Ultrasonographic Evaluation of the Lymphedema

Un Cheol Yeo, M.D., Won Serk Kim, M.D., Ho Soo Chun, M.D., Eil Soo Lee, M.D., Byung-Boong Lee, M.D.,* Dong Ik Kim, M.D.,* Ji-Hye Hwang, M.D.**

Department of Dermatology, Department of General Surgery*, Department of Physical Medicine and Rehabilitation**, Samsung Medical Center, Seoul, Korea

Background: Lymphedema occurs when tissue swelling develops through a failure of lymph drainage in the face of a normal capillary filtration. Little is known about water behavior in lymphedema.

Objective: Our purpose was to investigate, by means of ultrasound, the distribution of intradermal fluid in patients with lymphedema in response to 2 weeks' physical therapy.

Method: Ten patients with lymphedema were treated by 2 weeks' physical therapy. Before and after 2 weeks' treatment, circumference and ultrasonographic evaluation was done. Ultrasound images were obtained with a 20 MHz scanner. The echogenicity of the dermis and the skin thickness were quantified by in-built image analyzer.

Results: Low echogenic pixels showed the most noticeable and consistent change after 2 weeks' physical therapy.

Conclusion: Ultrasonographic evaluation could be a useful tool in evaluating lymphedema.


Key Words: Lymphedema, Ultrasonography

The real pioneering era of dermatological ultrasound is now over. Due to the availability of a variety of high-quality equipment constructed especially for the study of skin the method can now be more widely used. In 1979, a stimulus was given to high-frequency ultrasound examination of skin by Alexander and Miller. Very soon prototype equipments operating at 20 MHz were constructed, and the basic principles became validated. Dermascan-C (Cortex technology, Denmark) provides an axial and lateral resolution of 50 μm and 300 μm. Each B-mode picture is composed of 224 A-scans. Gain and viewing fields can be adjusted on the live image. The width of the field of view is limited to 1.3 cm, and usually the depth of penetration does not exceed 1.5 cm. Because of these limitations, Dermascan-C is inappropriate for examining the subcutaneous tissue, but very useful for dermal lesions.

The potential applications of high-frequency ultrasound imaging technology in dermatology include assessment of disease activity in conditions such as psoriasis, morphea, eczema, contact dermatitis, evaluation of efficacy of H1 blockers and boundary definition of malignancies such as melanomas and basal cell carcinomas.

Ultrasound imaging has also been used to assess dermal edema. Age related diurnal changes of dermal edema and dermal edema in lipodermatosclerosis were evaluated. Recently, ultrasonographic evaluation of lymphedema was done on 10 patients with limb lymphedema. Lymphedema showed uniformly distributed edema in papillary and reticular dermis.

The aim of this study is to evaluate the usefulness of Dermascan-C in evaluating the effect of treatment on lymphedema.

MATERIAL AND METHODS

Patients

Ten patients with lymphedema who visited lymphedema clinic in Samsung medical center were
Table 1. Patients' profile

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex/Age</th>
<th>Primary Disease</th>
<th>Duration (years)</th>
<th>Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F/63</td>
<td>Cervix cancer</td>
<td>16</td>
<td>Lt. thigh</td>
</tr>
<tr>
<td>2</td>
<td>F/65</td>
<td>Cervix cancer</td>
<td>15</td>
<td>Lt. lower leg</td>
</tr>
<tr>
<td>3</td>
<td>F/45</td>
<td>Cervix cancer</td>
<td>3</td>
<td>Lt. thigh</td>
</tr>
<tr>
<td>4</td>
<td>F/22</td>
<td>Primary lymphedema</td>
<td>8</td>
<td>Lt. thigh</td>
</tr>
<tr>
<td>5</td>
<td>F/35</td>
<td>Breast cancer</td>
<td>2</td>
<td>Lt. upper arm</td>
</tr>
<tr>
<td>6</td>
<td>F/50</td>
<td>Cervix cancer</td>
<td>1.5</td>
<td>Lt. thigh</td>
</tr>
<tr>
<td>7</td>
<td>F/57</td>
<td>Cervix cancer</td>
<td>1</td>
<td>Lt. thigh</td>
</tr>
<tr>
<td>8</td>
<td>F/27</td>
<td>Primary lymphedema</td>
<td>17</td>
<td>Rt. thigh</td>
</tr>
<tr>
<td>9</td>
<td>F/57</td>
<td>Breast cancer</td>
<td>4</td>
<td>Rt. upper arm</td>
</tr>
<tr>
<td>10</td>
<td>F/54</td>
<td>Cervix cancer</td>
<td>2</td>
<td>Rt. thigh</td>
</tr>
</tbody>
</table>

Table 2. The results of pre- and post-treatment evaluation

<table>
<thead>
<tr>
<th>Case</th>
<th>pre-Treatment</th>
<th>post-Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CF(cm)</td>
<td>ST(mm)</td>
</tr>
<tr>
<td>1</td>
<td>73.0</td>
<td>2.64</td>
</tr>
<tr>
<td>2</td>
<td>39.2</td>
<td>2.11</td>
</tr>
<tr>
<td>3</td>
<td>54.0</td>
<td>2.16</td>
</tr>
<tr>
<td>4</td>
<td>53.2</td>
<td>2.53</td>
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<tr>
<td>5</td>
<td>29.4</td>
<td>2.11</td>
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<tr>
<td>6</td>
<td>53.2</td>
<td>2.06</td>
</tr>
<tr>
<td>7</td>
<td>49.0</td>
<td>2.06</td>
</tr>
<tr>
<td>8</td>
<td>52.0</td>
<td>1.74</td>
</tr>
<tr>
<td>9</td>
<td>25.9</td>
<td>1.79</td>
</tr>
<tr>
<td>10</td>
<td>54.5</td>
<td>1.84</td>
</tr>
</tbody>
</table>

CF : Circumference of affected limb
ST : Skin thickness is measured by region-of-interest function of Dermascan-C
LEPs : The proportion of LEPs(0-30) among all the pixels measured by Dermascan-C is expressed in percentage

included in this study. They were documented as having lymphedema of variable severity and etiology by physical findings and Tc99m-ASC lymphoscintigram (Table 1).

Physical therapy
Treatment was undertaken according to the "complex physical therapy(CPT)" program. This program comprise four components: meticulous skin hygiene care, 1 hour manual lymph drainage, bandaging and 30 minutes' exercise. This was repeated on five days out of seven for two weeks. Comparison of circumferencial limb measurements before and after a two weeks' treatment was performed. Data of clinical improvement were obtained based on the patients' statement.

Ultrasonographic evaluation
Skin scanning was performed before and after 2 weeks' treatment schedule on the same site where the circumference was measured. The selected sites were 15cm above popliteal fossa or 10cm above antecubital fossa.

A 20 MHz ultrasound scanner (Dermascan C, Cortex Technology, Denmark) was used to obtain cross-sectional images of the skin (B-mode). The instrument consists of three main parts: the C probe with the transducer, the elaboration system, and the data storing system. The ultrasonic wave is partially reflected at the boundary between adjacent structures and generates echoes of different amplitudes. The intensity of reflected echoes is evaluated by the microprocessor and visualized as a
Table 3. Changes in CF, ST and LEPs after 2 weeks' treatment.

<table>
<thead>
<tr>
<th>Case</th>
<th>CF2/CF1(%)</th>
<th>ST2/ST1(%)</th>
<th>LEPs2/LEPs1(%)</th>
<th>Clinical assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>93.80</td>
<td>100.0</td>
<td>61.20</td>
<td>improved</td>
</tr>
<tr>
<td>2</td>
<td>96.40</td>
<td>100.0</td>
<td>54.20</td>
<td>improved</td>
</tr>
<tr>
<td>3</td>
<td>99.10</td>
<td>92.70</td>
<td>79.20</td>
<td>improved</td>
</tr>
<tr>
<td>4</td>
<td>97.70</td>
<td>89.60</td>
<td>53.40</td>
<td>improved</td>
</tr>
<tr>
<td>5</td>
<td>97.30</td>
<td>102.5</td>
<td>97.30</td>
<td>stationary</td>
</tr>
<tr>
<td>6</td>
<td>101.6</td>
<td>102.5</td>
<td>756.0</td>
<td>aggravated</td>
</tr>
<tr>
<td>7</td>
<td>97.30</td>
<td>92.30</td>
<td>1,956</td>
<td>aggravated</td>
</tr>
<tr>
<td>8</td>
<td>96.90</td>
<td>100.0</td>
<td>5.260</td>
<td>improved</td>
</tr>
<tr>
<td>9</td>
<td>94.60</td>
<td>85.30</td>
<td>60.50</td>
<td>improved</td>
</tr>
<tr>
<td>10</td>
<td>97.20</td>
<td>94.80</td>
<td>97.40</td>
<td>improved</td>
</tr>
</tbody>
</table>

CF2/CF1: Circumference of post-treatment(CF2) divided by circumference of pre-treatment(CF1)
ST2/ST1: Skin thickness of post-treatment(ST2) divided by skin thickness of pre-treatment(ST1)
LEPs2/LEPs1: Low echogenic pixels of post-treatment(LEPs2) divided by low echogenic pixels of pre-treatment(LEPs1)

Fig. 1. Comparison of skin thickness using ultrasonographic image and histopathological findings in the same site of lymphedema patient.
(a) Histopathologic findings: skin thickness is 1.37 mm which was measured three times by optical micrometer and averaged.
(b) Ultrasonographic findings: skin thickness is 1.37 mm which was measured through automatic algorithm displayed by in-built image analyzer. Apex of arrow shows automatic algorithm which defines the dermo-subcutaneous junction.
(c) Measurement of LEPs using in-built image analyzer. White pixels indicated by the arrow are LEPs.

colored two-dimensional image. The color scale of echogenicity is white > yellow > red > green > blue > black. The gain compensation curve was adjusted in the horizontal position at 22 dB. This gain was previously found to give maximal A-scan peaks on the rubber phantom provided by the manufacturer. The velocity of ultrasound in the skin was set at 1580 m/sec. The position of the
transducer was assured by checking the parallel orientation of the ultrasound image of the membrane of the probe versus the epidermal entrance echo. Echographic images were stored on floppy disks and subsequently processed by image analysis.

In each image the number of low echogenic pixels (LEPs) was measured with an in built image analyzer. In this system the amplitudes of echoes of single image elements (pixels) are ascribed to a numeric scale (0 to 255). The low echogenic pixels extend from 0 to 30. The number of LEPs increases with the decrease of echogenicity. LEPs were determined in the cutis region excluding the subcutaneous fat layer.

By the region-of-interest (ROI) function, the full-block of cutis excluding the subcutaneous fat was outlined and the skin thickness (ST) was measured automatically by the equipment. In preliminary study, we compared histopathologic findings with ultrasonographic findings and the results were compatible (Fig. 1).

RESULTS

Figure 2 shows the typical example of the ultrasonographical measurement. Table 2 shows the measurement of circumference (CF), skin thickness (ST) and low echogenic pixels (LEPs) in pre and post-treatment. We divided the post-treatment measurement by the pre-treatment measurement, and these data are expressed in table 3 and figure 3.

There were clinical improvement in case 1, 2, 3, 4, 8, 9 and 10. In these cases, the changes in LEPs were the most noticeable parameter than those of ST or CF. Case 5 showed variable results in three parameters and there was not clinical improvement. In case 6 and 7 who showed aggravation
in the dermis, the majority of echoes are generated on the interface between rigid collagen fibers and surrounding matrix composed mostly of water. It could be predicted that in the case of edema, excess of water distends the collagen network, thus making the dermal image more echolucent (echo-poor). Indeed, early experience with dermatological ultrasonography (20 MHz high resolution B-mode scanner) uniformly showed edematous regions such as urticarial wheals, places of irritant or inflammatory reactions, skin in the post-thrombotic syndrome and some tumors, as echolucent structures\(^4\). Echogenicity is nowadays amenable for objective quantification with computer-based image analysis programmes. Amplitudes of echoes of single-image elements (pixels) are given values on a numerical scale (0-255). The hypoechogenic bandwidth from 0 to 30 represents the hypoechogenic part of the image typical for edema\(^2\). Investigators have successfully used this system for quantification of skin edema\(^1\)\(^4\). Sometimes subepidermal LEPs can be seen in association with distended blood vessels, psoriasis, contact dermatitis and actinic damage. So we should carefully rule out these pathologic change before jumping into edema evaluation by ultrasonography.

Recently Gniadecka\(^9\) made ultrasonographic evaluation of lymphedema, lipodermatosclerosis and cardiac insufficiency. This was the first report of using high frequency ultrasound in lymphedema evaluation. All three diseases are associated with dermal edema, but only lipodermatosclerosis is often associated with skin ulcer. This phenomenon could be explained by localizing the dermal edema in three diseases. In lipodermatosclerosis, edema was located in upper dermis in contrast to diffuse localization in lymphedema and lower dermal localization in cardiac insufficiency.

In lymphedema, fluid accumulates in the dermis and fat layer due to impaired lymphatic drainage. In the early stages, many cases of lymphedema exhibit easy displacement of fluid on pressure. Subsequently, with the development of fibrosis, the edema becomes firmer, and although some pitting may persist, a permanent non-pitting component is present. Fibrosis develops in the dermis as the end stage of the pathologic process in chronic lymphedema, which leads to thickening of skin. Little is known about the change in skin thickness in response to treatment. This can be evaluated by

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**DISCUSSION**

Echostucture of an organ, viewed during 2-dimensional (B-mode) ultrasonography, depends on the content of fluid in the tissue. Hepatic and renal cysts are uniformly echo-poor and the echogenicity of liver decreases with increase in water content\(^5\). Echogenicity of the tissue is directly related to the amplitude and number of individual echoes in a given area of the ultrasound image. The echoes are generated at the border between media of different acoustic impedance. It is conceivable that...
noninvasive repetitive ultrasonographic measurement. In this study we found that after short term treatment skin thickness could be decreased probably due to decreased dermal edema. This has opened a new method to inspect change of skin thickness in the pathologic process of lymphedema. However, long term follow up should be performed to confirm the effect of physical therapy on skin thickness. In case 6 and 7, LEPs nearly approached 50% after treatment making the LEPs2/LEPs1 very high (756.0% and 1,956% respectively). This kind of severe edema could be found initially in other patients such as case 1,5 and 8. Acute increase in LEPs after treatment was thought to be caused by acute shifting of fluids from the lower leg to the thigh. But, shifted fluid couldn't escape to the trunk due to severe lymphatic obstruction in the inguinal region. In case 6 and 7, very high LEPs2/LEPs1 ratio was caused by relatively low pre-treatment LEPs in the thigh (6.56% and 2.50% respectively). Among CF, ST and LEPs, LEPs altered most dramatically after treatment and well correlated with the clinical improvement or aggravation. These findings lead to the conclusion that LEPs can be used as a sensitive indicator of therapeutic effect in lymphedema.

REFERENCES