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Soft Tissue Pathology Detected By Ultrasound Seem To Be Risk Factors for Painful Flare in Osteoarthritic Knee

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Abstract

BACKGROUND: To our knowledge, the importance of US findings, pain (brief pain inventory (BPI)) and disability in osteoarthritic knee (OA) pain patients remain uncertain.

AIM: The objectives are to evaluate the correlation of US findings, pain (brief pain inventory (BPI)) and disability in OA pain patients.

MATERIALS AND METHODS: Eighty - three patients with OA knee were divided into two groups. The first group was OA as symptomatic knee group and the second group was an asymptomatic control group. The maximum sagittal height of synovial fluid in 12 scans at 0, 30, 60 and 90 degrees flexion knee in 3 major recesses were measured.

RESULTS: There were a significant positive correlation between BPI Pain severity index, or BPI function interference index and a maximum height of effusion at 30-degree flexion angle in a supra-patellar recess in painful symptomatic knees. But, there was a significant negative correlation between BPI Pain severity index, and BPI function interference index and cartilage thickness in painful symptomatic knees.

CONCLUSION: The increase of maximum height of synovial effusion at different angles of knee and decrease of cartilage thickness associated with pain and disability in OA pain patients and are being predictors for pain severity and disability in OA pain patients.

Introduction

To our knowledge, few studies have addressed the relationship between US findings, pain especially brief pain inventory (BPI) and disability in OA pain patients. Thus, the objective is to evaluate the correlation of US findings and pain and disability in OA pain patients.

Osteoarthritis (OA) is one of the most common medical conditions in older adults and 9.6% of men and 18.0% of women aged 60 years have symptomatic OA of the knees [1]. OA is also the most common reason for restricted daily activity with a significant impact on the quality of life among affected people [2].

The importance of soft tissue pathology in pain in knee osteoarthritis remains uncertain. US of the OA knee may be able to visualise inflammation to its full extent and be extremely sensitive in the detection of soft tissue changes in knee OA, including synovial fluid and synovial proliferation. Such abnormalities are correlated with symptomatic flares and have associated prognostic implications [3].

To our knowledge, few studies have addressed the correction of US findings, brief pain inventory (BPI) and disability in OA pain patients. Thus, the objectives were to evaluate the correlation

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of US findings, pain and disability in OA pain patients.

Materials and Methods

Eighty-three patients with primary knee osteoarthritis (OA) were divided into two groups according to symptomatic pain knee. The first group (n = 43, 36 females, 5 males and age of 57.37 ± 7.65) was OA with eighty-six symptomatic pain knees (at least 3 months duration) as symptomatic knee group (S) and the second group (n = 40, 33 females, 7 males and age of 53.77 ± 5.22) was OA with eighty asymptomatic Knees group (A) as control group. The brief pain inventory (BPI) and the US of suprapatellar effusion area were done as outcome measures of pain and effusion.

Those patients were chosen from the outpatient clinics, rehabilitation department and diagnosed according to the American College of Rheumatology (ACR) criteria [4]. The European League against Rheumatism (EULAR) recommends that the clinical diagnosis of knee OA should be based on three symptoms (persistent knee pain, limited morning stiffness and reduced function) and three signs (crepitus, restricted movement and bone enlargement). The presence of all these signs and symptoms increases the probability of radiographic knee OA to 99% [5].

Inclusion criteria of our patients included the patients with ages 40-68-year-old and chronic knee pain. The exclusion criteria included patients who had knee surgery, mechanical knee derangement, serious knee pathology (e.g., fractures, tumours, rheumatologic disorders or infective diseases), severe cardiopulmonary disease, pregnant, and a pacemaker or metal implants.

All patients gave their informed verbal voluntary consent to use the recorded data in their follow up sheets according to the protocol approved by the local ethics committee and by the ethical standards of the Helsinki Declaration. This randomised controlled clinical trial began on January 2016 to April 2017.

Outcome measures of knee pain and effusion included visual analogue scale (VAS) and brief pain inventory (BPI) as measured pain and functional disability. Visual analogue scale (VAS) is a measurement instrument that tries to measure pain intensity on a scale from zero (no pain) to 100 (most severe pain). For example, the amount of pain that a patient feels ranges across a continuum from none to an extreme amount of pain [6].

The brief pain inventory (BPI) was originally developed to evaluate cancer pain, but it has been shown to be a valid and reliable instrument for chronic non-cancer pain. The BPI consisted of 11 items, which was designed to evaluate the pain intensity (four items) and pain interference with function (seven

items) scores [7]. The BPI items consisted of pain severity (four items) and pain interference with function (seven items) scores. BPI pain severity index consists of four items to measure pain intensity and range of pain severity index from 0-40 (0 = no pain, 10 = pain as bad you can imagine) of 4 items with total 40 point scale. BPI Function interference index consists of the sum of seven items to measure the level of function interference caused by pain (general activity, mood, walking ability, normal work, relations with other persons, sleep, and enjoyment of life) using 0 (no interference) to 10 (complete interference) rating scales and total range of function interference index of 7 items about 70 point scale [8].

Sonographers used the following equipment: 12-MHz, portable ultrasound machine GR LOGIQ, General Electric. The company, USA and Ultrasound scans of the knees were obtained by a linear transducer. All ultrasonographic evaluation of effusion areas were evaluated by an examiner who has good experience in musculoskeletal ultrasonographic evaluation. Grey-scale ultrasound (GSUS) and Color Doppler ultrasound (CDUS) examinations of each knee were performed at the following 3 major suprapatellar pouch recesses: midline suprapatellar, medial parapatellar, and lateral parapatellar recesses. Examination of the midline suprapatellar recess was carried out in the sagittal plane at midline, while that of the medial parapatellar and lateral parapatellar recess was carried out in the midpatellar transverse plane 90° medial and lateral from midline, respectively.

The ultrasound scans of the 3 recesses were performed in the 4 knee positions at 0°, 30°, 60°, and 90° of flexion of the knee joint, yielding a total number of 12 scans for each knee joint. The degree of flexion was established with the use of a standard goniometer. The knee was unsupported by external support (e.g., foam block) during the procedure. For each examination generous amounts of gel were applied to the knee and each sonographer took care in applying only minimal pressure to the transducer during the examination in order not to displace the fluid collection [9]. Ultrasonographers performed a complete ultrasonographic examination of each knee by the EULAR guidelines [10]. The fluid collection was defined as an anechoic or hypoechoic area that is displaceable and does not exhibit Doppler signal according to the Outcome Measures in Rheumatology definition of synovial fluid [11].

An ultrasound examination at the anterior part of the knee was done for each recess in every examined angle of flexion. The greatest effusion height (mm) was calculated automatically by using a sagittal scan as a quantitative measurement of in the supra-patellar, lateral parapatellar, and medial parapatellar recesses by ultrasonography [12]. Moreover, an ultrasound examination of the knee was done to look for hyperemia and thickening of the synovial membrane; and the medial and lateral joint lines to look for osteophytes and meniscal protrusion

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of knees. Also, an ultrasound examination of cartilage thickness was done in complete flexion position of knees [12] [13].

Study data were analysed using the SPSS (Statistical Package from the Social Science Program) (version15.0) (SPSS Inc., Chicago, IL, USA). The normality of the population was done during statistical analysis. The Student's t-test indicates the magnitudes of the differences of means ± SD and therefore the magnitude of the observation and to assess the difference between patients and control subjects and considered P value of < 0.05 statistically as significant. Quantitative data were presented as mean (± SD). Correlation between variables was done, and the Pearson correlation coefficient was calculated. All tests were 2-tailed and considered statistically significant at P < 0.05.

Results

Demographic and clinical, findings in symptomatic and asymptomatic knees in patients with primary OA are shown in Table 1. A significant difference of mean (± SD) of VAS, BPI Pain severity index, and BPI function interference index in symptomatic as compared to results in asymptomatic knees in patients with primary OA knee.

Table 1: Demographic, clinical findings in symptomatic and asymptomatic knees in patients with primary OA

Mean ± SD	Symptomatic OA knees (n = 43)	Asymptomatic OA knees (n = 40)	p-value
Age, years	57.37 ± 7.65	53.77 ± 5.22	N.S.
Sex (female./male)	30/13	28/12	N.S.
Body Mass Index (BMI) (kg/m^2)	21.93 ± 2.19	22.39 ± 2.48	N.S.
Disease duration, years	11.3 ± 04	10.55 ± 1.83	N.S.
VAS of pain intensity - point scale.	8.20 ± 1.58	-	-
[1]BPI Pain severity index	-	-	-
– Pain at its worst	8.02 ± 1.45	-	-
– Pain at its least	4.32 ± 1.78	-	-
– Pain on average	5.72 ± 1.51	-	-
– Pain right now	3.95 ± 1.70	-	-
[1]BPI Pain severity index – total point scale.	21.65 ± 3.95	-	-
[2]BPI Function interference index	-	-	-
– General Activity interference	5.76 ± 1.28	-	-
– Mood interference	2.56 ± 1.63	-	-
– Sleep interference	2.97 ± 0.53	-	-
– Enjoyment of Life interference	2.93 ± 0.86	-	-
– Ability to walk	4.95 ± 1.23	-	-
– Ability to work	5.11 ± 0.98	-	-
– People interference	4.18 ± 1.33	-	-
	28.11 ± 6.78	-	-
[2]BPI Function interference index- total point scale.			
Knee pain involved	-	-	
– Right knee (n, %)	41 (47.7%)	-	-
– Left knee (n, %)	35 (52.2%)	-	-
– bilateral knee pain	10 (52.2%)	-	-
– Anti-inflammatory medication(n, %)	43 (100%)	-	-
– intra-articular injections of hyaluronic acid (n, %)	20 (46.5%)	-	-
– Aspiration (n, %)	16 (37.2%)	-	-

N.B: OA, osteoarthritis; VAS, Visual Analog Scale; BPI, Brief Pain Inventory; US, Ultrasound. N.S.: not significant, P > 0.05; 1, BPI Pain severity index with range = 0-40 (0 = no pain, 10 = pain as bad you can image) of 4 items and total 40 point scale; 2, BPI Function interference index with range = 0-70 (0 = does not interfere, 10 = interferes completely) of 7 items and total 70 point scale.

Moreover, ultrasonographic findings of maximum effusion height of the three recesses in the four knee positions at 0°, 30°, 60°, and 90° of flexion in symptomatic and asymptomatic OA knee patients were shown in Table 2.

Table 2: Ultrasonographic findings of maximum effusion height of the three recesses in the four knee positions at 0°, 30°, 60°, and 90° of flexion in symptomatic and asymptomatic OA knee patients

Mean ± SD	Symptomatic OA knees (n = 43)	Asymptomatic OA knees (n = 40)	P-value
US maximum effusion height at 0 degree extension , (mean ±SD), mm	- -	- -	- -
– at the supra-patellar recess,	3.00 ± 0.44	0.68 ± 0.13	p<0.001
– at the medial para-patellar recess	2.87 ± 0.31	0.56 ± 0.06	p<0.001
– at the lateral para-patellar recess	2.35 ± 0.60	0.30 ± 0.07	p<0.001
US maximum effusion height at 30 degree flexion, (mean ± SD), mm	- -	- -	- -
– at the supra-patellar recess,	5.02 ± 0.90	0.70 ± 0.01	p<0.001
– at the medial para-patellar recess	2.97 ± 0.38	0.50 ± 0.02	p<0.001
– at the lateral para-patellar recess	3.10 ± 0.59	0.46 ± 0.03	p<0.001
US maximum effusion height at 60 degree flexion , (mean ± SD), mm	- -	- -	- -
– at the supra-patellar recess,	3.17 ± 0.51	0.68 ± 0.01	p<0.001
– at the medial para-patellar recess	0.94 ± 0.65	0.63 ± 0.03	p>0.05.
– at the lateral para-patellar recess	2.77 ± 0.42	0.35 ± 0.01	p<0.001
US maximum effusion height at 90 degree flexion , (mean ± SD), mm	- -	- -	- -
– at the supra-patellar recess,	2.03 ± 0.33	0.36 ± 0.001	p<0.001
– at the medial para-patellar recess	1.30 ± 0.89	0.21 ± 0.002	p<0.001
– at the lateral para-patellar recess	0.40 ± 0.52	0.20 ± 0.001	p>0.05.

N.B: OA, osteoarthritis; US, Ultrasound; **P < 0.001 = highly significant; *P < 0.05 = significant; N.S.= not significant, P > 0.05.

Also, ultrasonographic findings of bone and soft tissue pathology in symptomatic and asymptomatic OA knee patients were shown in Table 3 and Figures (1-7).
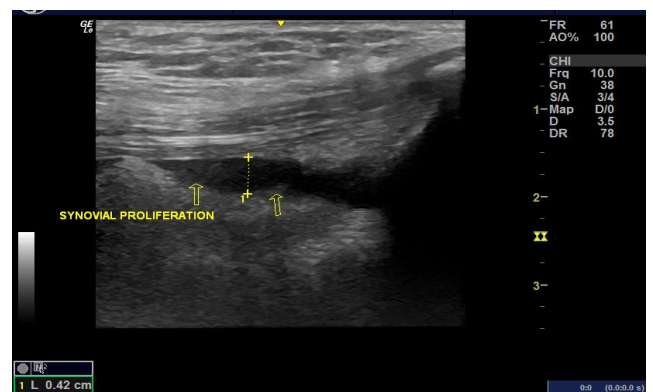

Figure 1: Representative images of synovial hypertrophy and a maximum height of suprapatellar effusion of 42 mm^2

We found increase of mean (± SD) of maximum height of synovial effusion at different angles of flexion in 3 recesses of knee and decrease of mean (± SD) of cartilage thickness in complete flexion position in symptomatic as compared to results in asymptomatic knees in patients with primary OA were shown in Tables 2 and 3.
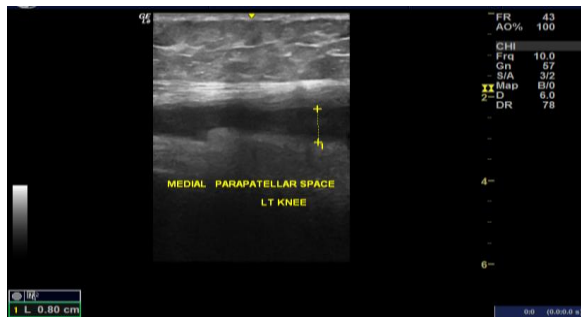
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Figure 2: Representative images of the maximum height of medial parapatellar effusion of 80 mm²

Moreover, in Table 4, there was a significant positive correlation between VAS, BPI Pain severity index, or BPI function interference index and maximum height of effusion at 30 degrees flexion angle in supra-patellar recess in symptomatic OK knees (r=0.822, p<0.001, r=0.733, p<0.05 and r=0.820, p<0.05 and) sequentially.

Table 3: Ultrasonographic findings of bone and soft tissue pathology in symptomatic and asymptomatic OA knee patients

Mean +SD	Symptomatic OA knees (n= 43)	Asymptomatic OA knees (n= 40)	p-value
US maximum effusion height at 30 degree flexion, (mean ±SD), mm	-	-	-
	-	-	-
-at the supra-patellar recess,	3.68±0.71	0.80±0.13↓	p <0.001
-at the medial para-patellar recess	3.00±0.38	0.75±0.16↓	p <0.001
-at the lateral para-patellar recess	2.87±0.37	0.38±0.02	p <0.001
US cartilage thickness, (mean±SD), mm	-	-	-
	-	-	-
-at medial epicondyle	1.51±0.24	2.93±0.09	p<0.001
-at intercondylar notch	1.42±0.30	2.76±0.12	p>0.05
-at lateral epicondyle	1.55±0.21	1.31±0.09	p>0.05
-US suprapatellar effusion (n, %)	28(65.1%)	5(12.5%)	p<0.001
-US synovial hypertrophy(>2 m),(n, %)	13(30.2%)	7(17.5%)	p<0.001
-Backer cyst (n, %)	9(20.9.9%)	3(7.5%)	p>0.05.
-US medial meniscal protrusion (>3 mm), n (%)	26(60.5%)	11(27.5%)	p<0.001
-US lateral meniscal protrusion (>3 mm), n (%)	7(16.3. %)	7(17.5%)	p>0.05
-US osteophyte (>3 mm), n (%)	8(18.6%)	3(7.5%)	p>0.05.

N.B: OA, osteoarthritis; US, Ultrasound. **p<0.001=highly significant; *p<0.05=significant; N.S.=not significant, p>0.05.

But, there was a significant negative correlation between VAS, BPI Pain severity index, or BPI function interference index and cartilage thickness at medial epicondyle in complete flexion position in symptomatic OA knees (r = 0.691, P < 0.05, r = 0.809, P < 0.05 and r = 0.715, P < 0.05) sequentially.
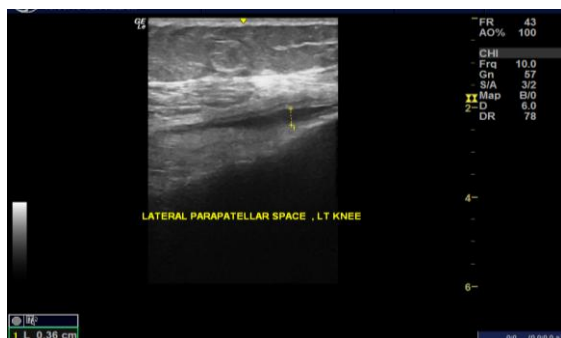

Figure 3: Representative images of the maximum height of lateral parapatellar effusion of 36 mm²

Figure 4: Longitudinal view of irregular cartilage thickness of the complete flexed knee joint

Discussion

Correlation of US findings and pain especially brief pain inventory (BPI) and disability in OA pain patients remains uncertain. Ultrasonographic (US) has become the first-line imaging technique chosen by rheumatologists to obtain real-time imaging information in patients with painful joints [14]. Also, few studies have addressed the relationship between the US of suprapatellar effusion area and knee pain. But, to our knowledge, the current study is the first to report on the association between brief pain inventory (BPI) and US findings in the osteoarthritic knee.

Table 4: Linear regression correlations (r-) between Soft tissue pathology detected by ultrasound and VAS as well as BPI pain severity index and IBP function interfere index in painful symptomatic OA knees

Variables, (mean ± SD)	VAS	BPI pain severity index	IBP function interfere index
Maximum Effusion height detected by ultrasound			
Maximum Effusion height at the supra-patellar recess at 30 degree of flexion , mm	r=0.822** p<0.001	r=0.737** p<0.001	r=0. .820** p<0.001
Effusion height at the medial para-patellar Recess at 30 degree of flexion , mm	r =0.270 p>0.05	r=0. .325 p>0.05	r=0.281 p>0.05
Effusion height at the lateral para-patellar recess at 30 degree of flexion, mm	r=0.323 p>0.05	r=0. .271 p>0.05	r=0.210 p>0.05
Cartilage thickness incomplete knee flexion detected by ultrasound			
Cartilage thickness at Medial epicondyle, mm	r=-0.691** p<0.001	r=-0.806** p<0.001	r=-0.715** p<0.001
Cartilage thickness at the intercondylar notch, mm	r=-0.555 p>0.05	r=-0.707 p>0.05	r=-0.561 p>0.05
Cartilage thickness at lateral epicondyle, mm	r=-0.729 p>0.05	r=-0.817 p>0.05	r=- 0775 p>0.05

N.B: US, Ultrasound; OA, osteoarthritis; VAS, visual analog scale; BPI, brief pain inventory; **P<0.001=highly significant; *p<0.05=significant; N.S.=not significant p>0.05.

Our results showed a significant difference of mean (± SD) of VAS of pain intensity, BPI Pain severity index, and BPI function interference index in symptomatic as compared to results in asymptomatic knees in patients with primary OA. Moreover, there was a significant positive correlation between VAS of

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pain intensity, BPI Pain severity index, or BPI function interference index with a maximum height of effusion at 30-degree flexion angle in a supra-patellar recess in painful symptomatic OK knees. But, there was a significant negative correlation between VAS of pain intensity, BPI Pain severity index, or BPI function interference index with cartilage thickness at medial epicondyle of the femur in complete flexion position in painful symptomatic OA.
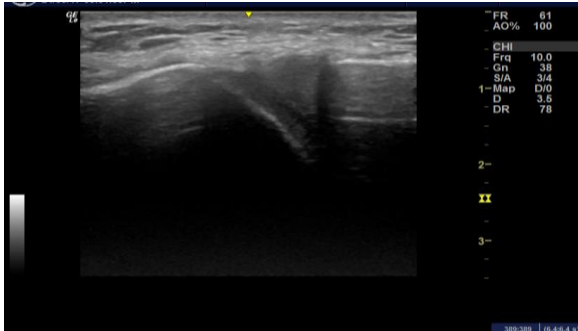

Figure 5: Longitudinal view of a medial aspect of the right knee joint. Meniscal protrusion present on the medial femoral condyle and tibia of right knee

Our findings are supported other publication; some authors reported that approximately 50% of patients with Inflammation in OA of the knee during flares of knee pain show US evidence of synovitis and/ or effusion as a possible explanation for their pain exacerbation [15].

Figure 6: Longitudinal view of a medial aspect of the knee joint. Small osteophytes present on the medial femoral condyle and tibia

Moreover, de Miguel- Mendieta et al. showed that patients with OA of knee and recent onset pain had a higher prevalence of Baker's cyst and joint effusion, as compared with painless OA knees [16].
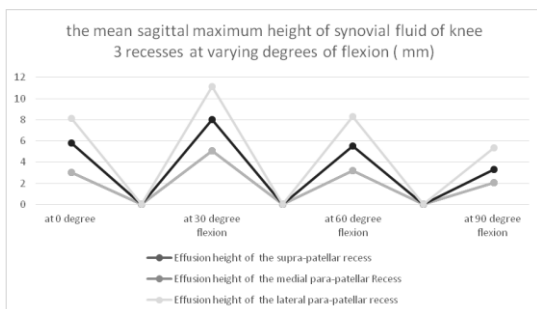

Figure 7: Plot diagram shows the Sonographic evaluation of the mean sagittal maximum height of synovial fluid of knee 3 recesses at varying degrees of flexion, using the extended position (0°) as a

reference. Dotted lines represent confidence intervals for each of the corresponding recesses. For each recess, corresponding graphs are marked with matching colours

Some studies reported that ultrasound with knee effusion has a positive correlation with pain score upon walking and stair climbing and this suggested that biomechanical derangement is an important aspect in OA knee pain.

Moreover, the presence of suprapatellar synovitis had higher pain score on sitting, and this suggested that Synovitis was considered to be an important predictor of pain [17]. This could be explained by a previous study conducted by the author that there exist two types of pain among OA knee patients: a mechanical pain and an inflammatory pain. The former, being biomechanical, is associated with joint movements such as walking and stair claiming whereas the latter is caused by flares of joint inflammation [17].

In the OA group, only suprapatellar effusion and medial compartment synovitis were significantly associated with knee pain. Visual analogue pain scale (VAS) scores on motion were positively linearly associated with suprapatellar effusion and medial compartment synovitis [18]. Some studies using MRI showed only moderate correlation/association between effusion/synovitis and pain [19]. Esen et al. correlated the inflammatory episodes in knee OA with suprapatellar effusion [20].

Similar findings are found in others studies. Knee effusion among OA knee has been shown to affect knee mechanics and muscle activity during gait in knee osteoarthritis and therefore can be a cause of the mechanical pain by itself. This suggests that the knee effusion among relates more to mechanical rather than inflammatory pain [21]. Moreover, Knee synovitis is accompanied by knee pain and cartilage destruction, and it induces synovial hypertrophy and the development of effusion in the joint cavity [22]. Several previous studies that used MRI and ultrasonography have reported that knee effusion worsens symptoms and pain [23].

In contrast to these findings, some authors have been demonstrated that imaging findings do not always correlate pain in OA patients and this suggests that The OA pain is multifactorial and the mechanism of its appearance is not completely understood [24] [25]. Other authors found no correlations between pain (VAS and WOMAC score) and joint effusion [26]. Some studies using MRI showed no correlation/association between effusion/synovitis and pain [27]. This finding is also consistent with the EULAR study, which showed no correlation between US inflammatory signs and pain intensity during physical activity [28]. This suggests that the psychological factors can interfere with pain which probably explains the differences with other studies. In contrast, neither US synovitis features nor other US features were associated with knee pain in knees

without OA. The results reflect the importance of synovitis in OA knee pain and the multifactorial origins of pain [29].

The mechanism of pain in OA knee is not well understood. Previous research has shown knee pain in OA to be multifactorial causes [30]. Inflammatory, mechanical, structural, bone-related factors, neurological and psychological factors play a role in the process that results in painful knee OA [31].

Some limitations of our study should be mentioned. One of the major limitations of our study is a small number of participants. The number of participants with more severe OA was excluded, and we studied both knees of one patient as an independent sample. Secondly, an important limitation is the lack of comparison of the US findings with MRI findings as we did not take into consideration the presence of bone marrow lesions as an important source of pain in OA knee.

In conclusion, the increase of maximum height of synovial effusion detected by ultrasound at different angles of flexion in 3 recesses of knee and decrease cartilage thickness incomplete knee flexion detected by ultrasound associated with pain and disability in OA pain patients and is being predictors for pain severity and disability in OA knee.

Acknowledgements

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