Relationship Between Pain Severity and Magnetic Resonance Imaging Features in Patients with Osteoarthritis of The Knee

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Abstract

Objective: To evaluate the association between clinical symptoms and magnetic resonance imaging (MRI) findings in patients with osteoarthritis (OA) of the knee.

Materials and Methods: Ten men and 24 women between 30 and 60 years of age, who fulfilled the American College of Rheumatology (ACR) criteria for knee OA, were included in the study. All patients underwent MRI of the more symptomatic knee and the MRI findings were evaluated by the same radiologist blinded to clinical findings, using a semi-quantitative whole-organ MRI scoring method (WORMS). The Western Ontario and McMaster University (WOMAC) osteoarthritis index was used to assess physical function, morning stiffness, and joint pain.

Results: Linear regression analysis revealed that the total WORMS score and effusion severity were the most important predictors of the WOMAC pain score. The volume of the effusion was significantly correlated with the WOMAC pain and disability scores (r=0.601, p<0.001; and r=0.626, p<0.001, respectively). There was also a positive correlation between the WOMAC pain score and the WORMS bone marrow edema (BME) score (r=0.508, p<0.01). Patients with synovial effusions had significantly higher WOMAC pain and disability scores compared to patients without synovial effusions (p<0.01 and p<0.001, respectively). Similar results were also observed in patients with BME compared to those without edema.

Conclusion: Our results demonstrated that the severity of synovial effusion on MRI was associated with increased pain and disability in knee OA. MRI allows the precise visualization of joint structures, such as cartilage, bone, synovium, ligaments, and menisci, so that the joint can be examined as a whole organ.

Key words: Knee, osteoarthritis, pain, Magnetic resonance imaging, WOMAC, WORMS

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Özet

Amaç: Diz ağrılı hastalarda klinik semptomlar ve manyetik rezonans görüntüleme (MRG) bulgularının birlikteliğini değerlendirmektir.

Yöntem ve Gereçler: 30-60 yaş arası, diz osteoartriti (OA) için Amerikan Romatoloji Birliği (ACR) kriterlerini karşılayan 10 erkek, 24 kadın hasta alındı. Hastaların tümünde daha semptomatik olan diz MRG’leri alındı. MRG’lerinin tümü hastaların kliniği bilmeyen bir radyolog tarafından değerlendirildi. MRG’leri semiquantitative whole organ skorlama metodu (WORMS) ile değerlendirildi. Fonksiyon, sabah tutuklu ve eklem ağrısı için Western Ontario ve Mc-Master University osteoarthritis (WOMAC) indeksi kullanıldı.

Bulgar: Lineer regresyon analizleri, total WOMAC skoru ve effüzyon siddetinin WOMAC ağrı skorunun en önemli belirleyicileri olduğunu gösterdi. Effüzyon siddeti, WOMAC ağrı ve disabilite skorları ile anlamlı korelasyondur (\(r=0.601, p<0.001\); \(r=0.626, p<0.001\)). WOMAC ağrı ve kemik iliği ödemi (KİÖ) skorları arasında da pozitif bir korelasyon vardır (\(r=0.508, p<0.01\)). Sinoviyal effüzyonlu hastalar, effüzyonu olmayan hastalardan anlamlı olarak daha yüksek WOMAC ağrı ve disabilite skorlarına sahiptiler (p<0.01 ve p<0.001). Benzer sonuçlar KİÖ’si olan ve olmayan hastalar arasında da gözlemdi.

Sonuç: Sonuçlarımız diz OA’inde sinoviyal effüzyon siddetinin, artmış ağrı ve disabilite ile birliktede olduğunu gösterdi. MRG kartilaj, kemik, sinoviyum, ligamentler ve menisküler gibi eklemi oluşturulanya tıkanmayı doygun zamanın ve böylece eklemi bütün bir organ gibi değerlendirilmesine izin verir.

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Anahtar sözcüklər: Diz, osteoartrit, ağrı, manyetik rezonans görüntüleme, WOMAC, WORMS

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Introduction

Osteoarthritis (OA) is the most common joint disease worldwide, and the prevalence increases with age (1). Although OA is traditionally known as a disease of the hyaline cartilage, it affects all of the articular structures, such as subchondral bone, fibrocartilage, ligaments, capsule, and synovium (2-4). Knee X-rays that are widely used for the assessment of painful joints are ineffective in demonstrating early changes in the joint (5, 6).

Knee OA is the major cause of pain and disability (1, 2). The primary goals of disease management are reducing pain and improving functional status. The exact source of pain in OA is not fully understood (3-6). There is no clear association between symptoms and radiographic findings. While there may be changes in articular cartilage and subchondral bone in the radiographies of patients without pain, individuals without radiographic OA may have significant pain symptoms (4, 6-9). This shows that in addition to changes in cartilage and subchondral bone, other joint structures are also affected and that OA should be considered as an organ failure (10).

Magnetic resonance imaging (MRI) techniques which have been developed in recent years allow simultaneous evaluation of all joint structures, along with the evaluation of the early changes in the cartilage (10, 11).

In this study, we aimed to determine the relationship between the structural changes in the joint observed by MRI and pain and disability in patients with knee OA.

Materials and Methods

Thirty-four patients (24 women and 10 men) between 30 and 60 years of age, admitted with knee pain to our outpatient clinic and diagnosed with OA of the knee according to the American College of Rheumatology (ACR) criteria, were included in the study (12). Patients with a history of knee trauma, surgical intervention, inflammatory disease, acute or chronic infection, metabolic disease, and those who received an intra-articular injection within the last year were excluded. Patients with any contraindications for MRI evaluation were also excluded. In patients with bilateral complaints, the more painful knee was tested. Weight, height, and body mass index (BMI; kg/m²) of the patients were recorded.

Pain, disability, and morning stiffness scores of the Western Ontario and Mc-Master University (WOMAC) OA index were used for the clinical assessment of the patients (13). Pain was also assessed by a 10 cm visual analog scale (VAS).

Anteroposterior radiographs of the knee were obtained in all patients. X-rays were staged using the Kellgren Lawrence system (14). Patients with stage 4 OA were excluded from the study.

Magnetic Resonance Imaging

Images were obtained by a 1.5 Tesla MRI system (Magnetom Symphony-Quantum; Siemens, Erlangen, Germany) using a knee coil. All X-rays and MR images were evaluated by a musculoskeletal radiologist blinded to the clinical condition of the patients. MRI evaluation was performed using the semi-quantitative whole organ MRI scoring (WORMS) method. A total of 14 regions, including the anterior, central, and posterior segments of the medial and lateral femur and tibia, as well as the medial and lateral patella, were assessed. Fourteen types of structural changes were recorded in these 14 regions: cartilage integrity, subarticular bone marrow (BM) edema, subarticular cysts, subarticular bone flattening, marginal osteophytes, medial-lateral meniscal tears, integrity of the anterior and posterior cruciate ligaments, integrity of the medial and lateral collateral ligaments, synovitis/effusion, loose body (joint mice), and periarticular cysts/bursitis (11). Cartilage structure (0, normal cartilage thickness and signal; 6, diffuse cartilage loss in >75% of the region), subarticular BM edema and cysts (0, absent; 3, in >50% of the region), subarticular flattening (0, mild concavity; 3, severe concavity), marginal osteophytes (0, absent; 6, large), ligament tears (0, absent; 1, present), meniscal tears (0, absent; 4, complete tear or degeneration), effusion severity (0, absent; 3, filling most of the synovial cavity), loose body (0, absent; 3, 3 or more), and synovial cyst/ bursitis (1, normal; 3, significant increase in size) were scored. The sum of all scores was recorded as the "total WORMS score". Those with an effusion score of 0 were considered as "absence of effusion", and those with an effusion score of 1-3 were considered as "presence of effusion". The patients were classified similarly according to BM edema.

Statistical Analysis

Statistical analysis of the data was performed using SPSS-10.0 software. Linear regression analysis was performed to determine the variables affecting pain. A non-parametric Spearman correlation test was used for correlation analysis. Patients with or without BM edema and patients with or without effusion were compared by a t-test. Inter-group comparison according to effusion severity was performed by Kruskal-Wallis analysis of variance and comparison of group pairs was performed by a Mann-Whitney-U test with Bonferroni correction. The level of statistical significance was set at p<0.05 for linear regression, correlation analysis and Kruskal-Wallis analyses, and at p<0.05/3=0.016 for the Mann-Whitney U test with Bonferroni correction.
Results

The mean age of the patients was 49.79±9.91 years and the mean duration of disease was 4.03±3.28 years. The mean total WORMS score was 24.84±14.16. The demographic and clinical characteristics of the patients are presented in Table 1.

Age and BMI were positively correlated with subarticular flattening (r=0.416, p=0.014; and r=0.462, p=0.006, respectively). The WOMAC pain score was significantly positively correlated with WOMAC disability, WORMS meniscus, and effusion scores (r=0.716, p=0.001; r=0.45, p=0.01; and r=0.601, p=0.001, respectively). There was also a significant positive correlation between WOMAC disability and effusion scores (r=0.63, p=0.01).

A significant positive correlation was also observed between the WORMS BM edema score and the VAS and WOMAC pain scores (r=0.488, p<0.01; and r=0.508, p<0.01, respectively).

The WORMS meniscus score was positively correlated with cartilage, osteophyte, and total WORMS scores (r=0.565, p=0.001; r=0.519, p=0.002; and r=0.396, p=0.02, respectively). The results of correlation analysis between the MRI findings are presented in Table 2.

Linear regression analysis, in which the WOMAC pain score was the dependent variable and the others were independent variables, revealed that WOMAC disability, effusion, and total WORMS scores were significant determinants for the WOMAC pain score (p<0.001, p<0.01, and p<0.05, respectively; Table 3).

WOMAC morning stiffness score was only positively correlated with the total cartilage score, which was close to significance (r=0.33, p=0.57).

A significant strong correlation was found between effusion and BM edema (r=0.451, p<0.01). Synovial effusion was present in 8 of 10 patients with BM edema. On regression analysis, the BM edema scores, although close, did not reach a significant level as a determinant of pain (p=0.06 for VAS pain and p=0.05 for WOMAC pain). Synovial hypertrophy was noted in 8 of 24 patients with effusion. Ligament injury was not noted in any of the patients. Loose bodies were noted in 2 patients, Baker’s cysts in 3 patients, and pes anserine bursitis in 4 patients. Synovial cysts were not observed in any of the patients.

When patients with or without BM edema were compared, WOMAC pain and disability scores were found to be significantly higher in patients with BM edema (p<0.001 and p<0.01, respectively). A similar significant difference was noted between patients with

<table>
<thead>
<tr>
<th>Table 1. Clinical and radiographic features of the patients</th>
</tr>
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<tbody>
<tr>
<td>Mean±SD</td>
</tr>
<tr>
<td>Age (years)</td>
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<tr>
<td>Disease duration (years)</td>
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<tr>
<td>BMI (kg/m²)</td>
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<tr>
<td>Total WORMS score</td>
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<tr>
<td>VAS pain</td>
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<td>WOMAC pain score</td>
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<td>WOMAC disability score</td>
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<tr>
<td>WOMAC morning stiffness (min)</td>
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<tr>
<td>Radiological grade (Kellgren-Lawrence)</td>
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<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
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<tr>
<td>3</td>
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</tbody>
</table>

Table 2. Correlations between the changes in the joint on magnetic resonance imaging

<table>
<thead>
<tr>
<th>WORMS cartilage</th>
<th>WORMS meniscus</th>
<th>WORMS flattening</th>
<th>WORMS osteophyte</th>
<th>WORMS subarticular cyst</th>
<th>WORMS effusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>r=0.891</td>
<td>r=0.545</td>
<td>r=0.543</td>
<td>r=0.814</td>
<td>r=0.714</td>
</tr>
<tr>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>p&lt;0.01</td>
<td>p&lt;0.001</td>
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<tr>
<td>WORMS cartilage</td>
<td>NS</td>
<td>r=0.643</td>
<td>r=0.422</td>
<td>r=0.627</td>
<td>r=0.638</td>
</tr>
<tr>
<td></td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td>p&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>WORMS meniscus</td>
<td>NS</td>
<td>NS</td>
<td>r=0.519</td>
<td>p&lt;0.01</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>p&lt;0.001</td>
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</tr>
<tr>
<td>WORMS flattening</td>
<td>NS</td>
<td>NS</td>
<td>r=0.446</td>
<td>p&lt;0.01</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>p&lt;0.001</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>WORMS osteophyte</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>r=0.318</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>p&lt;0.001</td>
<td></td>
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<tr>
<td>WORMS BM edema</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>r=0.451</td>
</tr>
<tr>
<td></td>
<td>p&lt;0.001</td>
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<td>p&lt;0.01</td>
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</table>

NS: Not significant, r: Correlation coefficient, WORMS: Whole organ magnetic resonance imaging scoring.
and without effusions (p<0.01 and p<0.001, respectively). Patients with moderate (8 patients) and severe effusions (5 patients) had significantly higher pain and disability scores compared to patients with mild effusions (7 patients; p<0.016 for each parameter).

**Discussion**

Knee OA is the major cause of pain and disability. However, there is little correlation between clinical symptoms and radiographic findings (6-8). Our cross-sectional study has demonstrated that the severity of effusion and total WOMA5 score were the significant determinants of knee pain. Although the severity of BM edema did not reach statistical significance as a pain determinant, we found a significant positive correlation between pain and BM edema.

Although OA is the most frequent cause of joint pain, the pathophysiology of pain has not been fully understood (2, 3, 15). Progressive cartilage destruction, observed as joint space narrowing on direct radiographies in later stages, is the most significant feature of OA (9, 16). Due to the lack of vascularization and innervation of articular cartilage, it is difficult to explain osteoarthritic pain by cartilage destruction (3, 17-20). It is likely that other joint structures, such as bone, synovial tissue, capsule, ligaments, and menisci, may be the source of pain in patients with OA. The fact that the essential changes in OA occur particularly in the subchondral bone, which has a rich innervation network, suggests that these changes in the subchondral bone may be the main source of pain (2, 3, 15, 21).

Cartilage destruction and reduction of its thickness leads to a decrease in its load-bearing capacity and an increase in friction. This, in turn, reduces the protection of subchondral bone, which is supported by cartilage (9, 21, 22). The increase in stress transfer to the subchondral bone leads to trabecular thickening. The increase in bone density further increases the physical stress on subchondral bone and bone marrow. This process results in increased stiffness of subchondral bone, flattening of the articular surface, and bone edema (4, 6, 23). In a cross-sectional study involving 143 patients, Torres et al. (24) found that the severity of knee pain was correlated with flattening, BM edema, meniscal tears, and effusions. Hernandez et al. (3) noted a significant correlation between the presence of knee pain and flattening (OR, 3.3; 95% CI, 2.5-4.5) in a recent study involving a Framingham OA cohort of 1627 patients. They have also reported that there is co-existing significant bone flattening and BM edema in 73% of the painful knees. The effect of flattening on pain did not reach statistical significance in our study (p=0.07). However, a significant positive correlation was noted between flattening and cartilage and osteophyte size. Similar to our results, Nagaosa et al. (25) also showed that there is a significant association between flattening and osteophyte size.

It is likely that changes in the cartilage and bone occur simultaneously. In a cross-sectional study, Felson et al. (17) found that BM edema was noted on MRI in 77.5% of the patients with knee pain. They reported a significant association between lesion size and pain (OR, 3.31; 95% CI, 1.54-7.41). They observed BM edema in 48% of the patients at stage 0 and in 100% of those at stage 4, according to Kellgren-Lawrence system. BM edema rates were lower in our study (30%). This might be explained by the fact that patients at stage 4 were not included in the study.

A possible explanation for the mechanism underlying BM edema, can be summarized as an increase in traumatic loading of the bone due to the reduction in cartilage thickness and an increase in subchondral bone stiffness. Local subchondral microfractures, inflammation, and edema occurs as a result of this process (4, 9, 21). Following bone injury, the lesion region fills with blood.
water, and other extracellular fluids. Bloody BM is slowly replaced by fatty and fibrotic BM. Non-specific necrosis, fibrosis, and trabecular abnormalities have been noted on histologic examination of the BM edema (9, 23, 27, 29). Another theory is that the formation of cavitation within the trabecular bone similar to the formation of subchondral cysts as a result of pumping of the synovial fluid to subchondral BM through the cartilage and bone defects. Impairment of venous drainage in the BM results in an increase in intraosseous pressure and pain (6, 17). The association of transient BM edema of the hip with pain also supports the hypothesis that this lesion is the source of pain (23, 28). Conversely, Sowers et al. (6) have found that BM edema findings were similar in patients with radiographic OA who did or did not have pain. However, they found that full-thickness cartilage and neighboring subchondral bone defect on MRI was significantly more common in patients with pain. We noted significantly higher pain and disability scores in patients with BM edema compared to those without edema.

Another potential source of knee pain might be synovitis/effusion, which leads to distention of the highly innervated capsule. Low-grade effusion accompanied by synovial thickening has been defined in 75% of osteoarthritic knees (3). Hill et al. (30) noted moderate-to-high effusions by MRI in 56.4% of the patients with knee pain and radiographic OA. Similar to our results, they also noted a significant correlation between pain and the presence and amount of effusion. Song et al. (31) found effusions on MRI in 61% of patients with knee OA while the rate of patients with effusions was 85% in the study conducted by Tarhan et al. (32). We found effusions in 58% of patients. The effusion severity was found to be the most significant determinant of pain. This finding suggests that pain intensity is proportionally increased by the amount of distention in the joint capsule.

Meniscal lesions are common in patients with OA. The role of meniscal tears on pain and functional disability is controversial. The prevalence of meniscal damage noted on MRI in symptomatic knee OA has been reported as 52%-92% in previous studies (9, 27, 33, 34). Bhattacharyya et al. (15) compared the MR images of patients with symptomatic knee pain and asymptomatic controls and found no significant difference between the groups in terms of pain and disability scores, and they noted meniscal tears in 67% of asymptomatic patients. Meniscal lesions were observed in 47% of our patients. The positive correlation between pain and meniscal damage may be interpreted as an increase in pain as the meniscal damage reaches to the fibers located in the outer one-third region of the meniscus. We also found a significant correlation between meniscal damage and cartilage destruction. In their 2-year follow-up study, Berthiaume et al. (34) found that volume loss was greater in the medial cartilage in patients with advanced medial meniscal tears. These results are supportive of the meniscal functions, including distribution of axial loading, protection of the neighboring cartilage, and stabilization of the joint.

The association between pain and osteophytes is also controversial. Boegard et al. (35) found a positive correlation between pain and osteophytes located at the medial femoral condyle observed on knee X-rays obtained at semiflexion position. However, in their study, including patients with chronic pain, these authors did not provide the details of the methods they used for pain assessment. Osteophytes are formed in the joint, as a proliferative response to inflammation of the neighboring synovial membrane or distention of the joint capsule, which gradually lose its stability with aging. Marginal osteophytes may become painful due to their close interaction with the synovium and joint capsule (9, 35). We did not find a correlation between pain and osteophyte scores. This might be due to presence of osteophytes in the later stages of OA. There were few patients at stage 3 and no patients at stage 4 in our study population. It has also been reported that osteophytes have a high positive predictive value for cartilage defects, as determined by MRI (9). We noted that osteophyte scores were significantly correlated with cartilage and meniscus damage. This suggests that changes in the articular cartilage, meniscus, and bone play a significant role in the development of osteophytes (9, 36).

Subchondral cysts are fluid-filled cavities and are often associated with joint space narrowing and sclerosis. The pathogenesis has been explained as the entrance of synovial fluid into subchondral bone subsequent to cartilage destruction. As the cyst is surrounded by fibrous tissue, the relation with the joint space is terminated (6, 10). Our finding of an association between subchondral cyst formation and cartilage destruction, osteophyte formation, and flattening is supportive of this hypothesis.

Our results suggest that the total WORMS score and severity of the effusion are the most significant determinants of pain. Along with the results of previous studies, our findings indicate that the source of osteoarthritic pain is multifactorial. OA is a disease in which changes in the cartilage, bone, and synovial tissue play a role. Genetic, metabolic, and cultural factors may also play a significant role in structural damage. MRI is a non-invasive method which allows comprehensive assessment and detection of early structural changes in osteoarthritic joints.
Conflict of Interest
No conflict of interest declared by the authors.

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