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Original Article

The Relationship Between Sarcopenic Obesity and Knee Osteoarthritis: The SARCOB Study

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Abstract

Background: To investigate whether sarcopenic obesity may contribute to knee osteoarthritis or not.
Methods: In this study, we assessed 140 community-dwelling adult patients. Their demographic data were recorded along with comorbidities. Anterior mid-thigh muscle thickness in the axial plane was measured on the dominant leg using ultrasound midway between the anterior superior iliac spine and the upper end of patella in millimeter. Then, the sonographic thigh adjustment ratio was calculated by dividing this thickness by body mass index. ISarcoPRM algorithm was used for the diagnosis of sarcopenia. Kellgren–Lawrence grading was used for knee osteoarthritis. Functional evaluation was performed using chair stand test, gait speed, and grip strength.
Results: There were 50 patients with knee osteoarthritis and 90 age- and gender-similar control subjects. When compared with controls, anterior thigh muscle thickness, gait speed, and grip strength were found to be similar between the groups, whereas body mass index and chair stand test values were higher in the knee osteoarthritis group (both $P < .05$). In addition, sarcopenic obesity was observed in 12 (13.3%) of control subjects and in 14 (28%) of osteoarthritis patients. When age, gender, exercise, smoking, and body composition type (i.e., nonsarcopenic nonobese, sarcopenic only, obese only, and sarcopenic obesity) were taken into binary logistic regression analyses, only sarcopenic obesity [relative risk ratio = 2.705 (95% CI: 1.079-6.779)] was independently related with the knee osteoarthritis ($P < .05$).
Conclusion: Our preliminary study has shown that neither sarcopenia nor obesity but sarcopenic obesity seems to be independently related to the knee osteoarthritis. Further longitudinal studies with larger samples are required for investigating the effects of obesity and sarcopenia on the development of knee osteoarthritis.
Keywords: Sarcopenia, body composition, ultrasound, muscle weakness, quadriceps

Introduction

Osteoarthritis knee (OA) is a chronic degenerative joint disease characterized by the deterioration of cartilage resulting in pain and functional limitation and is a common cause of disability in older adults.[1] An estimated 10%-15% of people over 60 years of age have some degree of knee OA, with a higher prevalence among women than men.[2] As the aging population size is increasing, the prevalence of knee OA is also on the rise. According to the United Nations, it has been estimated that people aged over 60 years will account for more than 20% of the world's population by 2050.[3] Established risk factors for knee OA include obesity, local trauma, and occupation, while the role of chronic disorders such as sarcopenic obesity, smoking, and sarcopenia is still debatable.[4]

On the other hand, sarcopenia is another important age-related disorder, which is characterized by age-related loss of muscle mass and muscle function, predominantly affecting lower extremity muscles, which have predominantly type II fibers (e.g., gastrocnemius and quadriceps).[5,6] As it is a precursor of adverse outcomes like physical frailty, mobility limitation, disability, increased risk of falls, and even premature death, early recognition of sarcopenia as well as understanding its association with other comorbid diseases are of paramount importance.[7]

Individuals with knee OA may be at a higher risk of sarcopenic obesity,[8] which is a co-occurrence of high adiposity (increase in subcutaneous and intramuscular fat) and sarcopenia.[9,10] The vicious cycle of pain, inactivity and muscle loss results in adiposity and/or obesity and aggravation of functional decline.

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To this end, our study aimed at investigating the relationship between the type of body composition (i.e., obesity only, sarcopenia only, or sarcopenic obesity) and knee OA. It is noteworthy to understand whether knee OA is related to loss of anterior thigh muscle mass/function and obesity.

Material and Methods

In this cross-sectional, case–control study, we recruited 50 consecutive patients with knee OA (15 males, 35 females) and 90 age- and gender-matched control subjects (27 males and 63 females) from the outpatient clinic of physical and rehabilitation medicine. The subjects of both genders aged ≥45 years were included in the study, having knee OA clinically and radiologically. Subjects having any neurologic disorders, peripheral neuropathy, depression or other psychiatric disorder, history of major orthopedic surgery, rheumatologic diseases other than knee OA, malignancy, and advanced organ failure/transplant were excluded. All participants were informed about the study protocol and consent was taken to participate in this study, after the local Ethics Committee of Combined Military Hospital Quetta, Pakistan approved the study (protocol no.13/A-22).

Age, weight, height, body mass index (BMI) and waist/hip circumferences, exercise/smoking habits, and chronic comorbidities including hypertension, diabetes mellitus (DM), and obesity were noted. Obesity was considered when BMI is ≥30 kg/m.[2] The diagnosis of symptomatic radiographic knee OA was defined according to the American College of Rheumatology classification criteria.[11] Kellgren–Lawrence (K–L) grading system was applied to the knee radiographs only in the patient group.[12]

Ultrasonographic Measurements

Using 5-12 MHz linear probe (Esaote MyLab 20, Italy), anterior mid-thigh muscle thickness was measured from the anterior superior iliac spine to the upper pole of the patella on the dominant side while subjects lied in the supine position using an abundant amount of gel. The muscle thickness was measured in the axial plane between periosteum of the femur and outer fascial layer of rectus femoris. Then, the anterior thigh muscle thickness (mm) was divided by BMI to calculate sonographic thigh adjustment ratio (STAR).[5]

Main Points

- The measurements of muscles rich in type II fibers (i.e., quadriceps), which are lost early and more rapidly in sarcopenia seems to affect the development of osteoarthritis (OA) in knees.
- Sarcopenic obesity seems to be independently related with the knee OA.
- Further longitudinal studies in larger samples are required for investigating the effects of deteriorated body composition (i.e., sarcopenic obesity) on knee OA.

Functional Evaluations

Grip strength was measured with a hand dynamometer (Preston hand dynamometer, New York, NY, USA). Subjects were instructed to sit with adducted shoulders and 90° flexed elbow. Three repeated measurements were taken from the dominant side and the maximum value was recorded for the analyses. Chair stand test (CST) was performed while subjects were asked to stand up and sit down from a chair without armrest for 5 times as quick as possible, with their arms crossed over their chests. For gait speed, subjects were asked to walk with their usual speed covering a 6 m path. Three measurements were recorded and median values were taken for the analyses.[3] All clinical and ultrasonographic measurements were performed by the same physiatrist (SR) who is an expert in performing musculoskeletal US with more than 8 years of experience.

Diagnosis of Sarcopenia

The diagnosis of sarcopenia was established if low muscle mass (i.e., STAR values <1.4 for males and <1.0 for females) was present along with low grip strength [<32 kg (males) and <19 kg (females)] and/or increased CST time (≥12 s) using ISarcoPRM algorithm.[6] Sarcopenic obesity was defined as sarcopenia in combination with obesity (BMI ≥30 kg/m^2).

Statistical Analysis

Statistical analysis was performed by using Statistical Package for Social Sciences (SPSS) version 21.0 (IBM SPSS Corp.; Armonk, NY, USA). Numerical variables are shown as mean ± SD and categorical variables as numbers and percentages (%). Normal distribution was measured by Kolmogorov–Smirnov test. Mean value comparisons for numerical variables were tested by Student's *t*-test or Mann–Whitney *U* test, and categorical variables were analyzed by Chi-square or Fisher's exact tests (where appropriate). To investigate the relationship between the presence of knee OA and the potential clinical/confounding variables (age, gender, smoking and exercise statuses and presence of obesity only and sarcopenic only, and the presence of sarcopenic obesity), binary logistic regression analysis was performed with backward selection. Since there was collinearity between BMI and body composition type, each was used in separate models. The most parsimonious and statistically significant models were presented as the final models. The Hosmer–Lemeshow test was used to check the goodness-of-the-fit test for logistic regression analyses. Statistical significance was set at $P < .05$.

Results

Comparison of the clinical data between patients with knee OA (median K–L grade of 2 on both sides) and control subjects are shown in Table 1. Fifty consecutive patients with knee OA and 90 age- and gender-similar control subjects were taken. When compared with control subjects, grip strength, gait speed, anterior thigh muscle thickness, and STAR values were found to be similar between the groups; in contrast, BMI and CST values were on the higher side in the knee OA group (both $P < .05$). In addition, sarcopenic obesity was observed in 12 (13.3%) control subjects and in 14 (28%) knee OA patients.

When age, gender, exercise and smoking habits, and BMI or body composition type (i.e., nonsarcopenic nonobese, sarcopenic only, obese only, and sarcopenic obesity) were taken into binary logistic regression analyses, while we found no independent relationship between BMI and knee OA in the former analysis, we found that the presence of sarcopenic obesity [RR = 2.705 (95% CI: 1.079-6.779)] was independently related with the development of knee OA in the latter with $P < .05$ (Table 2).

Discussion

In this study, we have shown that sarcopenic obesity was observed more commonly in patients with knee OA as compared to well-matched controls. In addition, among several clinical factors, neither sarcopenia nor obesity but sarcopenic obesity was found to be independently related to the development of knee OA.

Sarcopenia and knee OA are age-related disorders, together with several others like obesity, hypertension, dyslipidemia, insulin resistance, and metabolic syndrome.[13] Herewith, the most important one of those as regards knee OA seems to be obesity, particularly sarcopenic obesity, which may augment each other. Current literature still lacks any clear association between loss of muscle mass and knee OA, leading to a lack of uniformity in measuring this most important site (thigh) in the evaluation of sarcopenia.[14-16]

Table 1. Comparison of the Clinical Characteristics Between the Groups (N = 140)

	Knee OA (N = 50)	Controls (N = 90)	*P*
Age (year)	58.2 ± 8.6	56.1 ± 9.2	.765
Gender, male	15 (30.0)	27 (30.0)	1.000
Weight (kg)	75.4 ± 9.9	73.5 ± 10.6	.323
Height (m)	1.59 ± 0.06	1.61 ± 0.08	.132
BMI (kg/m^2)	29.9 ± 4.1	28.4 ± 4.8	.016
Exercise	8 (16.0)	19 (21.1)	.463
Smoking	3 (6.0)	5 (5.6)	.914
Circumference (cm)			
Waist	108.4 ± 9.9	107.4 ± 10.2	.477
Hip	108.1 ± 10.3	108.5 ± 9.6	.788
Comorbid disease			
Hypertension	7 (14.0)	15 (16.7)	.678
Diabetes mellitus	5 (10.0)	9 (10.0)	1.000
Anterior thigh MT (mm)	36.5 ± 6.5	35.5±5.7	.410
Functional test			
Grip strength (kg)	16.2 ± 7.2	17.2 ± 6.9	0.285
CST (s)	16.6 ± 4.2	15.3 ± 3.6	0.031
Gait speed (m/s)	1.03 ± 0.31	0.95 ± 0.19	0.090
Body composition type			0.189
Nonsarcopenic nonobese	22 (44.0)	51 (56.7)	
Sarcopenic only	5 (10.0)	9 (10.0)	
Obese only	9 (18.0)	18 (20.0)	
Sarcopenic obese	14 (28.0)	12 (13.3)	

Data are given as mean ± SD, or n (%). Statistically significant variables are shown as bold.
BMI, body mass index; CST, chair stand test; MT, muscle thickness; OA, osteoarthritis; s, second.

To begin with, sarcopenia is a site-specific disorder, with temporal and topographic variation in its distribution, and does not progress at the same rate in all regions.[17] There is evidence of heterogeneity in loss of muscle mass, predominantly affecting the muscle groups rich in type II fibers (i.e., anterior thigh and abdominal muscles) at a faster rate. Whereas the muscles dominantly having type I fibers (e.g., multifidus, tibialis anterior) or equal fiber distribution (e.g., anterior forearm muscles) are not effected by aging at the same rate. Herein, the anterior thigh region has also a particularly important relationship with knee OA. It is known that anterior thigh muscle group (i.e., quadriceps, rectus femoris, vastus medialis, vastus intermedius, and vastus lateralis) is affected in knee OA and its wasting plays a major role in the development and progression of degenerative changes in the knee joint. In other words, decreased knee extensor strength can cause knee OA and vice versa.

Table 2. Binary Logistic Regression Analyses Between Clinical Variables and Knee Osteoarthritis (N = 140)

Variables*	RR	95% CI	*P*
Nonsarcopenic nonobese	–	–	–
Sarcopenic only	1.288	0.387-4.285	.680
Obese only	1.159	0.451-2.978	.759
Sarcopenic obese	2.705	1.079-6.779	.034

CI, confidence interval; RR, relative risk ratio.
*Age, gender (female vs. male), smoking and exercise statuses, and body composition type (according to nonsarcopenic and nonobeses) were included in the analyses.
Statistically significant variables are shown as bold.

Muscles play a major role in joint function/stability during movements and atrophy/loss of muscle mass due to disuse, sedentary lifestyle, smoking or vitamin D deficiency may lead to the development of chronic degenerative joint changes. One study has shown that low skeletal muscle mass (measured by dual-energy x-ray absorptiometry) in the lower limbs is independently associated with knee OA.[18] In this regard, anterior thigh muscle mass is important from both perspectives, i.e., sarcopenia and knee OA, and it is further complicated by the presence of sarcopenic obesity and age-related other chronic comorbid diseases. In another study, Frontera et al[19] found a loss in knee extensor strength (24%-30%) and loss in quadriceps muscle cross-sectional area (16%) over a duration of 12 years. In case of quadriceps weakness, the patient's presentation ranges from difficulty in squatting, climbing upstairs and going downstairs, standing from a chair, and optimal/fast walking and maintaining balance.[20] Needless to say, quadriceps weakness can therefore be an important determinant of pain, impaired function, and disability in knee OA.[21] Herein, studies have also shown that there is a greater risk of falls secondary to a decrease in lower limb lean mass which is frequent in knee OA patients.[22-24]

It is still debatable whether muscle changes precede knee OA, or vice versa. There is growing evidence that low muscle quality and quantity are important contributors to knee OA, apart from mechanical influences.[22] The joint stability and health are effected by progressive loss of periarticular muscle mass/function.[21] On the contrary, pain, reduced movements, and functional decline secondary to knee OA can also result in the reduction of muscle mass and strength. These interconnected pathophysiological processes are further complicated by the presence of obesity. In addition, the combination of knee joint overloading, sarcopenia, and increased body mass with aging leads to muscle failure involving quadriceps, which can accelerate the development and progression of knee OA.[25] A recent study has shown that increased risk of knee OA was associated with sarcopenic obesity rather than sarcopenia alone.[26] The presence of the particular phenotype in which there is low skeletal muscle mass along with high adiposity has been described in patients with knee OA.[27-29] The combination of sarcopenia and obesity (i.e., sarcopenic obesity) is associated with impaired physical function and quality of life in patients with advanced knee OA.[30] Nonetheless, this shows compelling evidence that sarcopenia and/or obesity is present in knee OA but poorly

recognized/not recognized at all as sarcopenic obesity. This is very important to consider while assessing one of the abovementioned disorders.

In this study, we did not find any independent relationship between DM/hypertension and knee OA. Likewise, one study reported an inverse association between thigh circumference and cardiovascular mortality. [31] Age-related chronic metabolic disorders, such as hypertension, obesity, insulin resistance, DM, and dyslipidemia can overactivate the classical renin-angiotensin system (RAS) pathway resulting in increased angiotensin-II levels, which may ultimately lead to the development of sarcopenia.[12,32] It has been shown that classical RAS activity can result in deleterious effects not only on the cardiovascular system but also on the neuromusculoskeletal systems by acting on the protein turnover, cellular apoptosis, and collagen metabolism disrupting the balance between anabolic and catabolic processes.[12] All these metabolic processes are widely modulated by the RAS axes, whereby the classical axis induces protein degradation and the non-classical axis stimulates the anabolic processes of muscle protein synthesis and inhibits apoptosis.[33] In our study, possibly due to small sample size including relatively healthier and younger adults, associations regarding variables that might overactivate RAS such as exercise, smoking, and presence of DM and hypertension, and obesity/sarcopenia alone might have not reached statistical significance.

With growing awareness and global efforts to bring uniform guidelines for the definition and assessment of sarcopenia, and to slow down or even reverse its deleterious effects on the aging population, all aspects of sarcopenia need to be studied carefully. Of note, the burden of knee OA is physical, psychological, and socioeconomic and so is the case with sarcopenia.[34,35]

Limitations

This study had some drawbacks. First, it was a cross-sectional study including a small sample size. In addition, we could have not performed gender-specific analyses either. Second, we used low grip strength and/or high duration of CST for evaluating low muscle function in sarcopenia, but knee joint pain might be a confounding factor for evaluating these parameters. Lastly, our study included relatively healthier middle-aged and older adults in whom obesity and sarcopenia alone in knee OA might be less frequent. Nonetheless, our findings are important and worth discussing.

Our preliminary study has shown that sarcopenic obesity seems to be an independent factor in the development of knee OA. Definitely, further longitudinal studies in larger samples are required to investigate and study the effects of deteriorated body composition (i.e., sarcopenic obesity) on knee OA.[13]

Ethics Committee Approval: This study was approved by Ethics Committee of Combined Military Hospital, Quetta, Pakistan University (Approval No: 13/A-22, Date: January 19, 2022).

Informed Consent: Written informed consent was obtained from the participants who agreed to take part in the study.

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