Transcranial Doppler versus angiography in patients with vasospasm due to a ruptured cerebral aneurysm: a systematic review

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Authors' objectives
To evaluate the accuracy of transcranial Doppler (TCD) compared with angiography in the diagnosis of vasospasm in patients with subarachnoid haemorrhage due to ruptured aneurysm, and to evaluate its usefulness as a screening method in this setting.

Searching
MEDLINE (from 1966 to January 2001), EMBASE (from 1984 to January 2001) and the CENTRAL Register in the Cochrane Library (Issue 1, 2001) were searched; the keywords were listed. The reference lists of retrieved studies and relevant review articles were checked. No language restrictions were applied. Data from abstracts, letters and studies of animals were not considered. In addition, manufacturers were not contacted and unpublished data were not sought. Authors were contacted when the reported data were ambiguous.

Study selection
Study designs of evaluations included in the review
Diagnostic accuracy studies were eligible for inclusion.

Specific interventions included in the review
Studies of TCD were eligible for inclusion. TCD and angiography had to be performed within 24 hours of each other. Only studies that used conventional TCD devices were included (i.e. power colour TCD was not considered). In the studies included in the meta-analysis, the cut-off to define a positive TCD was defined as a flow velocity in the middle cerebral artery of 120, 130 or 140 cm/second.

Reference standard test against which the new test was compared
Studies that used cerebral angiography as the reference standard were eligible for inclusion. In the studies included in the meta-analysis, the cut-off to define a positive angiography was defined as a lumen reduction in any artery of at least 25 or 30%.

Participants included in the review
Studies of adults with subarachnoid haemorrhage due to ruptured aneurysms were eligible for inclusion.

Outcomes assessed in the review
No inclusion criteria relating to outcomes were specified. The outcome measures reported in the review were the positive and negative predictive values (PPV and NPV, respectively), positive and negative likelihood ratios (LRs), sensitivity and specificity.

How were decisions on the relevance of primary studies made?
Two authors screened all retrieved reports.

Assessment of study quality
The studies were scored according to the following criteria: study design, i.e. comparative versus case-control; consecutive patient selection; prospective data collection; observer blinding; description of test execution; complete verification of both tests; whether 2x2 data were reported; details of the study population; homogeneity of the study population; and the reporting of long-term outcomes. The studies were given one point for each criteria fulfilled, giving a maximum possible total of 10 points. Three authors independently read the papers and scored them for methodological quality. The authors then met to agree consensus and resolved any disagreements through discussion.
Data extraction
One author extracted dichotomous 2x2 data separately for different arteries. This was only done for trials that compared both tests in all patients. Two authors checked the extracted data. Any disagreements were resolved through discussion. Definitions of ‘positive’ TCD (increasing flow velocity) and ‘positive’ angiography (narrowing of arteries) were taken as reported in the original studies. Sensitivity, specificity, PPVs, NPVs, and positive and negative LRs were calculated for each valid study, together with 95% confidence intervals (CIs). For studies in which any of the 2x2 tables contained 0 cells, 0.5 was added to all cells before computing the summary measure.

Methods of synthesis
How were the studies combined?
The meta-analysis was performed when there was evidence of complete verification of both tests in a trial. When combined data were reported on different arteries and the data could not be separated, further analysis was not undertaken. Random-effects models were used to generate summary measures.

How were differences between studies investigated?
Differences between the studies were discussed in the text.

Results of the review
Twenty-six studies were included. However, dichotomous data for 2x2 tables could only be extracted from 9 studies, and in two of these verification was incomplete. Therefore, only 7 studies were included in the meta-analysis.

None of the included studies fulfilled all 10 methodological criteria. The median score was 4.5 (range: 1 to 8). Full details of the quality assessment were reported.

Middle cerebral artery (5 studies).
The sensitivity ranged from 38% (specificity 94%) to 91% (specificity 100%) and the specificity ranged from 94% (sensitivity 38%) to 100% (sensitivity 59 to 91%). The pooled sensitivity was 67% (95% CI: 48, 87) and the pooled specificity was 99% (95% CI: 99, 100). This corresponded to a pooled positive LR of 17 (95% CI: 5, 56) and a negative LR of 0.4 (95% CI: 0.2, 0.7).

Anterior cerebral arteries (3 studies).
The sensitivity ranged from 13% (specificity 100%) to 82% (specificity 71%) and the specificity ranged from 65% (sensitivity 18%) to 100% (sensitivity 13%). The pooled sensitivity was 42% (95% CI: 11, 72) and the pooled specificity was 76% (95% CI: 53, 100). This corresponded to a pooled positive LR of 1.7 (95% CI: 0.6, 4.9) and a pooled negative LR of 0.9 (95% CI: 0.6, 1.3).

Other arteries (internal carotid, posterior cerebral, basilar cerebral and vertebral cerebral) were each assessed in only one study; the results of these were presented in the paper.

Authors’ conclusions
For the middle artery, TCD is not likely to indicate a spasm when angiography does not show one (high specificity), and it may be used to identify patients with a spasm (high PPV). For all other situations and arteries, there was a lack of evidence of either accuracy or any usefulness of TCD. Most of these data were of a low methodological quality, bias could not be ruled out, and the data reporting was often uncritical.

CRD commentary
This was a well-conducted review that suffered from some weaknesses in the presentation of the results of individual studies and the synthesis of the results. The review addressed a clearly focused question and was supported by well-defined inclusion criteria. A detailed literature search, which did not involve any language restrictions, was undertaken. However, there were no attempts to identify unpublished studies, so the review may be subject to publication bias.
details of the review methodology were reported and these included appropriate attempts to avoid bias in the review process. A detailed quality assessment using appropriate criteria was undertaken, and the results of this were presented in tabular format and discussed in the 'Results' section.

The meta-analysis was limited to studies which reported appropriate data for pooling and which were not subject to verification bias. This appears to have been appropriate, but no results for studies that did not meet these criteria were presented. Consequently, a large amount of data that could potentially have been included in the review was discarded. The authors used methods for the meta-analysis that appear to have been appropriate. However, given the apparent differences between the studies, some discussion and testing of heterogeneity should have been carried out. Since some studies used different criteria to define a positive result, a summary receiver operator curve analysis might have been more appropriate, in addition to the simple pooling of summary diagnostic measures presented in the article.

Very few details of the studies were reported, which makes it difficult to assess the generalisability of the results, or for the reader to determine whether there were differences between the studies that could have accounted for the heterogeneity in the study results. The authors' conclusions appear to be supported by the results presented, but should be interpreted with some degree of caution due to the limitations highlighted.

Implications of the review for practice and research
Practice: The authors stated that if TCD of the middle cerebral artery in a patient who may have a spasm of that artery indicates the presence of a spasm, it is indeed likely that this patient has a spasm. If in the same patient TCD does not suggest a spasm of the artery, the operator does not know for sure that there is none. There is no evidence for any usefulness of TCD as a diagnostic tool for spasms of other cerebral arteries.

Research: The authors stated that in future trials, correlation coefficients rather than 2x2 tables based on arbitrary cut-offs would be more useful, and long-term outcomes should be studied.

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