Joint Bone Spine 79 (2012) 597–603

Available online at SciVerse ScienceDirect www.sciencedirect.com

Elsevier Masson France EM|consulte www.em-consulte.com/en

Original article

The KHOALA cohort of knee and hip osteoarthritis in France

Francis Guillemin[a,b,*], Anne-Christine Rat[a,b], Christian H. Roux[c], Bruno Fautrel[d], Bernard Mazieres[e], Xavier Chevalier[f], Liana Euller-Ziegler[c], Patrice Fardellone[g], Evelyne Verrouil[e], Johanne Morvan[h], Jacques Pouchot[a,i], Joel Coste[a,j], Alain Saraux[h], for the KHOALA cohort study

[a] *Lorraine University, Paris Descartes University, EA 4360 Apemac, France*
[b] *INSERM, CIC-EC CIE6, CHU de Brabois, Nancy, France*
[c] *University of Nice Sophia-Antipolis, Faculty of Medicine, University hospital l'Archet, Rheumatology department, Nice, France*
[d] *Pierre-et-Marie-Curie Paris 6 University, School of Medicine, Assistance publique–Hôpitaux de Paris, Pitié-Salpétrière University Hospital, Department of Rheumatology, Paris, France*
[e] *Paul-Sabatier University Faculty of Medicine, Purpan University Hospital, Rheumatology Centre, Toulouse, France*
[f] *Assistance publique–Hôpitaux de Paris, Henri-Mondor University hospital, Rheumatology department, Créteil, France*
[g] *INSERM U 1088, Faculty of Medicine, University hospital Amiens-Picardie, Rheumatology department, Amiens, France*
[h] *Cavale-Blanche University Hospital Rheumatology department, Brest, France*
[i] *Assistance publique–Hôpitaux de Paris, hôpital européen Georges-Pompidou, Department of internal medicine, Paris, France*
[j] *Unité de biostatistique et d'épidémiologie, hôpital Cochin, Assistance publique–Hôpitaux de Paris, Paris, France*

ARTICLE INFO

Article history:
Accepted 26 March 2012
Available online 20 June 2012

Keywords:
Osteoarthritis
Knee
Hip
Cohort
Quality of life
Health resources

ABSTRACT

Objectives: This study aimed to describe the prevalence of symptomatic knee and hip osteoarthritis (OA) and its course over time, as well as identify prognostic factors of OA course and determinants of costs and access to care in France in a patient cohort.
Methods: Subjects aged 40 to 75 years, with uni- or bilateral symptomatic hip and/or knee OA (ACR criteria), Kellgren and Lawrence (KL) stage 2 or greater, were recruited from a French national prevalence survey for the multicenter KHOALA cohort study. Data collected at baseline included sociodemographic and clinical data; WOMAC, IKS and Harris scores for pain and function; MAQ score for physical activity; functional comorbidity index; GHQ28 score for psychological status; and SF-36 (generic) and OAKHQOL (specific) scores for quality of life. Blood and urine samples were collected.
Results: Eight hundred and seventy-eight subjects were included, 222 with OA of the hip (mean age 61.2 ± 8.8 years), 607 knee (mean age 62.0 ± 8.5 years) and 49 both hip and knee (mean age 64.9 ± 7.9 years). Mean body mass index was 26.9 ± 4.5 for hip OA and 30.3 ± 6.3 for knee OA. Hip and knee OA patients had 1.99 and 2.06 comorbidities, on average, respectively. Disease severity on X-rays for KL stages 2, 3 and 4 for hip OA was 69.8, 26.1 and 4.1%, respectively, and for knee OA, 44.5, 30.3, and 25.2%. As compared with population norms, age- and sex-standardized SF-36 scores were greatly decreased for both knee and hip OA in all dimensions, particularly physical and emotional dimensions.
Perspectives: Patients will be followed up annually, alternately by mail and clinical visit. This cohort of representative patients with knee and hip OA will be an opportunity for future collaborative research.

1. Introduction

Knee and hip osteoarthritis (OA) is a frequent disease with important consequences for patient disability, quality of life (QoL) and costs to society. With the aging of the population, a change in disease profile emerges that needs to be monitored. Patient-reported outcomes, such as self-perceived pain, disability and health-related QoL, are becoming of major importance in this long-lasting disease, where access to care primarily relies on patient complaints and symptoms. The consequences of OA on self-perceived disability and health-related QoL have been insufficiently studied, and population-based data on OA severity are uncommon. Elucidating prognostic factors would be of great benefit to society in helping optimize resource allocation. As well, they would be of benefit to individuals in helping physicians in routine care identify needs and risk of severe deterioration and guide appropriate intervention. A recent literature review [1] found strong evidence of age, knee varus malalignment, and presence of OA in multiple joints, as well as hand OA [2], as predictors of knee OA progression and found body mass index a strong predictor of long-term OA progression. In contrast, conflicting results still persist for a number of potential prognostic factors, including modifiable parameters in lifestyle

* Corresponding author. Inserm CIC-EC, Service d'épidémiologie et évaluation cliniques, CHU de Nancy, 9, rue du Morvan, 54505 Vandœuvre-lès-Nancy, France. Tel.: +33 0 3 83 85 21 65; fax: +33 0 3 83 85 12 05.
E-mail address: francis.guillemin@chu-nancy.fr (F. Guillemin).

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doi:10.1016/j.jbspin.2012.03.011

and environment. Some patient characteristics and environmental aspects are clear predictors of severity and disability. In hip OA, age, joint space width at entry, femoral head migration, femoral osteophytes, bony sclerosis, Kellgren and Lawrence (KL) grade 3, baseline hip pain, and Lequesne score greater or equal to 10 are consistently associated with disease progression [3]. Outcomes to be predicted are generally radiographic joint deterioration and total joint replacement. Several factors determine delayed access to total joint replacement, which generates inequitable care [4].

Few cohorts of symptomatic OA patients at recruitment are currently ongoing, although other important cohorts such as in the Johnston County OA project [5] and the Framingham [6] or Chingford [7] study, mainly recruited on radiological criteria, are contributing to knowledge of OA. CASK [8], OAI [9], and MOST [10] studies are addressing prognosis of symptomatic knee OA. Only the CHECK cohort [11] includes both knee and hip OA patients, and no study has yet addressed broader outcomes. The recent health prevalence survey [12] conducted in France offered the opportunity to recruit a representative sample of population-based subjects with symptomatic knee and hip OA. From this sample, we established a multicenter French cohort of OA patients for the Knee and Hip Osteo-Arthritis Long-term Assessment (KHOALA) cohort study targeting a 10-year follow-up with the following objectives:

- to describe the current prevalence of knee and hip OA patients in the general population independent of any medical consultation or hospitalization;
- to study the course of OA over time, with a particular attention to patient QoL and cost to society;
- to identify prognostic factors of OA course in terms of perceived health, QoL and joint replacement;
- to identify the determinants of costs and access to care;
- to create a biobank for further research, including the search for prognosis biomarkers.

This paper reports on the baseline characteristics of patients included in and the structure of the ongoing KHOALA cohort study.

2. Methods

2.1. Sampling

Subjects were recruited from the 3000 OA two-stage population-based national prevalence survey conducted in France from April 2007 to March 2009 [12]. Briefly, the survey consisted of a random sample of households located within one-hour transportation distance of each investigating centre in six regions by using random digit phone dialing and the next-birthday method in each household. This survey allowed for gathering a representative sample of all cases in the selected age categories. All 1010 people with OA identified were invited to participate in the 10-year KHOALA cohort study. Inclusion criteria were both genders; age 40 to 75 years; uni- or bilateral, symptomatic hip and/or knee OA; clinical diagnosis confirmed and fulfilling American College of Arthritis criteria for knee [13] and hip OA [14]; and KL [15] score stage 2 or more on standard radiography. Subjects were excluded if they had a prosthesis for the symptomatic joint, previous osteotomy, severe comorbidity leading to significant deterioration of QoL or major health care consumption, isolated patello-femoral OA, or other joint disease. All subjects gave their written informed consent to be in the cohort before inclusion. The ethics committee CPP Est III gave approval for the cohort study (n° 07.01.01) registered at www.clinicaltrials.gov (n° NCT00481338).

2.2. Protocol

At baseline and at each annual clinical visit, subjects attend the clinical investigating centre in each region for blood and urine sampling and radiography, with clinical visits at baseline, 3 years, and every other year for 10 years. For alternate years, subjects are mailed a self-reporting questionnaire to be returned to the investigating centre. Subjects who cannot attend the centre can have a research nurse visit at home, and radiography and additional medical data are collected by their physician.

2.3. Outcomes

The primary outcomes are self-perceived pain, disability and health-related QoL and total hip or knee replacement. The secondary outcomes are radiographic disease progression and cost of care.

2.4. Data collection

At baseline, data collected included sociodemographic characteristics (age, sex, weight, height, education level, occupation) and clinical data (pain on a visual analogue scale [VAS], walking distance [meter], and IKS [16] score [0 = worse to 100 = best for movement and for function] and Harris [17] score [0 = none to 44 = maximal for pain; 0 = worse to 47 = best for function] for knee and hip functional ability, respectively); physical activity by the MAQ [18]; functional comorbidity index [19] (0 to 18 conditions); and mini-mental state [20] score (0 to 30 = normal) for cognitive abilities. Patient-reported outcomes included the WOMAC [21] score for pain, stiffness and function; the GHQ28 [22] score for psychological status; and the generic SF-36 [23] and specific OAKHQOL [24] scores for health-related QoL.

2.5. Radiological data

All X-rays are obtained by routine analogic or digital technology and are transferred on DVD to the centralised radiology reading centre in Toulouse for reading and storage. Radiographic data include weight-bearing anteroposterior (AP), posteroanterior semiflexed and axial/sky views of both knees and/or AP pelvis and oblique (Lequesne) views of both hips, according to symptomatic joint(s). All radiographs are read centrally by two readers (BM, EV) who are blinded to clinical condition and questionnaire results. Both readers were trained on a pilot study sample ($n = 1380$) [25]. Target hip and knee tibio-femoral compartments are scored by the KL method [15] on the basis of degree of osteophyte formation, joint space narrowing, sclerosis, and joint deformity in five grades (0: no OA, 1: doubtful, 2: minimal, 3: moderate, 4: severe).

2.6. Biological data

Blood and urine samples were collected in the morning, aliquoted for sera, stored for DNA and frozen at −80 °C in each centre, then transported for final storing in a biobank at Nancy University (INSERM U961). This biological collection was approved by CPP Est III (n° 07.01.01) and authorized by the ministry of education and research and regional hospitalisation agency (n° AC 2008-449).

2.7. Health resources

Data are collected annually on health resource use over the previous 12 months, including drug treatment, physiotherapy, alternative medicine, and surgery and prosthetic joint replacement.