

Significant Clinical Symptoms and Signs in Knee Osteoarthritis Patients: Relation to a Diagnosis of Knee Osteoarthritis

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Abstract: Osteoarthritis(OA) is often diagnosed by an overall clinical presentations based upon the patient's age and history, findings on physical examination, and laboratory and/or radiographic findings. The present study has thus helped in making a diagnosis of knee OA based upon significant clinical symptoms and signs of the disease condition which might help to detect the early stages of knee OA in patients with knee pain.

Keywords: Knee OA, Diagnosis, Clinical Symptoms and Signs, Knee Pain

1. Introduction

Osteoarthritis (OA) is the most prevalent arthritis of rheumatic diseases, and is the major cause of disability due to arthritis. OA is not a single disease or process; rather it is the outcome of the range of processes leading to pathological, structural and eventually symptomatic failure of one or more synovial joints. Cartilage damage can result from joint-level factors such as acute trauma, chronic joint instability, or other joint-tissue diseases. Besides these, individual-level factors contribute to disease progression, and both levels interact in a complex manner making OA treatment difficult [1].

It may be classified as primary (idiopathic) or secondary to other processes such as trauma, congenital/developmental, mechanical or local factors (for example obesity or hypermobility) or as a sequelae of other inflammatory arthritides [2, 3].

OA involves all tissues in the joint - initially there is loss of proteoglycan from the matrix of articular cartilage resulting in fibrillation, fissuring and degeneration [4, 5]. In more advanced disease, cartilage loss is such that the articulating surface is subchondral bone (eburnation). There is increased bone remodeling with subchondral osteosclerosis and cyst formation, articular surface deformity and osteophyte formation. Varying degrees of synovial

inflammation and ligament degeneration may also occur and OA is accompanied by peri-articular muscle wasting and biomechanical changes. These pathological processes lead to the characteristic X-ray features. There is often poor correlation between X-ray changes and symptoms [2, 6]. OA has multiple aetiological factors with gender, age and genetic factors increasing susceptibility and more local factors such as joint biomechanics, obesity, trauma and muscle weakness determining the site and severity of the disease [7, 8].

The diagnosis of OA depends on diagnostic criteria or classification tree because it occurs by multiple factors and its pathognomonic markers have not been identified. Diagnostic criteria or classification tree for the involved joints have developed. OA affects predominantly the hip, knee, fingers and spine. Knee OA is the most common form and diagnostic criteria for OA of the knee are most available at clinical practice. Diagnostic criteria for knee OA have been based on classic clinical findings or the addition of radiographic or laboratory findings to the clinical findings [9, 10].

It takes months or even years for radiographic findings to develop after onset of clinical symptoms and signs of knee OA [2]. It has suggested that early OA of the knee joint has not been detected by criteria with the addition of radiographic findings to clinical symptoms.

For the reason, some researchers have studied clinical characteristics of knee OA, including symptoms and signs, radiographic or laboratory results of knee OA, and proposed their options in relation to diagnostic criteria for knee OA for the past in our country [Ri Pohum (1994) Clinical Study of rational diagnosis and treatment of knee osteoarthritis. Doctoral dissertation, 111; Pak Kyonghue (2007) Clinical study of diagnosis and treatment of several rheumatic diseases. Doctoral dissertation, 82; Ri Mongson, et al. (2016) Revised diagnostic criteria for knee osteoarthritis. Internal Medicine 1, 33]. One researcher gave his opinion about a diagnosis of knee OA [Ri Pohum (1994) Clinical Study of rational diagnosis and treatment of knee osteoarthritis. Doctoral dissertation, 111]. His opinion was that the unique clinical symptoms and signs of knee OA would help to diagnose in the early stages of knee OA.

Hence the present study has focused on establishment of significant clinical symptoms and signs of knee OA, which are related to a diagnosis of OA of the knee, without radiographic or laboratory findings because pain of knee OA has mechanical characteristic and knee OA is non-inflammatory.

2. Methods

2.1. Study Design and Participants

All the participants gave written informed consent before entering the study. They were informed about purpose, content and the protocol of the study. The study was conducted at the Rheumatology department of Clinical institute, Pyongyang medical college, Kim Il Sung University. The design of study was approved by the Ministry of Health. Participants were selected among patients with the following inclusion criteria: typical knee joint pain, typical radiographic findings of knee OA, normal ESR and white blood cells, and eventual conformation of the knee osteoarthritic findings on arthroscopy. Diagnosis of knee OA was based on the clinical criteria defined by the American College of Rheumatology (ACR) [11, 12], and had radiographically assessed OA of the knee according to the Kellgren & Lawrence (K&L) scale [13]. All patients had a varus knee alignment. The study group also included patients who had clinical and laboratory findings of knee OA without radiographic findings, or had only radiographic findings over time. At the beginning of the study, 41 patients, who had clinical and laboratory findings of knee OA without radiographic findings, were not excluded and monitored until radiological changes occurred. At that time, they were included in the study. Disease duration of them was 1 year or less. They first had not got radiographic findings, but had typical clinical symptoms and signs of knee OA. Radiographic findings which 169 patients had at the beginning of the study were assessed in present study. Exclusion criteria were acute septic arthritis, inflammatory arthritis, and patients with a history of pathological osteoporotic fracture.

The study was conducted between December 2012 and November 2015. A total of 210 participants were included in the study according to the inclusion and exclusion criteria. Mean \pm SD age of them was 59.9 \pm 24.8 years and 122(58%) were women. Mean \pm SD symptom duration of them was 5.9 \pm 5.7 years. 191 patients fulfilled ACR criteria for rheumatoid arthritis, which had been last revised in 1987 [14], were designated for the control group.

2.2. Procedure

The French-Canadian version of the WOMAC OA index [15, 16] is a self-administered composite questionnaire with a three-dimensional measure of pain, joint stiffness and degree of difficulty in accomplishing daily life activities. The reliability and validity of this index have been approved by several studies [17, 18]. Each of these 24 questions is graded either on a five-point Likert scale or a 100-mm visual analogue scale (VAS) [19] ranging from 'no or 0' to 'extreme or 100'. In this study, we used the VAS as in the French-Canadian version [15]. The study used the following indicators to choose significant clinical symptoms and signs of knee OA; the WOMAC indicators more than 40mm on a 100-mm VAS, clinical symptoms and signs such as tenderness on medial epicondyle of femur, swelling of the knee, knee swelling with unremarked palpable redness of the knee, crepitus of the knee, asymmetric arthropathy of the knee and normal body temperature, laboratory finding, and radiographic changes including Heberden and Bouchard nodule.

2.3. Statistical Analysis

The data found via the electronic medical records were imported into Microsoft Excel. Positive incidence rates in both groups, OR (odds ratio) between the study and control group, and p-value via t -test, associated with the WOMAC indicators which were more than 40mm on a 100-mm VAS, clinical symptoms and signs, laboratory finding, and radiographic changes, were evaluated. Clinical symptoms and signs, which were OR $>$ 1 and p-value $<$ 0.05, were chosen up in the study group. We set up the coupled number of randomized clinical symptoms and signs which had sensitivity and specificity of more than 90%, respectively, for knee OA.

3. Results

3.1. Positive Incidence Rates, OR and P-value of the WOMAC Indicators more than 40mm on a 100-mm VAS

Positive incidence rates, OR (odds ratio), 95% confidence intervals (CI) and p-value of the 10 WOMAC indicators, which were more than 40mm on a 100-mm VAS, clinical symptoms and signs which described in UpToDate 2013 [9], laboratory finding, and radiographic changes including Heberden and Bouchard nodule [9, 10] were evaluated in the study and control group.

Table 1. Positive incidence rates, OR and p-value of indicators which most often occur in knee OA patients.

Indicators	Study (n=210)		Control (n=191)		OR	95% CI	P-value
	Positive (no.)	%	Positive (no.)	%			
knee joint pain at rest	135	64.28	171	89.5	0.21	64.22-64.35	2.89
nocturnal knee joint pain exacerbated by activity with weightbearing	195	92.8	165	86.38	2.04	92.82-92.89	0.032
more severe pain of the knee joint during going downstairs	189	90	159	83.24	1.81	89.95-90.04	0.046
knee joint pain when their walking begins	198	94.28	167	87.43	2.37	94.25-94.31	0.016
knee pain reduced sometime after their walking begins	187	89.04	157	82.19	1.76	89.00-89.08	0.049
knee pain at seating down	164	78.09	162	84.81	0.63	78.03-78.15	0.084
knee pain at standing up	154	73.33	153	80.1	0.68	73.27-73.39	0.1
tenderness on medial epicondyle of femur	201	95.71	170	89.00	2.75	95.68-95.74	0.01
swelling of the knee	157	74.76	153	80.10	0.73	74.70-74.82	0.2
knee swelling with unremarked palpable warmth(n=141)	139	98.58	182	95.28	3.43	98.56-98.59	0.035
redness of the knee	2	0.95	26	13.61	0.06	0.93-0.96	6.75
Flexion difficulty of the knee joint	141	67.14	170	89.00	0.25	67.07-67.20	1.6
Extension difficulty in the knee joint	138	65.71	165	86.38	0.30	65.65-65.77	1.5
crepitus of the knee	178	84.76	146	76.43	1.71	84.71-84.81	0.034
asymmetric arthropathy of the knee	180	85.71	133	69.63	2.61	85.66-85.76	0.0001
Heberden nodule	98	46.66	100	52.35	0.79	46.59-46.73	0.25
Bouchar nodule	44	20.95	88	46.07	0.31	20.89-21.00	8.9
morning stiffness	11	5.23	182	95.28	0.002	5.20-5.26	1.24
normal body temperature	198	94.28	167	87.43	2.37	94.25-94.31	0.01
ESR \leq 20mm/h	199	94.76	171	89.52	2.11	94.73-94.79	0.05
radiographic abnormalities of the knee joint	169	80.47	137	71.72	1.64	80.42-80.59	0.039

Indicators which were OR>1 and p-value<0.05 were 11; asymmetric arthropathy of the knee, tenderness on medial epicondyle of femur, knee joint pain when their walking begins, nocturnal knee joint pain exacerbated by activity with weightbearing, crepitus of the knee, knee swelling with unremarked palpable warmth, more severe pain of the knee joint during going downstairs, knee pain reduced sometime after their walking begins, normal body temperature, less than 20mm/h of ESR, and radiographic abnormalities of the knee joint (Table 1).

Normal body temperature and less than 20mm/h of ESR

are nonspecific to knee OA and radiographic abnormalities of the knee joint generally occur in the late stages of knee OA. Thus these indicators were excluded.

3.2. Significant Clinical Symptoms and Signs in Patients Knee OA

Each sensitivity and specificity of 8 clinical symptoms and signs less than 0.05 of p-value was calculated in the study group (Table 2).

Table 2. Sensitivity and specificity of clinical symptoms and signs of knee OA in the study group.

No	Clinical symptoms and signs	Sensitivity (%)	Specificity (%)
1	asymmetric arthropathy of the knee	85.71	30.36
2	tenderness on medial epicondyle of femur	95.71	10.99
3	knee joint pain when their walking begins	94.28	12.56
4	nocturnal knee joint pain exacerbated by activity with weightbearing	92.85	13.61
5	crepitus of the knee	84.76	23.56
6	knee swelling with unremarked palpable warmth	98.58	4.71
7	more severe pain of the knee joint during going downstairs	90	16.75
8	knee pain reduced sometime after their walking begins	89.04	17.80

Table 3. Changes of sensitivity, specificity and accuracy according to the coupled number of randomized clinical symptoms and signs.

Coupled number	Positive (no.)*	Negative (no.)**	Sensitivity (%)	Specificity (%)	Accuracy (%)
2	210	29	100	29.0	64.5
3	204	58	97.1	58.0	77.6
4	197	87	93.8	87.0	90.4
5	194	94	93.3	94.0	93.2
6	155	95	73.8	95.0	84.4
7	107	96	50.9	96.0	73.5
8	62	98	29.5	98.0	63.6

*Knee OA patients

**RA patients

Each clinical symptom and sign had high sensitivity, but low specificity. For increased in both sensitivity and specificity, the coupled number of randomized clinical symptom and sign was set up (Table 3). Five of the above clinical symptoms and signs resulted in a sensitivity and specificity for knee OA of 93.3 and 94.0%, respectively.

4. Discussion

Osteoarthritis (OA) is the most prevalent arthritis of rheumatic diseases, and is the major cause of disability due to arthritis. The diagnosis of OA is complicated by multiple factors. These include a lack of specific physical or

laboratory findings and discrepancies between symptoms and the results of radiographic examinations. As a result, OA is frequently diagnosed by an overall clinical presentations based upon the patient's age and history, findings on physical examination, and radiographic findings [7, 8]. Many studies had reported several criteria for knee OA for the past worldwide;

Yerov NK [20] reported clinical symptoms, signs, and radiographic findings associated with knee OA, such as knee pain which often occurs at night; knee pain which develops by physical activity and eliminates at rest; Heberden nodule, deformity of the knee joint, joint space narrowing, subchondral sclerosis, and osteophyte on X-ray. According to Alecsieva LE et al. [21], if the sum of the following findings point is 8, then it is distinct knee OA, if the sum is 4 to 7, it is almost distinct Knee OA (including mechanical pain and deformity of the knee joint), if the sum is less than 3, it is not knee OA: mechanical pain (3 points); knee pain occurred only by activity, but nocturnal pain caused by physical overloading; deformity of the knee joint associated with bony enlargement including Heberden nodule (4 points), joint space narrowing (2 points), subchondral sclerosis (5 points), and osteophyte (6 points) on X-ray. The classic criteria method for OA of the knee based upon the clinical characteristics; the presence of knee pain plus at least three of the following six clinical characteristics; greater than 50 years of age, morning stiffness for less than 30 minutes, crepitus on active motion of the knee, bony tenderness, bony enlargement, no palpable warmth [9]. The inclusion of laboratory criteria to these clinical characteristics; ESR less than 40mm/h, a rheumatoid factor titer less than 1:40, and synovial fluid suggestive of OA (clear color, viscous fluid, white blood cell count less than 2000/mm³) are added to the six clinical characteristics, the diagnostic criteria of knee pain and at least five of the nine features (six physical plus three laboratory) [9]. Knee joint pain and osteophyte on X-ray are added to one of the following three clinical findings; greater than 50 years of age, morning stiffness for less than 30 minutes, and crepitus on active motion of the knee [22]. In 1996, Altman R et al. [23] reported the following findings related to a diagnosis of knee OA: 50 years of age, morning stiffness for less than 30 minutes, crepitus on active motion of the knee, and osteophyte on X-ray. The following is the 1994 diagnostic criteria for knee OA: one of joint space narrowing or subchondral cysts, or subchondral sclerosis on X-ray, and no increased acute phase reactants on laboratory findings plus at least three of the following six clinical findings; more severe pain of the knee joint during going downstairs, knee joint pain when their walking begins, knee pain increased after overloading, tenderness on medial epicondyle of femur, crepitus of the knee [Ri Pohum (1994) Clinical Study of rational diagnosis and treatment of the osteoarthritic knees. Doctoral dissertation, 111]. In 2007, Pak Kyonghue suggested the clinical diagnostic criteria for knee OA: radiographic findings of the knee joint and normal acute phase reactant plus five of the following eight clinical findings; tenderness on medial epicondyle of

femur, knee joint pain when their walking begins, knee pain increased after overloading, crepitus of the knee, no palpable warmth, more severe pain of the knee joint during going downstairs, knee pain reduced sometime after their walking begins, and Heberden nodule [Pak Kyonghue (2007) Clinical study of diagnosis and treatment of several rheumatic diseases. Doctoral dissertation, 82].

The above diagnostic criteria depend upon the addition of radiographic and laboratory findings to clinical symptoms. Rheumatic diseases are generally divided into the early and late stages based upon a 6 month period after onset of symptoms. The incidence rates of any radiographic abnormalities of the knee were 83.9 (62/74) and 100% (156/156), respectively, in the early and late OA. Osteophyte is the most specific radiographic finding of OA [13]. But none of patients (n=74) with less than a year of breakout of symptoms had osteophyte on knee X-ray. As a result, radiographic abnormalities of knee OA suggested that patients whose medical history of knee OA was less than a year hadn't got any of joint space narrowing, subchondral sclerosis, subchondral cysts and osteophyte. It has been a certain time, approximately months or even years in patients with onset of OA symptoms, before radiographic abnormalities generally have occurred in knee OA [2]. Laboratory indicators are most often mild to moderate unless there are complications such as septic arthritis or rheumatoid arthritis [9]. Mean age of many patients with knee OA was more than 50 years, but recently knee OA has affected those with age of less than 50 years in randomized controlled trials [24, 25]. It is not clear whether palpable knee pain is bony or of soft tissue, and it needs skill of specialist to distinguish bony enlargement from soft tissue swelling. Thus we thought that more than 50 years' age limitation and bony enlargement might not be appropriate in making a diagnosis of knee OA.

Knee OA affects both medial and lateral patella-femoral compartments of the knee. But medial compartments are more often involved in population for the character of lesion location [26]. Most of patients with knee OA have complained of pain and tenderness on medial knee. It suggested that medial epicondyle would be anatomic landmark of tenderness to be clear about knee OA.

The primary pathological changes are loss of articular cartilage in OA, and are inflammatory process of synovium in inflammatory joint diseases including rheumatoid arthritis. Articular cartilage has a physical structure which acts as sponge-like slick surface, and makes synovial fluid absorbed at rest and oozed out by activity, leading to lubrication effect [27, 28, 29]. Osteoarthritis may result in less synovial fluid, decreased lubricity and buffering, and the knee pain. Tenderness on medial epicondyle of femur, knee joint pain when their walking begins, nocturnal knee joint pain exacerbated by activity with weightbearing, crepitus of the knee, more severe pain of the knee joint during going downstairs, knee pain reduced sometime after their walking may result from disturbance of lubricity and buffering.

Knee OA is non-inflammatory disease, but results in knee swelling with secondary synovitis due to mechanical stress [2]. Inflammatory process of secondary synovitis may be less severe

than of primary one of inflammatory joint diseases, and local warmth may be mild. Therefore we thought that expression of knee swelling with unremarked palpable warmth may be more suitable.

Knee OA is the relative local joint disease and may develop due to compensatory loading with promoting onset of disease. Bilateral disturbance of the knee joint generally haven't developed together because duration of onset and intensity of loading vary in bilateral knees. And we have applied the expression of asymmetrical arthropathy of the knee [27, 28, 29].

Finally, it is considered that clinical findings for knee OA have reflected clinical osteoarthritic symptoms of the knee, which are mechanical loading-related pain due to primary articular cartilage loss, leading to joint disease caused by the second synovitis. Although diagnostic criteria for knee OA based on clinical symptoms alone were reported in UpToDate 2013, it had a sensitivity of more than 90% and low specificity of 69%. As a result, clinical symptoms and signs with high sensitivity and specificity may help knee OA to be correctly diagnosed.

Patients with knee OA may have complaints of classic knee pain, but haven't got any of osteoarthritic radiographic abnormalities in the early stages. Such patients would have been diagnosed only when they have typical radiographic findings while following up. Clinical symptoms and signs we proposed, however, may be helpful to patients with the above, but not radiographic findings in the early stages. Thus we dose it is recommended the above as the early diagnostic significance and high cost-efficiency for knee OA.

5. Conclusion

In conclusion, this study has shown that significant clinical symptoms and signs in knee OA patients are as follows: asymmetric arthropathy of the knee; tenderness on medial epicondyle of femur; knee joint pain when their walking begins; nocturnal knee joint pain exacerbated by activity with weightbearing; crepitus of the knee; knee swelling with unremarked palpable warmth; more severe pain of the knee joint during going downstairs; knee pain reduced sometime after their walking begins.

Five of the above clinical symptoms and signs resulted in a sensitivity, specificity and accuracy for knee OA of 93.3, 94.0 and 93.2%, respectively. Such clinical symptoms and signs, as well as the coupled number of randomized clinical symptom and sign, related to a diagnosis of knee OA need to be investigated in further research.

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