Profile of osteophyte location in different grades of functional status in patients with knee osteoarthritis

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ABSTRACT

Background. Osteophyte is a reparative response to cartilage breakdown in osteoarthritis (OA) and osteophyte formation is a knee stabilizing factor. Disability could be found in patients with knee OA.

Objective. To identify the profile of osteophyte formation (location, size, and direction) based on knee radiograph and functional status examination in knee OA patients who presented to the Rheumatology Clinic, Cipto Mangunkusumo Central National General Hospital. Methods. Samples were taken by consecutive approach. Knee radiographs (weight bearing anteroposterior and 30 degrees flexion skyline views) and functional status examinations were performed on 100 patients with knee OA (90 females and 10 males with ages ranging from 51 to 74 years old). A radiologist assessed films for osteophyte profile such as location, size, and direction according to standard atlas. One knee with the severe radiological assessment based on OA grade was selected from one patient to be the profile. Lequesne Algofunctional Index was also taken from the patients.

Results. The site of osteophyte in patients with knee OA was mostly found at lateral femur (85/100 subjects). Based on specific location, grade 2 osteophyte at lateral femur was the most frequent size (49/100 subjects) and osteophyte extending toward the lower middle at lateral patella (65/100 subjects) was the most frequent direction of osteophyte. The most frequent profile for size and direction of osteophyte at specific location was the grade 2 osteophyte extending toward the lower middle at lateral patella (35/100 subjects). Severe functional status impairment was found in 53% of the patients. The most frequent functional status found according to specific location of osteophyte was severe functional status impairment in patients with osteophyte at lateral femur (46/100 subjects). The most frequent functional status of OA patients based on the size and direction of osteophyte at specific location was the severe functional impairment in the patients with grade 2 osteophyte at lateral femur (27/100 subjects) and the patients with osteophyte extending towards the lower middle at lateral patella (37/100 subjects) respectively.

Conclusions. Osteophyte at lateral femur, osteophyte at lateral tibiofemoral compartment, grade 2 osteophyte at lateral femur, and osteophyte extending toward the lower middle at lateral patella were the profiles of osteophyte which mostly showed severe functional status impairment in patients with knee OA.

Osteoarthritis (OA) is the most prevalent form of synovial arthritis. Around 56.7% of patients who were admitted to the Clinic of Rheumatology, Cipto Mangunkusumo Central National General Hospital suffered from one variation of OA in which knee OA is the most frequent variation. According to the degeneration theory of OA, OA will induce various enzymatic reactions producing proteolytic or colagenolytic enzymes by the chondrocyte. These enzymes will destroy cartilage matrix and this injury will induce subchondral bone reparative response through osteophyte formation. Along with this pathogenesis, inflammation process is also involved and the potential damage is caused by the release of destructive cytokines such as interleukin-1 and tumor necrosis factor α. Incompatibility between these destructive cytokines and modulator or anabolic growth factor cytokines further stimulates cartilage breakdown. This destructive inflammatory process will also induce reparative response by circulating bone growth factors, which are transforming growth factor-β and bone morphogenic protein-2, throughout osteophyte configuration.[1]

Patients with knee OA usually complain of knee pain and the discovery of osteophyte at the knee joint compartment showing significant correlation between early diagnosis of OA and knee pain. Therefore, finding osteophyte at specific knee compartment could be an important predictor and a reliable sign of knee pain.[2,3,4,5] Furthermore, limitation of movement or immobilization caused by knee pain would inhibit osteophyte formation whereas osteophyte was needed to stabilize the knee joint. Radiological figures of OA at tibiofemoral joint (TFJ) or patellofemoral joint (PFJ) are associated with osteophytosis at the same compartment.[5,6] Thus, finding osteophyte could become an efficient indicator to confirm diagnosis of OA at specific compartment.[7,8] Patients with radiographs of knee OA, even without definite symptoms, proved having lower quadriceps muscle strength. This source of muscle weakness could cause disability in patients with knee OA.[9] Accordingly, osteophyte could turn out to be an important indicator of determining functional disorder of knee OA.

The knee joint has three major compartments: lateral TFJ, medial TFJ, and PFJ. These compartments are further divided into 8 locations:

lateral femur, medial femur, medial tibia, lateral patella, medial patella, lateral femoral trochlea, and medial femoral trochlea. Cartilage breakdown as well as osteophyte development as a reparative response might occur at each of these locations.[4] Heterogenecity of structural changes, grade of disease, and functional status of patients with knee OA could be assessed by identification of osteophyte formation at specific location. This study is about exploring the profile of osteophyte location through radiograph examination in different grades of functional status by using Lequesne Algofunctional Index assessment in patients with knee OA.

METHODS

Subjects

The population of this study consisted of patients with knee OA who presented to the Clinic of Internal Medicine, Cipto Mangunkusumo Central National General Hospital and samples were taken consecutively from patients who fulfilled the inclusion criteria: had been clinically and radiologically diagnosed with ACR criteria; had not taken any analgesics, nonsteroid anti inflammation drugs, or traditional rheumatic medicines since 1 day before sample collection; had never been injected with intra articular hialuronan or intra articular corticosteroids since 3 months before sample collection; had no history of knee trauma or surgery; had no congenital or acquired knee deformity; had no lower extremity weakness; had no acute inflammation of the knee; and was willing to be involved based on the informed consent.

Data collections

Knee radiographs (weight bearing anteroposterior and 30 degrees flexion skyline views) and functional status examinations were performed on 100 patients with knee OA who fulfilled the inclusion criteria. A radiologist who was assigned by the Department of Radiology assessed films for osteophyte profile such as location, size, and direction according to standard atlas. One knee with the severe radiological assessment based on OA grade was selected from one patient to be the profile. Lequesne Algofunctional Index was also taken from these patients.

Statistics

The design of this study was cross sectional approach. The sample calculation was based on the profile of osteophyte location and functional status which can give the maximum subjects. The location of ostoephyte that can give the maximum amount was the medial femur (48.5% rounded to 50%). The functional status than can give the maximum amount was severe functional impairment (47.2% rounded to 50%). Therefore, this study needed 96 subjects, rounded to 100 subjects.

RESULTS

Characteristics of subjects

There were 100 patients with knee OA, 10 males and 90 females. Details are in table 1.

Table 1 Characteristic of the subjects (n=100)

Characteristic	Frequency
Sex	
Male	10
Female	90
Age	
51-62 years old	57
63-74 years old	43
Body mass index	
<23	22
≥23	78
Severity of osteoarthritis based on Kellgren Lawrence Score	
II	50
III	44
IV	6

Profile of osteophyte location

Osteophyte size at specific location

Osteophyte was commonly found at lateral femur (85/100 subjects). Grade 1 osteophyte at lateral femur (34/100 subjects) and grade 1 osteophyte at medial tibia (34/100 subjects), grade 2 osteophyte at lateral femur (49/100 subjects), and grade 3 osteophyte at medial femur (9/100 persons) were the most frequent specific size of osteophyte at specific location. Details are in table 2.

Table 2 Profile of osteophyte size at specific location (n = 100)

Osteophyte location	Grade of osteophyte			Total
	1	2	3	
Lateral femur	34	49	2	85
Medial femur	25	31	9	65
Lateral tibia	38	34	7	79
Medial tibia	34	30	2	66
Lateral patella	28	40	5	73
Medial patella	5	10	2	17
Lateral femoral trochlea	4	5	1	10
Medial femoral trochlea	23	18	6	47

Osteophyte direction at specific location

Osteophyte extending upward was found at lateral tibia or lateral femoral trochlea in only 1/100 subjects. Osteophyte extending toward the upper middle at lateral tibia (35/100 subjects), osteophyte extending outward at lateral femur (51/100 subjects), osteophyte extending toward the lower middle at lateral patella (65/100 subjects), and osteophyte extending downward at lateral patella (8/100 subjects) were the most frequent specific osteophyte direction at specific location. Further data of osteophyte direction is shown in figure 2.

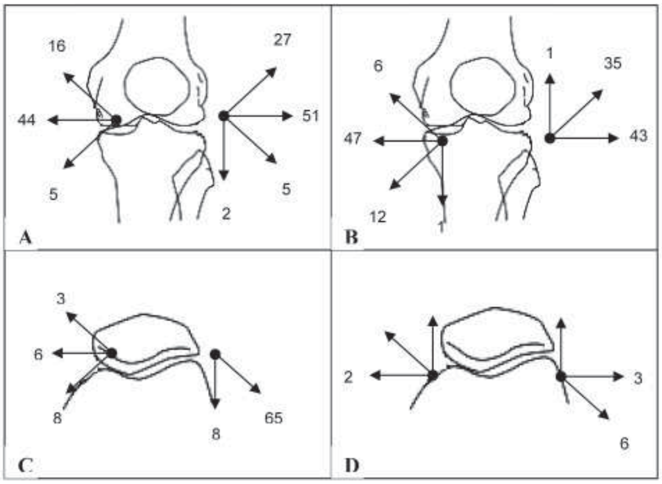
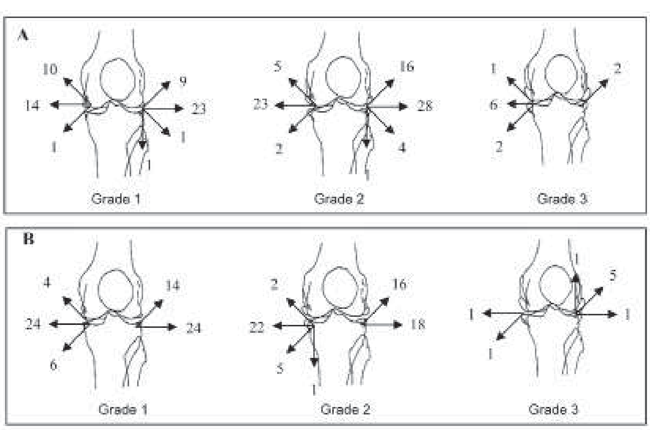


Figure 2 Profile of osteophyte direction among 100 subjects. Size of arrow reflects frequency of direction at each location. A. Femur. B. Tibia. C. Patella. D. Femoral trochlea.

Osteophyte size and direction at specific location

Grade 2 osteophyte extending outward at lateral femur (28/100 subjects) and grade 2 osteophyte extending outward at medial femur (23/100 subjects) are the most frequent osteophyte size and direction found at femur. Grade 1 osteophyte extending outward at lateral tibia (24/100 subjects) and medial tibia (24/100 subjects) are the most frequent osteophyte size and direction found at tibia. Grade 2 osteophyte extending toward the lower middle at lateral patella (35/100 subjects) and grade 2 osteophyte extending outward at medial patella (5/100 subjects) are the most frequent osteophyte size and direction found at patella. Grade 1 and grade 2 osteophytes (3/100 subjects each) extending toward the lower middle at lateral femoral trochlea and and grade 1 osteophyte extending outward at medial femoral trochlea (16/100 subjects) are the most frequent osteophyte size and direction found at femoral trochlea.



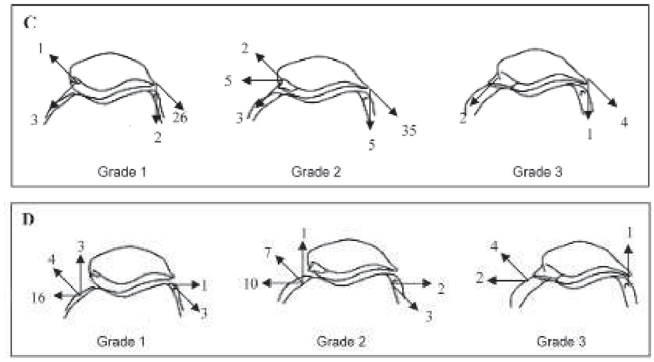


Figure 3 Frequency of osteophyte size and direction. A. Femur. B. Tibia. C. Patella. D. Femoral trochlea.

Profile of functional status

Patients with knee OA commonly suffered from severe functional status impairment (53%). Most male patients had moderate functional status impairment (8/10 subjects) whereas more females suffered from severe impairment (51/90 subjects).

Functional status based on specific osteophyte location

Severe functional status impairment in patients with osteophyte at lateral femur (46/100 subjects) was the most frequent functional status according to specific osteophyte location. Profile of functional status based on specific osteophyte location is shown in table 3.

Table 3 Profile of functional status based on osteophyte location (n = 100)

Osteophyte Location	Functional Status	
	Moderate	Severe
Lateral femur	39	46
Medial femur	30	35
Lateral tibia	35	44
Medial tibia	30	36
Lateral patella	32	41
Medial patella	10	7
Lateral femoral trochlea	4	6
Medial femoral trochlea	20	27

Functional status based on osteophyte size at specific location

Moderate functional status impairment was mostly found in patients with grade 2 osteophyte at lateral femur (22/100 subjects). Severe functional status impairment was mostly found also in patients with grade 2 osteophyte at lateral femur (27/100 subjects). Table 4 shows functional status based on the grade of osteophyte at specific location.

Table 4 Profile of functional status based on osteophyte size at specific location (n = 100)

Osteophyte size at specific location	Functional status	
	Moderate	Severe
Lateral femur		
Grade 1	16	18
2	22	27
3	1	1
Medial femur		
Grade 1	12	13
2	17	14
3	1	8
Lateral tibia		
Grade 1	18	20
2	15	19
3	2	5
Medial tibia		
Grade 1	15	19
2	15	15
3		2
Lateral patella		
Grade 1	15	13
2	15	25
3	2	3
Medial patella		
Grade 1	4	1
2	6	4
3		2
Lateral femoral trochlea		
Grade 1	1	3
2	2	3
3	1	
Medial femoral trochlea		
Grade 1	11	12
2	7	11
3	2	3

Functional status based on osteophyte direction at specific location

As shown in Table 5, moderate functional status impairment was mostly found in patients with osteophyte extending toward the lower middle at lateral patella (28/ 100 subjects), whereas severe functional status impairment was mostly found also in patients with same profile of osteophyte (37/100 subjects).

Table 5. Profile of functional status based on osteophyte direction at specific location (n = 100)

Osteophyte direction at specific location	Functional status	
	Moderate	Severe
Lateral femur		
Upper middle	**10**	**17**
Outward	**27**	**24**
Lower middle	**2**	**3**
Downward		**2**
Medial femur		
Upper middle	**5**	**11**
Outward	**22**	**22**
Lower middle	3	2
Lateral tibia		
Upward	1	
Upper middle	**18**	**17**
Outward	16	27
Medial tibia		
Upper middle	**2**	**4**
Outward	**20**	**27**
Lower middle	**8**	**4**
Downward		**1**
Lateral patella		
Lower middle	**28**	**37**
Downward	4	4
Medial patella		
Upper middle	3	
Outward	**4**	**2**
Lower middle	4	4
Lateral femoral trochlea		
Upward	1	
Outward	**1**	**2**
Lower middle	2	4
Medial femoral trochlea		
Upward	**3**	**1**
Upper middle	**7**	**8**
Outward	**10**	18

DISCUSSION

Osteophytes are reparative and remodelling response of OA. Osteophytes typically arise as a revitalization or reparative response by the remaining cartilage, but they may also develop from periosteal or synovial tissue. Osteophytes can be formed through the process of endochondral ossification in one or two ways. The first one involves vascular penetration into existing cartilage or also can be formed from the foci of cartilaginous metaplasia at joint margins.[4,10,11] Osteophyte formation is related to the increase of bone density and the influence of circulating bone growth factor and others such as insulin-like growth factor type-1, platelet-derived growth factor, fibroblast growth factor, transforming growth factor β, colony stimulating factor type-1, and bone morphogenic protein-2. Transforming growth factor β enhances production of extracellular pyrophosphate by chondrocytes through release of ATP whereas chondrocalcinosis in production of calcium pyrophosphate crystals had been confirmed to be associated with osteophyte formation and hypertrophic OA.[4,7, 12-14]

Joint instability is a biomechanical trigger of osteophyte formation; subsequently, osteophyte and bone remodelling is an effort to stabilize and widen the joint surface thus someone is capable of standing up under biomechanical weight pressure. Osteophytes develop in areas of a degenerating joint with lower stress so that it may be found at peripheral or marginal although they may appear at other articular location as well.[4,10] Osteophyte is frequently a sign of OA development. Osteoarthritis at specific joint compartment is diagnosed by finding osteophyte while grade of severity and disease progression are identified with assessment of joint space narrowing.[4,15] Radiological changes of knee OA were caused by the severity of joint damage at specific location as proven by Cicuttini et al. They discovered that there was a significant correlation between volumes of cartilage breakdown at femoral and tibial sites and radiological changes of knee OA at those sites.[16] In their trial on animal model, van Osch et al had concluded that cartilage breakdown would induce osteophyte formation in which the location of the osteophyte and the damage were correlated. This correlation is a compartment revitalization effort of osteoarthritic process.[17] The prevalence of osteophyte at specific compartment increased along with the narrowing of the joint space.[4] Neame et al came to the same conclusion regarding the significant association between osteophytosis and joint space narrowing.[5]

According to the theory, medial TFJ is a mechanically unstable knee compartment and gets the largest over pressure during activity so that this compartment dominantly suffers from cartilage breakdown of knee OA. Osteophytosis is more dominant at the contra lateral compartment (lateral TFJ) to stabilize the knee joint.[10,11] This study found that lateral femur was the most common location of osteophytes in patients with knee OA. Nagaosa et al reported that in over 204 patients with knee OA, lateral tibia was the most common site of osteophyte.[4] Even though the results were different, Nagaosa et al confirmed the same results that lateral TFJ was the most frequent site of osteophyte.

The location and size of osteophyte are related to joint space narrowing and knee malalignment.[4,15] Van Osch et al also found that the size of osteophyte was associated with the severity of cartilage damage of knee OA.[17] McCauley et al reported that marginal and central osteophyte were associated with progression of cartilage breakdown of knee OA.[18] Marginal osteophyte seemed to be larger if the joint space was obliterated than if just narrowed.[4] Kobayashi reported in his prospective study that there was an annual increase in osteophyte length evaluated in a seven-year study and this increase is significantly correlated with femorotibial angle changes that caused deformity of knee OA.[19]

Grade 2 osteophyte at lateral femur was the most common size of osteophyte according to specific location found in this study. Nagaosa et al found that grade 1 osteophyte**,** without specifically informing the location of osteophytes, as the most common size.[4] Even those results were different, specific size of osteophyte such as grade 1 and 2 at specific location could influence the severity grade of knee OA.

The direction of osteophyte development was influenced by how far at specific direction it should grow to widen the surface of the knee joint, to stabilize the knee joint, to protect against fracture and the restraints of adjacent fibrous structure as well.[4] This study found that osteophyte extending toward the lower middle at lateral patella was the most common direction of osteophyte among patients with knee OA. Nagaosa et al reported that osteophyte extending outward at medial tibia was the most frequent direction of osteophyte at specific location in his study.[4]

A 6 year prospective study of Miyazaki et al confirmed that dynamic loading of activity of the knee in patients with medial TFJ OA caused more severe progression of the disease at the same compartment. Disease progression is identified by assessing radiological changes such as joint space narrowing, osteophytosis, and the presence of deformity.[20] The importance of specifically identified radiological changes of knee OA was also supported by the study of Slemenda et al. They found that there were quadriceps muscle weaknesses in female patients who were radiologically diagnosed with TFJ OA although they had not yet complained of knee pain or suffered from muscle atrophy.[21] As reported by Hurley et al, cartilage breakdown of knee OA could cause quadriceps sensory- motor function disorder and decreased postural stability which are related to decreased functional performance.[22] O' Reilly et al also had the same conclusion that quadriceps muscle weakness is associated with knee pain and disability of knee OA.[23] Knee joint damage and chronic pain of OA cause muscle atrophy, decreased mobility, and worsened instability that ends in physical disability. Accordingly, OA is responsible of causing disability among the elderly. This disability could be detected by assessing radiological changes caused by cartilage breakdown of knee OA.[24,25]

Severe functional impairment was the most common functional status found in this study. Kertia et al reported that there was a correlation between inflammation and clinical degree of knee OA. They stated that severe functional impairment was the most common functional status of patients with knee OA so that it could be concluded that the inflammation involved could determine the functional status of patients with knee OA.[26]

A larger study reported that compared to TFJ angle changes, osteophyte at PFJ was more strongly correlated with knee OA pain. Osteophytes at TFJ was more assumed to be an early sign of OA.[2] Osteophytes at the unstable joint will be induced by joint movement and inhibited by immobilization. Osteophytes are important to stabilize the knee joint; therefore, removing osteophytes in arthroplasty surgery of knee OA would increase instability.[4]

A study conducted by McAlindon et al discovered that medial TFJ OA was associated with disability of knee OA. Osteophytes are more extensive at the lateral TFJ. However, they did not specifically study the location of osteophytes.[27] Severe functional impairment in patients who had osteophytes at lateral femur was the most common functional status in this study. Lateral femur is part of lateral TFJ so that the presence of osteophyte at lateral femur may be an indicator of the severity of functional disorder due to disability of knee OA. This study found that grade 2 osteophyte at lateral femur was the most common profile among patients with knee OA who had severe functional impairment. Larger osteophytes might not influence the more severe functional status but specific osteophyte size at specific location might influence the severity of disease and functional status among patients with knee OA.

Pottenger et al reported that after having gotten osteophyte removal surgeries, 20 patients of knee OA with varus-valgus deformity suffered an even worse knee instability.[28] In this case, osteophyte at specific location tended to grow laterally to widen the surface of the knee joint. Osteophytes could go vertically to stabilize the joint in order to reduce excessive valgus motion. Larger osteophytes predominantly extend upwards or downwards whereas the anatomical limitation of small osteophytes to grow laterally will be limited by the restraints of adjacent fibrous structure. The development of osteophytes at specific compartment of the knee joint depends on the need to widen and strengthen the osteophyte base to protect against fracture.[4]

Despite the absence of information about osteophyte direction, McAlindon et al reported that the prevalence of PFJ OA was significantly associated with knee pain and disability.[27] Cartilage breakdown at PFJ compartment is usually more frequently found at lateral site whereas osteophytosis is more extensive at the contra lateral site.[10,11]

This study found that osteophyte extending to lower middle direction at lateral patella was the most common characteristic among patients with knee OA who had severe functional impairment. Here we see that at lateral patella, osteophyte direction (not the size of osteophyte) gave more cases of knee OA with severe functional impairment. Until now there has not yet been a study about the profile of osteophyte direction in different grades of functional status of knee OA patients. Even a study on the association between osteophyte direction and grade of knee OA disease and/or disability causing functional impairment has never been conducted. The direction of osteophyte at this site could become an indicator of severe functional disorder in knee OA patients.

CONCLUSIONS

Osteophyte at the lateral femur, at the lateral tibiofemoral compartment, grade 2 osteophyte at lateral femur, and osteophyte extending toward the lower middle at lateral patella were the profiles of osteophyte which mostly showed severe functional status impairment in patients with knee OA. This specification of osteophyte location, size, and direction from knee radiograph assessment could inform the severity of knee OA, functional status, and disease progression; therefore, further studies with appropriate design, method, and sample size with the utilisation of other specific diagnosis devices such as MRI and OA biologic marker to detect disease progression are required to verify this association.

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