Transcranial Doppler ultrasonography to confirm brain death: a meta-analysis

CRD summary
This review found that ultrasound can be used to reliably diagnose brain death. These conclusions are supported by the data presented, but should be interpreted with some degree of caution given the limitations of the literature search.

Authors' objectives
To determine the accuracy of transcranial Doppler ultrasonography (TCD) in determining brain death.

Searching
PubMed was searched from 1980 to January 2004; the search terms, which were reported, did not include a diagnostic filter. The reference lists of retrieved articles were screened for additional studies.

Study selection
Study designs of evaluations included in the review
Prospective studies were eligible for inclusion. Case reports and reviews were excluded.

Specific interventions included in the review
Studies that assessed TCD flow patterns and specified a persistent intracranial flow pattern specific for cerebral circulatory arrest (oscillating flow or systolic spikes) were eligible for inclusion. Studies that only examined extracranial vessels were excluded. The vessels examined by the included studies were the middle cerebral artery, basilar artery, vertebral artery and internal carotid artery.

Reference standard test against which the new test was compared
Studies that included a specified reference standard and in which brain death was defined as non-reactive coma with complete loss of the brain-stem reflexes and apnoea were eligible for inclusion. The reference standards used in the included studies were clinical criteria alone or in combination with cerebral angiography, electroencephalogram or radionuclide scan.

Participants included in the review
Studies of neonates or infants (age under 1 year) were excluded. Details were only provided of patients who received a false-positive diagnosis.

Outcomes assessed in the review
Studies had to report extractable data for patients classified as brain dead or non-brain dead. The outcomes reported in the review were the sensitivity and specificity. Some studies only reported data on sensitivity.

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
Two reviewers independently assessed studies for methodological quality using the following criteria: (a) presence of an independent blind comparison with a ‘gold’ standard; (b) population studied was representative of those in whom the test would be used in practice; (c) enrolment of consecutive patients; and (d) sufficient description of TCD to allow reproduction of the method. High-quality studies were considered to be those that fulfilled all four criteria; low-quality studies were those that fulfilled criterion (a), although the comparison was not necessarily blinded, and criteria (d). All other studies were considered to be non-valid and were excluded from the review.
Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. Data from high- and low-quality studies were extracted as 2x2 tables of test performance. The sensitivity and specificity were calculated for each study.

Methods of synthesis
How were the studies combined?
In the absence of significant heterogeneity, the sensitivity and specificity were pooled for high-quality studies. Sensitivity analysis, to investigate the robustness of the conclusions, was carried out by adding low-quality studies to the pooled analysis.

How were differences between studies investigated?
Heterogeneity was assessed by visual examination of overlap of 95% confidence intervals (CIs) of estimates of sensitivity and specificity.

Results of the review
Ten studies (684 patients) were included.

Eight studies were judged to be of a low quality and two of a high quality. In the low-quality studies, the investigators were not blinded.

Only two studies reported false-positive results. Both of these patients became brain dead shortly after the false-positive diagnosis.

Meta-analysis of the two high-quality studies gave a pooled sensitivity of 95% (95% CI: 92, 97) and a pooled specificity of 99% (95% CI: 97, 100). When the low-quality studies were included in the analysis, the pooled sensitivity was decreased to 89% (95% CI: 86, 91) but the pooled specificity remained at 99% (95% CI: 99, 100). Visual assessment suggested that studies were homogeneous.

Authors' conclusions
TCD can be used to reliably diagnose brain death in combination with clinical criteria.

CRD commentary
The review addressed a focused question that was supported by inclusion criteria defined in terms of the intervention, reference standard, outcomes and study design. The literature search was limited to one electronic database and attempts were not made to locate unpublished studies. Relevant studies might, therefore, have been missed and the review may be subject to publication bias. A formal quality assessment based on appropriate criteria was conducted and appropriate steps were taken to minimise bias in this process. It is unclear whether such steps were also taken in the selection of studies and extraction of data.

Some details of the studies were tabulated but further details, especially in relation to the participants, would have been helpful. The methods used to pool the studies were adequate, but a more sophisticated analysis based on more complex methods would have been preferable. The authors' conclusions are supported by the data presented, but should be interpreted with some degree of caution given the limitations of the literature search.

Implications of the review for practice and research
Practice: The authors stated that TCD could be used to determine the appropriate timing of angiography. Research: The authors stated that a test to confirm brain death should have a specificity of 100%. Further research is required to confirm that TCD operates at this level of specificity.
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Record Status
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.