Subcutaneous Tissue Ultrasonography in Legs with Dependent Edema and Secondary Lymphedema

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Objectives: To elucidate the differences in subcutaneous ultrasound findings between dependent edema (DE) and secondary lower extremity lymphedema (LE).

Materials and Methods: Twenty legs in 10 patients with DE and 54 legs in 35 patients with LE, who first visited our clinic between April 2009 and December 2012, were studied retrospectively. Subcutaneous echogenicity and echo-free space (EFS) were assessed at 8 points on the thigh and leg using an 8–12 MHz ultrasound transducer.

Results: In DE, echogenicity was increased most in the lower leg, without a difference between the medial and lateral side. The EFS was most remarkable in the lower leg, and the lateral side was more severe. In the early stages of LE, echogenicity was similarly increased in the medial thigh and in the leg, while remarkable EFS was observed only in the lower leg. As clinical severity progressed, echogenicity increased in all parts of the lower extremity. EFS also increased in all parts of the leg, but the lower leg was still the most severe.

Conclusion: Echogenicity seemed to progress differently in DE and LE, but EFS progressed similarly and according to gravity. The current ultrasound findings may have added some diagnostic value in differentiating these conditions.

Keywords: ultrasonography, subcutaneous tissue, dependent edema, lymphedema

Introduction

As the elderly population becomes larger, the number of patients immobile because of severe gait disturbance is increasing. These people tend to sit for prolonged periods of time. Prolonged sitting with dependent legs leads to venous stasis, causing “dependent edema.” Venous stasis can result in skin changes, such as stasis dermatitis, hyperpigmentation, lipodermatosclerosis, white atrophy, and venous leg ulcers, as seen in advanced chronic venous insufficiency. Without these typical symptoms, however, dependent edema is often misdiagnosed as lymphedema because of the lack of objective diagnostic means, particularly by inexperienced physicians. Since these two types of leg edema are treated differently, they should be properly differentiated. In this study, we attempted to elucidate the differences in ultrasonographic findings between dependent edema and lymphedema.

Patients and Methods

This study was approved by the Institutional Review Board of Yamaguchi University Hospital (Ube, Yamaguchi, Japan), and the need for individual patient...
consent was waived because of the retrospective nature of the study.

We investigated patients who first visited our clinic between April 2009 and December 2012 complaining of leg edema who met the following inclusion criteria:

**Dependent Edema (DE)**

- A patient who sits during most of the day because of severe gait disturbance but is not bedridden.
- Normal lymph transport, as confirmed by lymphangioscintigraphy (LAS).
- No apparent symptoms indicating advanced chronic venous insufficiency, such as stasis dermatitis, hyperpigmentation, lipodermatosclerosis, white atrophy, or venous ulcers.
- Venous duplex ultrasound did not show any significant abnormalities.
- Systemic diseases that might cause leg edema were excluded.

**Lymphedema (LE)**

- Newly diagnosed with secondary leg lymphedema caused by oncologic surgery.
- Impaired lymph transport, as confirmed by LAS.
- No apparent gait disturbance.
- Venous duplex ultrasound did not show any significant abnormalities.
- Systemic diseases that might cause leg edema were excluded.

Twenty lower extremities in 10 patients with DE and 54 lower extremities in 35 patients with LE met the above requirements and were involved in the study. The characteristics of these patients are summarized in Table 1. The clinical stage of lymphedema was decided on the basis of the Consensus Document of the International Society of Lymphology.2

**Ultrasound**

During each patient's first visit, subcutaneous tissue was scanned using an ultrasound system (LOGIQ S6; GE Healthcare, Little Chalfont, Buckinghamshire, UK) with an 8–12 MHz linear transducer. The points of scanning were as follows:

- **Upper medial thigh**: Middle of the upper half of the thigh, immediately anterior to the great saphenous vein.
- **Upper lateral thigh**: Middle of the upper half of the thigh, lateral aspect of the quadriceps femoris muscle.
- **Lower medial thigh**: Middle of the lower half of the thigh, immediately anterior to the great saphenous vein.
- **Lower lateral thigh**: Middle of the lower half of the thigh, lateral aspect of the quadriceps femoris muscle.

At each scan point, the subcutaneous echogenicity was graded as described in our recent report (Fig. 1);3

**Subcutaneous Echogenicity Grade (SEG).**

- **Grade 0**: No increased echogenicity in the subcutaneous layer.
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leg, or between the same scan points from different legs. Spearman’s rank correlation was used to test the relationships between ISL stage and SEG or SEF. Statistical analyses were performed using Dr. SPSS II software (IBM, Armonk, New York, USA). A P value less than 0.05 was considered statistically significant.

Results

Subcutaneous echogenicity
The SEG in DE and LE are demonstrated in Fig. 2. In DE, the SEG was higher in the upper medial leg and the lower medial/lateral leg than in the upper medial thigh. No significant differences were found between the medial and lateral scan points at any of the same extremity levels.

In LE, the SEG of each scan point was significantly correlated with ISL stage. The difference in SEG between the upper medial thigh and the medial/lateral leg was not seen in any stage. In LE Stage I, the SEG in the medial thigh was higher than that in the lateral thigh. Differences in the SEG between the medial and lateral parts at the same extremity

Grade 1: Diffuse increases in echogenicity, but identifiable horizontal or obliquely oriented echogenic lines caused by connective tissue bundles.

Grade 2: Diffuse increases in echogenicity. Echogenic lines are not identifiable.

Since echogenicity is a relative evaluation and is easily changed by controlling B-mode gain, this was first adjusted to be observed as black using normal subcutaneous fat from another part of the body, or from a healthy subject.

In this study, we also graded the extent of echo-free space (EFS), which indicates identifiable edema by ultrasound, as specified below:

Subcutaneous Echo-Free Space Grade (SEF)
Grade 0: No EFS.
Grade 1: Horizontally oriented (<45° to the skin) only.
Grade 2: Presence of vertically oriented (≥45° to the skin) bridging the horizontally oriented EFSs.

Statistical analysis
A Mann–Whitney U-test was used to compare the SEG or SEF at the different scan points on the
level were not found in the leg nor in any part of the lower extremities in LE Stages II and III.

When the same scan points from DE and LE Stage I were compared, the SEG was significantly higher in the upper/lower medial thigh and was lower in the lower lateral leg in LE Stage I. In LE Stages II and III, the SEG was higher in all identical parts to DE, except in the lower leg.

**Subcutaneous echo-free space**

The SEF in DE and LE are shown in Fig. 3. In DE, the SEF was higher in all parts of the leg than in the upper medial thigh. The SEF was significantly higher in the lateral leg than in the medial leg.

In LE, the SEF of each scan point was significantly correlated with the ISL stage. For each stage, a significant increase in the SEF in the lower leg compared to the upper medial thigh was found. No significant differences were found between the SEF in the medial or lateral parts of any extremity levels in any stage of LE.

When the same scan points in DE and LE were compared, the SEF was significantly lower in the upper/lower lateral leg in LE Stage I and in the lower lateral leg in LE Stage II. On the contrary, the SEF was higher in the upper/lower medial thigh in LE Stage II, and in all parts in LE Stage III, except in the lower lateral leg.

**Discussion**

There were two major findings in the current study. First, in DE, increases in subcutaneous echogenicity and EFS were most evident in the lower lateral leg, while the upper medial thigh was preserved. Second, in LE, increases in echogenicity were evident in the medial thigh and the leg in earlier stages of the disease, while EFS was evident in the lower leg.

**Grading of subcutaneous echogenicity and echo-free space**

Increased echogenicity is not a finding specific to lymphedema, and is seen in various inflammatory conditions. However, the histological characteristics of the extracellular matrix in chronic lymphedema are similar to those in chronic inflammation. Therefore,
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Vertical fibrous septa separating the superficial fascial system. Fluid accumulation in these spaces will form a “cobblestone” appearance. In the current study, this sequence of fluid accumulation was graded. Because the terms “horizontally” and “vertically” were not clearly defined in the literature, we used a measurement of 45° to differentiate these conditions for convenience. Some of the vertically oriented EFSs may have been dilated lymphatics, but identification is quite difficult.

Subcutaneous echogenicity

Since edema is currently considered to be caused by an imbalance between capillary filtration and lymph drainage, but not venous capillary reabsorption, any form of edema can present with symptoms mimicking lymphedema. Therefore, we tried to investigate the changes in echogenicity in legs with DE as well as LE.

A new finding in the current study regarding echogenicity was the difference of distributions in DE and LE. In DE, the lower the leg level, the higher the vertical fibrous septa separating the superficial fascial system. Fluid accumulation in these spaces will form a “cobblestone” appearance. In the current study, this sequence of fluid accumulation was graded. Because the terms “horizontally” and “vertically” were not clearly defined in the literature, we used a measurement of 45° to differentiate these conditions for convenience. Some of the vertically oriented EFSs may have been dilated lymphatics, but identification is quite difficult.

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validity. These grades should be further examined in studies including larger numbers and wide varieties of subjects.

The finding of increased subcutaneous echogenicity involves potential problems. Since the superficial fascial system varies significantly as the level of adiposity changes, the connective tissue becomes indistinct in obese subjects. This is particularly evident in the upper medial thigh, where more fat is accumulated than in other parts of the lower extremity, such that the interpretation of the visibility of echogenic lines in this region more difficult. Furthermore, obesity itself is known to impede lymphatic flow, which leads to collection of protein-rich lymphatic fluid in the subcutaneous tissue and subsequent fibrosis mimicking lymphedema. Presently, there are no means to clearly separate normal and pathological fat accumulation, otherwise these conditions might not able to be separated. In increased edema, the extremity may present as lymphedema, CVI, or both. Each of these conditions exhibits a characteristic skin presentation caused by inflammation from different mechanisms, but these are not able to be differentiated by ultrasound at present.

Subcutaneous echo-free space
In DE, the most remarkable EFS (i.e., edema) was found in the lower leg, which is again presumed to be caused by gravity. An interesting finding is that edema was more severe on the lateral side. One possible explanation is that fluid in the medial side of the leg may be better drained by the VMB. Another possible explanation is a difference in compliance of the superficial fascia. The primary function of the superficial fascia is to encase, support, and shape the fat of certain body regions and to hold the skin onto the underlying tissue. Since it has been reported that the amount and thickness of superficial fascia varies in different parts of the body, it is estimated that the compliance of the subcutaneous tissue may be different in the medial and lateral lower leg.

Although mild edema was found in the medial thigh in LE Stages I and II, more severe edema was generally seen in the lower leg in all stages of LE. However, this distribution was different from that of echogenicity. It is now estimated that the extent of chronic inflammation resulting from lymph congestion may follow the distributions of lymph trunks, but fluid accumulation may be affected by both lymphatic transport and gravity. In LE Stage III, edema in the lower lateral leg seemed even more severe than in the medial side. It is assumed that advanced LE may show a mixed picture of LE and DE, because these patients can suffer significant gait disturbance from the heaviness of the extremity, reduced joint movement due to fibrosis of the surrounding tissue, and other related issues.

Limitations
Our SEG and SEF have not been supported by any pathological basis, but were simply defined based on empirical facts; accordingly, they might not hold any validity. These grades should be further examined in studies including larger numbers and wide varieties of subjects.

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Disclosure Statement
The authors have no conflicts of interest to declare.
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