Gender Differences in the Correlation between Symptom and Radiographic Severity in Patients with Knee Osteoarthritis

Hyung Joon Cho MD, Chong Bum Chang MD,
Jae Ho Yoo MD, Sung Ju Kim MS, Tae Kyun Kim MD

Published online: 4 March 2010
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Abstract

Background The effects of gender on the relationship between symptom manifestations and radiographic grades of knee osteoarthritis are not well understood.

Questions/purposes We therefore determined the increments of symptom progression with regard to radiographic grades of knee osteoarthritis and asked if those increments

differed by gender and whether symptom severity was differentially manifested by gender within the same grade. **Methods** We recruited 660 community residents; 368 (56%) women and 292 (44%) men. The mean subject age was 71.5 years (range, 65–91 years). Severity of symptoms was measured using the WOMAC and SF-36 scales, and the radiographic severity using Kellgren–Lawrence grades. Incremental changes in WOMAC and SF-36 scores were compared between adjacent Kellgren–Lawrence grades separately in men and women, and in the overall population. We compared symptom severity between men and women with the same radiographic grade.

Results For the entire cohort, the mean incremental change in symptom severity was not gradual between the adjacent radiographic grades but was greater between Kellgren–Lawrence Grades 1 and 2 and Grades 2 and 3 than between Grades 0 and 1 or Grades 3 and 4. The patterns of incremental changes in symptom severity differed between men and women: women had more severe symptom progression between Kellgren–Lawrence Grades 2 and 3 and Grades 3 and 4 than men. Furthermore, women had worse mean WOMAC and SF-36 scores than men with the same radiographic grade of knee osteoarthritis.

Conclusions These data suggest symptom progression is not gradual between adjacent radiographic grades, and for the same radiographic grade, symptoms are worse in women. **Level of Evidence** Level III, diagnostic study. See Guidelines for Authors for a complete description of levels of evidence.

One or more of the authors received funding from Pfizer Global Pharmaceuticals (Grant Number 06-05-039) (TKK) and Seongnam City Government in Korea (Grant Number 800-20050211) (TKK). Each author certifies that his or her institution has approved the human protocol for this investigation that all investigations were conducted in conformity with ethical principles of research, and that informed consent was obtained. This work was performed at the Joint Reconstruction Center, Seoul National University Bundang Hospital.

H. J. Cho, C. B. Chang, T. K. Kim (✉)
Joint Reconstruction Center, Seoul National University Bundang Hospital, 300 Gumidong, Bundangu, Seongnamsi, Gyunggido 463-707, Korea
e-mail: osktk@snuh.org

H. J. Cho
Department of Orthopaedic Surgery, Pusan National University School of Medicine, Pusan, Korea

C. B. Chang, T. K. Kim
Department of Orthopaedic Surgery, Seoul National University College of Medicine, Seoul, Korea

J. H. Yoo
Department of Orthopaedic Surgery, Kyung Hee University East-West Neo Medical Center, Seoul, Korea

S. J. Kim
Department of Statistics, Korea University, Seoul, Korea

Introduction

Clinically, knee osteoarthritis (OA) is diagnosed by clinical symptoms and radiographic evidence of degenerative

changes [3, 16, 39]. The severity of symptoms is commonly evaluated using the WOMAC scale, and general health status is generally estimated using the SF-36 scale [2, 6, 42, 43]. The radiographic severity of knee OA is frequently assessed using the Kellgren–Lawrence (K/L) grading system, which relies on specific radiographic findings: the presence of osteophytes, joint space narrowing, and subchondral sclerosis [7, 16, 23].

Many authors have investigated the relationship between symptom and radiographic severity [5, 8, 9, 11, 24, 26, 29, 31, 38, 44], and some authors found an association between them [9, 24, 31, 38], while others did not [5, 8, 11, 26, 29, 44]. However, the previous studies had limitations including limited radiographic views that might underestimate the structural abnormalities [5, 8, 31, 44] and unclear definitions of knee OA symptoms such as the mere presence of pain without using validated outcome scales [9, 15, 24, 45]. Furthermore, most previous studies were limited by focusing on the relationship between symptom and specific radiographic findings such as osteophyte, joint space narrowing and subchondral sclerosis [8, 9, 11, 24, 31, 44]. Overall radiographic grades may help physicians counsel patients in practice, and the K/L grading system has been frequently utilized for that purpose [7, 16, 23]. Nevertheless, few studies explore the relationship between symptom severity and overall radiographic grades [5, 26]. These studies include relatively small number of subjects [26] and analyzed only those with advanced knee OA and severe clinical symptom requiring TKA [5]. In addition to the controversial association of clinical and radiographic severity, it is not known whether the symptoms of knee OA gradually worsen in correspondence with radiographic severity or whether they become substantially worse between certain radiographic grades. Although it is generally agreed knee OA can be diagnosed at Grade 2 on the K/L scale [7, 12, 15, 25, 45], it is unknown whether knees of K/L Grade 2 OA have more severe symptoms than those of K/L Grade 1.

Female gender is a major predisposing factor of knee OA [14, 16, 30, 36] and is reportedly associated with worse clinical manifestations than in men [16, 18, 20, 22, 27, 33, 34, 40]. However, the effects of gender on the relationship between symptoms and radiographic grades of knee OA are not well understood, and thus the reported differences between men and women may relate to greater radiographic severity in women.

We therefore determined (1) mean symptom severity over entire radiographic grades of knee OA and the differences in mean incremental symptom severity between grades; (2) whether the patterns of changes in symptom severity between the grades differed in men and women; and (3) whether there were differences in severity between men and women at each grade.

Patients and Methods

This study was a part of the Korean Longitudinal Study on Health and Aging (KLoSHA) [32]. The KLoSHA was a population-based prospective cohort study on health, aging, and common geriatric diseases in elderly Koreans. It was conducted from September 2005 to August 2006 on residents aged 65 years or older in Seongnam, Korea. Seongnam is one of the largest satellite cities of metropolitan Seoul. It had a total population of 931,019 in 2005, and 61,730 (7%) of the residents were aged 65 years or older. A simple random sample ($n = 1118$) was drawn from a roster of elderly individuals aged 65 years or older using a computer-generated list of random numbers, and these individuals were invited to participate in the study by letter and telephone. All the subjects were ethnic Koreans. Mean subject age was 72.8 ± 6.5 years (range, 65–99 years), and 701 (63%) were women and 417 (37%) were men. Of the 1118 subjects, 673 agreed to participate in the study. However, 13 of 673 respondents had undergone previous TKA and were excluded. This left 660 subjects (a participation rate of 59%) (Fig. 1); 368 (56%) were women and 292 (44%) were men. The mean age of the participants was 71.5 ± 5.1 years (range, 65–91 years). Participants were younger (mean age of nonrespondents = 74.8 ± 7.7 years, $p < 0.001$ by the Mann–Whitney U test) and included a smaller proportion of women (percentage of women among nonrespondents = 73%, $p < 0.001$, chi square test) than nonparticipants. The mean body mass index (BMI) of participants was 24.3 kg/m^2 . Women were shorter and lighter but had a higher mean BMI than men (Table 1). This study was approved by the institution review board of our hospital, and informed consent was obtained from all participants.

The participants were surveyed for demographic information and symptom severity. Demographic information included gender, age, height, weight, and BMI, which are

Fig. 1 A flowchart shows the recruitment of participants.

Table 1. Demographic characteristics of study subjects

Parameter	Men (n = 292)	Women (n = 368)	P value
Age (years)	71.1 (4.8)	71.8 (5.3)	0.075
Height (cm)	165.0 (6.1)	150.9 (6.0)	< 0.001
Weight (kg)	65.4 (9.9)	56.0 (8.5)	< 0.001
Body mass index (kg/ m ²)	24.0 (3.2)	24.5 (3.2)	0.041

Values are expressed as means, with SDs in parentheses.

associated with symptom severity in knee OA [16, 28, 29, 41, 44]. Symptom severity was measured using the WOMAC index and the SF-36 scale. The WOMAC index contains 24 questions in total for three sections, namely, pain, stiffness, and function [2, 6, 43]. Each question has five response options (none, mild, moderate, severe, and extreme), and subtotal scores for pain (five items), stiffness (two items), and function (17 items) range from 0–20, 0–8, and 0–68, respectively. The SF-36 assesses general health-based quality of life and includes eight profiles of functional health and mental well-being scores, as well as physical and mental health summary measures as the physical component summary (PCS) and the mental component summary (MCS) [42, 43].

Three plain radiographs were used: both-leg standing anteroposterior (AP) view, 45° flexion posteroanterior (PA) view, and Merchant view. Both-leg standing AP and 45° flexion PA views were taken under weight-bearing conditions, and the Merchant views were taken at the position of 45° using a leg-holding device. All radiographic images were digitally acquired using a picture archiving and communication system (PACS) (Impax; Agfa, Antwerp, Belgium), and assessments were subsequently carried out using PACS software. Radiographs were evaluated by one of the authors (HJC) blinded to the clinical information of the subjects at the time of reading and allocated K/L grades [7, 23]. K/L grades were defined as follows: Grade 0, no features of osteoarthritis; Grade 1, small osteophyte of doubtful importance; Grade 2, definite osteophyte but an unimpaired joint space; Grade 3, definite osteophyte with moderate diminution of joint space; and Grade 4, definite osteophyte with substantial joint space reduction and sclerosis of subchondral bone [7, 23]. Each knee was divided into three compartments, that is, medial, lateral, and patellofemoral compartments, and each compartment was graded according to the presence of osteophytes, joint space narrowing, sclerosis, and cysts. To ensure the accuracies of radiographic assessments, we established the following reading criteria based on previous studies in the literature [7, 23]. A marginal osteophyte was defined as a definite osteophyte, but an osteophyte at the tibial eminence or intercondylar fossa was not regarded as a definite

osteophyte. Joint space narrowing was defined when the minimal joint space width was less than 3 mm for the tibiofemoral joint and less than 5 mm for the patellofemoral joint. We used the results of the worst compartments after grading each compartment according to the above-mentioned criteria, and similarly, if grades of right and left knees in one individual were different, we used the higher grade. In addition, the coronal limb alignment was investigated by measuring the anatomical tibiofemoral angle on the standing AP view. The anatomical tibiofemoral angle was defined as the angle between the anatomical axes of the distal femur (the line from the point bisecting the femur to the center of the femoral intercondylar notch) and the proximal tibia (the line from the point bisecting the tibia to the center of the tibial spine tips). The bisecting points of the anatomical axes were 15 cm removed from the lowermost portion of the lateral femoral condyle and the uppermost portion of the lateral tibial plateau. A negative value was given to knees in varus alignment.

To assess the reliabilities of K/L grade assessments and limb alignment measurements, two orthopaedic surgeons (HJC, CBC) performed measurements twice with an interval of 3 weeks in 50 patients who were randomly selected from the total cohort. The degree of measurement reliabilities was determined using kappa coefficients for the K/L grade assessments and intraclass correlation coefficients (ICC) for limb alignment measurements: we found kappa values of 0.91 for intraobserver reliability and 0.83 for interobserver reliability, and ICC values of 0.97 for intraobserver reliability and 0.94 for interobserver reliability, which allowed us to rely on the validities of the radiographic assessments and assessment data produced by the single investigator.

We categorized all study subjects by K/L grade, and then determined mean symptom severity (WOMAC and SF-36 scores) for each K/L grade. Incremental absolute score changes and percentage score changes [(higher grade score—lower grade score)/lower grade score × 100] were compared between adjacent K/L grades using the Mann–Whitney U test. To verify the differences in symptoms associated with the K/L grades were not confounded by other patient-related factors, we compared the age, BMI, and coronal limb alignment and found no differences between adjacent K/L grades ($p > 0.05$, the Mann–Whitney U test) (Table 2). We then determined whether there were differences in the patterns of changes in incremental symptom severity between adjacent K/L grades separately in men and women using the Mann–Whitney U test. Finally, we compared symptom severity between men and women at given radiographic grades by using the Mann–Whitney U test. In addition, power analyses were performed for the comparisons with a p value greater than 0.05 using a two-sided hypothesis test with an alpha level

of 0.05. We considered a difference greater than 6% of the maximum scores of WOMAC and SF-36 scales as being clinically important: WOMAC: pain = 1.2, stiffness = 0.5, function = 4.1; and SF-36: PCS = 4.9, MCS = 4.2 [4]. Statistical analyses were conducted using the SPSS® for Windows® statistical package (Version 15.0; SPSS Inc, Chicago, IL).

Results

Changes in symptom severity of all subjects were not gradual between the adjacent radiographic grades: worsening was greater between K/L Grades 1 and 2 and between K/L Grades 2 and 3 (Table 3, Fig. 2). WOMAC pain (Fig. 2A), stiffness (Fig. 2B), and function (Fig. 2C) scores increased with higher K/L grades, but WOMAC score increments between K/L Grades 1 and 2 ($p < 0.001$ in pain and function, $p = 0.001$ in stiffness) and between K/L Grades 2 and 3 ($p = 0.001$ in pain, $p = 0.035$ in stiffness, $p = 0.002$ in function) were greater than those between K/L Grades 0 and 1 and between K/L Grades 3 and 4 ($p > 0.05$ in every section). SF-36 PCS (Fig. 2D) and MCS (Fig. 2E) scores showed gradual decreases with higher K/L grades, but score reductions between K/L Grades 1 and 2 ($p = 0.005$ in PCS) and between K/L Grades 2 and 3 ($p = 0.001$ in PCS and $p = 0.005$ in MCS) were also larger than those between K/L Grades 0 and 1 and between K/L Grades 3 and 4. Power analyses revealed all the comparisons with a p value greater than 0.05 had a

power of greater than 80% to detect the defined meaningful differences.

When symptom severities in male and female subjects were analyzed separately, the patterns of change were notably different between women and men, although severity increased with higher K/L grades in both (Table 4, Fig. 3). In men, the differences in incremental score changes between adjacent K/L grades were similar ($p = 0.078$ – 0.979), although WOMAC pain (Fig. 3A) and function (Fig. 3B) scores showed a trend ($p = 0.078$ in pain, $p = 0.086$ in function) between K/L Grades 2 and 3. In contrast, women showed greater incremental changes in symptom scores in many scales between K/L Grades 2 and 3 and between K/L Grades 3 and 4. Between K/L Grades 2 and 3, the differences in symptom scores were greater for WOMAC pain (Fig. 3A, $p = 0.012$) and function (Fig. 3B, $p = 0.021$), and in SF-36 PCS (Fig. 3C, $p = 0.005$) and MCS (Fig. 3D, $p = 0.015$) scores. Likewise, between K/L Grades 3 and 4, women showed worsening in WOMAC function (Fig. 3B, $p = 0.013$) and SF-36 PCS (Fig. 3C, $p = 0.023$) and a trend for worsening in WOMAC stiffness (Fig. 3E, $p = 0.055$). In the power analyses, the comparisons in women had a power of greater than 80% whereas all the comparisons in men except between K/L Grades 0 and 1 had a power of less than 80%.

Women had more severe symptoms at the same K/L grades (Table 4, Fig. 3). Although in K/L Grade 3 the WOMAC pain ($p = 0.196$), stiffness ($p = 0.208$), and function ($p = 0.157$) of women were similar to those in men, women were worse in all other WOMAC scores in

Table 2. Demographic factors and coronal alignment in the five subgroups by the K/L grading system*

Parameter	Grade 0 (n = 101)	Grade 1 (n = 317)	Grade 2 (n = 80)	Grade 3 (n = 85)	Grade 4 (n = 77)
Age (years)	70.1 (4.1)	70.9 (5.1)	71.4 (4.8)	72.3 (4.7)	74.6 (5.7)
Body mass index (kg/m ²)	23.2 (2.8)	23.8 (3.1)	25.2 (2.7)	25.4 (3.3)	25.8 (3.4)
Anatomical tibiofemoral angle (degrees)	2.4 (1.9)	2.0 (2.3)	1.8 (2.8)	1.1 (2.8)	0.7 (5.6)

*Values are expressed in mean, with SDs in parentheses. No statistical significances were found between adjacent K/L grades ($p > 0.05$, Mann–Whitney U test).

Table 3. Summary of WOMAC and SF-36 scores according to Kellgren–Lawrence grade

Scale	Grade 0 (n = 101)	Grade 1 (n = 317)	Grade 2 (n = 80)	Grade 3 (n = 85)	Grade 4 (n = 77)
WOMAC					
Pain	2.3 (3.5)	2.5 (3.4)	4.2 (4.1)	6.5 (4.9)	7.3 (5.6)
Stiffness	1.0 (1.5)	1.2 (1.6)	2.0 (2.0)	2.7 (2.2)	3.3 (2.5)
Function	8.7 (10.5)	10.2 (11.1)	15.2 (12.8)	22.1 (15.1)	26.8 (17.7)
SF-36					
PCS	59.0 (12.6)	60.1 (12.2)	56.4 (10.4)	49.8 (13.3)	47.9 (16.3)
MCS	54.0 (8.9)	54.2 (9.2)	53.0 (9.9)	48.8 (10.6)	48.9 (11.6)

Values are expressed as means, with SDs in parentheses; PCS = physical component summary; MCS = mental component summary.

Fig. 2A–E Graphs show (A) WOMAC pain, (B) stiffness, and (C) function and (D) SF-36 PCS and (E) SF-36 MCS scores versus K/L grade of the entire cohort including men and women. Changes with p

values of less than 0.05 are marked with black lines and the absolute score change (proportional score change) and the exact p values are given.

K/L Grades 0, 1, 2, and 4 and in SF-36 MCS in K/L Grade 3, with a trend for worse SF-36 PCS ($p = 0.079$) in K/L Grade 3. Power analyses showed the comparisons for WOMAC pain, stiffness, and function and SF-36 PCS in K/L Grade 3 had a power of less than 80%.

Discussion

Although the relationship between radiographic findings and clinical symptoms in knee OA has been examined previously, the worsening of symptoms by radiographic grade has not been well documented, especially in the general population (Table 5) [5, 8, 9, 11, 24, 26, 29, 31, 38, 44]. Female gender is a major predisposing factor of knee OA [14, 16, 30, 36] and is reportedly associated with worse clinical manifestations of knee OA than in men [16, 18, 20, 22, 27, 33, 34, 40]. However, the effects of gender on the relationship between symptoms and radiographic grades of knee OA are not well understood. Therefore, we investigated symptom progression with regard to various radiographic grades in men and women separately, as well

as in a whole cohort, and determined whether symptom severity is differentially manifested by genders with the same radiographic severities.

Several limitations of this study should be noted. First, our study subjects were limited to one ethnic population. Symptom severity such as pain might be manifested differently in other ethnic populations [13]. Recent studies reported the existence of ethnic differences in symptom manifestation in OA population even in the same geographical area [17, 21]. These ethnic differences may be explained by differing biological (genetic), social, and cultural factors between ethnic populations. Second, we used the K/L grading system for radiographic evaluations and WOMAC and SF-36 scales for clinical assessments. There are other radiographic or clinical assessment tools with their own advantages such as that of Ahlbäck and Rydberg on weight-bearing radiographs [1, 7] and the American Knee Society Clinical Rating System [19]. Although the evaluation tools we used were considered appropriate for our study and have been used widely in similar studies [5, 8, 26, 29, 38, 44], it is possible the use of different evaluation tools would suggest differing

Table 4 Comparison of WOMAC and SF-36 clinical scales by gender and Kellgren–Lawrence grade

Scale	Grade 0			Grade 1			Grade 2			Grade 3			Grade 4		
	Men (n = 55)	Women (n = 46)	P value	Men (n = 188)	Women (n = 129)	P value	Men (n = 20)	Women (n = 60)	P value	Men (n = 11)	Women (n = 74)	P value	Men (n = 18)	Women (n = 59)	P value
WOMAC															
Pain	1.2 (1.9)	3.7 (4.4)	0.001	1.5 (2.2)	4.0 (4.2)	< 0.001	2.7 (3.9)	4.7 (4.1)	0.011	4.6 (3.9)	6.8 (4.9)	0.196	4.6 (4.7)	8.1 (5.7)	0.015
Stiffness	0.7 (1.1)	1.4 (1.8)	0.028	0.8 (1.2)	1.9 (1.8)	< 0.001	1.1 (1.6)	2.3 (2.0)	0.011	1.8 (1.5)	2.8 (2.2)	0.208	1.9 (2.1)	3.6 (2.5)	0.008
Function	6.0 (7.4)	11.9 (12.6)	0.007	7.2 (8.5)	14.5 (13.0)	< 0.001	10.1 (14.8)	16.9 (11.7)	0.001	15.9 (12.1)	23.0 (15.3)	0.157	15.6 (16.4)	30.2 (16.8)	0.001
SF-36															
PCS	62.8 (11.2)	54.5 (12.7)	0.001	63.2 (10.6)	55.7 (13.0)	< 0.001	61.3 (12.1)	54.7 (9.3)	0.007	56.0 (13.6)	48.9 (13.0)	0.079	60.1 (16.1)	44.1 (14.5)	< 0.001
MCS	56.3 (7.3)	51.3 (9.9)	0.006	56.0 (8.4)	51.6 (9.8)	< 0.001	55.7 (12.2)	52.1 (8.8)	0.026	55.0 (8.6)	47.9 (10.7)	0.030	56.6 (10.9)	46.5 (10.9)	0.001

Values are expressed as means, with SDs in parentheses; statistical analysis of gender differences within same grades was conducted using the Mann–Whitney U test; PCS = physical component summary; MCS = mental component summary.

conclusions. Third, we could not consider all factors which potentially confound the correlation between symptom and radiographic severities because this study was performed as a cross-sectional survey in a large cohort. Previous studies suggest many factors including quadriceps power, range of motion, psychosocial factors, comorbidities, or pain medication could influence symptom manifestations of osteoarthritic knees [10, 14, 28, 29, 35, 37, 44]. Fourth, subjects with K/L Grade 4 and severe knee symptoms might have had knee arthroplasty and were not recruited into the study. Therefore, symptom severity in the subjects with K/L Grade 4 may have been underestimated. It might also explain the relatively lower increase of symptom score from K/L Grade 3 to 4 compared to the increase from K/L Grade 2 to 3. Finally, while we had sufficient power for the comparisons between the adjacent K/L grades in the entire cohort and between men and women in the same grade, we did not have sufficient power for most of the separate comparisons in men between the adjacent K/L grades because the numbers of male subjects in K/L Grades 2, 3, and 4 were small.

The K/L scale is the scale most commonly used to evaluate the radiographic severity of knee OA [7, 12, 15, 16, 23, 25, 26, 45]. Although the presence of an osteophyte or cyst, joint space narrowing, and subchondral sclerosis are all considered when determining the radiographic severity, the presence of definite osteophytes, the key feature of K/L Grade 2, is commonly used as the diagnostic criterion of knee OA [7, 12, 15, 25, 45]. Based on symptom severity our findings support the appropriateness of the K/L Grade 2 as reflecting clinically important OA. We found worsening of symptom severity occurred between K/L Grades 1 and 2 whereas only a slight increase in severity occurred between K/L Grades 0 and 1. In addition, we believe the symptom worsening between K/L Grades 2 and 3 relates to joint space narrowing, the key feature of K/L Grade 3 and an important indicator of disease progression. Many conflicting assertions have been made about the relationship between radiographic findings and clinical symptoms (Table 5) [5, 8, 9, 11, 24, 26, 29, 31, 38, 44]. Some previous studies reported the presence of osteophytes was associated with knee pain [9, 24, 31, 38], whereas other studies found no association between them [11, 44]. The association between joint space narrowing and the presence of symptoms has also been debated [8, 9, 11, 24, 31, 38, 44], and one study concluded the presence of radiographic subchondral sclerosis is most closely associated with pain [38]. However, most previous studies were limited by focusing on the relationship between symptoms and specific radiographic findings [8, 9, 11, 24, 31, 44], having only a small number of subjects [26], or analyzing only those with advanced knee OA and severe clinical symptoms requiring TKA [5]. Our study on a large number

Fig. 3A–E Graphs show (A) WOMAC pain, (B) function scores, (C) SF-36 PCS and (D) SF-36 MCS scores and (E) stiffness with regard to K/L grade in men (■ linked with dotted line) and women (▲ linked with solid line) separately. Changes with p values of less than 0.05 are

marked with black lines and the absolute score change (proportional score change) and the exact p values are given in bold letters. Changes with statistical trend are marked in italic letters.

of subjects covering the entire spectrum of knee OA with the K/L grading system as an evaluating tool for overall radiographic severity indicated the presence of joint space narrowing could be objective evidence supporting symptom severity of knee OA.

The patterns of symptom progression in higher K/L grades were distinctively different between men and women. Although we observed incremental symptom change between K/L Grades 2 and 3 in the entire population, this change was more obvious in women than in men, and the pattern was even greater between K/L Grades 3 and 4. In contrast, we observed no worsening in mean symptom severity between K/L Grades 3 and 4 for the entire population, which may indicate symptom worsening in women was diluted by relatively small changes in men. Although the reasons for this different pattern in symptom progression between men and women are not clear, one interpretation might be that variation of symptoms with the progression of structural pathology was represented more sensitively in women than in men. Our finding that symptom progression with higher K/L grades is more substantial in women warrants special attention because it

indicates female patients with advanced knee OA are more likely to seek medical services for their knee symptoms than men [18]. However, the inadequate power for men does not allow this study to determine whether symptom progression between adjacent K/L grades is gradual in men or not. Further studies using an even larger cohort are warranted to determine the relationship between symptom and radiographic severities of knee OA in men.

Our data also suggest women have more severe symptoms than men in the same radiographic grade of knee OA. A possible explanation for these worse clinical symptoms in women compared with men is that women inherently tend to be more sensitive to pain and functional limitation than men: a recent study of pain in OA patients reported overall and current pain intensity was higher in women and interference of general activity due to pain was more easily developed in women [40]. Another study of the functional impairment in TKA candidates suggested women had more functional impairment in daily activity compared with men [33]. Other potential explanations include a higher prevalence of obesity in women and difference in daily physical activities between gender groups. Studies of the role of obesity in the clinical

Table 5. Summary of previous studies investigating the relationship between radiographic findings and clinical symptoms in knee osteoarthritis

Study	Number of subjects	Radiographs	Radiographic assessment	Clinical scales	Findings
Barker et al. [5]	123	Standing AP	K/L Grade	WOMAC	No correlation
Bruyere et al. [8]	212	Standing AP	Joint space narrowing	WOMAC	No correlation
Cicuttini et al. [9]	250	Standing AP, lateral, sky-line	Osteophyte, joint space narrowing	Pain	Present correlation between osteophytes and knee pain
Dieppe et al. [11]	500	Standing AP, lateral	Osteophyte, joint space narrowing, subchondral sclerosis	Pain, function (Steinbrocker index)	No correlation
Lanyon et al. [24]	452	Standing AP, sky-line	Osteophyte, joint space narrowing, subchondral sclerosis, cyst	Pain	Present correlation between osteophyte and knee pain, osteophyte as the best predictor for pain
Link et al. [26]	50	AP, lateral, sun-rise	K/L Grade	WOMAC	No correlation
McAlindon et al. [29]	159	Standing AP, lateral	K/L Grade	Pain, disability (Stanford Health Assessment Questionnaire)	No correlation
Ozdemir et al. [31]	84	Standing AP	Osteophyte, joint space narrowing	Range of motion	Correlation
Szebenyi et al. [38]	167	Standing AP, lateral	K/L Grade	Visual analogue scale (VAS) pain score, WOMAC function	Structural changes in both compartment are correlated with pain and loss of function and subchondral sclerosis is associated with pain
Zhai et al. [44]	500	Standing AP (semiflexed)	Osteophyte, joint space narrowing, subchondral sclerosis	WOMAC pain	No correlation
Cho et al. [current study]	600	Standing AP, 45° flexion PA, Merchant	K/L Grade	WOMAC, SF-36	Correlation (+), women had more substantial symptomatic progression with increasing grades of knee OA than men

symptoms of knee OA have yielded conflicting results but suggest obese subjects with knee OA are more likely to have worse clinical symptoms than nonobese subjects [16, 28, 41, 44]. Therefore, more severe obesity in women in our study cohort might partly account for the difference in clinical symptoms we observed. Finally, women in our society need kneeling and squatting postures in daily activities more often than men. If such activities were compromised, it would induce more discomfort in women.

In conclusion, incremental changes in symptom severity of knee OA are greater between K/L Grades 2 and 3, with less, but substantial worsening between Grades 1 and 2. These findings indicate joint space narrowing should be regarded as an indicator of the need for medical intervention and the presence of a definite osteophyte is meaningful in terms of making the diagnosis of knee OA. Furthermore, symptom severity of knee OA for given radiographic grades was distinctively different in men and women, and symptom worsening was more remarkable in women than

in men between K/L Grades 2 and 3 and even more substantial between K/L Grades 3 and 4. Our data suggest women have greater symptoms in knee OA than men at the same radiographic grades. Our findings should be considered in making a diagnosis and consulting patients to establish treatment plans based on radiographic findings.

Acknowledgments We thank Professor Kim, Ki Woong (Department of Neuropsychiatry, Seoul National University Bundang Hospital), the principal investigator of KLoSHA, for his generous support of this study.

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