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Estimation of muscle atrophy based on muscle thickness in knee surgery patients

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Summary

The purpose of this study was to establish an accurate estimation of muscle atrophy in the quadriceps femoris (QF) muscle group. Eighteen individuals who underwent meniscectomy participated in the study (nine men and nine women, mean age 44·4 years). Both operated and non-operated thighs were scanned by magnetic resonance imaging to determine the volume and thickness of the QF muscle group. Muscle volume was estimated using eleven axial images, and muscle thickness was measured at the anterior, lateral and medial regions of the proximal, mid- and distal thigh, respectively. A stepwise linear regression analysis was performed to obtain the relationship between the difference in muscle volume and the difference in muscle thickness between operated and non-operated limbs. There was no significant difference in muscle volume of the QF between operated ($806{\cdot}6 \pm 220{\cdot}0$ cm^3) and non-operated ($913{\cdot}7 \pm 241{\cdot}5$ cm^3) limbs. Based on the stepwise linear regression analysis, the difference in muscle volume was significantly correlated with the difference in muscle thickness at the anterior proximal thigh and lateral mid-thigh and anterior mid-thigh ($R = 0{\cdot}93$, $P<0{\cdot}01$). In conclusion, the difference in muscle volume between operated and non-operated limbs can be estimated accurately by measuring muscle thickness of the QF at three sites: the anterior proximal thigh, the lateral mid-thigh and anterior mid-thigh. Muscle thickness can be measured easily using imaging techniques such as ultrasonography. We propose that this method provides an easy and accurate estimate of knee surgery-induced muscle atrophy in clinical medicine.

Introduction

It is well known that atrophy is induced in the quadriceps femoris (QF) muscle group after knee surgery, including meniscectomy and anterior cruciate ligament (ACL) reconstruction (Eriksson & Haggmark, 1979; Eriksson, 1981; Arangio et al., 1997; Brindle et al., 2001; Akima & Furukawa, 2005; Ericsson et al., 2006). Assessing muscle size of the thighs or calves of patients with knee injury and surgery-related disuse is of concern for orthopaedic surgeons, physical therapists and sports trainers. Such an assessment is helpful in considering a patient's recovery from knee surgery.

To our knowledge, leg circumference using a tape measure is the most widely used technique for the estimation of changes in muscle size for patients who have undergone knee surgery (Young et al., 1980; Arangio et al., 1997). Although this method is simple to apply, previous studies have shown that circumference measurements do not accurately estimate the change in muscle size (Young et al., 1980; Narici et al., 1989; Arangio et al., 1997; Mathur et al., 2008). Large differences were found in the relative change in muscle size between cross-sectional area (CSA; 8·6%) and circumference (1·8%) in patients with ACL reconstruction (Arangio et al., 1997). Thus, methods for estimating disuse-induced muscle atrophy could be improved. Non-invasive imaging techniques, that is, magnetic resonance (MR) imaging and ultrasonography, could be used to more accurately quantify muscle size. Ultrasound devices are considered small and economical compared with other imaging techniques, and ultrasonography can be used in clinical and sports-related circumstances (Ishida et al., 1995; Abe et al., 1997; Pillen et al., 2008). In addition, ultrasonography has proven to be a highly reliable technique for measuring muscle thickness (Sanada et al., 2006). However, studies have reported that compression to the tissue by transducer could affect muscle and/or subcutaneous fat thickness measurements because of tissue distortion (Heckmatt et al., 1988; Reeves et al., 2004), which may lead to poor estimates of the true muscle thickness. While it is well known that muscle volume, rather than CSA or muscle thickness, is the most accurate measure for estimating muscle size (Roman et al., 1993; Miyatani et al., 2002, 2004; Akima & Furukawa, 2005), there are currently no quantitative data to suggest that muscle thickness, as measured by ultrasound, reflects muscle volume. Hence, we endeavour to explore methods to accurately estimate changes in muscle volume.

Previous studies have investigated the use of ultrasonography to measure muscle thickness of the QF at the anterior mid-thigh as an indicator of muscle size (Sipila & Suominen, 1991, 1993; Abe et al., 1997). However, there is no consensus that the anterior mid-thigh is the best representative region for measuring muscle thickness of the QF. Akima et al. (1997) demonstrated that the change in the individual muscles of the QF is different along the longitudinal axis of the thigh after 20 days of bed rest. Narici et al. (1989) also reported that the degree of hypertrophy in each of the four QF muscles by strength training was not the same along the length of the thigh. These reports suggest that a single measurement for determining muscle size may lead to inaccurate estimates where changes in muscle size occur. It is yet to be determined how many sites should be measured to assess global muscle atrophy along the length of the thigh. Therefore, the purpose of this study was to establish an accurate estimation of QF muscle atrophy in patients who underwent knee surgery, using MR imaging to assess muscle thickness at several sites. We hypothesized that measuring muscle thickness at multiple sites would be a better estimate of muscle volume change than at a single site.

Methods

Subjects

Eighteen individuals (nine men, nine women; mean age ± standard deviation (SD) 44·4 ± 14·4 years) who underwent arthroscopic knee surgery participated in the study. The patient demographics and their history of injury are shown in Table 1. All subjects participated after giving written informed consent. The study was approved by the Ethics Committee of the Research Center of Health, Physical Fitness & Sports, Nagoya University, in accordance with the guidelines in the Declaration of Helsinki.

Table 1 Patient demographics.

	Mean ± SD	Range
Age (years)	44·4 ± 14·4	23–70
Height (cm)	163·1 ± 8·1	148–175
Weight (kg)	63·2 ± 11·4	50–97
Duration from injury to surgery (months)	7·8 ± 22·8	1–99
Duration from surgery to measurement (months)	4·5 ± 3·2	0–9

SD, standard deviation.

Magnetic resonance imaging

To determine muscle volume and muscle thickness, the operated and non-operated thighs of each patient were scanned by MR imaging, according to the methods of our previous study (Akima & Furukawa, 2005). MR imaging was performed with a 0·2 T Signa Profile OpenSpirit (GE Healthcare, Waukesha, WI, USA). T2-weighted spin echo, axial-plane imaging was performed with the following variables, TR = 1600 ms, TE = 30 ms, matrix = 256 × 128, field of view = 320 mm, number of excitations = 1, slice thickness = 10 mm, interslice gap = 10 mm. The participants were imaged in a prone position with the knee and ankle joints held at 180° and ~120°, respectively, with 180° being the full extension of each joint. The number of axial images obtained for an individual was 11. Figure 1 shows representative MR images of the mid-thigh of the operated (Fig. 1a) and the non-operated (Fig. 1b) limbs of a 41-year-old female patient. All images were analysed by one investigator (MH).

Muscle volume

The muscle volume of the QF, including rectus femoris (RF), vastus lateralis (VL), vastus intermedius (VI) and vastus medialis (VM), was estimated using 11 axial images. Outlines of each muscle were traced on the series of axial images. The traced images were transferred to a personal computer (Let's note, Panasonic, Osaka, Japan) to estimate the anatomical cross-sectional areas (ACSAs) using the public domain NIH Image software package (National Institute of Health, Bethesda, MD, USA). The muscle volume was determined by multiplying the sum of the ACSA of each image by the sum of the thickness (10 mm) and the interslice gap (10 mm) of each section. The coefficients of variation for the muscle volume measurements of the operated and non-operated limbs were 27·3% and 26·4%, respectively.

Muscle thickness

The muscle thickness of the QF was measured at seven sites, at the anterior and lateral proximal thigh (70% of the length of the thigh; 70% Lt); at the anterior, lateral and medial mid-thigh (50% Lt); and at the lateral and medial distal thigh (30% Lt). The length of the thigh was defined by the distance between the greater trochanter and lateral femoral condyle. The medial proximal thigh and the anterior distal thigh were not measured, because we could not find any muscle at these sites in the MR images. Muscle thickness measurements at the anterior proximal thigh and the anterior mid-thigh included the RF and VI muscles; at the lateral proximal thigh, the lateral mid-thigh and the lateral distal thigh, the VL and VI muscles; and at the medial mid-thigh and the medial distal thigh, the VI and/or VM muscle. Figure 2 shows representative MR images of the proximal (a), middle (b) and distal (c) regions of the thigh. The procedure used to measure muscle thickness

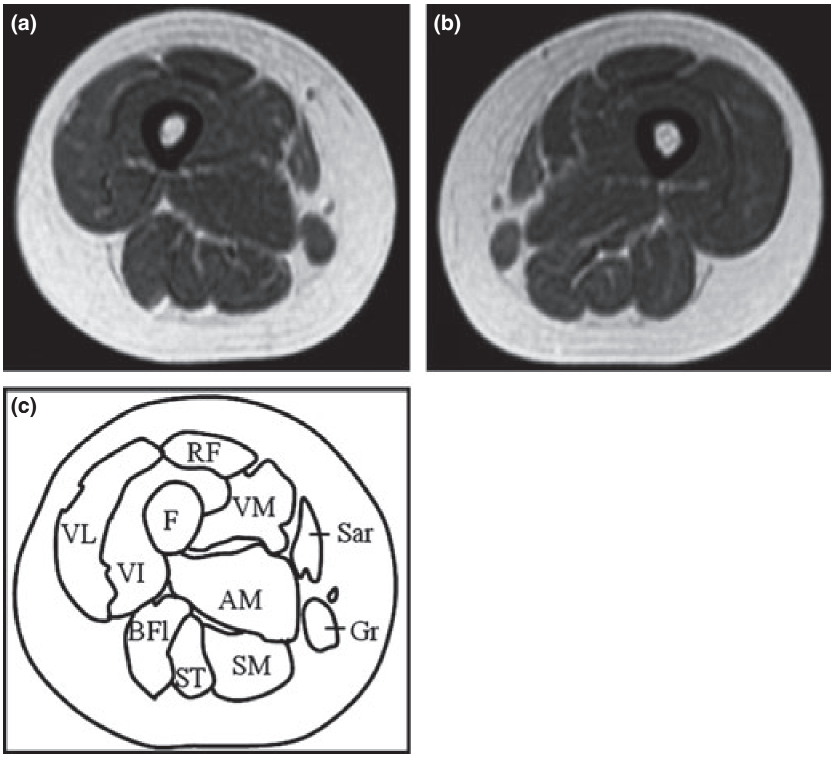

Figure 1 Representative axial magnetic resonance images of the (a) operated and (b) non-operated limbs at the middle region (50% of the length of the thigh) for a female patient and (c) thigh muscle anatomy. RF, rectus femoris; VL, vastus lateralis; VI, vastus intermedius; VM, vastus medialis; BFl, biceps femoris long head; ST, semitendinosus; SM, semimembranosus; Gr, gracilis; Sar, Sartorius; AM, adductor magnus; F, femur.

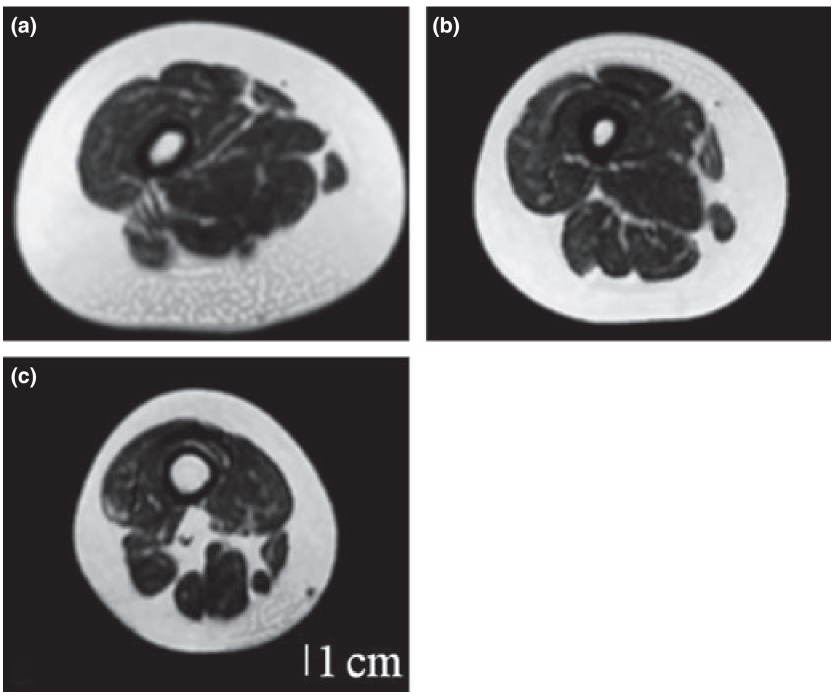

Figure 2 Representative axial images of the thigh on magnetic resonance imaging: (a) proximal region (70% of the length of the thigh; 70% Lt), (b) middle region (50% Lt) and (c) distal region (30% Lt).

is shown in the representative image in Fig. 3. For example (see Fig. 3a), muscle thickness measurements at the anterior mid-thigh were made as follows: (i) the centroid of the femur was marked on the image, (ii) two broken lines were drawn from the centroid of the femur to both edges of the RF, (iii) the angle formed by the two straight lines in step 2 was bisected by a solid line, and (iv) the distance from the superficial plain of the RF to the femur along the solid line was considered as the muscle thickness of the anterior mid-thigh. Based on this concept, muscle thickness of the QF at the lateral (Fig. 3b) and medial (Fig. 3c) regions were also measured.

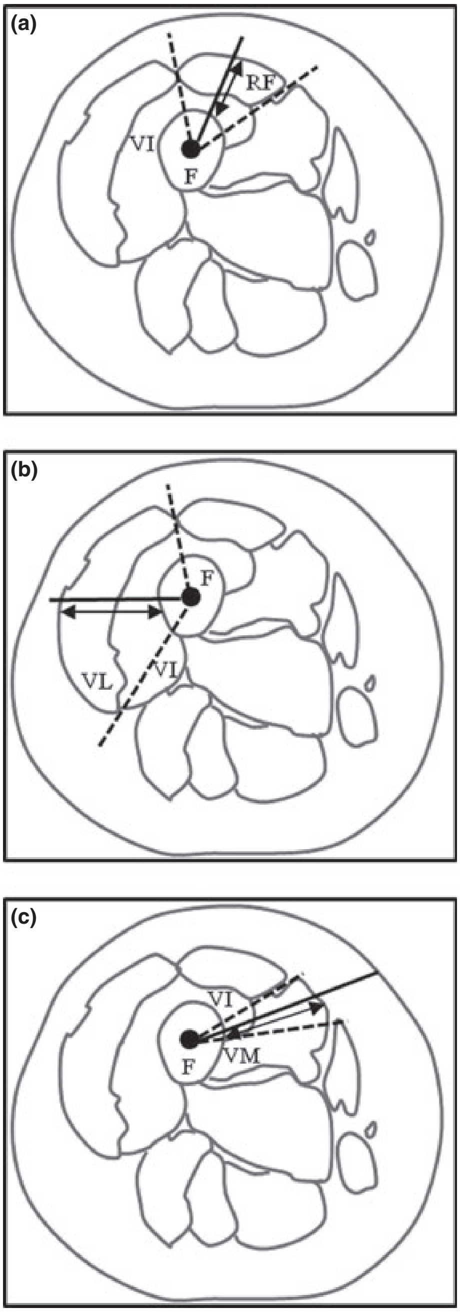

Figure 3 Representative axial magnetic resonance image for a female patient to demonstrate the methods for measuring muscle thickness at the anterior (a), lateral (b) and medial (c) mid-thigh. Image landmarks corresponding to the femur (F) and the edges of the muscle were digitized using appropriate software (see Methods). Muscle thickness was calculated as the distances between the arrows. RF, rectus femoris; VL, vastus lateralis; VI, vastus intermedius; VM, vastus medialis; F, femur.

Statistics

The difference in muscle volume of the QF between operated and non-operated limbs was determined using the Mann–Whitney test. Spearman's rank correlation coefficients were used to determine the relationship for the difference in muscle volume of the QF between operated and non-operated limbs and the difference in muscle thickness of the QF between operated and non-operated limbs at each of the seven sites. The correlation between the difference in muscle volume of the QF and the difference in muscle thickness of the QF between operated and non-operated limbs at each of the seven sites was determined by stepwise linear regression analysis (forward step) for the dependent variable (the difference in muscle volume of the QF between operated and non-operated limbs). Seven independent variables (the difference in muscle thickness of the QF at each of the seven sites) were entered into the stepwise linear regression if they represented a significant contribution to the explained variance (F to enter $\geq$ 2·00, F to remove $\leq$ 1·99) corresponding to an alpha level $P<0{\cdot}05$. All analyses were performed using the SPSS statistical package (Version 13; SPSS Inc., Chicago, IL, USA). The level of significance was set at $P<0{\cdot}05$.

Results

There was no significant difference in muscle volume of the QF between operated ($806{\cdot}6 \pm 220{\cdot}0$ cm^3) and non-operated ($913{\cdot}7 \pm 241{\cdot}5$ cm^3) limbs. Figures 4–6 show the relationship between the difference in muscle volume of the QF between operated and non-operated limbs and the difference in muscle thickness of the QF between operated and non-operated limbs at each of the seven sites. We found a significant correlation for the difference in muscle volume of the QF between the operated and non-operated limbs and the difference in muscle thickness of the QF at the anterior proximal thigh ($r = 0{\cdot}73$, $P<0{\cdot}01$), the anterior mid-thigh ($r = 0{\cdot}71$, $P<0{\cdot}01$) and the lateral distal thigh ($r = 0{\cdot}62$, $P<0{\cdot}01$) between the operated and non-operated limbs. However, there was no significant correlation at the lateral proximal thigh ($r = -0{\cdot}20$, $P = 0{\cdot}42$), the lateral mid-thigh ($r = 0{\cdot}34$, $P = 0{\cdot}17$), the medial mid-thigh ($r = -0{\cdot}12$, $P = 0{\cdot}63$) or the medial distal thigh ($r = 0{\cdot}45$, $P = 0{\cdot}06$).

Table 2 shows a summary of the stepwise linear regression analysis. The difference in muscle volume of the QF between operated and non-operated limbs was significantly correlated with the difference in muscle thickness of the QF between operated and non-operated limbs at the anterior proximal thigh, lateral mid-thigh and anterior mid-thigh ($R = 0{\cdot}93$, $P<0{\cdot}01$, $R^2 = 0{\cdot}86$). Seven independent variables (the difference in muscle thickness of the QF between operated and non-operated limbs) were used in this multiple stepwise linear regression analysis to select for variables that could explain the difference in muscle volume of the QF between operated and non-operated limbs. Table 3 shows the multiple regression equations of steps 1–3. The final multiple regression equation was calculated as follows:

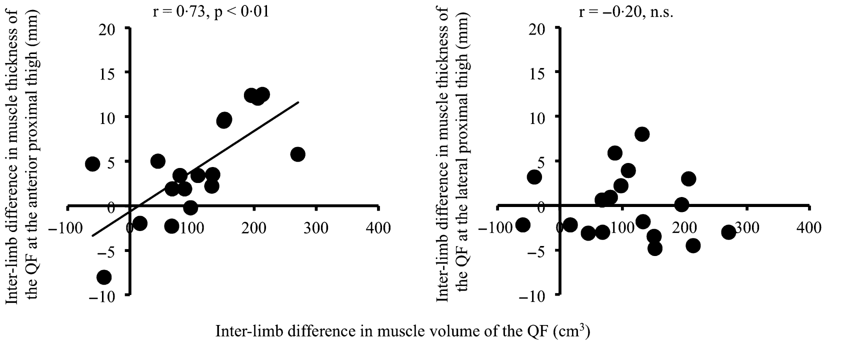

Figure 4 Relationship between the difference in muscle volume of the quadriceps femoris (QF) between operated and non-operated limbs and the difference in muscle thickness of the QF between operated and non-operated limbs at the anterior, lateral proximal thigh (70% of length of the thigh).

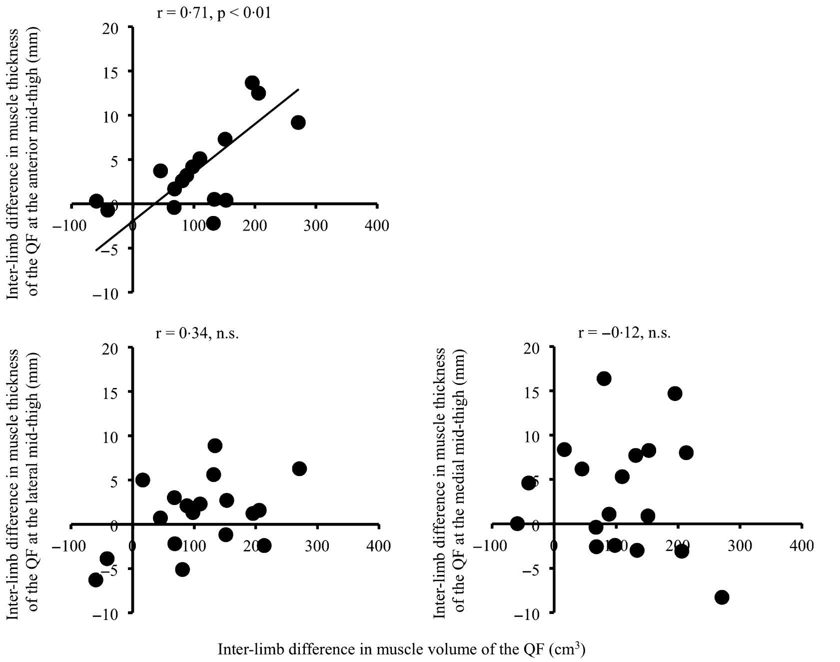

Figure 5 Relationship between the difference in muscle volume of the quadriceps femoris (QF) between operated and non-operated limbs and the difference in muscle thickness of the QF between operated and non-operated limbs at the anterior, lateral, medial mid-thigh (50% of length of the thigh).

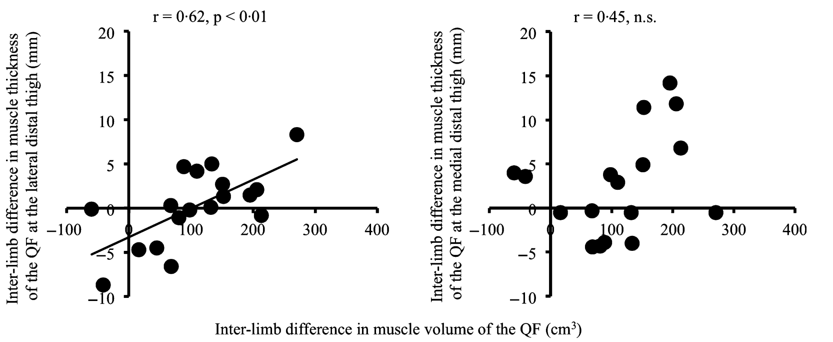

Figure 6 Relationship between the difference in muscle volume of the quadriceps femoris (QF) between operated and non-operated limbs and the difference in muscle thickness of the QF between operated and non-operated limbs at the lateral, medial distal thigh (30% of length of the thigh).

$$\begin{aligned}&\text{Inter-limb difference in muscle volume}\\&= 47.1 + 4.2(\text{Inter-limb difference in muscle thickness at the anterior proximal thigh}) + 12.1(\text{Inter-limb difference in muscle thickness at the lateral mid-thigh})\\&\quad + 7.5(\text{Inter-limb difference in muscle thickness at the anterior mid-thigh})\end{aligned} \tag{1}$$

Discussion

The aim of this study was to determine the appropriate combination of muscle thickness sites for improved estimation of QF muscle group atrophy in patients after meniscectomy. To accomplish this objective, we investigated the relationship between the difference in muscle volume and the difference in muscle thickness at seven sites of the QF between operated and non-operated limbs using a stepwise linear regression analysis.

Table 2 Stepwise linear regression analysis.

Dependent variable	Independent variables	Standardized regression coefficient	SE	Regression coefficient	*P*	*R*	R^2
Difference volume	Step 1						
	Anterior proximal thigh	0·704	2·760	10·941	0·001	0·704	0·495
	Step 2						
	Anterior proximal thigh	0·710	2·180	11·033	0·005	0·840	0·705
	Lateral mid-thigh	0·458	2·992	9·768			
	Step 3						
	Anterior proximal thigh	0·268	2·403	4·164	0·002	0·925	0·855
	Lateral mid-thigh	0·566	2·256	12·080			
	Anterior mid-thigh	0·598	1·975	7·503			

Difference volume: The difference in muscle volume of the quadriceps femoris (QF) muscle group between operated and non-operated limbs. Anterior proximal thigh: The difference in muscle thickness of the QF between operated and non-operated limbs at the anterior proximal thigh. Lateral mid-thigh: The difference in muscle thickness of the QF between operated and non-operated limbs at the lateral mid-thigh. Anterior mid-thigh: The difference in muscle thickness of the QF between operated and non-operated limbs at the anterior mid-thigh. SE, standard error; R^2, adjusted *R* value.

Table 3 Multiple regression equation by stepwise linear regression analysis.

Step 1	Difference volume = 61·2 + 10·9 (Anterior proximal thigh)
Step 2	Difference volume = 50·2 + 11·0 (Anterior proximal thigh) + 9·8 (Lateral mid-thigh)
Step 3	Difference volume = 47·1 + 4·2 (Anterior proximal thigh) + 12·1 (Lateral mid-thigh) + 7·5 (Anterior mid-thigh)

Difference volume: The difference in muscle volume of the quadriceps femoris (QF) muscle group between operated and non-operated limbs. Anterior proximal thigh: The difference in muscle thickness of the QF between operated and non-operated limbs at the anterior proximal thigh. Lateral mid-thigh: The difference in muscle thickness of the QF between operated and non-operated limbs at the lateral mid-thigh. Anterior mid-thigh: The difference in muscle thickness of the QF between operated and non-operated limbs at the anterior mid-thigh.

The difference in muscle thickness at the anterior proximal thigh, the lateral mid-thigh and anterior mid-thigh were selected as the variables to explain the inter-limb difference in muscle volume of the QF ($R^2 = 0{\cdot}86$, $P<0{\cdot}01$). This result statistically represents approximately 90% of inter-limb variance of muscle volume of the QF, as measured by the selected three muscle thickness sites. Interestingly, our findings are in agreement with our earlier studies showing that muscle atrophy occurs at the most bulky part of the muscle, which is adequately represented by the selected three muscle thickness sites (Akima *et al.*, 1997, 2000a,b; Akima *et al.*, 2001).

Several studies have reported the change in muscle size of the QF (e.g. atrophy or hypertrophy) based on changes in muscle thickness using ultrasonography (Sipila & Suominen, 1991, 1993; Abe *et al.*, 1997, 2000; Reid *et al.*, 2004). Muscle thickness at the anterior mid-thigh has been frequently used to estimate muscle size. Abe *et al.* (1997) reported that a significant correlation was observed between muscle thickness of the QF at the anterior mid-thigh by ultrasonography and CSA at the middle region by MR imaging. However, it is unclear whether the anterior mid-thigh is the best representative site for change in muscle volume of the QF. Previous studies suggested that a single region of CSA for determining muscle size would lead to a poor estimate of changes in muscle size (e.g. atrophy or hypertrophy; Narici *et al.*, 1989; Akima *et al.*, 1997); the percentage change in muscle size in individual muscles of the QF as a result of disuse or strength training differs along the length of the thigh. Akima *et al.* (1997) reported that the region showing greatest muscle loss after 20 days of bed rest was near the muscle belly (between 70% Lt and 30% Lt), rather than at the end of the muscle near its origin or insertion.

According to our result of simple correlation analysis, we found a significant correlation coefficients between the difference in muscle volume of the QF and difference in muscle thickness of the QF at the anterior proximal thigh, anterior mid-thigh and lateral distal thigh (r = 0·62–0·73; Figs 4–6). Furthermore, using a stepwise linear regression analysis, anterior proximal thigh, lateral mid-thigh and anterior mid-thigh were selected as independent variables to predict inter-limb differences in muscle volume ($R^2 = 0{\cdot}86$); this indicates that 86% of the variance in the muscle volume between operated and non-operated limb could be explained by differences in muscle thickness at these three selected sites. From a clinical standpoint, this information would be helpful in estimating accurately knee injury-related muscle atrophy using only three sites of muscle thickness. Interestingly, all four individual QF muscles are included within the selected three sites. Thus, overall, our study demonstrates a reasonable method with which to estimate atrophy-induced volumetric changes across the whole muscle. According to Trappe *et al.* (2001), aging-induced atrophy among the four individual QF muscles was similar. This suggests that measurements of muscle thickness at the three selected sites (the anterior proximal thigh, lateral mid-thigh and anterior mid-thigh) would reflect the atrophy-induced changes in muscle volume. In a study by Akima *et al.* (1997), the muscle belly of the VM was observed in the distal region of the thigh (approximately 30% Lt). The distal thigh was not selected as an independent variable in the stepwise linear regression analysis.

Using MR imaging, we calculated thigh muscle volume using eleven consecutive images. This number of images is fewer than that described by others in previous studies (Aagaard et al., 2001; Ogawa et al., 2012). As such, our results show lower absolute values for muscle volume than that described previously. Our imaging method was chosen to examine the region of the thigh with the maximum ACSA; this was determined with reference to earlier work that showed a significantly high correlation coefficient between torque and maximum ACSA (r = 0·705; Fukunaga et al., 2001). The maximum ACSAs of the RF, VL and VI were determined to be around the mid-thigh and that of VM slightly more distally (approximately 30% Lt; Akima et al., 1997). Thus, in this analysis, we adjusted the scanning so that the third scan would be positioned through the mid-thigh in the series, with two images obtained proximally and eight images distally from this point. From this arrangement, the maximal ACSAs of RF, VL, VI and VM would be covered within the eleven axial images; this is in line with previous reports (Akima et al., 2001, 2005; Akima & Furukawa, 2005). Thus, we speculate that these images provide a sufficient estimation of the 'true' muscle volume.

Anthropometrical measurements, such as tape measurements of thigh circumference, have been used in clinical medicine and in the sports medicine field to estimate changes in muscle size following physical injury-induced atrophy or training-induced hypertrophy. Because this method is simple, uncomplicated and economical, it is considered suitable for use in these applications. However, previous studies have reported that this method does not accurately represent changes in muscle size (Young et al., 1980; Narici et al., 1989; Arangio et al., 1997; Gruther et al., 2008; Mathur et al., 2008). Young et al. (1983) indicated an underestimation in the measurement of QF hypertrophy with the measurement of thigh circumference. Mathur et al. (2008) reported no significant correlation between muscle volume and thigh circumference in either healthy elderly individuals or patients with chronic obstructive pulmonary disease. These studies suggest that changes in muscle size cannot be inferred from thigh circumference measurements alone.

In this preliminary study, we should consider other non-invasive and clinically suitable techniques such as ultrasonography, which could be performed in lieu of MR imaging. Ultrasonography has been widely employed to achieve accurate estimations of muscle size. A previous study reports very close agreement between the measurements taken by ultrasound and by MR imaging, based on a regression analysis (r = 0·99; Reeves et al., 2004). Thus, it is likely that ultrasonography could also be used to measure muscle thickness at the anterior proximal thigh, lateral mid-thigh and anterior mid-thigh and potentially proved an accurate estimation of inter-limb differences in muscle volume. However, there are pitfalls with the use of ultrasonography, such as inter- and intra-observer variations in measurements of muscle thickness. Indeed, tissue compression and tilt angle transducer handling differences may affect measurements in ultrasonography (Pillen et al., 2008). Moreover, the thickness measurement depends on the skill and experience of the observer, suggesting that intra- and inter-observer variations could lead to significant errors in these sometimes subtle measurements. Therefore, it is important that standardized protocol for measuring muscle thickness is established in the future.

In conclusion, we found moderate to high correlations for inter-limb difference between muscle thickness and muscle volume in patients with a history of knee surgery. The variance in the inter-limb difference in muscle volume of the QF was explained by the variance in inter-limb muscle thickness at one to three different sites, from 50% to 86% based on the stepwise linear regression analysis. Thus, we suggest that inter-limb difference in muscle volume can be estimated by measuring muscle thickness at three key sites: at the anterior proximal thigh, lateral mid-thigh and anterior mid-thigh. This method would be useful for providing an accurate estimation of muscle atrophy induced by knee injury, after knee surgery and/or following bed rest. Future studies, however, need to compare the efficacy of ultrasonography with MR imaging when evaluating muscle atrophy.

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