Systematic review: diagnostic procedures to differentiate unilateral from bilateral adrenal abnormality in primary aldosteronism


CRD summary
This review concluded that accuracy of computed tomography/magnetic resonance imaging to distinguish between unilateral and bilateral adrenal abnormality in primary aldosteronism was poor compared with adrenal vein sampling. Limitations with the review, including the potential for bias and concerns regarding the comparability of the studies, suggested that the conclusions should be interpreted with caution as they may not be reliable.

Authors' objectives
To compare the accuracy of computed tomography or magnetic resonance imaging with adrenal vein sampling to distinguish between unilateral and bilateral adrenal abnormality in primary aldosteronism (hypertension).

Searching
PubMed, MEDLINE, EMBASE and The Cochrane Library were searched between 1977 and April 2009 for articles published in English, French, German or Dutch. Search terms were reported.

Study selection
Studies of patients over the age of 18 years with a diagnosis of primary aldosteronism and undergoing computed tomography/magnetic resonance imaging (CT/MRI) and adrenal vein sampling that reported results for both investigations on the extent of agreement were eligible for inclusion. Studies were excluded if they were review or practice guidelines, included only one patient, there was suspected inclusion bias or if it was not clear that diagnosis of primary aldosteronism was based on sodium chloride loading test, aldosterone renin ratio or plasma aldosterone concentration plus plasma renin activity.

The included studies were of male and female patients with a mean age of 50.8 years. The mean blood pressure was 157/97mm Hg. Approximately half of the patients had hypokalaemia. Diagnosis was confirmed using a sodium chloride loading test or a biochemical test (using the aldosterone-renin ratio or plasma aldosterone concentration plus plasma renin activity or concentration). Some of the included studies reported the cutoff value of selectivity criterion (used to determine if blood was drawn selectively from the adrenal veins and not from an adjacent vein during adrenal vein sampling) and lateralisation criterion (used to determine whether aldosterone hypersecretion was unilateral or bilateral). The primary outcome assessed was the accuracy of CT/MRI, that is, the number of times the CT/MRI (index text) results confirmed, or otherwise, the results for diagnosing unilateral or bilateral adrenal abnormality using adrenal vein sampling (reference standard). Some studies reported inaccuracy between tests when both tests showed unilateral abnormality, but on different sides.

Two reviewers independently screened the studies for selection Any discrepancies were resolved by consensus or referral to other reviewers.

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

Data extraction
The number (percentage) of CT/MRI results that agreed or did not agree with results from adrenal vein sampling were extracted. Where study details were unclear, authors were contacted. The authors did not state how many authors performed the data extraction.

Methods of synthesis
Percentages for accurate and inaccurate results were combined and reported as a narrative synthesis and in tables. Studies were grouped by the test used to confirm the diagnosis of primary aldosteronism and by the description of
selectivity and laterisation criteria, if used.

**Results of the review**

Thirty nine studies (n=950) were included in the review. Sample sizes ranged between one and 194 patients; most studies included fewer than 100 patients.

CT/MRI results were inaccurate in 37.8% of patients (n=359): in 14.6% of patients (n=139) adrenal vein sampling showed bilateral abnormality and CT/MRI showed unilateral abnormality; and in 19.1% of patients (n=181) adrenal vein sampling showed unilateral abnormality and CT/MRI showed a bilateral or no abnormality. In 3.9% of patients (n=37) adrenal vein sampling showed a unilateral abnormality on one side while CT/MRI showed it to be on the other side. In the remaining 62.2% of patients (n=591) 37.4% (n=355 patients) of the CT/MRI results were accurate for unilateral adrenal abnormality and 24.8% (n=236 patients) were accurate for bilateral abnormality.

**Authors’ conclusions**

CT/MRI performed poorly when compared to adrenal vein sampling as the criterion standard test for determining laterality of aldosterone secretion in patients with primary aldosteronism. Reliance upon this assessment tool could lead to inappropriate treatment of patients.

**CRD commentary**

The review question was well defined. It was supported by detailed inclusion criteria for participants and interventions, and more broadly for outcomes. There were no a priori criteria for study design and it was unclear from the review which study designs were included, thus the quality of the studies could not be estimated. Discrepancies were noted concerning the reported number of included studies and in the inclusion of a single-patient study, which conflicted with the a priori criteria. Relevant sources appeared to have been searched, including searches in a number of languages. However, the language restriction meant that language bias may have been introduced. As there was no apparent search for unpublished data, potentially relevant papers may have been missed. The authors did not state that they assessed validity, which meant that the robustness of the findings was uncertain. Steps were taken to reduce reviewer error and bias during study selection by screening in duplicate, but the same cannot be said for data extraction and bias cannot be ruled out completely. There was no obvious attempt to assess statistical heterogeneity, and as only few study and patient details were presented, it was unclear whether the studies were comparable. The authors' conclusions reflected the basic statistical analysis presented. The authors also mentioned a 20% inaccuracy rate with adrenal vein sampling, which raised questions whether comparison between the two assessment tools was appropriate. Given some of the methodological uncertainties mentioned above, the extent to which the authors' conclusions were reliable is unclear.

**Implications of the review for practice and research**

**Practice:** The authors stated that the conclusions may have major implications for facility planning in settings that still rely on CT/MRI. When using CT/MRI results alone, physicians should take into account that inaccuracy may lead to inappropriate treatment of patients with primary aldosteronism.

**Research:** The authors stated that future studies should include pathologic data, information on biochemical measures, blood pressure and medication use during follow-up to allow further analyses to determine whether adrenalectomy was appropriate.

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