hormonal and reproductive factors, and finally environmental influences, the main one being occupational and leisure time activities. The outcome of osteoarthritis and its predictors was also considered in a separate session. These themes were introduced by plenary lectures and an invited discussant then evaluated the material presented, together with newer data from the proffered abstracts. There is clearly a large number of groups currently active in the field and the workshop came to highlight both areas of agreement and possibilities for future research.

The workshop was only made possible by the generous sponsorship of the following bodies:

Spenshult's Hospital for Rheumatic Diseases, the County Health Authorities of Halland, Malmö General Hospital, and the following drug companies: Ciba Pharmaceuticals-Sweden, Pfizer Sweden, Rhône-Poulenc Rorer, Roche Pharmaceuticals, and Searle Scandinavia. The publication of these proceedings was financially supported by an educational grant from the UK Arthritis and Rheumatism Council and the County Health Authorities of Halland and Spenshult's Hospital for Rheumatic Diseases.

ALAN SILMAN

SESSION 1: DISEASE DEFINITION

Definition of hip osteoarthritis for epidemiological studies

Michael C Nevitt

The use of clear standardised criteria for defining hip osteoarthritis is important in epidemiological research so that differences among studies in disease frequency and risk factors may add to our understanding of the disease rather than sowing confusion. Despite the limited sensitivity of plain radiographs in detecting early pathological changes in cartilage^{1,2} and bone,³ the better imaging of bone abnormalities compared to cartilage loss,⁴ and concerns about cost and radiation exposure, standard radiographs have many advantages and remain the most important source of information for classification of hip osteoarthritis in community and population based epidemiological studies. Radiographs are practical in most study settings, they provide a permanent and objective record, and the imaging technique and classification procedures can be standardised and reproduced.⁴ While there clearly is not a one to one correspondence, radiographic abnormalities are strongly related to joint pathology,⁵ symptoms⁶⁻⁸ and clinical outcome.⁹ Other imaging methods that show promise in hip osteoarthritis, such as magnetic resonance imaging (MRI),¹⁰ remain experimental. Clinical findings may have a limited role in defining osteoarthritis for epidemiological studies,¹¹ but have not been well studied for the hip.

Kellgren-Lawrence grading

For nearly 40 years, epidemiological research on osteoarthritis has relied on standard criteria for case definition based on radiographic

features assessed according to the atlas based Kellgren-Lawrence (K/L) grading system.¹² The K/L grading system promotes a uniform set of criteria for all joints, and there have been several attempts to resolve apparent inconsistencies in the K/L criteria for different joints (table).^{13,14} However, limitations of the K/L grading system for the hip have long been apparent. Discrepancies between the original atlas photos and legends,¹⁵ which place greater emphasis on joint space narrowing and subchondral bone changes, and later revisions which emphasised osteophytes¹⁴ have created confusion.¹³ Emphasis on osteophytes as the initial defining feature of disease, and the implicit assumption of an invariant developmental sequence of bone and cartilage changes, were questioned early on by those who suggested that hip osteophytes without other changes are part of normal aging^{16,17} and more recently for failing to accommodate atrophic variants with little or no marginal bone reaction.¹⁸⁻²⁰ The small number of K/L atlas examples do not adequately illustrate thresholds (for example, possible versus definite osteophytes) or variations in the appearance of radiographic features. Evidence of high interobserver variability^{14,21-23} combined with the above mentioned inconsistencies in the criteria make it unlikely that the grades have actually been applied consistently so that discrepancies in hip osteoarthritis prevalence across studies^{24,25} are difficult to interpret.

The K/L grading scheme is also discordant with the emerging idea that osteoarthritis

Versions of the K-L grades for hip OA

- Grade 1**
 (a) possible JSN and possible osteophytes¹
 (b) minute osteophytes, doubtful significance²
- Grade 2**
 (a) definite JSN, definite osteophytes, slight sclerosis¹
 (b) no JSN, definite osteophytes^{2,3}
- Grade 3**
 (a) marked JSN, slight osteophytes, some sclerosis, cysts¹
 (b) moderate JSN²
 (c) definite JSN and osteophytes³
- Grade 4**
 (a) gross JSN, large osteophytes, sclerosis, cysts, deformity¹
 (b) marked JSN, sclerosis²

JSN, joint space narrowing;

¹ Empire Rheumatism Council, 1963.

² Lawrence, 1977; ³ Spector and Cooper, 1993.

includes a heterogeneous spectrum of disorders that are united by common risk factors and pathogenesis, but differentiated by the site of disease (both inter- and intra-articular localisation), variable degrees of degradation, repair, and bone reaction, and by wide variation in outcome.²⁶ This concept calls for radiographic criteria for case definition in epidemiological studies that are site specific and allow for a variable pattern of expression. Atlas standardised assessment and quantitative measurement of individual radiographic features of osteoarthritis are well suited to this concept, and several studies have shown that these measurements are reliable in the hip.^{6, 27–29} Still, uncertainties remain about how to define osteoarthritis for epidemiological studies using individual radiographic features.

Alternative radiographic schemes

Several alternatives to the K/L radiographic criteria have been proposed for the hip,^{6, 16, 28, 30, 31} with assessment of joint space narrowing playing an important role. Technical impediments to accurate imaging and assessment of joint space in the hip are less formidable than for the knee and hand.⁴ In 1964, Danielsson¹⁶ proposed that the radiographic classification of hip osteoarthritis should be based on the presence of joint space narrowing or structural changes (subchondral sclerosis or cysts), or both, but not osteophytes alone, allowing for a variable expression of radiographic features and challenging the K/L system's reliance on the osteophyte. This approach was supported by the findings of a long term study of orthopaedic clinic patients diagnosed with hip osteoarthritis which showed that after 11 years of follow up outcomes for patients with osteophytes alone were similar to those with no radiographic findings; both groups had rarely developed joint space narrowing or structural changes and were largely free of pain.¹⁶ Although this early study had a large potential for bias in both subject selection and loss to follow up, did not distinguish between femoral and acetabular osteophytes, and has not been replicated, it has influenced several later investigations.^{6, 32}

Croft and colleagues⁶ recently proposed that a single measurement of minimal joint space (the shortest distance between the femoral head margin and acetabulum) is the best

radiographic criterion for hip osteoarthritis for use in epidemiological studies. In a study using pelvis x rays taken for intravenous urograms in men aged 60–75 years, these investigators found that minimal joint space had superior inter-rater reliability and a somewhat stronger association with validation criteria (other radiographic features and hip pain) compared to other radiographic measurements (lateral, superior, and medial joint space, size of the largest osteophyte, and maximum thickness of subchondral sclerosis) and a modified K/L global assessment.

Problems with joint space narrowing

The use of joint space narrowing, especially quantitative measurement, as the primary criterion for hip osteoarthritis raises several issues. How should a narrowed joint space be defined from its continuous distribution? Danielsson¹⁶ arbitrarily defined narrowing as a joint space < 4 mm in persons less than age 70 years and < 3 mm in those 70 and over, contending that a different cutoff point was appropriate for older subjects because normal joint space decreases with age in the absence of disease. A later investigation by the same group used a more stringent cutoff point (< 2 mm) which did not differ by age.³³ Croft *et al*⁶ evaluated two definitions of joint space narrowing, 2.5 mm and 1.5 mm, based on the proportions of subjects each classified as abnormal. Only the more stringent cutoff point was clearly superior to other criteria in its association with validation measures, such as pain and other radiographic features. The more stringent definition was also more strongly associated with risk factors than the less stringent one.^{34, 35}

Whether the stronger relation to validation criteria of more stringent disease definitions is due to exclusion of milder cases, to a reduction in misclassification error, or to both is uncertain. Joint space narrowing, like osteoarthritis itself,²⁶ is a continuous rather than a dichotomous phenomenon; disease definitions require the selection of an arbitrary threshold with tradeoffs in sensitivity and specificity. Disease defined by more stringent cutoff points for joint space narrowing will, by definition, yield a lower prevalence of disease. The prevalence of hip osteoarthritis in men age 60–75 years using the 1.5 mm minimal joint space cutoff^{6, 36} is substantially lower than in studies that define cases using the K/L criteria.^{6, 21, 24, 36, 37} Joint space narrowing detectable on radiographs may be a relatively late stage phenomenon of osteoarthritis⁴; a stringently defined cutoff point for joint space narrowing (for example 1.5 mm), in particular, will tend to identify a severe and relatively late stage subset of disease.

Use of a less stringent cutoff point for joint space narrowing may increase sensitivity and will yield a higher prevalence of disease, but has lower specificity with respect to hip pain and other validation criteria⁶ and may be insensitive to true population differences in prevalence.³⁶ Isolated mild to moderate joint space narrowing in the hip may be as common as isolated osteophytes in the general

population^{6,36} and may likewise be a non-specific indicator of osteoarthritis. One study found an age related decrease in knee joint space in the absence of disease,³⁸ but the only published data for hip joint space found no decline with age.³⁹ There is likely to be substantial individual variation in the width of normal joint space and this could be systematically related to characteristics such as joint size, gender,^{22,38} and race, but this is not well studied. Normalisation of joint space to joint size or comparison to population specific normal distributions might improve the specificity of less stringent definitions

The specificity of definitions based on less stringent criteria for hip joint space narrowing may also be improved by requiring the presence of at least one other radiographic feature.³¹ One study suggests that narrowing and osteophytes are independent predictors of hip pain,⁷ arguing for a disease definition based on more than just a measure of joint space. Croft and colleagues evaluated a qualitative global grading system for the hip based on combinations of radiographic features.⁶ Unlike the original K/L grades, this modified global approach accommodates variable expressions of radiographic abnormalities and separately classifies isolated osteophytes and isolated joint space narrowing. Global grades based on the presence of multiple radiographic features are reliable,^{16,40} though less so than definitions based on minimal joint space,^{6,22} and are strongly related to validation measures, including pain,^{6,7,16} range of motion,⁴¹ and risk factors.^{40,42} As with minimal joint space, more stringent definitions (that is, requiring a greater number of features) perform better.

Finally, if disease is defined in terms of joint space narrowing, how should individuals with hip osteophytes but little or no narrowing be classified? As not having osteoarthritis? As having mild disease? Or as part of a disease subset characterised by vigorous reparative processes and a more benign course?^{9,43} Is the location (for example, acetabular versus femoral, superior versus inferior), or overall extent of osteophytosis useful in disease classification?

Clinical criteria

In some studies clinical measures may be more practical to obtain than radiographs¹¹ or may add to the information obtained from radiographic measures. There are few data on the reliability of joint symptom or examination measurements for the hip. Strictly clinical criteria have been proposed for hip osteoarthritis³⁰ as well as criteria that combine clinical (for example, pain, range of motion, erythrocyte sedimentation rate) and radiographic findings.^{30,31} The American College of Rheumatology (ACR) criteria for hip osteoarthritis have been evaluated only in a highly selected patient sample presenting with a variety of arthropathies and relatively severe hip pain; their value in population studies is uncertain.⁴⁴ However, this work suggests that osteophytes are useful in distinguishing symptomatic hip osteoarthritis from other diagnoses, including rheumatoid arthritis,

within a clinical population with diverse musculoskeletal disorders.

Because of discordance between joint symptoms and radiographic findings, it may be useful to define a clinically relevant entity of symptomatic radiographic hip osteoarthritis.⁴⁵ Identification of such cases in population studies has usually been accomplished by obtaining both symptom and radiographic data on all subjects. However, it would also be possible to obtain radiographs only in subjects who screen positive for hip symptoms. While efficient, there are potential drawbacks to this approach. Joint pain is subjective and variable, and hip pain in particular is a very non-specific marker for hip osteoarthritis.^{6,46} Studies are needed to determine which characteristics of hip pain (location, relation to activity, duration, intensity) improve its specificity and sensitivity with respect to both radiographic and clinical disease. Moreover, important insights into the pathogenesis and outcome of osteoarthritis may come from studying radiographic disease associated with mild, infrequent, or no symptoms. Oliveria and colleagues⁴⁷ and others⁴⁸ have used a case-finding approach for symptomatic or clinical hip osteoarthritis that applies standard radiographic criteria (for example, K/L grades) to x ray reports found in medical records in order to confirm the diagnosis in subjects identified as having hip osteoarthritis in large patient databases. This approach is promising but may be limited by factors affecting who seeks treatment and by poor agreement between a standardised research reading and a clinical reading of radiographic osteoarthritis. Some studies have defined cases of hip osteoarthritis as those admitted to hospital for total joint replacement.⁴⁹ The generalisability of these studies is questionable, however, because of the many psychosocial and local economic factors that influence allocation of costly surgical procedures.

Conclusion

In conclusion, atlas standardised assessment of individual radiographic features and quantitative measurement of joint space appear, at present, to be the most practical and valid data for use in defining hip osteoarthritis in epidemiological studies. Clinically meaningful disease subsets can be readily identified from these data (for example, atrophic versus trophic variants; pattern of femoral head migration).^{20,34} Although alternatives to the K/L radiographic criteria for hip osteoarthritis have been proposed, no consensus exists on the best approach. A single measure of minimal joint space has the advantage of high interobserver variability, but may lack sensitivity and be biased toward severe, late stage disease when more stringent and valid cutoff points are used. The combination of a quantitative or qualitative measure of narrowed joint space plus other radiographic features, or taking into account sources of systematic variation in normal joint space, may enhance the validity of less stringent definitions based on joint space. Further study is needed to evaluate

these approaches and clarify the status of isolated joint space narrowing and osteophytes. Exclusion or separate analysis of intermediate, mild, and uncertain categories of disease may further reduce misclassification and increase the likelihood of detecting biologically meaningful relations.⁵⁰

A single definition of hip osteoarthritis may be neither feasible, nor desirable, for epidemiological research. Valuation of the tradeoffs between validity, reliability, and practicality will depend, in part, on the design and research question of a particular study.²⁶ Perhaps the most appropriate goal would be to strive for a high standard of clarity and simplicity, as well as detailed description of measurements and criteria within each study, so that definitions can be applied reproducibly across studies.

Supported by US Public Health Service grant 1-RO1-AG05407

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