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ORIGINAL ARTICLE

Is There a Possible Neuropathic Pain Component in Knee Osteoarthritis?

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ABSTRACT

Objectives: This study aims to investigate the neuropathic pain (NP) component in patients with osteoarthritis (OA) of the knee and its association with physical function, risk factors, and stages of OA.

Patients and methods: A total of 109 patients (16 males, 93 females; mean age 62.5±8.5 years; range 44 to 81 years) diagnosed with knee OA according to the American College of Rheumatology criteria were enrolled in this study between July 2014 and June 2015. Patients were evaluated with visual analog scale for pain severity, PainDETECT questionnaire for presence and severity of neuropathic pain, Western Ontario and McMaster Universities osteoarthritis index for physical function, and the Kellgren-Lawrence system for severity of OA. Presence of the associated risk factors were also questioned.

Results: A total of 12 patients (11%) were classified as having likely NP and 23 patients (21.1%) were classified as having possible NP. PainDETECT scores were significantly correlated with the visual analog scale scores and Western Ontario and McMaster Universities osteoarthritis index pain, physical function and total scores. Patients with neuropathic pain had significantly longer symptom duration than the patients without NP. However, we found no relationship between the other risk factors and NP.

Conclusion: This study demonstrated that some of the knee OA patients had a NP component as the underlying cause of knee pain. Patients with NP had longer symptom duration, increased severity of pain, and disability. Therefore, the presence of NP component in these patients should be considered. Once it is determined, appropriate intervention strategies for NP should be incorporated in the routine treatment modalities of knee OA.

Keywords: Knee osteoarthritis; neuropathic pain; physical function; risk factors.

Osteoarthritis (OA) is a common progressive joint disease characterized by loss of articular cartilage and periarticular bone remodeling. It causes joint pain and pain is the most common disabling symptom for patients with OA.[1-3] The pain of knee OA is generally classified as nociceptive, due to cartilage damage. However, since cartilage is both an avascular and aneural tissue, the mechanism of pain is likely to be complex and the synovium, bone and soft tissue probably contribute to pain generation.[4,5] In addition, subchondral bone pathology may cause neuropathy after destruction of the chondral structure, because the subchondral bone is densely innervated.[4] Rat models of knee OA have shown that sensory nerve fibers innervating the knee are significantly damaged with destruction of subchondral bone junction and induce neuropathic pain (NP).[6] Like other chronic pain conditions, central sensitization may contribute to OA pain arising from chronic nociceptor stimulation and subsequent modification of central pain transmitting neurons.[7-9] Central sensitization in OA may present with several clinical features which are characteristic for NP conditions.[10] The characteristic verbal complaints include burning, prickling, itching, electric shock feeling, pins and needles, numbness, tingling,

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and sensitivity to heat, cold, touch or pressure.[11] Due to the characteristic complaints of NP reported by our patients, we consider that there is a NP component in the pain of knee OA. Although the risk factors for symptomatic knee OA have been identified,[12] to our best knowledge, a limited number of studies have evaluated the relationship between risk factors and NP in knee OA.[10] Therefore, in this study, we aimed to investigate the NP component in patients with OA of the knee and its association with physical function, risk factors, and stages of OA.

PATIENTS AND METHODS

A total of 109 knee OA patients (16 males, 93 females; mean age 62.5±8.5 years; range 44 to 81 years) who applied to Ankara Physical Medicine and Rehabilitation Training and Research Hospital between July 2014 and June 2015 were enrolled. Knee OA was diagnosed according to the American College of Rheumatology classification criteria.[13] Ankara Physical Medicine and Rehabilitation Training and Research Hospital Ethics Committee approved the study protocol. A written informed consent was obtained from each patient. The study was conducted in accordance with the principles of the Declaration of Helsinki.

All patients had knee pain for more than three months. Patients with any previous history of knee surgery, infection, rheumatoid arthritis and other pain/neurological conditions such as radiculopathies, diabetes mellitus, vitamin B12 deficiency, coxarthrosis, stroke, traumatic brain injury, and patients who were already receiving medical treatment for NP were excluded. Patients were questioned about the affected knee, pain duration, and sociodemographic factors including age, sex, job, education, and body mass index (BMI).

All patients completed the visual analog scale (VAS) for pain at rest and at movement, Western Ontario and McMaster Universities osteoarthritis index (WOMAC) scale and the painDETECT questionnaire (PDQ). WOMAC scale was used to assess the functional status. It consists of subsections for pain (five questions), stiffness (two questions), and physical functionality (17 questions). In 5-point Likert form, 0 is none while 4 is extreme pain, with 0 as the best and 96 as the worst. The Turkish reliability and validity studies were conducted.[14] The Leeds Assessment of Neuropathic Symptoms and Signs pain scale, the neuropathic pain questionnaire, the Douleur Neuropathique (Neuropathic Pain) with four questions, and the PDQ have been developed for the measurement of NP.[15-18] Among existing measures, the PDQ appears to be the most appropriate assessment tool for use in OA.[19]

PainDETECT questionnaire was used to assess the features of pain experienced by participants in the preceding four weeks. It contains a body drawing for patients to indicate the sites of pain and any radiation present, assessment of pain quality with a marker of severity from hardly noticed to very strongly, pattern of pain and measures of current, worst and average pain severity. The painDETECT score ranged from 0 to 38. Patients were divided into three groups: likely NP (score ≥19), possible NP (score ≥13 to ≤18), and unlikely NP (score ≤12).[18] The Turkish version of the PDQ was developed and validity and reliability studies were conducted.[20]

Each patient's knee X-rays were taken while the patient was standing, knee extended in anteroposterior position. We used the Kellgren-Lawrence grading system.[21]

Statistical analysis

Data were analyzed by using SPSS version 11.5 (SPSS Inc., Chicago, IL, USA). Distribution of continuous variables was assessed by Shapiro-Wilk test. Descriptive statistics were expressed as mean ± standard deviation for continuous variables and as median (minimum-maximum) for discrete variables. Correlation analysis between the painDETECT scores and age, BMI, disease duration, VAS, and WOMAC scores were performed with Spearman correlation test. Comparisons between patients with likely, possible and unlikely NP groups in terms of sociodemographic and clinical characteristics were measured by Kruskal-Wallis test for continuous variables and Chi-square test (or Fisher's exact test) for categorical variables. Post-hoc analysis was performed to detect which pairs of groups differ significantly. $P<0.05$ was considered statistically significant.

Table 1. Socio-demographic characteristics of patients

	n	Mean±SD	Range
Age (year)		62.5+8.5	44-81
Sex			
Female	93		
Male	16		
Body mass index (kg/m^2)		33.7+6.0	
Work status			
Working	7		
Housewife or retired	102		
Educational status			
Illiterate	21		
Primary school	76		
High school-university	12		

SD: Standard deviation.

RESULTS

Table 1 shows the socio-demographic characteristics of patients, while clinical variables were shown in Table 2.

In this study, 12 patients (11%) were classified as likely NP, 23 patients (21.1%) were classified as possible NP, and 74 patients (67.9%) were classified as unlikely NP.

PainDETECT score was weakly and positively correlated with the VAS at rest and at movement (r=0.272, p=0.044, and r=0.333, p<0.001), WOMAC pain score (r=0.358, p<0.001), WOMAC physical function score (r=0.220, p=0.022) and WOMAC total score (r=0.280, p=0.003).

Table 3 shows the demographic and clinical characteristics of patients based on PainDETECT scores. There were differences in symptom duration (p=0.001), pain VAS at rest (p=0.034), pain VAS at movement (p=0.041), WOMAC pain (p=0.004), WOMAC physical function (p=0.030), and WOMAC total score (p=0.008) between likely NP and unlikely NP groups.

DISCUSSION

In this study, we have demonstrated that knee OA patients with longer symptom duration have NP component in their knee pain and that patients with NP component have severe pain and disability than patients without NP component. Also, we have found no relationship between NP and risk factors and stages of OA.

Historically, the pain of OA knee has been considered to be nociceptive pain; however, cumulative data suggest that both nociceptive and neuropathic mechanisms can play role in the pain of OA.[8,22] Hochman et al.[10] evaluated 80 knee OA patients and found that 34% of patients reported NP descriptors including burning, tingling, numbness, and pins and needles. Similarly,

Table 2. Clinical properties of patients

	n	%	Mean±SD	Median	Min-Max
Symptom duration (month)			50.4+42.2		
Visual analog scale pain					
At rest				4	0-10
At movement				8	2-10
WOMAC scores					
Pain			10.7+3.4		
Stiffness			2.1+1.7		
Physical function			31.2+12.0		
Total			44.1+15.1		
PainDETECT questionnaire scores			8.1+6.6		
PainDETECT questionnaire groups					
Unlikely neuropathic pain	74	67.9			
Possible neuropathic pain	23	21.1			
Likely neuropathic pain	12	11			
Kellgren-Lawrence grade					
Grade 1	14				
Grade 2	34				
Grade 3	49				
Grade 4	12				

SD: Standard deviation; Min: Minimum; Max: Maximum; WOMAC: Western Ontario and McMaster Universities osteoarthritis index; PainDETECT questionnaire groups: Likely neuropathic pain (score ≥19), possible neuropathic pain (score ≥13 to ≤18), and unlikely neuropathic pain (score ≤12).

Table 3. Demographic and clinical characteristics patients based on PainDETECT scores

	Unlikely NP (n=74)			Possible NP (n=23)			Likely NP (n=12)			
	n	Median	Min-Max	n	Median	Min-Max	n	Median	Min-Max	*p*
Age (year)		63	44-80		60	50-81		62	50-77	0.379
Body mass index (kg/m²)		32.84	22.86-60		34.4	26.4-47.1		31.5	27.5-41.1	0.57
Sex										0.07
Female	59			22			12			
Male	15			1			0			
Work status										0.11
Working	7			0			0			
Not working	67			23			12			
Educational status										
Illiterate	14				7		0			0.25
Primary school	50			14			12			
High school-university	10			2			0			
Symptom duration (months)		24	4-240		60	6-120		120	36-180*	0.001
Pain Visual Analog Scale										
At rest		4	0-8		4	2-8		5	2-10*	0.034
With motion		7	2-8		7	4-8		8	7-10*	0.041
WOMAC										
Pain		10	3-18		12	8-20*		13.5	8-17*	0.004
Stiffness		2	0-6		2	0-6		4	0-6	0.159
Physical function		29.5	3-52		33	14-56		41.5	22-50*	0.030
Total		42.5	9-75		46	25-70		58.5	34-71*	0.008
Kellgren-Lawrence grade										0.67
Grade 1	11			2			1			
Grade 2	22			8			4			
Grade 3	33			12			4			
Grade 4	8			1			3			

NP: Neuropathic pain; Min: Minimum; Max: Maximum; WOMAC: Western Ontario and McMaster Universities osteoarthritis index; * Significantly different compared with unlikely neuropathic pain; PainDETECT questionnaire groups: Likely neuropathic pain (score ≥19), possible (score ≥13 to ≤18) and unlikely (score≤12).

Oteo-Álvaro et al.[23] found high prevalence of NP features in patients with knee OA. Our study is in accordance with these studies in terms of NP component in the pain of OA knee.

We investigated the association between NP component and physical function in the knees of OA patients. Ohtori et al.[4] found that painDETECT scores were correlated with WOMAC pain score, but there was no correlation with WOMAC physical function score. On the other hand, we found that painDETECT scores were correlated with WOMAC pain score and WOMAC physical function score. Therefore, we consider that patients with NP component in their knee pain may have severe pain and disability. The investigators have reported that NP occurs in association with damage to nerves innervating subchondral bone in late stage.[4,6] Because of this data, we hypothesize that the increased symptom duration may influence development of NP component in knee OA. Likewise, Hochman et al.[10] suggested that longer term nociceptive input may lead to more alterations in central pain processing and increase the possibility of developing NP. They determined that patients who used NP descriptors had a longer OA duration compared with patients who did not use NP descriptors in their study. In our study, there was a significant difference in symptom duration between unlikely NP and likely NP groups. Therefore, in late stage, patients with longer symptom duration may have a NP component in their knee OA pain. Thus longer symptom duration may be considered as a risk factor of NP.

Risk factors for symptomatic knee OA have been reviewed[12] but only one study has examined the relationship between risk factors and NP in knee OA.[10] Female sex, age, and BMI are well-known risk factors for OA, as shown in previous studies.[24-28] Also, in the literature, a low level of education was found to be a significant factor associated with OA.[29,30] Hochman et al.[10] compared age, sex, and educational level in knee OA patients between those who used NP descriptors and who did not use NP descriptors. They found that the patients who used NP

descriptors were younger and were more likely to be females, although only the age difference reached statistical significance and there was no significant difference in level of education between the groups. In our study, there was no difference in sex, age, and educational level between unlikely NP and likely NP groups and there was also no correlation between painDETECT scores and BMI. We consider that this may be a result of most of our patients being housewives and having a low level of education. According to these findings, we believe that level of education, age, sex, and BMI are not risk factors for NP in knee OA.

In this study, we investigated the association between radiographic severity and NP component in knee OA. The association between radiographic severity in OA and pain remains indeterminate. There are many patients who have radiographic evidence of OA in the absence of pain and those who have little radiographic evidence of OA with moderate to severe pain.[31] Finan et al.[32] suggested that central sensitization in knee OA is apparent among patients with high levels of pain in the absence of moderate-to-severe radiographic evidence of knee OA. In our study, there was significant correlation between painDETECT scores and the VAS score, but we found no correlation between painDETECT scores and the Kellgren-Lawrence grades. Based on our observations, findings on radiographic evaluation appear to correlate with the patient's age rather than the patient's symptoms. The relationship between radiographic severity in OA and pain requires further examination.

There are several limitations of our study. First, although psychological factors may contribute to central sensitization and NP in knee OA,[8,33] they were not evaluated in this study. Hochman et al.[19] showed the association between depression and NP presence. Second, the reliability of PDQ for NP in knee OA has not been conducted. Although PDQ was developed and validated in adults with chronic low back pain, we used it to evaluate NP component in knee OA like the other studies.[4,34] PDQ was modified for use in knee OA by Hochman et al.[19] and they claim that the modified PDQ may facilitate the identification of a neuropathic component in knee OA.

Despite limitations, to our knowledge, this is one of the rare studies that examined the association between risk factors and NP in knee OA. We detected that some patients have a NP component in their knee OA pain and patients with NP have longer symptom duration. Therefore, the presence of NP component in these patients should be considered. Once it is determined, appropriate intervention strategies for NP should be incorporated in the routine treatment modalities of the knee OA.

Declaration of conflicting interests

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