a study reported by Suami et al (31). These findings suggest that DBF may also appear from the proximal ends of the arm on lymphoscintigraphy images of upper limb lymphedema and thus be confirmed only in the hand in the most severe cases.

On the basis of the above assumption, we previously reported the classification of lymphoscintigraphy findings, with an emphasis on the sites of DBF, in patients with lower limb lymphedema (25). In addition, in the present study, we considered the report by Szuba et al (29) and examined the timing of when lymph nodes around the clavicle were visualized on images. As shown in *Table 3*, approximately 54% and 41% of patients in Type II and Type III groups, respectively, were classified as Subtype E or L. These results suggest that collateral routes form more frequently in the upper limbs than in the lower limbs (31). On the other hand, the prevalence of Subtype 0 was higher in Type IV and Type V, suggesting that disruption of the lymph system worsens in proximal sites (30,31). Taken together, we believe that the type classification proposed in this study reflects the severity of secondary lymphedema, despite the fact that the Kruskal Wallis H-test did not indicate statistical significance, which may be due to the small sample size examined.

One of the patients examined in the present study developed lymphedema after SNB but not axillary lymph node dissection. This patient was a clinical stage 1 patient, and the upper arm volume was changed by 3.49% after surgery. However, a lymphoscintigraphy image of the same patient was judged as Type 2-Subtype L and intraoperative ICG lymphangiography indicated DBF in the hand, forearm, and upper arm, presenting many similarities to the case reported by Suami et al (31). Considering that approximately 5% of patients who undergo SNB reportedly develop lymphedema (32), this patient may fall into this subpopulation that develops lymphedema after SNB.

Szuba et al reported a lymphedema severity scoring system based on the findings from lymphoscintigraphy performed in 19 patients who developed upper limb lymphedema after breast cancer surgery (29). Similarly, Pecking et al reported a lymphedema severity staging system based on the findings of 4,328 patients with lower limb lymphedema (33). We have also previously reported a classification of lymphoscintigraphy findings with an emphasis on the relation to indications for microsurgery for lower limb lymphedema using a simpler classification method than the previous two lymphoscintigraphy-based systems (25). This system's usefulness as an indicator for microsurgery in lower limb lymphedema has already been confirmed (25). High-resolution magnetic resonance (MR) lymphangiography is another static image-based approach that has been shown to be effective for diagnosing lymphatic flow disturbances (34). Although MR lymphangiography clearly depicts functional lymphatic vessels, the timing of scanning is difficult to control among patients. Thus, it is not suitable for comparative studies requiring identical examination conditions or for severity classification.

TABLE 8
Comparison Between Pre and Postoperative Scintigraphy

Affected side	Preoperative type	Post-operative type	Duration from surgery to postoperative scintigraphy
L	2-E	2-L	12 months
L	4-L	4-L	21months

Subtype E, detectable on early images taken 30 min after injection; Subtype L, detectable on late images taken 120 min after injection

We performed surgery for secondary lymphedema in 20 patients in this study. Based on our experience with patients with secondary lower limb lymphedema, we performed surgery in two Type I patients, regardless of their subtype: one with a high swelling rate (affected arm versus healthy arm) determined by measurement of arm circumference and volume; and another who strongly requested withdrawing from treatment that used a compression stocking. Swelling continued in the former patient after surgery, but use of an elastic compression stocking was successfully withdrawn approximately 1 year after surgery in the latter patient. Furthermore, the number of anastomosis sites in Type I patients was not markedly different from that in the other types, albeit on the basis of comparisons of a limited number of cases (*Table 6*). Taking these findings together, unlike Type I secondary lower limb lymphedema (25), surgical therapy might be indicated in a few cases of Type I secondary upper limb lymphedema, as in our two cases.

Lymphaticovenous anastomosis is our preferred surgical procedure for the treatment of secondary lymphedema. Prior to making skin incisions, we perform two-color lymphangiography using a 5% patent blue dye and ICG to identify the anastomosis sites (27,28). In this procedure, we can identify only superficial lymphatic drainage that is suitable for microscopic LVA. The sites of DBF identified by ICG lymphangiography shifted from the proximal to distal end of the arm as lymphedema progressed from Type I to Type V. The number of anastomosis sites in each part of the arm showed similar trends (*Table 6*). The number of cases of each type was insufficient for statistical analysis, so the differences among the types were not statistically tested. Nevertheless, our results suggested that possible sites for anastomosis can be found throughout the arm – from the hand to the upper arm – in patients with Type I-II, while such sites are mainly in the hand (the dorsum) and not in the upper arm in patients with Type V secondary lymphedema. Patients with lymphedema of the dorsum of the hand must wear an elastic glove in everyday life, and this sometimes leads to decreased ADL. Thus, the effects of anastomosis will be significant for patients when lymphedema is alleviated by this surgical treatment.

On the basis of the reduction in arm volume, Type II and Type III lymphedema are the most likely indications for microscope-assisted lymphaticovenous anastomosis. On the other hand, we routinely initiate complex physical therapy approximately 1 week after surgery. Therefore, the results shown in *Table 7* were not solely attributed to surgery, and the effects of complex physical therapy should be taken into consideration. In addition, surgery was performed in only 20 of the 78 patients in this study, and like our previous study on secondary lower limb lymphedema (25), the type classification did not reflect several factors such as elapsed time after breast cancer surgery, exposure to radiation, history of previous chemotherapy, occupation, and lifestyle. Indeed, postoperative lymphoscintigraphy was performed in two of our cases, which showed little change from the preoperative images (*Table 8*). In the protocol of this study, postoperative lymphoscintigraphy was not included because the late patency of every anastomosed site would not have been indicated clearly, although decreased DBF could have indirectly shown the effectiveness of LVA (35). Given the results of this study, postoperative lymphoscintigraphy should be included in future research protocols. In addition, prospective studies that give consideration to the timing and procedures of physical therapy are necessary in order to closely examine the usefulness of the proposed type classification as an indicator for surgery and to determine the significance of the subtypes.

CONCLUSION

Here we established a simple classification method, employing a commonly used diagnostic method, for classifying type of lymphoscintigraphic findings in secondary upper limb lymphedema, with an emphasis on the sites of DBF and visualization of lymph nodes around the clavicle. We believe that lymphoscintigraphy is effective for assessing patients with secondary upper limb lymphedema before lymphaticovenous anastomosis. Patients meeting the criteria for Type I secondary upper limb lymphedema, unlike previously reported criteria for Type I secondary lower limb lymphedema, might have indication for lymphaticovenous anastomosis. Our results suggest that lymphaticovenous anastomosis can be performed throughout the arm, from the hand to the upper arm, and its outcome is likely to be good in Type II and Type III patients, regardless of subtype. On the other hand, the sites and numbers of lymphatic vessels suited for anastomosis appear limited in Type IV patients with more severe lymphedema and Type V patients with DBF only in the hand.

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