



Effective Health Care

Comparative Effectiveness of Management Strategies for Renal Artery Stenosis

Executive Summary

Background

Renal artery stenosis (RAS) is defined as the narrowing of the lumen of the renal artery. Atherosclerosis accounts for 90 percent of cases of RAS. Atherosclerotic RAS (ARAS) is a progressive disease that may occur alone or in combination with hypertension and ischemic kidney disease. The prevalence of ARAS ranges from 30 percent among patients with coronary artery disease to 50 percent among the elderly and those with diffuse atherosclerotic vascular diseases. In the United States, 12 to 14 percent of new patients entering dialysis programs have been found to have ARAS.

Most authorities consider the goals of therapy to be improvement in uncontrolled hypertension, preservation or salvage of kidney function, and improvement in symptoms and quality of life. Treatment alternatives include medications alone or revascularization of the stenosed renal artery or arteries. Combination therapy with multiple antihypertensive agents, usually including angiotensin converting enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs), calcium channel blockers, and/or beta blockers, is frequently prescribed with a goal of normalizing blood pressure. Some clinicians also recommend statins to lower low density lipoprotein (LDL) cholesterol and

Effective Health Care Program

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antiplatelet agents, such as aspirin or clopidogrel, to reduce thrombosis.

The current standard for revascularization in most patients is percutaneous transluminal angioplasty with stent



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placement across the stenosis. Angioplasty without stent placement is less commonly employed. Revascularization by surgical reconstruction is generally used only for patients with complicated renal artery anatomy or for patients who require pararenal aortic reconstructions for aortic aneurysms or severe aortoiliac occlusive disease.

The American College of Cardiology and the American Heart Association recently published guidelines for the management of patients with peripheral arterial disease, including renal artery stenosis. These guidelines provide recommendations about which patients should be considered for revascularization; however, there remains considerable uncertainty on which intervention provides the best clinical outcomes. Among patients treated with medical therapy alone, there is the risk of deterioration of kidney function, with worsening morbidity and mortality. Renal artery revascularization may provide immediate improvement in kidney function and blood pressure; however, as with all invasive interventions, it may result in substantial morbidity and mortality in some patients.

Placement of renal artery stents can resolve dissections, minimize stenosis recoil and restenosis, and correct transluminal pressure gradients. The evidence for durability of benefit is unclear; the majority of published studies on stent placement in ARAS had followup duration of less than 2 years. Comparison among studies on the effect of revascularization on hypertension and kidney function is limited because of differences in medical therapy, target blood pressure, and criteria for improvement.

Considerable controversy remains regarding optimal strategies for evaluation and management of patients with ARAS. The evidence supporting benefit of aggressive diagnosis and treatment remains unclear. Meanwhile, a Medicare claims analysis found that the rate of percutaneous renal artery revascularization rapidly increased from 7,660 interventions in 1996 to 18,520 in 2000.

To determine which patients with ARAS, if any, would most benefit from angioplasty with stent placement, as opposed to continued aggressive medical treatment, the National Institutes of Health has sponsored the large, multicenter Cardiovascular Outcomes in Renal Atherosclerotic Lesions (CORAL) trial. This trial is currently enrolling subjects and plans to report results in 2010. Meanwhile, the Agency for Healthcare Research and Quality (AHRQ) has commissioned a

review of the evidence on the effectiveness of renal artery angioplasty with stent placement vs. aggressive medical therapy. This review was commissioned under Section 1013 of the Medicare Modernization Act, which calls for comparative effectiveness reviews on medications and devices. AHRQ requested that the Tufts-New England Medical Center Evidence-based Practice Center (Tufts-NEMC EPC) conduct a review of the literature on the comparative effectiveness of management strategies for renal artery stenosis.

This report summarizes the evidence evaluating the effect and safety of angioplasty with stent placements and medical therapies in the treatment of ARAS, particularly after long-term followup. The key questions and principal definition of terms were determined with the assistance of a technical expert panel.

Key questions addressed in this report are:

1. For patients with atherosclerotic renal artery stenosis in the modern management era (i.e., since JNC-5 in 1993¹), what is the evidence on the effects of aggressive medical therapy (i.e., antihypertensive, antiplatelet, and antilipid treatment) compared to renal artery angioplasty with stent placement on long-term clinical outcomes (at least 6 months), including blood pressure control, preservation of kidney function, flash pulmonary edema, other cardiovascular events, and survival?
 - 1a. What are the patient characteristics, including etiology, predominant clinical presentation, and severity of stenosis, in the studies?
 - 1b. What adverse events and complications have been associated with aggressive medical therapy or renal artery angioplasty with stent placement?
2. What clinical, imaging, laboratory, and anatomic characteristics are associated with improved or worse outcomes when treating with either aggressive medical therapy alone or renal artery angioplasty with stent placement?

¹ JNC-5 is the 5th Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure. The JNC-5 guidelines, issued in 1993, marked a substantial change from previous guidelines in treatment recommendations for hypertension, including more aggressive blood pressure targets. The guidelines were issued around the same time that ACE inhibitors began to be used more routinely for patients with severe hypertension.

3. What treatment variables are associated with improved or worse outcomes of renal artery angioplasty with stent placement, including periprocedural medications, type of stent, use of distal protection devices, or other adjunct techniques?

Conclusions

Key Question 1: Clinical outcomes—Angioplasty with stent vs. aggressive medical therapy

There is no published evidence directly comparing angioplasty with stent placement and “aggressive” medical treatment with currently available drugs for ARAS (Table A). Therefore, this review covers direct comparisons of angioplasty with or without stent and various medical regimens, and indirect comparisons between angioplasty with stent, surgical interventions, various medical therapies, and natural history. All the studies reviewed either implicitly or explicitly included only patients with generally stable blood pressure, kidney function, and cardiovascular status. Patients with acute decompensation due to progressive ARAS were not included. Therefore this review does not pertain to this important class of patients.

Overall, the evidence does not currently support one treatment approach over the other for the general population of people with ARAS (Table B). Notably, almost two-thirds of the studies were of poor methodological quality and more than half were of limited applicability to the population of interest. A very limited evidence base directly compares angioplasty without stent placement and medical treatment. While there was a benefit in blood pressure after angioplasty, particularly in patients with bilateral disease, there was no difference in kidney function outcomes. Possibly there were no differences in mortality and cardiovascular event rates, although studies generally included too few patients and were of too short a duration to make definitive assessments regarding these clinical event outcomes. Comparison of adverse events and complications across the various interventions is difficult. However, it is clear that various complications after revascularization do occur in a small percentage of patients, and each of the antihypertensive drugs has associated adverse events.

Description of reviewed studies

No study directly compared angioplasty with stent placement to aggressive medical therapy (Table A). Two randomized controlled trials directly compared angioplasty without stent placement to medical treatment, with outcomes primarily reported at 6 and 12 months. A third randomized trial compared angioplasty without stent placement at the start of the trial to angioplasty delayed by 3 months in half of the remaining patients and medical treatment alone in the other patients. The remaining seven comparative studies (one of which was a nonrandomized subgroup of one of the randomized trials) compared multiple types of revascularization to a variety of medical treatments for a wide range of durations—from about 6 months to 7 years—in both prospective and retrospective studies.

Hundreds of studies of cohorts of patients receiving angioplasty, both prospective and retrospective, have been published since 1980. Of these, the 25 prospective studies that analyzed at least 30 patients who received angioplasty mostly after 1993 and reported long-term (6 months) outcomes of interest were reviewed. Few studies specifically evaluated the effect of medical treatments that are currently common in patients with ARAS. Only four cohort studies evaluated ACE inhibitors or “triple therapy,” treatment with three classes of antihypertensive agents. An additional eight natural history studies evaluated cohorts of patients who mostly received medical treatment (although for the most part this is not clear). Four surgical cohorts analyzed at least 100 patients who received angioplasty mostly after 1993 and reported long-term outcomes of interest. Thirty-seven of these studies reported on adverse events.

Mortality (study duration 6 months or greater, Table B)

One small randomized controlled trial of angioplasty (without stent) vs. medical treatment, 3 other comparative studies, and 31 cohort studies of various interventions reported mortality data. Although studies were generally too small to detect any but large differences in mortality rates, no differences in mortality were found between interventions, up to about 5 years. Very high mortality rates, over 40 percent within 6 years, occurred mostly in studies of patients with either high-grade stenosis (>75 percent) or bilateral disease.

Weak evidence suggests no difference in mortality rates with medical treatment alone or with angioplasty.

Kidney function (Table B)

The two randomized controlled trials of angioplasty vs. medical treatment and the seven other studies with direct comparisons between revascularization and medical treatment mostly found no clinical or statistically significant differences in kidney outcomes. Among 17 cohort studies of angioplasty with stent, improved kidney function ranged from 8 to 51 percent. There were small to modest changes in creatinine clearance (–2 to +8 mL/min) or serum creatinine (–0.1 to +0.2 mg/dL). Only a single cohort study of medical treatment reported change in serum creatinine over an average of 1.5 years, an increase of 0.3 mg/dL. Seven natural history studies found similar increases in serum creatinine or progressive decreases in kidney function.

Overall, cohort studies of angioplasty with stent placement found changes in kidney function similar to those found in the medical and natural history studies. However, only in the studies of angioplasty with stent placement were some patients reported to have improved kidney function. This implies that, at least in a subset of patients with ARAS, kidney function is more likely to improve after angioplasty with stent placement than with continued medical treatment.

There is acceptable evidence that overall there is no difference in kidney outcomes between patients treated medically only and those receiving angioplasty. However, improvements in kidney function were reported only among patients receiving angioplasty.

Blood pressure control (Table B)

Two trials of angioplasty vs. medical treatment, 7 other comparative studies, all 25 angioplasty studies, all 4 medical studies, 2 natural history studies, and 2 surgical cohort studies reported blood pressure outcomes. Both trials and most of the other comparative studies found some evidence of greater blood pressure improvement after angioplasty than with medical treatment, although the benefit of angioplasty may be limited to patients with bilateral disease. The cohort studies generally found better blood pressure control among patients treated medically alone than among those who received revascularization. However, almost all cohort studies of angioplasty with stent placement reported that some—up to 18 percent of patients—were cured of hypertension (generally defined as maintaining blood pressure control without medication).

Across all studies of angioplasty with stent placement, blood pressure fell after revascularization between 6-32/0-17 mm Hg. Among the medical and natural history studies, blood pressure generally decreased by 20-50/8-42 mm Hg with combinations of multiple antihypertensive drugs. It is not possible to draw conclusions about the relative effect of the different interventions on blood pressure measurements.

There is acceptable evidence that combination antihypertensive treatment results in large decreases in blood pressure. There is also acceptable evidence that angioplasty is more likely than medical treatment alone to result in better blood pressure control, including cure of hypertension.

Cardiovascular outcomes (Table B)

One trial of angioplasty vs. medical treatment and a comparative study of surgery and medical treatment reported cardiovascular outcomes. In the angioplasty trial, no differences were found in event rates for congestive heart failure, stroke, or myocardial infarction, regardless of intervention, for up to 54 months of followup. In the surgery trial, near-identical rates of a combined outcome of atherosclerotic cardiovascular event, death, diastolic hypertension, or worsening kidney function were found for surgery and medical treatment. The reporting of cardiovascular outcomes in cohort studies was inadequate to allow cross-study comparisons. No study of medical interventions reported cardiovascular outcomes.

There is weak evidence suggesting similar rates of cardiovascular events between interventions; however, it is likely that the studies were too small to detect different rates of cardiovascular events.

Restenosis rate (after angioplasty with stent placement only)

A total of 17 studies of angioplasty with stent placement evaluated restenosis rates during followup of 3 to 40 months; rates ranged from 10 to 21 percent. Only one study noted a statistically significantly higher rate of restenosis among those who had undergone stent placement for ostial lesions compared to those with nonostial lesions.

Adverse events (including 30-day mortality, Table B)

Adverse events were reported in 37 studies, including both angioplasty trials and one retrospective comparative trial. No direct comparisons were made of differences in adverse event rates between

interventions. Adverse events reported in 16 angioplasty studies included 30-day mortality in up to 3 percent of patients, transient deterioration of kidney function in 1 to 13 percent, renal artery or parenchymal injury in up to 5 percent, and periprocedural cardiovascular events in up to 3 percent. Other adverse events reported included hemorrhage and hematomas, and renal artery occlusion. Medical studies did not report mortality within 30 days of being followed. Adverse events related to blood pressure medications (ACE inhibitors, beta blockers, and hydralazine) included orthostatic hypotension, central nervous system symptoms, digestive symptoms, Raynaud's phenomenon, and others.

The evidence does not adequately assess the net harms due to adverse events and complications of medical treatment or angioplasty.

Key Question 2: Baseline predictors of outcomes (Table B)

Among the studies reviewed, the value of diagnostic tests either for predicting long-term outcomes or for helping determine the best treatment is unclear. A variety of indicators of the severity of ARAS and of health problems, such as poorer kidney function, worse blood pressure, and coexisting cardiovascular disease, predict poorer outcomes in patients with ARAS. The reviewed studies did not report any indicators that may predict improved outcomes.

Randomized controlled trials of angioplasty vs. medical treatment

Neither trial directly analyzed whether any baseline predictors, including diagnostic tests, would predict relative outcomes between interventions. However, in one trial patients with bilateral stenosis had larger decreases in blood pressure after angioplasty than with medical treatment, in contrast to patients with unilateral disease.

Other direct comparisons

Another randomized trial, comparing early vs. either delayed or no revascularization, found that in contrast to patients with unilateral disease, patients with bilateral disease had better improvement in diastolic blood pressure, but not in creatinine clearance. Captopril test, renogram, recent hypertension, and stenosis >80 percent were not predictors of either worse outcome overall or of which intervention would result in better outcomes.

Angioplasty and comparative studies that combined interventions for analyses

Worse baseline kidney function was associated with increased mortality, poor clinical outcomes, and relatively worse blood pressure after revascularization. A history or markers of some cardiovascular diseases were associated with increased mortality, poor clinical outcomes, and relatively worse kidney function after revascularization.

Age and beta blocker or diuretic use at baseline were not significant predictors of mortality or other clinical outcomes. Baseline captopril test, renogram, arterial norepinephrine, and ACE genotype were generally not associated with outcomes. The association between baseline predictors and outcomes was uncertain for several factors, including baseline kidney function as a predictor of followup kidney function, baseline cardiovascular disease as a predictor of blood pressure effect, percent stenosis before angioplasty, bilateral vs. unilateral ARAS, and sex.

Cross-study (indirect) comparisons

No conclusions could be reached from noncomparative studies regarding which patients might have better outcomes with or without revascularization.

Natural history studies

Associations between baseline variables and outcomes in natural history studies are generally weak, since each association was analyzed by one or two studies only. Among the studies, worse kidney function, higher grade stenosis, various markers of cardiac disease, and older age were associated with higher mortality or dialysis. Patients with nonspiral blood flow in the renal arteries had significant progression in kidney impairment, while those with spiral flow did not.

Key Question 3: Treatment variables as predictors of outcomes after angioplasty (Table B)

Two prospective cohort studies found no difference in blood pressure and kidney outcomes between patients who had stents placed and those who did not. However, no study that met eligibility criteria reported analyses of whether other periprocedural interventions, such as different drugs or different approaches, affected either complications or long-term outcomes.

Populations studied compared to the ongoing CORAL trial

The CORAL trial is enrolling patients with ARAS ≥ 60 percent and systolic hypertension who are on two or more antihypertensive medications. Those with advanced chronic kidney disease (serum creatinine ≥ 3.0 mg/dL) or very small kidneys (< 7 cm), as well as certain patients with cardiovascular disease, are being excluded. The two published randomized controlled trials that compare angioplasty to medical treatment alone used somewhat different eligibility criteria, suggesting that patients with a different severity of ARAS are being enrolled in CORAL. One trial used similar criteria for percent stenosis, but only in patients with unilateral disease; blood pressure and kidney function criteria were narrower, indicating that, on average, hypertension and kidney disease were less severe. The other trial included patients with lower grade stenosis (> 50 percent) but did not exclude patients with more severe hypertension and included patients with more severe kidney disease. Among the remaining studies that compared revascularization to medical treatment and the noncomparative cohort studies, there were a wide range of eligibility criteria, such that patients with stenosis as low as 50 percent were commonly included, and patients with either more or less severe blood pressure and kidney function than those in the CORAL trial were often included. Across studies, there was no clear evidence that differences in eligibility criteria were predictive of outcomes—except possibly that patients with bilateral disease had greater improvement after angioplasty compared to those with unilateral disease. It was evident, by comparing mortality rates or change in kidney function across studies, that the severity of disease of enrolled patients differed among studies, although eligibility criteria, including percent stenosis, blood pressure, kidney function, and others, were not clearly associated with overall outcomes. Furthermore, the evidence does not adequately address how differences in eligibility criteria may affect the comparison between angioplasty and medical treatment.

Remaining Issues

In comparison with the CORAL trial, for which patients are currently being enrolled, the two published randomized controlled trials comparing angioplasty to medical treatment alone differed either in whether patients with bilateral disease were included or the severity of hypertension and kidney disease allowed.

Other studies also varied widely in their eligibility criteria. Combining the criteria, studies could not be classified adequately based on their severity of ARAS. Overall, with the possible exception of inclusion of patients with bilateral or unilateral disease, the eligibility criteria (or the severity of disease) of the published studies were not predictive of outcomes in a manner that would be applicable to patients who are not being enrolled in the CORAL trial.

There are additional topics of interest that the CORAL trial may be able to evaluate, primarily through post hoc analyses, but that may require additional studies to address adequately. These include the value of different diagnostic tests to determine which intervention would be best for individual patients; other baseline characteristics as predictors of relative outcomes; the value of cointerventions at the time of angioplasty, alternative methods of performing angioplasty with stent placement, or alternative types of stents; and the effect of different combinations of antihypertensive medications with other interventions such as lipid lowering and antiplatelet drugs.

The challenge of treating ARAS to achieve the targeted outcomes of improved blood pressure control and preservation of kidney function lies in the significant overlap between etiologic factors of aortorenal vascular disease and parenchymal kidney disease. While diabetes mellitus, dyslipidemia, and elevated blood pressure are associated with atherosclerotic narrowing of the renal arteries and consequent worsening of blood pressure and kidney function, they are independently associated with direct kidney injury. In a great many cases, overcoming the renal artery lesion fails to improve hypertension or kidney function, which may be mediated not only by ARAS but also by underlying kidney disease. Systematically evaluating the role of ARAS in hypertension and kidney dysfunction will assist in determining whether intervention should be directed toward improving kidney perfusion through angioplasty with stent placement or more aggressively targeting the underlying factors of parenchymal kidney disease with combination medical therapy.

Additional randomized controlled trials would be required to address the issues that will not be covered by the CORAL trial. Without such trials, there is the risk that the findings of the CORAL trial will be broadened to be considered applicable to patients with less or more severe ARAS than those patients included in the CORAL trial.

In addition, the ARAS research community should consider how to improve and/or standardize definitions of ARAS and severity of disease. These considerations should be based on how these definitions and the disease severity scale would correlate with clinical outcomes. The CORAL trial and other studies of ARAS should use the current suggested methods for estimating kidney function, including preferential use of estimated glomerular filtration rate (GFR) over serum creatinine, and stage of chronic kidney disease. The community of clinicians and professional organizations involved in performing renal artery angioplasty should consider how to improve procedural techniques and minimize variations in techniques and clinical outcomes across the clinicians performing the interventions, as clinically warranted. This may require quality improvement and other types of studies.

As the reviewed studies did not explicitly address the population of patients who may need acute intervention because of rapid clinical deterioration, the conclusions of this review do not apply to these patients.

Full Report

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Table A. Summary of Reviewed Studies

Study type and intervention	No. of studies	Quality			Applicability			No. of subjects	Intervention years
		Good	Fair	Poor	High	Moderate	Low		
Randomized trial of angioplasty with stent vs. medical therapy	0							—	—
Randomized trial of angioplasty without stent or combination of angioplasty with and without stent vs. medical therapy	2 ²	2			1	1	103	1992-95 and no data ³	
Comparison studies of revascularization vs. medical therapy ¹	28	2	6	1	7	597	1981-2003 and no data ³		
Cohort studies of medical treatment	4	1	3	3	1	83	No data		
Cohort studies of natural history	8	3	5	5	3	721	1970-98 and no data ³		
Cohort studies of angioplasty with stent only	21	10	11	2	14	3,368	1989-2002 and no data ³		
Cohort studies including angioplasty with and without stent	4	3	1	1	2	427	1993-99		
Cohort studies of surgical revascularization	4	4			4	921	1980-2004		
Studies that reported adverse events	37					5,378	1980-2005 and no data ³		

¹ Combination angioplasty and surgery or surgery vs. medical therapy, either randomized or nonrandomized, or angioplasty vs. medical therapy in a nonrandomized study.

² One study had both a randomized and nonrandomized component.

³ Some studies did not report the intervention years.

Table B. Summary of Comparative Data in Treatments of Renal Artery Stenosis

Key Questions	Strength of evidence	Summary/conclusion/comments
Key Question 1: Comparisons		
Angioplasty with or without stent vs. medical treatment	N/A	<ul style="list-style-type: none"> • 2 RCTs evaluated long-term outcomes comparing angioplasty without stent placement to various medical treatments; 6 nonrandomized prospective or retrospective studies compared angioplasty (with or without stent) or surgical revascularization to various medical treatments. • 20 prospective cohorts that met criteria evaluated angioplasty with stent placement; 4 cohort studies evaluated angioplasty with or without stents. • Studies that compared stent placement to no stent placement found no difference in outcomes. • 3 cohort studies evaluated different antihypertensive medical treatments; no studies evaluated anti-hyperlipidemia or lipid-lowering drugs; 8 cohort studies evaluated the natural history of patients with RAS, on various management regimens.
Mortality	Weak	<ul style="list-style-type: none"> • 1 RCT, 3 nonrandomized comparative studies, and 31 cohort studies of various interventions suggest no difference in mortality up to about 5 years between revascularization and medical treatment.
Kidney function	Acceptable	<ul style="list-style-type: none"> • 2 RCTs found no difference in kidney outcomes, mostly at 6 and 12 months. • Among 7 other comparative studies, most found no difference in kidney outcomes, although 2 found some supporting evidence for better kidney function after angioplasty (with or without stent). • The cohort studies mostly support the conclusion that kidney outcomes are similar with either angioplasty or medical treatment, although improvements in kidney function were reported only among the angioplasty cohort studies.
Blood pressure	Acceptable	<ul style="list-style-type: none"> • The 2 RCTs both found some evidence of greater blood pressure improvement after angioplasty than with medical treatment, although this relative effect may be limited to patients with bilateral disease. • Most other comparative studies found larger blood pressure reductions among patients having revascularization than medical treatment alone, although the difference was often clinically small and statistically nonsignificant. However, 2 studies found larger reductions in blood pressure among patients treated without revascularization, although the differences were not statistically significant.

Table B. Summary of Comparative Data in Treatments of Renal Artery Stenosis (continued)

Key Questions	Strength of evidence	Summary/conclusion/comments
Key Question 1: Comparisons (continued)		
Blood pressure (continued)		<ul style="list-style-type: none"> Among cohort studies, larger reductions in blood pressure were found among medical treatment or natural history studies than in angioplasty studies, although the effect of pre-angioplasty antihypertensive medication use cannot be corrected for. Only in cohort studies of angioplasty were patients cured of hypertension, no longer requiring medication to maintain normal blood pressure.
Cardiovascular	Weak	<ul style="list-style-type: none"> 1 RCT found similar rates of cardiovascular events at 3 to 54 months of followup after angioplasty or with continued medical treatment. Reporting of cardiovascular outcomes was too sparse among studies to make meaningful indirect comparisons.
Adverse events	N/A	<ul style="list-style-type: none"> The evidence does not support meaningful conclusions about relative adverse events or complications from angioplasty compared to medical treatment.
Key Question 2: Baseline predictors of outcomes		
Angioplasty with or without stent vs. medical treatment	Weak	<ul style="list-style-type: none"> In one RCT, patients with bilateral disease had larger decreases in blood pressure after angioplasty compared with medical treatment, in contrast to patients with unilateral disease.
Angioplasty	N/A	<ul style="list-style-type: none"> 5 comparative studies and 15 cohort studies analyzed baseline variables as possible predictors of outcomes. Most of the comparative studies, however, did not distinguish between interventions in these analyses.
Baseline kidney function	Acceptable	<ul style="list-style-type: none"> The 10 studies that evaluated baseline kidney function generally found that poorer kidney function (with a wide range of definitions) predicted higher mortality, poorer clinical outcomes including cardiovascular events, and/or poorer blood pressure control. However, among 4 studies, 2 found that kidney function after angioplasty improved more among patients with worse baseline kidney function, 1 found no difference in effect among patients with different baseline kidney function, and 1 found less improvement in kidney function among patients with worse baseline kidney function.
Baseline RAS severity	Weak	<ul style="list-style-type: none"> 4 studies evaluated baseline percent stenosis. The studies were heterogeneous in their analyses and their conclusions. 1 found a borderline increase in mortality among patients with >70% stenosis. 1 found that higher percent stenosis was associated with higher blood pressure after revascularization. 1 found no association with either kidney function or diastolic blood pressure. 1 found that patients with higher grade stenosis had greater benefits in their kidney function than patients with lower grade stenosis.

Table B. Summary of Comparative Data in Treatments of Renal Artery Stenosis (continued)

Key Questions	Strength of evidence	Summary/conclusion/comments
Key Question 2: Baseline predictors of outcomes (continued)		
Baseline RAS severity (continued)		<ul style="list-style-type: none"> 11 studies evaluated whether bilateral vs. unilateral RAS was a predictor of outcomes. The studies were heterogeneous in their analyses and their conclusions. 2 found bilateral disease was associated with increased mortality, but 2 found no association (although 1 of these did find an association with a combined poor clinical outcome). Among 7 studies, most found no association with either change in kidney function or blood pressure, but 2 found that patients with bilateral disease had better improvement in blood pressure, and 1 found better improvement in kidney function than patients with unilateral disease.
Baseline cardiovascular disease	Acceptable	<ul style="list-style-type: none"> Among 6 studies, a range of cardiovascular measures, including history of disease, were found to be associated with increased risk of death, new cardiovascular events, or decreased likelihood of improvement in kidney function after revascularization. 2 studies, though, found that some baseline cardiovascular factors, including history of myocardial infarction, CHF, or hyperlipidemia, or reduced ejection fraction, did not predict increased mortality.
Diagnostic tests	Weak	<ul style="list-style-type: none"> 3 diagnostic tests were evaluated by 4 studies. The captopril test, renogram, and unilateral renin secretion were not associated with differential outcomes in blood pressure, kidney function, or mortality. 2 studies evaluated a resistance index of over 80%; 1 found that these patients had worse kidney and blood pressure outcomes and 1 found that they had better changes in both kidney function and blood pressure levels.
Demographics	Weak	<ul style="list-style-type: none"> Among 5 studies evaluating age, 1 found that older patients had higher followup blood pressure, 1 that they had lower followup blood pressure, and 3 found that after adjustment for other predictors, age was not associated with poor clinical outcomes. Among 3 studies evaluating sex, 2 found that men had worse outcomes than women, but 1 found no difference after adjustment for other predictors.
Medical treatment	N/A	<ul style="list-style-type: none"> No study evaluated potential predictors of outcomes.
Natural history	N/A	<ul style="list-style-type: none"> 4 natural history studies examined various predictors, 2 of which performed multivariate analyses.
Baseline kidney function	Weak	<ul style="list-style-type: none"> 1 study found that lower baseline GFR was independently associated with higher mortality or dialysis.
Baseline RAS severity	Weak	<ul style="list-style-type: none"> 2 studies found that higher grade stenosis was independently associated with higher mortality (1 by multivariate, 1 univariate analysis); 1 study found that bilateral disease was not associated with kidney disease prognosis.

Table B. Summary of Comparative Data in Treatments of Renal Artery Stenosis (continued)

Key Questions	Strength of evidence	Summary/conclusion/comments
Key Question 2: Baseline predictors of outcomes (continued)		
Baseline cardiovascular disease	Weak	<ul style="list-style-type: none">1 study found that various markers of cardiac disease predicted mortality in patients with coronary artery disease and RAS.
Diagnostic tests	Weak	<ul style="list-style-type: none">1 study found that patients with nonspiral blood flow in the renal arteries had significant progression in kidney impairment, while those with spiral flow did not.
Demographics	Weak	<ul style="list-style-type: none">1 study found that older age predicted mortality in patients with coronary artery disease and RAS.
Key Question 3: Effect of periprocedural interventions on outcomes		
Angioplasty with or without stent	Weak	<ul style="list-style-type: none">2 studies found no difference in blood pressure and kidney outcomes between patients who had stents placed and those who did not.
Other interventions	N/A	<ul style="list-style-type: none">No study that met eligibility criteria reported analyses of whether other periprocedural interventions, such as different drugs or different approaches, affected either complications or long-term outcomes.

Abbreviations: CHF = congestive heart failure; GFR = glomerular filtration rate (or creatinine clearance); N/A = not applicable; RAS = renal artery stenosis; RCT = randomized controlled trial.