Do Risk Factors for Incident Hip Osteoarthritis (OA) Differ from Those for Progression of Hip OA?

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Our understanding of risk factors associated with hip osteoarthritis (OA) is derived largely from cross-sectional studies or retrospective case-control studies. As David Felson points out elsewhere in these proceedings[1], it is important to distinguish between radiographic OA and symptomatic OA, insofar as many persons identified as having radiographic OA in population surveys will not have symptoms. Symptomatic OA is often studied in the context of the patient who is undergoing total hip arthroplasty (THA).

A number of case-control studies from Scandinavia and the United Kingdom have focused on differences between individuals undergoing THA for OA and controls drawn from the population. The factors that appear to be associated with hip OA in such studies include age and higher body mass index (BMI), although the strength of the association between hip OA and BMI is not as strong as that for knee OA. With hip OA (as with knee OA), the association with obesity is stronger for bilateral disease than for unilateral disease. A history of trauma or joint injury is also associated with hip OA (more strongly with unilateral than bilateral disease), as is occupational exposure in jobs that require heavy lifting and, particularly, farming. A systematic review published by the group from Rotterdam nicely summarizes the literature on vocational exposure and hip OA[2]. Finally, as is well known to orthopedic surgeons, congenital and developmental disorders, such as acetabular dysplasia, lead to the development of hip OA in subjects in their 20s and 30s.

What factors are associated with the progression of hip OA? Several studies — mainly of hospital-based or clinical populations, some in France and others in the UK — have addressed this. In a recent systematic review[3] that employed the best-evidence type of summary, the authors divided the progression of hip OA into clinical progression (e.g., progressing to THA) and radiographic progression. The factors predicting clinical progression included smaller joint space width (JSW) in the baseline radiograph, age > 70 years, female sex, and superolateral migration of the femoral head. Predictors of radiographic progression were superolateral migration of the femoral head and an atrophic, rather than hypertrophic, bone response.

Insight into risk factors for incidence and progression of hip OA has been gleaned also from the Study of Osteoporotic Fractures (SOF)[4], a longitudinal cohort study that has received continuous funding from the US National Institutes of Health (NIH) since 1985. Initially, 9704 white women who were at least 65 years of age were recruited from the general population in 4 clinical centers: the initial hip OA component of the SOF study utilized data that were, in fact, obtained without a plan to study hip OA but to estimate femoral neck bone mass using the old Singh index. Therefore, all women underwent an AP radiograph of the pelvis at the baseline visit.

Nancy Lane, Michael Nevitt, Harry Genant, and I developed an atlas of individual radiographic features of hip OA[5]. We showed that intra- and inter-reader variability was very good to excellent. With that background, Drs. Lane, Nevitt, and I embarked on a project that involved the reading of a consecutive sample of 5818 pelvis radiographs of SOF subjects for features of hip OA. Each radiograph was assigned a Kellgren-Lawrence grade and the severity of individual radiographic features of OA was scored using our standard atlas. Following recommendations of Peter Croft[6], we derived a global severity grade based on individual radiographic features and certain combinations of these features. We also measured the minimum interbone distance (i.e., JSW), using the technique of chondrometry described by Michel Lequesne[7]. Our baseline data showed that the prevalence of hip OA was about 12% in this group of older women, as defined by a grade ≥ 2 on the modified Croft scale, i.e., the presence of 2 or more definite individual radiographic features of OA, or a minimum JSW ≤ 1.5 mm.

Was this definition valid? We found a significant correlation between radiographic severity and a report of pain in or around the hip at the baseline visit or pain on motion or limitation of motion of the hip on physical examination. In examining specific radiographic features and their relationship to complaints of pain (Table 1) we found that superolateral joint space narrowing (JSN) exhibited a severity-response relationship. Severe superomedial JSN and femoral, but not acetabular, osteophytes were also related to pain in and around the hip. In cross-sectional analyses published in the mid-to-late 1990s[8,9], we reported

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Table 1. Correlation of individual radiographic features with reported pain, pain on motion, or limitation of motion on physical examination. Data from Scott JC, *et al*. Arthritis Rheum 1992; 35 Suppl:S81.

Individual Risk Factors	Adjusted Odds Ratio
Superolateral JSN = 2	1.4*
Superolateral JSN > 2	2.2**
Superomedial JSN = 2	1.0
Superomedial JSN > 2	1.6*
Femoral osteophyte	1.6**
Acetabular osteophyte	1.3

* $p < 0.05$. ** $p < 0.01$.

an association between radiographic hip OA and higher adjusted bone mineral density (BMD) at the femoral neck and other sites. In addition, we noted an association between hip OA and radiographic hand OA, supporting the construct of generalized OA[9].

We also found evidence of an association between hip OA and use of estrogen replacement therapy[10]. In addition, in these cross-sectional studies, we found an association between hip OA and avocational physical activity, particularly during young adulthood[11]. We found no cross-sectional association, however, between hip OA and radiographic evidence of acetabular dysplasia[12], confirming results of cross-sectional studies by Croft in the UK[13] and a study of elderly Chinese men in Hong Kong[14].

In longitudinal analyses of the hip OA data from the SOF study we found an association between radiographic hip OA and a decrease in the rate of bone loss at the hip, but no association with the rate of subsequent fractures or falls[15].

To provide further information about the incidence and progression of hip OA, we obtained funding for repeat AP pelvis radiographs of subjects during their fifth biannual visit in SOF. Nearly 6000 (62%) of the original participants and 73% of the survivors underwent a repeat AP pelvis radiograph at a mean interval of 8 years after their initial radiograph.

We performed standardized readings of the paired radiographs, blinded to sequence, and measured minimum JSW. As outcome measures, we used the development of OA in subjects who were at risk for incident hip OA and the progression of OA in subjects who had mild, moderate, or severe hip OA at baseline.

We identified 9318 hips that were at risk for development of incident hip OA, based on one of the following 3 definitions: development of minimum JSW ≤ 1.5 mm; development of an osteophyte score ≥ 2 on a scale of 0–3 (this approach eliminates very small osteophytes and requires a moderate–large osteophyte at the femoral neck); or a modified Croft grade ≥ 2. Insofar as they correlated with self-reported hip pain and a reduced range of motion on examination of the joint, these definitions were valid (see above).

Incident hip OA. What factors did we find to be associated with incident hip OA? Initially, we performed nested case control studies. In contrast to the findings derived from the cross-sectional analysis (see above), we found that the presence of acetabular dysplasia in the baseline radiograph was significantly associated with incident hip OA. Thus, mild dysplasia in women whose average age was in the early 70s put them at risk for development of radiographic hip OA some 8 years later[16].

In addition, we found that low serum levels of 25-hydroxy vitamin D were associated with an increased risk of radiographic hip OA[17]. We therefore asked whether higher BMD in subjects with radiographically normal hips was associated with an increased risk of incident radiographic hip OA.

Obviously, in a study of osteoporosis and osteoporotic fractures, such as SOF, an ample number of BMD studies are available. At the baseline visit, subjects from SOF underwent single-photon absorptiometry of the distal radius and calcaneus. At the second visit, a dual x-ray absorptiometry scan of the hip was performed. We adjusted for a number of covariates, including age, height and weight, estrogen therapy, level of physical activity and smoking, and examined the relationship between age-adjusted BMD and development of hip OA[18].

The baseline characteristics of the 5242 women who were at risk for development of hip OA are shown in Table 2. Most were physically active; a small proportion were current hormone users or current smokers. The incidence of radiographic hip OA in the 8 year interval between the baseline and followup examinations was about 3%, regardless of whether we defined incident disease as development of minimum JSW ≤ 1.5 mm, the presence of a definite osteophyte, or a Croft grade ≥ 2. The results indicated a dose-response relationship between the quartile of baseline BMD, measured at either the forearm or total hip, and the incidence of radiographic hip OA. In marked contrast, when we based the definition of hip OA solely on a minimum JSW ≤ 1.5 mm, we found no relationship between baseline BMD and the incidence of radiographic hip OA. The results were similar after adjustment for the number of vertebral defor-

Table 2. Baseline characteristics of women in SOF study who were at risk for incident hip OA*. Values are mean ± SD or percentages. Modified with permission, from Lane, *et al*. Arthritis Rheum 2003; 49:752-8.

Age, yrs	70.6 ± 4.6
Weight, kg	67.5 ± 12.2
Height, cm	159.3 ± 6.0
Walk ≥ 1 block/day, %	55
Current ERT, %	15
Current smoker, %	8
Total hip BMD, g/cm^2	0.77 ± 0.13

* See text. ERT: estrogen replacement therapy; BMD: bone mineral density.

mities in baseline radiographs of the spine, or when BMD of the calcaneus was substituted for distal radius BMD, or when we restricted the analysis to the hip ipsilateral to the site of the BMD measurement. We concluded that a greater BMD increases the risk that an elderly white woman will develop radiographic hip OA when the diagnosis of OA is based upon osteophytosis (and other changes in subchondral bone, such as sclerosis and bone cysts), but not when the diagnosis is based upon the development of JSN alone.

Progression of hip OA. What about the progression of hip OA? We identified 745 women in whom 936 hips exhibited radiographic OA at baseline and could be considered at risk for progressive OA[19]. We characterized these women as having either symptomatic or asymptomatic hip OA. The former group was defined as having radiographic hip OA with "hip pain on most days of at least one month" in the past year or as having radiographic changes and hip pain elicited during examination of the range of motion of the joint.

Our objective was to evaluate the progression of symptomatic and asymptomatic radiographic hip OA in these elderly women in a community-based sample. It is important to recall that in the systematic review mentioned above[3], in comparison, studies were based on clinic populations or hospital-based populations. We defined progression of hip OA by the presence of at least one of the following 4 criteria: THA for hip OA, confirmed by hospital records; reduction in minimum JSW > 0.5 mm, based on data obtained in the ECHODIAH study[20]; an increase of 1 or more units in the global grade; or an increase of 2 or more units in osteophyte score.

We examined the association between progression and the presence of symptomatic or asymptomatic disease at baseline, after adjustment for several relevant covariates[19]. Table 3 provides a baseline comparison of women who had painful hip OA and those who had asymptomatic (or only mildly symptomatic) disease. Those with symptoms were slightly younger and a little heavier (consistent with other studies that have suggested that increased weight is associated with symptom-reporting in individuals with OA), but the 2 groups did not differ with respect to height, hormone use, or level of physical activity.

Table 3. Baseline characteristics of women in whom risk factors for progression of hip OA were excluded*. From Lane, *et al*. Arthritis Rheum 2000; 43 Suppl:S172.

	Hip Pain	No Hip Pain
Number	347	396
Age, yrs	71.4	72.2**
Weight, kg	70.2	66.8**
Height, cm	159.7	159.1
Current ERT use, %	13.4	11.9
Walks ≥ 1 block daily, %	49	53

* See text. ** $p < 0.05$. ERT: estrogen replacement therapy.

Table 4. Association between baseline hip pain and progression of OA. From Lane, *et al*. Arthritis Rheum 2000; 43 Suppl:S172.

	Adjusted OR (95% CI)
THA score	8.1 (4.2, 15.4)
Croft score ≥ 1	1.5 (1.0, 2.1)
Decrease in minimum joint space width ≥ 0.5 mm	1.9 (1.4, 2.6)
Osteophyte score ≥ 2	2.0 (1.4, 2.9)

THA: total hip arthroplasty; OR: odds ratio; CI: confidence interval.

Table 5. Association between individual radiographic features of OA at baseline and progression to hip arthroplasty. From Lane, *et al*. Arthritis Rheum 2000; 43 Suppl:S172.

Individual Radiographic Features	Adjusted Odds Ratio
None	–
Superolateral JSN + 2	2.6*
Superolateral JSN > 2	14.9**
Superomedial JSN + 2	1.7
Superomedial JSN > 2	5.0**
Femoral osteophytes	2.7**
Acetabular osteophytes	1.5

* $p < 0.05$. ** $p < 0.01$. JSN: joint space narrowing.

When we examined the percentage of hips that showed progression of OA in relation to the presence or absence of hip pain at the baseline examination, we found a large difference between the 2 groups with respect to the incidence of THA, a less striking difference when the definition of OA progression was based on an increase in osteophytosis, and only a minimal difference when progression was defined as an increase in Croft grade or change in JSW.

The odds of undergoing THA among subjects with symptomatic hip OA at baseline was 8-fold greater than that in subjects who had asymptomatic radiographic hip OA at baseline (Table 4). However, the adjusted odds ratios for progression based on our other 3 definitions were much lower, ranging from 1.5 to 2.0, although all were statistically significant. These results were independent of the definition of radiographic hip OA at baseline (JSW or Croft grade), and the relationships persisted after adjustment for the covariates mentioned above.

When we considered the association between the presence of individual radiographic features of hip OA at baseline and progression to THA (Table 5), we found a striking increase in risk among patients with superolateral migration, as has been reported in hospital-based and clinical studies[3]. In our cohort, the risk for progression to THA approached 15 among subjects with severe superolateral narrowing. Superomedial narrowing and the presence of femoral osteophytes also were significantly associated with progression to THA, but the association between acetabular osteophytes or mild superomedial narrowing and THA was not significant.

Thus, in this community-based sample of elderly white women with radiographic hip OA, hip pain was a strong predictor of progression. However, symptomatic hips exhibited a slower rate of progression in our subjects than that reported in clinical trials, such as the ECHODIAH study[20]. Further, the global grade of severity of hip OA (based on JSN and bony features) identified more women with baseline OA than did severe JSN alone, although the rate of OA progression in women who were diagnosed with OA on the basis of the different sets of criteria was similar.

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