

# Osteoarthritis and Cartilage



## Coexisting lateral tibiofemoral osteoarthritis is associated with worse knee pain in patients with mild medial osteoarthritis



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### SUMMARY

**Objective:** To examine the clinical impact of coexisting lateral osteoarthritis (OA) in knees with mild medial OA.

**Design:** In patients with Kellgren/Lawrence (K/L) grade 2 OA in the medial compartment ( $n = 100$ ; age: 56–89 years; 80.0% female), anteroposterior knee radiography was used to assess the presence of lateral OA, using grading systems from the Osteoarthritis Research Society International (OARSI) atlas and the K/L classification. The Japanese Knee Osteoarthritis Measure (JKOM), knee range of motion (ROM), and performance-based functional measures (10 m walk, timed up and go and five repetition chair stand maneuvers) were evaluated. The outcomes were compared between patients with and without lateral OA using an analysis of covariance (ANCOVA) or nonparametric rank ANCOVA. Furthermore, ordinal logistic regression analysis was performed, with responses on individual JKOM pain questionnaires as the outcomes and lateral OA as the predictor.

**Results:** Knees with coexisting lateral OA had a significantly worse score of JKOM pain question compared with those without, after adjusting for covariates. The presence of lateral OA was significantly associated with knee pain while ascending/descending stairs and standing. These results were consistent between different definitions of the K/L and OARSI grading systems. The knee ROM and performance-based functional measures were not significantly different between patients with and without lateral OA.

**Conclusion:** Knees with concomitant lateral and mild medial OA may be more symptomatic compared to those without lateral OA. These findings might help to define a clinically distinct subgroup based on a simple radiographic finding in mild knee OA.

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### Introduction

Osteoarthritis (OA) of the knee, a leading cause of knee pain and chronic disability worldwide<sup>1</sup>, is the most common type of

arthritis<sup>2</sup> and is a heterogeneous disease<sup>3</sup>. The Kellgren/Lawrence (K/L) classification<sup>4</sup> is a widely accepted scale that is used to grade disease severity and to define the presence of OA, in which grade 2 is usually used as the disease threshold<sup>5</sup>. Unlike the Osteoarthritis Research Society International (OARSI) atlas grading system defined by Altman and Gold<sup>6</sup>, the K/L classification grades medial or lateral compartment features without distinction. However, knee OA is a tricompartmental disease<sup>7</sup>, which indicates the importance of compartment-specific assessment and the need to investigate the pathogenesis and clinical impact of knee OA based on different radiographic patterns.

Although knee OA commonly affects the medial tibiofemoral compartment of the knee joint<sup>8,9</sup>, possibly because of a higher

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percentage of loading in the medial compartment<sup>10</sup>, a coexisting marginal osteophyte in the lateral compartment in medial OA has been reported<sup>11,12</sup>. For example, Faschingbauer *et al.*<sup>11</sup> showed that 170 (49.4%) of 344 knees with medial OA of K/L grade 2 or 3 had a radiographic-defined osteophyte in the lateral compartment. Coexisting medial and lateral OA has been suggested to be more of a synovial inflammatory disease than is isolated medial OA<sup>13</sup>. This finding indicates that bicompartamental (medial and lateral) and unicompartmental (medial alone) OA may belong to different subgroups, or may represent different stages of the same disease. However, no previous study has examined the clinical impact of coexisting lateral disease in medial knee OA, including knee pain and functional measures. Such knowledge would contribute to defining a subgroup of knee OA using simple radiographic features, and might help resolve the discordance between clinical symptoms and radiographic findings in heterogeneous OA disease<sup>14</sup>.

This cross-sectional study sought to examine the clinical impact of coexisting lateral OA in knees with mild medial OA. Since mild knee OA shows a wide variability in clinical outcomes among patients, the current study focused on knees with K/L grade 2 in the medial compartment, thereby defining a potential subgroup in mild knee OA as suggested by Felson *et al.*<sup>15</sup>. We hypothesized that knees with coexisting lateral OA would have worse clinical symptoms, poorer physical function, and a more restricted knee range of motion (ROM) compared to knees without lateral OA.

## Method

### Patients

The ethical committee of Kyoto University approved the study (approval number: E1923), and written informed consent was obtained from all participants before their enrollment. For the current cross-sectional study, we used data obtained from January 2014 to January 2015.

Patients were identified through the medical record system, and were recruited from the community orthopedics clinic in Hiroshima which is located in a rural mountainous community. We distributed an advertisement requesting patients who were visiting the clinics for conservative treatment of knee OA. All recruited patients had a history of pain in one or both knees. Patients were included in this study if they met the following inclusion criteria: (1) age  $\geq 50$  years; (2) radiographic OA (K/L grade 2 according to the original version<sup>4</sup>) in one or both knees in the medial tibiofemoral compartment, evaluated using weight-bearing anteroposterior radiographs of the tibiofemoral joint; and (3) ability to walk independently on a flat surface without any ambulatory assistive device. Patients with bilateral knee OA were not considered separately from unilateral cases. The exclusion criteria were (1) a history of knee surgery, (2) rheumatoid arthritis, (3) periarticular fracture, (4) present neurological problems, or (5) lateral knee OA (i.e., isolated lateral OA or coexisting medial and lateral OA but lateral OA is more severe than medial OA). Lateral knee OA was defined as a knee having a K/L grade  $\geq 2$ , along with lateral joint space narrowing (JSN)  $>$  medial JSN, and lateral osteophytes  $>$  medial osteophytes using an OARSI atlas<sup>6</sup> according to previously described methods<sup>16,17</sup>.

### Outcome measurements

For all patients, the following outcome measurements were evaluated: (1) radiographic evaluation, (2) passive knee ROM measurement, (3) three functional performance measurements (the 10 m walk, timed up and go [TUG], and five repetition chair stand [5CS]), and (4) an OA-related health domain measure (the

Japanese Knee Osteoarthritis Measure [JKOM]). Measurement of ROM and functional performance were evaluated by trained physical therapists (HI and NF) who had  $>6$  years of clinical experience with musculoskeletal disorders and a postgraduate master's (HI) or doctor's (NF) degree-level qualification.

### Radiographic evaluation

Anteroposterior radiographs of the index knees in the fully extended weight-bearing and foot map positions were obtained within 3 months of enrollment. The index knee was defined as the more painful knee, as described in the [Statistical analysis](#) section. The beam was positioned parallel to the floor with no angle at the joint space. Fluoroscopic guidance with an anteroposterior X-ray beam was used to properly visualize the joint space. The radiographic severity of the lateral compartment in the tibiofemoral joint was assessed by trained examiner (HI) and experienced physician who had a  $>10$  years of clinical experience as an orthopedic surgeon (KN) using the standard scale from the OARSI atlas<sup>6</sup> and K/L classification system. Disagreement between two independent examiners was discussed and consensus was achieved. OARSI JSN (lateral tibiofemoral joint) and osteophytes (lateral femoral and tibial compartment) were graded on a four-point scale (0–3; 0: normal; 1: mild; 2: moderate; 3: severe) following the radiograph examples in the OARSI atlas<sup>6</sup>. Radiographic OA of the lateral compartment by the OARSI atlas grading system was considered to be present if: (1) JSN  $\geq$  grade 2, (2) the sum of the two marginal osteophyte grades from the lateral compartment  $\geq 2$ , or (3) grade 1 JSN combined with a grade 1 osteophyte in the lateral compartment. Although this definition is supposed to be equivalent to grade 2 OA in the K/L classification<sup>18</sup>, a recent study showed that the OARSI atlas grading system differs from the K/L classification regarding the prevalence of radiographic knee OA<sup>19</sup>. Thus, we also defined radiographic OA according to the K/L grading system as the presence of a definite osteophyte (K/L grade = 2) in the lateral compartment of the tibiofemoral joint in a compartment-specific manner<sup>20</sup>. Specifically, the K/L grade in the lateral compartment was scored as follows: 0 = normal; 1 = possible osteophyte; 2 = definite osteophytes; 3 = osteophytes and JSN; 4 = large osteophytes, marked JSN, and definite deformity. We defined lateral OA if marginal osteophytes were confirmed in either femur or tibia. Although this definition of K/L grade 2 was different from the original version<sup>4</sup>, varus knee would be expected to lead to a lateral lift off, which affects JSN grading in the lateral compartment. Thus, radiographic lateral OA in the current study was defined only according to the presence of a definite marginal osteophyte. This is also an alternative criterion used in large studies, such as the Framingham study<sup>21</sup>.

To assess intra-rater reliability, 100 randomly selected radiographs were rescored by the same examiner (HI) more than 1 week after the first assessment. The intra-rater reliabilities were excellent<sup>22</sup> for JSN ( $\kappa = 0.84$ , 95% confidence interval [CI]: 0.73–0.96), osteophyte grade (femur,  $\kappa = 0.87$ , 95% CI: 0.81–0.93; tibia,  $\kappa = 0.90$ , 95% CI: 0.86–0.95), and K/L grade in the lateral compartment ( $\kappa = 0.88$ , 95% CI: 0.83–0.92). The inter-rater reliability between two examiners (HI and KN) was fair to good<sup>22</sup> for JSN ( $\kappa = 0.66$ , 95% CI: 0.48–0.85), osteophyte grade (femur,  $\kappa = 0.73$ , 95% CI: 0.62–0.84; tibia,  $\kappa = 0.63$ , 95% CI: 0.50–0.75), and K/L grade in the lateral compartment ( $\kappa = 0.68$ , 95% CI: 0.56–0.80).

### Statistical analysis

To minimize any bias produced by similarities between the right and left knees of the same patients, only one knee per patient was analyzed ("index knee"; [Supplementary methods](#)).

Data analyses were performed using JMP 11 (SAS Institute, Cary, NC, USA) or R (R Foundation for Statistical Computing, Vienna,

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