Original Article

Symptoms and physical findings of early knee osteoarthritis

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Background: There is an increasing need on identifying symptoms and physical findings of the early knee osteoarthritis (KOA). The purpose of this study was to clarify clinical manifestation of early KOA detected by ultrasonography (US) and standard radiographs, and to characterize them for early detection of KOA.

Methods: A total of 1,090 participants (2,180 knees) recruited at residential health examinations were evaluated by visual analogue scale of pain, the Japanese Knee Osteoarthritis Measure (JKOM) score as a health-related score, knee extension muscle strength, and images (US and radiographs). Among them, 663 knees with Kellgren-Lawrence Grade (KLG) 0 and 1 were divided into four groups; Group A (with no pain and echo-negative OA findings, n=192), Group B (with no pain and echo-positive OA findings, n=284), Group C (with pain and echo-negative OA findings, n=84), and Group D (with pain and echo-positive OA findings, n=103).

Results: Group C and D indicated a significant higher JKOM score than Group A and B, especially in terms of disturbance of activities of daily living (ADLs) such as ascending upstairs or descending downstairs, standing up, and squatting. Group B showed significant higher subscales in disturbance of these ADLs than Group A, although Group B has no pain. Maximum knee extension muscle strength in Group C and D were weaker than Group A and B. Group D indicated the weakest knee extension muscle strength among the groups. In women, weak knee extension muscle strength was significantly correlated with pain and echo-positive OA findings. The risk factors of early KOA were woman, high BMI, and weak extension muscle strength.

Conclusions: This study showed that symptoms of early KOA might be not only pain but also the disturbance of ADLs such as ascending upstairs or descending downstairs, standing up, and squatting with weak knee extension muscle strength. Pain-free knees with positive US findings, when disturbing these ADLs, might be the pre-stage of early KOA, namely super-early KOA. For not only treatment of the established KOA, but also prevention of proceeding to early KOA, strengthening of the knee extension muscle to maintain these ADLs might be recommended.

Keywords: Symptom; early osteoarthritis; knee; JKOM; muscle strength

Received: 08 September 2018; Accepted: 19 September 2018; Published: 29 September 2018.
doi: 10.21037/aoj.2018.09.06
View this article at: http://dx.doi.org/10.21037/aoj.2018.09.06

Introduction

There is an increasing need on identifying symptoms and physical findings of early knee osteoarthritis (KOA), which is never recovered once destroyed (1). More than 21 million people suffered from osteoarthritis (OA) and elderly Americans aged 70 or older have some degree of radiographic knee OA in the U.S. (2-4). In Japan, a rapid

super-ageing society, KOA affects approximately 25 million people, estimated 48.2% and 51.6% in the age groups 70–79 and >80 years in men, and 71.9% and 80.7% in women, respectively (5). Symptomatic KOA deteriorates activity of daily living (ADL), impairs the health-related quality of life (HRQoL), and consumes a significant amount of healthcare resources. A systemic review showed that the total annual average direct and indirect costs per patient with OA varied from US$1442 to US$21,335 and from US$238 to US$29,935, respectively, both in USA (6). In addition, joint replacement surgeries are most often indicated for knee and hip OA; 905,000 knees and hips were replaced in 2009 at a cost of $42.3 billion (7). World Health Organization (WHO) estimates that the number of people over 60 years will rise 900 million to 2 billion between 2015 and 2050, and address that OA is one of the greatest causes of disability and comprehensive public health action will require fundamental shifts in how we think about ageing and health (8).

There are several established definitions of OA and classification criteria of KOA (9-11), however, it is more complicated to diagnose the early KOA than the established KOA. To identify it clinically relevant, and to contribute to classifying patients for clinical trials, Luyten *et al.* proposed the criteria for early KOA as follows (12):

(I) Pain in the knee.
(II) Radiographic grading as classified by Kellgren-Lawrence grade < II.
(III) Structural findings proven by arthroscopy and/or MRI:
  (i) Arthroscopic findings of cartilage lesions as defined by International Cartilage Repair Society (ICRS) I–IV in two compartments or II–IV in one compartment (13);
  (ii) MRI findings of cartilage lesions defined as Whole-Organ Magnetic Resonance Imaging (WORMS) 3–6 (14), or Boston Leeds Osteoarthritis Knee Score (BLOKS) grades 2–3 (15), meniscus injury defined by BLOKS grades 3 and 4, or bone marrow lesion.

These criteria including pain and radiographic findings might be indeed easily used for clinicians, however structural criteria including arthroscopic and/or MRI findings might be sometimes difficult clinically and epidemiologically in terms of invasive test and high-demanded costs. Therefore, we propose the usage of non-invasive, fast, easy-to-use and safe ultrasonography (US) in addition to standard radiographs to detect early KOA.

In this paper, we demonstrate clinical manifestation of early KOA detected by US and standard radiographs and characterize them for early detection of KOA. In addition, we address the importance of recognition of symptoms and physical findings in the pre-stage of early KOA, namely super-early KOA to prevent from proceeding to early KOA.

Methods

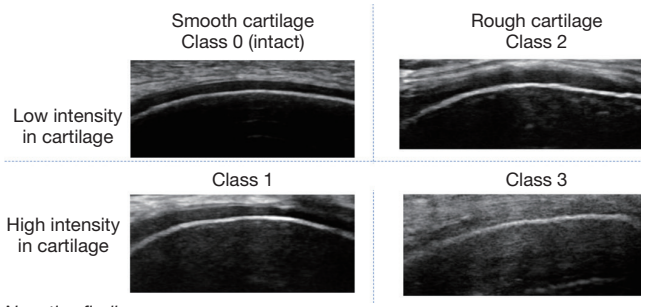
The Ethics Committee of Shimane University School of Medicine approved the present study, and all participants provided written informed consent. Participants were recruited at residential health examinations held in Shimane prefecture from 2011 through 2014. In total, 1,060 participants (2,120 knees) were recruited. Measurements of height and weight were performed on site. They answered questionnaires about their musculoskeletal symptoms, especially of knee joints, their past and present medical history, occupation, family history, and health-related quality of life. And they underwent a radiographic examination, muscle power test, and US.

Clinical manifestations

The severity of pain was measured by a visual analog scale (VAS, 0 to 100). The clinical symptoms, activities and health conditions were evaluated by the Japanese Knee Osteoarthritis Measure (JKOM) score (13). The JKOM score is a patient-based, self-answered evaluation score that consists of four subscales: pain and stiffness (0 to 32), ADLs (0 to 40), social activities (0 to 20), and general health conditions (0 to 8) with 100 points as the maximum score. The JKOM score is higher in KOA patients with more pain and physical disability, and this evaluation modality have been shown to be a reliable and stable outcomes measure for studies of the clinical outcomes of Japanese subjects with knee OA (16). Statistical evaluation and comparison have also proven its enough reliability and validity with other health-related scales, such as the Western Ontario and McMaster Universities Arthritis Index (WOMAC) and the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) (16).

Radiographs and US

One of the authors (HT, who has 10 years of experience as orthopedists) categorized radiographs of both knees in the



Negative finding

(Class 0) smooth superficial layer and low intensity of cartilage

Positive findings

(Class 1) smoothness and high intensity of cartilage

(Class 2) roughness and low intensity of cartilage

(Class 3) roughness and high intensity of cartilage

Figure 1 Classification based on the US findings. US, ultrasonography.

standing position based on the Kellgren-Lawrence grade (KLG) (17). The knees were classified as follows:

(I) KLG 0 (no radiographic features of OA);

(II) KLG 1 [doubtful joint space narrowing (JSN) and possible osteophytic lipping];

(III) KLG 2 (definite osteophytes and/or possible JSN);

(IV) KLG 3 (multiple osteophytes, definite JSN, sclerosis, possible bony deformity), and;

(V) KLG 4 (large osteophytes, marked JSN, severe sclerosis and definite bony deformity).

Two of the authors (SK and NK who have 5 years of experience in ultrasonographic evaluation of early KOA) evaluated all ultrasound scans. The subjects were examined sitting on the table with a flexed knee in the deep flexed position. The longitudinal sagittal scan to the distal end of the midline medial and lateral condyle were obtained by a linear transducer probe (14–16 MHz, Avius®; HITACHI ALOKA Ltd., Tokyo, Japan). The cartilage was subjectively evaluated using 4 classifications based on the US findings of the condition of the superficial layers (smooth or rough) and the intensity of cartilage (monotonous anechoic or hyper echogenicity) as follows (15): class 0 (smooth surface and monotonous echogenicity), class 1 (smooth surface and increased echogenicity), class 2 (rough surface and monotonous echogenicity), and class 3 (rough surface and hyper echogenicity). Class 0 is regarded as echo-negative, and Class 1 or more as echo-positive findings (*Figure 1*). Statistical evaluation and comparison with arthroscopic findings have been shown enough reliability and validity of the US (18-21).

Muscle strength

Finally, we (YU and HT) evaluated maximum knee extension muscle strength of the subjects by the Locomo Scan® (ALCARE Co., Ltd., Tokyo, Japan) (22). The subjects extended their knee joint by putting their knee joint on the knee-holding part of the Locomo Scan®, with the load pressure applied to the Locomo Scan® in the popliteal region at this time measured and displayed as the isometric knee extension strength (quadriceps muscle strength). The maximum voluntary contraction of the quadriceps muscle was measured for each leg with the Locomo Scan® and recorded the better value of the two measured values. The value divided by weight was used as the extension muscle strength for statistical analysis. The average muscle strengths in total men and women were calculated as reference.

Statistical analysis

The means and standard deviations (SDs) were calculated for weight, height, BMI, and maximum knee extension muscle strength of each leg per weight, in each category.

Results were analyzed using one-way analysis of variance, multiple comparison by scheffe method, and logistic regression analysis from SPSS 22, IBM®. A P value ≤ 0.05 was considered statistically significant.

Results

Subject characteristics

The present study was participated by 1,090 individuals (345 men, 745 women; mean age: 71 years, 40–91 years). The means (range) of weight, height, and body mass index (BMI) in the present study are 153.8 cm (129.3–181.5 cm), 54.3 kg (28.2–98.6 kg), and 22.9 (14.2–35.9), respectively. Number of the participants classified by sex, KLG and US class are summarized in *Table 1*.

Clinical manifestation

To clarify clinical characteristics of early knee OA, 663 knees with KLG 0 and 1 were divided into four groups in terms of pain and US findings; Group A (with no pain and echo-negative findings, n=192), Group B (with no pain and echo-positive findings, n=284), Group C (with pain and echo-negative findings, n=84), and Group D (with pain and echo-positive findings, n=103).

VAS of pain was significantly different among the groups

Table 1 Characteristics of participants

KLG	Total (n)	Men (n)	Women (n)	US findings (%)				
				Class 0	Class 1	Class 2	Class 3	Positive ratio
0/1	663	335	328	41.6	5.9	38.8	13.7	52.5
2	817	231	586	22.7	3.2	44.7	23.2	67.9
3/4	700	124	576	4.3	3.0	41.1	51.6	92.7

KLG, Kellgren-Lawrence grade; US, ultrasonography.

Table 2 Demographic data of the Groups A-D, objectively measured knee pain and physical function

Evaluation items	Group A	Group B	Group C	Group D	P value
Pain VAS	0	0	28±22	32±22	<0.001
JKOM subscale					
1. "morning stiffness"	0.19±0.43	0.18±0.52	0.81±0.76	0.64±0.84	<0.001
2. "morning pain"	0.15±0.40	0.19±0.47	0.76±0.77	0.74±0.77	<0.001
3. "sleeping pain"	0.08±0.34	0.10±0.43	0.36±0.64	0.32±0.62	<0.001
4. "walking pain"	0.15±0.40	0.14±0.41	0.63±0.68	0.55±0.66	<0.001
5. "pain while upstairs"	0.17±0.42	0.20±0.47	0.80±0.81	0.82±0.85	<0.001
6. "pain while downstairs"	0.18±0.41	0.20±0.49	0.77±0.80	0.79±0.86	<0.001
7. "pain while standing up"	0.27±0.50	0.32±0.69	0.96±0.86	1.03±0.93	<0.001
8. "pain while standing"	0.20±0.44	0.17±0.47	0.66±0.69	0.71±0.74	<0.001

Group A: with no pain and echo-negative findings, Group B: with no pain and echo-positive findings, Group C: with pain and echo-negative findings, and Group D: with pain and echo-positive findings.

(*Table 2*). There were no significant differences in BMI among the groups in men, however, BMI was significantly increased with pain and US findings in women (*Figure 2*).

Group C and D indicated a significant higher JKOM score than Group A and B, especially in terms of the disturbance of ADLs such as ascending upstairs or descending downstairs, standing up, and squatting. Subtotal JKOM score of ADLs, social activities and general health conditions except pain and stiffness was increased with pain and US findings (*Tables 2,3* & *Figure 3*). Group B showed significant higher subscales** in the disturbance of those ADLs than Group A, although Group B has no pain (*Figure 3*).

Muscle strength

Maximum knee extension muscle strength in Group C and D were weaker those in Group A and B. Group D indicated the weakest muscle strength among the groups. The muscle strength weakness in women was significantly correlated with pain (*Figure 4*).

Risk factors

Adjusted odds ratios of proceeding Group D from Group B in women, high BMI (≥25), and muscle weakness (< average knee extension muscle strength) were 1.30 (95% CI: 0.80–2.14, P=0.290), 1.86 (95% CI: 1.04–3.33, P=0.034), and 1.19 (95% CI: 0.74–1.91, P=0.162). Adjusted odds ratios of proceeding Group B from Group A in women, high BMI (≥25), and muscle weakness (< average knee extension muscle strength) were 1.30 (95% CI: 0.80–2.14, P=0.290), 1.86 (95% CI: 1.04–3.33, P=0.034), and 1.19 (95% CI: 0.74–1.91, P=0.162).

Discussion

In a large residential health examination of Japanese with

confirmed early KOA by US and radiographs, ADLs such as ascending upstairs or descending downstairs, standing up, and squatting were most likely to be the first disturbances with pain. This study also demonstrates that painful knees indeed disturbed these ADLs, however did so even pain-free knees with US findings. This means that pain was not always necessary to disturb these ADLs. Women, high BMI, and weak knee extension muscle strength except pain might be contributed to the disturbances. Weight-bearing bending of the knee in these ADLs needs muscle power to maintain the posture and physical activity. Women who have weak knee extension muscle strength, high BMI which cause over load stress to the knee joint, and weak knee extension muscle strength are the risk factors proceeding to early KOA. Therefore, early detection of the disturbances of these ADLs might benefit care management of high-risk members in a community, monitoring for their process and prevention of established KOA.

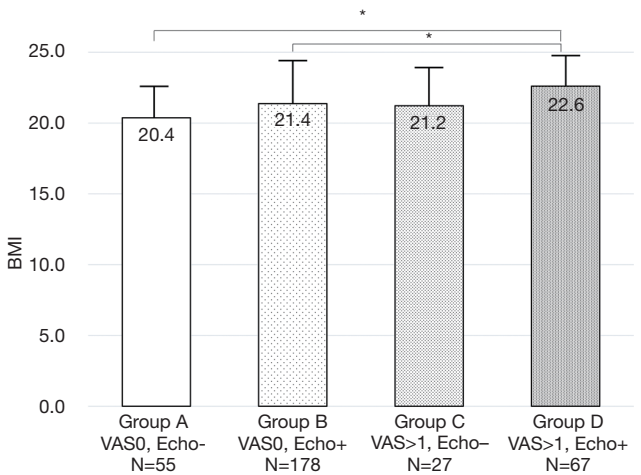


Figure 2 BMI in terms of pain and US findings (women). *, P<0.05. US, ultrasonography.

To our knowledge it is the first study to determine which activities might be associated with pain of early KOA. According to Madry *et al.* (23), one of the first symptoms is pain while climbing stairs and the severity of pain is increased while kneeling or squatting activities. However, they did not show clinical evidences referred to these findings. It might be theoretically right that activities to bend the knee joint with weight seem to cause initial pain following development of KOA, but this might have not been proven. Hensor *et al.* assessed the WOMAC data of 4673 people obtained from the Osteoarthritis Initiative (OAI), determining which activities might be related to the start of knee pain (24). With Rasch analysis to rank the WOMAC pain questions (activities), they concluded that knee pain would appear first during weight-bearing activities regarding bending of the knee, such as using stairs. Our results that ADLs such as ascending upstairs or descending downstairs, standing up, and squatting were disturbed even in early KOA, were well corresponded to those of Hensor *et al.* (24). Moreover, pain-free knees with

Table 3 Demographic data of the Groups A-D, objectively measured activities of daily living and social activities

JKOM subscale	Group A	Group B	Group C	Group D	P value
9. “ascending upstairs, descending downstairs”	0.27±0.61	0.37±0.79	0.81±0.88	0.70±0.96	<0.001
10. “squatting, standing up”	0.35±0.67	0.44±0.81	0.89±1.01	0.87±1.00	<0.001
11. “rising from chair”	0.05±0.28	0.10±0.37	0.21±0.56	0.19±0.51	<0.001
12. “putting on pants”	0.10±0.35	0.13±0.38	0.34±0.61	0.31±0.61	<0.001
13. “pulling on stockings”	0.13±0.35	0.17±0.50	0.43±0.77	0.35±0.61	<0.001
14. “walking”	0.21±0.59	0.26±0.65	0.26±0.64	0.28±0.58	<0.001
15. “using a cane”	0.13±0.57	0.11±0.54	0.19±0.77	0.17±0.56	<0.001
16. “shopping”	0.06±0.35	0.11±0.51	0.11±0.35	0.22±0.58	<0.001
17. “light housekeeping, e.g., washing dishes”	0.06±0.30	0.09±0.41	0.16±0.48	0.16±0.50	<0.001
18. “heavy housekeeping, e.g., cleaning room”	0.09±0.40	0.20±0.65	0.35±0.69	0.36±0.74	<0.001
19. “going in the neighborhood”	0.02±0.23	0.03±0.16	0.08±0.32	0.08±0.30	<0.001
20. “going a long way”	0.03±0.30	0.05±0.31	0.16±0.59	0.07±0.39	<0.001

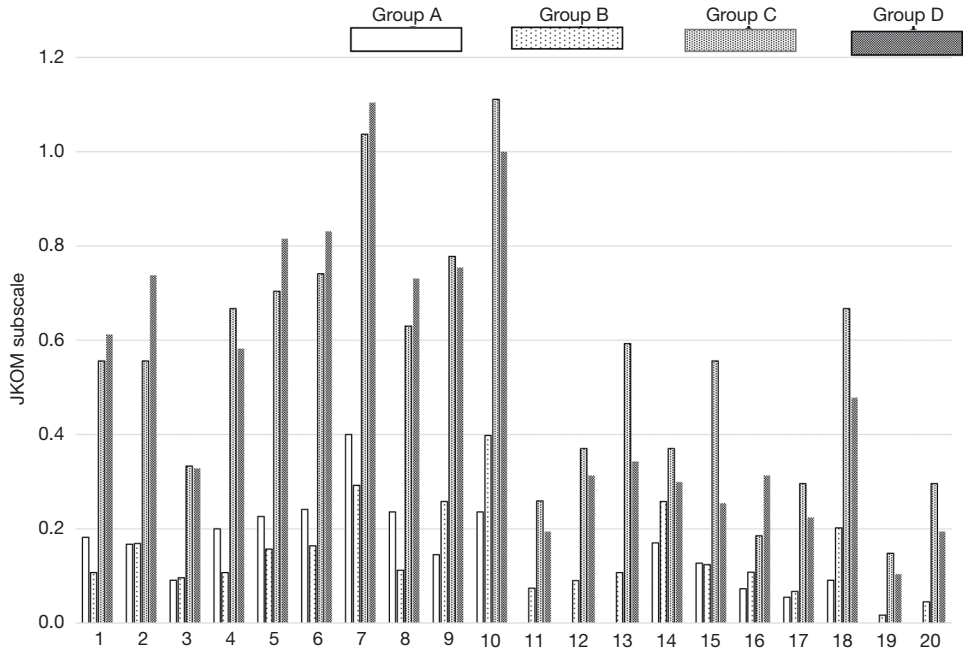


Figure 3 JKOM subscale in the Groups A-D in women. JKOM, Japanese Knee Osteoarthritis Measure.

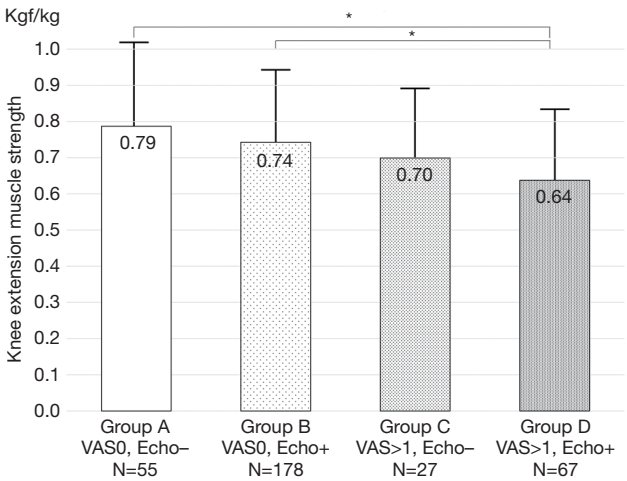


Figure 4 Knee extension muscle strength in the Groups A-D in women. *, P<0.05.

OA positive US finding also disturbed these ADLs, which might be not caused by pain but weak knee extension muscle strength.

From a practical point of view, Nguyen *et al.* (25) reviewed and summarized that strengthening the quadriceps may improve joint stability (26), and that optional strengthening the quadriceps and medial or lateral muscle to decrease the load in the medial compartment (27) or the lateral patellofemoral compartment. The OA Research Society International (OARSI) recommendations in 2014 (28) said that muscle training was even regarded as a core treatment of KOA and is proposed for all patients. Brosseau *et al.* reviewed 26 high-quality studies and showed that strengthening exercise programs significantly improved pain relief, physical function and quality of life (29). Strengthening knee extension muscle might not only provide pain relief and functional improvement of established KOA, but also prevent from proceeding pre-stage of early KOA to the early or established one.

There are some restrictions to the current study. This is a cross-sectional study using participants recruited at residential health examinations, not a longitudinal cohort study. It is impossible to accurately predict the onset of early KOA from pain-free knee, but the present study might indicate some risk factors such as woman, high BMI, and weak knee extension muscle strength. Another restriction is the usage of US to detect early KOA, instead of arthroscopy and/or MRI. Arthroscopy and MRI would confirm structural deterioration of KOA which is not apparent with standard radiographs. For residential health examinations, however, US is a fast, easy-to-use, safe, and low cost for public health service.

In conclusion, symptoms of early KOA might be not only pain but also the disturbance of ADLs such as ascending

upstairs or descending downstairs, standing up, and squatting with weak knee extension muscle strength (as the physical finding of early KOA). Even pain-free knees with positive US findings when disturbing those ADLs, might be the pre-stage of early KOA, namely super-early KOA. For prevention of proceeding to early KOA, strengthening of the knee extension muscle might be important to maintain these ADLs.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Annals of Joint* for the series "Early Osteoarthritis: Definition, Pathogenesis, Diagnosis, Management and Prevention". The article has undergone external peer review.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/aoj.2018.09.06). The series "Early Osteoarthritis: Definition, Pathogenesis, Diagnosis, Management and Prevention" was commissioned by the editorial office without any funding or sponsorship. YU served as the unpaid Guest Editor of the series. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The Ethics Committee of Shimane University School of Medicine approved the present study, and all participants provided written informed consent.

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doi: 10.21037/aoj.2018.09.06
Cite this article as: Uchio Y, Takuwa H, Kuwata S, Kumahashi N. Symptoms and physical findings of early knee osteoarthritis. Ann Joint 2018;3:79.