Meta-analysis: test performance of ultrasonography for giant-cell arteritis
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CRD summary
This generally well-conducted review found that ultrasonography may be helpful in diagnosing giant-cell arteritis, but that it is important to interpret the ultrasound results based on the clinical presentation and pre-test probability of disease. Given the potential for missed studies and the diversity of the included studies, the authors’ conservative conclusion seems appropriate.

Authors' objectives
To determine the diagnostic performance of ultrasonography for giant-cell arteritis.

Searching
MEDLINE, EMBASE and the Cochrane Library were searched in April 2004 for published articles; the search terms were reported. No language restrictions were applied. The reference lists of retrieved articles and review articles were screened, and experts in the area were contacted for additional relevant studies. Abstracts were not eligible for inclusion.

Study selection
Specific interventions included in the review
Studies of temporal artery ultrasonography were eligible for inclusion, regardless of the ultrasound method used. Studies of multiple cranial arteries were only eligible for inclusion if they provided separate data for the temporal artery. The ultrasound abnormalities assessed were halo, stenosis or occlusion. The ultrasound techniques evaluated were colour duplex imaging with ultrasound frequencies of 5 to 15 MHz, and grey-scale ultrasound biomicroscopy with a 50-MHz probe.

Reference standard test against which the new test was compared
Studies that used temporal artery biopsy or the American College of Rheumatology (ACR) criteria were eligible for inclusion. The ACR requires 3 of 5 criteria to be met for the classification of giant-cell arteritis: age at onset at least 50 years; new onset of localised headache; temporal artery tenderness or decreased pulse; erythrocyte sedimentation rate of at least 50 mm/hour; and an artery biopsy specimen showing vasculitis characterised by a predominance of mononuclear cells or granulomatous inflammation.

Participants included in the review
Studies of patients with giant-cell arteritis (suspected or confirmed) were eligible for inclusion. Some participants had suspected or confirmed polymyalgia rheumatica. The mean age of the participants ranged from 67 to 76 years and the proportion of women ranged from 40 to 76%.

Outcomes assessed in the review
The primary outcomes reported were the sensitivity and specificity for the detection of halo sign, stenosis or occlusion. Estimates of the post-test probability of disease based on three different pre-test probabilities of disease (10%, 50% and 90%) were also reported.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.
Assessment of study quality
Study quality was assessed using 13 items covering 6 dimensions of study quality: technical quality of ultrasonography, technical quality of biopsy, application of the reference standard, blinding, description of study sample and cohort assembly. Two reviewers independently graded each study for methodological quality. Any discrepancies were resolved through discussion.

Data extraction
The data were extracted using a standard form. Two investigators independently extracted data for the 2x2 tables. Any disagreements were resolved by referral to a third reviewer. Authors were contacted when clarification was needed and for missing data.

Methods of synthesis
How were the studies combined?
Estimates of accuracy were calculated separately for studies that used biopsy and ACR criteria as the reference standard, and for the different ultrasound abnormalities. Meta-analyses using fixed-effect (Mantel-Haenszel) and random-effects (DerSimonian and Laird) models were carried out using weighted independent estimation of sensitivity and specificity. Likelihood ratios were derived from this meta-analysis. Weighted and unweighted summary receiver operating curves were also estimated. The post-test probability of giant-cell arteritis was estimated by transforming the pre-test odds of disease into the post-test odds using the positive and negative likelihood ratios.

How were differences between studies investigated?
Heterogeneity was assessed using the Fisher exact method. The authors examined the effect of year of publication, language, number of participants, and individual aspects of study quality on the diagnostic performance of ultrasonographic findings. Subgroups were compared using general variance methods to estimate the standardised difference in effect sizes. Differences between the studies were also discussed in the text.

Results of the review
Twenty-three diagnostic accuracy studies met the inclusion criteria (n=2,036; 1,043 underwent ultrasound and biopsy, 1,172 ultrasound and ACR, and 409 ultrasound, biopsy and ACR). Five studies were diagnostic case-control studies (n=994).

One study met all methodological quality criteria, 12 studies fulfilled at least half the criteria, 3 studies met only 1 criterion, and one met none of the criteria. The criteria satisfied least often were adequacy of blinding during interpretation of imaging and histologic results, and adequacy of description of the technical aspects of biopsy.

Biopsy as the reference standard.
Halo sign (14 studies, 532 patients).

The pooled sensitivity was 69% (95% confidence interval, CI: 57, 79) and the pooled specificity 82% (95% CI: 75, 87). There was considerable heterogeneity in both the sensitivity and specificity (P<0.03). Post-test probabilities with a positive/negative ultrasound result were 30%/4% with a 10% pre-test prevalence, 79%/27% with a 50% pre-test prevalence and 97%/77% with a 90% pre-test prevalence.

Arterial narrowing (stenosis or occlusion (15 studies, 813 patients).

The pooled sensitivity was 68% (95% CI: 49, 82) and the pooled specificity 77% (95% CI: 65, 85). There was considerable heterogeneity in both the sensitivity and specificity, with trade-off between estimates of sensitivity and specificity (P<0.001). Post-test probabilities with a positive/negative ultrasound result were 25%/4% with a 10% pre-test prevalence, 75%/29% with a 50% pre-test prevalence and 96%/79% with a 90% pre-test prevalence.

Any vessel abnormality (halo, stenosis or occlusion (7 studies, 332 patients).
The pooled sensitivity was 88% (95% CI: 74, 95) and the pooled specificity 78% (95% CI: 71, 84). There was no statistical evidence of heterogeneity (P=0.20). Post-test probabilities with a positive/negative ultrasound result were 31%/2% with a 10% pre-test prevalence, 80%/13% with a 50% pre-test prevalence and 97%/58% with a 90% pre-test prevalence.

ACP criteria as the reference standard.

Halo sign (7 studies; 1,092 patients).

The pooled sensitivity was 55% (95% CI: 36, 73) and the pooled specificity 94% (95% CI: 82, 98). There was considerable heterogeneity in both the sensitivity and specificity (P<0.001). Post-test probabilities with a positive/negative ultrasound result were 50%/5% with a 10% pre-test prevalence, 90%/32% with a 50% pre-test prevalence and 99%/81% with a 90% pre-test prevalence.

Arterial narrowing (stenosis or occlusion) (4 studies, 933 patients).

The pooled sensitivity was 66% (95% CI: 32, 89) and the pooled specificity 95% (95% CI: 78, 99). There was considerable heterogeneity in both the sensitivity and specificity, with trade-off between estimates of sensitivity and specificity (P<0.001). Post-test probabilities with a positive/negative ultrasound result were 59%/4% with a 10% pre-test prevalence, 93%/26% with a 50% pre-test prevalence and 99%/76% with a 90% pre-test prevalence.

Any vessel abnormality (halo, stenosis or occlusion) (3 studies, 853 patients).

The pooled sensitivity was 87% (95% CI: 80, 91) and the pooled specificity 96% (95% CI: 89, 98). There was no statistical evidence of heterogeneity (P=0.48 for sensitivity and P=0.082 for specificity). Post-test probabilities with a positive/negative ultrasound result were 71%/2% with a 10% pre-test prevalence, 96%/12% with a 50% pre-test prevalence and 99%/55% with a 90% pre-test prevalence.

Diagnostic performance did not differ significantly with date of publication, sample size, or language. The halo sign appeared to perform better in studies of higher technical ultrasound quality and in those that fulfilled the quality criteria for cohort assembly.

Authors' conclusions

Ultrasoundography may be helpful in diagnosing giant-cell arteritis, but cautious interpretation of the test results based on clinical presentation and pre-test probability of disease is imperative.

CRD commentary

This was a generally well conducted and reported review of the area. It addressed a focused objective that was supported by well-defined inclusion criteria. The literature search was limited using diagnostic terms (accuracy, false negative and specificity), which might have led to relevant studies being missed. The review appears to have been limited to published studies, thus there is also the possibility of publication bias. Appropriate steps to minimise bias during the data extraction and the validity assessment processes were undertaken. It was unclear whether the same steps were taken to reduce the potential for selection bias. A detailed quality assessment was carried out, and the results were reported in tabular format and incorporated into the analysis. The methods used to synthesise the studies were appropriate, while a graphical presentation of the results provided a helpful overview of the results of the primary studies. Bearing in mind the potential for missed studies and the heterogeneity between the included studies, the authors' conservative conclusion seems appropriate.

Implications of the review for practice and research

Practice: The authors stated that when the pre-test probability of disease is low (<10%), negative results on ultrasonography practically exclude giant-cell arteritis and eliminate the need for temporal artery biopsy; positive results are inconclusive. When the pre-test probability of disease is very high (90%), biopsy is probably unavoidable as the treatment is not trivial. In these cases ultrasonography is meaningful only for high-risk patients who do not agree to
biopsy. When giant-cell arteritis is likely but several other diagnoses are possible (pre-test probability 50%), ultrasonography is of considerable value. Abnormal findings boost the likelihood of disease high enough to justify a biopsy, while negative results decrease the post-test probability to within a range in which biopsy should be considered on an individual basis.

Research: The authors stated that additional studies are needed to clarify the accuracy of ultrasound in patients with polymyalgia rheumatica or systemic illnesses.

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