Comparative effectiveness of management strategies for renal artery stenosis

CRD summary
This review aimed to compare the effectiveness and safety of angioplasty with aggressive medical therapies for the treatment of atherosclerotic renal artery stenosis. The authors concluded that the available evidence does not clearly support one treatment approach over another. In view of the poor quality of the identified studies this conclusion appears appropriate; however, other relevant studies might have been missed.

Authors' objectives
To compare the effectiveness and safety of angioplasty (with or without stent placement or surgical revascularisation) with aggressive medical therapies for the treatment of atherosclerotic renal artery stenosis (RAS).

Searching
MEDLINE was searched from inception to September 2005 for studies published in full in the English language; the search terms were reported. The reference lists of related systematic reviews, selected narrative reviews and primary studies were also reviewed. Members of the review's technical expert panel were also invited to provide additional relevant studies.

Study selection
Study designs of evaluations included in the review
Both controlled and uncontrolled studies were eligible for inclusion. Uncontrolled studies that enrolled all patients prior to the publication of the 5th Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure guidelines (see Other Publications of Related Interest no.1) in 1993 were not eligible for inclusion. The studies had to include at least 10 participants to be eligible for inclusion; some study designs and interventions required the number of participants to be higher for the study to be included in the review (see report for details). The studies included in the review were randomised controlled trials (RCTs), non-randomised controlled trials, cohort studies, and other studies reporting adverse events.

Specific interventions included in the review
Studies of angioplasty (with or without stent placement) and aggressive medical therapies (defined as antihypertensive drugs, antilipid drugs and antiplatelet drugs) were eligible for inclusion. The authors also included studies of surgical revascularisation, any medical treatment, or a variety of generally undefined strategies. However, studies of surgical procedures that were considered not to be comparable to angioplasty, such as endarterectomy, renal ablation or nephrectomy, were not eligible for inclusion. The majority of the included studies used angioplasty without stent placement. The medical therapies included atenolol, bedrofluazide and calcium-channel blockers.

Participants included in the review
Studies of adults with RAS that was severe enough to warrant aggressive management, either due to resistant hypertension, evidence of kidney damage, or the high likelihood of poor outcomes, were eligible for inclusion. The definitions of RAS used by the primary study authors were accepted. The authors only included studies where at least 80% of the participants had atherosclerotic RAS, as opposed to fibromuscular dysplasia, arteritis-associated RAS, acute embolic stenosis and other nonatherosclerotic stenosis, or where the results were reported separately for a subgroup of patients with atherosclerotic RAS. Studies of participants with RAS in the setting of a transplanted kidney, renal artery aneurysms requiring repair, aortic disease or concurrent cancer were excluded, as were studies of participants who had received previous surgical or angioplasty interventions for RAS. The majority of the included studies only included patients with generally stable blood-pressure, kidney function and cardiovascular status.

Outcomes assessed in the review
The primary outcomes of interest were long-term (6 months or more) mortality, kidney function, changes in blood-
pressure control, restenosis, flash pulmonary oedema or congestive heart failure events, other cardiovascular events and adverse events (including 30-day mortality).

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
An existing grading system was used to assess the quality of the included studies. For RCTs, the authors considered the following criteria: method of randomisation, allocation concealment, blinding, level of drop-outs, reporting of primary outcomes, and whether the results were reported on an intention-to-treat basis. For non-randomised controlled trials and cohort studies, the authors considered the following criteria (where applicable): study’s eligibility criteria, similarity of the groups at baseline, crossovers, loss to follow-up, description of outcomes and results, and whether the results were reported on an intention-to-treat basis. The studies were categorised as good, moderate or poor quality. Only RCTs could achieve a ‘good’ rating.

The authors also categorised studies according to how applicable they were to the target population of interest. The studies were categorised as high (study population was representative of the target population), moderate (study population was representative of a relevant subgroup of the target population), or low (study population was representative of a narrow subgroup of the target population and was of limited applicability to other subgroups).

At least two reviewers performed the validity assessment.

Data extraction
One reviewer extracted the data from the included studies, whilst a second reviewer checked the extraction.

Data on the baseline, follow-up and change from baseline for each outcome of interest, including information on statistical significance, were extracted. Only long-term effectiveness results were extracted from the included studies: 6 months, 12 months and each subsequent year, so long as at least 10 participants were evaluated at each time point.
When the outcome data were only reported as overall outcomes, without a specific time point, the mean or median time of follow-up was used. All adverse event data were extracted, regardless of length of follow-up.

Subgroup analyses reported in included studies that assessed the effects of different participant and intervention characteristics on the results were also extracted from primary studies.

Methods of synthesis
How were the studies combined?
A narrative synthesis was presented.

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

Results of the review
Fifty-five studies were included in the review: 2 RCTs, 8 non-randomised controlled studies and 45 cohort studies. A further 5 studies were included in the review, solely for data on adverse events.

None of the included studies were rated as good quality, most were rated as poor quality. Very few studies were rated as highly representative of the target population: over half of the included studies were rated as having a low level of applicability to the target population.

Kidney function.

Two RCTs (n=103), 7 non-randomised controlled studies (n=428) and 34 cohort studies (n=4,916) found no significant
difference in kidney function between angioplasty and medical treatment alone. Improvements in kidney function were reported in cohort studies only among patients receiving revascularisation.

Blood-pressure.

Two RCTs (n=103), 8 non-randomised controlled studies (n=597) and 34 cohort studies (n=4,275) found some evidence for a greater reduction in blood-pressure after angioplasty than medical treatment alone, particularly in patients with bilateral disease. Cure of hypertension was reported in cohort studies only among patients receiving revascularisation.

Other outcomes.

There was weak evidence to suggest that there were no large differences in mortality or cardiovascular events between angioplasty and medical treatment alone. There was insufficient evidence on adverse events to draw meaningful conclusions.

Baseline clinical characteristics associated with improved or worse outcomes.

There was moderate evidence to suggest that poorer kidney function or concomitant cardiovascular disease was associated with higher mortality rates and poorer clinical outcomes among patients who had angioplasty. There was weak evidence to suggest that patients with bilateral disease may benefit more from angioplasty than medical treatment alone. There was insufficient evidence to assess other clinical factors that may be predictive of improved or worse outcomes.

Treatment characteristics associated with improved or worse outcomes.

There was insufficient evidence to assess whether any treatment characteristics were associated with improved or worse outcomes.

**Authors' conclusions**

The available evidence did not clearly support one treatment approach over another for atherosclerotic RAS.

**CRD commentary**

The review question was clear in terms of the study designs, participants, interventions and outcomes of interest. The authors made limited attempts to identify relevant studies and only included published English language studies, thus increasing the potential for publication bias and language bias. The authors did not state how the studies were assessed for relevance, therefore the potential for reviewer bias and error cannot be assessed. Two reviewers were involved in the data extraction process (one extracted the data and the other checked it) and at least two reviewers performed the validity assessment, which reduces the potential for reviewer bias and error. The criteria for assessing study validity seemed appropriate.

In view of the differences between study populations and interventions, a narrative synthesis appeared appropriate. The quality of the included studies was generally poor, with limited applicability to the population of interest. Therefore, the authors' conclusions that the available evidence does not clearly support one treatment approach over another seems appropriate; however, other relevant studies might have been missed.

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

Practice: The authors did not state any implications for practice.

Research: The authors stated that further research is required to assess the role of atherosclerotic RAS in hypertension and kidney dysfunction to determine whether intervention should be directed towards improving kidney perfusion through angioplasty with stent placement, or more aggressively targeting the underlying factors of parenchymal kidney disease with combination medical therapy. The authors discussed an ongoing trial sponsored by the National Institutes
of Health, the results of which are expected to be reported in 2010 (Cardiovascular Outcomes in Renal Atherosclerotic Lesions, CORAL). The authors also stated that researchers should consider how to standardise definitions of atherosclerotic RAS and severity of disease.

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**Bibliographic details**

**Original Paper URL**
http://effectivehealthcare.ahrq.gov/search-for-guides-reviews-and-reports/?pageaction=displayproduct&amp;productID=53

**Additional Data URL**
http://www.annals.org/cgi/reprint/145/12/901

**Other publications of related interest**


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Subject indexing assigned by CRD

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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.