



# Implications of evaluating leg muscle mass and fat mass separately for quadriceps strength in knee osteoarthritis: the SPSS-OK study

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Received: 24 September 2019 / Revised: 16 November 2019 / Accepted: 4 December 2019 / Published online: 30 December 2019  
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## Abstract

**Objective** To examine the influence of obesity on quadriceps strength by separately analyzing body mass index (BMI) as fat mass and leg muscle mass in patients with knee osteoarthritis (KOA).

**Methods** The Screening for People Suffering Sarcopenia in Orthopedic cohort of Kobe (SPSS-OK) study was a single-center cross-sectional study that recruited 906 patients with KOA. Fat mass and leg muscle mass were measured by bio-impedance. Isometric knee extension torque (Nm) was measured as quadriceps strength. A series of general linear models were fitted to estimate the continuous associations of BMI and fat mass with quadriceps strength, with adjustment of confounders. In the fitted models, both BMI and fat mass were treated as restricted cubic spline functions.

**Results** A continuous, non-linear relationship between BMI and quadriceps strength was found ( $P = 0.008$  for non-linearity). In patients with a BMI of 16–25 kg/m<sup>2</sup>, increasing quadriceps strength was observed. However, in patients with a BMI of 25–40 kg/m<sup>2</sup>, quadriceps strength seemed similar. Additionally, an inverted U-shaped relationship between fat mass and quadriceps strength was demonstrated ( $P = 0.04$  for non-linearity). In those with a fat mass of 10–20 kg, increasing quadriceps strength was seen. However, in patients with a fat mass of 20–30 kg, quadriceps strength showed a decreasing trend. Independent of fat mass, leg muscle mass was linearly associated with greater quadriceps strength.

**Conclusion** Our study suggests that there are independent associations between the leg muscle mass, fat mass, and quadriceps strength. It is difficult to easily predict quadriceps strength using only BMI.

## Key Points

- An increase in body mass index (BMI) up to 25 kg/m<sup>2</sup> was associated with increasing quadriceps strength.
- Quadriceps strength remained almost unchanged among patients with a BMI of > 25 kg/m<sup>2</sup>.
- The association between fat mass and quadriceps strength had an inverted U-shaped relationship, suggesting the importance of the separate assessment of fat mass and muscle mass in patients with knee osteoarthritis, especially those who are overweight or obese.

**Electronic supplementary material** The online version of this article (<https://doi.org/10.1007/s10067-019-04879-6>) contains supplementary material, which is available to authorized users.

**Keywords** Body mass index · Fat mass · Knee osteoarthritis · Obesity · Quadriceps strength

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## Introduction

Osteoarthritis (OA) of the knee is one of the most common age-related diseases of the musculoskeletal system, and it is a major cause of pain and disability in the elderly. Quadriceps strength is crucial for averting disability by exerting functional movement and is a potential target for rehabilitation in patients with knee OA [1, 2]. Separately, obesity is associated with worse knee function in patients with knee OA owing to the increased mechanical stress [3] and the inflammatory mediators derived from adipose tissues [4]. Indeed, intentional weight loss is reported to be effective for improving knee function in overweight and obese patients with knee OA [5,

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6]. However, “to what extent” reduction in obesity is associated with an increase in quadriceps strength in patients with knee OA remains unclear.

With regard to the association of body mass index (BMI) and quadriceps strength among healthy elderly individuals, those with extreme obesity (BMI > 35 kg/m<sup>2</sup>) have less quadriceps strength than those with normal weight [7]. However, overweight (BMI 25 to < 30 kg/m<sup>2</sup>) and obese elderly (BMI 30 to < 35 kg/m<sup>2</sup>) individuals exhibited greater quadriceps strength than normal weight individuals. This inverted U-shaped relationship between BMI and quadriceps strength has not been tested in patients with OA and may be attributable to the complexity of BMI as a measure of obesity [8]. Indeed, BMI is affected not only by body fat mass but also by lean body mass. Thus, an estimate of obesity expressed as BMI is erroneously considered as “decreased” if the amount of lean body mass is decreased without a decrease in true fat mass [9, 10]. Given that muscle mass is positively correlated with muscle strength, it is uncertain whether a reduction in BMI is positively associated with quadriceps strength (due to a reduction in fat mass) or negatively (due to a reduction in muscle mass). Thus, decomposing BMI into fat mass and muscle mass and elucidating each association with quadriceps strength among patients with knee OA is more important and informative than examining the association between BMI and quadriceps strength.

In this study, we aimed to examine the association between BMI and fat mass and quadriceps strength in patients with knee OA, using the “Screening for People Suffering Sarcopenia in Orthopedic cohort of Kobe study” (SPSS-OK).

## Methods

### Design, setting, and participants

This single-center cross-sectional study was conducted at an institution in central Kobe City. From August 2016 to April 2019, we recruited only patients with knee OA who were scheduled for their 1st knee replacement surgery to avoid the potential interference of an implanted artificial joint during bio-impedance analysis (BIA). The exclusion criteria included patients with stroke, Parkinson’s disease, severe cognitive impairment, severe psychiatric impairment, and severe cardiac, pulmonary, or musculoskeletal disorders. In addition, we excluded older adults with artificial implants, such as cardiac pacemakers and joints, which did not permit the measurement of bioelectrical impedance. The study was approved by the local institutional review board (No. 57, January 26, 2017) and by the Research Ethics Committee of Fukushima Medical University School of Medicine (No. 2850, September 28, 2016). All patients provided written informed consent prior to participation.

## Conceptual framework

A conceptual framework is shown in Online Resource 1. First, we focused on the relationship between BMI as the exposure variable and quadriceps strength as the outcome variable, with the severity of knee OA as a confounder (analysis #1). Next, we focused on the relationship between fat mass and leg muscle mass as the exposure variables and quadriceps strength as the outcome variable (analysis #2). In analysis #2, the severity of knee OA was treated as both a confounder and an effect modifier for the relationship between leg muscle mass and quadriceps strength based on the findings of our previous study [2].

### Body mass index, fat mass, and leg muscle mass

BMI was calculated based on the following equation: body weight/height<sup>2</sup> (kg/m<sup>2</sup>). Body weight was measured using a digital scale, and height was measured using a fixed stadiometer. Fat mass and leg muscle mass were measured using a biometrical impedance system (MC-780A; TANITA CO, Ltd., Tokyo, Japan) while the patient was in a stable condition. The monitor is a multifrequency device that measures bio-impedance at 3 frequencies between 5 and 250 kHz. The results were analyzed using a body composition analyzer that was incorporated into the device. Validation of the BIA method using the dual-energy X-ray absorptiometry (DXA) method (DPX-L, GE Healthcare) showed very high correlations with the two methods for both fat mass and appendicular skeletal muscle mass [2].

### Quadriceps strength

Isometric knee extension torque (Nm) was measured as quadriceps strength using a handheld dynamometer (HHD) ( $\mu$ Tas F1; Anima, Chofu, Japan). Patients were placed in a sitting position, with their hips flexed at 90° and the knees flexed at 75°. We positioned the HHD in the area that was slightly above the ankle joint and used a belt to fix the HHD. This method has been shown to be highly reliable [11]. Following submaximal efforts, patients performed two maximal trials for 3 s while receiving verbal encouragement to facilitate maximal volitional force production. The peak force (newton) from two maximal contractions was used to measure quadriceps strength.

### Measurement of covariates

Covariates measured in the study were sociodemographic characteristics including age, sex, presence of type 2 diabetes, and severity of knee OA. The presence of type 2 diabetes was defined as having glycosylated hemoglobin (HbA1c) values of  $\geq 6.5\%$  according to the National Glycohemoglobin

Standardization Program. Radiographs were evaluated by a single trained observer (O.W.) based on the Kellgren-Lawrence radiographic grading system [12]. Intra-rater reliability for radiographic severity was assessed by reassessment of 100 randomly selected radiographs 2 weeks later and found to be excellent ( $\kappa = 0.89$ ). Chronic kidney disease was defined as estimated glomerular filtration rate (eGFR) values  $\leq 60$  mL/min/1.73 m<sup>2</sup>, which were calculated based on the 3-variable Japanese equation using age, serum creatinine level, and sex as follows [13]:  $eGFR = 194 \times \text{serum creatinine}^{-1.094} \times \text{age}^{-0.287} \times 0.739$  (if female).

## Statistical analysis

All statistical analyses were conducted using Stata/SE version 15 (Stata Corp., College Station, TX). Complete case analyses were done because the proportion of patients with missing data was small. Baseline characteristics were described using appropriate summary statistics. In addition, we categorized the BMI values into five groups (< 20, 20 to < 25, 25 to < 30, 30 to < 35, and  $\geq 35$  kg/m<sup>2</sup>) and described summary measures of fat mass, leg muscle mass, and leg muscle mass/fat mass ratio by these 5 categories.

For both analyses #1 and #2, the unit of analysis was limbs, as the outcome variable (i.e., quadriceps strength) and some predictor variables (i.e., leg muscle mass and knee OA severity determined by X-ray) are limb specific [14]. For this reason, we fitted general linear models with cluster-robust variance to account for correlation of paired-outcome data among single individuals [15]. For analysis #1, we estimated mean differences in quadriceps strength by differences in BMI, with adjustment for age, sex, diabetes, and knee OA severity. In the model, to estimate the non-linear, continuous relationship between BMI and the quadriceps strength, BMI was represented as a restricted cubic spline function. Splines are a series of cubic polynomials fitted among the BMI segments and connected at knots that provide a smooth curve to assess the

relationship between continuous BMI variables and quadriceps strength [16]. Three knots were placed at 10th, 50th, and 90th percentiles of BMI. Non-linearity was assessed by the Wald test. From the multivariable adjusted model, predicted mean quadriceps strength by BMI was visually presented using Stata's *adjustrcspline* command with fixation of covariates at mean values.

Next, for analysis #2, we estimated mean differences in quadriceps strength by differences in fat mass and leg muscle mass, with adjustment for age, sex, diabetes, and knee OA severity. Similar to BMI, fat mass was expressed as restricted cubic spline function to investigate the continuous, non-linear relationship between fat mass and the quadriceps strength, with placement of three knots. In the model, leg muscle mass was included as a linear term while knee OA severity was included as a confounder and an effect modifier (i.e., product term of knee OA severity and leg muscle mass) of the relationship between leg muscle mass and the quadriceps strength, based on the findings of our previous study [2]. From the multivariable adjusted model, predicted mean quadriceps strength by fat mass and leg muscle mass were visually presented using Stata's *adjustrcspline* and *margins* commands. A *P* value < 0.05 was considered to indicate statistical significance.

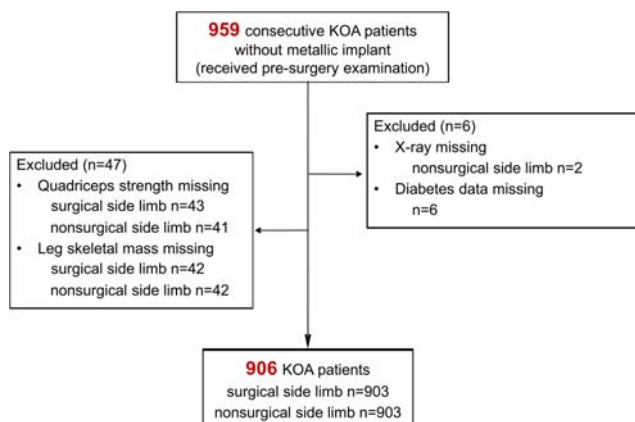
## Results

### Patient flow and descriptive statistics

Initially, 959 patients with knee OA who met the inclusion criteria were identified. Of these, 6 patients without knee OA severity categories or diabetes were excluded. After further exclusion of patients who lacked exposure and outcome variables for the analyses, 906 patients were included in our analyses (Fig. 1). Table 1 summarizes the baseline characteristics of the study population. The patients' mean age (standard deviation) was 73.0 (7.7) years, and over three-quarters (78%) of the patients were women. Online Resource 2 summarizes fat mass, leg muscle mass, and leg skeletal mass/fat mass ratio by BMI categories. As the BMI increased, fat mass and leg muscle mass increased, whereas the leg muscle mass/fat mass ratio decreased.

### BMI and quadriceps strength

In the covariate-adjusted restricted cubic spline model, the splines demonstrated a non-linear relationship between BMI and quadriceps strength ( $P = 0.008$  for non-linearity). The predicted quadriceps strength defined at the continuous BMI value is shown in Fig. 2. From a BMI of 16–25 kg/m<sup>2</sup>, increasing quadriceps strength was seen (for example, at a BMI of 16, 20, and 25 kg/m<sup>2</sup>, quadriceps strength was 44.9 Nm (95%



**Fig. 1** Patient flowchart. Exclusion of patients who lacked exposure and outcome variables for analyses. Finally, 906 patients were included

**Table 1** Characteristics of patients with knee osteoarthritis

	Total N = 906
Age, years	73.0 (7.7)
Female sex, n (%)	711 (78%)
Body mass index, kg/m <sup>2</sup>	25.2 (3.7)
Fat mass, kg	20.2 (7.9)
Diabetes, n (%)	91 (10%)
Chronic kidney disease, n (%)	252 (28%)
Knee osteoarthritis grade, n (%)	
Surgical side	
Grade 1	1 (0.1%)
Grade 2	42 (4.6%)
Grade 3	193 (21.3%)
Grade 4	670 (74.0%)
Nonsurgical side	
Grade 1	12 (1.3%)
Grade 2	243 (26.9%)
Grade 3	246 (27.2%)
Grade 4	403 (44.6%)
Missing n = 2	
Leg skeletal mass, kg	
Surgical side	6.6 (1.6)
Nonsurgical side	6.6 (1.7)
Quadriceps strength, Nm	
Surgical side	47.3 [34.3; 63.3]
Missing n = 3	
Nonsurgical side	57.1 [44.3; 74.3]
Missing n = 2	

<sup>a</sup> Continuous variables summarized as mean and standard deviation (in parentheses)

<sup>b</sup> Continuous variables are summarized as median and 25th percentile and 75th percentile values (in square brackets)

Note: The 906 patients all had complete data on quadriceps strength and knee X-ray images for either the right side or left side

confidence interval (CI) 39.9–49.8 Nm), 50.5 Nm (95% CI 48.0–53.1 Nm), and 56.7 Nm (95% CI 54.7–58.7 Nm), respectively). However, from 25 to 40 kg/m<sup>2</sup>, quadriceps strength was similar (for example, at a BMI of 30, 35, and 40 kg/m<sup>2</sup>, quadriceps strength was 57.2 Nm (95% CI 55.0–59.3 Nm), 56.2 Nm (95% CI 51.5–60.8 Nm), and 55.2 Nm (95% CI 47.4–62.9 Nm), respectively). Adjusted differences in quadriceps strength by covariates are shown in Table 2. Increasing KOA severity, increasing age, and female sex were associated with lower quadriceps strength independent of BMI.

### Fat mass, leg muscle mass per leg, and quadriceps strength

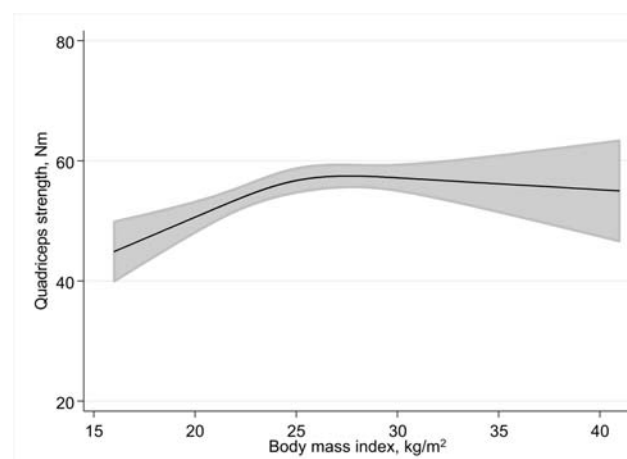
In the covariate-adjusted restricted cubic spline model, the splines demonstrated a non-linear, inverted U-shaped relationship

between fat mass and quadriceps strength ( $P = 0.04$  for non-linearity). The predicted quadriceps strength defined at the continuous fat mass value is shown in Fig. 3. From a fat mass of 10–20 kg/m<sup>2</sup>, increasing quadriceps strength was seen (for example, at a fat mass of 10, 15, and 20 kg/m<sup>2</sup>, quadriceps strength was 53.8 Nm (95% CI 50.9–56.8 Nm), 55.5 Nm (95% CI 53.6–57.3 Nm), and 56.4 Nm (95% CI 54.5–58.3 Nm), respectively). However, from 20 to 30 kg/m<sup>2</sup>, quadriceps strength showed a decreasing trend (for example, at a fat mass of 25 and 30 kg/m<sup>2</sup>, quadriceps strength was 55.9 Nm (95% CI 54.0–57.8 Nm) and 54.7 Nm (95% CI 52.4–57.0 Nm), respectively). Adjusted differences in quadriceps strength by covariates are shown in Table 3. Increasing age and female sex were associated with lower quadriceps strength independent of fat mass. Increasing lower leg muscle mass was associated with greater quadriceps strength. However, the magnitude of the association between the lower leg muscle mass and quadriceps strength decreased with increasing severity of knee OA grade ( $P$  for interaction = 0.005).

## Discussion

This study investigated the consequences of decomposing the association of BMI with quadriceps strength in patients with knee OA by examining the association between fat mass, leg muscle mass, and quadriceps strength. The results showed that an increasing BMI of up to 25 kg/m<sup>2</sup> was associated with increasing quadriceps strength, and quadriceps strength had minimal change among patients with a BMI of > 25 kg/m<sup>2</sup>. The association between fat mass and quadriceps strength had an inverted U-shaped relationship.

The result of increased quadriceps strength with an increasing BMI of up to 25 kg/m<sup>2</sup> in this study was in accordance with the



**Fig. 2** Predicted quadriceps strength by body mass index (BMI). Using the multivariable adjusted general linear model including age, sex, diabetes, and knee osteoarthritis (OA) severity, adjusted mean quadriceps strength by BMI was predicted. The solid line indicates point estimates. The gray shadow indicates 95% confidence intervals

**Table 2** Adjusted differences in quadriceps strength among patients with knee osteoarthritis

Quadriceps strength, Nm Covariates	Mean difference	(95% CI)	P value
Knee osteoarthritis grade			
1 or 2	Reference		
3	- 3.54	(- 6.88 to - 0.20)	0.038
4	- 6.03	(- 9.11 to - 2.96)	< 0.001
Age, per 10 years	- 7.69	(- 9.48 to - 5.90)	< 0.001
Sex, female	- 33.09	(- 36.98 to - 29.20)	< 0.001
Diabetes, yes	- 0.22	(- 5.19 to 4.74)	0.930

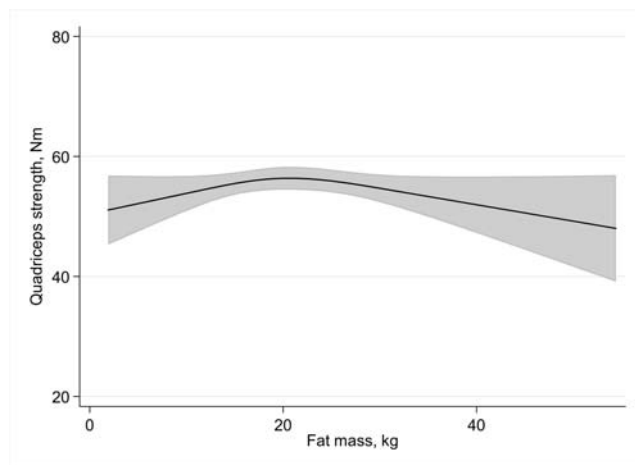
Analysis of 1806 limbs among 906 patients with knee osteoarthritis. General linear model adjusted for age, sex, diabetes, and knee osteoarthritis severity with consideration for intra-individual correlation using cluster variance. Italic font indicates significance at  $P < 0.05$  in P value column. The association between BMI and quadriceps strength was non-linear ( $P$  for non-linearity = 0.008)

finding of a previous study involving healthy but overweight elderly individuals [7]. In the previous study, the mechanism for increased quadriceps strength in overweight patients could be explained by the adaptation of the quadriceps muscle mass for carrying their heavy body weight. On the other hand, our results showing almost unchanging quadriceps strength among patients with knee OA who were overweight or within the obese range was contradictory to the previous study reporting increased quadriceps strength among healthy elderly individuals with obesity. This discordance could be attributable to the different proportions of fat mass and lean body mass between obesity complicated by knee OA and uncomplicated obesity. For example, muscle mass, which is positively correlated with muscle strength, may increase with increasing BMI in healthy but obese elderly individuals. On the one hand, among obese patients with knee OA, increasing BMI leads to a relatively greater increase in fat mass rather than in muscle mass. Indeed, in patients with knee OA and obesity, the finding of decreasing leg muscle mass/fat mass ratio with

increasing BMI categories in this study suggests that fat mass increases more than leg muscle mass with increasing BMI.

With regard to the relationship between leg muscle mass and quadriceps strength, the quadriceps strength increased linearly with increasing leg muscle mass, consistent with the result of previous studies [2, 17]. More interestingly, an inverted U-shaped relationship between fat mass and quadriceps strength was observed. The association of greater fat mass with decreased quadriceps strength could be explained by three reasons. First, fat mass accumulation causes low-grade inflammation in the musculoskeletal system by producing inflammatory mediators [4], which are associated with decreased muscle strength [18]. Second, adipose tissue in the thigh inhibited the central activation of knee extension, which is crucial for muscle force production [19]. Thus, we speculated that the low-grade inflammation and central activation inhibited by adipose tissue are greater with greater fat mass accumulation, thereby leading to decreased quadriceps strength in obese patients with knee OA. Third, physical inactivity related to obesity among patients with knee OA [20] may mediate the relationship between fat mass accumulation and decreased quadriceps strength [21]. On the other hand, an extremely low fat mass was also associated with decreased quadriceps strength. This mechanism remains unclear. It may be possible that an appropriate amount of fat mass is necessary for efficient muscle force production. A previous study suggested that underweight elderly individuals have a decreased metabolic activity of fat free mass [22]. Thus, impaired energy metabolism during muscle contraction may lead to decreased quadriceps strength among patients with knee OA with extremely low fat mass.

Our findings have two implications in the clinical setting. First, our results provide additional meaning in the interpretation of the relationship between BMI values and quadriceps strength in patients with knee OA. Our results suggested that the deleterious effect of fat mass on quadriceps strength may not be apparent in patients with a BMI of up to 25 kg/m<sup>2</sup>. On the other hand, quadriceps strength will decrease by increasing fat mass among



**Fig. 3** Predicted quadriceps strength by fat mass. Using the multivariable adjusted general linear model including age, sex, diabetes, lower limb muscle mass, knee osteoarthritis severity, and the product term of lower muscle mass and knee osteoarthritis severity, adjusted mean quadriceps strength by fat mass was predicted. The solid line indicates point estimates. The gray shadow indicates 95% confidence intervals

**Table 3** Adjusted differences in quadriceps strength among patients with knee osteoarthritis<sup>a</sup>

Quadriceps strength, Nm Covariates	Mean difference	(95% CI)	P value
Lower limb muscle mass per limb, kg <sup>a</sup>			
Knee osteoarthritis grade 1 or 2	7.97	(5.78 to 10.16)	< 0.001
Knee osteoarthritis grade 3	5.34	(3.08 to 7.60)	< 0.001
Knee osteoarthritis grade 4	4.12	(2.29 to 5.96)	< 0.001
Knee osteoarthritis grade			
1 or 2	Reference		
3	13.96	(− 0.13 to 28.06)	0.052
4	19.20	(6.97 to 31.44)	0.002
Age, per 10 years	− 4.94	(− 6.84 to − 3.03)	< 0.001
Sex, female	− 18.86	(− 25.32 to − 12.41)	< 0.001
Diabetes, yes	− 1.18	(− 6.19 to 3.84)	0.645

Analysis of 1806 limbs among 906 patients with knee osteoarthritis. General linear model adjusted for age, sex, diabetes, lower limb muscle mass, knee osteoarthritis severity, and the product term of lower muscle mass and knee osteoarthritis severity with consideration for intra-individual correlation using cluster variance. *Italic font indicates significance at  $P < 0.05$  in  $P$  value column. The association between fat mass and quadriceps strength was non-linear ( $P$  for non-linearity = 0.04)*

<sup>a</sup> Within each knee osteoarthritis grade subcategory, the adjusted mean differences are estimated because the grade modified the association between lower limb muscle mass and quadriceps strength ( $P$  for interaction = 0.005)

patients with a BMI of  $\geq 25$  kg/m<sup>2</sup>. Second, our findings provide data for improving quadriceps strength in patients with knee OA according to their BMI and fat mass values. This may influence the concept provided in the OARSI guideline that choice of the nonsurgical management for patients with knee OA should be determined by comorbidities such as obesity [23]. For example, a weight reduction regimen is considered to be appropriated for all individuals. However, the present study suggests that in underweight or normal weight patients with knee OA, clinicians should increase muscle mass through resistance training and avoid excessive fat mass reduction (i.e., weight reduction may be contradictory). On the other hand, in patients with knee OA and obesity, not only resistance training for increasing muscle mass but also aerobic exercise for decreasing fat mass could be effective in improving quadriceps strength.

This study has several strengths. First, our study evaluated the relationship between obesity and quadriceps strength among patients with knee OA, which is rarely investigated despite the known importance of both obesity and quadriceps strength as targets for improving functional movement. Second, its large-scale, single-center design enabled us to measure BMI, fat mass, and quadriceps strength in a uniform manner to effectively assess our research question. Third, our study attempted to analyze both limbs in each patient using a suitable statistical method. Accordingly, the findings of this study can be applied to both legs of a patient with knee OA, given that knee OA often develops bilaterally.

This study has also several limitations. First, we assessed fat mass and muscle mass using BIA instead of using computed tomography or magnetic resonance imaging. However, the validation of the BIA method via DXA showed very high

correlations between the two methods for fat mass as described before, and BIA is recommended as an option for measuring muscle mass by the EWGSOP2 and AWGS [24, 25]. Second, the cross-sectional design does not enable us to estimate the causal relationships. A longitudinal study is warranted to validate our findings further in consideration of the concept that obesity leads to a reduction in physical activity, leg muscle mass, and leg strength. Third, the participants in this study were not representative of all patients with knee OA because most of the participants had severe radiographic knee OA and were scheduled for knee replacement surgery. We believe that the association of obesity with quadriceps strength is a valuable finding that should be validated in patients who do not require surgical treatment. Separate measurement of muscles and fat mass may be more clinically meaningful and help the physician if the observed relationship between leg muscle mass, fat mass, and quadriceps strength is true for patients who are physically active but have less severe knee OA with obesity.

In conclusion, the association of increasing quadriceps strength with increasing BMI was observed in patients with knee OA and normal weight but not in those who were overweight or obese. By decomposing BMI into fat mass and muscle mass, we also were able to show that quadriceps strength followed an inverted  $U$ -shaped curve with increasing fat mass. These findings suggest that clinicians should evaluate fat mass and muscle mass separately rather than solely evaluating BMI when considering an individualized rehabilitation program for improving quadriceps strength in patients with knee OA. Further studies are warranted to examine whether such a customized program based on fat mass and leg muscle mass effectively increases quadriceps strength and achieves optimal weight.

**Acknowledgements** The authors greatly thank the following research assistant and medical staff members for their assistance in collecting the clinical information used in this study: Takehiro Kaga, Tomohiro Oka, Yoriko Tamura, Hiroshi Nishi, Yuichi Isaji, Yutaka Sato, Tomohiro Takagi, Kaho Shibata, Maho Wakai, Chisato Shindoh, Kenta Hirose, Takuma Ota, Tatsuya Arita, Yuuki Ikawa, Tsuyoshi Fukui, Riuji Nakagawa, Taisuke Hayashida, Shuto Fujii, Keisuke Yoneya, Kazuaki Mori (Anshin Hospital, Kobe-city, Hyogo), Lisa Shimokawa (Fukushima Medical University Hospital, Fukushima-city, Fukushima).

**Funding information** This study was supported by JSPS KAKENHI (Grant Number: JP15K16518). The JSPS had no role in this study except for funding.

**Compliance with ethical standards** The study was approved by the local institutional review board (No. 57, January 26, 2017) and by the Research Ethics Committee of Fukushima Medical University School of Medicine (No. 2850, September 28, 2016). All patients provided written informed consent prior to participation.

**Disclosures** None.

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