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INVESTIGATION OF CLINICAL FACTORS AFFECTING PERCEIVED PAIN INTENSITY IN FEMALE PATIENTS WITH KNEE OSTEOARTHRITIS

DİZ OSTEOARTRİTLİ KADIN HASTALARDA ALGILANAN AĞRI ŞİDDETİNİ ETKİLEYEN KLİNİK FAKTÖRLERİN İNCELENMESİ

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ABSTRACT

Objective: The present study aimed to identify the clinical variables influencing perceived pain intensity at rest, during activity, and at night in female patients with knee osteoarthritis (OA).

Method: One hundred-six female patients with knee OA (mean age, 58.50±9.48 years; mean BMI, 30.73±5.53 kg/m^2) were included. The Visual Analogue Scale (VAS), active range of motion (AROM), strength of the iliopsoas, gluteus medius, quadriceps femoris, and hamstring muscles, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and Short Form-12 (SF-12) were outcome measures. A multivariate or univariate regression analysis was conducted to examine the relationship between the VAS ratings and AROM, muscle strength, WOMAC, SF-12, and Kellgren-Lawrence classification.

Results: The mean values for VAS-rest, VAS-activity, and VAS-night were 3.02±2.32, 6.62±1.96, and 3.89±2.72, respectively. A significant correlation was found between VAS-rest and quadriceps femoris muscle strength, as well as the WOMAC score. Similarly, VAS-activity showed a significant association with hip flexion and knee extension AROM, quadriceps femoris muscle strength, Grade 3 or Grade 4 OA, physical component score of SF-12, and WOMAC score ($p<0.05$). There was also a significant association between VAS-activity and age (β:-0.194, 95%CI:-0.043 - 0.021, p=0.04).

Conclusion: The quadriceps femoris muscle strength and functional level of the patients with knee OA significantly predict both pain intensity at rest and during activity. In addition, pain intensity during activity was found to be associated with hip flexion and knee extension AROM, Kellgren-Lawrence grading, the physical component of quality of life, and age.

Key Words: Function, Knee, Osteoarthritis, Pain, Regression

ÖZ

Amaç: Bu çalışmanın amacı, diz osteoartriti (OA) olan kadın hastalarda dinlenme anında, aktivite sırasında ve gece algılanan ağrı yoğunluğunu etkileyen klinik değişkenleri belirlemekti.

Yöntem: Diz OA'lı 106 kadın hasta (ortalama yaş, 58.50±9.48 yıl; ortalama VKİ, 30.73±5.53 kg/m^2) çalışmaya dâhil edildi. Sonuç ölçümleri Vizüel Analog Skala (VAS), aktif eklem hareket açıklığı (AEHA), iliopsoas, gluteus medius, kuadriseps femoris ve hamstring kas kuvveti, Western Ontario ve McMaster Üniversiteleri Osteoartrit İndeksi (WOMAC) ve Kısa Form-12 (SF-12) idi. VAS skorları ile AEHA, kas kuvveti, WOMAC, SF-12 ve Kellgren-Lawrence sınıflandırması arasındaki ilişkiyi incelemek için çok değişkenli veya tek değişkenli regresyon analizi yapıldı.

Bulgular: VAS-dinlenme, VAS-aktivite ve VAS-gece için ortalama değerler sırasıyla 3.02±2.32, 6.62±1.96 ve 3.89±2.72 idi. VAS-dinlenme ile kuadriceps femoris kas kuvveti ve WOMAC skoru arasında anlamlı bir ilişki bulundu. Benzer şekilde, VAS-aktivite ile kalça fleksiyonu ve diz ekstansiyonu AEHA, kuadriceps femoris kas kuvveti, Evre 3 veya Evre 4 OA, SF-12 fiziksel komponent skoru ve WOMAC skoru arasında anlamlı bir ilişki bulundu ($p<0.05$). VAS-aktivite ile yaş arasında da anlamlı bir ilişki vardı (β:-0.194, %95CI:-0.043 –0.021, p=0.04).

Sonuç: Diz OA'lı hastaların kuadriseps femoris kas gücü ve fonksiyon seviyesi, hem istirahat hem de aktivite sırasındaki ağrı şiddetini anlamlı olarak öngörmektedir. Ayrıca aktivite sırasındaki ağrı yoğunluğunun kalça fleksiyonu ve diz ekstansiyonu AEHA, Kellgren-Lawrence derecelendirmesi, yaşam kalitesinin fiziksel bileşeni ve yaş ile ilişkili olduğu bulundu.

Anahtar Kelimeler: Fonksiyon, Diz, Osteoartrit, Ağrı, Regresyon

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INTRODUCTION

Osteoarthritis (OA) is the most common joint disease in individuals over 60 years of age globally [1]. OA, seen in 10% of older adults, is a dynamic process affecting all joint structures, especially cartilage and bone tissue [2]. Although the cause of OA remains unclear, it most commonly affects the knee and hip joints [2-4]. The current evidence indicates that it depends on many factors that affect cartilage homeostasis [5]. The most important risk factor for OA is the female sex [4,6]. It is suggested that some features often found in females, such as the increased prevalence of obesity, reduced muscle tone, and heightened joint hypermobility, contribute to varied degrees of joint instability [3-5]. This instability may create a favorable environment for the occurrence of recurrent microtrauma, ultimately resulting in irreparable joint damage [3-5]. Other risk factors include obesity [7], genetic characteristics [8], excessive physical work, sports, or occupational work [9], previous knee joint trauma [10], vitamin D deficiency [11], and chondrocalcinosis [12].

Patients with knee OA commonly describe symptoms like joint pain, joint stiffness, and reduced joint functionality, which can ultimately lead to disability [13]. Pain and disability often occur when there are functional limitations, structural alterations in the subchondral bone, cartilage degradation, and the involvement of surrounding soft tissue [14]. Patients often experience two types of pain: occasional but typically severe or intense pain and persistent background pain characterized by aching sensations [15,16]. The progression of pain associated with osteoarthritis (OA) can be observed through several stages. In the initial stages, patients typically experience pain that is triggered by physical activity. As the condition advances, this discomfort gradually becomes more persistent and is punctuated by intermittent, intense pain [16,17]. In the more advanced stages of the disease, pain can be continuous, disrupting sleep patterns at night, and causing deterioration in the patient's psychological health. Social and recreational activities, subsequently reducing the health-related quality of life [17].

When reviewing the literature, many valuable studies focus on the impact of various treatment approaches on knee OA pain, but few studies investigate the pain intensity and influencing factors in untreated patients with knee OA. Therefore, the present study aimed to identify the clinical factors that influence the perceived pain intensity at rest, during activity, and at night in female patients with knee OA.

METHOD

Study Design and Setting

The present study was a cross-sectional study conducted in İstanbul, Türkiye.

Participants

All participants with knee OA who consulted the orthopedic clinics of İstanbul University and Avrasya Center for Orthopedics between February 2022 and August 2023 were recruited to the study after undergoing an assessment that considered the predefined criteria for participation. Orthopedic surgeons performed a clinical examination and radiological imaging assessment to diagnose knee OA of grades 2 to 4 based on the Kellgren and Lawrence (1957) scale [18]. Volunteer participants who met the clinical criteria for diagnosis of knee OA, as outlined by the American College of Rheumatology standards (pain in the knee and at least three of the following: age >50 years, stiffness <30 min, crepitus, bony tenderness, bony enlargement, and no palpable warmth) were included [19]. The criteria for exclusion were as follows: (1) a confirmed diagnosis of neurologic diseases, rheumatoid arthritis, radiculopathy, peripheral neuropathy, or psychiatric diseases; (2) a documented history of knee surgery or intraarticular corticosteroid injection in the last 6 months; (3) disclosed use of oral or topical analgesics for knee pain in the last 6 months; (4) participation in a lower limb physical therapy program in the last six-months; (5) inability to read and write; (6) inability to understand and follow simple instructions; and (7) presence of visual or hearing impairments.

Sample Size Calculation

The sample size was calculated by using the G*Power 3.1.9.2 sample size calculation program. The calculations were based on a moderate effect size ($\rho^2|=0.13$), an alpha level of 0.05, a 95% confidence interval, the desired power of 80%, and the number of predictors ranging from 1 to 4 [20]. The parameters result in a sample size of 60-103 participants. A total of 110 patients were invited to the study.

Outcome Measures

Outcome measures included perceived pain intensity, active range of motion (AROM), muscle strength, functional status, and health-related quality of life. All eligible individuals were questioned regarding their age, body mass index (BMI), dominant extremity, affected extremity, education, and occupation. The Charlson Comorbidity Index was used as a metric for assessing the presence of comorbidities.

The *Visual Analogue Scale (VAS)* was used for the perceived pain intensity under three conditions: at rest (VAS-rest), during activity (VAS-activity), and at night (VAS-night). This assessment was made using a 10 cm line scale ranging from no pain (0) to severe pain (10). The score was determined by measuring the distance on a 10 cm line [21].

Active Range of Motion: The measurement of AROM for hip flexion, knee flexion, and knee extension was conducted according to the methodology outlined by Norkin and White [22], utilizing a digital goniometer (Baseline Evaluation Instrument® Fabrication Enterprises, Inc). All participants were provided with verbal instructions regarding the testing technique. The affected side was measured three times, with a 30-second interval between tests, and the average value was computed.

Muscle Strength: The isometric muscle strength of the iliopsoas, gluteus medius, quadriceps, and hamstring muscles was assessed using the methodology outlined by Mentiplay et al. [23], employing a hand-held dynamometer (The Lafayette Instrument Company, Lafayette, Indiana, model 01160). All participants were provided with verbal instructions regarding the testing technique. Each limb was measured three times, with a 30-second interval between tests, and the average value was computed.

The *Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)* is a reliable and valid tool for assessing outcomes in patients with knee OA. It consists of 24 items and is divided into three main categories. The items are rated on a 5-point Likert scale ranging from none to extreme. The WOMAC score ranges from 0 to 96, with higher values indicating lower function levels [24,25].

The Short Form-12 is a reliable and valid tool for assessing subjective health-related quality of life perception. It consists of 12 items, including seven items related to physical components (PCS-12) and five items related to mental components (MCS-12). Both scores range from 0 to 100, with higher values indicating a better health-related quality of life [26,27].

Ethical Approval

The study protocol was approved by the Non-Interventional Clinical Research Ethics Committee at Haliç University (approval number 2021-147 on June 24, 2021). The study was carried out in accordance with the Declaration of Helsinki. The trial was registered on ClinicalTrials.gov with the registration number NCT05238857. Before the data collection, all participants provided written informed consent.

Statistical Analysis

Statistical Package for Social Science (IBM SPSS Statistics New York, USA) version 20.0 was used to perform statistical analyses. Descriptive statistics are presented as mean±standard deviation for continuous data, whereas binary and categorical variables are shown as numbers and frequencies. Regression analysis was performed to examine the relationship between VAS-rest, VAS-activity, and VAS-night, as well as potential factors that may contribute to pain severity in patients with knee OA. A multivariate linear regression analysis was conducted to examine the relationship between AROM, muscle strength, SF-12, VAS-rest, VAS-activity, and VAS-night. The association between WOMAC, age, VAS-rest, VAS-activity, and VAS-night was analyzed with univariate regression analysis. Analysis for Kellgren-Lawrence classification was conducted with logistic regression due to being a categorical variable. The significance level was set at p<0.05.

RESULTS

One hundred ten participants with a clinical diagnosis of knee OA were assessed for eligibility, and a total of 106 voluntary participants were included in the study. The sociodemographic and clinical characteristics of the participants are presented in Table 1. The mean scores were 3.02±2.32 for VAS-rest, 6.62±1.96 for VAS-activity, and 3.89±2.72 for VAS-night. The mean WOMAC score was 50.54±16.61, the mean PCS-12 score was 36.42±8.74, and the mean MCS-12 score was 44.29±8.72.

Table 1. Sociodemographic and clinical characteristics of the participants (n=106)

Characteristics		
Age (years)		58.50±9.48
BMI (kg/m²)		30.73±5.53
CCI (score)		2.83±2.24
WOMAC (score)		50.54±16.61
BMI (n,%)	<25	12 (11.3)
	25-30	37 (34.9)
	≥30	57 (53.8)
Affected extremity (n,%)	Unilateral	52 (49.1)
	Bilateral	54 (50.9)
Education (n,%)	Illiterate	5 (4.7)
	Primary school	59 (55.7)
	Secondary school	18 (17.0)
	High school	12 (11.3)
	College/University	12 (11.3)
Pain Intensity (cm)	VAS-rest	3.02±2.32
	VAS-activity	6.62±1.96
	VAS-night	3.89±2.72
Muscle Strength (kg.N^{-1})	Iliopsoas	9.03±2.84
	Gluteus medius	7.22±2.83
	Quadriceps femoris	8.99±2.05
	Hamstring	8.61±4.46
Kellgren-Lawrence Classification (n,%)	Grade 2	24 (22.6)
	Grade 3	56 (50.0)
	Grade 4	29 (27.4)
Dominant Side (n,%)	Right	102 (96.2)
	Left	4 (3.8)
Occupation (n,%)	Active worker	17 (16.0)
	Housewife	68 (64.2)
	Retired	21 (19.8)
Active Range of Motion (°)	Hip flexion	110.34±17.16
	Knee flexion	116.54±17.03
	Knee extension	-5.04±2.87
Short Form-12 (score)	PCS-12	36.42±8.74
	MCS-12	44.29±8.72

BMI:Body Mass Index, CCI:Charlson Comorbidity Index, MCS-12:Mental Component Summary score of SF-12, PCS-12:Physical Component Summary score of SF-12, SF-12:Short Form-12, VAS:Visual Analogue Scale, WOMAC:The Western Ontario and McMaster Universities Arthritis Index.

Linear regression analysis between the AROM, muscle strength, and VAS scores is shown in Table 2. A significant correlation was found between VAS-rest and quadriceps femoris muscle strength. VAS-activity was associated with hip flexion and knee extension AROM, and quadriceps femoris muscle strength (p<0.05). However, VAS-night was not found to be associated with AROM or muscle strength (p>0.05).

Linear regression analysis between disease-related outcome measurements, age, and VAS scores is shown in Table 3. VAS-rest was found to be associated with the WOMAC score (p=0.021). VAS-activity was found to be associated with PCS-12 score, WOMAC score, and age (p<0.05). In addition, there was a significant association between VAS-activity and having Grade 3 or Grade 4 knee OA. However, VAS-night was not found to be associated with disease-related outcome measurements or age (p>0.05).

DISCUSSION

The findings of the present study revealed that perceived pain intensity during rest was correlated with quadriceps femoris muscle strength and WOMAC score, whereas perceived pain intensity during activity was correlated with age, hip flexion, and knee extension AROM, quadriceps femoris muscle strength, having a Grade 3 and Grade 4 knee OA, physical health-related quality of life, and WOMAC score. The correlation ranged from mild to strong. Current evidence indicates that sleep disturbance is associated with altered pain processing, with the severity of knee OA further exacerbating the problem [28, 29]. However, an association between the outcome measures of the current study and the perceived pain intensity at night was not found. Following a focus group study on night pain in knee OA, it was reported that simple dichotomous questions at a single time point or pain severity measures like a VAS might not accurately measure night pain in knee OA [30]. In our study, the possible relationship between night pain and clinical variables may not have been revealed due to our pain assessment method.

The predisposing factors for perceived pain intensity in patients with knee OA were always a topic of interest since the findings would allow clinicians to shape their rehabilitation programs accordingly. Literature suggests that there are many links between the pain of the patient and numerous factors. For instance, in one of the latest articles on this topic, Bjerre-Bastos et al. [31] reported that pain at rest was significantly correlated with the WOMAC score in patients with knee OA. Moreover, the association between pain at activity and WOMAC was stronger than the association between pain at rest and WOMAC. Our findings were in line with the results reported in the study by Bjerre-Bastos et al. [31]. This result is reasonable considering that activities, especially those involving weight-bearing, trigger biochemical mechanisms causing pain [31, 32]. Another rationale for this notion could be that the data from the literature indicate that patients with early OA have more pain in weight-bearing conditions than at rest, and the association between pain at rest and the WOMAC score weakens as the disease progresses [33]. These findings also support the association found in the current study between pain during activity and having Grade 3 and 4 levels of knee OA, health-related quality of life, and age.

A recent study indicated that aging reduces pain sensitivity for lower pain intensities [34]. Besides, pain during activity is significantly associated with a decline in health-related quality of life, particularly in the elderly [35]. The experience of chronic pain tends to increase with age, particularly in the context of osteoarthritis, and pain can lead to decreased quality of life, with the latter being further affected by functional limitations [36]. Therefore, reducing knee pain is crucial for improving functionality and health-related quality of life in patients with knee OA. Furthermore, literature findings collectively suggest that perceived pain intensity in patients with knee OA was correlated with weaker quadriceps femoris muscle strength, and this association was especially prominent in females [37] because of the quadriceps

Table 2. Linear regression analysis between the active range of motion, muscle strength, and VAS scores

	VAS-rest		VAS-activity		VAS-night	
Model-1: ROM	**β (95% CI for B)**	***p***	**β (95% CI for B)**	***p***	**β (95% CI for B)**	***p***
Hip flexion	-0.082 (-0.309-0.136)	0.444	-0.281 (-0.065-0.001)	*0.033**	-0.120 (-0.065-0.027)	0.412
Knee flexion	-0.028 (-0.042-0.035)	0.846	-0.002 (-0.032-0.031)	0.991	-0.097 (-0.060-0.029)	0.494
Knee extension	-0.047 (-0.212-0.135)	0.664	0.197 (-0.008-0.278)	*0.040**	0.118 (-0.090-0.314)	0.274
Model-2: Muscle Strength	**β (95% CI for B)**	***p***	**β (95% CI for B)**	***p***	**β (95% CI for B)**	***p***
Iliopsoas	-0.140 (-0.341-0.102)	0.288	-0.156 (-0.302-0.076)	0.215	-0.003 (-0.270-0.263)	0.982
Gluteus medius	0.236 (-0.122-0.518)	0.222	-0.094 (-0.339-0.206)	0.876	-0.160 (-0.540-0.227)	0.420
Quadriceps femoris	-0.095 (-0.104-0.008)	*0.021**	-0.258 (-0.583-(-0.061))	*0.016**	-0.077 (-0.427-0.200)	0.475
Hamstring	-0.176 (-0.107-0.028)	0.251	0.107 (-0.037-0.078)	0.488	0.147 (-0.042-0.120)	0.348

**p<0.05, VAS-rest:Visual Analogue Scale score at rest, VAS-activity:Visual Analogue Scale score during activity, VAS-night:Visual Analogue Scale score at night.*

Table 3. Linear regression analysis between disease-related outcome measurements, age, and VAS scores

Model-3: Kellgren-Lawrence Classification	VAS-rest		VAS-activity		VAS-night	
	β (95% CI for B)	***p***	**β (95% CI for B)**	***p***	**β (95% CI for B)**	***p***
Grade 2	-	-	-	-	-	-
Grade 3**	0.966 (0.806-1.158)	0.711	1.288 (1.013-1.638)	*0.004**	0.926 (0.797-1.077)	0.321
Grade 4**	1.152 (0.947-1.402)	0.157	1.874 (1.178-2.105)	*0.002**	1.036 (0.873-1.230)	0.685
Model-4: SF-12	**β (95% CI for B)**	***p***	**β (95% CI for B)**	***p***	**β (95% CI for B)**	***p***
PCS-12	-0.048 (-0.066-0.041)	0.636	-0.314 (-0.158-(-0.038))	*0.002**	-0.144 (-0.077-0.012)	0.155
MCS-12	0.123 (-0.021-0.086)	0.227	-0.003 (-0.061-0.059)	0.103	0.165 (-0.008-0.082)	0.975
Model-5: WOMAC	**β (95% CI for B)**	***p***	**β (95% CI for B)**	***p***	**β (95% CI for B)**	***p***
Score	0.224 (0.005-0.058)	*0.021**	0.551 (0.046-0.084)	*<0.0001**	0.062 (-0.022-0.042)	0.525
Model-6: Age	**β (95% CI for B)**	***p***	**β (95% CI for B)**	***p***	**β (95% CI for B)**	***p***
	-0.152 (-0.341-0.102)	0.123	-0.194 (-0.043 - 0.021)	*0.041**	-0.161 (-0.540-0.227)	0.334

***:Reference category is Grade 2, *p<0.05, MCS-12: Mental Component Summary score of SF-12, PCS-12: Physical Component Summary score of SF-12, SF-12: Short Form-12, VAS-rest: Visual Analogue Scale score at rest, VAS-activity: Visual Analogue Scale score during activity, VAS-night: Visual Analogue Scale score at night, WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.*

femoris muscle strength and this association was especially prominent in females [37] because of the quadriceps femoris muscle atrophy, neuromuscular alterations, and inflammatory processes [31]. However, it is not clear whether quadriceps femoris muscle strength is the result or the reason for pain in patients with knee OA. For instance, Bokaeian et al. [32] reported that strength training for quadriceps femoris muscle did not result in improvement in pain and functional status in patients with knee OA, suggesting that quadriceps femoris muscle strength was not associated with pain. On the other hand, DeVita et al. [33] showed that 12 weeks of strengthening program decreased the pain and increased the function in patients with knee OA, suggesting an increase in quadriceps femoris muscle strength would result in an improvement in knee pain. Our findings conclusively suggest that quadriceps femoris muscle strength was associated with both pain at rest and pain during activity. There is conflicting evidence from the literature and differences among the studies, but a recent paper may explain this reason. According to a recent article by Alshahrani et al. [31], the association between muscle strength of quadriceps femoris and pain was not a causative relationship. Rather, pain was a mediator between muscle strength and postural control, thus affecting overall functional mobility [31]. These findings underscore the importance of addressing pain and muscle strength in the management of knee OA to improve functional mobility. Another important finding of the current study was that AROM in hip flexion and knee extension was associated with pain during activity,

however, this association was weak. Although the association between OA and AROM has already been well-known for years [34], the knowledge regarding the association between knee extension ROM and pain was just recently broadened by a paper stating that decreased knee extension ROM was observed during gait in patients with OA [35]. The potential consequences of a reduction in normal terminal knee extension can significantly impact knee mechanics during ambulation and weight-bearing activities [36]. Similarly, hip flexion ROM was also stated as a determinant of increased pain in patients with hip and/or knee OA [37]. The loss of ROM was particularly underlined since this could result in the development of secondary OA and/or increased pain, especially during daily tasks [38]. Therefore, it is important to target both strengthening and stretching training when treating patients with knee OA [39].

Limitations

This study has some limitations that should be mentioned. Firstly, all participants were female, which impedes the generalization of the results. Secondly, pain at rest, during activity, and at night was assessed with a single-item pain-intensity measure. However, the VAS is a reliable scale, with the smallest errors in the measurement of knee OA pain [38]. Another limitation of this study was that gluteus maximus muscle strength, and hip internal and external rotation ROM were not evaluated. Restricted joint mobility in the external rotation of the hip was found to be an important determinant of impairment in patients with OA [39].

CONCLUSION

To summarize, our findings pointed out that hip flexion and knee extension AROM, quadriceps femoris muscle strength, and age are significant predictors of pain intensity during activity. In addition, pain intensity during activity was also associated with the physical component of quality of life and function. The present findings and the evidence suggest that enhancing the AROM in knee extension and hip flexion, along with augmenting the strength of the quadriceps femoris muscle, is important for the rehabilitation of knee OA, particularly in terms of decreasing the perceived pain intensity at rest and during activity. However, none of the factors investigated in this study were associated with the pain experienced at night. Therefore, further studies are still required to determine the possible predisposing factors for night pain in patients with knee OA.

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