### Osteoarthritis and Cartilage



# Incidence, prevalence, natural course and prognosis of patellofemoral osteoarthritis: the Cohort Hip and Cohort Knee study



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#### ARTICLE INFO

Article history: Received 22 April 2016 Accepted 1 December 2016

Keywords: Osteoarthritis Patellofemoral joint Tibiofemoral joint Cohort Knee

#### SUMMARY

*Objective:* To examine the proportion of isolated patellofemoral osteoarthritis (PFOA) compared to tibiofemoral osteoarthritis (TFOA) in middle-aged participants with early osteoarthritis (OA) symptoms of the knee; to describe the natural course of PFOA compared with that of TFOA and to identify whether patients with PFOA have a different phenotype compared to patients with TFOA, or with combined PFOA and TFOA (combined osteoarthritis (COA)).

*Design:* Participants with early OA symptoms of the knee were selected, completed questionnaires, underwent physical examination, and had knee radiographs at baseline, and at 2 and 5 years follow-up. Based on radiographs, participants were classified as having isolated TFOA, isolated PFOA, COA, or no radiographic OA. Multivariate logistic regression was used to identify participant characteristics associated with a specific group of OA at 2 years follow-up.

*Results:* The cohort comprised 845 participants (mean age 55.9 years). At baseline, 116 had PFOA, none had TFOA or COA. Of these 116 participants, 66.3% had developed COA at 5 years follow-up. At 2 years follow-up, PFOA, TFOA and COA were present in 77 (10.8%), 39 (5.5%) and 83 (11.6%) participants, respectively. Multivariate regression analyses at 2 years follow-up showed that participants with radiographic PFOA or TFOA were not significantly different from each other with respect to signs and symptoms.

*Conclusions:* These results suggest that OA is more likely to start in the patellofemoral joint and then progress to COA in individuals with symptoms of early knee OA. No differences in TFOA and PFOA phenotypes were determined with respect to signs and symptoms.

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#### Introduction

The most common condition to affect the knee joint is osteoarthritis (OA)<sup>1,2</sup>. The knee joint consists of two compartments the tibiofemoral (TF) and the patellofemoral (PF) compartment. OA in the knee can occur solely in the TF joint [isolated tibiofemoral osteoarthritis (TFOA)] or in the PF joint [isolated patellofemoral osteoarthritis (PFOA)] or can be present in both joints [combined TFOA and PFOA (combined osteoarthritis (COA))]. Most research on OA has focused on the TF joint, although the prevalence of isolated PFOA might be higher than isolated TFOA<sup>3-6</sup>. Furthermore, radiographic signs of PFOA are associated with symptoms such as pain and disability<sup>7-10</sup>.

Although the main goal of treatment for OA is pain relief, not every participant responds equally well to treatment<sup>11,12</sup>. One possible reason for this difference is that the heterogeneous OA population consists of persons with different phenotypes of  $OA^{12-14}$ . Identification of the distinct phenotypes in OA may help classify which preventive measures are suitable for an individual<sup>14</sup>. Therefore, it is suggested to target interventions to different OA phenotypes<sup>15–18</sup>. However, Mills and Hunter stated: '*due to the inclusion of homogenous study groups based on TFOA in clinical trials*,

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*the phenotype specific effects of OA can be masked*<sup>19</sup>. Therefore, large cohort studies that include participants with COA and isolated TFOA and PFOA are needed to determine whether participants with PFOA have a different phenotype compared to those with TFOA or COA.

Additionally, evidence from a study including participants aged >50 years with knee complaints suggests that OA in the knee starts in the PF joint and subsequently progresses to the TF joint<sup>20</sup>. This was recently strengthened by Stefanik et al. (2016) who found that knees with structural damage in one compartment of the knee do not develop structural damage in another compartment. Moreover, knees that developed mixed structural damage were more likely to start with isolated to the PF joint<sup>21</sup>. Therefore, more insight is required in the natural course of PFOA and how its natural course differs from TFOA. The few studies describing the prevalence and natural course of TFOA and PFOA included participants with severe signs of OA on radiographs<sup>22</sup> or studied a general population including individuals without knee complaints<sup>9,23</sup>. Other studies focussing on TFOA and PFOA included participants with a relatively high age (mean age 68.4, 65.2 and 62.5 years, respectively)<sup>20,21,24,25</sup> Although two studies evaluated the prevalence of PFOA in a younger population (aged 34-55 years), these participants had chronic knee complaints<sup>26</sup> or no baseline X-ray data of the PF joint were available so that progression could not be evaluated<sup>27</sup>. Thus, most research has focused on older participants with a longer symptom duration of knee pain, or on the general population and therefore little is known on the incidence and prevalence rates, as well as the natural course of PFOA and TFOA, in relatively young subjects with a recent onset of knee complaints.

Therefore, the aim of this study is to 1) determine the proportion PFOA compared to TFOA in individuals with early knee OA symptoms; 2) describe the natural course of PFOA at 2 and 5 years follow-up compared with that of TFOA; and 3) identify whether participants with PFOA have a different phenotype of signs and symptoms compared to those with TFOA, and those with COA.

#### Methods

#### Study population

The present study used baseline data, and data from 2 to 5 years follow-up of the Cohort Hip and Cohort Knee study (CHECK). A detailed description of this cohort is published elsewhere<sup>28,29</sup>. In brief, the cohort included 1002 participants recruited between October 2002 and September 2005. Inclusion criteria were: participants aged 45–65 years with hip and/or knee complaints (pain or stiffness) who had never visited a general practitioner (GP) for their complaints, or had visited a GP no longer than 6 months previously.

Participants were excluded if they had a pathologic disorder (based on medical history and physical examination) that also could explain the symptoms (e.g., for the knee; other rheumatic disease, ligament or meniscus injury, knee joint replacement, plica syndrome, Baker's cyst); had a serious comorbidity that did not allow physical evaluation/follow-up for up to 10 years; and did not have adequate understanding of the Dutch language<sup>28</sup>.

For the current study only those participants that reported knee pain or knee stiffness at baseline were included (n = 845). Ethical approval was obtained and participants provided informed consent prior to commencement of the study<sup>28</sup>.

#### Questionnaires

Self-reported questionnaires were filled in yearly by all participants. At baseline and at follow-up the following domains were assessed by questionnaires: 1) Socio-demographic characteristics: age (in years), sex (male/female), body height (m) and weight (kg), 2) Knee symptoms: duration of complaints (only assessed at baseline), side of knee pain, number of subjects with hip and knee symptoms, and the Western Ontario and McMaster Universities Index (WOMAC)<sup>30</sup> for knee function (higher scores indicating worse function). Moreover, information on pain when going up/ down upstairs and when walking on a flat surface was obtained by means of a five-point Likert scale ('none', 'slight', 'moderate', 'severe', 'extreme')<sup>30</sup>.

#### Physical examination

All participants underwent a standardised physical examination at baseline, and at 2 and 5 years follow-up. For the present study, we used data of the physical examination at baseline and data of the 2-year follow-up of the index knee (i.e., the most affected knee)<sup>31</sup>. Of the 845 participants with knee pain, 384 (44.5%) had unilateral symptoms. For participants with bilateral symptoms the index knee was based on the following decision tree as described by Holla *et al.*<sup>31</sup> 1) highest Kellgren/Lawrence score, 2) lowest degree of active knee flexion, 3) highest pain during knee flexion, and 4) crepitus during knee flexion. In participants for whom we could not define an index knee based on these signs, we randomly assigned an index joint.

Range of joint motion was measured with a goniometer (in degrees). To assess knee effusion the refill test was used (present or absent), palpable warmth was determined by comparing both knees with each other (present or absent), and bony enlargement, joint line tenderness, crepitus (during squatting) and PF grinding test were all scored for presence or absence by palpation.

#### Radiographs

At baseline and at 2 and 5 years follow-up, weight-bearing posterior-anterior (PA), with 7-10°; knee flexion; lateral weightbearing radiographs with 30° of knee flexion; and skyline view with the knees in 30° flexion were made of both knees separately. For the PA radiographs individual features of OA were scored according to the atlas of Altman *et al.*<sup>32</sup> The following features of OA were scored: joint space narrowing (none, doubtful, mild or moderate), femoral medial and lateral osteophytes, and tibial medial and lateral osteophytes (none to moderate). The original Kellgren & Lawrence (K&L) criteria were used to score the severity of TFOA of the involved knee on the PA radiographs<sup>33</sup>. On the lateral views osteophytes (none to moderate) were scored and on the skyline view osteophytes (none to moderate) and joint space narrowing (none to moderate) were scored according to Burnett *et al.*<sup>34</sup>. All the above-mentioned features were scored by five observers independently, according to a paired reading procedure (inter-reader reliability:  $(0.62)^{35}$ .

#### Definition of radiographic OA per compartment

The type of OA was defined for the index knee of the individual. Patients were classified having no OA, isolated PFOA, isolated TFOA or combined OA. Patients classified having isolated PFOA only had signs of OA in the PF joint, patients with isolated TFOA only had signs of OA in the TF joint, and none in the PF joint. and patients with COA had signs of OA in both the TF and the PF joint (Table 1). No radiographic OA was defined if none of the definitions was fulfilled. Incident cases at 2 or 5 years follow-up were defined as participants with radiographic signs of OA at baseline or at 2 years follow-up<sup>4,23</sup>.

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