CLINICAL AND LABORATORY ASSESSMENTS IN RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS

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SUMMARY

Clinical and laboratory assessments in rheumatoid arthritis and osteoarthritis precede imaging methods in both defining diagnosis and determining response to therapy. Some assessments are similar in both diseases, e.g. measuring joint pain, the number of involved joints and functional impairment. There are also areas of difference; for example, rheumatoid arthritis is a systemic disease with immune disturbance and positive tests for rheumatoid factor and elevated acute phase markers while osteoarthritis is a more local disease with little systemic upset. In both diseases pain and progressive joint damage result in increasing disability. There is agreement on a core data set in rheumatoid arthritis which comprises: swollen joint counts, tender joint counts, pain assessment, patient’s global assessment, an acute phase marker such as the ESR and a self-administered functional questionnaire. There is less agreement on the core data set in osteoarthritis, though pain and functional impairment are both important. Combined or overall indices have been used in both rheumatoid arthritis (e.g. the disease activity score) and in osteoarthritis (e.g. the Lequesne functional index), but there is no general agreement on their value. In both diseases plain radiology is useful to define diagnostic groups and follow progression in long-term studies. Mortality is increased in rheumatoid arthritis and is useful for defining the long term effects of the disease; little is known about mortality in osteoarthritis. Standardizing clinical methods is important and much work is needed in this area.

KEY WORDS: Assessment, Key data sets, Osteoarthritis, Rheumatoid arthritis.

THE ASSESSMENT of rheumatoid arthritis (RA) and osteoarthritis (OA) involves clinical measures and laboratory assessments. Some assessments are similar in both diseases, e.g. measuring joint pain, the number of involved joints, functional impairment and disability, and assessing joint damage, while other assessments differ—RA has major systemic disturbances involving the immune system whereas OA is a more local disease with little systemic upset. In both RA and OA joint pain and progressive damage cause considerable disability.

Clinical and laboratory assessments are key issues for clinical practice. There has been considerable international standardization of assessments in RA and attention is now being given to OA. Key components in assessment are measuring the severity of joint involvement and determining its effects on general health, functional status and laboratory changes.

THE CORE DATA SET IN RA

International consensus has resulted in an agreed core data set (Table I) [1]. The core data set measures give a good overall picture of RA, assess progression and are responsive to changes in disease activity. European collaborative studies across multiple centres [2] have shown that the most useful measures are the number of swollen joints, the number of tender joints and the ESR. The best single variable is probably the number of swollen joints. Morning stiffness has not been included within the core set due to its variability between patients and poor response to changing clinical status.

JOINT SWELLING AND TENDERNESS IN RA

Swelling is soft tissue swelling detectable along joint margins. A synovial effusion invariably means the joint is swollen. Neither bony swelling nor deformity of joints constitute joint swelling. Fluctuation is characteristic of swollen joints and may influence the range of joint movement. Tenderness is pain in a joint found: at rest with pressure; on movement of the joint; or from questioning about joint pain, e.g. pain upon movement of the hip joints. Pressure to elicit tenderness should be exerted by the examiner’s thumb and index finger sufficient to cause ‘whitening’ of the examiner’s nail bed.

JOINT COUNTS IN RA

Various joint counts have been used. Prevoo et al. [3] contrasted several methods, including the Ritchie index [4], the Thompson–Kirwan index [5] and the 28 joint index. Each index had similar reliability and validity, and the simple 28 joint index was adequate. This was
confirmed by Smolen et al. [6], who showed the 28 joint count to be as informative as more extensive joint counts.

**POOLED INDICES IN RA**

RA is multidimensional, involving several domains, and it is appealing to use an index which pools several outcome measures to give a single measure of disease activity. Such a combined index needs to use appropriately selected and weighted measures, e.g. the disease activity score of van der Heijde et al. [7] and the Stoke index [8]. However, pooled indices may be difficult to calculate and their interpretation is often controversial.

**FUNCTIONAL MEASURES IN RA**

The most familiar instruments used in RA are the Health Assessment Questionnaire (HAQ) [9] and the Arthritis Impact Measurement Scales (AIMS) [10]. Both were developed for RA and are ‘disease-specific’ measures. There are also several questionnaires designed for a wide range of health problems—‘generic’ measures. Several have been used in RA, including the Nottingham Health Profile (NHP) and the SF-36 [11]. The various instruments seem to have similar contents but may produce different evidence about patients’ well-being. For example, one study in RA patients compared findings in a disease-specific instrument (AIMS) with a generic instrument (NHP) [12]. Patients’ scores for mobility agreed substantially with both instruments but those for emotional distress and social function did not. This raises the question about which measure correctly reflects patients’ health status. Despite such concerns, current consensus favours the HAQ and SF-36 to determine function and health status respectively.

**LABORATORY MEASURES IN RA**

Rheumatoid factor levels indicate disease type and severity, and are important indicators of progressive RA. Isomaki [13] found that outcome was worst in seropositive rheumatoid patients and best in seronegative oligoarthritis of unknown aetiology. Progressive joint damage is also more likely in seropositive patients [14].

**THE ACUTE PHASE RESPONSE IN RA**

Active RA is characterized by an elevated ESR, a high C-reactive protein level, and associated changes in other plasma proteins such as orosomucoid and immunoglobulins. Single laboratory measures of disease activity are weak predictors of clinical course. A combination of measures or multiple values are better. Hassell et al. [15] evaluated disease activity annually over 7 yr in 127 patients using the area under the curve for each variable with time. Persistent disease activity with a high acute phase response was related to progressive joint damage and functional outcome.

**IMAGING IN RA**

Imaging includes plain radiology, bone scans and isotope labelling methods, DEXA scans for peri-articular osteoporosis and MRI. Conventional X-rays are the gold standard for diagnosis and determining progression. X-rays of the hands and feet can be scored by simple standardized methods like those of Sharp et al. [16] and Larsen et al. [17]. These are reproducible [18] and composite indices combining mainly joint space loss and erosions.

**MORTALITY AND MORBIDITY IN RA**

RA leads to premature mortality. In hospitalized RA patients nearly 20% of deaths are directly caused by RA. Wolfe et al. [19] reported results from a large study examining 922 deaths in 3501 RA patients. The standardized mortality ratio was 2.3. A similar increased mortality rate has been seen in many other studies [20]. The causes of mortality in RA do not differ much from those in the normal population, though there is an excess of deaths from infection and lymphatic malignancies. Patients with severe RA are most likely to die early. The shortening of life is in the region of 4–5 yr, so death is not a useful outcome measure in studies lasting 1–5 yr.

There is considerable morbidity from pain and persisting joint inflammation. Functional measures reflect morbidity and quantitative measures of functional status such as grip strength, walking time, the button test and questionnaires on activities of daily living decline in >80% of hospital cases during 10 yr follow-up [21]. Patients with extra-articular disease show the most functional decline.

**DIFFERENCES BETWEEN RA AND OA**

The clinical assessment of OA is less well defined than RA, though this will soon be addressed through new international collaboration. The main assessments in OA are measures of joint pain, joint tenderness and swelling, and functional impairment. The duration of morning stiffness and post-exercise stiffness are also relevant. Laboratory measures are less useful, though defining the extent of cartilage and bone damage may be important biochemical measures in the future. A comparison of the clinical assessment of RA and OA is shown in Table II.

**CLINICAL MEASURES IN OA**

Measuring pain is the key assessment in OA. Either descriptive 4–5 point Lickert scales or visual analogue scales are used. We prefer using 100 mm horizontal visual analogue scales. Pain assessments can be for pain at rest, at night, on movement or overall pain [22]. It is often best to record pain at specific sites such as the knee rather than global overall pain. Tenderness is

<table>
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<tr>
<th>Assessments</th>
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<td>Pain</td>
<td>Visual analogue scale (VAS)</td>
<td>VAS</td>
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<tr>
<td>Joint counts</td>
<td>28, 66 or Ritchie index</td>
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<td>ESR or C-reactive protein</td>
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<td>Auto-antibodies</td>
<td>Rheumatoid factor</td>
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**TABLE II**

Comparison of assessments in RA and OA
widely used. There have been attempts to devise numerical articular indices similar to those used in RA. The Doyle index [23] is the best known, but it is of limited value.

OVERALL INDICES IN OA

There is no equivalent to the Disease Activity Score, but the Lequesne index [24] gives an accepted overall assessment of both hip and knee OA. It combines pain, morning stiffness, walking distance and general activities.

FUNCTIONAL INDICES IN OA

Disability can be assessed by specific measures such as the HAQ, though this concentrates on upper limb function and is better in RA. A specific functional measure for OA is the WOMAC [25], which is the best disease-specific measure. Generic measures can be used though more work is needed on their utility in OA.

LABORATORY MEASURES IN OA

Tests for rheumatoid factor and acute phase proteins have no role. Excluding crystal deposition, disease by synovial fluid microscopy helps in differential diagnosis. At present no tests have a major role in assessing OA, but investigations based on connective tissue biochemistry will be available in the future. They comprise measures of derivatives of collagen metabolism, cartilage breakdown products and mediators of connective tissue turnover.

Keratan sulphate has been the most widely studied compound. It is a metabolite of cartilage degradation and can be measured in synovial fluid and blood. Serum levels of keratan sulphate may reflect proteoglycan metabolism. Its serum levels are elevated in some patients with OA, but this may merely reflect a negative acute phase reactant [26] and may not always reflect cartilage damage. The measurement of other cartilage products, such as the expression of chondroitin sulphate epitopes by monoclonal antibodies (e.g. 3B3 antibody), may be more helpful, but this work is at an early stage. Collagen degradation leads to pyridinoline and deoxypyridinoline cross-link fragments in blood and urine which can be measured in chromatographic or immunochemical assays. They are the most widely used markers in OA [27], though they have not progressed beyond clinical trials.

IMAGING IN OA

Several scoring systems quantify radiological changes in the knees and hips. The most widely known, by Kellgren and Lawrence [28], grades damage on a 0–4 scale using standard films. A review of the radiographic criteria to assess progression in OA showed that joint space narrowing and changes in subchondral bone were more significant indicators of progression than a lone osteophyte [29].

MORTALITY AND MORBIDITY IN OA

Relatively little is known about whether OA increases mortality. The National Health and Nutrition Examination Survey from North America included many patients with OA and there was no evidence that they had increased mortality [30]. There is considerable morbidity from the persistent pain and discomfort of large joint OA and there is considerable evidence that obesity is a risk factor for disability, especially in elderly patients [31]. Further work is needed to define the mortality and morbidity of OA.

CONCLUSIONS

Clinical measurement remains an inexact science. There is more information available about RA than OA, though this situation will soon be corrected through international consensus. Standardization is important to ensure that studies evaluate comparable cases in similar ways. Imaging joints will remain the gold standard by which to judge the end results of treatment, with clinical and laboratory measures a rough yardstick to determine therapeutic response.

REFERENCES