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CORRELATION AMONG BIOIMPEDANCE ANALYSIS, SONOGRAPHIC AND CIRCUMFERENTIAL MEASUREMENT IN ASSESSMENT OF BREAST CANCER-RELATED ARM LYMPHEDEMA

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ABSTRACT

New approaches for assessment of lymphedema using ultrasonography (US) have been introduced recently and are reported to be reliable and simple. Ultrasonography provides detailed information about physical properties of the tissue in addition to volume and size. There have been only limited studies comparing bioimpedance analysis (BIA), US, and circumferential measurement (CM), which is considered a standard measurement. The aim of this study was to determine the relationship between US, BIA, and CM. Twenty-eight patients with lymphedema after breast cancer surgery underwent BIA, US, and CM. Impedance, which reflects the amount of extracellular fluid, was measured with 1 kHz frequency in affected and unaffected arms. Circumferences were measured at 10cm proximal and distal to the elbow and a truncated cone method used to calculate estimated volumes for upper arm and forearm. We found that interlimb forearm subcutis thickness differences measured by US were highly correlated with CM measurements and that interlimb upper arm subcutis thickness differences measured by US were moderately correlated with CM measurements and BIA ratios. However, the interlimb ratio of compressibility measured by US showed no or only weak correlation with impedance measurements and circumferential measurements. Our results also show that compressibility measured by US could not be predicted from BIA or CM measurements despite a high degree of concordance among subcutis thickness measured by US, CM, and BIA.

Keywords: breast cancer, bioelectrical impedance, BIS, lymphedema, ultrasonography, measurement

Upper limb lymphedema is a clinical manifestation that can arise from an obstruction or disruption of the lymphatic system as a consequence of breast cancer surgery, radiation therapy, or malignancy (1). The reported incidence of upper limb lymphedema is quite variable from less than 10% to more than 50%, with a prevalence of 13-42% of breast cancer patients (2-4) depending on factors such as different times and methods of assessment. In order to document exact incidence and treatment outcomes, reliable, valid, and practical measurements and quantifications of upper limb lymphedema are crucial. There are various definitions used to diagnose lymphedema such as interlimb circumference difference more than 2 centimeters, interlimb volume difference more than 8 to 10% or

200ml or subjective reports of limb heaviness (5-7). Conventional measurements include a circumferential measurement (CM) such as a tape method and calculated volume which is derived from circumference measures by using the formula for a truncated cone (8,9). Due to its convenience and cost-effectiveness, this is the most widely used method to assess lymphedema. Because circumferential measurements assess total limb volume, these are indirect measures and have limitations to detect early changes of lymphedema. Also, reliability issues have been raised (10,11). Total limb volume includes not only the extracellular fluid, which accounts for approximately 25% of total limb volume but also bone, muscle, fat, and other soft tissues (12,13).

New measurement methods have been introduced to evaluate upper limb lymphedema. Bioelectrical impedance (BIA) measurements are used to quantify the amount of extracellular fluid directly (14) by measuring the response of the body to an applied electrical current to estimate body composition (12). Ultrasonography (US) has been used to evaluate lymphedema for investigational purposes (15), and it can analyze physical properties of tissue and structural alterations in real time (16). Long standing lymphedema can cause increased fibrosis which makes tissues stiffer and less compressible (17). In clinical practice, it is confusing to diagnose lymphedema when the clinician recognizes a difference in stiffness based on palpation but there is no definite circumferential difference. There have been trials to measure stiffness objectively, and US has been suggested as one of simplest way to measure stiffness and compressibility in an objective way. The compressibility of the skin and subcutis has been reported as an important index to monitor the progress of lymphedema (18).

Although a few trials have investigated the relationship between CM and water displacement or perometry (19), the relationship between US for tissue thickness and compressibility and other measurements such as BIA, CM, and volume measurements has not been reported so far. Therefore, the objective of this study was to determine the relationship among US, BIA, and CM assessment measurements. In addition, we further examined which parameters from those measurements would be more correlated to other measurement methods.

METHODS

Subjects

Patients with secondary unilateral lymphedema that developed after surgery for breast cancer and was confirmed by clinical and lymphoscintigraphic examination were eligible. For clinical diagnosis, the circumference of the affected arm measured at forearm and upper arm had to exceed that of the unaffected arm by two or more centimeters. Lymphoscintigraphy evaluated the obstructive pattern of lymphatic drainage in the affected limb and the accumulation of lymphatic fluid. Patients who had primary lymphedema, whose lymphedema was not related to the treatment for breast cancer, or had bilateral lymphedema, were excluded. The participants were recruited from the outpatient clinic of Department of Rehabilitation Medicine, and the study protocol was approved by the institutional review board of our hospital (IRB No.1108-101-374). All study parameters were explained in detail and informed consent was obtained from all participants.

Demographic and clinical variables of patients were obtained. Demographic variables included age at study enrollment and body mass index (BMI). Clinical variables included the side of the dominant hand, type of surgery, time after surgery, history of lymph node dissection, radiation therapy, and chemotherapy, tumor stage, and duration of lymphedema.

Measurements of Lymphedema

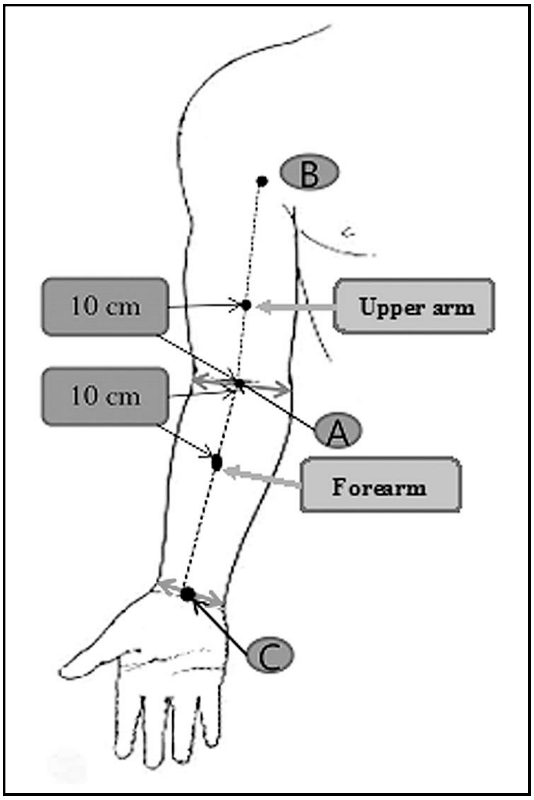

Fig. 1. Schematic demonstrating reference points used to measure for circumferential and ultrasonographic measurements in the upper arm and forearm. For the upper arm, the measurement point was orientated on a line from midpoint of medial and lateral epicondyle (point A) to bicipital groove (point B) and the measurements taken at a location 10cm proximal along this line from point A. For the forearm, the measurement point was orientated along the line from point A to the midpoint of radial and ulnar styloid process (point C) at a location 10cm distal from point A.

Lymphedema was measured with BIA, US, and CM at the same day and time. Bioimpedance and circumference were measured by one experienced physical therapist. One fully experienced ultrasonographer measured skin thickness, subcutis thickness, and compressibility using ultrasonography.

Circumferential measurement

The circumferences were measured with a measuring tape. Circumferences were measured at upper arm, elbow and forearm on both sides. On the upper arm, the location of measurement was 10 centimeter proximal from the elbow crease along the line between the midpoint of the medial and lateral epicondyles of the humerus and the bicipital groove. On the forearm, the location of measurement was 10cm distal from the elbow crease along the line between the midpoint of the medial and lateral epicondyles and the midpoint of radial and ulnar styloid processes *(Fig. 1)*.

One experienced therapist measured circumferences. The volumes of forearm and upper arm were derived from circumference measures by using the formula for a truncated cone (20). The interlimb circumference difference, interlimb volume difference, and interlimb volume ratios were calculated and used for an analysis.

Bioimpedance measurement

A multifrequency impedance plethysmograph body composition analyzer (InBodyS10, Biospace, Seoul, Korea) was used to measure extracellular fluid volume. It takes readings from the body using an eight-point tactile electrode method. During impedance measurements, all participants were lying supine on a bed. Previous literature showed that the best frequency to detect extracellular fluid is 0 kHz (or DC). However, measurement at this frequency is not possible in practice due to the high skin impedance at DC, and an estimate is usually determined from low frequency measurements because single low frequency measurements sufficiently provide information for the purpose of the lymphedema assessment indistinguishable from bioimpedance measurement with 0 kHz (21). Impedance measured with 1 kHz frequency in affected and unaffected arms was used for analysis in this study. Impedances obtained directly from the device were used to calculate impedance ratios. Because impedance decreases with increased fluid,

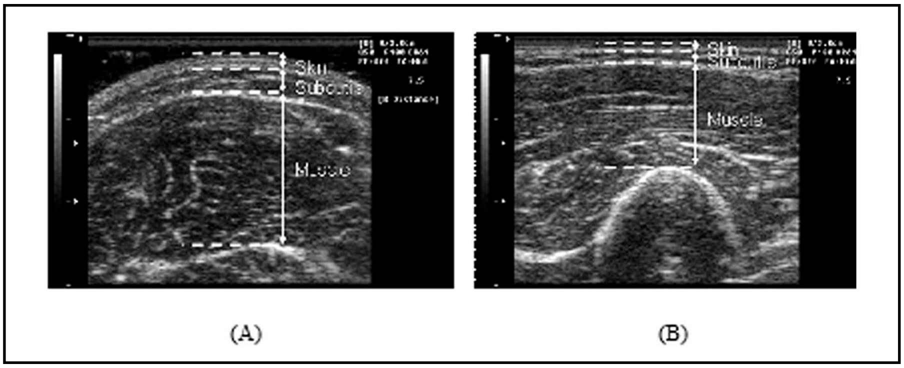

Fig. 2. Ultrasound images of a patient with breast cancer-related lymphedema demonstrating imaging with negligible pressure (A) and with control of precise 2N pressure (B).

the ratio was expressed as impedance on unaffected limb/impedance on affected limb to provide a lymphedema index greater than 1.

Ultrasonographic measurement

The subjects were placed supine on an examination table with the forearm supinated and relaxed. An ultrasound unit (Accuvix V10EX-DOM-00, Medison Co., Seoul, Korea) evaluated the soft tissue on the upper arm and forearm with a 7.5MHz linear-array transducer. Ultrasonographic measurements were performed at the same points with circumferential measurements for upper arms and forearms on both affected and unaffected sides.

Imaging of the skin, subcutis, muscle, and sometimes bone was possible. Ultrasound gel was applied liberally to the skin and the probe placed transversely on the arm. To measure the thickness of the skin and subcutis, an ultrasonographer applied negligible pressure by applying a sufficient amount of lubricant so that the contour of the tissue beneath a transducer was not distorted. Ultrasonographic measurements of skin and subcutis thickness at upper arm and forearm in affected and unaffected upper limbs were performed with control of precise pressure. A portable pressure sensor (HF-1, Japan Instrumentation System Co., Yokohama, Japan) was attached to the probe, and the examiner precisely controlled pressure as 2N to provide same amount of pressure to all participants by monitoring the sensor. The previous study showed at least 2N needs for achieving a high reliability (22).

One experienced technician examined all subjects to exclude the possible inter-rater variability. Our previous study reported that intra-rater reliability was 0.848-0.900 in forearm and 0.539-0.760 in upper arm while intra-rater reliability was 0.952-0.962 in forearm and 0.904-0.974 in upper arm (23). Skin thickness was defined as distance between the bottom of the entry-echo and the skin-subcutis boundary. Subcutis thickness was measured between the skin-subcutis boundary and the subcutis-muscle boundary *(Fig. 2)*.

On the images captured on the upper arm and forearm, the thickness of skin and subcutis were measured by using console measurement tools on the ultrasound unit.

The compressibility was calculated as: thickness measured without pressure - thickness measured with pressure over thickness measured without pressure.

Data Analysis

SPSS 18.0 program for Windows was

TABLE 1 Participant Characteristics	
Characteristic	
Age (year) (mean±SD)	54.8±9.7
BMI (Kg/m^2) (mean±SD)	24.3±3.1
Affected limb	18R:10L
Surgery	
quadrantectomy	12 (42.9%)
breast conserving surgery	6 (21.4%)
modified radical mastectomy	6 (21.4%)
Others	4 (14.3%)
Axillary lymph node dissection	
Yes	21 (75.0%)
No	2 (7.1%)
N/A	5 (17.9%)
Chemotherapy	25 (89.3%)
Radiotherapy	24 (85.7%)
Time since surgery (months) (mean±SD)	57.2±53.2
Time since onset of lymphedema (months) (mean±SD)	30.4±26.7

used for the statistical analysis with a value of $p<0.05$ considered significant. We compared CM with US and BIA ratios by Pearson's correlation analysis. Comparison of compressibility between affected and unaffected side was performed using Student's t-test.

RESULTS

Subjects

Baseline characteristics of participants are summarized in *Table 1*. Twenty-eight women, ages 30-77 years (54.8 ± 9.7, mean ± SD) were enrolled. All patients had undergone previous breast cancer operative treatment. Twelve (42.9%) underwent quadrantectomy, 6 (21.4%) underwent breast conserving surgery, and 6 (21.4%) underwent modified radical mastectomy. Axillary lymph node dissection was performed in 21 patients (75.0%). 25 patients (89.3%) received chemotherapy and 24 patients (85.7%) received radiotherapy. Eighteen patients (64.3%) were affected on the right side and 10 (35.7%) on the left. Lymphangioscintigraphy was performed in 20 patients (71.4%). It showed definite obstruction in 7 (25.0%), suspicious obstruction in 11 (39.3%) and no definite obstruction in 2 (7.1%).

Circumferential Measurement

The mean circumferential difference at 10cm distal and at 10cm proximal from the elbow crease was 2.72 ± 2.68 and 2.84 ± 2.23, respectively (*Table 2*). The mean interlimb volume difference at the forearm and upper arm was 0.11 ± 0.12cm^3 and 0.12 ± 0.12cm^3, respectively. The mean interlimb ratio at the forearm and upper arm was 1.24 ± 0.26 and 1.22 ± 0.21, respectively.

Bioimpedance Measurement

The mean values of impedance for affected side and unaffected sides were 331.62 ± 79.60 and 402.59 ± 44.90, respectively. The mean value for the interlimb ratio of impedance (unaffected side/affected side) was 1.27 ± 0.31.

Ultrasonographic Measurement

Upper arm

Skin thickness measured with negligible pressure at the affected and unaffected sides in the upper arm was 0.19 ± 0.08 and 0.16 ± 0.03, respectively *(Table 3*). Subcutis thickness measured with negligible pressure at affected and unaffected sides in the upper arm was 0.91 ± 0.41 and 0.72 ± 0.20, respectively. Interlimb subcutis thickness with negligible pressure in the upper arm was 0.19 ± 0.42. Skin thickness measured with control of precise pressure at affected and unaffected sides in the upper arm was 0.15 ± 0.05 and 0.13 ± 0.02, respectively. Subcutis thickness measured with control of precise pressure at affected and unaffected sides in the upper arm was 0.58 ± 0.27 and 0.43 ± 0.11, respectively. Interlimb subcutis thickness with control of precise pressure in upper arms was 0.16 ± 0.28.

TABLE 2
Circumferential Measurements

	Affected (mean±SD)	Unaffected (mean±SD)	Interlimb difference	Ratio (mean±SD)
Circumference at the MCP (cm)	19.01±0.90	18.88±1.38	0.13±1.23	
Circumference at the wrist (cm)	17.34±1.53	16.30±0.99	1.04±1.28	
Circumference at forearm (cm)	25.51±3.19	22.79±1.60	2.72±2.68	
Circumference at the elbow (cm)	27.36±3.43	24.80±1.73	2.56±2.71	
Circumference at upper arm (cm)	31.10±3.38	28.26±2.60	2.84±2.23	
Volume at forearm (cm^3)	0.56±0.15	0.45±0.06	0.11±0.12	1.24±0.26
Volume at upper arm (cm^3)	0.69±9.16	0.56±0.09	0.12±0.12	1.22±0.21

TABLE 3
Ultrasonographic Measurements

	Subcutis thickness with negligible pressure		**Subcutis thickness with precise pressure**	
	Affected	**Unaffected**	**Affected**	**Unaffected**
Forearm	1.24±0.90	0.77±0.31	0.86±0.78	0.46±0.23
Upper arm	0.91±0.41	0.72±0.20	0.58±0.27	0.43±0.11
	Skin thickness with negligible pressure		**Skin thickness with precise pressure**	
	Affected	**Unaffected**	**Affected**	**Unaffected**
Forearm	0.65±0.55	0.18±0.05	0.15±0.06	0.13±0.03
Upper arm	0.19±0.08	0.16±0.03	0.15±0.05	0.13±0.02
	Subcutis compressibility at affected limb		**Subcutis compressibility at unaffected limb**	
Forearm	0.35±0.16		0.38±0.21	
Upper arm	0.34±0.15		0.39±0.13	

Compressibility of skin and subcutis measured in the affected upper arm was 0.02 ± 1.23 and 0.34 ± 0.15. The compressibility of skin and subcutis measured in the unaffected upper arm was 0.19 ± 0.14 and 0.39 ± 0.13. There was no difference in the compressibility of skin and subcutis between affected and unaffected sides.

Forearm

Skin thickness measured with negligible pressure at affected and unaffected sides in the forearm was 0.65 ± 0.55 and 0.18 ± 0.05, respectively (*Table 3*). Subcutis thickness measured with negligible pressure at affected and unaffected side in the forearm was 1.24 ± 0.90 and 0.77 ± 0.31, respectively. Interlimb subcutis thickness with negligible pressure in the forearm was 0.47 ± 0.91. Skin thickness measured with control of precise pressure at affected and unaffected side in the forearm was 0.15 ± 0.06 and 0.13 ± 0.03, respectively. Subcutis thickness measured with control of precise pressure at affected and unaffected side in the forearm was 0.86 ± 0.78 and 0.46 ± 0.23, respectively. Interlimb subcutis thickness with control of precise pressure in the forearm was 0.16 ± 0.28.

Compressibility of skin and subcutis measured at the affected forearms was 0.51 ± 0.37 and 0.35 ± 0.16. The compressibility of skin and subcutis measured at the unaffected forearms was 0.25 ± 0.19 and 0.38 ± 0.21. There is no difference in the compressibility of skin and subcutis between affected and unaffected sides.

TABLE 4
Correlation Among Bioimpedance, Circumferential And Ultrasonographic Measurements

	r (p-value)	
	Forearm	**Upper arm**
Impedance ratio vs circumferential measurements		
Interlimb circumference difference	0.872(<0.001)	0.789(<0.001)
Interlimb volume difference	0.851(<0.001)	0.836(<0.001)
Interlimb volume ratio	0.841(<0.001)	0.802(<0.001)
Impedance ratio vs ultrasonographic measurements		
Interlimb subcutis thickness difference without pressure	0.623(<0.001)	0.555(0.002)
Interlimb subcutis thickness difference with pressure	0.504(0.006)	0.561(0.002)
Interlimb ratio of compressibility	0.228(0.244)	0.255(0.190)
Ultrasonographic measurements vs circumferential measurements		
Interlimb subcutis thickness difference with negligible pressure vs		
Interlimb circumference difference	0.725(<0.001)	0.598 (0.001)
Interlimb volume difference	0.798 (<0.001)	0.597 (0.001)
Interlimb volume ratio	0.767 (<0.001)	0.527 (0.004)
Interlimb subcutis thickness difference with precise pressure vs		
Interlimb circumference difference	0.756 (<0.001)	0.541 (0.003)
Interlimb volume difference	0.826 (<0.001)	0.516 (0.005)
Interlimb volume ratio	0.809 (<0.001)	0.452 (0.016)
Interlimb ratio of compressibility vs		
Interlimb circumference difference	0.393 (0.039)	0.236 (0.226)
Interlimb volume difference	0.346 (0.072)	0.165 (0.400)
Interlimb volume ratio	0.391 (0.040)	0.178 (0.364)

r: Pearson's correlation coefficient

Relationship Between CM and BIA Measurement Methods

Impedance ratios measured at the upper arm and forearm were highly correlated with circumferential difference [0.789 (p<0.001) and 0.872 (p<0.001), respectively] and interlimb volume difference [0.836 (p<0.001) and 0.851 (p<0.001), respectively] (*Table 4*). Impedance ratios measured at the upper arm and forearm were also highly correlated with interlimb volume ratio [0.802 (p<0.001) and 0.841(p<0.001), respectively].

Correlation Between CM and US Measurements

Upper arm

The interlimb subcutis thickness differences measured with negligible pressure and with 2N precise pressure in the upper arm were correlated with interlimb circumferential difference [0.541 (p=0.003) and 0.598 (p=0.001), respectively], with interlimb volume difference [0.516 (p=0.005) and 0.597(p=0.001), respectively], and with interlimb volume ratio [0.452 (p=0.016) and 0.527 (p=0.004), respectively]. The interlimb ratio of compressibility in the upper arm was not correlated with interlimb circumferential difference [0.236 (p=0.226)], with interlimb volume difference [0.165 (p=0.400)], and with interlimb volume ratio [0.178 (p=0.364)].

Forearm

The interlimb subcutis thickness differences measured with and without pressure were correlated with interlimb circumferential difference [0.756 (p<0.001) and 0.725 (p<0.001), respectively], with interlimb volume difference [0.826 (p<0.001) and 0.798 (p<0.001), respectively], and with interlimb volume ratio [0.809 ($p<0.001$) and 0.767 ($p<0.001$), respectively]. The interlimb ratio of compressibility was weakly correlated with interlimb circumferential difference [0.393 ($p=0.039$)], with interlimb volume difference [0.346 ($p=0.072$)], and with interlimb volume ratio [0.391 ($p=0.040$)].

Correlation Between BIA and US Measurements

Impedance ratios measured at upper arm were correlated with interlimb subcutis thickness difference with and without pressure [0.504 ($p=0.006$) and 0.623 ($p<0.001$), respectively] and those measured at forearm [0.561 ($p=0.002$) and 0.555 ($p=0.002$), respectively]. However, the interlimb ratios of compressibility at upper arm and forearm were not correlated with impedance ratio [0.255 ($p=0.190$) and 0.228 ($p=0.244$), respectively].

DISCUSSION

We found that there is a strong agreement of circumferential measures with impedance ratios at the upper arm and forearm and circumferential measures with interlimb subcutis thickness difference at forearm measured by ultrasonography. However, only a moderate agreement (less than 0.7 of r value) of impedance ratios with interlimb subcutis thickness difference at upper arm and forearm and circumferential measures with interlimb subcutis thickness difference at upper arm.

Documenting differences in limb size and determining quantitative discrepancies between patients' unaffected and affected limbs is critical in the evaluation of lymphedema. Assessment of lymphedema is most commonly based on abnormal limb size determined from circumferential measurements of the limb. Irrespective of how limb size is determined, circumference and volume are affected by tissues that may change independently from lymphedema, such as muscle and fat (24). Size differences from left-right dominance, muscle atrophy, fibrous tissue deposition, or weight gain may be inaccurately attributed to fluid accumulation (25). In addition, it requires a significant amount of time to perform the measurements, and there is a high potential for measuring error (14). Bioimpedance analysis is a convenient and quick method and has proven to be useful in discerning limb size and fluid accumulation differences in patients with lymphedema (12,13,26-28). Although bioimpedance analysis can accurately measure extracellular accumulation of lymphatic fluid because low frequency currents selectively pass through extracellular fluid compartments, it cannot quantify the other tissue elements that increase aside from the interstitial fluid, such as fibrous tissue (14).

Exact reference values for impedance ratios is not well established especially in Asian populations although there are published trials to determine the reference value for impedance ratios in American and Australian populations (29,30). Also, impedance (arm to arm) ratios in patients with bilateral lymphedema can be anticipated as normal (30). In this case, Ward et al. suggested extracellular/intracellular fluid ratios as an alternative method to determine the diagnosis of bilateral lymphedema (28). In addition, ultrasonographic measurements, which can demonstrate the components of the volume and thickness, can be used to help diagnose bilateral lymphedema.

Impedance measurements showed relatively poor correlation with ultrasonographic measurement. BIA analysis measures along the length of the arm as an index of extracellular fluid volume. The changes in thickness measured by ultrasonography may not parallel changes in extracellular fluid volume. Alternatively, impedance measurements in the transverse direction rather than in the longitudinal direction may overcome this limitation (27,31,32).

Ultrasonography can safely and simply assess structural alterations and the severity of lymphedema. Ultrasonography is easily accessible in a clinic and can visualize architecture in real time. The results from the present study demonstrated that an increase of circumference and calculated volume in an affected limb was mirrored by an increase of subcutis thickness measured by ultrasonography. However, skin thickening was minimal in the lymphedematous limbs. We anticipated that severely lymphedematous limbs would be more fibrotic and less compressible and therefore, evaluated compressibility by a dynamic method with pressure. The compressibility failed to show a strong correlation with the severity measured by CM and BIA. This may be due to limitations in evaluating compressibility by applying pressure with an ultrasound probe and calculating the deformation of the tissue using the ultrasound image. Our methods assessed only stress and strain at the tissue surface, so it was impossible to discriminate whether the estimated value indicated the superficial part or the deep part. For example, if the shallow part is fibrotic, the deep part would be estimated to be less soft than it really is. Fukuda et al suggested a soft tissue model composing three-layered structure. The skin, subcutis, and muscle compose a layered structure, and the lymphatic fluid remains in the subcutaneous tissue layer in a patient with lymphedema (18). Every layer has its own compressibility, and three layers have three different compressibilities. Even though we estimated subcutis compressibility separately, compressibility of other tissues could affect the measured value to each other. To quantify compressibility and fibrosis, new assessment methods need to be developed.

One weakness of this study is that only a few patients who had fibrotic change in the lymphedematous arm were included in this present study. A larger number of patients with a wide range of elasticity will be required to evaluate the compressibility in future studies. In clinical practice, it is difficult to diagnose lymphedema when the physician recognizes a difference in stiffness based on palpation with no definite circumferential difference. Fortunately, staging of lymphedema is reported on the basis of tissue fibrosis as well as a circumferential difference when lymphedema assessment is carried out in a clinic. It is also known that the early stage of lymphedema without fibrotic change is more responsive to treatment (33,34), so assessment of fibrosis can be an important prognostic factor. However, there is no definite measurement method to examine stiffness and fibrosis objectively. Ultrasonography has been introduced as a simple way to measure stiffness and compressibility in an objective way. The present study shows US, BIA, and CM measurements are all valuable for measuring the volume status and that US can simultaneously evaluate the characteristics of subcutis layer and compressibility. The results from this study can be used to develop clinical methods for measuring fibrosis objectively.

CONCLUSION

There was a high degree of concordance among CM and impedance ratios as determined by BIA and subcutis thickness measured by US.

Impedance ratios measured at upper arm and forearm were highly correlated with interlimb circumferential difference, interlimb volume difference, and interlimb volume ratio. Impedance ratios measured at upper arm and forearm were correlated with subcutis thickness on the affected side measured by ultrasonography. Also, subcutis thickness at the affected side measured by ultrasonography was correlated with interlimb circumferential difference, interlimb volume difference, and interlimb volume ratio. BIA and US measurements correlated with CM but they also have different advantages in evaluating patients with upper limb lymphedema. The aim of the evaluation, availability, and cost should be considered when choosing an appropriate method for use in individual clinical settings.

Conflict of Interests

The authors declare that no conflicts of interest and no commercial party had a direct financial interest in the results of the research and/or supported this article nor will confer a benefit upon the authors or upon any organization with which the authors are associated.

REFERENCES

1. Murdaca, G, P Cagnati, R Gulli, et al: Current views on diagnostic approach and treatment of lymphedema. Am. J. Med. 125 (2012), 134-140.
2. Petrek, JA, MC Heelan: Incidence of breast carcinoma-related lymphedema. Cancer 83 (12 Suppl Am) (1998), 2776-2781.
3. Ridings, P, TE Bucknall: Modern trends in breast cancer therapy: Towards less lymphoedema? Eur. J. Surg. Oncol. 24 (1998), 21-22.
4. Deo, SV, S Ray, GK Rath, et al: Prevalence and risk factors for development of lymphedema following breast cancer treatment. Indian J. Cancer 41 (2004), 8-12.
5. Stout Gergich, NL, LA Pfalzer, C McGarvey, et al: Preoperative assessment enables the early diagnosis and successful treatment of lymphedema. Cancer 112 (2008), 2809-2819.
6. Armer, JM: The problem of post-breast cancer lymphedema: Impact and measurement issues. Cancer Invest. 23 (2005), 76-83.
7. Hayes, S, B Cornish, B Newman: Comparison of methods to diagnose lymphoedema among breast cancer survivors: 6-month follow-up. Breast Cancer Res. Treat. 89 (2005), 221-226.
8. Tewari, N, PG Gill, MA Bochner, et al: Comparison of volume displacement versus circumferential arm measurements for lymphoedema: Implications for the SNAC trial. ANZ J. Surg. 78 (2008), 889-893.
9. Deltombe, T, J Jamart, S Recloux, et al: Reliability and limits of agreement of circumferential, water displacement, and optoelectronic volumetry in the measurement of upper limb lymphedema. Lymphology 40 (2007), 26-34.
10. Gerber, LH: A review of measures of lymphedema. Cancer 83 (12 Suppl Am) (1998), 2803-2804.
11. Sander, AP, NM Hajer, K Hemenway, et al: Upper-extremity volume measurements in women with lymphedema: A comparison of measurements obtained via water displacement with geometrically determined volume. Phys. Ther. 82 (2002), 1201-1212.
12. Cornish, B: Bioimpedance analysis: Scientific background. Lymphat. Res. Biol. 4 (2006), 47-50.
13. Cornish, BH, IH Bunce, LC Ward, et al: Bioelectrical impedance for monitoring the efficacy of lymphoedema treatment programmes. Breast Cancer Res. Treat. 38 (1996), 169-176.
14. Warren, AG, BA Janz, SA Slavin, et al: The use of bioimpedance analysis to evaluate lymphedema. Ann. Plast. Surg. 58 (2007), 541-543.
15. Han, Nm, Yj Cho, Js Hwang, et al: Usefulness of Ultrasound examination in evaluation of breast cancer-related lymphedema. J Korean Acad. Rehabil. Med. 35 (2011), 101-109.
16. Saijo, Y: High resolution biomedical imaging-multimodal ultrasound microscope and combination with optics. J. Acoust. Soc. Am. 131 (2012), 3495.
17. De Cock, HE, VK Affolter, ER Wisner, et al: Progressive swelling, hyperkeratosis, and fibrosis of distal limbs in Clydesdales, Shires, and Belgian draft horses, suggestive of primary lymphedema. Lymphat. Res. Biol. 1 (2003), 191-199.
18. Fukuda, O, M Tsubai, N Ueno: Impedance estimation of soft tissue using ultrasound signal. Conf. Proc. IEEE Eng. Med. Biol. Soc. 2007 (2007), 3563-3568.
19. Jain, MS, JV Danoff, SM Paul: Correlation between bioelectrical spectroscopy and perometry in assessment of upper extremity swelling. Lymphology 43 (2010), 85-94.
20. Taylor, R, UW Jayasinghe, L Koelmeyer, et al: Reliability and validity of arm volume measurements for assessment of lymphedema. Phys. Ther. 86 (2006), 205-214.
21. York, SL, LC Ward, S Czerniec, et al: Single frequency versus bioimpedance spectroscopy for the assessment of lymphedema. Breast Cancer Res, Treat. 117 (2009), 177-182.
22. Hwang, BK, DH Lee, JE Park, et al: Optimal pressure measurements of lymphedema with ultrasonography in post operative breast cancer patients. Proceedings of the 13th International Congress on Clinical Ultrasound of the Spanish Society of General Medicine, Apr 22-24 2012. Madrid, Spain.
23. Kim, W, SG Chung, TW Kim, et al: Measurement of soft tissue compliance with pressure using ultrasonography. Lymphology 41 (2008), 167-177.
24. Czerniec, SA, LC Ward, KM Refshauge, et al: Assessment of breast cancer-related arm lymphedema—comparison of physical measurement methods and self-report. Cancer Invest. 28 (2010), 54-62.

25. Mikes, DM, BA Cha, CL Dym, et al: Bioelectrical impedance analysis revisited. Lymphology 32 (1999), 157-165.
26. Cornish, BH, M Chapman, C Hirst, et al: Early diagnosis of lymphedema using multiple frequency bioimpedance. Lymphology 34 (2001), 2-11.
27. Cornish, BH, LC Ward, BJ Thomas, et al: Quantification of lymphoedema using multi-frequency bioimpedance. Appl. Radiat. Isot. 49 (1998), 651-652.
28. Ward, L, A Winall, E Isenring, et al: Assessment of bilateral limb lymphedema by bioelectrical impedance spectroscopy. Int. J. Gynecol. Cancer 21 (2011), 409-418.
29. Ridner, SH, MS Dietrich, J Deng, et al: Bioelectrical impedance for detecting upper limb lymphedema in nonlaboratory settings. Lymphat. Res. Biol. 7 (2009), 11-15.
30. Ward, LC, E Dylke, S Czerniec, et al: Confirmation of the reference impedance ratios used for assessment of breast cancer-related lymphedema by bioelectrical impedance spectroscopy. Lymphat. Res. Biol. 9 (2011), 47-51.
31. Dylke, E, L Ward, C Stannard, et al: Bioimpedance for the spot measurement of tissue density. J. Physics: Conference Series, 2013. IOP Publishing: 012054.
32. Ward, L, B Cornish, N Fuller, et al: Bioelectrical impedance analysis: The electronic skin-fold caliper? Bioelectromagnetism, 1998. Proceedings of the 2nd International Conference on, 1998. IEEE: 101-102.
33. Casley-Smith, JR: Alterations of untreated lymphedema and it's grades over time. Lymphology 28 (1995), 174-185.
34. Ramos, SM, LS O'Donnell, G Knight: Edema volume, not timing, is the key to success in lymphedema treatment. Am. J. Surg. 178 (1999), 311-315.

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