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Age-related quadriceps-dominant muscle atrophy and incident radiographic knee osteoarthritis

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Abstract Muscle atrophy is common in the elderly. However, the etiologic role of muscle atrophy associated with osteoarthritis of the knee has not been studied in detail. We assessed the association between age-related muscle atrophy around the knee joint and incident radiographic osteoarthritis of the knee. Twenty-one women in their thirties and 17 women in their sixties participated. They had no history, symptoms, or objective findings of any knee problems, and none of the participants was limited in performing daily activities. Radiographs of the knee joint were graded for the presence of osteoarthritis, and the cross-sectional imaging around the knee joint was carried out using computed tomography. Incident radiographic osteoarthritis was observed in 6 of the 17 women in their sixties. Quadriceps-dominant muscle atrophy was marked in the elderly women with radiographic osteoarthritis. In a multivariate analysis, the risk of incident radiographic osteoarthritis of the knee was significantly increased among women with a higher hamstrings/quadriceps cross-sectional area ratio. The results suggest the possibility that age-related quadriceps-dominant muscle atrophy may play a role in the pathogenesis of osteoarthritis of the knee.

Key words Aging · Muscle atrophy · Computed tomography · Osteoarthritis of the knee

Introduction

Muscle atrophy is commonly observed with aging. In the lower extremity, several studies reported that age-related reduction in muscle mass is greater in the quadriceps than in the hamstrings.[5,20] Muscle atrophy is a major contributor to reduced muscle strength,[4,13,17] and age-related quadriceps weakness is reported to be associated with decreased functional performance and increased incidence of falls.[2] Therefore, quadriceps muscle atrophy is likely to be strongly associated with disability in the elderly population.

Osteoarthritis (OA) of the knee has been reported to be the most common cause of chronic disability in the elderly.[7] Several studies have found that quadriceps weakness, which is common in patients with knee OA, plays a more important role in disability than the severity of either the pain or the radiographic changes of the knee.[16,18] For treatment of knee OA, exercises designed to strengthen the quadriceps muscles are often advocated and recommended. Quadriceps muscle exercises have been found to have beneficial effects not only on strength but also on pain and function.[19]

It is widely believed that quadriceps weakness is due to disuse atrophy secondary to joint pain among patients with knee OA. However, recently, some studies have proposed that quadriceps weakness can become one of the risk factors for knee OA. The age-related deterioration in proprioception of muscle[10] and reduced quadriceps strength relative to body weight among women[24] have been reported as possible causes of damaged articular cartilage. Furthermore, regarding muscle mass, the role of reduced lower extremity lean body mass per body weight in the pathogenesis of knee OA has been suggested.[28] However, the role of age-related changes in individual muscle mass around the knee joint has not been examined.

The purpose of the present study was to investigate the cross-sectional areas of the muscles and fat tissues around the knee joint among women using computed tomography (CT) and to examine the association between age-related muscle atrophy around the knee joint and incident radiographic knee OA.

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Methods

Subjects

Sixty new female outpatients with problems such as trauma or arthralgia in the upper extremity for a few days were enrolled in the present study. They consisted of 27 women in their thirties and 33 women in their sixties.

Among the 60 participants, 2 women in their thirties and six in their sixties were excluded from the analysis because swelling or tenderness in the knee joint was observed when they were examined. In the remaining 52 participants, 4 women in their thirties and 7 in their sixties were excluded because they had a history of knee problems and injuries in the lower extremities that had required immobilization of the joint for more than 1 week. Furthermore, three women in their sixties had a history of neuromuscular condition or organic disease that could impair skeletal muscle function or influence body composition; they also were excluded. Ultimately, 38 participants remained for the analysis.

The subjects consisted of 21 women in their thirties with a mean ± SD age of 34.4 ± 2.5 years and 17 women in their sixties with a mean ± SD age of 64.5 ± 3.5 years. They had no swelling or tenderness in the knee joint and no history of any knee problems, and none was limited in performing daily activities. All participants received a sufficient explanation of the purpose and procedures of the examination and gave their consent. The present study was approved by the ethics committee of Oita University.

Procedure

The height and body weight of each subject were measured, and the body mass index (BMI) was calculated as weight (kg)/height (m^2).

A standing anteroposterior radiograph of the right knee joint obtained with the knee in 45° of flexion (Rosenberg's method)[21] was used for the radiographic evaluation of incident knee OA. When a radiograph showed a finding with grade 2 or greater using Kellgren and Lawrence criteria,[12] the knee joint was identified as having radiographic knee OA.

The cross-sectional CT images at the level 20 cm proximal from the tibial tuberosity and 10 cm distal from the tibial tuberosity were obtained from lower extremities of each subject. The subjects were imaged in the supine position with the arms above the head and toes directed toward the top of the gantry, with lower extremities extended flat on the table. The cross-sectional images were obtained using the GE High-speed Advantage CT scanner operating at 120 kV, 230 mA, 512 × 512 matrix, and a 420 mm^2 field of view. Technical factors were slice width 5 mm and a scanning time of 1 s.

The CT images were input into a personal computer and analyzed with Scion Image Beta version 4.02 using manual planimetry by three observers who did not have any information on the subjects. On the CT images, the outline was drawn manually along the margin of each muscle with care taken that no pixels for bone were included in the muscle area of the right lower extremity. After that, the cross-sectional areas (cm^2) in the outlines, such as for the quadriceps, hamstrings, and plantar flexors were measured.

Similarly, for measurement of the fat tissue area of the thigh, the lines were drawn manually along the skin and the deep fascial plane surrounding the thigh muscles. The intermuscular fat tissue was distinguished from the subcutaneous fat tissues by a line along the deep fascial plane. The cross-sectional areas of the muscles and fat tissue were measured three times (1 week apart) by each observer to obtain mean values. The average intraobserver difference among the measured data of the cross-sectional area of each component was 2.1%, and the interobserver difference was 4.5%.

All the subjects were interviewed about their histories of occupations and participation in sports since leaving school. Occupational physical activity was classified into five grades according to strength demand as reported by Felson et al.[3] This strength demand was based mostly on the weight of objects one must lift, carry, push, or pull on the job. The five grades of occupational activities were as follows: sedentary (lift 10 lb maximum, only occasional walking or standing); light (lift 20 lb maximum with frequent lifting or carrying of up to 10 lb; walking or standing frequent); medium (lift 50 lb maximum with frequent lifting or carrying of up to 25 lb); heavy (lift 100 lb maximum with frequent lifting or carrying of up to 50 lb); very heavy (lift over 100 lb maximum with frequent lifting or carrying objects over 50 lb).

Data analysis

Data were analyzed using the StatView version 5.0 for Macintosh. Student's *t*-tests were used to compare mean values between groups. The data are presented as means ± SD. Multivariate analysis of associations with radiographic knee OA was examined using logistic regression; age, height, and weight-adjusted odds ratios (OR) for radiographic knee OA together with 95% confidence intervals (95% CI) were presented. Statistical significance was accepted at $P < 0.05$.

Table 1. Comparison of the characteristics of the women in the two groups

Characteristic	Mean (SD), by age		P
	Thirties (n = 21)	Sixties (n = 17)	
Age (years)	34.4 (2.5)	64.5 (3.5)	<0.001
Height (cm)	157.6 (4.8)	155.1 (4.0)	0.11
Weight (kg)	52.4 (5.9)	50.4 (6.0)	0.33
BMI (k/m^2)	21.0 (1.9)	20.9 (2.7)	0.93

BMI, body mass index

Table 2. Comparison of the characteristics of the women in their sixties with and without incident radiographic knee OA

Characteristic	Mean (SD)		P
	OA (n = 6)	Non-OA (n = 11)	
Age (years)	65.1 (3.7)	63.8 (3.2)	0.44
Height (cm)	155.3 (4.3)	155.0 (4.1)	0.89
Weight (kg)	49.0 (5.7)	51.2 (6.5)	0.50
BMI (k/m^2)	20.3 (1.8)	21.4 (3.1)	0.46

OA, osteoarthritis

Results

There was no statistical difference in the height, body weight, or body mass index between the women in their thirties and sixties, as shown in Table 1. Incident radiographic knee OA was observed in 6 of 17 women (6/17 knee joints) in their sixties but was not observed among those in their thirties. All six knees showed the findings of grade 2 using Kellgren and Lawrence criteria; there were no grade 3 or 4 knees. The mean body weight of the women with incident knee OA was not statistically different from that of those without incident knee OA in the present study (Table 2).

In the CT images, the cross-sectional areas of the muscles were smaller among the women in their sixties than in those in their thirties. The intermuscular low-density regions (i.e., fat and loose connective tissue) were greater among the women in their sixties than among those in their thirties.

The measurements of the cross-sectional areas of the total thigh, quadriceps, hamstrings, and plantar flexors are shown in Tables 3 and 4. The areas of the total thigh and each muscle of the women in their sixties were significantly smaller than those of the women in their thirties. The percentage reduction in the cross-sectional area of each component between women in their thirties and sixties was, on average, greatest in the quadriceps (23.8%), whereas it was 17.0% in the total thigh, 12.9% in the hamstrings, and 17.7% in the plantar flexors (Table 3).

Among the women in their sixties, the cross-sectional areas of the quadriceps in those with incident knee OA were significantly smaller (on average, 12%) than those without knee OA. However, the areas of the total thigh, hamstrings, and plantar flexors were not significantly different between the women with and without incident knee OA (Table 4).

The hamstrings/quadriceps cross-sectional area ratio (H/Q ratio) was 0.50 for the women in their thirties and 0.58 for those in their sixties. Furthermore, among those in their sixties the H/Q ratio was 0.62 for the women with incident knee OA and 0.55 for those without incident knee OA. Table 5 shows the associations of incident radiographic knee OA with the H/Q ratio and the cross-sectional areas of the muscles and fat tissue among women in their sixties. A significant increase in risk of radiographic knee OA was observed in those with a high H/Q ratio (OR 2.50, 95% CI 1.02–6.18).

The cross-sectional areas of the subcutaneous fat were also significantly smaller among the women in their sixties than in those in their thirties, as shown in Table 3. However, the area occupied by the subcutaneous fat as a proportion of the total thigh was 34.6% among the women in their sixties. Its value was not significantly different from 37.2% among those in their thirties (p = 0.056). In contrast, the cross-sectional areas of the intermuscular fat were significantly greater among the women in their sixties than in those in their thirties. The area occupied by the intermuscular fat as a proportion of the total thigh among the women in their sixties was also higher: 13.3% vs. 9.3% among those in their thirties ($P < 0.001$).

Of 21 women in their thirties, 19 were in occupations requiring sedentary or light activity and 2 were in occupations requiring medium activity. Among the women in their sixties, all of their occupations were classified in sedentary or light activity. None was in an occupation requiring heavy or very heavy physical demands.

Of the 38 women included in the present study, 9 had a history of sports participation since leaving school. They participated in recreational activity once every 3–4 weeks on average. None was an athlete or performed resistance weight training. The grades of occupational physical activity and the histories of participation in sports did not yield significant differences in the cross-sectional areas of the muscles and fat tissue (data not

Table 3. Cross-sectional areas of the thigh and leg components measured from CT images

Component (cm^2)	Area (cm^2), by age: Thirties (n = 21)	Sixties (n = 17)	Mean difference (%)	P
Total thigh	169.2 (30.5)	139.9 (27.3)	−17.3	<0.001*
Quadriceps	47.7 (7.8)	36.4 (6.2)	−23.8	<0.001*
Hamstrings	23.7 (4.7)	20.7 (3.7)	−12.9	0.003*
Plantar flexors	40.9 (7.7)	33.7 (5.8)	−17.7	<0.001*
Subcutaneous fat	62.9 (17.4)	48.4 (16.2)	−23.1	<0.001*
Intermuscular fat	15.7 (4.0)	18.6 (3.4)	+18.5	<0.001*

Results are the mean (SD)
CT, computed tomography
*Significant

Table 4. Mean cross-sectional areas of the thigh and leg components among women in their sixties

Component (cm^2)	Area (cm^2): OA (n = 6)	Non-OA (n = 11)	P
Total thigh	139.2 (21.1)	141.1 (30.4)	0.86
Quadriceps	33.3 (5.8)	37.9 (5.9)	0.04*
Hamstrings	20.4 (3.0)	20.8 (4.0)	0.77
Plantar flexors	33.5 (6.8)	33.8 (5.4)	0.88
Subcutaneous fat	52.1 (14.6)	46.6 (17.9)	0.39
Intermuscular fat	19.1 (1.9)	19.8 (3.7)	0.54

Results are the mean (SD)
*Significant

Table 5. Association of incident knee OA with cross-sectional areas of the muscles and fat tissue, H/Q ratio, occupational physical activity, and participation in sports

Factor	Adjusted odds ratio[a]	95% CI	P
Total thigh	1.03	0.98–1.08	0.307
Quadriceps	0.90	0.76–1.05	0.182
Hamstrings	1.12	0.85–1.49	0.409
H/Q ratio per 0.1 difference	2.50	1.02–6.18	0.046*
Plantar flexors	0.99	0.85–1.15	0.914
Subcutaneous fat	1.13	0.99–1.29	0.066
Intermuscular fat	0.92	0.61–1.38	0.677
Occupation	1.21	0.22–6.62	0.825
Sports	1.18	0.13–10.41	0.880

H/Q ratio: the hamstrings/quadriceps cross-sectional area ratio; 95% CI, 95% confidence interval
[a] All analyses were adjusted for age, height, and weight
*Significant

shown) and were not associated with radiographic knee OA among the women in their sixties (Table 5).

Discussion

Our observations of changes in body composition that occur with aging were comparable to those in previous reports. Overend et al. examined the thigh composition using CT imaging and reported that in elderly men (65–77 years old) there was a significantly smaller cross-sectional area of quadriceps in 26.4% and of hamstrings in 17.9% than in young men (19–34 years old).[20] Similarly, Young et al. reported that the mean quadriceps cross-sectional area in elderly women (71–81 years old) was 33% smaller than that in young women (20–29 years old).[29] The age-related muscle atrophy seems to be characterized by a loss of fibers that begins at about 25 years of age and a reduction in fiber size that can be explained mostly by smaller type 2 fibers.[15]

Regarding the imaging site of the thigh, several sites were used as "mid-thigh" in previous reports (e.g., at the middle of the medial edge of the greater trochanter and the intercondyloid fossa[6] or at the middle of the pubic symphysis and the lower pole of the patella[5]). In the present study, the imaging site was 20 cm proximal from the tibial tuberosity. This was because when we examined the radiographs of the lower extremity of the subjects (148.0–170.0 cm in height) prior to CT imaging the site used previously was found to be 18.3–22.6 cm proximal to the tibial tuberosity.

Several studies have shown that the increase in the intermuscular and intramuscular fat tissue is apparent especially in elderly persons, obese persons, and women.[6,20] In elderly persons, the reduction in the number and size of muscle fibers are first seen in skeletal muscle, followed by subsequent replacement with fat and fibrous tissue.[15] In addition, aging human skeletal muscle has an increase in the relative proportion of type 1 muscle fibers, which have greater lipid content.[1,14] These phenomena are likely to explain in part the cause of the age-related increase in intermuscular and intramuscular fat tissues.

The association between body composition and knee OA has also been discussed in previous studies. It is reported that an increase in fat tissue is frequently observed in patients with knee OA.[8] Furthermore, Slemenda et al. reported that the women who developed incident knee OA had more lower extremity muscle mass, and their knee extensor strength after adjustment for body weight was 18% lower at baseline than that of the controls without knee OA.[24] These results seemed to be strongly associated with obesity. In contrast, Toda et al. reported that women with early-phase knee OA had a reduced lower extremity muscle mass compared with similar-weight controls without knee OA; and they noted that reduced lower extremity muscle mass may be an important cause of knee OA.[28] However, they did not evaluate individual muscle groups around the knee joint.

In the present study, quadriceps-dominant muscle atrophy was observed in association with aging and was marked among elderly women with incident knee OA compared with those without knee OA. The subjects had similar height and weight, on average, in these two subgroups of elderly women. Although it is widely known that the quadriceps muscle can be selectively inhibited by pain and a collection of fluid in the knee joint,[27] all 38 subjects in the present study had no history, symptoms, or signs of any knee problems. Furthermore, although some previous studies have noted that the strength demand and the frequency of occupation and sports were associated with the change in body composition and the increase in knee OA risk,[3,22,26] no subjects showed high activity in either occupation or sports activity. These results suggest that disuse atrophy is not primarily responsible for the pathogenesis of knee OA and that age-related quadriceps-dominant muscle atrophy may play a role.

Hurley proposed that the reason for quadriceps-dominant muscle atrophy in comparison with hamstrings is because hamstrings are biarticular; by spanning the knee and the hip joints, they can be contracted and stretched even if the knee is immobilized, in contrast to the monoarticular quadriceps with the exception of rectus femoris as a weak hip flexor.[9] The quadriceps are important for maintaining knee joint stability, and they play a role in attenuating the lowering speed of a lower limb at the end of each swing phase and in reducing the shock to the knee joint during heel strike when walking. Therefore, it is thought that when quadriceps strength is reduced and the proprioception deteriorates with aging, the knee joint is shocked more strongly and becomes unstable, making it easier for knee joint cartilage to be damaged.[11]

There are some limitations to the present study. One is the small sample size available for comparisons among women in their sixties. We had 52% power to detect a 13% difference in the cross-sectional area of the quadriceps between those with and without knee OA. Almost 25% difference between the two groups would have been required to provide more than 80% power.

The second limitation is that knee alignment, proprioception, bone density, and genetic factors, among others are well-recognized risk factors for knee OA,[23,25] but we did not investigate these factors. If they were included in the calculation of logistic regression, the adjusted odds ratio of muscle mass for incident radiographic knee OA might have been influenced.

The third limitation is that because the present study is a cross-sectional study calculating a predictive value of each independent variable to incident knee OA may not be suitable. However, characteristics of subjects between those in their thirties and those in their sixties, or between those in their sixties with or without incident knee OA were similar. Therefore, we propose that age-related quadriceps-dominant muscle atrophy (i.e., the H/Q ratio) may have predictive value for incident knee OA.

Conclusions

We examined the changes in body composition with aging and the association between age-related muscle atrophy around the knee joint and incident radiographic knee OA in women. The cross-sectional areas of the muscles were smaller in the women in their sixties compared with those in their thirties, and the areas of intermuscular fat tissue were greater among those in their sixties. The degree of reduction in the cross-sectional area of each muscle group between women in their thirties and those in their sixties was greatest in the quadriceps. Moreover, among the women in their sixties the mean cross-sectional area of the quadriceps among those with incident knee OA was significantly smaller than that among the women without knee OA, and the risk of incident knee OA had significantly increased among women with a higher hamstrings/quadriceps cross-sectional area ratio. These results suggest the possibility that the age-related quadriceps-dominant muscle atrophy may play a role in the pathogenesis of knee OA.

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