Quadriceps Weakness in Individuals with Coexisting Medial and Lateral Osteoarthritis

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Background: This study examined whether individuals who have mild medial osteoarthritis (OA) of the knee with co-existing lateral OA have less muscle strength than individuals who do not have lateral OA.

Methods: A series of 153 individuals (84% of whom were women) between 48 and 88 years old who had Kellgren and Lawrence (KL) grade-2 OA in the medial compartment of the knee underwent radiographic evaluation to assess the presence of lateral OA, which was graded with the system of the Osteoarthritis Research Society International (OARSI) atlas as well as the KL system. The isometric maximum strengths of the quadriceps, the hip abductors, and the hip extensors were evaluated with use of a handheld dynamometer.

Results: Individuals who had coexisting medial and lateral OA had more severe knee pain and weaker quadriceps than those who did not have lateral OA. The study adjusted for age and sex both for the OARSI atlas system (adjusted difference in mean strength: 0.272 Nm/kg, 95% confidence interval [CI]: 0.143 to 0.401 Nm/kg) and for KL grading (adjusted difference in mean strength: 0.185 Nm/kg, 95% CI: 0.061 to 0.309 Nm/kg). Logistic regression analysis showed that weakness of the quadriceps increased the odds of the presence of lateral OA sevenfold after adjustments using the OARSI atlas were made for age, sex, anatomical axis, range of motion of the knee, and intensity of pain in the knee.

Conclusions: Individuals who had coexisting medial and lateral OA had weaker quadriceps than individuals who had mild medial OA alone. Paying close attention to quadriceps weakness might provide a key to clarifying the pathogenesis of bicompartmental disease in the tibiofemoral joint.

Level of Evidence: Prognostic Level III. See Instructions for Authors for a complete description of levels of evidence.

Osteoarthritis (OA) is a progressive chronic disease that results in pain and disability[1]. It has recently been suggested that OA is a syndrome comprising multiple distinct subgroups rather than a single disease[2]. The identification of clinically relevant subgroups of OA of the knee and their relevance to clinical outcomes have recently gained attention[3]. Patients who have less severe disease as seen on radiographs respond better to therapeutic interventions than those with severe disease; therefore, identifying subgroups of OA that are less severe, as was previously done by Felson et al.[4], can have a therapeutic advantage.

The utilization of radiographic evaluation to determine the potential subgroup is useful because of its simplicity and wide use in the clinical setting. A recent cross-sectional study of 100 subjects who had Kellgren and Lawrence (KL) grade-2 OA[5] in the medial compartment of the knee identified a subgroup[6]: individuals who had coexisting lateral osteophytes and mild medial OA had more severe pain in the knee than those who had medial OA alone[6]. The 2 groups of patients may have had different clinical profiles. Although the pathogenesis of bicompartmental tibiofemoral joint disease has not been elucidated, impaired muscle function in the lower limb is a potential factor associated with this subgroup, and the reverse may also be true. Quadriceps weakness[7] and inactivation during gait[8] result in decreased shock absorption and thereby increase the load transmitted through the entire tibiofemoral joint, which may be responsible for OA changes in the medial and lateral compartments[9]. Conversely, bicompartmental disease may

induce more severe pain that then impairs quadriceps muscle contractions[10]. A plausible hypothesis is that individuals who have coexisting lateral and medial OA have less muscle strength. This hypothesis is supported by evidence demonstrating that cells from the knees of subjects who had bicompartmental disease (medial and lateral OA) showed a greater inflammatory response than cells from the knees of subjects who had unicompartmental disease[11]; inflammation is a significant factor associated with decreased strength of the quadriceps in individuals who have knee OA[12,13].

This study tested the hypothesis that individuals who have lateral OA have less muscle strength than those without lateral OA. This knowledge should provide us with new insight into understanding subgroups of OA of the knee and their relevance to clinical outcomes.

Materials and Methods

Participants

Community-dwelling elderly individuals who had pain in the knee were identified through a mailed survey and were invited to attend a research meeting at Kyoto University in September 2017. The ethics committee of Kyoto University approved the study, and written informed consent was obtained from all participants before their enrollment. All recruited participants had a history of pain in 1 or both knees in the last month. Eligibility criteria included (1) age more than 45 years; (2) mild medial tibiofemoral OA (KL grade 2) in 1 or both knees, evaluated using weight-bearing anteroposterior radiographs; and (3) the ability to walk without assistive devices. Individuals who had a history of knee surgery, rheumatoid arthritis, current neurological problems, or lateral OA of the knee were excluded from this study. Lateral OA was defined as a KL grade of ≥1 with joint-space narrowing graded >0 in the lateral compartment and 0 in the medial compartment[14]. Medial and lateral OA of the knee have distinct characteristics[15], and the medial type is the most common in Japan[16,17], so individuals in whom the severity of lateral OA exceeded the severity of medial OA were excluded from this study. We previously reported excellent interrater reliability scores for the severity of radiographic changes in the medial compartment[18,19].

Measurements

Radiographic assessment of the knee was performed and the lower-limb muscle strength of the participants was measured. Demographic characteristics, a self-reported measure of pain related to the OA of the knee, and range of motion of the knee were also assessed as covariates.

Radiographic Assessment

Anteroposterior radiographs of both knees, fully extended and weight-bearing, were made at the time of enrollment in the study. The radiographic severity of OA in the lateral compartment was assessed by a trained examiner (H.I.) in accordance with the previous study[6]. In brief, the Osteoarthritis Research Society International (OARSI) atlas[14] and KL grading system[5] were used for radiographic evaluation in a compartment-specific manner[20] because these systems provide a different prevalence rate of radiographic evidence of OA[21]. Radiographic evidence of OA in the lateral compartment, determined with use of the OARSI atlas, was considered to be present if 1 or more of the following criteria were present: (1) joint-space narrowing was grade 2, (2) the sum of the 2 marginal osteophyte grades was 2, or (3) grade-1 joint-space narrowing was combined with a grade of 1 for marginal osteophytes[22]. Radiographic evidence of lateral OA according to the KL grading system was considered to be present if the presence of marginal osteophytes in either the femur or the tibia was definitely confirmed[23]. We previously reported fair to good interrater reliability for osteophyte grade, joint-space narrowing, and KL grade in the lateral compartment[6].

Muscle Strength

The maximum isometric strengths (Nm/kg) of the quadriceps, hip extensors, and hip abductors of both legs were measured using a hand-held dynamometer (μTas F-1; Anima) in accordance with a method previously validated for community-dwelling elderly fallers[24]. Details about the measurement procedure for each muscle are provided in the Appendix and shown in Appendix Figure E-1. The minimum detectable change (MDC95) was calculated using 100 randomly selected participants (200 knees) to indicate the smallest degree of change that is outside the error of the strength testing. The MDC95 was 0.227, 0.211, and 0.132 Nm/kg for quadriceps, hip extensor, and hip abductor strengths, respectively. The intrarater reliability was excellent for quadriceps strength (intraclass correlation [$ICC_{1,1}$]: 0.939, 95% confidence interval [CI]: 0.921 to 0.954), hip extensor strength ($ICC_{1,1}$: 0.942, 95% CI: 0.925 to 0.956), and hip abductor strength ($ICC_{1,1}$: 0.936, 95% CI: 0.916 to 0.951).

Covariates

Data on age, sex, and height were self-reported by the participants. Weight was measured with a weighing scale, with the participants clothed but not wearing shoes. The severity of knee pain and self-reported physical function were evaluated using the Japanese Knee Osteoarthritis Measure (JKOM)[25]. The anatomical axis angle (AAA) with sex-specific correction[26] was assessed on the anteroposterior short view made with the individual bearing weight (see Appendix, Method 2). The range of passive flexion and extension of the knee was also evaluated (see Appendix, Method 3).

Statistical Analyses

To minimize any bias generated by similarities between the right and left knees of the same person, only 1 knee per individual (the index knee) was analyzed. The index knee was defined as the knee that was considered more painful in either the past or the present. If an individual perceived that the 2 knees were equally painful, the index knee was selected randomly with use of a computer-generated permuted

block randomization scheme[27]. A sample-size calculation based on the pilot data of quadriceps strength was performed. In this manner, it was determined that a minimum of 141 participants were required for the present study (see Appendix, Method 4).

To check the reproducibility of the previous study, which had been conducted to determine whether individuals who have bicompartmental tibiofemoral joint disease are more symptomatic than those who have OA in the medial compartment only[6], the JKOM scores were compared using an analysis of covariance (ANCOVA) adjusted for age, female sex, and body mass index. Subsequently, the muscle strength of individuals who did and did not have OA in the lateral compartment was compared with use of the ANCOVA adjusted for age and sex.

To test the hypothesis that decreased muscle strength is significantly associated with the presence of lateral OA, logistic regression analysis was performed with muscle strength as an independent variable (continuous; per −1 Nm/kg) and the presence of lateral OA as a dependent variable (0: no, 1: yes). Age, female sex, the corrected AAA of the index knee, the range of motion of the index knee, and the JKOM pain score were included as covariates. These covariates were determined a priori based on clinical judgment and on potential association with muscle strength and the presence of OA in the lateral compartment[6]. Muscle strength was normalized to body mass, so body mass index was not included as a covariate, although it may be a potential confounder[6]. Data analyses were performed using JMP Pro 13.0 (SAS Institute). A p value of <0.05 was considered significant.

Results

Of the 296 participants evaluated, 143 (48%) were excluded for the following reasons: (1) missing data, 6 individuals; (2) no definitive radiographic evidence of OA (KL grade 1), 106 individuals; or (3) radiographic evidence of moderate to severe OA (KL grade 3 or 4), 31 individuals. Thus, the final analysis included 153 participants. The mean age was 69.3 years (range,

TABLE I Comparison of Characteristics of Individuals Who Had Mild Medial OA with and without Lateral OA (N = 153)						
	OARSI Atlas*			KL Classification*		
Variable†	With Lateral OA (N = 45)	Without Lateral OA (N = 108)	P Value‡	With Lateral OA (N = 58)	Without Lateral OA (N = 95)	P Value‡
Age (yr)	70.0 ± 9.60	69.0 ± 9.30	0.612	70.1 ± 9.75	68.8 ± 9.15	0.449
Women (no. [%])	41 (91.1)	87 (80.6)	0.108	51 (87.9)	77 (81.1)	0.264
Height (m)	1.54 ± 0.07	1.57 ± 0.08	0.033§	1.54 ± 0.08	1.57 ± 0.07	0.014§
Weight (kg)	56.5 ± 12.5	54.0 ± 9.90	0.340	55.7 ± 12.0	54.2 ± 9.90	0.465
Body mass index (kg/m²)	23.7 ± 4.12	21.9 ± 2.93	0.003§	23.3 ± 3.78	21.8 ± 3.06	0.006§
Index knee corrected AAA (°)	178.3 ± 3.37	177.2 ± 3.55	0.078	178.3 ± 3.58	177.0 ± 3.40	0.021§
Alignment [no. (%)]			0.330			0.099
Neutral (corrected AAA ≥179° but <182°)	12 (26.7)	23 (21.3)		13 (22.4)	22 (23.2)	
Valgus (corrected AAA ≥182°)	6 (13.3)	8 (7.4)		9 (15.5)	5 (5.3)	
Varus (corrected AAA <179°)	27 (60.0)	77 (71.3)		36 (62.1)	68 (71.6)	
Lateral joint-space narrowing in index knee (no. [%])			0.880			0.300
Grade 0	44 (97.8)	106 (98.1)		56 (96.6)	94 (98.9)	
Grade 1	1 (2.2)	2 (1.9)		2 (3.4)	1 (1.1)	
Grade 2	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	
Grade 3	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	
JKOM pain subscale (points)	6.87 ± 5.04	4.33 ± 3.95	0.002§	6.45 ± 5.08	4.28 ± 3.81	0.008§
JKOM ADL subscale (points)	4.59 ± 4.15	2.08 ± 2.55	<0.001§	3.88 ± 3.93	2.19 ± 2.69	0.005§
JKOM total score (points)	16.5 ± 10.5	10.3 ± 7.60	0.001§	15.4 ± 10.4	10.2 ± 7.52	0.004§
Flexion ROM of index knee (°)	144.5 ± 8.44	149.2 ± 8.40	0.002§	145.1 ± 7.76	149.4 ± 8.80	<0.001§
Extension ROM of index knee# (°)	−2.67 ± 5.42	−0.37 ± 4.17	0.002§	−2.16 ± 5.32	−0.37 ± 4.11	0.022§

*Values are given as the mean and the standard deviation, except where otherwise noted. †ADL = activities of daily living, and ROM = range of motion. ‡P values are calculated using the Student t test (height, index corrected AAA), Mann-Whitney U test (age, weight, body mass index, JKOM scores, ROM of the knee), and chi-square test (female, alignment, and lateral joint-space narrowing). §Significant result. #A negative value indicates flexion of the knee joint.

TABLE II Muscle Strengths of Individuals Who Had Mild Medial OA with and without Lateral OA—Comparison Using ANCOVA (N = 153)						
	OARSI Atlas			KL Classification		
Variable	With Lateral OA (N = 45)	Without Lateral OA (N = 108)	Adjusted Difference in Mean* (95% CI)	With Lateral OA (N = 58)	Without Lateral OA (N = 95)	Adjusted Difference in Mean* (95% CI)
Index knee						
Quadriceps strength (Nm/kg)	0.998 ± 0.296	1.298 ± 0.412	0.272 (0.143, 0.401)†	1.084 ± 0.388	1.287 ± 0.397	0.185 (0.061, 0.309)†
Hip extensor strength (Nm/kg)	1.184 ± 0.381	1.476 ± 0.562	0.249 (0.073, 0.424)†	1.286 ± 0.464	1.454 ± 0.561	0.138 (−0.028, 0.305)
Hip abductor strength (Nm/kg)	0.716 ± 0.212	0.829 ± 0.325	0.120 (0.017, 0.224)‡	0.743 ± 0.240	0.828 ± 0.328	0.093 (−0.005, 0.191)
Non-index knee						
Quadriceps strength (Nm/kg)	1.063 ± 0.303	1.355 ± 0.442	0.250 (0.114, 0.386)†	1.148 ± 0.393	1.343 ± 0.431	0.166 (0.035, 0.296)‡
Hip extensor strength (Nm/kg)	1.221 ± 0.378	1.535 ± 0.507	0.275 (0.113, 0.437)†	1.345 ± 0.487	1.502 ± 0.489	0.128 (−0.028, 0.284)
Hip abductor strength (Nm/kg)	0.721 ± 0.249	0.835 ± 0.358	0.122 (0.005, 0.238)‡	0.744 ± 0.262	0.837 ± 0.367	0.100 (−0.009, 0.210)

*Adjusted for age and sex. †$P < 0.01$. ‡$P < 0.05$.

48 to 88 years), and 84% of the participants were women. Radiographic evidence of OA in the lateral compartment was present in 45 individuals (29%) according to the criteria of the OARSI atlas compared with 58 individuals (38%) according to the KL criteria. Table I shows the comparison of characteristics between individuals with and without lateral OA. Of the 153 individuals, 99 (65%) had a history of knee pain within the past month; of these, 56 (57%) felt the pain ≥3 days per week. The mean duration of the pain was 41.0 months (range, 0.5 to 360 months), and individuals who had OA in the lateral compartment had a significantly longer duration of complaints (means, 60.8 and 58.6 months when the OA was graded with the OARSI and KL systems, respectively) than those without

lateral OA (means, 30.8 and 28.1 months when graded with the OARSI and KL systems). The JKOM pain score in individuals who had lateral OA was more severe than it was in individuals without lateral OA, regardless of radiographic criteria, after adjusting for the covariates; the mean difference in JKOM pain score was 2.495 (95% CI, 0.950 to 4.040) points and 2.099 points for OA graded with the OARSI and KL systems, respectively.

Table II shows the comparison of strength in the muscles of the lower limb of the index and non-index knees for individuals with and without lateral OA. The quadriceps, hip extensor, and hip abductor muscles of both lower limbs were weaker in individuals who had lateral OA than in those without

TABLE III Association Between Weaker Muscle Strength and the Presence of Lateral OA in Individuals with Mild Medial OA—Binary Logistic Regression Analyses (N = 153)				
	OARSI Atlas		KL Classification	
	OR (95% CI) of the Presence of Lateral OA*		OR (95% CI) of the Presence of Lateral OA*	
Independent Variable	Crude Model	Adjusted Model	Crude Model	Adjusted Mode
Index knee				
Quadriceps strength, per −1 Nm/kg	11.3 (3.69, 39.9)†	6.53 (1.81, 27.1)†	4.13 (1.66, 11.3)†	2.00 (0.71, 6.03)
Hip extensor strength, per −1 Nm/kg	3.25 (1.56, 7.31)†	2.02 (0.85, 5.06)	1.87 (0.99, 3.68)	1.08 (0.49, 2.37)
Hip abductor strength, per −1 Nm/kg	4.83 (1.24, 22.2)‡	2.23 (0.42, 14.2)	2.95 (0.90, 11.1)	0.90 (0.21, 3.82)
Non-index knee				
Quadriceps strength, per −1 Nm/kg	8.23 (2.87, 27.2)†	7.12 (2.07, 28.6)†	3.37 (1.43, 8.65)†	2.70 (0.99, 8.01)
Hip extensor strength, per −1 Nm/kg	4.63 (2.03, 11.6)†	2.82 (1.11, 7.68)‡	1.97 (0.99, 4.09)	0.99 (0.43, 2.28)
Hip abductor strength, per −1 Nm/kg	3.85 (1.10, 15.9)‡	1.84 (0.41, 10.1)	2.71 (0.90, 9.45)	1.22 (0.35, 5.16)

*OR (odds ratio) was calculated per −1 Nm/kg to indicate predictive ability of weaker muscle strength. Adjustments were made for age and sex and for corrected AAA, extension range of motion, flexion range of motion, and JKOM scores for pain and stiffness of the index knee. †$P < 0.01$. ‡$P < 0.05$.

lateral OA after adjusting for age and sex. Significant differences in hip muscles were determined only when the OARSI atlas were used.

We performed logistic regression analyses to determine whether muscle weakness was significantly associated with the presence of lateral OA (Table III). A weaker quadriceps was associated with 6.5-fold and 7.1-fold increases in the odds of the presence of lateral OA in the index and non-index knees, respectively. However, these differences were statistically significant only when the OARSI classification was used.

Discussion

A significant finding of the current study is that individuals who had coexisting lateral OA had weaker muscles, particularly the quadriceps muscle, after adjusting for the covariates. Consistent with the previous study[6], individuals who had coexisting medial and lateral OA had greater pain in the knee, indicating that these patients had a more symptomatic disease than those with medial OA alone. Our findings indicate that if closer attention is given to the weaker quadriceps, this information may provide a key in clarifying the pathogenesis of bicompartmental disease in the tibiofemoral joint.

The prevalence of lateral OA in this study was similar to or slightly less than has been reported in previous studies[6,28,29]. We considered lateral OA to be present if osteophytes were detected in either the tibia or the femur, which is different from the original version of KL grading. Thus, the prevalence according to KL grading was less than that determined when the OARSI atlas was used for grading. Racial differences might also contribute the lower prevalence of lateral OA in this study[29,30]. The magnitude of between-group difference in knee pain was approximately equal to the minimal clinically important difference (MCID)[31], indicating that these 2 groups may have different pain profiles. The complaints of individuals with lateral OA were of longer duration, a finding that supports the above-mentioned interpretation. A prospective cohort study is warranted to address the causal relationship between greater pain in the knee and bicompartmental disease in the tibiofemoral joint.

Muscle strength was evaluated using a handheld dynamometer, with which the test-retest reliability was similar to that reported in a previous study[32]. The group difference in quadriceps strength might be affected by knee pain during testing[33,34]. The impact of pain during testing would be expected to be small; however, the data should be interpreted with caution. Because individuals who had lateral OA also had greater pain, the precise difference in the strength of the quadriceps between those who did and did not have lateral OA may be less than the values provided in the present study. On a related note, the mean difference of muscle strength in the quadriceps and hip extensors, when OA was determined by the OARSI atlas criteria, exceeded the MDC95 value, indicating that in individuals who had coexisting lateral OA, muscle strength was diminished by more than the measurement error of muscle-strength testing. However, the mean differences in quadriceps and hip extensor strength when OA was determined

by the KL classification were lower than the MDC95; thus, close attention is needed when translating our research findings into clinical practice. Furthermore, the mean difference in hip abductor strength was lower than the MDC95 regardless of the radiographic OA classification used, although the MDC95 of hip abductor muscle strength was lower than that reported in a previous study[35].

The mechanism responsible for lesser muscle strength in individuals who have lateral OA has not yet been clarified; however, it has been suggested that individuals who have bicompartmental OA have a more inflammatory disease than those with unicompartmental OA[11]. The elevated inflammatory response may contribute to weakness of the quadriceps[12,13,36], and this should be considered in future studies. These systemic effects may explain why the muscles in the non-index knee of the participants in this study who had lateral OA were also significantly weaker than they were in the individuals who did not have lateral OA.

An important implication of this study is that a weak quadriceps may be a factor associated with bicompartmental disease in the tibiofemoral joint, although the cross-sectional nature of the present study limits our interpretation of any causal relationship. Race is known to be associated with bicompartmental disease[29,30]; however, previous studies did not consider the effects of strength of the muscles of the lower limb. It should be highlighted that the difference in quadriceps strength between the 2 groups in the present study exceeded the MCID value (6% reduction in muscle strength) for self-reported functional decline[37]. Quadriceps weakness or inactivity during gait could result in large loads at the tibiofemoral joint[7,8] and might be responsible for OA changes in the lateral compartment. A previous meta-analysis revealed moderate to high-quality evidence that a rehabilitation program targeting the quadriceps increased muscle strength, with a small to moderate effect[38]. Therefore, the difference in quadriceps strength between individuals with and without lateral OA might be treatable through a non-pharmacological method. However, bicompartmental OA could contribute to weakness of the quadriceps because severe pain in the knee impairs quadriceps contractions[10]. A longitudinal cohort study is warranted to clarify whether weakness of the quadriceps is a modifiable risk factor associated with bicompartmental disease.

The present study has some limitations. A lack of information about patellofemoral OA restricted our analysis. Patellofemoral OA contributes to quadriceps weakness[39]. Thus, the decreased strength of the quadriceps in individuals who have lateral OA may be attributable to the greater prevalence of disease in the patellofemoral joint. Additionally, we lacked information about the patients' history of injury. A previous injury such as a rupture of the anterior cruciate ligament, which is a risk factor for progression of radiographic evidence of lateral OA[40], might explain the weaker quadriceps in individuals who have lateral OA. We had no data on forms of muscle contraction other than isometric strength, and this restricted our analysis of the relationship between muscle

strength and the presence of coexisting medial and lateral OA. Individuals who have OA of the knee have impaired eccentric quadriceps contraction compared with concentric and isometric contractions[41]; this should be a subject of future studies.

In conclusion, in this study, individuals who had coexisting medial and lateral OA had decreased muscle strength, particularly of the quadriceps, in conjunction with more severe knee pain compared with individuals who did not have lateral OA. Weakness of the quadriceps may be an important manifestation of bicompartmental OA and has demonstrated associations with important clinical outcomes, including knee pain. Close attention to quadriceps weakness might provide the key to clarification of the pathogenesis of bicompartmental disease in the tibiofemoral joint.

Appendix

eA Additional details regarding the methods used in the present study (including references[42-46], which are cited only in the Appendix) and a figure demonstrating measurement of lower-limb muscle strength are available with the online version of this article as a data supplement at jbjs.org (http://links.lww.com/JBJSOA/A83). ∎

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