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The use of high-frequency skin ultrasound in the diagnosis of lipodermatosclerosis

Witold Woźniak¹, Anna Danowska¹, Robert K. Mlosek²

¹ *First Department of General and Vascular Surgery, Faculty of Medicine, Medical University of Warsaw, Poland*

² *Ultrasound Diagnostic Department Faculty of Medical Sciences, Medical University of Warsaw, Warsaw, Poland*

Correspondence: Witold Woźniak, First Department of General and Vascular Surgery, Faculty of Medicine, Medical University of Warsaw, Kondratowicza 8, 03-242 Warsaw, Poland; e-mail: drww@onet.pl

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Abstract

Introduction: Lipodermatosclerosis is a symptom of severe venous insufficiency, the diagnosis of which is based on the clinical picture. Although the histopathology of the skin and the subcutaneous tissue allows for the most reliable diagnosis, it is not recommended due to healing disorders. **Aim:** The aim of this study was to assess the usefulness of high-frequency ultrasound in the diagnosis of lipodermatosclerosis. **Materials and methods:** The study included 10 patients with lipodermatosclerosis who underwent Duplex Doppler ultrasound of lower limb veins, high-frequency ultrasound of the tibial skin, and radiography of the lower leg, all of which were analyzed in correlation with clinical symptoms. **Results:** The study group included 9 women and 1 man aged 39–81 years. Manifestations of lipodermatosclerosis were detected in 14 limbs. High-frequency ultrasound showed that the mean dermis thickness at the affected sites was 2.63 mm, and was significantly thicker compared to healthy skin (1.45 mm) ($p = 0.00002$). Higher echogenicity was detected in the affected body regions in 85.7% of cases for the skin and 92.9% of cases for the subcutaneous tissue. Subcutaneous and vascular wall calcifications were detected in 92.9% and 78.6% of cases, respectively. Fibrosis was observed in all limbs, and compression sonoelastography showed that the compliance of the subcutaneous tissue was lower than that of muscles. The border between the skin and the subcutaneous tissue was blurred in 57.1% of cases. Radiography revealed thickening of the affected skin regions in all limbs, with calcifications detected in 85.7% of cases. A blurred border between the skin and the subcutaneous tissue was observed in 35.7% of limbs. **Conclusion:** High-frequency ultrasonography of the skin and the subcutaneous tissue in the lower legs supported with radiological findings is highly useful in the diagnosis of lipodermatosclerosis.

Introduction

Lipodermatosclerosis is one of the symptoms of severe chronic venous insufficiency (CVI). It is a limited chronic inflammation and fibrosis of the skin and the subcutaneous tissue, which is sometimes accompanied by scarring and contracture of the Achilles tendon. The clinical picture of lipodermatosclerosis is characterized by brownish red, flaky skin prone to ulceration. Atrophy and fibrosis of the subcutaneous tissue lead to the characteristic appearance of distal lower limbs, which after some time start to resemble an 'upside-down champagne bottle'^(1,2). However, pain and edema, which particularly increase in the evening, dominate in patients, thus significantly reducing their quality of life. The differential diagnosis of lipodermatosclerosis should include lupus erythematosus, systemic sclerosis, or erythema nodosum⁽³⁾.

The diagnosis is based mainly on the clinical picture. Focal necrosis of adipose tissue with microcysts and calcium deposition into elastin fibers, adipose tissue, and the immediate vicinity of blood vessels is a typical histopathological picture⁽³⁻⁵⁾. The whole picture is complemented by hemosiderin deposits (siderosomes) in the form of granules, dispersed within both the dermis and the subcutaneous tissue. However, a significant amount of siderosomes is absorbed by the macrophages of the dermis, which, along with hemosiderin granules between collagen fibers, are responsible for the brownish-red color of the skin⁽⁶⁾. Therefore, histopathological examination of full-thickness sections of the skin and subcutaneous tissue would be important for the diagnosis, but unfortunately, this is associated with a high risk of hard-to-heal ulcers, which is why it is rarely performed in clinical practice^(3,4). Therefore, minimally invasive methods, such as high-frequency ultrasound (HFU) of the tibial skin or radiology of the tibial soft tissues have become increasingly important. Precise assessment of radiological and ultrasonographic manifestations typical of lipodermatosclerosis has become necessary for both the diagnosis and monitoring of disease progression.

Aim

The aim of this study was to assess the usefulness of high-frequency ultrasound in the diagnosis of lipodermatosclerosis in correlation with the clinical picture and tibial radiography.

Materials and methods

A prospective study was conducted among 10 patients with advanced lipodermatosclerosis in the first quarter of 2020 (Fig. 1). Correlation between clinical symptoms of lipodermatosclerosis and venous insufficiency in the lower limb confirmed in Duplex Doppler ultrasound was an inclusion criterion. The exclusion criteria were as follows: congenital vascular malformations, lower limb ischemia (ankle-brachial index, ABI <0.8), severe systemic comorbidity (cancer, severe heart disease, severe kidney failure, severe liver



Fig. 1. Clinical picture of advanced CVI

failure, etc.), coexisting autoimmune diseases, and connective tissue diseases. Pregnant and breastfeeding women were also excluded from the study group.

All patients underwent general medical and phlebological examination. CVI was staged based on the following classification systems: CEAP: clinical (C), etiological (E), anatomical (A), pathophysiological (P) classification, and Venous Clinical Severity Scale (VCSS). DUS was performed in each patient using Philips HD15 ultrasound. The examination was performed in an upright and supine position. A broadband linear transducer was used for peripheral veins (L12-3 MHz). The presence of thrombi and venous competence was assessed by performing manual compression, while the venous flow was evaluated with Color Doppler with the forced flow in the venous trunks. The presence of reflux was verified each time with Pulsed Wave Doppler in the vessels in the longitudinal section with simultaneous peripheral compression on the vessels. The vessels were considered incompetent if the reflux measured in an upright position was greater than 0.5 s. Skin HFU was performed with Philips Epic ultrasound equipped with an L18-5 transducer with static elastography. DermaMed (Dramiński S.A., Olsztyn, Poland) ultrasound equipped with 48 MHz sector array transducer was used for the measurement of dermis thickness. The thickness of the dermis was measured and compared to the thickness of the uninvolved dermis of the thigh. We also assessed the echogenicity of the dermis and the subcutaneous tissue, comparing it against the echogenicity of femoral structures. Furthermore, we looked for

Tab. 1. Basic demographic data of patients with lipodermatosclerosis

Patients (n)	10
Mean age (range)	66.3 ± 14.3 (39–81)
Sex (males vs females)	1:9
BMI (range)	32.7 ± 3 (27–37)
Limbs (n) (right vs left vs both)	14 (4:2:4)
Hypertension (%)	9 (90)
Diabetes (%)	6 (60)
Ischemic heart disease (%)	5 (50)

calcifications in the venous walls and the subcutaneous tissue when performing the ultrasound. We also verified the presence of fibrosis in the subcutaneous tissue. Since the disease causes subcutaneous tissue hardening, we assessed this tissue using static elastography. Strain rate (SR) was calculated by comparing the strain of the muscle under the involved subcutaneous tissue (as a reference area) against the tissue located above. In healthy individuals, the subcutaneous tissue is elastic and more compliant to strain than the underlying muscles⁽⁷⁾.

PA and lateral radiology of the tibia was performed to assess skin thickening, the presence, and severity of skin and subcutaneous tissue calcifications, as well as blurring of the border between the tibial skin and the subcutaneous tissue.

Statistica 13.1 software was used for statistical analysis. Descriptive statistics were mainly used. The W Shapiro-Wilk test was used to assess the normality of the distribution of variables, and after confirming that the distribution was normal, the t-test for independent samples was used. The significance level was set at $\alpha = 0.05$.

Results

The study group included 9 women and 1 man aged 39–81 years, with clinical manifestations of lipodermatosclerosis in 14 limbs. Basic demographic data is shown in Tab. 1.

The stage of CVI in the study group

As already mentioned, 14 limbs with advanced CVI were assessed. Based on the CEAP clinical classification (C), 3 limbs (21.4%) were classified as C4, 4 limbs (28.6%) were classified as C5, and 7 limbs (50%) were classified as C6. According to medical history collected in the study group, a past incident of venous thromboembolism or superficial thrombophlebitis was reported for 6 lower limbs, and no such event was noted in the remaining 8 limbs. Therefore, primary and secondary CVI was diagnosed in 8 (57.1%) and 6 (42.9%) lower limbs, respectively. DUS revealed VSM insufficiency in 11 limbs (78.6%) and VSP insufficiency in 3 limbs (21.4%). Post-thrombotic deep venous insufficiency was found in 4 limbs (28.6%), and coexisting perforating vein insufficiency was detected in 11 limbs (78.6%). DUS also allowed for the determination of the pathophysiological mechanism underlying CVI. Pathophysiological changes in the form of reflux were detected in 10 (71.4%) limbs, while mixed mechanism (reflux and deep vein stenosis) was showed

Tab. 2. Stage of chronic venous insufficiency

	Limbs (n)	14
C	C ₁ (%)	0 (0)
	C ₂ (%)	0 (0)
	C ₃ (%)	0 (0)
	C ₄ (%)	3 (21.4)
	C ₅ (%)	4 (28.6)
	C ₆ (%)	7 (50)
E	E _p (%)	8 (57.1)
	E _s (%)	6 (42.9)
A	A ₁ (%)	14 (100)
	A ₂ (%)	11 (78.6)
	A ₃ (%)	12 (85.7)
	A ₄ (%)	3 (21.4)
	A ₁₁ (%)	3 (21.4)
	A ₁₃ (%)	2 (14.3)
	A ₁₄ (%)	2 (14.3)
P	A ₁₈ (%)	11 (78.6)
	P _R (%)	10 (71.4)
	P _O (%)	0
	P _{R+O} (%)	4 (28.6)
Mean VCSS (range)		13.8 ± 5.1 (6–21)

E_p – no history of DVT; E_s – at least one confirmed DVT incident; A₁ – telangiectasias and reticular veins; A₂ – great saphenous vein above the knee; A₃ – great saphenous vein below the knee; A₄ – small saphenous vein; A₁₁ – common femoral vein; A₁₃ – femoral vein; A₁₄ – popliteal vein; A₁₈ – tibial perforator veins; P_R – the pathophysiological mechanism due to reflux alone; P_O – the pathophysiological mechanism caused by deep venous obstruction; P_{R+O} – mixed pathophysiological mechanism: reflux and post-thrombotic changes in the deep veins in the form of venous sequestration and/or significant thickening of the venous wall

for 4 (28.6%) limbs. The severity of CVI was assessed based on VCSS, the mean value of which was 13.8. Detailed data on the stage of CVI is summarized in Tab. 2.

High-frequency ultrasound

HFU findings (Tab. 3) clearly showed that the thickness of the dermis within the affected areas was higher than in the reference area on the thigh (Fig. 2, Fig. 3). The mean thickness of the dermis was 2.63 mm for the involved skin vs 1.45 mm for healthy skin. The observed difference was statistically significant, as confirmed by the t-test for independent samples: $t = 6.15$; $p = 0.00002$.

It was also found based on the collected data that the involved skin showed increased echogenicity compared to the skin of the thigh. Increased echogenicity of the dermis was observed in 12 cases (85.7%). A comparison of the echogenicity of the subcutaneous tissue demonstrated that it was the same as in the examined regions in 1 case (7.1%) and higher in the affected region in 13 cases (92.9%).

Subcutaneous tissue calcifications in the affected skin were detected in 13 cases (92.9%) (Fig. 4), including multiple calcifications in 9 limbs (64.3%) and sporadic calcifications in 4 (28.6%) limbs. No subcutaneous tissue calcifications were detected in 1 case (7.1%).

Tab. 3. Skin and subcutaneous tissue HFU findings

No.	Dermis thickness (mm)		Echogenicity of the dermis: involved vs healthy (thigh)	Echogenicity of the subcutaneous tissue: involved vs healthy (thigh)	Subcutaneous calcifications: 0 – absent, 1 – sporadic, 2 – multiple	Vascular wall calcifications: 0 – absent, 1 – sporadic, 2 – multiple	Subcutaneous fibrosis: 0 – absent, 1 – present	Compression elastography: subcutaneous tissue to the muscle	SR (Strain Ratio): subcutaneous tissue to the muscle – involved region	Border between the dermis and the subcutaneous tissue: 0 – blurred, 1 – clear
	Involved	Healthy (thigh)								
1	3.67	1.65	higher	higher	2	2	1	harder	4.32	0
2	3.34	1.43	higher	higher	2	2	1	harder	5.42	1
3	2.34	1.65	higher	higher	1	1	1	harder	2.87	1
4	1.98	1.12	no difference	no difference	2	0	1	harder	1.56	1
5	1.87	0.98	higher	higher	1	0	1	harder	1.83	0
6	3.84	2.11	higher	higher	2	1	1	harder	6.72	0
7	2.45	1.74	higher	higher	2	2	1	harder	3.67	1
8	2.13	1.23	no difference	higher	2	1	1	harder	3.21	1
9	2.67	1.35	higher	higher	2	1	1	harder	2.74	1
10	3.23	1.46	higher	higher	2	1	1	harder	6.32	0
11	2.19	1.45	higher	higher	1	1	1	harder	2.61	0
12	2.72	1.62	higher	higher	1	1	1	harder	2.56	0
13	2.34	1.01	higher	higher	2	1	1	harder	3.71	0
14	2.03	1.54	higher	higher	0	0	1	harder	1.96	0

We also used ultrasound to search for calcifications in vascular walls (Fig. 5). No such lesions were found in 3 cases (21.4%). Isolated and multiple calcifications in vascular walls were detected in 8 (57.1%) and 3 (21.4%) cases.

Fibrosis was observed in all evaluated limbs (100%) (Fig. 6).

Similarly, compression elastography showed lower compliance (higher hardness) of the subcutaneous tissue compared to muscles (Fig. 7, Fig. 8). Contrasting findings were obtained for healthy skin (thigh). This was also confirmed by the strain ratio (SR), which is 3.53 on average and indicates that the subcutaneous tissue is harder than the muscle.

Tab. 4. Skin and subcutaneous tissue radiographic findings

No.	Thickened dermis	Calcifications in the skin and subcutaneous tissue: 0 – absent, 1 – sporadic, 2 – multiple	Blurred border between the skin and the subcutaneous tissue: 0 – blurred, 1 – clear
1	Yes	1	1
2	Yes	2	0
3	Yes	0	1
4	Yes	2	1
5	Yes	1	1
6	Yes	2	0
7	Yes	1	1
8	Yes	2	0
9	Yes	2	1
10	Yes	2	0
11	Yes	1	1
12	Yes	1	1
13	Yes	2	0
14	Yes	0	1

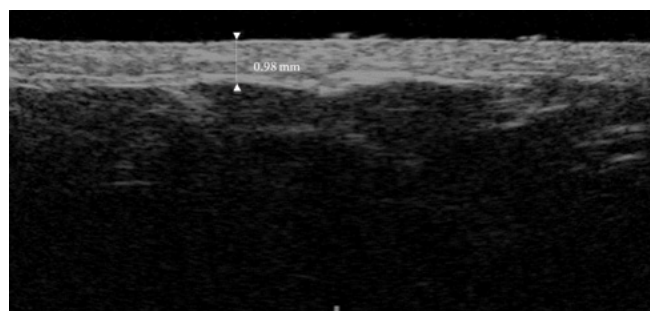


Fig. 2. Clinical picture of healthy skin of the thigh – a 48 MHz transducer

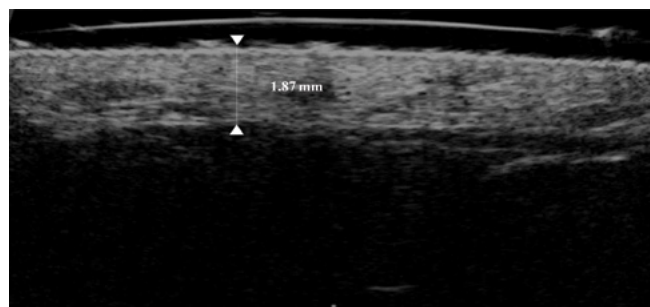


Fig. 3. Involved tibial skin – a 48 MHz transducer

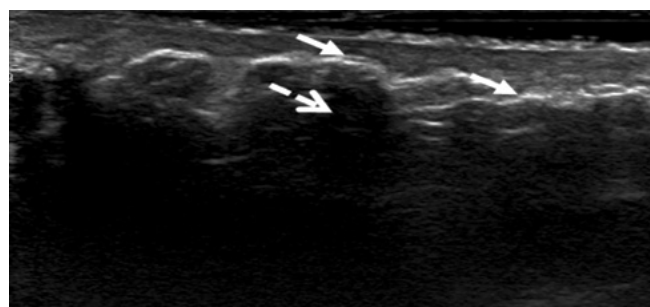


Fig. 4. Massive calcifications (the dashed arrow shows reflexions from calcifications and a shadow behind calcifications)

The border between the dermis and the subcutaneous tissue was the last parameter assessed on ultrasound. This border was blurred in 8 (57.1%) cases and readily visible in the remaining 6 (42.9%) cases.

Radiography

Increased skin thickness in the area of the largest skin lesions compared to unaffected regions was detected in all limbs (100%, Tab. 4). Skin and subcutaneous tissue calcifications were detected in 12 limbs (85.7%), including isolated calcifications in 5 cases, and massive calcifications merging into large conglomerates infiltrating the skin in the other 7 limbs (Fig. 9). Radiography showed no calcifications in 2 limbs (14.3%).

A blurred border between the skin and the subcutaneous tissue of the tibia was detected in 5 limbs (35.7%).

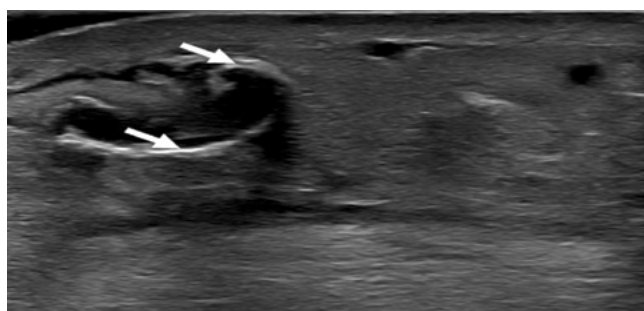


Fig. 5. Calcifications in the vessel walls (arrows)

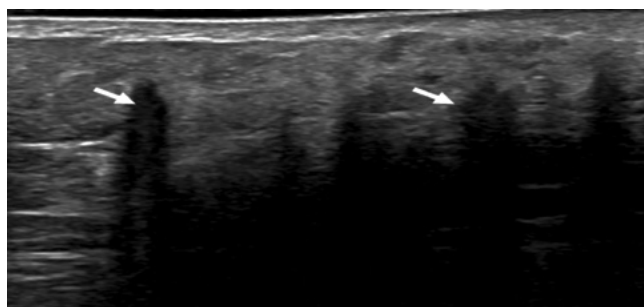


Fig. 6. Subcutaneous fibrosis (the arrow points to the fibrotic shadow)

Concordance between high-frequency ultrasound and radiography

High-frequency ultrasound and radiology showed 100% concordance for detecting thickening of the involved skin. High concordance between these two modalities was also found for detecting skin and subcutaneous tissue calcifications. Radiologically detected calcifications were confirmed in HFU. In only one case (7.1%), the calcification on HFU was not visible on the radiograph. A blurred border between the skin and the subcutaneous tissue was seen on radiography and HFU images in 37.5% and 57.1% of patients, respectively. Therefore, the two modalities showed concordance for detecting the blurred border between the skin and the subcutaneous tissue in only 3 limbs. In the case of a visible border between the skin and the subcutaneous tissue, concordance was achieved for only 4 limbs.

Discussion

Lipodermatosclerosis is an important clinical and therapeutic problem affecting all age groups. It is associated with pain and often ulcerations, which consequently lead to limb dysfunction. Although the most reliable diagnosis of lipodermatosclerosis is based on histopathology of skin and subcutaneous tissue specimens, biopsy is not recommended due to the risk of impaired healing of the tibial wound. Therefore, minimally invasive diagnostic imaging of lipodermatosclerosis is needed.

It was already 25 years ago that Welzel *et al.*⁽⁸⁾ used HFU for the diagnosis of lipodermatosclerosis. The authors used a 20 MHz transducer and found a more than 2-fold increase in the thickness of skin and its increased echogenicity in patients

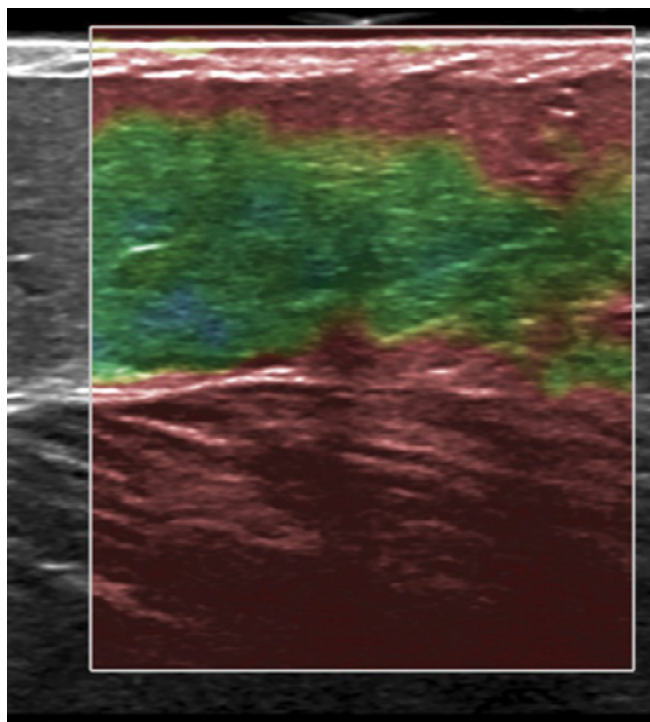


Fig. 7. Compression elastography of the femoral skin

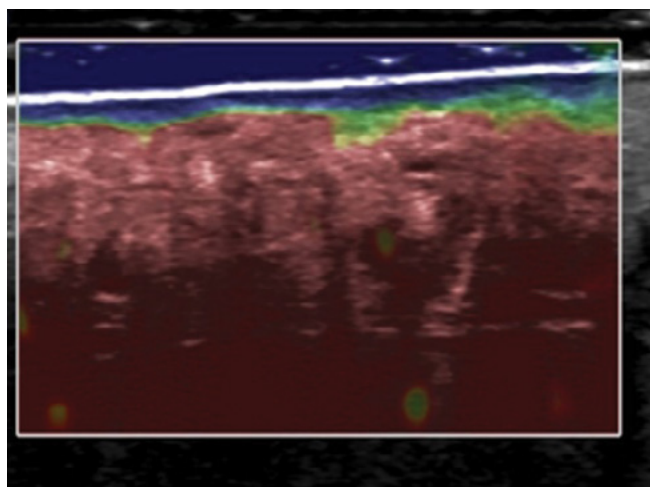


Fig. 8. Compression elastography of the tibial skin

with advanced CVI. These authors also confirmed the efficacy of HFU in detecting subcutaneous tissue calcifications. Additionally, they noticed a blurred border between the skin and the subcutaneous tissue in all patients, which was caused by chronic inflammation⁽⁸⁾. The enormous technological progress in skin diagnostic ultrasound was associated with the introduction of 20–100 MHz transducers⁽⁹⁾. In our research, we used a 48 MHz transducer (DermaMed, Dramiński S.A., Olsztyn, Poland), which significantly improved the imaging of pathological changes within the skin and the subcutaneous tissue typical of CVI. HFU allowed for easy visualization of increased skin thickness and echogenicity, as well as calcifications and fibrosis, which are an important element of the diagnosis of lipodermatosclerosis.

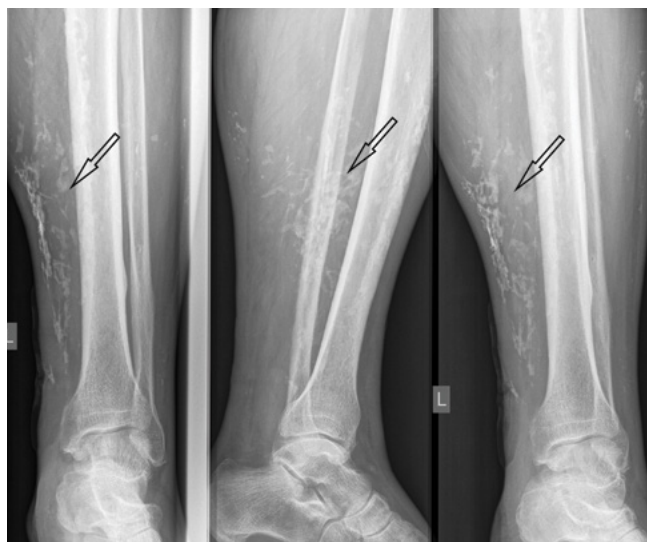


Fig. 9. Radiography of the tibia involved by lipodermatosclerosis (the arrows point to multiple confluent calcifications)

Tokoro *et al.*⁽¹⁰⁾, on the other hand, used PA and lateral tibial radiographs for the diagnosis of lipodermatosclerosis. They confirmed the presence of skin and subcutaneous tissue calcifications in 65% of patients with lipodermatosclerosis, which were either punctate-type calcifications or merged into conglomerates referred to by the authors as trabecular calcifications⁽¹⁰⁾. In their paper, the authors confirmed a large percentage of calcifications in patients with advanced CVI, which was also confirmed by HFU. Here, ultrasound was slightly more accurate compared to conventional radiography.

Imaging of blood vessels, including small veins, is another advantage of HFU⁽¹¹⁾. Our study pointed to its high effectiveness in detecting calcifications in the walls of fine vessels, which are typical for advanced CVI.

Modern, high-class ultrasounds feature static and dynamic sonoelastography options⁽¹²⁾. Static compression elastography used in our study made it possible to easily confirm reduced compliance of the subcutaneous tissue in lipodermatosclerosis. The strain ratio clearly indicated that the adipose tissue (or what has left of it) was harder than muscles.

In conclusion, it should be emphasized that HFU and radiography have characteristic features that facilitate the diagnosis of lipodermatosclerosis. Their non-invasiveness may be an important asset in the monitoring of disease progression, and these two modalities may become useful tools for the assessment or treatment of lipodermatosclerosis in the future.

Conclusions

High-frequency ultrasonography of the skin and the subcutaneous tissue in the lower legs, supported with radiological findings, is highly useful in the diagnosis of tibial lipodermatosclerosis. It would be very useful to determine fixed parameters that would allow for a rapid diagnosis. This, however, requires further studies.

Conflict of interest

Authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

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