Title page

Enhanced echo intensity and a higher extracellular water-to-intracellular water ratio are helpful clinical signs for detecting muscle degeneration in patients with knee osteoarthritis

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Abstract

Introduction/objectives: Enhanced muscle echo intensity (EI) with ultrasound imaging and a higher extracellular water-to-intracellular water (ECW/ICW) ratio with segmental-bioelectrical impedance spectroscopy (S-BIS) represent muscle quality loss. This study aimed to clarify quadriceps muscle degeneration characteristics, focusing on muscle quality changes in patients with knee osteoarthritis (OA).

Method: Forty-one women with knee OA (mean age, 71.4±6.0 years) and 27 healthy women (mean age, 75.6±4.9 years) participated. Ultrasonography was used to evaluate the muscle thickness (MT) and the EI of each quadriceps compartment. The ECW/ICW ratio was obtained by S-BIS. MT, EI, and ECW/ICW ratio differences between the two groups were tested using univariate analysis of variance, adjusting for age and body mass index. Logistic regression analyses were performed with the group as the dependent variable, and the MT and EI of the vastus medialis (VM) and the ECW/ICW ratio as independent variables.

Results: Patients with knee OA had a significant decrease in VM MT, enhanced VM, and vastus intermedius EIs and a higher ECW/ICW ratio compared with healthy participants. Logistic regression analysis showed that the VM EI (odds ratio [OR], 1.19; 95% confidence interval [CI], 1.06–1.35) and the ECW/ICW ratio were independently associated with knee OA (OR, 1.19; 95% CI, 1.00–1.42).

Conclusions: VM EI and the ECW/ICW ratio, rather than VM MT, characterised quadriceps muscle degeneration in patients with knee OA. Therefore, enhanced EI and a higher ECW/ICW ratio are helpful clinical signs for detecting muscle degeneration in patients with knee OA.

Key Points

- Echo intensity (EI) of the vastus medialis and the extracellular-to-intracellular water (ECW/ICW) ratio significantly increased in patients with knee osteoarthritis (OA).
- Enhanced EI and a higher ECW/ICW ratio are useful clinical signs for detecting muscle degeneration in patients with knee OA.

Keywords: knee osteoarthritis, quadriceps muscle degeneration, echo intensity, extracellular-to-intracellular water ratio, muscle quality.

Introduction

Quadriceps muscle degeneration, which includes loss of muscle mass and quality, is a known risk factor for knee osteoarthritis (OA) development and the decline of functional abilities [1-3]. A recent meta-analysis [4] indicated that muscle fat infiltration (i.e., poor muscle quality) was higher in patients with knee OA than in healthy participants. A more recent study [5] also showed that poor muscle quality, but not muscle mass loss, is associated with functional disabilities. Therefore, muscle quality assessment may be fundamental for elucidating the association between muscle dysfunction and functional disabilities in knee OA.

Evaluating morphological and composition changes of the quadriceps femoris is important for estimating knee OA pathogenesis [6,7]. However, the use of imaging modalities, such as magnetic resonance imaging and dual-energy X-ray absorptiometry, are often limited in research fields. By contrast, muscle thickness (MT) and muscle echo intensity (EI) can be non-invasively and easily measured via ultrasound images in a clinical setting and are widely used for muscle quantity and quality indices [8-10]. Previous studies have reported that an EI increase occurred at an earlier age and OA stage than did an MT decrease [9,11,12]. Specifically, the vastus medialis (VM) muscle EI in patients with knee OA significantly increased compared with healthy participants [12], suggesting that muscle quality assessment using the VM EI was useful for detecting muscle degeneration in patients with knee OA.

The relative increase of the extracellular water (ECW) compartment within the skeletal muscle is also an important determinant of muscle quality [13]. Segmental-bioelectrical impedance spectroscopy (S-BIS) is a convenient, affordable, and non-invasive tool for evaluating muscle quality. Skeletal muscle tissue contains a large amount of water, and S-BIS can distinguish intracellular water (ICW) and ECW from total body water [14,15]. Generally, ICW represents muscle cell mass, and ECW represents non-contractile tissue, including interstitial fluid in the extracellular space [16]. A higher ECW/ICW ratio indicates a relative increase of non-contractile tissue to muscle mass (i.e., muscle quality loss) [17]. Although a high ECW/ICW ratio in patients with knee OA was associated with physical dysfunction [5], it remains unclear whether the ECW/ICW ratio in patients with knee OA is higher than that in healthy participants.

Furthermore, a previous study that simultaneously investigated EI and the ECW/ICW ratio suggested that these indicators represent different qualitative changes within the skeletal muscle [18]. Ultrasound images cannot distinguish a liquid component from muscle composition. Therefore, EI assessment is assumed to reflect mainly adipose and fibrous tissue. Conversely, the ECW/ICW ratio indicates an expansion of the extracellular space based on increased water content [18]. To our knowledge, no studies have simultaneously investigated EI and the ECW/ICW ratio in patients with knee OA. Specifically, it is unknown if an enhanced EI and a higher ECW/ICW ratio can be used to characterise knee OA muscle degeneration, which would indicate a loss of muscle quality.

This study aimed to clarify the characteristics of quadriceps muscle degeneration by focusing on muscle quality changes in patients with knee OA. We hypothesized that (1) the VM EI and the ECW/ICW ratio in patients with knee OA are increased compared to that of healthy participants; and (2) these indicators, which suggest a loss of muscle quality rather than muscle quantity, could be used to characterise quadriceps muscle degeneration in patients with knee OA.

Materials and Methods

Study participants and selection

Forty-one female patients with symptomatic medial knee OA were recruited from one community orthopaedic clinic. Twenty-seven healthy control women were also recruited from local communities in Kyoto and neighbouring cities. All study procedures were approved by the Ethics Committee of the Kyoto University Graduate School of Medicine and were conducted following the Declaration of Helsinki principles. All participants were informed regarding the purpose and procedures of this study and gave written informed consent.

All patients with knee OA were diagnosed based on the American College of Rheumatology criteria for osteoarthritis of the knee [19] and classified using the Kellgren-Lawrence (KL) grading system ≥2 for unilateral or bilateral knees [20]. The inclusion criteria for knee OA were symptomatic and radiographic knee OA, the ability to live independently, and the ability to walk with or without assistive devices. The exclusion criteria for all patients were a surgical history for the back or both limbs, rheumatoid arthritis, and cardiovascular or neurological disorders. In the case of bilateral knee OA, the more severe side was selected for data analysis. If the participant had equal OA severity for both knees, the more painful side was selected. Of 41 patients with knee OA, the KL grades were as follows: grade 2, n = 19; grade 3, n = 13; grade 4, n = 9.

The inclusion criteria in the healthy control group were no self-reported history of knee pain, the ability to live independently, and the ability to walk with or without assistive devices. The exclusion criteria for healthy control participants were the same as that used for the knee OA group, and the right knee was selected for data analysis. Based on a previous study that reported the VM EI between knee OA and healthy control groups [12], an effect size of 0.98 was applied for the sample size calculation with an α level of 0.05 and a β level of 0.20. The sample size was calculated using G*Power software (version 3.1.9.7, Universität Kiel, Germany); 18 participants were needed in each group.

Self-reported knee function and symptoms

The Knee Society's Knee Scoring System (KSS) 2011 was used to evaluate knee function and symptoms. The KSS 2011 is a self-administered measurement tool for knee conditions, and the validity of KSS has been confirmed in the Japanese population [21]. There are four KSS subcategories:

symptoms, satisfaction, expectations, and functional activities. This study focused on the functional activities and symptoms categories. The functional activities category was chosen to evaluate the degree of physical dysfunction during daily activities. This category has four components: walking and standing, standard activities, advanced activities, and discretionary activities. The symptom category has three components: the degree of knee pain during walking, the degree of knee pain when travelling up or down stairs, and knee stiffness. The maximum possible functional activities and symptom scores are 100 and 25 points, respectively, and lower scores represent worse functional activity abilities and symptoms.

Muscle thickness and echo intensity measurements using ultrasound images

Transverse ultrasound images were acquired using a B-mode ultrasound imaging device with an 8 MHz linear-array probe (LOGIQ e; GE Healthcare UK Ltd., Chalfont, UK). The participants rested for more than 3 min in the relaxed supine position, and then ultrasound image measurements were performed. All measurements were taken by the same investigator using the same equipment settings (58-dB gain and 69-dB dynamic range). The dynamic focus depth was set to the middle of the muscle of interest. The measurement sites of each muscle followed a previous study [12], and the MTs of the rectus femoris (RF), vastus intermedius (VI), vastus lateralis (VL), and VM were measured. The MT was measured on the ultrasound images using an electronic calliper. EI was measured by converting the image pixels to an 8-bit grey-scale using image processing software (ImageJ-WinJP; LISIT, Japan). The average EI in the region of interest was calculated on a 256-point scale from 0 to 255, with the high EI values indicating more augmented fat and connective tissue within the muscle [22]. All EI analyses were conducted by another investigator who did not know the group attributes. The reliability of the MT and EI measurements were confirmed by estimating the intra-class correlation coefficients (ICC) for the between-day test-retest reliability. The ICC values of MT and EI ranged from 0.94 to 0.85 and 0.88 to 0.81, respectively. Ultrasound measurements were performed as previously described [18].

Quantification of the ECW/ICW ratio in the upper thigh

The S-BIS measurement procedure was conducted following the ultrasound measurements to avoid body water re-distribution. The ECW/ICW ratio was assessed with a multi-frequency S-BIS device (Fig. 1). The S-BIS device (SFB7, ImpediMed Inc., Australia) measures bioelectrical impedances using a logarithmic distribution of 256 frequencies (ranging from 4 kHz to 1000 kHz) with disposable tab-type electrodes (Red Dot TM; 3M Inc., Japan). The S-BIS measurements were performed for three consecutive repetitions, and the average bioelectrical impedance value was used for analysis. The acquisition, storage, and data processing were conducted using SFB7 Bioimp software (ImpediMed Inc., Australia). The resistance of zero (R_0) and infinity (R_∞) were estimated and obtained by fitting the spectrum of impedance data to the Cole-Cole model. The R_0 and R_∞ indicate the ECW compartment (i.e., $R_0 = R_{ECW}$) and the total body water compartment (TBW; i.e., $R_\infty = R_{TBW}$). The resistance of the ICW compartment (R_{ICW}) was calculated as $1/[(1/R_{TBW}) - (1/R_{ECW})]$. The ECW and ICW in the thigh were calculated by applying the estimation algorithm as follows: ECW = $\rho_{ECW} \times L^2/R_{ECW}$ and ICW = $\rho_{ICW} \times L^2/R_{ICW}$, where ρ represents the specific resistivity (ρ_{ECW} = 47 Ωcm) and intracellular resistivity (ρ_{ICW} = 273.9 Ωm). L indicates the segment length (cm), which corresponds to the distance between the anterior superior iliac spine and the proximal end of the patella. Then, the ECW/ICW ratio was converted to ECW against ICW. The ICC value for the test-retest reliability in between-day was 0.99 in the ECW/ICW ratio. The detailed description of S-BIS measurements is indicated elsewhere [18].

Statistical analysis

All values are presented as means and standard deviations (SDs). After normal distributions were confirmed with the Kolmogorov-Smirnov test, unpaired t-tests were applied to the participant characteristics and KSS scores. Univariate analysis of variance (ANOVA) was performed to investigate the differences in MT, EI, and the ECW/ICW ratio between the groups, and the adjusted mean difference between the groups was also estimated, with adjustments for age and BMI. Furthermore, we conducted logistic regression analyses to characterise quadriceps muscle degeneration in patients with knee OA. Logistic regression analysis was performed with the knee OA group (reference, healthy control group) as the dependent variable and MT, VM EI, and the ECW/ICW ratio as independent variables, after adjusting for age and BMI. To identify a cut-off for muscle degeneration characterisation in knee OA, receiver operating characteristic (ROC) curve analysis using the Youden index was performed on the significant variables selected by logistic regression analysis. ROC curve analysis also calculated the area under the curve (AUC), sensitivity, and specificity.

All statistical tests were conducted with SPSS software version 25.0 (SPSS Japan Inc., Tokyo, Japan). Statistical significance was set at p <0.05.

Results

Table 1 presents the characteristics of the patients with knee OA and healthy control participant. The knee OA group was significantly younger than the healthy control group, but body mass and BMI in the knee OA group were significantly higher. The KSS function and symptom scores in the knee OA group were significantly lower than those in the healthy control group.

Univariate ANOVAs with adjustment for age and BMI showed significant group differences in the VM MT, EIs of VI and VM, and the ECW/ICW ratio (Table 2). The VM MT was significantly smaller in the knee OA group than in the healthy control group (adjusted mean difference, -0.44 cm; 95 % confidence interval [CI], -0.65 to -0.23). Additionally, the EIs of VI and VM in the knee OA group were significantly higher than those in the healthy control group, and the adjusted mean difference in the VM EI was remarkably higher in the knee OA group compared to the healthy control group (22.24 arbitrary units [a.u.]; 95% CI, 15.19 to 29.29). Figure 2 shows representative ultrasound images of the VM in healthy controls and patients with knee OA. Moreover, the ECW/ICW ratio in the knee OA group significantly increased compared with the healthy control group (0.10 a.u.; 95% CI, 0.05 to 0.15).

Logistic regression analysis showed that the VM EI (odds ratio [OR], 1.19; 95% CI, 1.06 to 1.35) and the ECW/ICW ratio were independently associated with knee OA (OR, 1.19; 95% CI, 1.00 to 1.42), but the VM MT was not (Table 3). ROC curve analyses determined that the optimal cut-off points for characterising muscle degeneration in knee OA were 80.4 a.u. for VM EI and 0.45 a.u. for the ECW/ICW ratio (Fig. 3). The ROC model on VM EI had high accuracy, with an AUC of 0.90, sensitivity of 0.81, and specificity of 0.89.

Discussion

This was the first study to clarify the characteristics of quadriceps muscle degeneration in patients with knee OA, focusing on muscle quality changes. In agreement with a previous report [12], the VM MT in patients with knee OA significantly decreased, and EIs of the VI and VM in patients with knee OA increased compared to healthy participants. The novel finding in this study was that the ECW/ICW ratio in patients with knee OA was higher than that in healthy participants, consistent with our hypotheses.

Moreover, the logistic regression analysis indicated that both enhanced EI of the VM and a higher ECW/ICW ratio could distinguish between OA and healthy knees, also supporting our hypotheses. These findings suggest that quadriceps muscle degeneration in patients with knee OA is characterised by muscle quality loss rather than muscle quantity.

Previous studies investigating muscle size and fat content using magnetic resonance imaging indicated that muscle atrophy and fat infiltration of VM in patients with knee OA were associated with cartilage loss and worsening symptoms [1,23]. This study measured MT and EI using ultrasound and found an MT decrease and an EI increase in the VM of patients with knee OA. Since the VM in patients with knee OA exhibits selective atrophy of type 2 fibres and fatty degeneration [24], these morphologic and composition changes can be indirectly assessed by measuring MT and EI using ultrasound. Although this was known, we found that the ECW/ICW ratio measured using S-BIS was significantly higher in patients with knee OA than in healthy participants, which is new. Increases in the EI and the ECW/ICW ratio indicate lower muscle quality, reflecting the relative increase of non-contractile tissue to muscle mass. Interestingly, Noehren et al. [25] confirmed the expansion of the extracellular matrix in muscle cells by biopsy of patients with knee OA with lower quadriceps function. The ECW compartment on bioelectrical impedance theoretically reflects interstitial fluid in the extracellular space. Therefore, the ECW/ICW ratio could be associated with the expansion of the extracellular matrix, suggesting that assessing the ECW/ICW ratio can effectively evaluate quadriceps muscle degeneration in patients with knee OA. Although the mechanism for an increasing ECW/ICW ratio is unknown, some reports suggest that high inflammation within the muscle in knee OA may be involved in muscle degeneration [26-28].

Notably, our finding indicated that quadriceps muscle degeneration in patients with knee OA was characterised by an EI and ECW/ICW ratio increase rather than an MT decrease. Kumar et al. [7] also suggested that the quadriceps intramuscular fat fraction, rather than muscle size, was associated with the structural and symptomatic severity of knee OA. These suggestions support the need to focus on both the accumulation of adipose and fibrous tissues and the expansion of extracellular water contents within the skeletal muscle, rather than only muscle size, to assess muscle degeneration in patients with knee OA. Therefore, simultaneously assessing the EI and the ECW/ICW ratio was helpful for a more accurate characterisation of muscle quality loss in knee OA. Additionally, the ROC curve analysis results showed that the discrimination accuracy for characterising muscle degeneration in knee OA was high in the VM EI. A possible reason for this difference is that the EI measured using ultrasound can assess individual muscles, such as VM, whereas the ECW/ICW ratio measured using S-BIS cannot divide the quadriceps muscle group into four individual muscles. Given the poor muscle quality in the VM of patients with knee OA, the ECW/ICW ratio (which cannot evaluate individual quadriceps muscles) may underestimate specific muscle degeneration. The ECW/ICW ratio was a useful biomarker for poor functional disabilities [5]. However, our findings suggested that the EI assessment of VM was more sensitive for detecting muscle degeneration in patients with knee OA.

As a clinical suggestion, assessments of muscle quality using ultrasound images and/or S-BIS are recommended in primary care to better understand the exact function of the quadriceps regardless of knee pain. Although EI assessment using ultrasound is useful for detecting a decline of individual muscle quality, ECW/ICW ratio assessment using bioelectrical impedance equipment can also be substituted. Previous studies suggested that these muscle quality indicators changed during 8–12 weeks of training intervention and detraining [29-31], and thus regular monitoring of 8–12 weeks on muscle degeneration is required for physicians. In the future, given that decline of muscle quality occurred at an earlier age and OA stage than did loss of muscle mass [9,11,12], muscle quality indicators could be a predictor of knee OA development.

The present study had several limitations. First, the cross-sectional design of our study could not determine a causal relationship between quadriceps muscle degeneration and the presence of knee OA. Since a previous study already reported that higher intramuscular fat content is associated with knee OA progression [23], future studies should evaluate whether muscle quality loss (i.e., enhanced EI and a higher ECW/ICW ratio) results in knee OA development and progression. Second, the participants of both groups were only older women, and there were also significant differences in age and body mass between the two groups. Although the prevalence of knee OA is higher in older and obese women [32,33], our findings might not be generalizable to older men because there is also a difference between the sexes on quadriceps muscle function in patients with knee OA.

In conclusion, patients with knee OA had significantly decreased MT, an enhanced VM EI, and an increased ECW/ICW ratio compared with healthy participants. Furthermore, an increase in the VM EI and the ECW/ICW ratio characterised quadriceps muscle degeneration in patients with knee OA. Therefore, enhanced EI and a higher ECW/ICW ratio are helpful clinical signs for detecting muscle degeneration in patients with knee OA.

Declarations

Funding

This study was supported by the JSPS KAKENHI Grant-in-Aid for Scientific Research (18H03164 and 20K19376). The grant was used for data collection, data analysis, and writing the manuscript in this study.

Conflicts of Interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

Availability of data and material

Data are not available due to ethical restrictions.

Code availability

Not applicable

Authors' contributions

All authors have made substantial contributions to (1) the conception and design of the study; (2) revising it critically for important intellectual content; and (3) final approval of the version to be submitted. The specific contributions of each author are as follows:

(1) Analysis and interpretation of the data: MT, YF, MY, YY, and NI.

(2) Drafting of the article: MT, YF, MY, and NI.

Ethics approval

All study procedures were approved by the Ethics Committee of the Kyoto University Graduate School of Medicine and were conducted in accordance with the principles of the Declaration of Helsinki.

Consent to participate and consent for publication

Written informed consent was obtained from all participants.

Acknowledgements

We would like to thank Editage (www.editage.jp) for English language editing.

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Table 1. Knee OA and healthy control participant characteristics

	Healthy control n = 27	Knee OA n = 41	p-value	95% CI
Age, y	75.6 (4.9)	71.4 (6.0)	0.004	[-6.97, -1.42]
Height, cm	151.7 (5.6)	153.7 (5.6)	0.144	[-0.72, 4.83]
Body mass, kg	48.9 (5.1)	57.2 (9.3)	<0.001	[4.35, 12.17]
Body mass index, kg/m^2	21.3 (2.1)	24.2 (3.7)	<0.001	[1.37, 4.47]
KSS function score, /100	92.0 (11.3)	67.1 (15.4)	<0.001	[-31.87, -18.11]
KSS symptom score, /25	24.0 (1.5)	15.7 (5.1)	<0.001	[-10.35, 6.31]

Variables are presented as means (SDs).

Abbreviations: OA, osteoarthritis; CI, confidence interval; KSS, Knee Society Score.

Table 2. Muscle property differences between the knee OA and healthy control groups

	Unadjusted mean (SD)		Adjusted mean (SE)		p-value	Adjusted mean difference [95% CI]
	Healthy control	Knee OA	Healthy control	Knee OA		Knee OA against healthy control
Muscle thickness, cm						
Rectus femoris	1.82 (0.35)	1.80 (0.28)	1.88 (0.06)	1.76 (0.05)	0.153	-0.12 [-0.29, 0.05]
Vastus intermedius	1.52 (0.42)	1.58 (0.47)	1.63 (0.09)	1.51 (0.07)	0.312	-0.12 [-0.36, 0.12]
Vastus lateralis	1.65 (0.26)	1.72 (0.36)	1.74 (0.06)	1.66 (0.05)	0.324	-0.08 [-0.25, 0.08]
Vastus medialis	1.95 (0.36)	1.67 (0.42)	2.05 (0.08)	1.61 (0.06)	<0.001	-0.44 [-0.65, -0.23]
Echo intensity, a.u.						
Rectus femoris	92.5 (10.3)	92.7 (13.3)	91.6 (2.5)	93.3 (1.9)	0.611	1.69 [-4.93, 8.32]
Vastus intermedius	56.5 (13.6)	60.0 (14.5)	52.9 (2.8)	62.4 (2.2)	0.014	9.48 [2.01, 16.95]

Vastus lateralis	83.7 (9.7)	89.2 (15.0)	85.2 (2.6)	88.2 (2.0)	0.387	3.02 [-3.91, 9.94]
Vastus medialis	70.1 (8.9)	91.4 (14.3)	69.5 (2.6)	91.8 (2.1)	<0.001	22.24 [15.19, 29.29]
ECW/ICW ratio, a.u.	0.41 (0.10)	0.47 (0.10)	0.39 (0.02)	0.49 (0.01)	<0.001	0.10 [0.05, 0.15]

Univariate ANOVAs with adjustment for age and BMI were conducted to investigate the muscle property differences between groups. The adjusted mean differences were calculated and presented as the knee OA group values against the healthy control group.

Abbreviations: OA, osteoarthritis; SD, standard deviation; SE, standard error; CI, confidence interval; ECW/ICW; extracellular-to-intracellular water; a.u., arbitrary unit.

Table 3. Logistic regression and ROC analyses for clarifying muscle degeneration characteristics in knee OA patients

	Logistic regression analysis		ROC analyses				
	OR [95% CI]	p-value	AUC	p-value	Cut-off value	Sensitivity	Specificity
Muscle thickness in vastus medialis	0.47 [0.04, 5.56]	0.547	-				
Echo intensity in vastus medialis	1.19 [1.06, 1.35]	0.004	0.90	<0.001	80.4	0.81	0.89
ECW/ICW ratio	1.19 [1.00, 1.42]	0.047	0.69	0.008	0.45	0.56	0.74

Logistic regression analyses were conducted with the group (reference, healthy control group = 0; knee OA group = 1) as the dependent variable and the MT, VM EI, and the ECW/ICW ratio as independent variables (after adjusting for age and BMI). The ROC analyses were performed to obtain the AUC, cut-off value, sensitivity, and specificity for characterising muscle degeneration in knee OA.

Abbreviations: OR, odds ratio; CI, confidence interval; ROC, receiver-operating characteristic; AUC, area under the curve; ECW/ICW; extracellular-to-intracellular water.

Figure Caption

Fig. 1 The setting for the measurement of segmental-bioelectrical impedance spectroscopy in the thigh

To evaluate the bioelectrical impedance of the thigh, two sensing electrodes were placed on the anterior superior iliac spine and the lateral knee articular condyles, and injection electrodes were placed on the dorsal surfaces of the hand and forefoot.

Fig. 2 Representative ultrasound images of the vastus medialis (VM) in (a) healthy control and (b) knee OA patient

Legend: The arrows represent the thickness of the VM. The entire VM in patients with knee osteoarthritis is white, implying that the mean echo intensity increases.

Fig. 3 Receiver operating characteristic (ROC) curve analyses of echo intensity in the vastus medialis and extracellular water-to-intracellular water (ECW/ICW) ratio for clarifying muscle degeneration characteristics in patients with knee osteoarthritis.

Legend: The bullet in ROC curve represents a cut-off point.

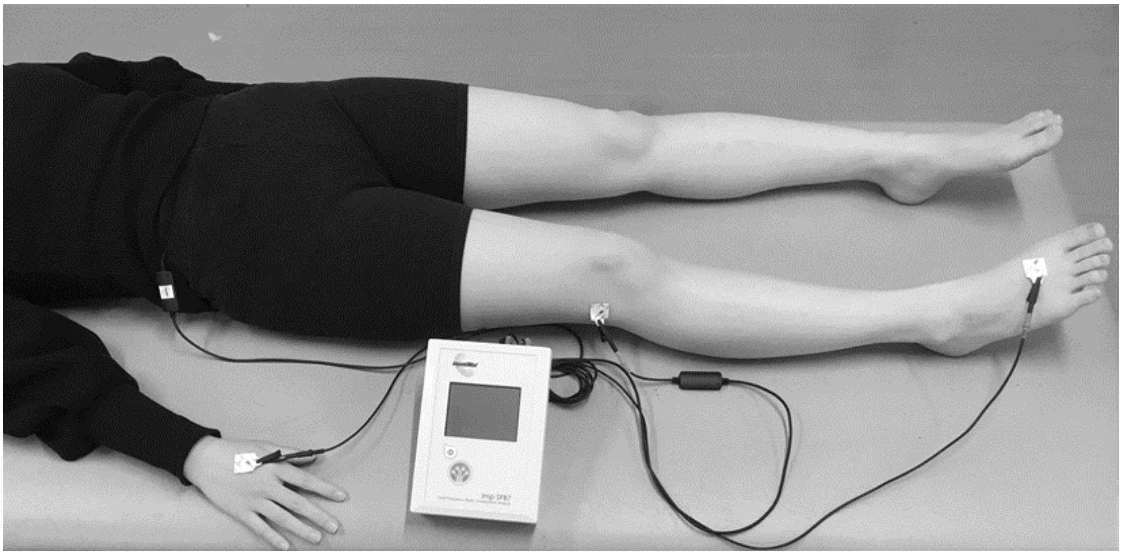

Fig. 1

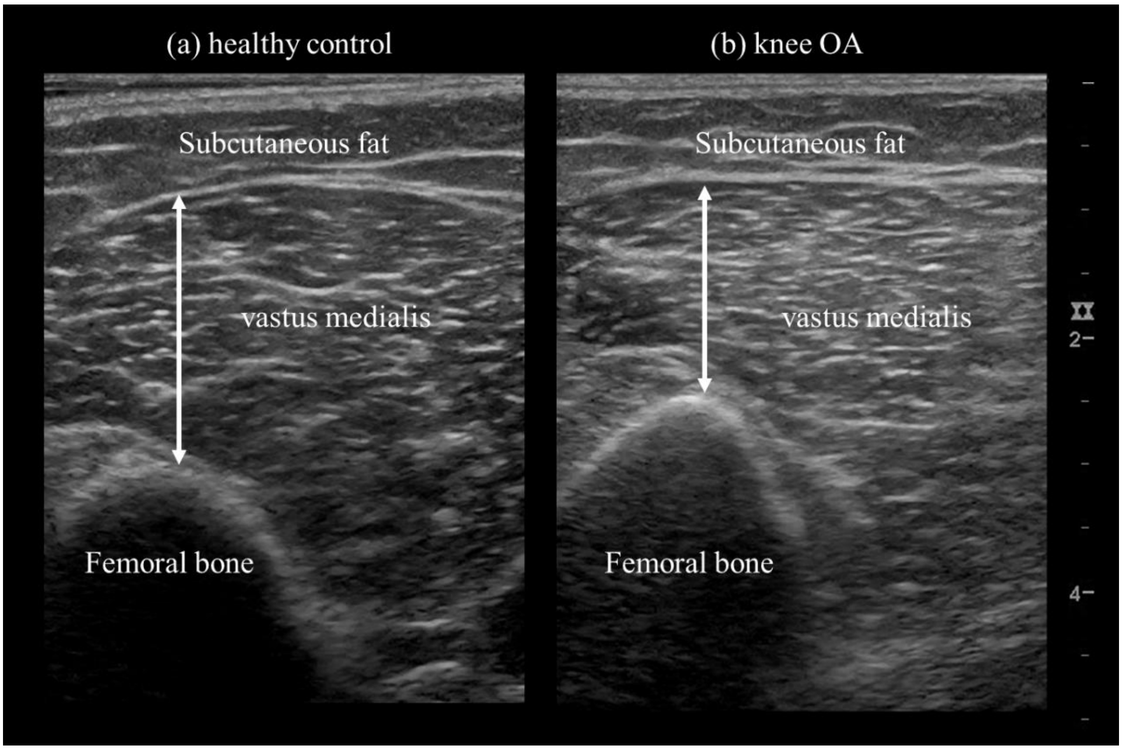
(a) healthy control
(b) knee OA
Subcutaneous fat
vastus medialis
Femoral bone
Subcutaneous fat
vastus medialis
Femoral bone
2
4

Fig. 2

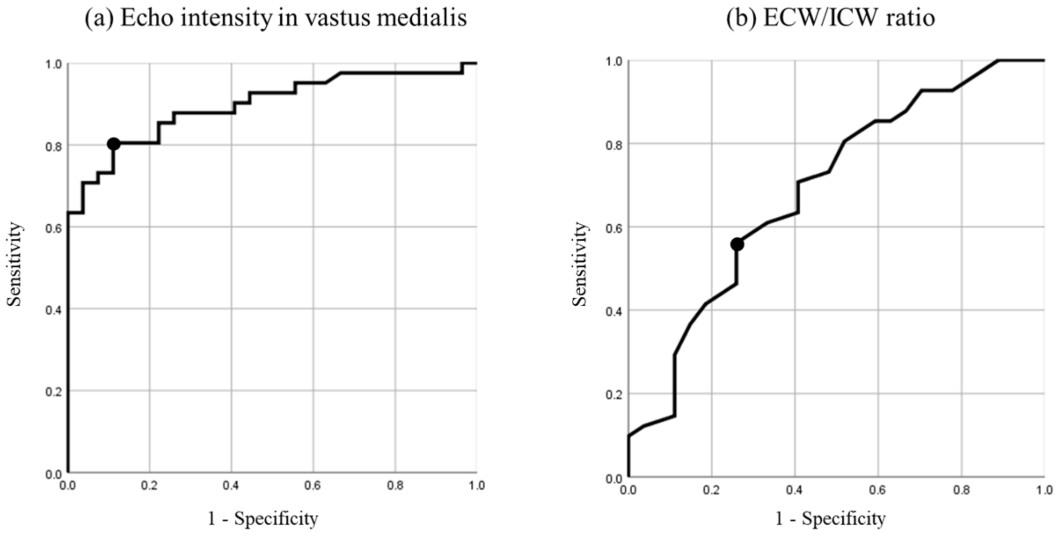
(a) Echo intensity in vastus medialis
Sensitivity
1 - Specificity
0.0
0.2
0.4
0.6
0.8
1.0
(b) ECW/ICW ratio
Sensitivity
1 - Specificity
0.0
0.2
0.4
0.6
0.8
1.0

Fig. 3