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Quadriceps Muscle Atrophy in Patients with Varus Gonarthrosis

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Abstract

Objective: This study aimed to investigate which section of the quadriceps muscle has more evident muscle atrophy, in knees with gonarthrosis and genu varum.

Methods: In patients operated on because of gonarthrosis and varus alignment, intraoperative muscle biopsies are taken from the vastus lateralis (VL), vastus medialis (VM), and vastus intermedius (VI). The materials obtained were evaluated for connective tissue and fatty tissue and the ratio of atrophic muscle cells. The statistical evaluation is used to determine the relationship between atrophy and the varus angle.

Results: The mean varus angle is 11.7°. The results showed that the amounts of connective tissue in the VM muscle was significantly greater than in the VL and VI muscles (p=0.018). Additionally, no difference is determined between VM, VI, and VL with respect to the ratio of atrophic muscle cells to total muscle cells. The ratio of fatty tissue in the VL muscle was found to be statistically significantly greater in females than in males (p<0.05). The connective tissue was generally determined at a significantly higher rate in the VM muscle than in the VL and VI muscles.

Conclusion: With an increase in the varus angle of the knee, atrophy is seen to increase in the VM and VI muscles, and is more evident than atrophy in the VL muscle. Therefore, strengthening exercises directed at the VM for patients varus knees would be useful in the prevention of gonarthrosis.

Keywords: Gonarthrosis, atrophy, quadriceps weakness, knee

INTRODUCTION

The presence of osteoarthritis in the knee constitutes a significant morbidity. Several factors impact the development of osteoarthritis, but the etiology is not yet been fully understood. Knee alignment is seen as a factor affecting osteoarthritis development. The natural normal knee joint alignment is 2°-3° of varus compared with the mechanical axis. Changes in knee alignment cause changes in lateral and medial weight-bearing (1,2).

In knees with normal alignment, 60%-80% of compressive loads passing from the knee pass immediately medial of the midline. In a varus knee, more of the load is transferred from the inner compartment. The adduction moment forces the knee into varus and therefore causes compression in the medial compartment while walking because the grand reaction force vector passes from the medial of the knee joint (2). A greater adduction moment causes greater loading in the medial compartment. Sufficient quadriceps strength in healthy knees has a protective effect against the development of osteoarthritis.

The function of the muscles around the knee is to create movement, absorb loads, and provide dynamic stability of the joint (3). The weakness of the quadriceps muscle increases the load on the knee joint, causing pain and function loss in patients with osteoarthritis in the knee joint. There is up to 40% more weakness in the quadriceps muscle of patients with osteoarthritis compared with healthy individuals (4). A reduction in proprioception or sensory innervation of the knee joint with

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advancing age causes an imbalance in the activity of the muscles stabilizing the joint, and this plays a role in the development of osteoarthrosis (2). Structural changes in the muscles added to this imbalance in muscle function can inhibit the protective effect of the muscle system and thus contribute to the development of osteoarthrosis (2). Muscle weakness is a significant additional risk factor in patients susceptible to the development and progression of knee osteoarthrosis, particularly those with a misalignment of the lower extremity.

This study determines the presence of atrophy by histopathological examitation of the quadriceps muscle and investigate the relationship with the varus angle and which section of the quadriceps muscle affected the most in patients with varus knee who have undergone surgery for gonarthrosis.

METHODS

Approval for the study was obtained from the Giresun University Faculty of Medicine Local Research Ethics Committee (decision date: 21.06.2017, number of decisions: 8). Informed written consent was obtained from all patients.

The study included 32 patients who applied with total knee prosthesis for the diagnosis of primary gonarthrosis. All the patients who presented with complaints of severe knee pain were aged >50 years, had primary gonarthrosis and genu varum, and agreed to participate in the study.

The overall anatomic tibiofemoral angle was measured on standard length, standing anteroposterior knee radiographs measuring 14×17 in. The patients included in the study were diagnosed with grade 4 osteoarthritis according to the Kellgren-Lawrence classification on the semi-flexed radiographs and underwent surgical intervention (5).

Patients were excluded from the study if they had valgus knee alignment, inability to walk, any neurological problems, alcohol dependence, arthritis in the hip or knee, gonarthrosis that developed secondary to trauma, infection or inflammatory disease, a history of fracture to the same lower extremity, a history of surgery to the lower extremities, limb length discrepancy, hip dysplasia, diabetes mellitus, loss of muscle strength, Lasegue and reverse Lasegue positivity, or any neurological disease.

Biopsy

Surgery was performed in all patients using an anterior midline incision and medial parapatellar arthrotomy. From the proximal of the skin incision, the muscle fibers of the vastus lateralis (VL), vastus intermedius (VI), and vastus medialis (VM) obliquus are reached. Muscle fiber biopsies, 1×0.5 cm in size, were obtained from all patients at approximately 1 cm proximal to the musculotendinous junction.

Histopathological Evaluation

The pieces of muscle tissue obtained were fixed in 10% buffered formalin, then embedded in paraffin blocks in a manner that allows us to take sections both horizontally and transversely. Slices of 4 μm thickness were cut with a microtome from the paraffin blocks, then stained with hematoxylin and eosin (HE). The HE-stained specimens were evaluated under a light microscope using a pathology specialist (IC) and the results were recorded.

The evaluation criteria were as follows:

1- The presence and amount of fatty tissue within the muscle tissue (Figure 1),

2 - The presence and amount of connective tissue within the muscle tissue (Figure 2),

3- Ratio of atrophic muscle fibers to all muscle fibers (evaluated in 3 magnification areas).

No histomorphological atrophic muscle scoring system can be found in the literature. Therefore, for this study, reference was taken from the radiological classification of rotator cuff muscle fat degeneration of Goutallier et al. (6), and a scoring system was formed for the histomorphological evaluation of the presence of fatty tissue and fibrosis. Thus, the presence of fatty tissue and fibrosis within muscle tissue were evaluated separately and scored as follows:

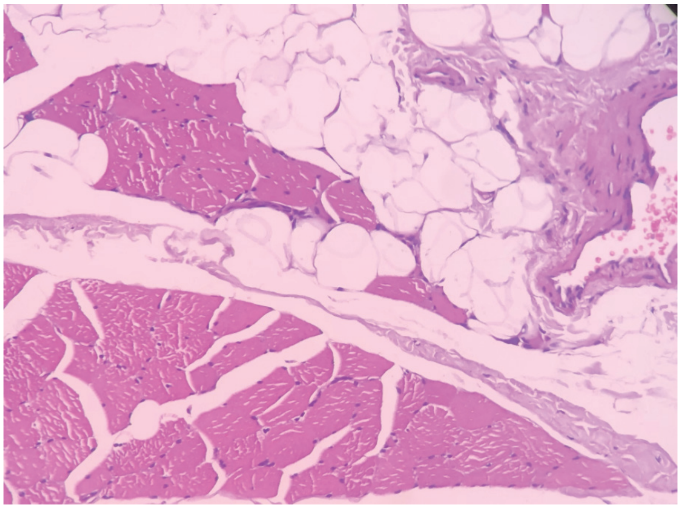

Figure 1. Atrophic muscle tissue with increased fat and connective tissue (hematoxylin and eosin stain, 10x100)

Score 0: Normal muscle structure,

Score 1: Occasional fatty or connective tissue,

Score 2: <50% fatty tissue or fibrosis,

Score 3: 50% fatty tissue or fibrosis,

Score 4: >50% fatty tissue or fibrosis.

The ratio was determined in each specimen by counting the total muscle fibers and number of atrophic muscle fibers under 3 separate magnification areas (the number of atrophic muscle fibers/the total number of muscle fibers). The section in which atrophy was observed to be most intense, the ratio was determined in each specimen.

Statistical Analysis

Data obtained in the study were analyzed statistically using SPSS 22.0 software. Descriptive statistics of the data were stated as mean ± standard deviation, median, minimum and maximum values, number (n) and percentage (%). The conformity of the data to a normal distribution was assessed with the Kolmogorov-Smirnov test. The Mann-Whitney U test was used in the evaluation of quantitative data. In the evaluation of dependent qualitative data, the Cochrans c-test and the McNemar test were used, and in the analysis of dependent quantitative data, the Friedman test was used. The chi-square test was applied in the analysis of dependent qualitative data and when chi-square test conditions were not met, the Fischer's exact test was applied. In the determination of correlations, Spearman's correlation analysis was performed. A value of $p<0.05$ was set as statistically significant.

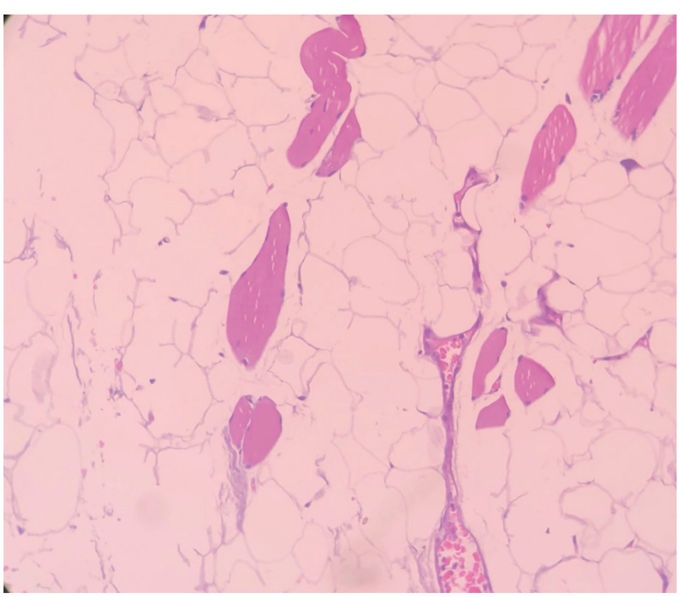

Figure 2. Atrophic muscle fibers in adipose tissue (hematoxylin and eosin stain, 10x100)

RESULTS

The evaluation was made of 32 patients comprising 5 (15.6%) males and 27 (84.4%) females with a mean age of 67.62 years (range, 53-77 years). Surgery was performed on the right knee in 15 (46.9%) patients and the left knee in 17 (53.1%). All the patients were determined by grade 4 gonarthrosis according to the Kellgren-Lawrence classification (25). The mean lower extremity alignment of all patients was determined as 11.666° (range, 4°-22°) genu varum.

Atrophic Muscle Cell Ratio

No significant difference was determined in the atrophic muscle cell ratio of the VL, VM ve VI ($p>0.05$) (Table 1). No significant correlation was observed between age and gender and the atrophic muscle cell ratios of the VM, VL, and VI muscles ($p>0.05$). No significant correlation was determined between the varus angle and the atrophic muscle cell ratio of the VL muscle. A statistically significant positive correlation was determined between the varus angle and the atrophic muscle cell ratio of the VM and VI muscles ($p<0.05$) (Table 2).

Fatty Tissue

No significant difference was observed between the fatty tissue results of the VM, VL, and VI muscles ($p>0.05$). Fatty tissue in the VL muscle was determined at a statistically significantly higher rate in females ($p<0.05$). No significant difference was observed between males and females with respect to the fatty tissue results of the VM and VI muscles ($p>0.05$).

Connective Tissue

Generally, the connective tissue in the VM muscle was determined at a significantly greater rate than in the VL and VI muscles ($p=0.018$).

Table 1. The ratio of atrophic muscle cells to healthy muscle cells

Muscle from which biopsy was taken	Maximum-minimum	Median	Mean ± SD
Vastus lateralis	5.3%-29.6%	17.2%	16.8%±5.6%
Vastus medialis	5.0%-25.4%	18.0%	17.7%±5.2%
Vastus internedius	4.1%-26.7%	16.3%	16.5%±5.5%

SD: Standard deviation

Table 2. Correlations between the varus angle and the atrophic cell ratio

		Atrophic muscle cell ratio		
		VL	VM	VI
Varus angle	r	-0.035	0.436	0.386
	p	0.853	0.013	0.029

VL: Vastus lateralis, VM: Vastus medialis, VI: Vastus intermedius

No significant difference was observed between males and females with respect to the connective tissue results of the VL, VM and VI muscles (p>0.05).

Correlations Between Atrophic Muscle Cell Ratios and the Amounts of Fatty and Connective Tissue

In the VL muscle, no statistically significant difference was seen between the fatty tissue and the atrophic muscle cell ratios in the absent-mild group and the moderate-severe groups (p>0.05). In the VM muscle, the atrophic muscle cell ratio was significantly higher in the moderate-severe fatty tissue group than in the absent-mild fatty tissue group (p<0.05). In the VI muscle, the atrophic muscle cell ratio was significantly higher in the moderate-severe fatty tissue group than in the absent -mild fatty tissue group (p<0.05).

No significant difference was determined in the atrophic muscle cell ratios between the groups with absent-mild and moderate-severe connective tissue in the VM, VL, and VI muscles (p>0.05) (Table 3).

Table 3. Correlations between the atrophic cell ratio and the amount of fatty tissue and connective tissue

	Fatty tissue absent-mild		Fatty tissue moderate-severe		p
	Mean ± SD %	Median %	Mean ± SD %	Median %	
Atrophic muscle cell ratio					
VL	16.55±8	13.1	17.65±5	19.2	0.255
VM	14.75±8	16.0	19.24±4	20	0.031
VI	12.65±0	11.3	18.74±6	18.2	0.006

VL: Vastus lateralis, VM: Vastus medialis, VI: Vastus intermedius, SD: Standard deviation

DISCUSSION

In this study, examinations were made on knees with grade 4 gonarthrosis, varus alignment, and severe pain. The quadriceps muscle sections were evaluated separately, to determine whether there was any correlation between the atrophy of the sections and varus alignment.

The lower extremity muscles provide functional stability of the knee joint and function as a shock absorber (7). In a knee with normal alignment, quadriceps strength is not related to osteoarthritis. However, greater strength or weakness of the quadriceps in the presence of malalignment or laxity is associated with the progression of knee osteoarthritis (8). If the strength of the quadriceps muscle weakens, the rate of loading formed in the knee is higher (7).

Noehren et al. (3) reported that in the pathological examinations of the quadriceps muscle in knees with a moderate degree of osteoarthritis, the extracellular matrix is increased and the regeneration capacity of the muscle in these knees is significantly reduced compared with the knees of healthy individuals. The quadriceps muscle strength decreases with an increase in the stores of fibrotic collagen in the muscles (3). In animal models, muscle strength is decreased by excessive fibrosis (9). Corresponding to an evident decrease in satellite cells in patients with osteoarthritis, fibrosis is increased in the extracellular matrix (3). To evaluate quadricep's atrophy in the current study, pathological evaluations were made of the amount of fibrosis and fatty tissue in the muscle and the ratio of atrophic muscle cells to healthy muscle cells. The results showed that the amounts of connective tissue in the VM muscle was significantly greater than in the VL and VI muscles (p=0.018).

Although the findings of the risk of the development of osteoarthritis are controversial in patients with strong quadriceps muscles and malalignment or those with knee laxity (8,10,11), increased quadriceps strength prevents cartilage degeneration on the lateral surface of the patella-femoral compartment (10). Impaired activation of the quadriceps muscle additional to osteoarthritis is usually associated with a decrease in sensory receptors in the knee joint because stimulation of alpha motor neurons was reduced with spinal and/or supraspinal mechanisms in these patients (7).

In a prospective cohort study magnetic resonance imaging (MRI) examinations, it was reported that when the quadriceps muscle is strong, cartilage loss in the lateral patella-femoral joint is reduces, but there is no effect on cartilage loss in the tibiofemoral joint. The presence of a strong quadriceps muscle has a chondroprotective effect (10). In another later cohort study, females with normal knee alignment were followed up for 30 months, and the study reported a correlation between the weak quadriceps muscle and increased narrowing of the joint space (12). The ratio of hamstrings to quadriceps has not been shown to affect the narrowing of the joint in males or females (12).

Lim et al. (13) examined the electromyographic (EMG) activity of quadriceps muscles in patients with knee osteoarthritis. There is not found to be any relationship between the ratio of the VM to the VL and the peak quadriceps torque and severity of varus malalignment of the knee. The EMG of the VM was found to be greater than that of the VL, and the mean VM/VL ratio is approximately 1.3 (13).

MRI examinations have found the VM/VL ratio to be higher in varus knees than in neutral or valgus knees (14). During the flexion-extension movement of the knee in individuals with no pain, the ratio of VM obliquus and VL activity is almost 1:1 (15).

Malalignment of the joint and excessively disproportional axial loading on the knee joint may be found in the pathogenesis of the formation of knee osteoarthritis. In knees with malalignment (deviations of >5° from the mechanical axis), there is an increase in loading on the quadriceps, which increases knee laxity (defined as a varus-valgus deviation >6.5°) (4). Therefore, unbalanced loading on the joint leads to focal stress in the joint.

Disproportionately increased loading in the joint in the frontal plane causes progressive cartilage loss and deformity in the medial or lateral joint surfaces of the knee (14). While varus alignment increases the risk of progression of medial osteoarthritis, valgus alignment increases the progression of lateral osteoarthritis. Also, varus or valgus alignment exceeding 5° can cause functional impairment in a short period of 18 months (1). Among patients included in the current study, the mean varus angle of the knees was 12°.

Malalignment of the knee affects the external knee moment in the frontal plane during walking. Apart from the bone and joint geometry, the alignment the knee depends on the strength of the muscles around the knee or joint laxity. Of these factors, muscle strength can be modified and is reversible. Quadriceps weakness is a well-known risk factor in the development and progression of gonarthrosis (14), so strengthening of the quadriceps is important in the rehabilitation of gonarthrosis.

In MRI examinations, the VM/VL ratio is significantly higher in varus knees than in neutral or valgus knees (10). A previous study has shown that gender affects medial and lateral osteoarthritis, with lateral osteoarthritis seen more in women (16). In this study, the ratio of fatty tissue in the VL muscle was found to be significantly higher in females than in males. This greater amount of fatty tissue in the VL muscle in females could indicate greater weakness in the VL muscle and could therefore be a reason for osteoarthrosis. The more frequent observation of lateral osteoarthrosis in females could be explained by the more frequent observation of valgus alignment in females (17,18). In contrast, Brouwer et al. (19) reported that while varus malalignment was associated with the development of osteoarthrosis, the effect of valgus malalignment

On deviations of more than 5° from the mechanical axis, there is an increase in loading on the quadriceps, which increases knee laxity (defined as a varus-valgus deviation >6.5°) (4). Therefore, unbalanced loading on the joint leads to focal stress in the joint.

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This muscle weakness is seen particularly in the early stages of osteoarthritis. It may have been present before the onset of the disease (4). Quadriceps muscle strengthening exercises are a treatment approach recommended by some authors. A strong quadriceps muscle is important in pain control. However, this patient group is composed of the elderly, and a widespread decrease in muscle mass with aging is expected (21).

Study Limitations

There were some limitations to our study. Biopsy samples were taken from fresh cadavers with varus alignment but no gonarthrosis used as a control group. Another limitation was the wide confidence intervals in some analyses, which was due to the small sample size. The findings of this study highlight the need for further research. Evaluations of muscle atrophy in gonarthrosis at earlier stages while determining the relationship with alignment would be especially helpful in revealing the progression of atrophy (cadaver studies). If it can be shown how muscle atrophy progresses and which quadriceps muscles are affected in the early stage of osteoarthritis, treatment directed to this pathology may be useful in decreasing pain, slowing disease progression, and increasing quadriceps muscle capacity.

Muscle weakness is been well defined and accepted in knees with osteoarthritis, but the measurement is not easy, and it has not always been well reported in osteoarthritis studies.

CONCLUSION

In conclusion, in this study, the histopathological analysis was applied to VM, VL, and VI muscles, taken from patients with gonarthrosis. The frequency of structural changes was analyzed in addition to atrophy and associations were examined with clinical parameters, such as the alignment of the knee.

The amount of fatty tissue and fibrosis is important in the determination of muscle atrophy, as these are indicators of poor muscle quality. The results of the current study showed that with an increase in varus angle, there was observed be a significant increase in the ratio of atrophic cells in the VM and VI muscles. Muscle rehabilitation plays an important in gonarthrosis treatment. Good rehabilitation increases joint integrity, reduces symptoms and prevents disease progression. Rehabilitation directed to the VM muscle, which is atrophic and weak, will improve symptoms and correct the joint structure. The current study results demonstrated a significantly greater amount of fatty tissue and fibrosis and atrophic cell ratio in the VM muscle compared to the VL and VI. Atrophy in the VM and VI was seen to increase in correlation with the varus angle. Atrophy in the VL muscle did not show a correlation with the varus angle (Table 2). Therefore, it would be more appropriate to apply physical therapy directed to the VM, in particular, to prevent muscle fibrosis in varus knees.

Ethics

Ethics Committee Approval: Approval for the study was obtained from the Giresun University Faculty of Medicine Local Research Ethics Committee (decision date: 21.06.2017, number of decisions: 8).

Informed Consent: Informed written consent was obtained from all patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: K.A., C.Z.E., Concept: C.Z.E., Design: İ.Ç., K.A., D.E., Data Collection or Processing: İ.Ç., K.A., Analysis or Interpretation: İ.Ç., C.Z.E., Literature Search: D.E., Writing: İ.Ç., D.E., C.Z.E.

Conflict of Interest: No conflict of interest was declared by the authors.

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