EXTENDED REPORT

Predictive factors of total hip replacement due to primary osteoarthritis: a prospective 2 year study of 505 patients

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Objectives: To determine the 2 year total hip replacement (THR) rate and to identify factors predictive of THR due to primary osteoarthritis (OA).
Methods: A 2 year prospective cohort study. Inclusion criteria were primary hip OA, with a history of pain for 6 months, and patients' pain assessment of ⩾30 mm on a visual analogue scale (0–100 mm). Predictive factors of THR were identified by univariate then multivariate analysis using logistic regression. Potential predictors considered were demographic, radiographic (localisation and severity of OA), and patients' assessment of symptomatic severity of OA.
Results: Of the 741 patients enrolled, 505 (68.2%) patients, mean (SD) age 64.0 (10.1) years, mean (SD) disease duration 4.7 (5.2) years, had complete 2 year data. There was no difference between the completer and non-completer groups. During follow up, 189/505 (37.4%) patients had a first THR. By multivariate analysis, predictors of THR were Kellgren-Lawrence radiographic grade (grade III: odds ratio (OR) = 3.3 (95% confidence interval (95% CI) 1.7 to 6.4); grade IV: OR = 5.3 (95% CI 2.6 to 10.8)), high mean patient global assessment during the first 6 months (OR = 2.2 (95% CI 1.4 to 3.2)), and previous non-steroidal anti-inflammatory drug (NSAID) intake (OR = 1.5 (95% CI 1.0 to 2.4)). For two of these factors together, OR = 3.0 (95% CI 1.6 to 5.9), for three factors together, OR = 5.6 (95% CI 2.6 to 12.2).
Conclusion: The 2 year rate of THR was high in this group of patients with painful hip OA: 37.4%. Radiological grade, mean patient global assessment, and the need for NSAIDs were predictive of THR.

Hip osteoarthritis (OA) affects 7–25% of white people over the age of 55 years.[1–4] In addition to the related pain and discomfort, hip OA has substantial economic consequences.[5] OA is the most common indication for total hip replacement (THR) in the elderly. Because of an aging population, high prevalence of OA among the elderly, and technical improvements in arthroplasty, the demand for total joint arthroplasties has been steadily increasing.[6] However, the prevalence of THR continues to be debated in this disease and there are few longitudinal studies of predictive factors of THR due to primary OA. Such longitudinal studies are important for identifying those at greatest risk for development of clinically significant disease and disability and discovery of factors that may slow progression. Recently, a systematic review analysed the evidence concerning prognostic factors of progression in hip OA (either radiographic joint space narrowing or recourse to surgery).[7] This review clearly showed that more data are needed in this field.

In this study we report results for an outpatient population with painful hip OA, after a total of 2 years of follow up. The objectives of this study were to determine the 2 year THR rate and to identify predictive factors of THR in primary hip OA.

PATIENTS AND METHODS

Setting

The cohort studied was community based, recruited through 741 French rheumatologists (thus, secondary care setting). Patients were initially entered into a therapeutic trial.[8] This article reports results of the 2 year follow up.

Study design

This was a 2 year, longitudinal prospective cohort study involving 741 patients. The initial 24 week study was a therapeutic trial comparing patient administered assessment tools and an unsupervised home based exercise programme in OA.[8] For the initial trial, patients were treated continuously with rofecoxib 12.5 or 25 mg/day; after the end of this phase, no standardised treatment was given, and patients were followed up by their usual physician. This work reports the 2 year follow up of this cohort.

Patients

The selection of patients has been described elsewhere.[8] Briefly, inclusion criteria were: ambulatory outpatients aged 40 years or more; hip OA according to the American College of Rheumatology definition[9]; history of hip pain of >6 months; pain scored by the patient on a 100 mm visual analogue scale (VAS) ⩾30; and pain for at least 14 days during the previous month.

Exclusion criteria were: (*a*) secondary arthritis as defined by the Osteoarthritis Research Society International (OARSI[10]); (*b*) an operation scheduled within the 12 months after inclusion; (*c*) any type of surgery, including arthroscopy, of the study hip in the previous 2 years; (*d*) serious concomitant illnesses (neoplasia, infectious diseases, unstable metabolic or cardiovascular diseases, systemic diseases); (*e*) any intra-articular injection (hyaluronic acid or corticosteroids) during the 2 months before inclusion, joint lavage in the 3 months before inclusion, or recent introduction of slow acting anti-osteoarthritic drugs (in the 2 months before the study); (*f*) contraindication of rofecoxib; and (*g*) participation in another research study.

Abbreviations: CI, confidence interval; NSAID, non-steroidal anti-inflammatory drug; OA, osteoarthritis; OR, odds ratio; THR, total hip replacement; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index

Table 1 Patients' baseline characteristics*

	All patients with 2 year follow up (n = 505)	Patients lost to follow up or with missing data (n = 236)	p Value
Age (years)	64.0 (10.1)	63.7 (10.3)	0.73
Sex, No (%) female	309 (61.2)	151 (64.0)	0.47
Body mass index (kg/m^2)	26.3 (4.6)	26.3 (4.6)	0.89
Duration of symptoms (years)	4.7 (5.2)	4.3 (5.0)	0.34
Pain (0–100 mm VAS)	55.0 (15.8)	56.8 (16.3)	0.16
WOMAC function score (0–100)	44.4 (16.2)	45.9 (16.9)	0.31
Patient global assessment (0–100 mm VAS)	57.8 (18.4)	59.3 (18.7)	0.30
Radiological grade (Kellgren-Lawrence), No (%)			0.27
III	273 (54.1)	119 (50.4)	
IV	142 (28.1)	63 (26.7)	
Previous treatment, No (%)			
NSAIDs	331 (65.5)	164 (69.5)	0.26
Intra-articular injections	20 (4.0)	3 (1.3)	0.05

*Except where otherwise indicated, values are the mean (SD).
VAS, visual analogue scale; NSAIDs, non-steroidal anti-inflammatory drugs; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

All patients agreed to be enrolled in the study and provided their signed informed consent. The study was approved by the ethics review board of Cochin Hospital (Paris, France).

Data collection

Data collection at baseline

The following evaluation data were collected at baseline:

- *Demographic data*: age, sex, body mass index
- *Patient history*: duration of symptoms in the target joint, concomitant illnesses. Any previous intra-articular injections in the target hip, any previous non-steroidal anti-inflammatory drug (NSAID) use, previous or current slow acting symptomatic OA drug use, and concomitant treatments
- *Clinical status*: clinical severity estimated through patients' global assessment of pain (VAS), patients' global assessment of disease severity (VAS), and functional impairment, measured by the physical function subscale of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC, normalised to a 0–100 score)[11]
- *Radiography*: the following baseline data: radiological grade according to Kellgren and Lawrence's classification[12] and the pattern of migration of the femoral head within the acetabulum in the target hip: superolateral, superomedial or global.

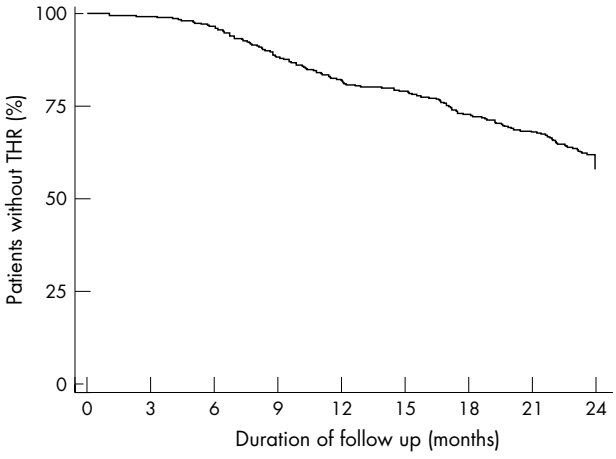

Figure 1 Cumulative occurrence of THR over time in a cohort of 505 patients with painful hip OA: Kaplan-Meier survival analysis.

Data collection during the first 6 months

Pain, functional impairment, and patient assessment of disease activity were evaluated at four time points during the first 6 months of follow up in 246 patients, and at baseline and 6 months for another 202 patients, permitting calculation of mean values of these three variables over the first 6 months for 448 patients (for 246 patients, these mean values were thus calculated based on four values).

Data collection of the outcome measure after 2 years of follow up

The primary outcome criterion was the occurrence of THR during the 2 years of follow up. This information was collected through a specific research file. The 741 rheumatologists taking part were contacted by fax, then if necessary by telephone (two phone calls for each physician). They were asked to obtain information about their patients, by telephone or by a visit. Information collected was date of last contact with the patient, status of the target joint: surgery yes/no and if yes, date.

Statistical methods

A survival curve according to Kaplan-Meier's method was established to estimate the cumulative occurrence of THR over time.

Predictive factors of the occurrence of THR after 2 years were identified by univariate analysis (χ^2 and t tests) and multivariate analysis (logistic regression with stepwise procedure). The potential predictive variables included in the multivariate model were selected using univariate analysis ($p \leqslant 0.20$). Mean symptomatic outcome variables over the first 6 months of follow up were transformed into binary variables using the median value as the cut off point. An additional analysis was performed to determine the odds ratio for THR if several of the predictive factors identified were present simultaneously. Statistical analysis was performed using SAS statistical software (SAS institute Inc, Cary, NC).

RESULTS

Demographic, clinical, and radiological features of the patient cohort

Seven hundred and forty one patients with hip OA were enrolled.[8] Two hundred and thirty six (31.8%) were lost to follow up at 2 years: 115/741 (15.5%) patients were lost to follow up by their rheumatologist (3 patients died, 63 refused further follow up by their rheumatologist or moved out of the

Table 2 Predictive factors of THR in painful hip OA: univariate analysis

	THR (n = 189)	No THR (n = 316)	p Value
Age (years)	65.0 (9.8)	63.4 (10.3)	0.09
Sex, No (%) female	119 (63.0)	190 (60.1)	0.53
Body mass index (kg/m^2)	26.3 (3.9)	26.1 (3.9)	0.55
Duration of symptoms (years)	4.4 (4.7)	4.9 (5.5)	0.28
Location of hip OA, No (%)			
Superolateral	117 (61.9)	189 (59.8)	0.64
Superomedial	30 (15.9)	59 (18.7)	0.42
Global	52 (27.5)	79 (25.0)	0.53
OA in contralateral hip, No (%)	68/184 (37.0)	128/305 (42.0)	0.27
Radiological grade (Kellgren-Lawrence), No (%)			<0.0001
III	101 (53.4)	172 (54.4)	
IV	73 (38.6)	69 (21.8)	
Previous treatment, No (%)			
NSAIDs	139 (73.5)	191 (60.4)	0.003
Hip intra-articular injections	8 (4.2)	12 (3.8)	0.81
Baseline pain (0–100 mm VAS)	57.0 (16.2)	53.8 (15.4)	0.03
Baseline WOMAC function score (0–100)	45.7 (15.9)	43.7 (16.3)	0.17
Baseline patient global assessment (0–100 mm VAS)	60.7 (19.1)	56.1 (17.7)	0.006
Mean pain over the first 6 months >42 (0–100 mm VAS), No (%)*	282 (62.9)	189 (42.2)	<0.0001
Mean WOMAC function score over the first 6 months >26 (0–100 mm VAS), No (%) *	268 (59.8)	197 (44.0)	0.001
Mean patient global assessment over the first 6 months >47 (0–100 mm VAS), No (%)*	282 (62.9)	189 (42.2)	<0.0001

Except where otherwise indicated, values are the mean (SD).
VAS, visual analogue scale; NSAIDs, non-steroidal anti-inflammatory drugs.
*Mean values of symptomatic outcome variables over the first 6 months were obtained for 448 patients and were dichotomised according to the median value.

area, for 49 there was no specified reason) and for 121/741 (16.3%) data were missing at the 2 year evaluation owing to the absence of an answer from the rheumatologist.

Table 1 shows the baseline characteristics of the patients. For the 505 patients with complete data, mean (SD) age at inclusion was 64.0 (10.1) years and mean (SD) symptom duration at inclusion was 4.7 (5.2) years. Mean (SD) pain at inclusion (VAS, 0–100) was 55.0 (15.8), mean (SD) WOMAC function score (0–100) was 44.4 (16.2), mean (SD) patient global assessment of disease activity (VAS, 0–100) was 57.8 (18.4). Hip OA was radiologically severe: 415/505 (82.2%) patients presented a Kellgren-Lawrence grade III or IV. The baseline characteristics of the patients lost to follow up did not differ from those of the rest of the cohort clinically or radiologically except for fewer previous hip intra-articular injections.

Occurrence of THR

Figure 1 shows the cumulative occurrence of THR over the 2 years of follow up for the 505 patients with 2 year data, according to Kaplan-Meier's life table method.

During follow up, 189/505 (37.4%) patients had a first THR due to primary OA.

Predictive factors of hip replacement

The analysis of predictive factors was performed only for the 505 patients for whom complete 2 year follow up data were available.

Univariate analysis

Table 2 presents the results obtained by univariate analysis of the studied variables.

- Analysis of the baseline variables collected for the 505 patients showed that radiological grade was predictive of THR, as were baseline patient global assessment and baseline pain, and previous treatment by NSAIDs.
- Analysis of the mean values for symptomatic outcome variables obtained during the first 6 months in 448 patients indicated that mean values of pain, of patient global assessment, and of WOMAC function score above the median were predictive of THR.
- No other analysed factor showed predictive value.
- There was no association between the occurrence of THR and inclusion in one of the intervention groups carrying out home based exercises for OA for the initial 6 month phase (p = 0.88).

Table 3 Predictive factors of THR in painful hip OA: multivariate analysis in 448 patients

	Odds ratio	95% CI	p Value	Patients at risk (n)	% THR	
					In group at risk	In group not at risk
Radiological grade			<0.0001			
III	3.3	1.7 to 6.4		249	39.0	16.9 (grade II)
IV	5.3	2.6 to 10.8		122	52.5	16.9 (grade II)
Previous NSAID intake	1.5	1.0 to 2.4	0.049	296	43.2	30.3
Mean patient global assessment over the first 6 months >47* (0–100 mm VAS)	2.2	1.4 to 3.2	0.0002	222	48.2	29.3

*47 is the median value for mean patient global assessment over the first 6 months.

Stepwise multiple logistic regression

Multiple regression was performed in the 448 patients in whom mean values over the first 6 months were obtained: 174 (38.8%) had THR performed, 274 (61.2%) did not (table 3). Independent predictors of THR were Kellgren-Lawrence radiographic grade III or IV (versus grade II), mean patient global assessment during the first 6 months above the median (47 mm), and any previous NSAID intake.

If two of these three factors (radiographic grade III or IV, mean patient global assessment above the median, and previous NSAID intake) were present, the odds ratio (OR) for THR was 3.0 (95% confidence interval (95% CI) 1.6 to 5.9); if three of the factors were present, OR = 5.6 (95% CI 2.6 to 12.2) and the estimated probability of having THR was then 63% (95% CI 53 to 73%).

DISCUSSION

In this group of patients with painful hip OA, the 2 year THR rate was 37.4%. Radiological grade III or IV, high mean patient global assessment during the first 6 months, and previous treatment with NSAIDs were predictive of the occurrence of THR.

The main limitation of our study is the high rate of loss to follow up. This occurred owing to the study design, which involved an important number of participating rheumatologists so as to best reflect the natural progression pattern and treatment pattern of hip OA in the population (in our country, a high proportion of patients with OA are referred to rheumatologists). Every effort was made to obtain information about all patients; a high proportion of data is missing because rheumatologists themselves refused to answer. Nevertheless it should be noted that baseline characteristics of patients lost to follow up did not differ from those of completers, reducing the risk of bias. For the incidence of THR in our cohort, if we were to take the hypothesis of maximal bias related to our patients lost to follow up—that is, if we consider that no patient lost to follow up had THR, the hypothetical rate of THR would then be 24.8%. As for the analysis of prognostic factors of THR, there is no specific reason to believe this analysis was modified by follow up loss.

Several publications report the THR rate in hip OA. In previous publications we reported the outcome for 506 patients with symptomatic hip OA participating in a randomised controlled trial of diacerein and found that THR occurred in 6% within 12 months and 21% within 36 months.[13 14]

Ledingham *et al* showed evidence of the highest rate of surgery: in patients with hip OA referred to a hospital rheumatology and orthopaedic clinic they found that 53% had a THR after a median of 14 months of follow up.[15]

Danielsson performed a long term follow up on 117 patients in Sweden from 1950 to 1954. After 10 years, 26 (22%) patients had undergone hip surgery.[16] This percentage of THR is much lower than in our study but in the 1960s arthroplasty was not as standard; furthermore, in Danielsson's study patients had radiographic but often asymptomatic hip OA.

Lane *et al* examined radiographic progression of hip OA and recourse to surgery over 8 years in a community sample of 745 elderly white women with baseline radiographic hip OA.[17] During follow up, 12.9% had a THR. Progression was greater in the 37% of hips and 47% of women with painful hip OA at baseline: among these painful hips, 23.6% progressed to THR (versus 2.7% without pain). Here again, recourse to surgery is much lower than in our study, even in the group with painful hip OA; part of this difference may be due to patient selection (Lane studied elderly women, perhaps presenting with more comorbidity—that is, contraindications to surgery), part to differences in healthcare systems.

Birrell *et al* also studied rates of THR in England[18]: 195 patients attending with a new episode of hip pain were followed up for a median of 36 months; 16% had THR. However, in our study mean symptom duration was 4.7 years, whereas in Birrell's patients, only 28% had pain duration of more than 12 months.

The high rate of THR in this study might be explained by the fact that this cohort was constituted as a follow up of a therapeutic trial. Thus these patients (*a*) were given the opportunity to enter the trial by their rheumatologists; (*b*) agreed to participate. This probably constitutes a group of patients with particular symptomatic severity, and indeed our patients had a high baseline level of pain; perhaps also these patients had certain social, educational, and psychological characteristics, all of which might impact on their future need to have a hip replacement. On the other hand, we might have excluded patients with a more severe disease by excluding those who were due to have surgery in the subsequent 12 months, or those who had had recent intra-articular injections.

Furthermore, there is inherent variability in the decision to perform surgery. Recourse to surgery reflects the severity of OA, but also other factors, related (patient's age, willingness, or concomitant diseases,…) or not (doctor's and/or surgeon's opinion, healthcare system, economic activity, family circumstances,…) to the patients' condition.[19–22] This raises the issue of external validity: it may be that the results for our populations might not totally be applicable to other groups or to other healthcare systems.

As reported recently by Lievense *et al* in a systematic review,[7] two studies on predictive factors of THR in hip OA indicate that baseline radiographic grade is an important predictive factor,[23 24] and this is confirmed here (Kellgren-Lawrence radiographic grade is predictive of THR in univariate and multivariate analysis). In Birrell's study, THR was predicted by pain, use of a walking stick, and radiographic severity.[18] Rapid radiographic change is also probably important but was not studied here. Radiographic aspects have been classified according to the pattern of migration of the femoral head within the acetabulum,[25–28] and the pattern of bone response to cartilage loss.[28 29] Strong evidence now exists for a more rapid progression of hip OA when there is a superolateral migration of the femoral head, as compared with a medial migration.[15 23 29] The evidence for an association between sex, obesity, or age and the progression of hip OA is conflicting.[7 30–32] This study did not confirm the role of the pattern of migration of the femoral head, of sex, of obesity, or of age.

More recently, pain and functional status have been associated with THR.[14 15 18] In this study, mean pain, function, and global assessment over 6 months were predictive of THR in univariate analysis; mean patient global assessment over 6 months was predictive in multivariate analysis. This supports the logical assumption that the indication for arthroplasty is based on the association of radiographic severity and of symptomatic severity: patient perceived sustained pain and functional impairment.

Furthermore, this study indicates a predictive value of requirement for NSAIDs. Data on NSAIDs were collected as binary information: previous NSAID intake yes/no; thus we have no information on the type of NSAID or the total dose ingested. Requirement for NSAID treatment should probably be considered here only as reflecting a more symptomatic severe disease,[14] as was the case for previous use of analgesics in Birrell's study.[18]

In this study of patients with painful hip OA, we obtained high figures for recourse to surgery and suggest that

radiographic characteristics, patient perceived severity, and the need for NSAIDs can identify patients with poor outcome from hip OA. Further studies are required to confirm these results and better define the profile of patients with hip OA requiring surgery.

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