Role of ultrasonography in diagnosing early rheumatoid arthritis and remission of rheumatoid arthritis - a systematic review of the literature


CRD summary
The review concluded that ultrasound appeared to have an added value to clinical examination for diagnosing and evaluating remission of rheumatoid arthritis. In light of several review limitations, the reliability of the processes used was uncertain. Given the heterogeneity across studies, the conclusions may be too strong.

Authors' objectives
To clarify the added value of ultrasonography to clinical examination for diagnosing early rheumatoid arthritis and in assessing remission of rheumatoid arthritis.

Searching
PubMed, EMBASE and The Cochrane library were searched to 2011 for published studies in English or Dutch; search strategies were reported in an appendix. Reference lists of relevant articles were also examined to identify further studies.

Study selection
Eligible studies were of ultrasound either for diagnosing rheumatoid arthritis or for evaluating signs of synovitis in rheumatoid arthritis patients who were clinically in remission. Studies had to be in adult populations and inflammation had to be assessed. Case reports and reviews were excluded.

Diagnostic studies: Most were published between 2009 and 2011. Populations varied: inflammatory, rheumatoid and undifferentiated arthritis populations were studied, as were patients with oligoarthritis. Doppler ultrasound and greyscale ultrasound (four studies), or greyscale ultrasound alone (two studies) was used. In most studies metacarpophalangeal joints were assessed as the minimum. Definitions of synovitis varied across studies.

Remission studies: Most studies scanned between six and 16 joints (range six to 44 joints). The wrist and metacarpophalangeal joints of the dominant hand were scanned in all studies. Doppler ultrasound and greyscale ultrasound were used in all studies. Remission definitions varied.

One reviewer screened titles and abstracts. It appeared that two reviewer assessed full papers, with disagreements resolved by discussion.

Assessment of study quality
For studies that evaluated diagnosis, study quality was assessed using QUADAS-2 with an extra question on sample size. For studies that evaluated remission, a quality items list was devised by the authors which examined parameters relating to the population, study design, and statistical analyses (each parameter was described as being good, bad or unclear). An adaptation of the phases (levels) in diagnostic studies proposed by Sackett and Haynes to reflect the clinical relevance of studies was also used.

The authors did not state how many reviewers performed quality assessment.

Data extraction
One reviewer extracted data on basic study characteristics, number and type of joints under investigation and ultrasonography parameters.

Methods of synthesis
A narrative synthesis was presented; the authors stated that heterogeneity in study design and methods precluded pooling the results.
Results of the review

Diagnosis (six studies, 582 patients): Four studies had bias limitations in the flow and timing domain. Other biases (specific to individual studies) were also summarised. In most studies it appeared that clinical diagnosis at follow-up was the reference standard.

In one study, ultrasound predicted progression to clinically detectable joint inflammation of the subset of joints showing a positive power Doppler ultrasonography signal, after a median follow-up of 26 months, with an odds ratio of 5.50 (95% CI 2.57 to 11.9). Another study showed that adding ultrasound parameters at baseline to clinical parameters increased the pre-test probability of 6% to 94% post-test for the progression to inflammatory arthritis at 12 month follow-up. One study suggested ultrasound had a sensitivity of 35% (95% CI 24 to 48) and a specificity of 78% (95% CI 67 to 86). Further results of individual studies were reported.

Remission (11 studies, 928 patients): Study results generally had wide confidence intervals. Definitions of ultrasound inflammation varied across studies.

For greyscale ultrasound, all 11 studies identified signs of synovitis in 73% to 95% of patients in clinical remission. For Doppler ultrasound, the range was 9% to 62%. The predictive value of greyscale ultrasound for clinical flares was not significant (three studies) or not reported (one study). For Doppler ultrasound (three studies) the odds ratios ranged from 3.6 to 13.0. Further results were reported.

Authors' conclusions

Ultrasound appeared to have added value to clinical examination for diagnosing rheumatoid arthritis when scanning at least metacarpophalangeal, wrist and metatarsophalangeal joints, and when evaluating remission of rheumatoid arthritis, scanning at least wrist and metacarpophalangeal joints of the dominant hand. For both purposes primarily power Doppler ultrasound might be used since its results were less equivocal than those of greyscale ultrasound.

CRD commentary

The review addressed a clear question and was supported by reproducible eligibility criteria. Although several databases were searched, the restriction to searching only for studies published in English or Dutch means that some relevant studies may have been missed (and the review may have been subject to publication or language bias). The authors did not use methods which could minimise the risk of reviewer error and bias during all stages of the review - only one reviewer screened titles/abstracts, and only one reviewer extracted data.

A narrative synthesis was presented; the authors noted the studies were too heterogeneous to pool their results. It was unclear whether attempts were made to derive 2x2 data to allow easier comparison of results across studies. Sample sizes for several studies were small. Adequate primary study details were provided, except for the study quality assessment results; only basic summary information was reported from using QUADAS-2, a tool devised to enable more transparent reporting of study quality. This made it difficult to evaluate the strength of the evidence.

In light of the aforementioned limitations, the reliability of the review processes used was uncertain. Given the heterogeneity across studies, the conclusions may be too strong.

Implications of the review for practice and research

Practice: The authors’ recommendation when scanning for diagnosis of early rheumatoid arthritis could be to scan at the minimum the wrists, metacarpophalangeal and metatarsophalangeal joints bilaterally using Doppler ultrasound; proximal interphalangeal joints could also be included. They added that for both diagnosis and remission evaluation it was not necessary to scan large joints.

Research: The authors stated that large prospective longitudinal studies were necessary to evaluate the additional value of ultrasound in diagnosing rheumatoid arthritis, scanning joints and evaluating the predictive validity of other signs such as ultrasound-detected tenosynovitis.

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