Ann Vasc Dis Vol. 16, No. 3; 2023; pp 174–180

Online June 30, 2023
doi: 10.3400/avd.oa.22-00132

Original Article

Dependent Leg Edema in Older Patients with or without Skin Lesion

Kotaro Suehiro, MD, Noriyasu Morikage, MD, Takasuke Harada, MD, Yuriko Takeuchi, MD, Soichi Ike, MD, Ryo Otsuka, MD, Ryunosuke Sakamoto, MD, Hiroshi Kurazumi, MD, Ryo Suzuki, MD, and Kimikazu Hamano, MD

Objective: This study aimed to clarify the features and causes of dependent edema (DE) in the legs of patients in geriatrics.
Patients and Methods: We retrospectively reviewed 224 patients with DE, aged ≥65 years, who visited our clinic from April 2009–March 2022. DE was defined as bilateral leg edema in patients without known systemic edemagenic conditions, venous insufficiency confirmed by duplex venous scanning, or a cancer treatment history in the pelvic/inguinal lesions.
Results: The median patient age was 77 years (range: 65–94 years), where 74% were female. Overall, 198 patients (88%) had gait disturbances caused mainly by musculoskeletal disorders, but 58 (26%) walked without aid. Compared with patients with DE only (N=129), patients with DE and venous stasis-related skin lesions (N=95) included a larger number of those with obesity than did those with DE only (26% vs. 14%, p=0.02).
Conclusion: The primary cause of DE in older patients was the sedentary lifestyle secondary to aging and gait disturbance, not solely because of reduced leg function. The complications of obesity are associated with increased venous stasis-related skin lesions.

Keywords: leg edema, chronic venous disease, lymphedema

Division of Vascular Surgery, Department of Surgery and Clinical Science, Yamaguchi University Graduate School of Medicine, Ube, Yamaguchi, Japan

Received: December 19, 2022; Accepted: May 19, 2023
Corresponding author: Kotaro Suehiro, MD. Division of Vascular Surgery, Department of Surgery and Clinical Science, Yamaguchi University Graduate School of Medicine, 1-1-1 Minamikogushi, Ube, Yamaguchi 755-8505, Japan
Tel: +81-836-22-2260, Fax: +81-836-22-2423
E-mail: ksuehiro-circ@umin.ac.jp

Introduction

Bilateral leg edema of unknown cause in older patients is often encountered clinically. Such leg edema has been described as dependent edema (DE)[1]: gravitational edema,[2] filtration edema,[3] and so on. However, to date, DE remains inconclusive. Although DE is commonly observed, most textbooks do not list it as a causal condition for leg edema. Many physicians remain unaware of DE. However, such patients continually visit us with complaints of leg heaviness, walking and sitting difficulty, etc. Some DE cases are complicated by weeping blisters and/or leg ulcers. For these patients, the pathophysiology of DE must be explained and treated. Moreover, DE can complicate other edemagenic conditions, such as lymphedema or chronic venous insufficiency, and significantly affect edema volume.[4,5] Hence, DE's effect must be considered when managing leg edema, particularly in older patients. Currently, no methods can measure DE independently; however, recognizing its presence and features is important. In this study, we retrospectively reviewed the background, symptoms, and examination results of patients with DE to clarify its features. Furthermore, we discuss the pathophysiology of DE based on these observations.

Patients and Methods

This retrospective study was approved by the Institutional Review Board of Yamaguchi University Hospital (Ube, Yamaguchi, Japan, 2022-108), and the need for individual informed consent was waived. Between April 2009 and March 2022, 1394 patients visited our clinic with complaints of leg swellings. Of these, 432 patients were aged 65 years or older during their initial visits and had bilateral leg edema. Patients with the following conditions were excluded:

- Known edemagenic conditions, such as cardiac/renal/hepatic failure, hypothyroidism, terminal cancer, etc.
- Venous insufficiency and/or occlusion confirmed by duplex venous scan.
- A history of cancer treatment for pelvic/inguinal le-

sions (excluding possible secondary lymphedema).

Finally, 224 patients met all the criteria and were studied. **Table 1** presents patient characteristics. Among 224 patients with DE, 129 (58%) had bilateral DE without skin lesions (Group 1). The remaining patients (N=95, 42%) had skin lesions in either leg alongside bilateral DE (Group 2).

In the outpatient setting, the patients' walking condition was assessed while they moved from the waiting room to the consulting room; if their walking cycle: heel strike, weight on, ankle pivot, tip toe, weight off, dorsiflexion, and foot forward[6] was not smooth and symmetrical, they were regarded to have walking disturbance. History taking and physical examinations were performed in the consulting room. The presence of edema in the legs was confirmed by a pitting sign and subcutaneous echo-free space (SEFS), as described below. The circumference measurements were taken at the following levels: calf, level of the calf at its maximum diameter; ankle, level of the upper edge of the medial malleolus; and foot, level of the middle of the foot arch. We routinely performed a venous duplex ultrasound, skin and subcutaneous tissue ultrasonography, and air plethysmography. In the skin and subcutaneous tissue ultrasonography, the leg was scanned at nine points (upper/lower, medial/lateral, thigh/leg, and pedal) using an 8–12 MHz linear transducer, as per our previous report.[7] The SEFS was graded as follows: grade 0, no SEFS; grade 1, horizontally oriented (<45° to the skin) SEFS only; and grade 2, presence of a vertically oriented (≥45° to the skin) SEFS bridging the horizontally oriented SEFS. We previously reported that SEFS grading is well correlated with the severity of edema assessed using bioelectrical impedance analysis, and therefore, it is a semi-quantitative measure of leg edema.[8] Using air plethysmography, the venous filling index (VFI), an index of venous reflux and arterial inflow, and ejection fraction (EF), an index of calf muscle pump function, were obtained.[9] Epifascial lymphangioscintigraphy was performed only when patients consented. The images were obtained 15, 60, and 180 min after injecting the first interdigital web with an intradermal tracer (111 MBq of 99mTc suspended in 0.1 mL human serum albumin). When the entire superficial lymph

Table 1 Patient characteristics and symptoms

Characteristics	Overall (N=224)	Patients with leg edema only (Group 1) (N=129)	Patients with leg edema and skin lesions (Group 2) (N=95)	p-value (Group 1 vs. 2)
Age (years)	77 (65–94)	77 (65–91)	78 (65–94)	0.9967
>75 y	145 (65%)	83 (64%)	62 (65%)	0.8865
Female	165 (74%)	93 (72%)	72 (76%)	0.3964
Height (cm)	152 (128–190)	153 (131–176)	150 (128–190)	0.1485
Weight (kg)	58 (29–120)	56 (29–97)	62 (34–120)	0.0235*
BMI (kg/m^2)	24 (15–43)	24 (15–41)	26 (16–43)	0.0005*
<17 kg/m^2	5 (4%)	5 (4%)	3 (3%)	0.7944
>30 kg/m^2	43 (19%)	18 (14%)	25 (26%)	0.0175*
Gait disturbance	198 (88%)	110 (85%)	88 (93%)	0.0379*
Clutch, Walker	102 (46%)	54 (42%)	48 (51%)	0.1731
Wheelchair	38 (17%)	18 (14%)	20 (21%)	0.1509
Causes				
OA/RA	88 (39%)	43 (33%)	45 (47%)	0.0348*
Physical frailty	54 (24%)	35 (27%)	19 (20%)	0.221
LBP	46 (21%)	27 (21%)	19 (20%)	0.4481
CND	38 (17%)	20 (16%)	19 (20%)	0.6270
Others	35 (16%)	12 (9%)	23 (24%)	
Skin lesion				
Hyperpigmentation	88 (39%)	N.A.	88 (94%)	
Stasis dermatitis	33 (15%)	N.A.	33 (55%)	
Lipodermatosclerosis	32 (14%)	N.A.	32 (34%)	
Corona phlebectatica	6 (3%)	N.A.	6 (6%)	
Venous ulcer	19 (8%)	N.A.	19 (20%)	
Stemmer's sign	8 (4%)	N.A.	8 (8%)	

BMI: body mass index; OA: osteoarthritis; RA: rheumatoid arthritis; LBP: lower back pain; CND: cranial nerve disorders; N.A.: not applicable

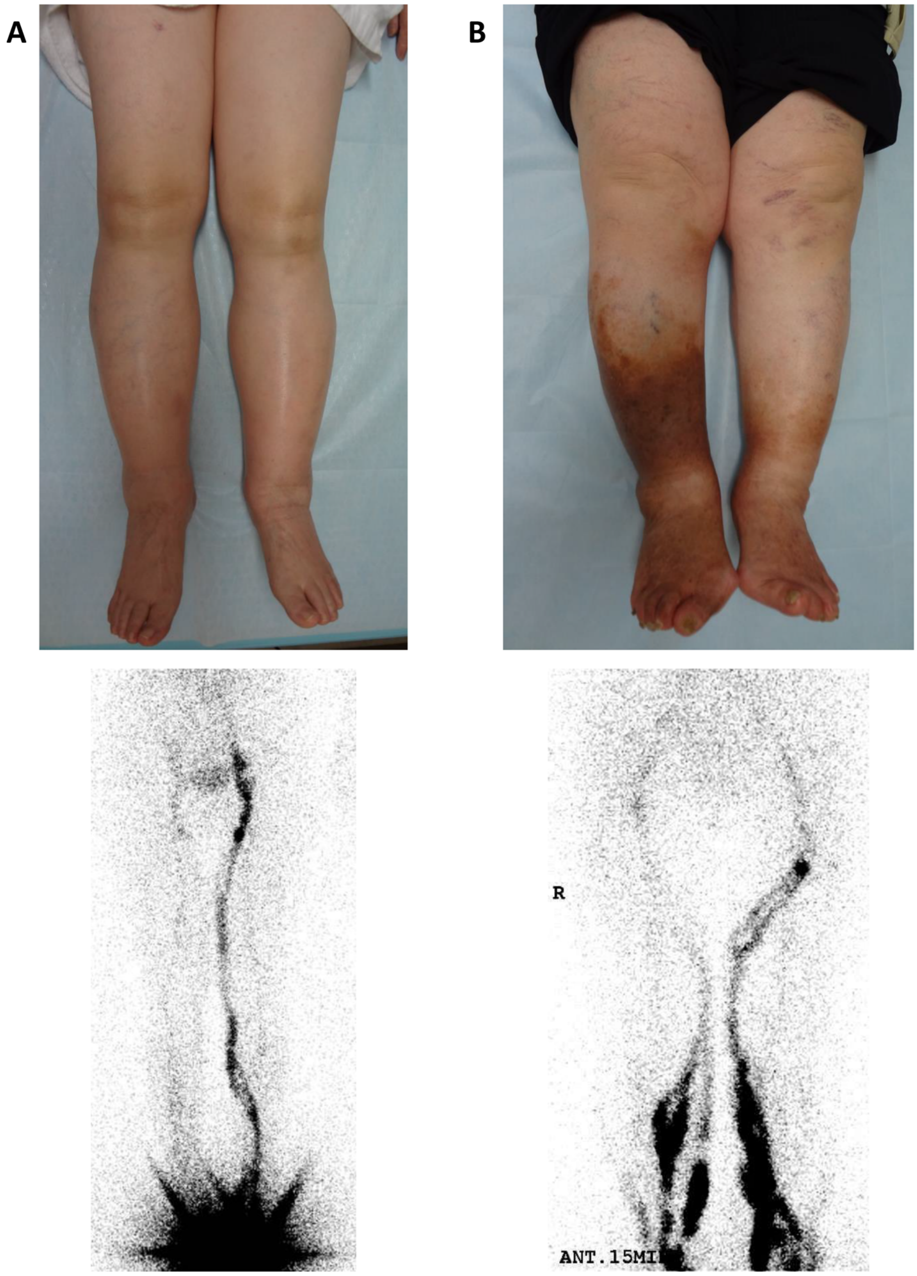

Fig. 1 Representative pictures of the legs with dependent edema and lymphangioscintigraphy images. (**A**) the patient with leg edema only, (**B**) the patient with leg edema and skin lesions (lipodermatosclerosis). Lymphangioscintigraphy images were obtained 15 min from tracer injection into the first interdigital web.

trunk and inguinal nodes were visualized within 15 or 60 min, followed by washout until 180 min, we considered the lymph transport system hyperactive or normal, respectively. Otherwise, the lymph transport system was considered insufficient.[10] Bioelectrical impedance analysis using a bioimpedance spectrometer (U-400, Impedimed Ltd., Brisbane, Australia) was performed only when the device was available. We calculated the ratio of intracellular fluid resistance to extracellular fluid resistance (R*i*/R*e*) in each leg as a measure of the amount of extracellular fluid,[11] and the ratio of extracellular fluid resistance in the affected leg to extracellular fluid resistance in the (right) arm (R*e*L/R*e*A) as a measure of the severity of edema.[5]

Statistical analysis

The results are expressed as median (range) or count unless otherwise indicated. The Mann–Whitney U test was used to evaluate the between group differences in patient data. The χ^2 test was used to test categorical variables. Simple linear regression analysis was used to test the cor-

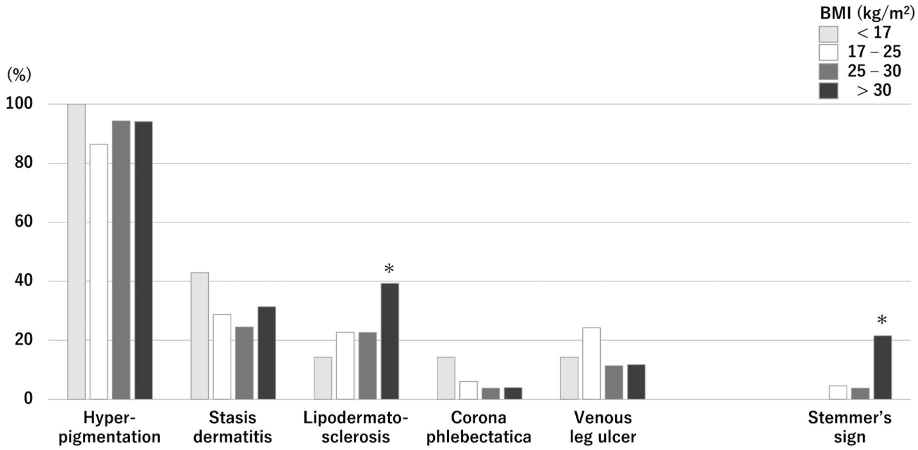

Fig. 2 Prevalence of skin lesions according to body mass index among patients with skin lesions in either leg along with bilateral dependent edema (Group 2).
* $p<0.05$, compared with the other groups.
BMI: body mass index

relation between the parameters. Statistical analyses were performed using JMP 11.0 (SAS Institute, Cary, NC, USA). Statistical significance was set at $p<0.05$.

Results

Representative pictures of the legs with DE and lymphangioscintigraphy images are shown in **Fig. 1**.

Characteristics in the patients with DE without skin lesions (Group 1)

In Group 1, the median age was 77 years, where 72% were female, and the median body mass index (BMI) was 24 kg/m^2. Only 9% and 7% of patients had obesity (BMI >30 kg/m^2) and low body weight (BMI <17 kg/m^2), respectively. In Group 1, 85% of patients had gait disturbance; among whom, 42% used clutches and/or walkers and 14% used wheelchairs. The causes of gait disturbance were osteoarthritis and/or rheumatoid arthritis, physical frailty, lower back pain, and cranial nerve disorders. Meanwhile, 15% had no evident problems in ambulation and 44% were walking without aid. In physical examinations, the calf, ankle, and foot circumferences, the severity and distribution of SEFS, and R*i*/R*e* and R*e*L/R*e*A were all similar between each patients' legs. Regarding air plethysmography, 69% of the patients in Group 1 could not complete the exercise protocol because of insufficient leg function and/or physical frailty. Among those who completed the protocol, the median EF was 59%. No significant difference was found between the legs in VFI and EF. Twenty-two patients in Group 1 agreed to undergo lymphangioscintigraphy. Insufficiency of the superficial lymphatic trunk was absent in any of the legs, and more than two-thirds of the legs were hyperactive. No differences in lymphatic function were observed between each patient's legs. Dermal backflow limited to the calf was observed in only one leg.

Comparison of patients and legs with and without skin lesions

Compared to Group 1, Group 2 included more patients with obesity, gait disturbance, and osteoarthritis or rheumatoid arthritis; other patient characteristics were similar between Group 1 and 2. In Group 2, 97% of the skin lesions found were listed in the Clinical, Etiological, Anatomical, Pathophysiological (CEAP) classification.[12] Of these, 84%, 55%, 44%, and 50% of hyperpigmentation, stasis dermatitis, lipodermatosclerosis, and venous leg ulcer lesions were found bilaterally, respectively. Lipodermatosclerosis and Stemmer's signs were observed more frequently in patients with a BMI of >30 kg/m^2 compared to each smaller BMI group (**Fig. 2**).

Next, we compared the results of physical examinations and function tests in legs with DE only (N=271) and those with DE and skin lesions (N=177) (**Table 2**). The calf, ankle, and foot circumferences were larger in the legs with DE and skin lesions. On skin and subcutaneous tissue ultrasonography, the SEFS in the lateral upper calf was increased in the legs with DE and skin lesions. Although the number of tested legs was limited, the R*i*/R*e*, R*e*L/R*e*A, VFI, and EF were not significantly different between the groups. Superficial lymph trunk function was similar in both groups. Dermal backflow limited to the calf was found in four legs among those with DE and skin lesions; this incidence was higher than that among the legs with DE only ($p<0.05$). The four legs with dermal backflow were both legs of an 81-year-old female with a BMI of 32 kg/m^2, the right leg of an 82-year-old male with a BMI of 29 kg/m^2, and the right leg of a 78-year-old female with a BMI of 35 kg/m^2. Lipodermatosclerosis complicated

Table 2 Comparing physical examination results in legs with edema only and those with edema and skin lesions

	Legs with edema only (N=271)	Legs with edema and skin lesions (N=177)	p-value
Circumference			
Calf (cm)	34.8 (20.2–49.8)	38.3 (29.2–55.0)	<0.0001*
Ankle (cm)	24.0 (15.5–39.0)	26.3 (19.3–40.0)	<0.0001*
Foot (cm)	23.6 (17.9–30.2)	24.5 (20.0–40.0)	0.0036*
Skin ultrasonography			
SEFS (Grade 0:1:2, %)			
Medial upper thigh (mm)	96:04:00	97:03:00	0.4920
Lateral upper thigh (mm)	84:12:04	85:12:03	0.7822
Medial lower thigh (mm)	82:14:04	82:17:01	0.0500
Lateral lower thigh (mm)	76:18:06	74:17:09	0.5008
Medial upper calf (mm)	66:24:10	61:29:10	0.6822
Lateral upper calf (mm)	53:26:21	38:32:30	0.0237*
Medial lower calf (mm)	16:44:40	20:48:32	0.3244
Lateral lower calf (mm)	6:29:65	3:27:70	0.6697
Dorsum of foot (mm)	24:29:47	28:34:38	0.3875
Bioelectrical impedance analysis	(N=36)	(N=16)	
R*i*/R*e*	4.05 (1.03–13.96)	3.97 (1.17–6.41)	0.8007
R*e*L/R*e*A	0.63 (0.27–0.95)	0.64 (0.33–0.80)	0.6788
Air plethysmography	(N=114)	(N=28)	
VFI (mL/s)	2.1 (0.7–7.1)	2.3 (0.4–7.1)	0.3403
EF (%)	54 (13–121)	63 (24–175)	0.0812
Lymphangioscintigraphy	(N=48)	(N=22)	
Hyperactive	34 (71%)	15 (71%)	0.8222
Normal	14 (29%)	7 (33%)	0.8222
Insufficiency	0 (0%)	0 (0%)	
DBF (Thigh)	0 (0%)	0 (0%)	
DBF (Calf)	1 (2%)	4 (19%)	0.0152*

Table 2 shows the SEFS, R*i*/R*e*, R*e*L/R*e*A, VFI, EF, and DBF.
SEFS: subcutaneous echo-free space; R*i*/R*e*: the ratio of intracellular fluid resistance to extracellular fluid resistance; R*e*L/R*e*A: the ratio of extracellular resistance in the leg to extracellular resistance in the (right) arm; VFI: venous filling index; EF: ejection fraction; DBF: dermal backflow

all these legs, but a positive Stemmer's sign was noticed only in both legs of the 81-year-old female with a BMI of 32 kg/m^2.

Discussion

We previously reported that venous stasis due to immobility was considered the primary cause of DE.[13] However, in the current study, 12% of patients with DE did not have gait disturbance and 41% walked without aid. In addition, the median EF was above the normal limit, i.e., >40%, among patients who could complete the exercise protocol during air plethysmography, indicating that calf muscle pump function was maintained. Accordingly, the assumed primary cause of DE might be immobility due to reduced leg function and sedentary lifestyle caused by aging, musculoskeletal disorders, associated chronic pain, physical frailty, physical disability due to cranial nerve disorders, etc. Eifell et al. also reasoned that walking intensity and time spent sitting were associated with the severity of chronic venous insufficiency.[14] DE was more prevalent among female patients in the current study. This might be because the number of females in this study was higher, and musculoskeletal disorders, such as osteoarthritis and physical frailty, are more prevalent among older females than males.[15]

While the physical constitution of most patients in Group 1 was healthy, more patients with obesity were included in Group 2. Obesity causes venous hypertension by increasing intra-abdominal pressure[16] and is more frequently associated with venous stasis-related skin lesions.[17,18] Increased prevalence of venous stasis-related skin lesions, particularly lipodermatosclerosis, was also confirmed in this study. DE is commonly found in patients with a healthy physical constitution; it is primarily caused by aging and a sedentary lifestyle, and obesity worsens venous stasis-related skin complications. Chronic inflammatory processes affected by lipometabolism in obesity also causes venous stasis-related skin lesions.[18)]

In the current study, the insufficiency of superficial lymphatic trunk was not confirmed in any legs with DE; rather, the lymph transport was hyperactive in more than two-thirds of the cases. This indicates that the primary cause of DE is unlikely to be reduced lymph transport. Meanwhile, dermal backflow was observed particularly in the legs with lipodermatosclerosis, i.e., the leg with inflammation and fibrosis in the skin and subcutaneous tissue. Currently, many specialists support the idea that "all patients with chronic venous insufficiency (C3–C6) should be considered as lymphedema patients."[19)] Namely, the high-output lymphatic insufficiency due to venous diseases is considered as a form of lymphedema. However, the International Society of Lymphology persistently states that high-output lymphatic insufficiency should be distinguished from lymphedema.[20)] Whether these conditions, namely hyperactive lymph transport with/without localized dermal backflow, should be diagnosed as phlebolymphedema must be discussed further.

Limitations

First, the amount of data regarding bioelectrical impedance analysis and lymphangioscintigraphy, which should provide objective and definitive information on the pathophysiology of DE, was limited in the current study. However, performing lymphangioscintigraphy for all patients with DE seems over-indicated. Second, aging was reported to be associated with changes in structures and function of veins[21)] and lymphatics,[22)] and reduced skin viscoelasticity[23)] all of which could affect DE. However, these factors could not be assessed in this study. Since these are important factors, their effects should be studied in the future. Finally, the definition of SEFS grades is based on empirical facts rather than supported by any pathological data, and inter- and intra-observer differences in assigning SEFS grades were not determined. These issues should be addressed in future research.

Conclusion

In the present study, the primary cause of DE in older patients was assumed to be venous hypertension derived from a sedentary lifestyle secondary to aging and gait disturbance of various causes. Obesity appears to be an additional risk factor for developing skin lesions.

Acknowledgments

None.

Funding

This research received no specific grant from any funding agency in the public, commercial, or non-profit sectors.

Declaration of Conflicting Interests

The authors declare no conflict of interest.

Author Contributions

Study conception: KS
Data collection: KS, TH, YT, SI, RO, RS, HK, RS
Analysis: KS
Investigation: KS
Writing: KS
Funding acquisition: NM, KH
Critical review and revision: all authors
Final approval of the article: all authors
Accountability for all aspects of the work: all authors

References

1) Ely JW, Osheroff JA, Chambliss ML, et al. Approach to leg edema of unclear etiology. J Am Board Fam Med 2006; **19**: 148-60.
2) Piérard-Franchimont C, Letawe C, Fumal I, et al. Gravitational syndrome and tensile properties of skin in the elderly. Dermatology 1998; **197**: 317-20.
3) Mortimer PS, Levick JR. Chronic peripheral oedema: the critical role of the lymphatic system. Clin Med (Lond) 2004; **4**: 448-53.
4) Suehiro K, Morikage N, Ueda K, et al. Correlation between changes in extremity volume and bioelectrical impedance in arm and leg lymphedema. Lymphat Res Biol 2018; **16**: 385-9.
5) Suehiro K, Morikage N, Harada T, et al. Extracellular fluid content in the legs of patients with chronic venous disease. Ann Vasc Surg 2021; **71**: 215-9.
6) Lattimer CR, Franceschi C, Kalodiki E. Optimizing calf muscle pump function. Phlebology 2018; **33**: 353-60.
7) Suehiro K, Morikage N, Murakami M, et al. Subcutaneous tissue ultrasonography in legs with dependent edema and secondary lymphedema. Ann Vasc Dis 2014; **7**: 21-7.
8) Suehiro K, Morikage N, Ueda K, et al. Local echo-free space in a limb with lymphedema represents extracellular fluid in the entire limb. Lymphat Res Biol 2018; **16**: 187-92.
9) Christopoulos DG, Nicolaides AN, Szendro G, et al. Air-plethysmography and the effect of elastic compression on venous hemodynamics of the leg. J Vasc Surg 1987; **5**: 148-59.
10) Szuba A, Shin WS, Strauss HW, et al. The third circulation: radionuclide lymphoscintigraphy in the evaluation of lymphedema. J Nucl Med 2003; **44**: 43-57.
11) Cornish BH, Thomas BJ, Ward LC, et al. A new technique for the quantification of peripheral edema with application in both unilateral and bilateral cases. Angiology 2002; **53**:

41-7.
12) Lurie F, Passman M, Meisner M, et al. The 2020 update of the CEAP classification system and reporting standards. J Vasc Surg Venous Lymphat Disord 2020; **8**: 342-52.
13) Suehiro K, Morikage N, Murakami M, et al. A study of leg edema in immobile patients. Circ J 2014; **78**: 1733-9.
14) Eifell RKG, Ashour HY, Heslop PS, et al. Association of 24-hour activity levels with the clinical severity of chronic venous disease. J Vasc Surg 2006; **44**: 580-7.e1.
15) Kasajima M, Eggleston K, Kusaka S, et al. Projecting prevalence of frailty and dementia and the economic cost of care in Japan from 2016 to 2043: a microsimulation modelling study. Lancet Public Health 2022; **7**: e458-68.
16) Arfvidsson B, Eklof B, Balfour J. Iliofemoral venous pressure correlates with intraabdominal pressure in morbidly obese patients. Vasc Endovascular Surg 2005; **39**: 505-9.
17) van Rij AM, De Alwis CS, Jiang P, et al. Obesity and impaired venous function. Eur J Vasc Endovasc Surg 2008; **35**: 739-44.
18) Vlajinac HD, Marinkovic JM, Maksimovic MZ, et al. Body mass index and primary chronic venous disease—a cross-sectional study. Eur J Vasc Endovasc Surg 2013; **45**: 293-8.
19) Lurie F, Malgor RD, Carman T, et al. The American Venous Forum, American Vein and Lymphatic Society and the Society for Vascular Medicine expert opinion consensus on lymphedema diagnosis and treatment. Phlebology 2022; **37**: 252-66.
20) Executive Committee of the International Society of Lymphology. The diagnosis and treatment of peripheral lymphedema: 2020 Consensus Document of the International Society of Lymphology. Lymphology 2020; **53**: 3-19.
21) Molnár AÁ, Nádasy GL, Dörnyei G, et al. The aging venous system: from varicosities to vascular cognitive impairment. GeroScience 2021; **43**: 2761-84.
22) Filelfi SL, Onorato A, Brix B, et al. Lymphatic senescence: current updates and perspectives. Biology (Basel) 2021; **10**: 1-13.
23) Piérard GE, Paquet P, Piérard-Franchimont C. Skin viscoelasticity in incipient gravitational syndrome. J Cosmet Dermatol 2014; **13**: 52-5.