SESSION 5: PROGNOSIS Guest editor: Alan Silman

Prognosis of osteoarthritis

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The course and prognosis of osteoarthritis have been the subject of several recent reviews. In addition, potential limitations of clinical and epidemiological studies designed to assess the course and prognosis of osteoarthritis have been identified and discussed. In this article I shall cover the "natural" history of osteoarthritis by joint group affected, and factors associated with variation in outcomes.

Mortality
Mortality among subjects with radiographic features of osteoarthritis of the hip and knee, and by self report of arthritis diagnosis and symptoms, has been examined in data from the First National Health and Nutrition Examination Survey (NHANES-I), conducted in the United States between 1971 and 1975, and the epidemiological follow up to NHANES-I (NHEFS). The presence of definite knee osteoarthritis was associated with reduced survival in both men and women in univariate analyses; after adjustment for possible confounding variables including age, years of schooling, race, marital status, body mass index, and blood pressure, women but not men with radiographic knee osteoarthritis still had reduced survival. The presence of definite hip osteoarthritis was also associated with reduced survival in both men and women in univariate analyses; after adjustment for possible confounding variables, survival was not significantly reduced in either men or women. None of the arthritis symptoms was significantly related to reduced survival after adjustment for age in either gender.

Morbidty
The prognosis of osteoarthritis can also be assessed by measuring the development of morbidity; relevant outcomes include total joint arthroplasty, difficulty with tasks or physical disability, and health care use. Data from NHANES-I and the NHEFS have also been examined to determine the occurrence of disability in survivors by presence of radiographic features of knee osteoarthritis at baseline and to examine other baseline variables in relation to these disability outcomes. Subjects with definite knee osteoarthritis, especially if associated with complaints of knee pain, were at significantly greater risk of developing mobility and lower extremity disability than subjects with normal knee radiographs; women experienced difficulty with more activities than men. Furthermore, persons with comorbid medical conditions, particularly heart and lung disease, were also at greater risk of developing lower extremity disability than those with knee osteoarthritis alone.

Radiographic progression
The course and prognosis of osteoarthritis has also been measured by radiographic progression at the hands, hips, and knees, and analyses have been conducted to examine factors associated with variations in progression of the disease.

HANDS
Data from three studies provide information of the course of hand osteoarthritis. In data from the Baltimore longitudinal study of aging, the rate of progression of osteoarthritis was faster in the distal than in the proximal interphalangeal joints of the hands. In addition, the rate of progression was slower in joints with greater baseline severity than in those with milder disease, suggesting a "burnout" phenomenon. Older age, but neither greater body mass index nor metacarpal cortical bone mass, was associated with a higher rate of progression of hand osteoarthritis in both sexes. Lane and colleagues found that radiographic features of hand osteoarthritis, particularly osteophytes, progressed over both two and five years of follow up in men and women participating in a longitudinal study of runners aged 50 years and above and age matched community controls. Harris and colleagues examined paired radiographs from 59 patients with hand osteoarthritis with a mean follow up of 10 years and mean age at follow up of 69 years. Progression was noted in about one half the patients; gender, body mass index, and presence of knee osteoarthritis at baseline were all not associated with progression of hand osteoarthritis.

What factors other than older age might be related to progression of hand osteoarthritis? Gerster reported two cases in whom the presence of calcium apatite crystals in synovial fluid removed from osteoarthritic interphalangeal joints predicted the development of erosive osteoarthritis. Hutton and colleagues examined the relationship between findings on...
a baseline 99mTc bone scan of the hands and progression of hand osteoarthritis in 14 patients with generalised nodal osteoarthritis who had a mean age of 62 years followed for a mean of 4 years.\(^1\) The proportion of progressive changes of individual distal and proximal interphalangeal joints on radiographs was significantly greater among those with an initially positive bone scan: 45% of scan-positive joints progressed compared with 14% of scan-negative joints.

HIPS
There have been few longitudinal studies of patients with hip osteoarthritis. Danielsson, in his classic doctoral thesis, made several seminal observations: first, that only one of 84 subjects with osteophytosis alone on their baseline radiograph developed joint space narrowing over an 11 year follow up period; and second, that two thirds of patients with symptomatic hip osteoarthritis had radiographic progression while 5% showed radiographic regression.\(^2\) He also noted that the majority of symptomatic hips became less painful over time despite the presence of flexion contractures in almost three quarters and reports of difficulty dressing in a similar proportion. As no comments were made regarding treatment, it appears that in most patients symptoms may improve despite progressive restriction in motion and loss of function.

What factors might be related to progression of hip osteoarthritis? Ledingham and colleagues measured radiographic progression as well as progression of disability and total hip replacement in 136 patients with osteoarthritis of the hip with a mean age of 65 years, and examined factors related to variation in these outcomes.\(^3\) Only 15% of osteoarthritic hips showed radiographic progression by Kellgren-Lawrence grade over a median interval of 28 months; 64% of hips, however, showed changes in severity of at least one individual radiographic feature. Women were more likely than men to show radiographic progression; hips with superior migration patterns or atrophic bone response were also more likely to progress. Age, body mass index, presence of nodal interphalangeal osteoarthritis, and chondrocalcinosis did not significantly influence radiographic progression. Those hips showing greatest radiographic progression were more likely to be replaced during follow up; other factors predicting total hip replacement included presence of rest or night pain or worse functional capacity at baseline. Functional deterioration during follow up most strongly correlated with worsening symptoms, radiographic progression, and reported worsening in exercise tolerance. These results regarding radiographic and symptom progression are similar to those from an earlier study of Seifert and colleagues.\(^4\)

KNEES
The majority of the literature on radiographic progression of osteoarthritis is based on studies of knee osteoarthritis. Hernborg and Nilsson examined the long term course of knee osteoarthritis in 71 patients with osteophytes and sclerosis on baseline radiographs with a mean age of 63 years after a follow up time of 10 to 18 years.\(^5\) Radiographic progression occurred in the majority of cases, was more common in women than in men, and correlated with worsening symptoms and angular deformity; development of joint space narrowing could not be examined because films were taken in the supine position. This contrasts with the situation in subjects with only knee osteophytes, where only one third developed radiographic progression.\(^6\)

Several more recent studies of patients with knee osteoarthritis have been reported. Dougdos and colleagues performed a one year follow up study of 353 patients with a mean age of 67 years and disease duration of 7.3 years.\(^7\) The proportion of individual radiographic changes which showed progression varied from 26.8% to 38.1%; improvement occurred in between 8.2% and 15.8% of subjects. Although minimum joint space did not change significantly over the one year period, factors which correlated with worsening of joint space narrowing were presence of obesity, a greater number of joints affected by osteoarthritis, daily consumption of non-steroidal anti-inflammatory drugs, and having undergone a synovial fluid aspiration.

Massardo and colleagues re-evaluated 31 patients with knee osteoarthritis with a mean age of 72 years and duration of symptoms of 19 years after eight years.\(^8\) Paired radiographs in 26 subjects showed deterioration in 16; however, radiographic progression did not correlate with symptomatic changes. Spector and colleagues re-evaluated 63 patients with knee osteoarthritis with a mean age of 60 years after a mean follow up of 11 years.\(^9\) One third of knees showed progression by Kellgren-Lawrence grade; 38% of knees with grade 2 and 16% with grade 3 changes at baseline worsened over time. Improvement was noted in about 10% of knees. There were no significant correlations between worsening of symptoms and progression of radiographic changes. Lane and colleagues found that radiographic features of knee osteoarthritis, particularly osteophytes, progressed over five years of follow up in men, but not women, participating in a longitudinal study of runners aged 50 years and over and age matched community controls.\(^10\)

What factors might be related to progression of knee osteoarthritis? Ledingham et al measured radiographic progression in 188 patients with knee osteoarthritis with a mean age of 71 years and duration of symptoms of nine years after a median follow up of two years.\(^11\) Progression of at least one individual radiographic feature occurred in almost three quarters of knees; progression in joint space narrowing, osteophytosis, bone attrition, and sclerosis was noted in 52%, 32%, 30%, and 14% of knees, respectively. In multivariate logistic regression analysis, only particular osteoarthritis, especially nodal generalised osteoarthritis, and higher body mass index were associated with progression, defined
using Kellgren-Lawrence grade, or joint space narrowing and osteophyte grade. Radiographic progression correlated with worsening of symptoms and deterioration in exercise tolerance.

The role of overweight as a factor associated with progressive joint space narrowing was also noted in the longitudinal follow up of subjects with radiographic knee osteoarthritis identified in the Zoetermeer study.29 Schouten reexamined baseline radiographs in 233 subjects initially felt to have knee osteoarthritis: on rereading, 142 were felt to have definite knee osteoarthritis, and progressive cartilage loss was identified in 34% after a mean of 12.2 years. Older age, higher body mass index, presence of Heberden’s nodes, and diagnosis of generalised osteoarthritis were all associated with a significantly greater odds of progressive cartilage loss. Spector et al showed that overweight was associated with an increased risk of developing contralateral knee osteoarthritis in middle aged women who had unilateral knee osteoarthritis at baseline.29 Of 58 women with unilateral knee osteoarthritis with a mean age of 57 years, 47% of those with a baseline body mass index of 26 kg m² or more developed contralateral knee osteoarthritis, compared to only 10% of those with a body mass index below 23 kg m². Preliminary data from the Baltimore longitudinal study of aging based on 151 subjects with a median follow up of four years show that, after adjustment for gender, older age and higher body mass index are associated with increased risk of osteophyte progression,30 while the presence of osteophytes on the baseline film is associated with progression of joint space narrowing.31

Bone scintigraphy and serum concentrations of biochemical markers of cartilage degradation were examined as predictors of progression of knee osteoarthritis in a follow up study of 94 patients with knee osteoarthritis with a mean age of 64 years and duration of symptoms of nine years, conducted by the Bristol rhematology unit; 75 patients were reexamined after five years.32 An abnormal baseline 99mTc labelled hydroxyethylidiphosphonate (HMDP) bone scan was a significant predictor of radiologic change or progression: 60% of knees with a scan abnormality progressed while none of the knees with a normal bone scan progressed.33 Thus the negative predictive value of a normal bone scan for radiographic progression was 100%. A subset of 63 patients had baseline serum samples available for measurement of cartilage oligomeric matrix protein (COMP).34 Baseline COMP levels were not related to either results of baseline 99mTc-labelled HMDP bone scans or progression of knee osteoarthritis, defined as either joint space narrowing of 2 mm or more or knee joint surgery. Baseline serum hyaluronic acid levels, measured in 60 patients, were significantly higher in patients with progression compared to nonprogressors.34 After adjustment for possible confounding variables, a linear regression analysis, higher baseline serum level of hyaluronic acid, higher weight-to-height ratio, and the number of joints affected by osteoarthritis were all independently related to progression of knee osteoarthritis. Baseline serum concentrations of keratan sulphate, however, were not related to progression of knee osteoarthritis.

Finally, Schouten and colleagues used data from the longitudinal component of the Zoetermeer survey to examine the relations between baseline serum levels of insulin-like growth factor-1 (IGF-1) and progression of knee osteoarthritis.35 Previous cross sectional studies had failed to show an association between serum levels of IGF-1 and the presence of knee osteoarthritis.36,37 After adjustment for age, gender, and body mass index, subjects with serum levels of IGF-1 in the highest tertile were more likely to experience growth of osteophytes and overall progression, but not cartilage loss, than those in the lowest tertile; statistical significance was lacking, however, possibly due to type II error.


