Computed tomographic angiography for detecting cerebral aneurysms: implications of aneurysm size distribution for the sensitivity, specificity, and likelihood ratios
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CRD summary
This review aimed to determine the diagnostic accuracy of computed tomographic angiography (CTA), compared with intra-arterial digital subtraction angiography or surgical findings, for the detection of cerebral aneurysms after adjusting for size distributions. The author concluded that CTA is useful in the descriptive imaging of a known aneurysm. Although the author’s conclusions appear consistent with the results obtained, methodological limitations may restrict interpretation.

Authors’ objectives
To determine the diagnostic accuracy of computed tomographic angiography (CTA), compared with intra-arterial digital subtraction angiography (IA-DSA) or surgical findings, for the detection of ruptured and unruptured cerebral aneurysms after adjusting for size distributions. A secondary objective was to determine whether accuracy was affected by aneurysm prevalence.

Searching
As described in an earlier review (see Other Publications of Related Interest), MEDLINE and EMBASE were searched from January 1988 to December 1998 for published studies in any language; the search terms were reported. The bibliographies of retrieved articles were screened for additional references. The RSNA Index to Imaging Literature and relevant journals were also handsearched for applicable publications. Only articles published in full were eligible for inclusion. The author stated that the literature review was updated in September 2002.

Study selection
Study designs of evaluations included in the review
Diagnostic accuracy studies involving more than 20 cases were eligible. The interpreting radiologists were required to be blinded to the results of the reference standard.

Specific interventions included in the review
Studies evaluating the diagnostic accuracy of a noninvasive imaging examination (CTA) were eligible for inclusion in the review.

Reference standard test against which the new test was compared
Studies using IA-DSA or autopsy reports as the reference standard of diagnosis were eligible for inclusion. Of the included studies, seven compared CTA with an IA-DSA while five compared CTA with the surgical findings from an autopsy report.

Participants included in the review
Studies of patients with ruptured or unruptured aneurysms were eligible. Studies of patients who were known, or suspected, to have had a recent subarachnoid haemorrhage or intracranial aneurysm, or who had symptoms that could be attributed to an underlying aneurysm, were included in the review. The average number of aneurysms per person in the included studies ranged from 0.4 to 1.1.

Outcomes assessed in the review
The included studies were required to report the sensitivity and specificity of CTA for the detection of cerebral aneurysms, with sensitivity stratified by aneurysm size. The reviewers calculated the following measures of diagnostic accuracy: the likelihood ratio (LR) for a positive test, LR for a negative test, sensitivity and specificity. False-negative aneurysms outside the study volume of the CTA were excluded. The average aneurysm rates (per individual patient) were also presented.
How were decisions on the relevance of primary studies made?
The author did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The author did not state that they assessed validity.

Data extraction
The author did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
How were the studies combined?
A Bayesian logistic regression model was used to estimate the sensitivity of CTA according to aneurysm size. The model included an estimated size change above which CTA has an assumed sensitivity of 100%. Patient level data were used. The size distributions of false-positive aneurysms, identified on CTA, were modeled using a Bayesian multinomial-Dirichlet conjugate model using non-informative prior probability. The size distributions for ruptured and unruptured aneurysms were derived using the bootstrap method. Hierarchical Monte Carlo methods were used to perform computer-generated probabilistic simulations of cases screened with CTA. Each simulation was based on 30,000 cases.

How were differences between studies investigated?
A Bayesian hierarchical logistic regression model was used to estimate variance between the studies.

Results of the review
Nine studies (n=619) were included in the review, and were used to estimate the size-specific sensitivity of CTA.

The size distributions for ruptured aneurysms (2,787 aneurysms) and for unruptured aneurysms (901 aneurysms) were each estimated from 6 studies.

The crude sensitivity ranged from 66 to 98%. The predicted change point in aneurysm size was 7.7 mm (95% confidence interval, CI: 7.0, 8.9), above which false negatives did not occur. The sensitivities stratified by aneurysm size ranged from 53% (95% CI: 44, 62) for 2-mm aneurysms to 95% (95% CI: 92, 97) for 7-mm aneurysms. The crude specificity ranged from 77 to 100%. The overall estimated specificity for the studies was 98.9% (95% CI: 91.5, 99.99), but there was between-study heterogeneity. The rate of aneurysms per case, sensitivity of the study, and study size were not statistically associated with between-study heterogeneity. The medium sensitivity for ruptured aneurysms, as derived from computer simulations, was 92% (95% CI: 90, 94); the corresponding medium sensitivities for unruptured aneurysms and for aneurysms greater than 5 mm were 82% (95% CI: 78, 86) and 92% (95% CI: 89, 95), respectively.

The LR for negative tests was 0.18 for unruptured aneurysms, 0.012 for unruptured aneurysms of at least 6 mm, and 0.081 for ruptured aneurysms. The LR for positive tests for unruptured aneurysms with a low probability ranged from 15 for 2-mm aneurysms, to 61 for 5-mm aneurysms, to 99 for 6-mm aneurysms. The LR for positive results for ruptured aneurysms with a 50% pre-test probability ranged from 3.9 (2-mm aneurysm) to 56 (5-mm aneurysm). The LR for positive results for a solitary ruptured aneurysm with a high pre-test probability (85%) ranged from 3.4 (2-mm aneurysm) to 40 (5-mm aneurysm).

Interpretation of CTA results derived from computer simulations.

Negative CTA with a suspected unruptured aneurysm.

For a low pre-test probability of 2%, a negative CTA resulted in a post-test probability of 0.37%. For a high pre-test probability of 10%, the post-test probability would be 2.0%.
Positive CTA with a suspected unruptured aneurysm. For a low pre-test probability of 2%, the post-test probability of an identified 2-mm aneurysm was 23%, while that of an identified 5-mm aneurysm was 56%. With a high pre-test probability of 10%, the post-test probabilities for a 2-mm and 5-mm aneurysm were 62% and 87%, respectively.

Negative CTA with a suspected ruptured aneurysm. For a pre-test probability of 5%, the post-test probability after a negative CTA was 0.42%. For a pre-test probability of 50%, the post-test probability was 7.5%, while for a high pre-test probability of 90%, the post-test probability was 42%.

Positive CTA with a suspected ruptured aneurysm. For a low pre-test probability of 5%, the post-test probability of a 2-mm identified aneurysm being ruptured was 18%. A 5-mm identified aneurysm has a probability of 78% of being a ruptured aneurysm. For a pre-test probability of 50%, the post-test probabilities for a 2-mm and 5-mm aneurysm being ruptured were 69% and 92%, respectively. With a pre-test probability of 90%, the post-test probabilities for a 2-mm and 5-mm aneurysm being ruptured were 82% and 99%, respectively. The likelihood of a false-positive aneurysm is very small for aneurysms of greater than 5 mm, identified on CTA.

When screening for an unruptured aneurysm of at least 6 mm, with a low pre-test probability of 2%, a negative CTA resulted in a post-test probability of 0.024%. For a high pre-test probability of 10%, the post-test probability after a negative CTA was 0.13%. For a pre-test probability of 2% the post-test probability of a true-positive was 68%, and for a pre-test probability of 10%, the post-test probability was 92%. False-positives for aneurysms greater than 6 mm are unlikely.

Authors' conclusions
CTA is useful in the descriptive imaging of a known aneurysm. Small aneurysms detected by CTA should be investigated further, unless there is a high pre-test probability of a ruptured aneurysm. When screening for ruptured aneurysms, a negative CTA should be investigated further. However, a negative CTA results in a very low probability of a clinically important aneurysm when screening for unruptured aneurysms.

CRD commentary
The author addressed a clear question, which was supported by well-defined inclusion and exclusion criteria. A thorough literature search appears to have been carried out, although the search strategy was restricted to published studies and publication bias was not assessed. The author, however, acknowledged that this might have introduced publication bias. The procedures implemented for the selection of primary studies, data extraction and quality assessment were not reported, thus the likelihood of reviewer error or bias at these stages could not be assessed.

The statistical analyses undertaken were appropriate, and the author explored some differences in the characteristics of the selected studies. The author acknowledged that the use of uniform distributions might have caused a small overestimation of the sensitivity of CTA for small aneurysms and an underestimation of the sensitivity of small-to-medium aneurysms. In addition, when there was more than one observer interpreting the CTA results, the results of the most accurate were selected. Since no intra-observer variability data were reported, it is impossible to assess the likely differences between the data selected and that which would derive from normal clinical practice.

The author's conclusions appear consistent with the results obtained, but are perhaps too firm if the methodological limitations and the small size of the data set supporting the model simulations are considered.

Implications of the review for practice and research
Practice: The author stated that if the post-test probability is sufficiently high and the imaging is satisfactory, then treatment decisions can be made. If the post-test probability is sufficiently low, then diagnosis of an aneurysm can be excluded for clinical purposes.

Research: The author stated that further research into the interaction between the prevalence of aneurysms, the suspicion of the interpreter, and the sensitivity and specificity of CTA is needed. In addition, further research is
required into the usefulness of novel computer modeling and its application for clinicians, the optimum method of presenting the results, and whether these models and the information derived from these models improves decision-making.

**Bibliographic details**

**PubMedID**
12943576

**Other publications of related interest**

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Aneurysm, Ruptured /radiography; Cerebral Angiography /statistics & numerical data; Evaluation Studies as Topic; Humans; Intracranial Aneurysm /radiography; Likelihood Functions; Logistic Models; Meta-Analysis as Topic; Reproducibility of Results; Sensitivity and Specificity; Severity of Illness Index; Tomography, X-Ray Computed /statistics & numerical data

**AccessionNumber**
12003001927

**Date bibliographic record published**
31/01/2006

**Date abstract record published**
31/01/2006

**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.