Lymphedema

20

Takumi Yamamoto and Nana Yamamoto

20.1 Etiology and Clinical Manifestations of Lymphedema

Lymphedema is an edematous disease caused by abnormal lymph circulation [1–5]. There are various types of lymphedemas, and most of them are intractable and progressive. Lymphedema is largely classified into primary lymphedema and secondary lymphedema [1, 3, 4, 6–8]. Secondary lymphedema has an evident cause of the disease such as infection, trauma, and surgical intervention to lymphatic system, and lymphedema other than secondary lymphedema is called primary lymphedema [1, 2, 8]. Majority of lymphedema cases are secondary lymphedema [2–4, 9–11]. In tropical areas, filaria infection is a major cause of secondary lymphedema; filarial lymphedema. In developed countries, cancer treatments are major causes of secondary lymphedema; cancer-related lymphedema or cancer treatment-related lymphedema [3, 7–9].

As the lymphatic system plays important role in fluid balance, immune system, and lipid metabolism, various clinical manifestations can be seen in lymphedema [1, 8, 12]. Lymph retention causes edematous changes in various tissues especially subcutaneous fat tissue [1–4, 9, 13]. Abnormal lymph circulation deteriorates immune system and lipoprotein profile [1, 3, 9, 10, 14]. Long-lasting inflammation may lead to development of angiosarcoma; Stewart–Treves syndrome [5, 10, 15, 16]. As lymph flow deterioration progresses subclinically, appropriate evaluations including lymph flow visualization are important for lymphedema management [1, 2, 9, 11, 17–21].

T. Yamamoto (✉) · N. Yamamoto
Department of Plastic and Reconstructive Surgery, Center Hospital of National Center for Global Health and Medicine, Tokyo, Japan
e-mail: tyamamoto-tky@umin.ac.jp

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20.1.1 Etiology of Primary Lymphedema

Various conditions cause primary lymphedema. Although specific gene mutations are reported in familial lymphedema cases, most primary lymphedema cases are sporadic and their causes are unknown [1, 2, 8, 9]. Various abnormalities during development of the lymphatic system can cause primary lymphedema.

One of the most genetic mutations causing primary lymphedema is VEGFR3 causing Milroy disease. Others include GJC2 (Meige disease), FOXC2 (lymphedema distichiasis syndrome), KIF11/VEGFC (Milroy-like disease), RASA1 (Parkes-Weber syndrome), AKT/PIK3/mTOR (CLOVE/fibroadipose hyperplasia), AKT1 (Proteus syndrome), CCBE1 (Hennekam syndrome), GATA2, and several genes causing syndromic lymphedema such as Turner syndrome, Fabry disease, and yellow nail syndrome [1, 2, 8, 12].

Most primary lymphedema cases are sporadic and their causes are unknown [1, 2, 8]. Some are clarified to be associated with malformation and/or dysfunction of lymph nodes and lymph vessels including the collecting lymph vessels, the pre-collecting lymph vessels, and the lymphatic capillaries.

20.1.2 Etiology of Secondary Lymphedema

Majority of lymphedema cases are secondary lymphedema [3–7, 9, 10, 22, 23]. Secondary lymphedema has obvious causes of development of the disease such as trauma, surgery, radiation, infection, tumor, malformation, and venous diseases. Any injury to the lymphatic system can cause secondary lymphedema [3, 4, 6, 7, 10, 22]. The most common causes are parasite infection in tropical regions, and cancer treatments in developed countries.

Filarial infection is the commonest cause of secondary lymphedema in the world [3, 5, 12]. Infection by the filaria, *Wuchereria bancrofti*, causes multi-site inflammation in the lymph vessels and nodes, resulting in lymph flow obstructions. In spite of effective antimicrobial agents to the parasite, there are still many new filarial lymphedema cases because of limited availability of the drug and neglect of the disease's significance in developing tropical countries.

Cancer treatments are the leading cause of secondary lymphedema in most developed countries [3, 6, 10, 12, 22]. Surgical resection and/or irradiation of regional lymph nodes causes lymph flow obstruction. Extensive lymph node dissection with radiation has a higher risk of developing secondary lymphedema. Extensive intra-lymphatic metastasis of tumor cells can also cause lymph flow obstruction and subsequent lymphedema.

Venous stasis ultimately causes abnormal lymph circulation, as lymph flows into venous circulation [2, 12, 24]. Advanced venous congestion can be associated with lymphedema; phlebolymphedema. Phlebolymphedema manifests as more progressive edematous disease with frequent inflammatory episodes of cellulitis and ulceration complicated with lymphorrhea.

20.1.3 Clinical Manifestations and Prognosis of Lymphedema

Abnormal lymph circulation causes dysfunction in fluid balance, lipid metabolism, and immune system [1, 3, 9, 10, 12]. Clinical manifestations are caused by edematous changes, poor lipid metabolism, and local immune-insufficiency in affected regions.

Lymph retention leads to volume changes mostly in the adipose tissue via edematous changes [4, 10, 11, 23]. Lymph, protein-rich fluid, retains in the interstitial tissue, manifesting pitting edema. Protein-rich fluid in the interstitial tissue causes subclinical inflammation and adipose tissue deposition, manifesting non-pitting edema with significant duration after lymphedema development. Long-lasting inflammation finally leads to fibrotic changes of the dermis and the adipose tissue, manifesting elephantiasis. In advanced lymphedema, dermal lymphatic capillaries are dilated in the very superficial layer in the dermis, manifesting lymphocyst. Lymphocyst is likely to be ruptured spontaneously, causing leakage of lymph called lymphorrhea [4, 9, 12, 20, 25, 26].

Inflammation is caused either by interstitial lymph retention itself or by infectious conditions [1, 10, 16, 25]. Clinically evident inflammation can be seen in lymphedematous regions, called lymphangitis or cellulitis. Bacterial infection is more frequently seen in progressed lymphedema complicated with lymphorrhea or phlebolymphedema, and is sometimes life-threatening because of sepsis. Decades-long inflammation eventually causes malignant mutation of the lymph vessels' cell gene, causing life-threatening lymphangiosarcoma or angiosarcoma called Stewart–Treves syndrome [6, 10, 15].

Lymphedema starts from subclinical conditions with abnormal lymph circulation, and progresses to clinically evident edematous changes; first with pitting edema, then non-pitting edema [3, 9, 11, 17, 25, 27]. Although the progression is gradual and not rapid in most cases, lymphedema is progressive and non-curable in nature, and its treatment requires life-long time. Lower hemi-body lymphedema, lower extremity lymphedema, and genital lymphedema have poorer prognosis compared with upper extremity lymphedema.

20.2 Diagnosis and Evaluation of Lymphedema

The most important point in lymphedema evaluation is to understand that clinical manifestations can be confirmed only after abnormal lymph circulation significantly progresses [10, 11, 27]. Lymph flow obstruction leads to distal lymphatic hypertension and dilatation of lymph vessels, causing retrograde lymph flows as lymphatic valvular insufficiency takes place due to lymphatic dilatation. Only after significant retrograde lymph flow takes places, lymph retains in the interstitial spaces, which is manifested as clinically evident pitting edema. Long history of lymph retention in the interstitial spaces and inflammation in the soft tissue causes fat deposition, manifested as non-pitting edema and skin fibrosis. Classical physical examinations, such as Stemmer sign, can be useful only for already significantly progressed cases [1, 3, 12, 21, 27].

20.2.1 Conventional Examinations and Gene Testing

History taking helps a medical staff to suspect lymphedema. When an edematous patient has a past history of treatment for malignancy with lymph node dissection and/or radiation, travel to or residence in tropical regions where filarial infection is common, trauma or surgical intervention to major lymphatic pathways, or family history of lymphedema, probability of lymphedema becomes higher as a cause of the edema [1, 2, 5–7, 12, 22, 23]. Other medical and social history, which may influence edematous conditions such as several organs failure and hormonal conditions, should be assessed to rule out other edematous diseases. Systemic involvement can be seen in some primary lymphedema cases, and non-edematous body parts and related symptoms should also be assessed, such as the eyelid (lymphedema distichiasis), nail (yellow nail), skin color change (Stewart–Treves syndrome), and diarrhea (protein-losing enteropathy due to intestine lymphangiectasia) [1, 2, 8, 12]. Blood tests, X-ray, and electrocardiogram may be used to rule out other edematous diseases. Specific gene testing is needed for definitive diagnosis of above-mentioned primary lymphedema due to gene mutation.

20.2.2 Volumetry

As fluid retention is the most evident clinical manifestation of lymphedema, volume evaluation is the most common routine assessment for lymphedema [3, 9, 10, 12, 28]. There are various volume evaluations, including circumference measurements, water displacement method, image-based volumetry, and other volumetric methods. Although objective measurement, volumetry cannot evaluate lymph circulation itself which is the most important for lymphedema evaluation.

Circumference measurement is the most commonly applied lymphedema evaluation. Various extremity parts are measured with tape, and followed to assess therapeutic courses of lymphedema. A major drawback of circumference measurement is that it is 1-dimensional evaluation in spite that lymphedematous volume change is 3-dimensional (3D). Therefore, circumference measurement data should be used to calculate 3D volume using truncated cone model or lymphedema index formula (Fig. 20.1) [28–31].

Water displacement method is used to directly measure limb volume. A limb is inserted into water-container fulfilled with fixed volume of water, and water volume overflowed from the container is measured to represent the limb volume. Although used as a gold standard for volumetry, water displacement method is time consuming and non-convenient, which is not practical in most daily lymphedema clinics [3, 28, 30].

Computed tomography (CT) and magnetic resonance imaging (MRI) can be used to calculate volume. Although reconstruction of images and calculation of limb volume take some time, CT- and MRI-based volumetry allows accurate and reproducible volume measurement. A major drawback is high cost for CT and MRI, and they are not practical for routine follow-up methods [3, 21, 31].

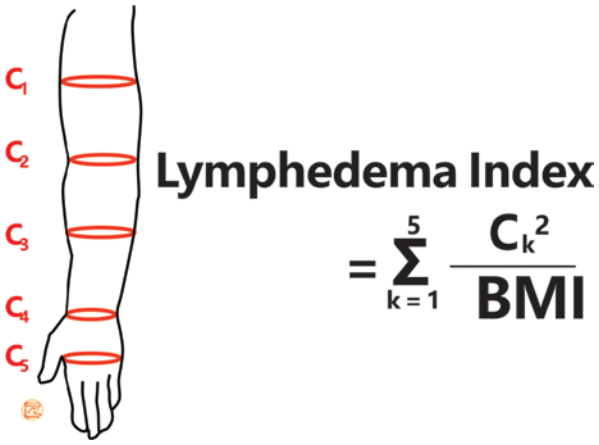

Fig. 20.1 Formula for lymphedema index

Other volumetry methods include specialized volumetry measures such as laser-scan volumetry and 3-dimensional photography [3, 21, 32]. Laser-scan volumetry and 3D photography-based volumetry allow limb volume measurement via laser scanning and 3D reconstructed image, respectively. Unlike CT-based volumetry, laser scanning and 3D photograph are free from radiation exposure.

20.2.3 Bio-Impedance Spectroscopy

Bio-impedance spectroscopy (BIS) quantifies fluid balance in the human body by measuring various parts' impedance to calculate fluid components in the muscle and the fat tissues of various body parts. BIS is not invasive and its data is easily available, allowing clinically practical routine evaluation method. BIS can detect small changes of fluid retention, and allows early diagnosis of lymphedema [3, 11, 28, 33]. A major drawback is that BIS only quantifies fluid balance and cannot assess lymph circulation which is crucial for lymphedema evaluation. Small change of fluid balance can occur in daily activity or physiological and non-pathological leg edema. Therefore, it is necessary for definitive diagnosis of lymphedema to rule out other edematous conditions with other modalities.

20.2.4 Imaging Studies Other than Lymph Flow Imaging

Edematous changes can be detected by CT, MR, and ultrasound (US). Fluid retention is represented as higher density area in CT, higher intensity area in T2 weighted MRI, and hypoechoic area in US [3, 12, 21, 22]. Typically, fluid retention is seen mostly in the deep fat layer above the deep fascia in lymphedema, whereas venous edema shows fluid retention also in the deeper tissues such as the muscles. CT and MRI have an advantage that edema distribution is visualized three-dimensionally. CT allows quick scanning to obtain images, but has a risk of radiation exposure.

MRI visualizes 3D distribution of fluid and fat without radiation exposure, but requires longer scanning time than CT. US allows real-time visualization and sometimes visualizes the collecting lymphatic vessels, but its image quality largely depends on an examiner [10, 22, 34].

20.2.5 Lymph Flow Imaging Studies

Lymph flow visualization is the most important for lymphedema evaluation, and basically necessary for definitive diagnosis. There are several lymphography methods, including direct oil-contrast lymphangiography (LAG), lymphoscintigraphy (LSG) and single photon-emission computed tomography-computerized tomography (SPECT-CT), magnetic resonance lymphography (MRL), and indocyanine green fluorescent lymphography (ICG-L) [3, 8, 9, 17, 19, 21, 35–39].

Direct LAG using oil-contrast such as lipiodol used to be a gold standard for direct lymphatic visualization [3, 36, 39]. Oil-contrast is injected directly into the collecting lymphatic vessel via a small skin incision and cannulation, and radiographic images are taken. Although anatomy of the collecting lymphatic vessels proximal to the injection site is clearly visualized, LAG has a risk of lymphedema worsening because oil-contrast evokes inflammation and subsequent obstruction of the enhanced lymph vessels. Therefore, LAG is not currently used for lymphedema evaluation, and mainly used for diagnosis and treatment for lymph leakage diseases such as lymphorrhea, chyloabdomen, and chylothorax (Fig. 20.2) [3, 39].

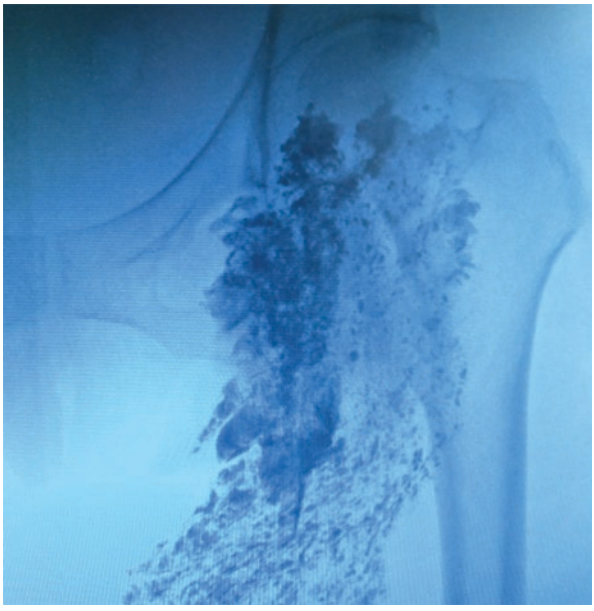

Fig. 20.2 LAG showing the inguinal lymph nodes and lymphatic leakages

LSG is currently considered a gold standard for lymph flow evaluation [2, 3, 8, 12, 17, 22, 36]. Contrast agent combined with radioisotope is subcutaneously injected at the distal limb, and scintigram scan images are obtained after injection. LSG visualizes superficial and deep lymph flows in a whole body, and is necessary for primary lymphedema evaluation with systemic involvement. Major drawbacks include obscure image and a risk of radiation exposure (Fig. 20.3) [3, 20, 36]. LSG can be combined with CT image; SPECT-CT. SPECT-CT allows 3D evaluation of lymph circulation (Fig. 20.4). With advancement of lymphatic reconstructive surgeries, LSG or SPECT-CT images are not enough for precise localization of lymph vessels suitable for lymphatic surgery, and the following new modalities are becoming popular [36, 39–41].

Contrast-agent for MRI, gadolinium, can be injected subcutaneously, which visualizes lymph vessels on MRI; MRL. MRL allows both fluid/fat balance evaluation on non-enhanced images and lymph flow visualization on MRL images. Unlike LSG or SPECT-CT, MRL images are clear enough to consider indication and design of lymphatic surgeries [3, 21, 36, 39]. Major drawbacks include obscure image and a risk of radiation exposure (Fig. 20.5). Although MRL gives abundant information of lymphedema, subcutaneous injection of gadolinium has a risk of injected site skin necrosis which may result in severe sequela of cellulitis worsening lymphedema, and is contraindicated for patients with renal failure.

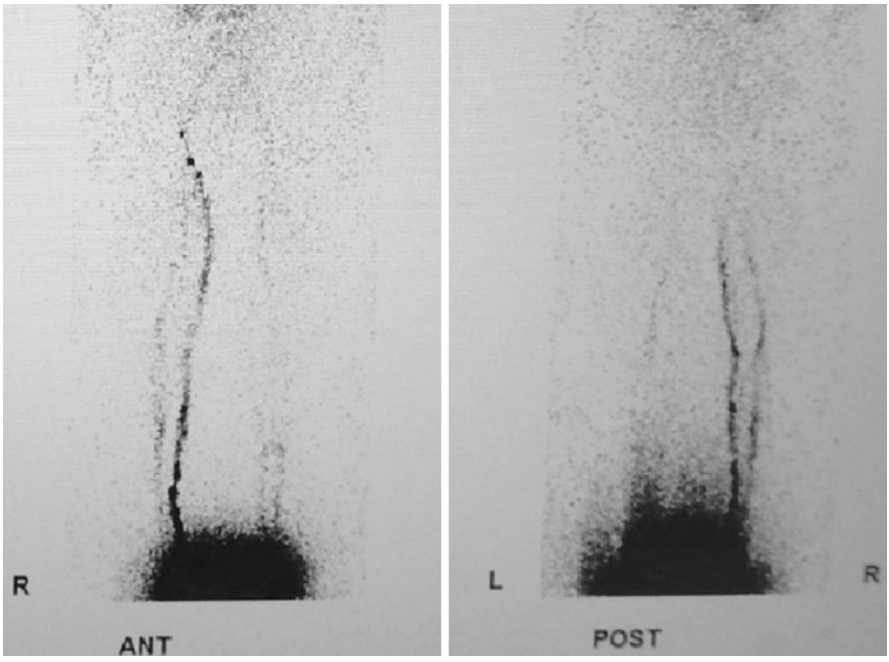

Fig. 20.3 LSG images showing lower extremity lymph flows

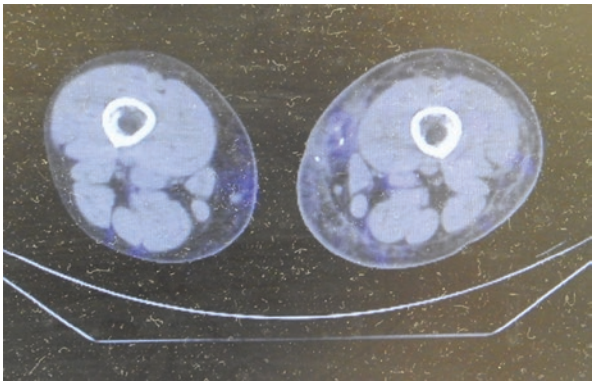

Fig. 20.4 SPECT/CT image showing 3D location of the lymph vessels

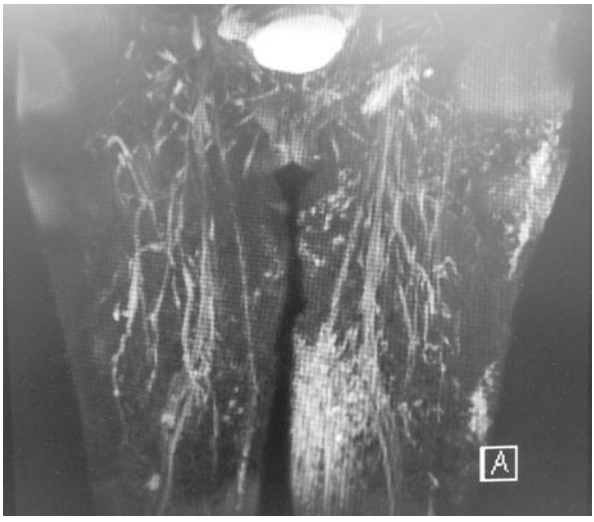

Fig. 20.5 MRL showing the lymph vessels and DB; veins are also shown

ICG-L images are obtained using a near-infrared camera after subcutaneous injection of ICG. Superficial lymph circulation is clearly visualized without a risk of ionized radiation exposure [3, 17, 20, 35, 38] (Fig. 20.6). Unlike any other lymph flow imaging methods, ICG-L allows real-time imaging, which is clinically useful for intra-interventional evaluation of lymph circulation; a surgeon can evaluate lymph flow conditions intraoperatively and use it for intraoperative navigation, and a physiotherapist can evaluate efficacy of manual lymph drainage (MLD) [17, 23, 40–48]. Compared with other modalities, ICG-L allows the earliest detection of abnormal lymph circulation, dermal backflow (DB), leading to diagnosis of subclinical lymphedema and possible radical prophylactic intervention. With its usefulness and convenience, ICG-L is becoming popular and one of the most important evaluation for lymphedema management in most advanced lymphedema centers. A major drawback is that ICG-L visualizes only superficial lymph flows 2-cm in depth from the skin surface and cannot directly visualize deep lymph flows.

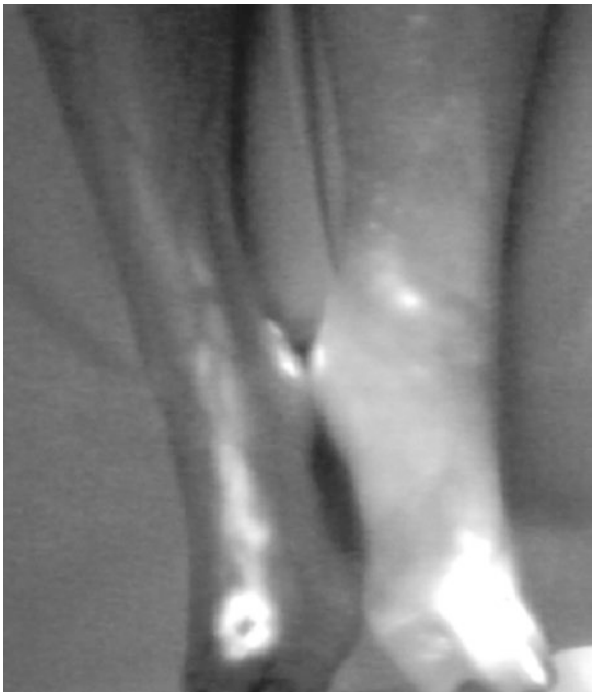

Fig. 20.6 ICG-L showing superficial lymph flows. Linear pattern is seen in the right leg and DB pattern in the left leg

20.3 Classification and Severity Evaluation

As various conditions take place with progression of lymphedema, various classification and severity staging systems are reported. Most classifications are based on physical findings such as edematous conditions and volume changes, and on lymph circulation. Although most commonly applied in daily clinics, physical finding-based classifications does not always represent pathophysiological conditions of lymphedema, and lymph flow-based classifications should be utilized as possible.

20.3.1 Staging Based on Physical Examination

Physical finding-based stages utilize edematous conditions such as temporary edema, pitting and non-pitting edema, and fibrotic changes such as elephantiasis. The most popular and widely used classification is International Society of Lymphology (ISL) stage [3, 5, 45]. ISL stage consists of stage 0, stage I, stage II, and stage III. ISL stage 0 represents no edema but with impaired lymphatic transport, ISL stage I mild temporary edema which can be resolved with limb elevation, ISL stage II pitting or non-pitting edema which cannot be subsided with limb

elevation, and ISL stage III elephantiasis. There are several clinical stages similar to ISL stage, and some include limb volume change as criteria.

20.3.2 Primary Lymphedema Classification

Onset age is most commonly used classification for primary lymphedema, and primary lymphedema is classified into congenital lymphedema, lymphedema praecox, and lymphedema tarda [1, 2, 8]. Cutoff values of age are 0 and 35 years; congenital lymphedema represents primary lymphedema seen at birth, lymphedema praecox from 0 to 35 years old, and lymphedema tarda after 35 years old. Although the most popular classification, onset age-based classification does not represent its pathophysiology and is not useful to predict prognosis. For some primary lymphedema with specific gene mutation, gene-based classification or diagnosis can be used for clinical evaluation and management [8, 12].

Image-based classification has been reported useful for pathophysiology-based classification and prognosis prediction. ICG lymphography classification consists of proximal DB (PDB), distal DB (DDB), less enhancement (LE), no enhancement (NE) types (Table 20.1) (2). DB pattern is seen predominantly in the proximal region in PDB type, and in the distal region in the DDB type. In LE type, Linear pattern is seen in the distal region, but no enhancement is observed in the proximal region. In NE type, no enhancement is observed other than ICG injected sites. PDB type has similar prognosis to secondary lymphedema, and DDB type is more frequently associated with cellulitis. LE type has better prognosis, and compression therapy alone is enough to control lymphedema. NE type is clinically most severe form and has the worst prognosis against physiotherapy or lymphatic bypass surgery.

20.3.3 Secondary Lymphedema Staging

Various lymphatic images are used to classify secondary lymphedema severity. US, MRI, and CT-based classification utilizes fluid retention and its contribution/extension as criteria. These images-based volumetry is also used to classify secondary lymphedema severity [3, 9, 10, 21, 36, 38]. As mentioned before, they just represent fluid retention and do not represent pathophysiological conditions.

Table 20.1 ICG classification for primary lymphedema

ICG classification	Lymphography findings
PDB type	DB pattern mainly in the proximal region
DDB type	DB pattern mainly in the distal region
LE type	Linear pattern only in the distal region (no DB pattern)
NE type	No enhancement (no linear or DB pattern)

ICG indocyanine green, *DB* dermal backflow, *PDB* proximal, *DB*. DDB, distal DB. *LE* less enhancement, *NE* no enhancement

LSG is a widely used lymphatic imaging study to evaluate pathophysiological conditions of secondary lymphedema [3, 36, 37]. Based on visibility of lymphatic image and extension of DB, LSG stage and transport index are determined. LSG is clarified useful for secondary lymphedema diagnosis, and there are several reports of usefulness of LSG for prognosis prediction and considering surgical indication.

ICG-L stages are reported for secondary lymphedema of the various body parts; upper extremity, lower extremity, genitalia, face/head/neck, and breast [17, 20–25]. ICG-L findings are divided into normal Linear pattern and abnormal Splash (mild DB) pattern, Stardust (moderate DB) pattern, and Diffuse (severe DB) pattern (Fig. 20.7) [17, 27]. ICG stage consists of stage 0 (Linear pattern only), stage I (Linear and Splash pattern), stage II (Linear and Stardust/Diffuse pattern in 1 region), stage III (Linear and Stardust/Diffuse pattern in 2 regions), stage IV (Linear and Stardust/Diffuse pattern in 3 regions), and stage V (Stardust/Diffuse pattern only) (Table 20.2) [18, 27, 46, 49]. Using ICG-L, ISL stage 0 can be divided into 3 stages; ICG stage 0 (no lymphedema) with no risk of progression, ICG stage I

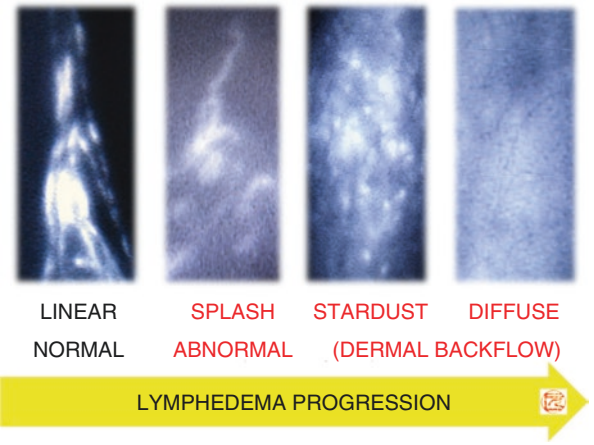

Fig. 20.7 Characteristic ICG lymphography findings. Normal Linear pattern and abnormal DB patterns (Splash, Stardust, and Diffuse pattern)

Table 20.2 ICG stage for secondary lymphedema

ICG stage	Lymphography findings
Stage 0	Linear pattern only (no dermal backflow pattern)
Stage I	Linear pattern + splash pattern[a]
Stage II	Linear pattern + stardust/diffuse pattern (1 region)[b]
Stage III	Linear pattern + stardust/diffuse pattern (2 regions)[b]
Stage IV	Linear pattern + stardust/diffuse pattern (3 regions)[b]
Stage V	Stardust/diffuse pattern only (no linear pattern)

ICG indocyanine green

[a] Splash pattern is usually seen around the axilla/groin

[b] Upper/lower extremity are divided into 3 regions; the upper-arm/thigh, the forearm/lower-leg, and the hand/foot. Face/head/neck is divided into 3 regions; the neck, and the lower/upper hemi-face below/above the eye level. Genitalia is divided into 3 regions; the lower abdomen above the mons pubis, the scrotum/labia majora, and the penis/labia minora

(subclinical lymphedema) with 10–30% risk of progression, and ICG stage II (early lymphedema) with 30–100% risk of progression; lower extremity and genital lymphedema have higher risks, whereas upper extremity, breast and face/head/neck lymphedema have lower risks. ICG stage III-V represent progressed lymphedema with 100% risk of progression.

20.4 Management of Lymphedema

Mainstays of lymphedema management are conservative treatments, and surgical treatments are considered for compression-refractory cases [3–5, 9, 10, 15, 22, 23]. Prophylactic lymphatic reconstructive surgery may be considered for primary prevention of lymphedema after cancer treatments. Multidisciplinary approach is essential for management of this challenging disease.

20.4.1 Conservative Treatments

Complete decongestive therapy (CDT), consisting of skin care, compression therapy, appropriate exercise, and MLD, is performed by specialized lymphedema therapists. Compression therapy using lymphedema-specialized garment is the most important one among CDT [3, 5, 9, 10, 12, 22, 26, 50]. Although mainstay for lymphedema management, CDT is basically anti-symptomatic therapy and does not address pathophysiology of lymphedema; abnormal lymph circulation is not improved by CDT. Therefore, conservative treatments are required basically for a life-long period.

Several medications have been used to treat lymphedema, but most of them are abandoned due to adverse effects without therapeutic efficacy; for example, diuretics are now contraindicated for lymphedema. Some advanced medical treatments can be considered for limited cases. Gene therapy and growth factor therapy may be applied in some primary lymphedema cases, but would be contraindicated for cancer-related lymphedema because of risks of facilitating cancer metastasis [1, 3, 8, 12]. Some herbal medicines are undergoing clinical trials.

20.4.2 Surgical Treatments

Surgical treatments are divided in to debulking surgery and reconstructive surgery [3, 7, 9, 10, 12, 13, 16, 26, 40–44, 50]. Debulking surgery, including surgical resection and liposuction, aims to remove edematous tissue, resulting in immediate volume reduction but deterioration of lymph circulation. Surgical resection is associated with high postoperative wound complication rates and morbidities, and liposuction requires even more strict compression therapy for a life-long period.

Reconstructive surgery aims to improve lymph circulation by diverting congested lymph flow via bypass or by implanting an intact lymphatic tissue [7, 9, 26, 40, 42, 43]. Lymphatic bypass surgeries include lymphaticolymphatic bypass and

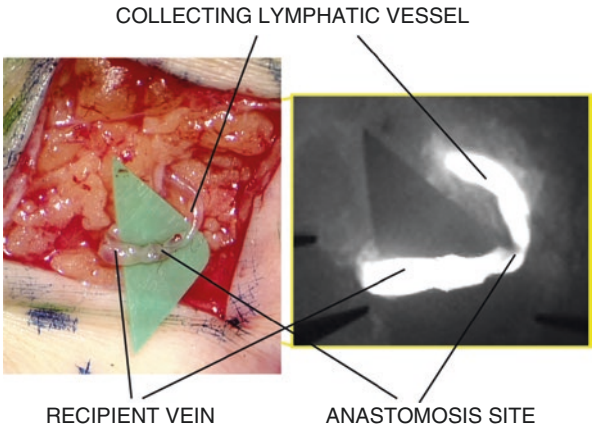

Fig. 20.8 Supermicrosurgical LVA. A collecting lymphatic vessel is anastomosed to a nearby venule or a small vein in an intima-to-intima coaptation manner. Intraoperative ICG-L shows patency of the anastomosis

lymphaticovenous bypass. Lymphaticolymphatic bypass requires a long lymph vessel graft which may cause donor site lymphedema [3, 9, 16]. Lymphaticovenous bypasses include lymph node-to-venous coaptation, lymphaticovenous implantation (telescopic anastomosis), and supermicrosurgical lymphaticovenular anastomosis (LVA); former 2 procedures are done with microsurgical technique, and tissues other than the endothelium are exposed inside the lumen, which would result in anastomosis site thrombosis when venous reflux occurs [9, 10, 22, 26, 40, 44, 50]. On contrary to microsurgical implantations, intima-to-intima coaptation is utilized in LVA, which has a far less risk of anastomosis site thrombosis even with venous reflux. LVA is becoming popular with its efficacy and minimally invasiveness (Fig. 20.8).

Lymphatic tissue transfers include lymph node transfer (LNT), lymph vessel transfer (LVT), and lymph-interpositional-flap transfer (LIFT) [7, 9, 10, 22, 43]. Lymph node/vessel and its surrounding tissue are transferred with microvascular anastomosis in LNT/LVT. In LVT, additional LVA is basically required to optimize its efficacy. In LIFT, vascularized soft tissue including lymph vessels is transferred with microvascular anastomosis, and its lymph vessels' stumps are approximated to recipient lymph vessels' stump to bridging lymphatic gaps. LNT and LVT are indicated for severe lymphedema cases where LVA hardly works due to lymphosclerosis, and LIFT is indicated for soft tissue defect cases associated with defects of major lymph pathways (Fig. 20.3) [7, 9, 10, 43, 46].

20.5 Summary of Recent Advancements

Significant achievements have been established recently regarding diagnosis and treatment of lymphedema. Many genes related to primary and secondary lymphedema are identified, and some of them are applied in gene therapy mainly for primary lymphedema. ICG-based lymphography has been widely applied in evaluation and navigation of lymphedema interventions, including near-infrared imaging and photoacoustic imaging. Combined surgical approach using debulking and

reconstructive surgery is becoming popular to achieve lymphedema cure with complete lymphedematous volume reduction and compression-free conditions.

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