Diagnostic performance of antineutrophil cytoplasmic antibody tests for idiopathic vasculitides: metaanalysis with a focus on antmyeloperoxidase antibodies

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Authors' objectives
To undertake a meta-analysis that examined the diagnostic value of assays for detecting antmyeloperoxidase antibodies (anti-MPO) for the detection of Wegener's granulomatosis (WG), microscopic polyangiitis (MPA), the Churg-Strauss syndrome (CSS) and isolated pauci-immune necrotising and crescentic glomerulonephritis (iNCGN).

Searching
MEDLINE was searched from 1966 to October 1998 for English language papers only. The search terms were detailed in the paper. In addition, manual searches of the reference lists of included papers and review articles were undertaken.

Study selection
Study designs of evaluations included in the review
Studies which had random or consecutive patient selection were included in the review. Both prospective and retrospective studies were eligible for inclusion. Case-series studies without controls were excluded, as were case reports, letters, reviews and editorials.

Specific interventions included in the review
Studies had to assess values of anti-MPO tests, regardless of other antineutrophil cytoplasmic antibodies (ANCA) tests, to be eligible for inclusion. To be considered ANCA-positive, the sera had to be positive for both antiMPO and pANCA. The authors accepted the determinations of positivity reported by the individual studies. COMPARED>> Studies had to report the use of acceptable criteria, as defined, for the diagnosis of WG, MPA, CSS and iNCGN exclusive of ANCA test results (n=35). Case definitions were those matching the definition of the Chapel Hill consensus conference (see Other Publications of Related Interest no.1). iNCGN was defined as pauci-immune NCGN without features of systemic diseases. In addition, the criteria as defined by Fauci et al. for WG (see Other Publications of Related Interest no.2) were considered acceptable. Studies which did not specify a reasonably unbiased patient selection method, or the use of acceptable criteria for the diagnosis of WG, MPA, CSS or iNCGN exclusive of ANCA test results, were excluded. The methods of case definition reported in the studies were biopsy and Chapel-Hill biopsy.

Reference standard test against which the new test was compared
Studies had to report the use of acceptable criteria, as defined, for the diagnosis of WG, MPA, CSS and iNCGN exclusive of ANCA test results (n=35). Case definitions were those matching the definition of the Chapel Hill consensus conference (see Other Publications of Related Interest no.1). iNCGN was defined as pauci-immune NCGN without features of systemic diseases. In addition, the criteria as defined by Fauci et al. for WG (see Other Publications of Related Interest no.2) were considered acceptable. Studies which did not specify a reasonably unbiased patient selection method, or the use of acceptable criteria for the diagnosis of WG, MPA, CSS or iNCGN exclusive of ANCA test results, were excluded. The methods of case definition reported in the studies were biopsy and Chapel-Hill biopsy.

Participants included in the review
Studies had to specify a reasonably unbiased patient selection method (consecutive or random). Patients with suspected defined systemic vasculitic syndromes such as WG, MPA, CSS and iNCGN, were included in the review.

Outcomes assessed in the review
Studies that presented data allowing the construction of 2x2 tables were eligible for inclusion. The outcome measures used in the review were sensitivity and specificity.

How were decisions on the relevance of primary studies made?
The authors adopted a four-stage process (see paper for full description); two reviewers were involved at each stage in the selection of studies.
Assessment of study quality
No formal quality assessment was performed, but quality criteria (patient spectrum and appropriate reference standard) were used to select the studies for inclusion. The authors do not state how the papers were assessed for validity. Any discrepancies in judgement were resolved by consensus.

Data extraction
Data were extracted to construct 2x2 contingency tables for patients with and without the spectrum of vasculitis compared with patients with and without positive anti-MPO test results.

Methods of synthesis
How were the studies combined?
Summary estimates of sensitivity and specificity were calculated by pooling results weighted by the number of participants in each study. A fixed-effect model was applied in the case of no heterogeneity, while a random-effects model was used when there was heterogeneity. The 95% confidence intervals (CIs) were calculated.

How were differences between studies investigated?
The chi-squared test of homogeneity was evaluated for all selected studies. In the case of heterogeneity, summary receiver operating characteristic (SROC) curves were constructed.

Results of the review
Seven studies (n=4,261) were included in the review: 3 case control (n=1,481) and 4 cohort studies (n=2,780).

The summary estimates of sensitivity and specificity (assessed in disease controls only) of assays for anti-MPO testing for the diagnosis of systemic necrotising vasculitides (n=7) were 37.1% (95% CI: 26.6, 47.6) and 96.3% (95% CI: 94.1, 98.5), respectively. When the pANCA pattern by indirect immunofluorescence (IIF) was combined with anti-MPO testing (n=6), the specificity improved to 99.4% (95% CI: 99.0, 99.9), with a lower sensitivity of 84.7% (95% CI: 70.7, 98.7). The combined ANCA testing system (anti-MPO plus pANCA or antiPR3 plus cANCA)(n=5) increased the sensitivity to 84.7% (95% CI: 70.7, 98.7), with a specificity of 98.6% (95% CI: 97.9, 99.3). The SROC univariate analyses suggested that the studies of case-control design or the earliest studies found significantly better performance of anti-MPO tests than those of cohort design or later. There was statistically-significant heterogeneity in both the sensitivities and specificities, both with all controls (p<0.001) and with disease control only (p<0.001), across the seven papers.

Authors’ conclusions
The authors conclude that ‘the results suggest that while anti-MPO is relatively specific for the diagnosis of systemic vasculitis, the combination system of immunoassays for anti-MPO and IIF for pANCA is highly specific and both tests should be used together’.

CRD commentary
The authors conducted a limited literature search, searching only one electronic database and restricting their search to only English language studies, although they did undertake a reference list review as well. However, there remains the possibility that some studies may have been missed. The authors provided details on the processes by which the papers were selected and the data extracted. The authors’ conclusions appear to follow from the evidence presented.

Implications of the review for practice and research
Practice: The authors state that, although immunoassays for anti-MPO are relatively specific for the diagnosis of systemic vasculitis, the combination system of immunoassays for anti-MPO and IIF for pANCA is highly specific and both tests should be used together. Furthermore, because patients with ANCA-associated vasculitis have either anti-
MPO with pANCA or antiPR3 with cANCA, and rarely both, a combined ANCA testing system including anti-PR3/cANCA and anti-MPO/pANCA is recommended to optimise the diagnostic performance of ANCA testing.

Research: The authors did not state any implications for further research.

Bibliographic details

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11469466

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Antibodies, Antineutrophil Cytoplasmic /analysis; Churg-Strauss Syndrome /diagnosis /immunology; Glomerulonephritis /diagnosis /immunology; Granulomatosis with Polyangiitis /diagnosis /immunology; Humans; Myeloblastin; Peroxidase /immunology; Serine Endopeptidases /immunology

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.