6 Investigations of Lower Limb Edema

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6.1 Introduction

The diagnosis of leg edema is currently based upon clinical history and laboratory investigations regarding systemic or local disorders (Table 6.1), followed by the local evaluation of objective signs.

In most cases, the local evaluation of limb edema is based upon the visual appearance of the leg, followed by skin palpation and, at the most, tape measurement of the ankle circumference.

Other techniques of edema quantification and characterization are poorly used in daily clinical practice, even be simple execution. Some of these techniques are

Table 6.1 Differential diagnosis of swollen legs

Causes of monolateral leg edema	
Local factors	Venous insufficiency, lymphatic disorders, skin diseases, inflammation or infections, trauma, previous surgery, osteoarticular, and/or neuromuscular disorders
Causes of bilateral symmetric leg edema	
Systemic diseases	Dyscrasia and dysproteinemia (renal and/or hepatic disorders), cardiac insufficiency, pulmonary disorders, malnutrition, hormonal disorders
Lifestyle	Obesity, sedentary
Drug therapies	Anti-inflammatory drugs, antihypertensive treatments, and others

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currently used only for research purposes. In turn, data obtained with these methods may help to refine the diagnosis as well as to furnish the information useful in decision-making regarding the therapy for each case.

In daily clinical practice, the more frequent cause of lower limbs edema is chronic venous disease (CVD). The presence of edema is currently considered an accurate index of CVD severity. In fact, grade 3 of the “C” score of the Clinical-Etiologic-Anatomic-Pathophysiologic classification (CEAP) consists of the presence of edema (C3) [1] Leg edema is also included in both the original and the modified versions of the Venous Clinical Severity Score (VCSS). The severity of edema is just classified as “absent” (grade 0), mild (grade 1, evening only), moderate (afternoon, grade 2), and severe (grade 3, morning) [2]. This grading is insufficient to quantify the severity of venous edema at all. In turn, a correct clinical categorization of venous edema needs a more detailed quantification of edema and characterization of tissue changes. Moreover, a correct quantification of edema is important for both the daily practice and research purposes. In addition, it seems appropriate to identify the pathogenesis of edema, necessary to plan the more appropriate treatment.

For all these reasons, even if patient history and visual inspection are enough to diagnose the presence of edema, more accurate tests are necessary for a correct overview of the clinical contest [3]. These can be shared in tests for the quantification of edema and tests for its characterization.

Quantification of edema can be performed by various methods, which can be summarized in the following three:

– Static leg circumference measurements
– Static leg volume measurements
– Dynamic leg volume measurements

Characterization of edema can be performed by radiologic (TC, MR), ultrasonographic, and physical techniques.

6.2 Static Leg Circumference Measurements

The simplest method consists of the direct measurement of the circumference of the leg at one or several points by a tape measure. Data obtained by these tests are compared with those from the contralateral leg (in the case of monolateral leg edema) or repeated to evaluate the efficacy of treatment.

More frequently, the leg circumference is evaluated 3–4 cm above the internal/medial malleolus or at the largest circumference of the calf. Accuracy of “hands-free” tape measurements can be improved using the “Leg-O-Meter” which allows for reproducible and consistent repeated evaluations because it takes into account the height at which the circumference has been measured. The Leg-O-Meter consists of a large tape measure fixed to a stand attached to a platform on which the

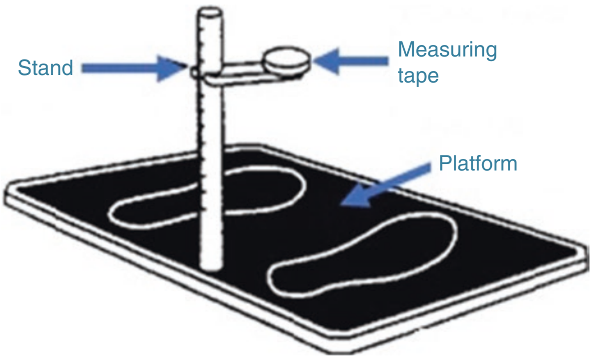

Fig. 6.1 The Leg-O-Meter

patient is in standing position. The tape measure is fixed at a fixed distance from the platform in order to obtain consistent standardized measurements by ensuring that repeated measurements are taken at the same point each time (Fig. 6.1) This is a simple and fast method and has been shown to be a reliable and standardized instrument to assess patients over time [4].

6.3 Static Leg Volume Measurements

The simplest method for leg volume measurements in static conditions is water displacement volumetry (WDV) and those based upon mathematical calculations on multiple measurements of limb circumference. Several other devices have been used to evaluate static leg volume: optoelectronic methods, computed tomography (CT), magnetic resonance (MR), and dual X-ray absorptiometry. The latter are expensive and not all of them have been validated. However, they seem to be the future investigations of choice because they allow us to discriminate the respective increase of volume of the superficial and deep compartments, as well as to furnish important information regarding the presence of muscular or osteoarticular lesions, possibly responsible for leg edema.

6.4 Water Displacement Volumetry (WDV)

WDV is generally regarded as the gold standard for measurement of lower limb volume and has become a routine screening test for assessment of leg edema (Fig. 6.2) [5]. It consists of a plexiglass box filled with water. When the leg is immersed, the displaced water spills out into a graduated receptacle. This is an inexpensive piece of equipment which allows us to measure the leg and foot volume in both the standing or sitting positions [6, 7].A variant water volumeter measures directly the level of the water in the container before and after the limb immersion. [6]

Fig. 6.2 The principle of WDV

6.5 The "Truncated Cone"

The "truncated cone" (Fig. 6.3) method is based upon the assumption that the leg approximates to the shape of one or more truncated cone(s) [8]. In its simplest version, this method is based upon the measurements of the leg circumference at the highest and lowest points of the leg segment under investigation, and on the distance between these two levels. A mathematical formula is then applied to these values to calculate the approximate volume of the leg segment between the two measurements. This technique does not include the volume of the foot.

An evolution of the truncated cone is based upon the application of the same Khunke's formula to multiple circumference measurements of the leg, with the volume measurement extending to the thigh by evaluating 11 perimeters which delimits 10 truncated cones [6, 9]. Limb volume is finally calculated as a summation of the multiple truncated cones. The perimeters are measured by weighted tapes attached every 4 cm to a semirigid stainless steel bar. The advantages of this simple device are the regular space, the horizontal position, and the reproducible traction on the tape. Both these techniques are currently used in scientific reports to evaluate the effects of pharmacologic, surgical, or physical treatments on the leg volume [5].

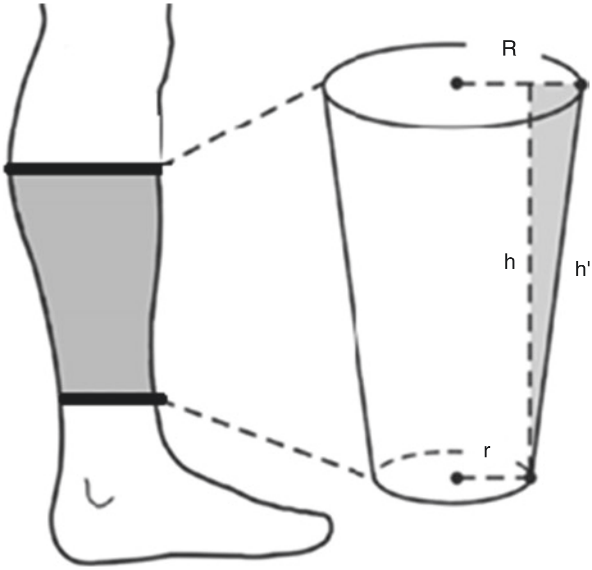

Fig. 6.3 The truncated cone

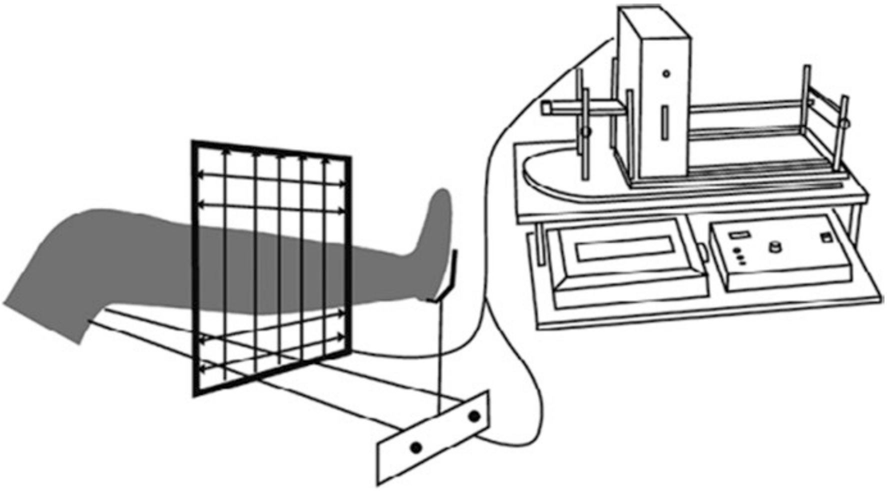

Fig. 6.4 Modified from Rabe et al., 2018

6.6 Optoelectronic Systems

Optoelectronic measurements of the leg volume are based upon infrared phototransistors which evaluate the circumference of the leg at multiple levels and calculate the volume electronically [10–13]. The leg passes through a four-sided sliding metal frame, which is equipped with infrared-detecting diodes. These emit an infrared beam that allows a three-dimensional image of the limb to be created indirectly. The volume of thin slices can then be calculated to provide an estimate of limb volume mainly in the supine position (Fig. 6.4).

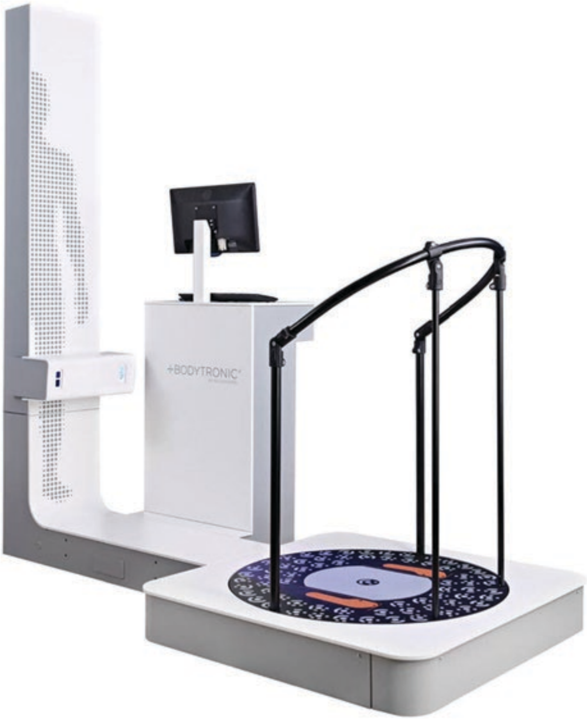

Fig. 6.5 The Bodytronic©

Recently, a novel optical three-dimensional (3D) volumetric measurement system (BODYTRONIC® 600) for the assessment of lower limb circumference and volume in standing position was introduced. Data obtained with Bodytronic was comparable to those furnished by CT [14] (Fig. 6.5).

6.7 Dynamic Volume Measurements

A few other techniques have been used to evaluate changes of leg volume provoked by special tests, i.e., postural, dynamic, or compressive maneuvers: strain gauge plethysmography and air plethysmography. These instruments evaluate changes of the calf circumference (strain gauge plethysmography) (Fig. 6.6) or of the calf volume (air plethysmography) (Fig. 6.7), for example during the elevation of the limb, during walking, during immersion, etc. [15, 16]. Accordingly, these methods are more an assessment of the venomuscular pump, vein competence, venous compliance, and/or venous outflow more than to quantify absolute volume variations [16].

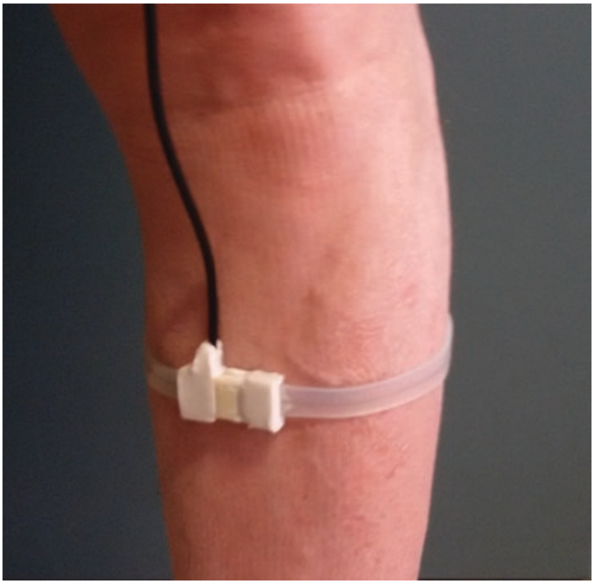

Fig. 6.6 Strain gauge plethysmography. By courtesy of Giorgio Bergamo, Microlabitalia, Padua (I)

Fig. 6.7 Air plethysmography. By courtesy of Giorgio Bergamo, Microlabitalia, Padua (I)

6.8 Techniques for the Qualitative Evaluation of Leg Edema

In clinical practice, palpation is the most widely used technique to assess lower limb edema: the physician applies pressure with the index finger to a single point on the patient's ankle skin provoking or not a fovea (pitting or non-pitting edema). This maneuver allows us to evaluate the pit depth and the time necessary for the skin to return to its original appearance. The test is empirically graded with a score ranging from 0 to 4 (Table 6.2). While commonly used in clinical practice, this is an unvalidated, qualitative, and subjective measure of edema.

Pitting edema occurs in most diseases. Non-pitting edema occurs in thyroid disorders (myxedema), skin trauma, and infections. It is also reported to occur in lymphedema. However, in the first stages of lymphedema, skin edema may be compressible. Similarly, in the same conditions of venous disorders edema is not or poorly pitting. In these cases, pitting is painful and pain allows to exert only light and short compressions.

Recently, a new method was proposed to exactly measure the depth of the fovea, and a positive correlation between depth of the fovea and skin thickness was demonstrated [17].

Bioelectrical Impedance

Measurements of bioelectrical impedance are used to evaluate volume changes in human limbs [7, 18, 19]. A low intensity constant electrical current is applied to a subject's limb, and surface electrodes measure the resulting voltage. This technique is used to estimate relative changes in liquid distribution, also provoking a change in limb volume. A reduction of the leg bioimpedance with lower voltage with respect to the baseline corresponds to an increase of the fluid content of the limb and vice versa. Bioimpedance allows us to evaluate the extra- and intracellular water rates. In fact, due to the high impedance of the cell's membranes, using frequencies below 1 kHz, it is possible to evaluate the flow through extracellular fluid to quantify this parameter [20]. Bioimpedance can be performed without cloth removal and can be used in legs with dermatitis or ulcers (which cannot be tested by water immersion techniques). On the contrary, individuals with pacemakers and metal implants cannot be measured using this technique.

Table 6.2 Grading of skin pitting

Grade	Depth of the fovea	Definition
1	2 mm or less	Slight pitting, no visible distortion, disappears rapidly
2	2–4 mm	Somewhat deeper pit, no readably detectable distortion, disappears in 10–25 s
3	4–6 mm	Pit is noticeably deep. May last more than a minute. Dependent extremity looks swollen and fuller
4	6–8 mm	Pit is very deep. Lasts for 2–5 min. Dependent extremity is grossly distorted

6.9 Computed Tomography and Magnetic Resonance Leg Imaging

Computed tomography (CT) [21, 22] and magnetic resonance (MR) [23, 24] imaging may be used not only to measure the leg volumes but also to evaluate vascular, musculotendinous, or osteoarticular lesions in the deep or superficial compartments causing edema. CT and MRI can quantify edema in the different compartments of the limb. In particular, they are the only techniques allowing us to diagnose volume increase of the deep compartment. CT and MRI are also useful to possibly discriminate various causes of leg edema by differentiating lymphedema, lipedema, and venous edema.

In particular, MRI is even more used in the diagnosis and staging of limb lymphedema. Recent studies demonstrated the possible role of contrast less MRI in diagnosis of early-stage lymphedema in patients with borderline clinical measurements. MRI is particularly indicated in the long-term follow-up, especially if considering it is noninvasive and more readily accessible compared to lymphoscintigraphy or to lymphangiography.

6.10 Dual X-Ray Absorptiometry

Dual-energy X-ray absorptiometry (DXA) is capable of measuring regional body composition providing information about fat mass, lean mass, and bone mass for both total body and subregions. DXA was successful in the evaluation of limbs lymphedema and of lipedema of the leg [25–27].

6.11 Ultrasonography

High-frequency ultrasound allows us to visualize tissues of the superficial compartment. In swollen legs, US shows two patterns of subcutaneous thickening: (1) diffuse soaking with light increase of tissue echogenicity or (2) anechoic lacunae of variable size and extension. Moreover, US is the only technique allowing for an easy demonstration of dermal edema which can accompany or not subcutaneous edema.

Skin morphology is evaluated by the same probes used for Duplex evaluation of superficial veins. US allows us to exactly measure the thickness of the superficial compartment, its difference between the two limbs, and changes following treatment [28–30].

Besides skin thickness, US allows us to evaluate tissue echogenicity: the increase or reduction of tissue echogenicity corresponds respectively to increased cellularity (inflammation) or increase of water content. The latter can be diffused or concentrated in anechoic folds. Moreover, US allows us to identify the presence of dermal edema consisting of the increase of dermal thickness [29]. Edema of the dermis (alias: dermal edema, DE) may be present or not in legs with venous insufficiency.

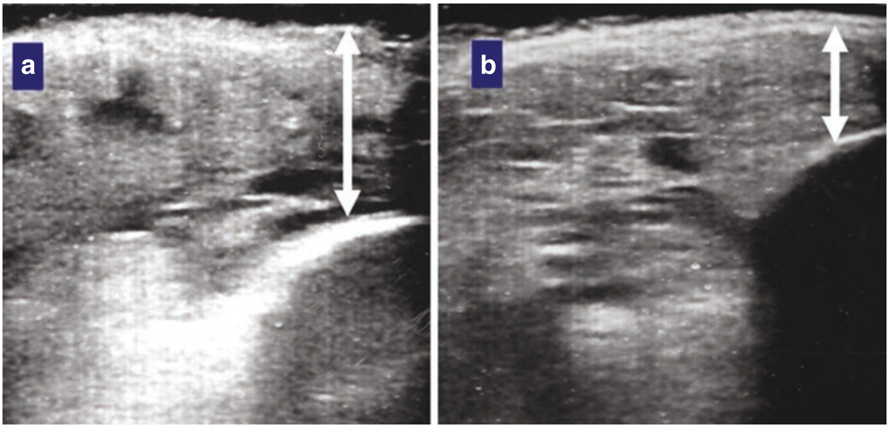

Fig. 6.8 Pitting test by US probe: (**a**) A positive squeezing test by US. (**b**) The thickness of the subcutaneous layer reduces significantly with disappearing of dermal edema

DE consists of an increase of water content of the dermis, with dermal thickening and hypoechogenicity. In most cases, edema is limited to the papillary dermis.

Tissue echogenicity is evaluated by the visual comparison of US findings from the swollen limb areas and the adjacent or contralateral homologous areas.

Finally, US allows us to better evaluate the pitting phenomena by compressing the skin with the probe instead of the finger. This maneuver allows us to quantify the compression-related reduction of skin thickness, the time of recovery of the initial conditions, and structural changes provoked by the pressure exerted on the skin. (Fig. 6.8). Skin squeezing by the US probe is negative in the presence of inflammatory processes and lipedema.

A positive squeezing test (Fig. 6.8) easily reveals those legs in which a mechanical treatment (manual or pneumatic lymphatic drainage, massotherapy, etc.) may effectively reduce the SCL or CL edema.

However, US does not allow for a differential diagnosis of the cause of leg edema. In fact, current knowledge is limited to the differential diagnosis between edema of the subcutaneous layer and increase in volume of the muscular compartment. With regard to subcutaneous edema, US allows us to discriminate between inflammatory and non-inflammatory causes.

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References

1. Vasquez MA, Rabe E, McLafferty CK, Shortell RB, Marston WA, Gillespie D, et al. Revision of the venous clinical severity score: venous outcomes consensus statement: special communication of the American venous forum ad hoc outcomes working group. J Vasc Surg. 2010;52:1387–96.

2. Wittens C, Davies AH, Baekgaerd N, Broholm R, Cavezzi A, Chastanet S, et al. Editor's choice. Management of chronic venous disease: clinical practice guidelines of the European Society for Vascular Surgery (ESVS). Eur J Vasc Endovasc Surg. 2015;49:678–737.
3. Rabe E, Carpentier P, Maggioli A. Understanding lower leg volume measurements used in clinical studies focused on venous leg edema. Int Angiol. 2018;37(6):437–43.
4. Berard A, Kurz X, Zuccarelli F, et al. And the VEINES group: reliability study of the leg-O-meter, an improved tape measure device, in patients with chronic venous insufficiency of the leg. Angiology. 1998;49:169–73.
5. Mosti G, Caggiati A. The effects of water immersion and walking on leg volume, ankle circumference and epifascial thickness in healthy subjects with occupational edema. Phlebology. 2021;36(6):473–80. https://doi.org/10.1177/0268355520984065. Epub 2021 Jan 6. PMID: 33407051
6. Rabe E, Stucker M, Ottilinger B. Water displacement leg volumetry in clinical studies. A discussion of error sources. BMC Med Res Methodol. 2010 Jan;13(10):5. https://doi.org/10.1186/1471-2288-10-5.
7. Wall R, Lips O, Seibt R, Rieger MA, Steinhilber B. Intra- and inter-rater reliability of lower leg water plethysmography, bioelectrical impedance and muscle twitch force for the use in standing work evaluation. Physiol Meas. 2017;38(5):701–14.
8. Devoogdt L, Van Nuland G, Christiaens C, Van Kampen M. A new device to measure upper limb circumferences: validity and reliability. Int Angiol. 2010;29(5):401–7.
9. Perrin M, Guex JJ. Edema and leg volume: methods of assessment. Angiology. 2000;51:9.12.
10. Blume J, Langenbahn H, Champvallins M. Quantification of edema using the volumeter technique: therapeutic application of Daflon 500 mg in chronic venous insufficiency. Phlebology. 1992;2(Suppl):37–40.
11. Tierney S, Aslam M, Rennie K, et al. Infrared optoelectronic volumetry, the ideal way to measure limb volume. Eur J Vasc Endovasc Surg. 1996;12:412–7.
12. Northfield JW, Holroyd B, et al. Validation of an optoelectronic limb volumeter (Perometer). Lymphology. 1997;30:77–97.
13. Veraart JCJM, Neumann HAM. Leg volume measurements with a modified optoelectronic measurement system. Phlebology. 1995;10:62–4.
14. Tischer T, Oye S, Wolf A, Feldhege F, Jacksteit R, Mittelmeier W, Bader R, Mau-Moeller A. Measuring lower limb circumference and volume - introduction of a novel optical 3D volumetric measurement system. Biomed Tech (Berl). 2020;65(2):237.
15. Mosti G, Bergamo G, Oberto S, Bissacco D, Chiodi L, Kontothanassis D, Caggiati A. The feasibility of underwater computerized strain gauge plethysmography and the effects of hydrostatic pressure on the leg venous Haemodynamics. EJVES Vasc Forum. 2020;47:60–2.
16. Rosfors S, Persson LM, Blomgren L. Computerized venous strain-gauge plethysmography is a reliable method for measuring venous function. Eur J Vasc Endovasc Surg. 2014;47(1):81–6.
17. Kogo H, Murata J, Murata S, Higashi T. Validity of a new quantitative evaluation method that uses the depth of the surface imprint as an indicator for pitting edema. PLoS One. 2017;12(1):e0170810.
18. Nishibe T, Nishibe M, Akiyama S, et al. Bioelectrical impedance analysis of leg edema and its association with venous functions in patients with saphenous varicose veins. Int Angiol. 2020;39:284–9.
19. Barnes MD, Mani R, Barrett DF, et al. How to measure changes in edema in patients with chronic venous ulcers? Phlebology. 1992;7:31–5.
20. Jaffrin MY, Morel H. Body fluid volumes measurements by impedance: a review of bioimpedance spectroscopy (BIS) and bioimpedance analysis (BIA) methods. Med Eng Phys. 2008 Dec;30(10):1257–69.
21. Marotel M, Cluzan RV, Pascot M, et al. Tomodensitomtrie de 150 cas de lymphoedemes des membres inferieurs. J Radiol. 1998;79:1373–8.
22. Ling H, et al. Volumetric differences in the suprafascial and subfascial compartments of patients with secondary unilateral lower limb lymphedema. Plastic Reconstr Surg. 2020;145:1528–37.

23. Cluzan RV, Pereti IDDI, Alliot AF, et al. Cutaneous and subcutaneous changes in lymphedema analysed with high resolution MR imaging, indirect lymphography and lymphoscintigraphy. In: Whitte M, Whitte C, editors. Progress in lymphology XIV. Lymphology; 1994. p. 305–8.
24. Arrivé L, Derhy S, Dahan B, El Mouhadi S, Monnier-Cholley L, Menu Y, Becker C. Primary lower limb lymphoedema: classification with non-contrast MR lymphography. Eur Radiol. 2018 Jan;28(1):291–300.
25. Czerniec SA, Ward LC, Meerkin JD, Kilbreath SL. Assessment of segmental arm soft tissue composition in breast cancer-related lymphedema: a pilot study using dual energy X-ray absorptiometry and bioimpedance spectroscopy. Lymphat Res Biol. 2015 Mar;13(1):33–9.
26. Dietzel R, Reisshauer A, Jahr S, Calafiore D, Armbrecht G. Body composition in lipoedema of the legs using dual-energy X-ray absorptiometry: a case-control study. Br J Dermatol. 2015;173(2):594–6. https://doi.org/10.1111/bjd.13697. Epub 2015 Jul 2. PMID: 25641018
27. Hidding JT, Viehoff PB, Beurskens CH, van Laarhoven HW, Nijhuis-van der Sanden MW, van der Wees PJ. Measurement properties of instruments for measuring of lymphedema: systematic review. Phys Ther. 2016;96(12):1965–81.
28. Caggiati A. Utrasonography of skin changes in legs with chronic venous disease. Eur J Vasc Endovasc Surg. 2016 Oct;52(4):534–42.
29. Caggiati A, Caggiati L. Sonography of leg venous edema. Acta Phlebologica. 2018;19:59–62.
30. Caggiati A. Ultrasound of verrucous hyperplasia of the skin related to venous stasis and effects of compression treatment. J Vasc Surg Cases Innov Technol. 2019;5(3):225–7.