EXTENDED REPORT

Sex differences in hip osteoarthritis: results of a longitudinal study in 508 patients

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Objective: To evaluate sex differences in the clinical and structural presentation, and natural history of hip OA.

Methods: A multicentre, prospective, longitudinal, five year follow up study of 508 patients (302 women, 206 men, mean age 63 (7) years) with painful hip OA. Data collected were baseline demographics, symptomatic, therapeutic, and structural variables; symptomatic variables and changes in joint space width (JSW) during the first year's follow up; requirement for total hip arthroplasty (THA) between the end of the first and fifth years. Statistical analysis: evaluation of sex differences (*a*) at baseline, in the main characteristics of hip OA using multivariate logistic regression; (*b*) during the first year of follow up, in the radiological progression of the disease; (*c*) during the five years of follow up, in the requirement for THA using Kaplan-Meier curves and the log rank test, and of the parameters related to THA, using a multivariate Cox analysis.

Results: At entry, women presented more frequently than men with polyarticular OA (mean (SD) articular score 306 (162) *v* 235 (127)), and superomedial migration of the femoral head (40% *v* 19%), and had more severe symptomatic disease (patient's overall assessment 46 (23) *v* 40 (26)). The change in JSW did not differ between women and men after one year, but a greater proportion of women had rapid structural progression (OR=2.34, 95% CI 1.1 to 5.2). THA was performed more often in women. Multivariate analysis suggested that the decision to perform surgery was related more closely to the symptomatic and structural severity of the disease than to the sex of the patient.

Conclusion: Hip OA in women is more frequently part of a polyarticular OA, and displays greater symptomatic and structural severity.

The prevalence of hip osteoarthritis (OA) ranges from 3 to 25% in adults aged 55 years and older in white populations, and is a leading cause of disability and handicap.[1–7] Management includes treatments that can be non-pharmacological (patient education, physical therapy, use of cane, weight management programme in overweight patient, etc), pharmacological (non-steroidal anti-inflammatory drugs, analgesics, intra-articular injections of corticosteroids or hyaluronic acid), or surgical (osteotomy, arthroplasty).[8 9]

Several studies suggest that the characteristics of hip OA might differ in men and women as hip OA in women is more commonly an element of polyarticular OA, and has greater symptomatic and structural severity,[10–15] However, studies evaluating hip OA in men and women either had a retrospective or cross sectional design, or a recruitment bias (hydrotherapy, patients referred to hospital), or a small sample size. This study aims at understanding the natural history of hip OA with regard to the sex of the patient, using a large cohort of patients enrolled in a long term (five years) longitudinal prospective follow up.

PATIENTS AND METHODS

Study design

Patients who had participated in a multicentre, prospective, randomised, controlled, double blind three year clinical trial evaluating the structure modifying effects of diacerein (ECHODIAH study)[16] were subsequently prospectively followed up for an additional two years (for a total of five years of follow up). During the additional two years patients were treated by their regular practitioners, who were allowed to prescribe any treatment. All patients agreed to the subsequent two year follow up study. The study protocol was approved by the local ethics committee (Cochin Hospital, Paris, France).

Inclusion criteria

Inclusion criteria have been previously described.[16] Briefly, outpatients visiting a rheumatologist and fulfilling the American College of Rheumatology criteria for the diagnosis of hip OA[17] were enrolled after written informed consent. Other inclusion criteria were age between 50 and 75 years and hip pain every day for at least one month during the past three months. Exclusion criteria were radiological joint space width <1 mm at the narrowest point, radiographic medial or axial femoral head migration, and secondary hip OA.

Data collection

During the three year trial, symptomatic and structural data were repeatedly collected. Conversely, patients were not seen during the two additional years of follow up: one of the investigators telephoned the patients once each year and asked whether they had undergone total hip arthroplasty (THA) during the year.

Demographic, symptomatic, and therapeutic variables

The following characteristics were collected at entry: age, sex, body mass index (BMI), and duration of the disease. Other joints affected by OA were recorded by the following procedure: for hand OA, diagnosis was based on clinical symptoms and physical examination. For other locations

Abbreviations: JSW, joint space width; BMI, body mass index; OA, osteoarthritis; THA, total hip arthroplasty; VAS, visual analogue scale

Table 1 Baseline demographics, symptomatic and structural variables of the 508 patients. Values are mean (SD) unless indicated otherwise

Parameters	Women (n=302)	Men (n=206)
Demographic variables		
Age (years)	64 (7)	61.6 (7)
Disease duration (years)	4.7 (4.8)	4.2 (4.8)
Body mass index (kg/m^2)	25 (4)	27 (3)
Concomitant OA		
Hand OA (%)	53	30
Spine OA (%)	81	73
Knee OA (%)	40	20
Articular index	306 (162)	235 (127)
Symptomatic variables		
Pain (mm)	47 (20)	42 (20)
Lequesne's index	8.0 (2.6)	7.5 (2.7)
Patient's overall assessment (mm)	46 (23)	40 (26)
Structural variables		
Femoral head impact		
Superolateral: % of patients	50	72
Superomedial: % of patients	40	19
Concentric: % of patients	11	9
Joint space width (mm)	2.2 (0.8)	2.3 (0.9)

(spine and knee, in particular), OA was recorded if it had been diagnosed during a previous radiological evaluation of a painful joint. No systematic radiological evaluation of other joints was made, except the hip contralateral to the study hip, because both hips are visible on the hip radiograph. The extent of OA was evaluated using the articular score derived from the Lansbury index.[18] Each patient was evaluated by a single rheumatologist at entry, then every three months for three years. The following data were collected at each visit: pain occurring after physical activities during the previous two days (100 mm visual analogue scale (VAS)), functional disability (Lequesne's index, a 0–24 scale of the impact of hip OA on daily activities),[19] and patient's overall assessment of disability (100 mm VAS).

Structural variables

An anteroposterior weightbearing radiograph of the pelvis with the lower limbs in 15° internal rotation was taken at entry and then every year for three years. All films were collected and analysed by a single doctor (ML). The type of femoral head migration (superomedial, superolateral, concentric) and the structural severity was assessed by an experienced rheumatologist. Joint space width (JSW) at the narrowest point in mm (using a 0.1 mm graduated magnifying glass) was measured at baseline and after one year.

Decision for total hip arthroplasty

Decision for THA was made jointly by the rheumatologist and the surgeon, referring to the last follow up *x* ray findings (but not to radiographic change) and analysis of objective symptomatic variables, and by the patient. The date of surgery was noted.

Some disparity in the decision to perform surgery can be accounted for because it involved two doctors and the patient, and because the study was multicentric. We have previously reported that the place of residence does not influence the requirement for surgery.[20] The results cannot be influenced by economic considerations because the French national health insurance covers virtually everyone. Notably, there is no undue delay between the decision to perform surgery and the date of surgery.

Statistical analysis

The analysis involved three steps:

- Evaluation of the characteristics of the patient at baseline (demographic data, OA localisation, symptomatic and structural severity), with regard to the sex of the patient, using multivariate regression logistic analysis, in which sex was the dependent variable and the other data at baseline were the independent variables.
- Evaluation of the progression rate of the disease during the first year, using multivariate regression logistic analysis, with regard to the sex of the patient. We compared the mean values of the symptomatic variables and the change in radiological JSW during the first year of follow up, by sex.
- Evaluation of the requirement for THA with regard to the sex of the patient. We performed Kaplan-Meier estimates of the cumulative probabilities of not proceeding to THA according to sex. Curves were compared using a log rank test. We subsequently conducted a Cox model multivariate analysis which evaluated THA performed as of the end of year 1, in order to include the mean values of symptomatic variables and radiographic progression during the first year.

Because this study was an analysis secondary to a large clinical trial, treatment was included as a covariate in the longitudinal analyses (steps 2 and 3).

RESULTS

Of the 508 recruited patients (mean age 63 (7) years), 302 (59.4%) were women. Table 1 summarises the main baseline characteristics of the patients.

Because some data were missing the multivariate regression logistic analysis, in which sex was the dependent variable, and other data at baseline, independent variables concerned 483 patients (199 men, 284 women). Table 2 shows the results obtained. The demographic characteristics (age and BMI) and also the presentation of OA differed between the sexes. Superomedial femoral head migration was more common in women, and other locations of OA were more common in women (in particular, the hand), resulting in a higher articular score. Variables evaluating symptomatic severity suggested more severe OA in women.

Table 2 Baseline measures related to the sex of the patient on multivariate logistic regression analysis (sex was the dependent variable and other baseline data were the independent variables). Results are shown as percentages

	Women (n=284)	Men (n=199)	Odds ratio (95 CI)	p Value
Age >60 years	73.9	55.2	1.9 (1.2 to 3)	0.0013
BMI ⩽27 kg/m^2	69.7	59.2	2.1 (1.3 to 3.3)	0.0043
Patient's overall assessment >40 (100 mm VAS)	64.4	47.2	2.6 (1.7 to 4)	<0.0001
Joint space width <3 mm	78.8	72.8	1.7 (1 to 2.9)	0.038
Superomedial hip OA	40.4	20.1	2.8 (1.7 to 4.6)	<0.0001
Associated hand OA	52.1	30.6	2.3 (1.5 to 3.6)	0.0003
Articular score >400	28.1	9	4.2 (2.3 to 8.1)	<0.0001

Table 3 Mean average values of symptomatic and therapeutic variables, and mean decrease in JSW during the first year of follow up, according to the sex of the patient. The symptomatic variables were collected at baseline and at months 1, 3, 6, 9, and 12. The structural variable was collected at entry and at year 1. Results are shown as mean (SD)

Measures	Women	Men	p Value (*t* test)	p Value (Wilcoxon test)
Symptomatic data				
Pain (mm)	39 (20)	34 (19)	0.005	0.02
Lequesne's index	6.7 (2.9)	5.7 (2.7)	0.001	0.0003
Patient's assessment of disability (mm)	37 (22)	31 (19)	0.001	0.005
Change in joint space width (mm)	0.31 (0.5)	0.30 (0.5)	0.84	0.7

During the first year of follow up, 38 patients (9 men, 27 women) underwent THA. Table 3 shows the mean values of symptomatic and therapeutic variables and the mean decrease in JSW in the remaining patients. There was a statistically significant difference between the groups in favour of a more symptomatically severe disease in women, with no difference in the mean structural progression.

Because some data were missing the multivariate analysis, in which sex was the dependent variable, and all baseline characteristics together with the changes in symptomatic and structural variables, the independent variables concerned 424 patients (179 men, 245 women). Apart from previously selected variables for the multivariate analyses performed at baseline (see table 2), this analysis suggested a greater proportion of rapid structural progression (decrease in JSW >50% during the first year) in women (12% in women and 8% in men, odds ratio=2.34, 95% confidence interval 1.1 to 5.2, p=0.03).

The requirement for surgery (THA) occurred more frequently and earlier in women than in men, illustrated by the Kaplan-Meier estimates of the cumulative probabilities of not undergoing surgery (fig 1, log rank test, p=0.0084). At the end of the fifth year of follow up, THA had been performed in 44 (6)% and 32 (6)% of women and men, respectively. However, when performing a multivariate analysis (in only 410 patients because of missing data) in which the requirement for surgery was the dependent variable and the demographics (including sex), symptomatic and structural variables were the independent variables, sex was not statistically associated with requirement to surgery (relative risk 1.256, 95% CI 0.872 to 1.822). On the other hand, symptomatic and overall structural variables were associated with requirement to surgery (data not shown).

Finally, inclusion of treatment as a covariate in the analysis did not significantly change the results (data not shown).

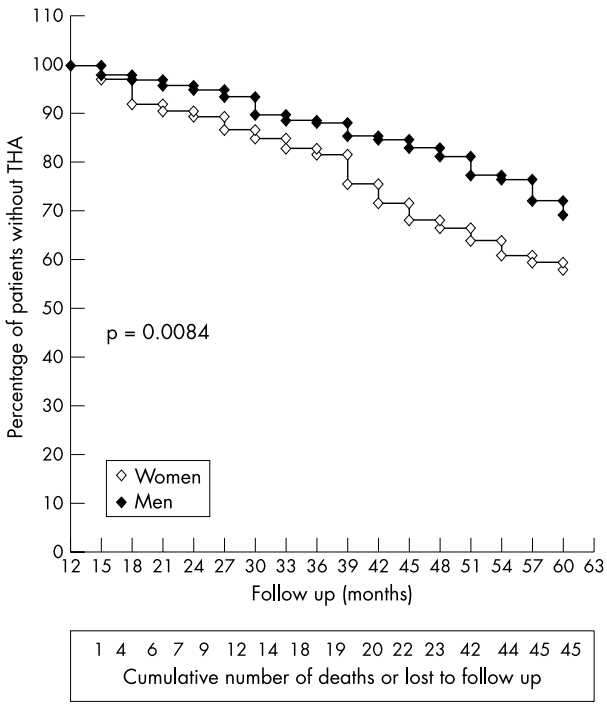

Figure 1 Kaplan-Meier estimates of the cumulative probabilities of not undergoing THA, between the ends of years 1 and 5, according to sex, in painful hip OA.

DISCUSSION

In this study hip OA in women was found to be more frequently part of a polyarticular OA, to have greater symptomatic and structural severity, and to require THA more often than OA in men.

It is noteworthy that the group was included in a therapeutic trial during the first three years of follow up. The treatment used in these first years and the criteria for inclusion in the trial might have introduced some bias. However, the characteristics of the patients included were those commonly seen in daily practice, and the results were unchanged in an analysis including the study treatment as a covariate. Also of note is that, owing to missing data, some patients were not included in the analyses. But the analyses were multivariate, which means that one missing piece of information was sufficient to exclude a patient from the analysis (without losing the patient to follow up). As the proportion of patients excluded from the analyses was low (<5–10%), we do not believe that this obviates the value of the study.

Although conflicting results have been reported, the prevalence of hip OA in men and in women is probably similar.[1–7] Our study, however, enrolled more women (60%). The patients' characteristics were those commonly seen in daily practice and in therapeutic trials evaluating treatment effects in hip OA. The male/female ratio in the French population aged from 40 to 74 years is 48.4/51.6%.[21] Therefore, the ratio in our study (40/60%) might suggest an unbalanced male/female ratio of patients visiting a practitioner for hip OA in daily practice, and thus a higher prevalence of symptomatic hip OA in women than in men. However, this study was not designed to be epidemiological. As such, it cannot indicate the prevalence or the male/female ratio of symptomatic hip OA in the general population. Other explanations for our study's unbalanced male/female ratio include chance and the criteria chosen for inclusion and exclusion.

As suggested elsewhere,[10 11] a polyarticular disease was observed more commonly in women with hip OA (associated hand OA, articular score >400). This may in part explain the greater symptomatic severity seen in women with hip OA. The

association between superomedial migration of the femoral head and women has been reported elsewhere.[11] It was suggested that this association was due to anatomical sex differences in the so-called CE angle (a measure of acetabular depth), which is larger in women.[11] Why symptomatic variables (pain, Lequesne's index) were higher in women at entry is more difficult to explain and may be related to factors other than hip OA (other OA affected joints, psychosociological factors). This observation at entry is obviously insufficient to infer that hip OA is more severe in women. However, the one year longitudinal evaluation suggested that the disease was more severe in women, as illustrated by higher mean values in symptomatic variables, without a higher mean rate of radiological progression, but with a higher proportion of patients with rapidly progressing structural damage.

Finally, on univariate analysis, women underwent THA significantly more often than men. On multivariate analysis, the sex of the patient was not related to THA, but to symptomatic and structural severity. These results suggest that the requirement for THA is directly related to symptomatic and structural variables, and only indirectly to the sex of the patient, through the female associated severity. This severity related to the sex of the patient may be due to a selection bias. Katz *et al* reported that women have worse functional status than men before THA.[22] Hawker *et al* reported that among patients with hip OA and potential need for arthroplasty, women are less likely to have discussed THA with a doctor, specifically with an orthopaedic surgeon.[23] This may be seen earlier in the history of hip OA, with women first visiting a rheumatologist later than men. But in our study, disease duration was similar in men and women. Additionally, rapid progression in a subgroup of women may explain why women have worse functional status than men before THA, and why women are less likely to have discussed THA. The difference between our study and that of Hawker *et al* may also be due to cultural differences between France and North America.

Explaining these sex differences in hip OA is not straightforward. Hip OA in women may be related more often to a systemic disease (as illustrated by the concomitant affected joints), and this systemic disease may be a more rapidly progressing form of the disease whatever its location.[24] Another explanation may be the influence of sex hormone on cartilage breakdown.[25]

Further studies are required to confirm these results in other sets of patients and to better understand the underlying mechanisms of differences between the sexes in hip OA.

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