Ultrasound in the assessment of early arthritis

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Introduction and overview
Inflammatory arthritis is potentially very aggressive and debilitating if left untreated. The most common type is rheumatoid arthritis (RA), with approximately 400,000 people affected in the UK (12,000 new cases per year).

The overall occurrence of RA is approximately three times greater in women than men and although the peak age of incidence in the UK is the 70s, people of all ages can develop the disease.

Around three quarters of people with RA are first diagnosed when of working age and one third of patients stop working within two years of diagnosis, this proportion increasing thereafter.

The total costs of RA in the UK, including indirect costs and work-related disability, have been estimated at between £3.8 and £4.75 billion a year with NHS costs at around £560 million a year. Clearly, this disease is costly to the UK economy and to individuals.

Helping to identify and treat this disease at an early stage may not only improve patient outcome, but may have longer term cost saving implications for the national economy.

Pathogenesis
The exact cause for the inflammatory arthritides is unknown but abnormalities in the immune system result in a cascade of events culminating in abnormal immune and inflammatory reactions, particularly targeting joints lined with synovium.

In rheumatoid arthritis, inflammatory cytokines such as tumour necrosis factor (TNF) and interleukin-1 (IL-1) result in increased blood flow to the joint (causing heat), thickening of the synovial lining of the joint (synovitis) and increased synovial fluid (causing swelling) and stretching of the pain receptors around the joint (causing pain).

If this inflammation is not suppressed, there is progression to the conversion of the synovium into pannus and the release of protein degrading enzymes, both of which can result in irreversible destruction of the bone and cartilage (causing secondary degenerative change and bony erosions) around the joint and subsequent deformity and disability. The degree to which this happens depends on the severity and duration of the synovitis.

Diagnosis
The presence of active synovitis should be documented as early as possible, so that appropriate treatment can be started to prevent irreversible joint destruction. The traditional diagnostic criteria for rheumatoid arthritis include clinical examination findings and blood tests including rheumatoid factor status, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) levels and anti-cyclic citrullinated peptide (anti-CCP). However, all of these may be normal in the early stages of disease.

The need for a more sensitive test to detect early active synovitis as well as advances in technology have resulted in imaging playing an increasingly important role in diagnosis and the decision to start treatment.

Treatment options
The aim of treatment is to relieve symptoms, the most important being pain, and modify the disease process to minimise the severity and duration of active synovitis so that progressive destruction of the joint is prevented, stopped or reduced. Analgesics and non steroidal anti-inflammatory drugs (NSAIDs) are used for symptom relief.

The mainstays of modifying the disease process are the disease modifying antirheumatic drugs (DMARDs), such as methotrexate, sulphasalazine and hydroxychloroquine.

As more has been understood regarding the pathogenesis of inflammation, biological DMARDs have been developed (such as anti-TNF agents and IL-1 inhibitors) which target the source (mediators) of inflammation. These tend to be used in conjunction with the more traditional therapies such as methotrexate.

On average, biological drugs cost around £9,500 per patient per year, compared with around £450 per year for conventional therapy. In addition, both types of DMARDs are associated with potential toxicity and adverse reactions. The literature suggests that the early appropriate introduction of DMARDs is associated with fewer adverse reactions and a better overall prognosis.

As such, it is important to start DMARDs as early as possible in the disease process but only in those patients with active synovitis in whom the benefits far outweigh the risks.

Early diagnosis: Which imaging modality?
The Royal College of Radiologists advocates the use of plain radiographs of the affected joint(s), hands and feet routinely for diagnosis with specialised use of ultrasound, MRI or nuclear medicine for diagnosing acute synovitis (see figure 1).
Conventional radiography

Plain film assessment is still required as a baseline in patients who present with symptoms and signs of an inflammatory arthropathy and may show alternative diagnoses. However, the typical signs of arthritis (periarticular osteopaenia, loss of joint space, subluxation and bony erosions) are all findings that occur late in the disease process, once there is already irreversible joint damage. Studies have shown that erosions (which are sensitive for inflammatory arthritis) are detected up to a year later than more sensitive imaging tests such as ultrasound or MRI. The radiographic findings of early synovitis are soft tissue swelling and joint space widening, both of which are non-specific and insensitive. Although radiographs are reproducible, relatively inexpensive and quick, their role is for monitoring disease progression rather than early detection.

MRI

MRI has been shown to assess synovial inflammatory activity well, in close correlation with histological findings. It assesses the joint with a more 'global view' providing information about the articular cartilage surfaces and the subchondral bone marrow, both of which other imaging tests are poor at assessing. While it is accurate and reproducible, it is also expensive and time consuming and many patients are unable to tolerate it or have contraindications to its use (such as a pacemaker). Ultrasound

There are many advantages to ultrasound as an imaging modality to assess arthritis:

• It is widely available and non-invasive with a high level of patient acceptability;
• It is cost-effective;
• It demonstrates soft tissues with high resolution;
• It demonstrates flow/hyperaemia;
• Prosthetic joints do not interfere with images;
• Any peripheral joints can be assessed as and when required without much planning and the patient can direct the imaging to areas of pain;
• Ultrasound examination has been shown to detect up to 20% more erosions than plain radiographs and compares well to MRI;
• It is also able to measure disease activity unlike a radiograph, with the presence of Doppler flow within the thickened synovium indicating active synovitis.

Disadvantages include that it is operator dependent and that it can have a long learning curve for an inexperienced operator. This may in itself pose time constraints to assessment in a busy clinic.

What to look for

In order to standardise the assessment of early arthritis on ultrasound examination, the Outcome Measurement Rheumatoid Arthritis Clinical Trial (seventh OMERACT conference), set definitions summarised as follows:

Synovial fluid

• Abnormal hypoechoic or anechoic relative to subdermal fat (sometimes isoechoic/hyperchoic);
• Intra-articular material – displaceable and compressible;
• No Doppler signal (figure 2A).

Synovial hypertrophy

• Abnormal hypoechoic (relative to subdermal fat), sometimes iso or hyperechoic;
• Intra-articular tissue;
• Non-displaceable;
• Poorly compressible;
• +/- Doppler signal (figure 2B);
• Synovial vascularity on quantitative Doppler can predict radiographic progression.13

Tenosynovitis

• Hypoechoic or anechoic thickened tissue with or without fluid within the tendon sheath;
• Seen in two perpendicular planes;
• +/- Doppler signal (figure 3).

Enthesopathy

• Abnormally hypoechoic (loss of normal fibrillar architecture) and/or thickened tendon or ligament at its bony attachment;
• Occasionally contains hyperechoic calcific foci;
• Seen in two perpendicular planes;
• +/- Doppler signal;
• +/- bone changes – enthesophytes, erosions, irregularity.

Bone erosion

Intra-articular discontinuity of the bone surface, visible in two perpendicular planes (most develop within the first two years in RA) (figure 4).

Where to scan

The hands are easily accessible and research shows the metacarpophalangeal and wrist joints accurately reflect inflammatory load in RA. A high frequency (eg 17MHz) linear probe should be used with power Doppler. In our institution, our ultrasound routine for detection of arthropathies is as follows:

1. Wrist
   • Radial styloid
   • Radiocarpal joint and extensor compartments
   • First carpometacarpal joint
   • Ulnar styloid

2. Hand
   • Metacarpophalangeal joints (MCPJ)
   • Proximal inter-phalangeal joints (PIPJ)

Important tips for technique

Metacarpophalangeal joints

1. Each MCPJ is examined dorsally in longitudinal section as synovitis and effusions are well demonstrated and this is a comfortable position for most patients. The probe position should be adjusted to obtain maximal height of the dorsal triangular joint space, taking care to include any dorsal spill of synovium over the metacarpal head.
2. Transverse images should be taken where lesions are seen.
3. It is particularly important to look for erosions at the radial aspect of the second metacarpal head, ulnar aspect of the fifth MC head and at the ulnar styloid. Erosions frequently develop in these areas within the first two years of the disease.

Proximal inter-phalangeal joints – dorsal views in longitudinal survey with transverse images for pathology.

Distal inter-phalangeal joints and flexor tendons are commonly involved in psoriatic arthropathy and should be included where appropriate.

Tenesynovitis is a frequent finding in early inflammatory arthritis; flexor digitorum, extensor digitorum and extensor carpi ulnaris tendons are most commonly involved and may demonstrate thickening +/- hyperaemia of the tendon sheath +/- fluid.

How do we influence patient management in our assessment?

The combination of appropriate symptoms and the ultrasound finding of active synovitis and/or erosions, particularly where there is positive serology, will hasten the use of DMARDs influencing the severity and course of disease. Up to one third of new patients referred do not demonstrate synovitis on ultrasound and are unlikely to benefit from DMARDs and may be spared their side effects. If erosions are found (which may not be visible on plain film), this is a poor prognostic factor.

Ultrasound can also help to differentiate between different types of arthropathy or an alternative cause for the symptoms experienced, such as the presence of enthesopathy (inflammation at the insertion of a tendon, more commonly a feature of a seronegative inflammatory arthritis such as psoriatic arthritis), or a simple primary tenosynovitis (inflammation of the tendon sheath), unrelated to an inflammatory arthropathy.

Experienced sonographers have transferrable skills that, after appropriate training, facilitate a sonographer-provided, radiologist-led approach to early diagnosis and treatment of inflammatory arthritis.

Treatment response

Good treatment response can be assessed with US in specific circumstances – where there will be reduction in synovial thickness and vascularity. The EULAR (European League Against Rheumatism) recommendations from 2010 advise that treatment should be implemented as soon as the diagnosis of RA is made and if the target of remission/low disease is not reached, treatment should be changed every 1-3 months with strict monitoring.14

Conclusion

Ultrasound assessment of early arthritis has therapeutic impact and is likely to influence patient outcome. For early diagnosis of patients with inflammatory arthropathies, the key findings are active synovitis and erosion.

References


Further recommended reading


