



# The relationship between body composition and knee osteoarthritis in postmenopausal women

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## ABSTRACT

**Objectives:** The aim of this study was to examine the relationship between the body composition measures and knee osteoarthritis (OA) in postmenopausal women to determine whether the fat mass or the lean mass was closely associated with knee OA.

**Patients and methods:** This retrospective, cross-sectional study included a total of 212 postmenopausal women (mean age 59.9±6.2 years; range, 46 to 76 years). Descriptive characteristics were recorded and height was measured using a stadiometer. Body weight, fat mass, and lean mass were estimated using bioelectrical impedance analysis. X-rays of the knees were obtained. Knee OA was radiographically diagnosed according to the Kellgren-Lawrence criteria. Based on the radiographic knee OA diagnosis the women were divided into two groups. Logistic regression analyses were used to examine the associations between the body composition measures and knee OA.

**Results:** Knee OA was present in 117 women. Body Mass Index, body weight, fat mass, and lean mass were all significantly associated with knee OA after adjusting for confounding factors such as age, height, and physical activity ( $p<0.001$ ). When assessed together with lean mass in a multivariate regression model, fat mass was closely and significantly found to be related to knee OA, compared to lean mass ( $p<0.001$ , OR: 1.17). Furthermore the fat mass/lean mass ratio was positively associated with knee OA ( $p<0.001$ ).

**Conclusion:** In postmenopausal women body weight was significantly and positively associated with knee OA and among the components that constitute body weight, fat mass was closely and significantly associated with knee OA compared to lean mass. This result suggests that the relationship between obesity and knee OA is mainly based on the fat mass, and supports the importance of systemic metabolic effects of adiposity in this relationship.

**Keywords:** Body composition; fat mass; knee osteoarthritis; lean mass; postmenopausal women.

Knee osteoarthritis (OA) is a common and disabling condition in the middle-aged adults and elderly and its prevalence has been growing with the increasing age of the population.<sup>[1,2]</sup> Obesity is a well-known risk factor for knee OA. Increased Body Mass Index (BMI) is associated with an increased risk of radiographic and clinical knee OA, particularly in women.<sup>[3]</sup> Although there is an evident relationship between obesity and knee OA, the exact mechanism of this relationship is still unclear.

Biomechanical impact of increased body weight is considered to have an important role in this relationship.<sup>[4]</sup> Being overweight is associated with the excess load and forces across a weight-bearing joint that can cause a damaged joint tissue.<sup>[5]</sup> However, obesity

is also associated with OA of non-weight-bearing joints such as joints of hand<sup>[6]</sup> which suggests that the relationship between OA and obesity may not be explained only by biomechanical stress. Body weight is composed of three components mainly; fat mass, lean mass, and bone mass. Recent studies have shown that fat mass and fat percentage are significantly associated with knee OA and knee cartilage defects in women.<sup>[7,8]</sup> However some other studies have demonstrated no such association.<sup>[9,10]</sup> In addition, skeletal muscle mass, a surrogate of lean mass, has been reported to be positively associated with knee OA.<sup>[11]</sup>

Body composition changes in women with aging and menopausal status even in the absence of a alteration in body weight. Fat mass increases and

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lean mass decreases with aging, and there is a decline of lean mass with menopause.<sup>[12,13]</sup> The incidence and severity of OA is higher in women, and more severe knee OA are seen after the menopause.<sup>[14,15]</sup> A better understanding of the relationship between the body composition and knee OA, particularly in postmenopausal women, would be beneficial to elucidate the interaction between the obesity and knee OA. However, there is a lack of data evaluating the relationship between the body composition measures and knee OA in postmenopausal women.

In this study, we, therefore, aimed to investigate the relationship between the body composition and knee OA in a sample of Turkish postmenopausal women to determine whether the fat mass or the lean mass was closely associated with knee OA.

## PATIENTS AND METHODS

This retrospective, cross-sectional study included data of 212 postmenopausal women (mean age 59.9±6.2 years; range, 46 to 76 years) who were admitted to our outpatient clinics between October 2014 and January 2016. Women who underwent radiographic examination of the knees, body composition measurements by bioelectric impedance analysis, experienced natural menopause for at least one year and, completed questionnaires on demographic and clinical data were eligible for the study. Those with comorbidities which could affect the body composition, such as concurrent inflammatory rheumatic diseases, cardiovascular, pulmonary, renal, endocrine, neurologic disorders, malignancies, also those who had previously been or were presently taking drugs such as estrogen, glucocorticoids, thyroid hormones, those who were on diet or losing or gaining weight, and those who were having muscle-strengthening exercises were excluded. The study protocol was approved by the local Ethics Committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Demographic and clinical data including physical activity levels were recorded. Women participating in physical activity such as walking, running, and cycling for more than 20 min and three days a week were considered physically active. Anthropometric measurements were obtained. Body composition measurements were performed through bioelectric impedance analysis (Body Composition Analyzer MC-780, Tanita Corp., Tokyo, Japan), according to the manufacturer's instructions. Body weight (kg), fat mass (kg), and lean mass (kg) were measured. Height was measured to the nearest 0.1 cm. Body Mass Index

was calculated as the body weight divided by the square of the height (kg/m<sup>2</sup>).

Radiographic assessment was done by analyzing the bilateral weight-bearing anteroposterior and lateral plain radiographs of the participants. The radiographic changes related to OA were evaluated by two clinicians according to the Kellgren-Lawrence grading system.<sup>[16]</sup> Participants were defined as having radiographic knee OA, when they had grade ≥2 radiography. Participants who had knee joint replacement and insufficient quality images were excluded. The women were divided into two groups according to the radiographic knee OA diagnosis; women with and without knee OA.

## Statistical analyses

Statistical analysis was performed using the IBM SPSS version 23.0 software (IBM Corp., Armonk, NY, USA). Descriptive statistics were presented in mean ± standard deviation (SD), and frequency, as appropriate. Univariate and multivariate logistic regression analyses were used to assess the relationship between body composition measures and knee OA. The presence/absence of knee OA was used as the outcome measure. Body weight, BMI, fat mass, lean mass, and fat/lean mass ratio were independent variables. In the univariate analyses, the relationship between knee OA and independent variables were assessed. In the multivariate analyses, independent variables were adjusted for the potential confounders of age, height, and physical activity, where appropriate. A further multivariate analysis was also performed including both fat mass and lean mass to evaluate the independent association of these variables with knee OA. Enter method was used and maximum five independent variables were entered to the models which provides requirement to perform logistic regression analyses. The overall

**Table 1.** Characteristics of the study population

|                          | n   | %    | Mean±SD   |
|--------------------------|-----|------|-----------|
| Age (year)               |     |      | 59.9±6.2  |
| Weight (kg)              |     |      | 70.5±11.7 |
| Height (cm)              |     |      | 155.0±5.1 |
| BMI (kg/m <sup>2</sup> ) |     |      | 29.4±4.7  |
| Fat mass (kg)            |     |      | 26.4±7.5  |
| Lean mass (kg)           |     |      | 41.9±4.9  |
| Fat mass / lean mass     |     |      | 0.6±0.1   |
| Knee osteoarthritis      |     |      |           |
| None                     | 95  | 45   |           |
| Osteoarthritis           | 117 | 55   |           |
| Physical activity level  |     |      |           |
| Non-active               | 131 | 61.8 |           |
| Active                   | 81  | 38.2 |           |

SD: Standard deviation; BMI: Body Mass Index;

**Table 2.** Relationship between the body composition measures and knee osteoarthritis

|                          | Univariate analysis |          | Multivariate analysis* |          | Multivariate analysis** |          |
|--------------------------|---------------------|----------|------------------------|----------|-------------------------|----------|
|                          | OR (95% CI)         | <i>p</i> | OR (95% CI)            | <i>p</i> | OR (95% CI)             | <i>p</i> |
| Weight (kg)              | 1.13 (1.09 to 1.17) | <0.001   | 1.14 (1.10 to 1.18)    | <0.001   |                         |          |
| BMI (kg/m <sup>2</sup> ) | 1.36 (1.24 to 1.48) | <0.001   | 1.34 (1.22 to 1.47)    | <0.001   |                         |          |
| Fat mass (kg)            | 1.21 (1.15 to 1.29) | <0.001   | 1.22 (1.15 to 1.30)    | <0.001   | 1.17 (1.08 to 1.26)     | <0.001   |
| Lean mass (kg)           | 1.23 (1.14 to 1.33) | <0.001   | 1.31 (1.20 to 1.44)    | <0.001   | 1.12 (0.99 to 1.25)     | 0.07     |
| Fat mass / lean mass     | 1.10 (1.06 to 1.13) | <0.001   | 1.09 (1.06 to 1.12)    | <0.001   |                         |          |

\* Odds ratio of knee osteoarthritis per unit increase in the body composition measures after adjustment for age, height, and physical activity levels (age and physical activity levels for BMI); \*\* Odds ratio of knee osteoarthritis per unit increase in fat mass and lean mass after adjustment for lean mass and fat mass including age, height, and physical activity levels; OR: Odds ratio; CI: Confidence interval; BMI: Body Mass Index;

classification of the models was between 67.9 and 72.2% for the univariate analyses, and between 72.6 and 75.5% for the multivariate analyses. The strength of the relationship between independent variables and knee OA was expressed in odds ratios (OR) with 95% confidence interval (CI) per unit increase in each variable. A *p* value of <0.05 was considered statistically significant.

## RESULTS

Radiographic knee OA was present in 117 women. Table 1 presents the characteristics of the study population including age, weight, height, BMI, fat mass, lean mass, fat mass/lean mass ratio, and physical activity levels.

The logistic regression models for assessing the associations between body composition measures and knee OA are presented in Table 2. In the univariate analysis, body weight, BMI, fat mass, lean mass, and fat mass/lean mass ratio were all significantly and positively associated with knee OA. In the multivariate analysis which was adjusted for age, height, and physical activity level, all variables remained significantly associated. After adjustment for fat mass and lean mass together, fat mass remained significantly and positively associated with knee OA (*p*<0.001), while lean mass was not found to be significantly associated with knee OA (*p*>0.05).

## DISCUSSION

In the present study, we investigated the relationship between body composition and knee OA in postmenopausal women. Body weight was positively associated with knee OA. Fat mass and lean mass, two components of body weight, were also significantly associated with knee OA; however, when adjusted together, fat mass became significantly and more closely associated with knee OA, compared to lean

mass. In addition, a high fat mass/lean mass ratio was found unfavorable for knee OA.

Our results support the importance of adipose tissue in the relationship between body composition and knee OA. The impact of obesity and excessive weight on knee OA are considered to occur due to different mechanisms such as; weight-bearing effects with excessive load on the knee joints, weight independent systemic metabolic effects or a combination of both. As fat mass remained positively and was significantly associated with knee OA after adjustment with lean mass and the significant association of lean mass with knee OA disappeared after adjustment with fat mass, we could argue that the relationship between obesity and knee OA is based on the fat mass in postmenopausal women and the systemic metabolic effects of adipose tissue seems to be more important in this relationship. If weight-bearing effects were the main factor, we would expect a similar impact of lean mass.

The findings of the study are in consistent with the recent studies evaluating the relationship between body composition and knee OA. Berry et al.<sup>[17]</sup> reported a positive association between fat mass and bone marrow edema and suggested that inflammatory factors released from the adipose tissue might contribute to the vascular changes seen in these lesions. In healthy adults, a negative effect of fat mass was found on knee cartilage properties and fat mass was considered to be an important factor in the development and progression of cartilage defects.<sup>[18]</sup> Visser et al.<sup>[7]</sup> reported fat mass and low skeletal muscle percentage to be significantly associated with knee OA in women, suggesting that metabolic syndrome and systemic inflammation seen in individuals with greater adiposity may cause it.

There is also growing evidence concerning the metabolic link between adiposity and OA which may clarify the possible causes of our result. Adipose tissue is defined as an active metabolic and endocrine

organ. It releases adipokines and also cytokines like interleukin-6 (IL-6) and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) which potentially causes low-level systemic inflammation in excess body fat.<sup>[19,20]</sup> A number of adipokines have been detected to mediate inflammatory effects and have catabolic roles in the pathophysiology of OA.<sup>[21,22]</sup> Serum leptin levels were associated with MRI assessed cartilage defects and knee joint damage in middle-aged women.<sup>[23]</sup> Leptin has been shown to increase the production of catabolic enzymes and proinflammatory mediators, such as matrix metalloproteinases, nitric oxide, IL-6, IL-8, and prostaglandin E2 in the cartilage.<sup>[24,25]</sup> Visfatin, another adipokine, was found significantly greater in knee osteoarthritic patients, compared to the control individuals, particularly in advanced knee OA grades and was found to be positively correlated with degradation biomarkers of OA.<sup>[26]</sup> Increased serum adiponectin were seen in female patients with erosive OA.<sup>[27]</sup>

Our study also showed that a high fat mass/lean mass ratio was unfavorable for knee OA in postmenopausal women. Weight loss is highly recommended for the non-surgical management of knee OA.<sup>[28]</sup> It may be more beneficial, if it originates from fat mass in postmenopausal women. Rehabilitative approaches that provide losing fat mass and maintaining or improving muscle mass in overweight and obese postmenopausal women seems to be protective for the risk of knee OA. In a study evaluating weight loss, exercise and physical function in obese older adults, a combination of weight loss and exercise which provided more decrease in fat mass, compared to lean mass, resulted in greater improvement in physical function measures.<sup>[29]</sup> Fat mass change was found to be related to symptomatic relief of obese patients with knee OA.<sup>[30]</sup> A greater fat loss was also associated with greater gain in muscle strength and quality in older obese adults with knee OA in a weight loss intervention combined with exercise.<sup>[31]</sup>

Another finding is that, rather than the body weight or BMI, body composition is important in the relationship between obesity and knee OA in women. Obesity is defined by BMI which is calculated by using body weight and height. However, BMI does not differentiate adipose and non-adipose body mass and consider obesity-related characteristics. Individuals with lower body weight would be at a higher risk of OA with an unfavorable body composition.<sup>[32]</sup>

Our study has certain limitations. Cross-sectional design of the study may be insufficient to evaluate the

causal relationship between body composition and knee OA. The body composition differences could have been influenced from knee OA. Longitudinal studies evaluating the relationship between the alteration of body composition and knee OA would be better. In addition, using bioelectric impedance analysis can be considered as a limitation, although it has good correlations with dual-energy X-ray absorptiometry for the assessment of body composition measures.<sup>[33]</sup> As the cohort of this study is the Turkish postmenopausal women, the ethnic differences seen in adiposity and body composition<sup>[34]</sup> would have affect the relationship with knee OA. On the other hand, in evaluating the relationship between the body composition measures and knee OA, we used potential confounders for adjustment such as physical activity, which is known to affect body composition by losing fat mass and maintaining muscle mass which is a surrogate of lean mass.<sup>[35]</sup>

In conclusion this study shows that body weight is significantly and positively associated with knee OA and, among the components that constitute body weight, fat mass is closely and significantly associated with knee OA in postmenopausal women when assessed together with lean mass. This result suggests that the relationship between obesity and knee OA is mainly based on the fat mass, and supports the importance of systemic metabolic effects of adiposity in this relationship. In addition, a high fat mass/lean mass ratio is unfavorable for knee OA. In clinical practice, losing fat mass and maintaining or improving lean mass must be aimed in overweight and obese postmenopausal women to prevent from knee OA. Further studies should aim to elucidate the roles of inflammatory cytokines and adipokines in the development of knee OA and also evaluate the effects of rehabilitative interventions which aim reducing the fat mass and maintaining or improving the lean mass in overweight and obese postmenopausal women to prevent knee OA.

#### **Declaration of conflicting interests**

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