Comparative Effectiveness Review
Number 179

Effective Health Care Program

Renal Artery Stenosis Management Strategies: An Updated Comparative Effectiveness Review

Executive Summary

Background

Atherosclerotic renal artery stenosis (ARAS) is increasingly common in an aging population with rising prevalence of diabetes, hypertension, obesity, dyslipidemia, and vascular disease. The goals of treatment are improvement in uncontrolled hypertension, preservation or salvage of kidney function, prevention or treatment of cardiac syndromes such as pulmonary edema or unstable angina, and ultimately improved survival. Treatment alternatives include medical therapy alone or renal artery revascularization with continued medical therapy. Medical therapy generally involves aggressive therapy with multiple antihypertensives, antilipidemics, and antiplatelet agents. Most commonly, revascularization is achieved through percutaneous transluminal renal angioplasty with stent placement (PTRAS) across the stenosis. Open surgical revascularization, once common, is generally reserved for patients who have complicated renal artery anatomy or who require aortic repair. After revascularization, patients generally continue aggressive medical therapy. The Tufts Evidence-based Practice Center conducted a Comparative Effectiveness Review of management strategies for ARAS in 2006, with an update in 2007. The review concluded that the evidence did not support one treatment approach over another for the general population of people with ARAS. There was weak or inadequate evidence for most interventions and outcomes and for whether any clinical or intervention characteristics affect outcomes.

Effective Health Care Program

The Effective Health Care Program was initiated in 2005 to provide valid evidence about the comparative effectiveness of different medical interventions. The object is to help consumers, health care providers, and others in making informed choices among treatment alternatives. Through its Comparative Effectiveness Reviews, the program supports systematic appraisals of existing scientific evidence regarding treatments for high-priority health conditions. It also promotes and generates new scientific evidence by identifying gaps in existing scientific evidence and supporting new research. The program puts special emphasis on translating findings into a variety of useful formats for different stakeholders, including consumers.

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Objectives

We sought to summarize the evidence evaluating the comparative effectiveness and safety of PTRAS, surgical revascularization, and medical therapy to treat ARAS in regard to clinically important outcomes. We evaluated what clinical, imaging, laboratory, and anatomic characteristics, and what PTRAS treatment variables are associated with outcomes.

Data Sources

We searched MEDLINE®, Embase®, the Cochrane Central Register of Controlled Trials, and Cochrane Database of Systematic Reviews from inception to March 16, 2016. We also included still-eligible studies from the original reports and screened studies from relevant existing systematic reviews; recent kidney, urology, and vascular surgery conference proceedings; and the U.S. Food and Drug Administration, World Health Organization, and ClinicalTrials.gov databases. Furthermore, we solicited studies via Scientific Information Packets from manufacturers.

Review Methods

We included comparative studies of any design of PTRAS, medical therapy, and/or surgical revascularization (where renal artery revascularization was the most common primary indication for surgery). We also included prospective studies of PTRAS (N ≥30), medical therapy alone (N ≥10), and surgery (N ≥10 if prospective, N ≥100 if retrospective). We further included the 20 most recently published case reports of patients with acute decompensation due to ARAS. The assessed outcomes included all-cause and cardiovascular mortality, cardiovascular events (including congestive heart failure and coronary or cerebral artery revascularization), renal replacement therapy (RRT) and other kidney events, hypertensive crises and other hypertension-related events, kidney function, blood pressure (BP) control, medication use, and adverse events. Clinical heterogeneity in terms of study design, particularly heterogeneity related to patient eligibility criteria, precluded meta-analysis of comparative studies; heterogeneity of outcome definitions and results precluded meaningful meta-analysis of observational studies.

Results

From 1,454 citations from the updated search, other literature sources, and the original reports, we included 78 relevant studies and 20 case reports. Nine randomized controlled trials (RCTs) and 11 other comparative studies compared treatment options; 67 individual cohorts of patients (in 63 studies) were treated with PTRAS in prospective studies; 20 cohorts of patients (in 17 studies) were treated with medical therapy alone in prospective studies; and 4 eligible cohorts of patients were treated surgically. Studies are double-counted because cohorts came from single-group and comparative studies. Findings are summarized by intervention and Key Question in Table A.

Comparative Studies

RCTs of PTRAS versus medical therapy were limited in their applicability to only patients for whom there was clinical equipoise between the two options. Patients with acute decompensation, including pulmonary edema or rapidly declining kidney function, make up about 23 percent of patients presenting with ARAS but were underrepresented in trials. Six RCTs found no statistically significant differences or, overall, minimal clinically important differences in mortality, RRT, cardiovascular events, or pulmonary edema, but the RCTs were not powered for these outcomes. Six RCTs mostly found no statistically significant difference in change in kidney function and seven RCTs mostly found no difference in BP control. Procedural adverse events were rare and no medication-related adverse events were reported. Effect size estimates were generally imprecise, and there was inconsistency in effect size estimates across studies. One RCT that compared open surgical revascularization with medical therapy alone found no statistically significant differences in mortality, RRT, or BP control. One RCT that compared PTRAS and surgery found no statistically significant difference in mortality, kidney function, or BP. While nonrandomized comparative studies did not require clinical equipoise between treatments, they failed to adequately account for fundamental differences between patients who undergo PTRAS and those who remain on medical therapy alone, or between those who undergo PTRAS or surgery. However, nonrandomized studies of PTRAS versus medical therapy found no statistically significant difference in mortality, but mostly found that PTRAS improved kidney function (e.g., 7–28% of participants had improvement with PTRAS vs. 6–8% with medical therapy) and BP control (e.g., 5 of 6 studies found net change in systolic BP of about −5 to −16 mmHg, favoring PTRAS) more than medical therapy. Studies of PTRAS versus surgery found no statistically significant difference in mortality or BP control, but one study found that kidney function improvement was more common after surgery (52% of patients) than PTRAS (24%).

Noncomparative Studies

The review summarizes clinical event rates and changes in kidney function and BP for the single-intervention studies. All 20 case reports describe patients who had clinical and symptomologic improvement (particularly related to pulmonary edema, severe acute kidney injury or RRT, and malignant hypertension) after revascularization.

Subgroup Analyses

Two RCTs found no patient characteristics that were significantly associated with different outcomes between PTRAS and medical therapy. A retrospective comparative study found that patients presenting with flash pulmonary edema or with both rapidly declining kidney function and refractory hypertension had decreased mortality with PTRAS (vs. medical therapy) compared with other patients. In single-intervention studies, worse pre-PTRAS kidney function or BP was generally associated with better improvement in these outcomes, and worse kidney function was associated with increased death. Studies were inconsistent regarding whether bilateral disease was associated with outcomes. In general, patients with histories of cardiovascular disease were at increased risk of adverse clinical outcomes, including death. In two medical therapy studies, having flash pulmonary edema, but not rapid kidney function decline or refractory hypertension, was associated with increased death or, separately, cardiovascular events but not RRT (1 study); patients with worse kidney function or with proteinuria were at significantly increased risk of RRT but not death. Two studies examined the association between specific medications and clinical outcomes, both of which found a strong association between statin use and reduced death, RRT, and cardiovascular outcomes, but conflicting findings regarding association of angiotensin inhibitors and outcomes. One study found no association between beta blocker use and outcomes. Two studies found no difference in composite cardiovascular and renal outcomes by age. In three PTRAS studies, use of gold-coated stents, sirolimus eluting stents, embolic protection devices, and intraluminal brachytherapy were not associated with improved outcomes.

Conclusions

Because of important limitations in the evidence base, there is low strength of evidence for all outcomes regarding the relative benefit of PTRAS and medical therapy alone for patients with ARAS. An important caveat in interpreting the results of RCTs, which lowered the overall strength of evidence, is their restriction to patients for whom there is clinical equipoise regarding the benefit between revascularization and medical therapy alone. Patients and clinicians had to agree to the possibility of not having PTRAS to be included in a trial. Because there is a strong belief that PTRAS is superior to medical therapy alone in the one-quarter of patients with ARAS who present with pulmonary edema or rapidly declining kidney function, these patients were generally not included in trials. Therefore, the RCTs may not apply to these patients. There is an intrinsic discordance between the RCTs that ask "How does PTRAS compare with current medical therapy?" and observational studies that, for the most part, ask either "How effective is medical therapy for patients who are thought not to require revascularization?" or "How effective is revascularization when used in patients who are thought to require it?" (usually because of "failed" medical therapy). There were several limitations to the evidence. Populations of eligible patients varied between and within studies. Only the CORAL (Cardiovascular Outcomes in Renal Atherosclerotic Lesions) trial explicitly incorporated translesional pressure gradient measurements into its eligibility criteria and assessment of stenosis severity. Other studies that did not diagnose severe renal artery stenosis as definitively may be biased to the null, since one would not expect revascularization to be as effective in patients with nonsevere stenosis. Not only did definitions of ARAS vary (affecting eligibility criteria), but the studies also were highly heterogeneous in terms of definitions of outcomes, particularly clinical and categorical outcomes related to BP control and kidney function. Conclusions across studies about incidence and relative rates of these outcomes are therefore limited. Furthermore, most studies (particularly the single-group studies) included and analyzed all-comers who had the intervention of interest, regardless of baseline kidney function or BP. This may also have biased the effect of the interventions toward the null as, for example, patients with normal kidney function at baseline would not be expected to have any improvement in kidney function with treatment. In addition, effect size estimates, particularly for clinical outcomes, were generally imprecise, and findings were commonly inconsistent across studies. Only one trial of PTRAS versus medical therapy had a primary clinical outcome (CORAL: composite cardiovascular and kidney events) and none were explicitly adequately powered for clinical outcomes. Also, while nonrandomized trials did not require clinical equipoise between treatments, they were inadequately adjusted to account for underlying differences between patients undergoing different interventions.

Thus, there is a low strength of evidence of no statistically significant or minimal clinically important difference in

important clinical outcomes (death, cardiovascular events, RRT) or BP control between PTRAS and medical therapy alone, but this conclusion is most applicable to those patients for whom there is clinical equipoise between the two treatments. There is low strength of evidence that kidney function may be improved in patients who undergo PTRAS versus medical therapy based on comparative studies and the indirect comparison between cohorts of patients who had PTRAS or continued medical therapy. Clinically important adverse events related to PTRAS are rare; however, studies generally failed to report medication-related adverse events.

Data on adverse events were, overall, sparse, particularly for medical therapy. While rates of PTRAS complications varied across studies, in the RCTs, which used rigorous criteria for enrolling and implementing PTRAS and prospectively collected adverse event data, complication rates were low.

Analyses of predictors of outcomes after PTRAS were mostly inconsistent, but a single observational study found that a subset of patients with flash pulmonary edema, rapidly declining kidney function, and refractory hypertension fared better with PTRAS than medical therapy, in contrast with other subpopulations of patients. Notably, though, this population was generally excluded from the RCTs. However, this finding comports with the generally good outcomes seen in case reports of patients with acute decompensation. Otherwise, the most consistent, although not universal, finding was that patients with worse kidney function or BP were more likely to have improvement in those outcomes after PTRAS than patients with less bad kidney function or BP. The evidence, however, does not provide support for any given PTRAS-related technique.

Since the original Agency for Healthcare Research and Quality review, new RCTs and more comprehensive nonrandomized and noncomparative studies have become available. Although limitations in the RCTs and other evidence remain, for patients similar to those enrolled in the RCTs (for whom there is clinical equipoise between PTRAS and medical therapy), we now have direct evidence of no statistically significant or minimal clinically important difference in long-term outcomes between treatment options. We also have more complete, if still inconclusive, evidence about which patients may best respond to PTRAS.

New studies or reanalyses of data in existing studies are needed to better understand the comparative effectiveness of PTRAS versus medical therapy for those patients who most commonly undergo PTRAS—namely, those who have a “clinical indication” for revascularization under current standard practice. Given the difficulties recruiting into RCTs a broad spectrum of study subjects who are fully representative of patients with ARAS, new analyses are needed of large databases, such as potentially a registry, that adequately account for fundamental differences between patients who have revascularization and those who remain on medical therapy alone. The larger existing trials and other studies also can be reanalyzed to further evaluate potential subgroup differences or predictors of outcomes (e.g., based on stenosis severity or cointerventions) Based on the evidence, subsets of patients benefit from revascularization (at least in terms of improved kidney function and BP control), but the evidence does not clearly define who these patients are. As evidenced from case reports, patients with acute decompensation can benefit from revascularization, but a study that includes an unbiased sample of these patients is needed.

Table A. Summary of findings by intervention comparisons and Key Questions

Variable	Topic /Findings
	PTRAS vs. medical therapy, overall
Risk of bias	Seven RCTs and 8 NRCSs compared PTRAS and medical therapy. Risk-of-bias concerns included unblinded outcome assessment, attrition bias, and selection bias, and selective outcome reporting among the NRCSs. The RCTs may not be fully representative of patients typically considering or undergoing PTRAS since both they and their clinicians had to have equipoise between PTRAS and continued medical therapy alone. Notably, the RCTs excluded patients with acute decompensation, which by 1 recent prospective study's estimate represents about half of patients presenting with ARAS. The NRCSs compared fundamentally different cohorts of patients—those for whom it was decided that PTRAS was indicated and those for whom PTRAS was not considered necessary (or an appropriate option). The NRCSs did not adequately adjust for the differences between patient cohorts.
	PTRAS vs. medical therapy, Key Question 1: Effects of interventions (comparative)
Mortality	Four RCTs and 5 NRCSs found no statistically significant difference or MCID between interventions, but no study was adequately powered for mortality.
RRT	Four RCTs and 5 NRCSs had wide differences in rates of RRT across studies. Imprecise estimates found no statistically significant differences or MCID in incident RRT between interventions.
Cardiovascular outcomes	Four RCTs and 3 NRCSs were heterogeneous in which outcomes were reported. No statistically significant differences or MCID between interventions were found.
Pulmonary edema	Three RCTs reported on incident pulmonary edema or CHF. No statistically significant differences or MCID between interventions were found.
Kidney function	Six RCTs and 7 NRCSs reported on changes in kidney function. Five of the RCTs found no statistically significant differences in either likelihood of improvement (or worsening) of kidney function or measures of kidney function (GFR or SCr). In contrast, 2 of 3 NRCSs found that patients' kidney function was more likely to improve (or less likely to worsen) after PTRAS than with medical therapy alone and 3 of 7 found larger improvements in measures of kidney function after PTRAS than on medical therapy alone; however, these analyses were not adjusted for underlying differences between the cohorts.
BP control	Six RCTs and 7 NRCSs reported on BP control. One RCT found no difference in improvement (or worsening) of BP control; 1 found that HTN was much more likely to be cured (PTRAS 11% vs. medical 0%), but similar percentages of patients had failure to improve (PTRAS 22% vs. medical 29%). All but 1 RCT found no statistically significant difference in changes in measured BP. Two trials both found that patients on average were prescribed 0.2 fewer antihypertensive medications than those who remained on medical therapy only. The 7 NRCSs reported highly heterogeneous results, except that all but 1 found no difference in changes in number of antihypertensive medications.
Adverse events	Five RCTs and 4 NRCSs reported on adverse events, but only related to PTRAS. PTRAS-associated adverse events included periprocedural all-caus deaths (about 0.5%), angioplasty-related dissection and other vessel injuries, vessel occlusion, distal embolization, groin hematoma or hemorrhage, acute kidney injury, and stent dislocation.
	PTRAS vs. medical therapy, Key Question 2: Patient factors predicting effects (comparative)
Patient factors	Three RCTs reported on analyses of patient factors as predictors of outcomes. Two RCTs found no factor that differentially predicted outcomes (between PTRAS and medical therapy); 1 prospective cohort found that patients with flash pulmonary edema or with both rapidly declining kidney function and refractory HTN (prerandomization) had significantly better outcomes after PTRAS.
	PTRAS vs. medical therapy, Key Question 3: Treatment factors predicting effects (comparative)
Treatment factors	No comparative studies addressed differences in treatment factors as a predictor of outcomes in the comparison of PTRAS vs. medical therapy.

Table A. Summary of findings by intervention comparisons and Key Questions (continued)

	Surgery vs. medical therapy, overall
Risk of bias	One RCT compared only surgery and medical therapy. The study was of low (or unclear) risk of bias.
	Surgery vs. medical therapy, Key Question 1: Effects of interventions (comparative)
Outcomes	No statistically significant differences or MCID were found between interventions for death, dialysis-free survival, or BP control. Adverse events were not reported.
	Surgery vs. medical therapy, Key Question 2: Patient factors predicting effects (comparative)
Patient factors	Patients with baseline elevated SCr had better outcomes if surgically revascularized, in contrast with the total cohort, but no significant interactions were found.
	Surgery vs. medical therapy, Key Question 3: Treatment factors predicting effects (comparative)
Treatment factors	No comparative studies addressed differences in treatment factors as a predictor of outcomes in the comparison of surgery vs. medical therapy.
	Surgery vs. PTRAS, overall
Risk of bias	One RCT and 3 NRCSs compared surgery and PTRAS. The RCT was of low (or unclear) risk of bias. The NRCSs suffered from selection and attrition biases; they also did not adjust their analyses for differences between patient cohorts.
	Surgery vs. PTRAS, Key Question 1: Effects of interventions (comparative)
Outcomes	One RCT found no difference in death, change in kidney function (SCr), BP, or antihypertensive treatment requirement. Periprocedural adverse events occurred in both groups. Two of 3 NRCSs reported only limited data, reporting no differences in mortality or HTN. One NRCS found similar rates of death and RRT, long-term kidney function, and BP control; perioperative complications were significantly more common with open surgery than with PTRAS.
	Surgery vs. PTRAS, Key Question 2: Patient factors predicting effects (comparative)
Patient factors	One of 2 studies found that patients with HTN as their indication for intervention were more likely to have better outcomes with surgery than PTRAS, but patients with renal salvage as their indication had similar outcomes regardless of revascularization approach; but the interaction between subgroups and interventions was not analyzed. The second study found similar associations between renal resistive index and mortality regardless of revascularization approach.
	Surgery vs. PTRAS, Key Question 3: Treatment factors predicting effects (comparative)
Treatment factors	No comparative studies addressed differences in treatment factors as a predictor of outcomes in the comparison of surgery vs. PTRAS.
	PTRAS, overall
Risk of bias	Sixty-seven cohorts of patients (in 63 prospective studies) reported outcomes after PTRAS. The studies were highly heterogeneous in both their included patients, indications for PTRAS, and specific PTRAS techniques. Many of the studies were deemed to be at high risk of bias for failure to adjust for different lengths of followup, attrition bias, and selective outcome reporting.

Table A. Summary of findings by intervention comparisons and Key Questions (continued)

	PTRAS, Key Question 1: Effects of interventions (noncomparative)
Mortality	In 31 studies, mortality ranged from 0 to 53% after 6 months to 5 years of followup (1 study reported at 15 years). Other than a general trend toward increased death with longer term followup, there was no clear explanation across studies for the difference in mortality.
RRT	In 7 studies, incident RRT occurred in 2.3 to 23% of patients between 1.25 and 5 years, but with no clear explanation of the heterogeneity across studies, including length of followup.
Cardiovascular outcomes	In 12 studies, various cardiovascular outcomes were reported to occur, but with highly heterogeneous percentages of patients (including CHF, 0-83%; MI, 1-82%; stroke, 1-19%).
Kidney function	In 4 studies, 2 to 82% of patients had episodes of acute kidney injury. In 21 studies, kidney function improved in 12 to 82% and worsened in 4 to 37% of patients. Twenty-one studies had a median change in GFR of 0 mL/min (range −9 to 10 mL/mL). There was no clear explanation across studies for the wide heterogeneity in change in kidney function.
BP control	In 2 studies, 0 and 4% of patients had new-onset HTN. In 19 studies, BP improved in 4 to 69% and stabilized or worsened in 7 to 67% of patients. In 36 studies, median changes in SBP were −17 mmHg (range, −51 to 28) and in DBP were −6 mmHg (range, −30 to 5). In 30 studies, the median change in number of antihypertensive medications was −0.3 (−1.4 to 1.2). There was no clear explanation across studies for the wide heterogeneity in change in BP control.
Adverse events	In 19 studies, adverse events included postoperative death, RRT, and acute renal failure, as well as severe bleeding, dissection, unplanned surgery, and thrombosis.
	PTRAS, Key Question 2: Patient factors predicting effects (noncomparative)
Patient factors	Twenty studies reported on analyses of patient factors as predictors of outcomes after PTRAS. Overall, the studies were heterogeneous in their analyses and findings. Among predictors analyzed by at least 3 studies, those with some indication of an association with favorable kidney and BP outcomes included worse pre-PTRAS kidney function (in 6 of 13 studies), bilateral stenosis (in 3 of 9 studies), higher pre-PTRAS BP (in 3 of 5 studies), higher grade of stenosis (in 2 of 5 studies). Absence of cardiovascular disease, female sex, and younger age were found to be significantly associated with better outcomes in only 1 of 4 or 5 studies. However, in contradistinction to their associations with intermediate outcomes, death, RRT, and composite clinical outcomes were associated with worse pre-PTRAS kidney function (in 3 of 5 studies), bilateral stenosis (in 2 of 5 studies), cardiovascular disease (in 2 of 4 studies), and CHF (in 3 of 5 studies). In addition, smoking and diabetes were associated with clinical events in only 1 of either 3 or 4 studies.
	PTRAS, Key Question 3: Treatment factors predicting effects (noncomparative)
Treatment factors	Three studies addressed differences in treatment factors as predictors of outcomes. No differences in outcomes were found with or without gold-coated stents, sirolimus eluting stents, embolic protection devices, or intraluminal brachytherapy.
	Medical therapy, overall
Risk of bias	Twenty cohorts of patients (in 17 prospective studies) reported outcomes in patients receiving medical therapy alone. The studies were highly heterogeneous in both their included patients and specific medical treatments (both within and across studies). Many of the studies were deemed to be at high risk of bias for failure to adjust for different lengths of followup and attrition bias.
	Medical therapy, Key Question 1: Effects of interventions (noncomparative)
Mortality	In 10 studies, mortality ranged from 9 to 56% after 2 to 9 years of followup. Other than a general trend toward increased death with longer term followup, there was no clear explanation across studies for the difference in mortality.

Table A. Summary of findings by intervention comparisons and Key Questions (continued)

	Medical therapy, Key Question 1: Effects of interventions (noncomparative) (continued)
RRT	In 7 studies, incident RRT occurred in 2 to 18% of patients between 3 and 5 years, but with no clear explanation of the heterogeneity across studies, including length of followup.
Cardiovascular outcomes	In 9 studies, various cardiovascular outcomes were reported to occur, but with highly heterogeneous percentages of patients (including CHF,1.4-13%; MI, 2.5-83%; stroke, 2.5-23%).
Kidney function	Ten studies reported on kidney function outcomes. Kidney function improved in 0 to 26% of patients and deteriorated in 19 to 38% of patients (4 studies). In 3 studies, GFR changed by −0.7 to 8 mL/min between 1 and 6 years of followup and SCr changed by −0.1 and 1.3 mg/dL at between 1 and 5 years of followup. In 4 studies, 2 to 82% of patients had episodes of acute kidney injury. In 21 studies, kidney function improved in 12 to 82% and worsened in 4 to 37% of patients. Twenty-one studies had a median change in GFR of 0 mL/min (range, −9 to 10 mL/mL). There was no clear explanation across studies for the wide heterogeneity in change in kidney function.
BP control	Twelve studies reported on BP outcomes. In 1 study, 4% of patients became newly hypertensive and 0 had a hypertensive crisis. In 10 studies, SBP changed by −6 to −22 mmHg and DBP by −1 to −13 mmHg. In 2 studies, the number of antihypertensive medications was unchanged after 1.75 years of followup and increased by 1.4 medications after 3.6 years.
ACEi/ARB use	Two studies found increases in the percentage of patients on ACEi or ARB after 1 year—from 79 to 83% in 1 study and from 38 to 43% in the other.
Adverse events	No study reported on adverse events related to medication use.
	Medical therapy, Key Question 2: Patient factors predicting effects (noncomparative)
Patient factors	Two studies reported on patient-level predictors of clinical outcomes. In 1 study each, statistically significant associations were found between flash pulmonary edema and both death and cardiovascular events, and between lower GFR and RRT, and a near-significant association was found between proteinuria and RRT. No associations were found between flash pulmonary edema and RRT, lower GFR and death, or rapid kidney function deterioration, refractory HTN, sex, or history of coronary artery disease and clinical outcomes.
	Medical therapy, Key Question 3: Treatment factors predicting effects (noncomparative)
Treatment factors	Two studies addressed differences in treatment factors as predictors of outcomes. One study found no association between beta blockers or ACEi and death or RRT, but the second study found that ACEi use was associated with reduced cardiovascular events and statin use was associated with reduced cardiorenal events, death, and RRT.
	Surgical revascularization, overall
Risk of bias	Four studies (3 retrospective, 1 prospective) reported outcomes in patients receiving surgical revascularization. The studies were highly heterogeneous in both their included patients and specific surgical techniques (both within and across studies). The retrospective studies were subject to high risk of bias related to attrition, selective reporting, and lack of adjustment for different lengths of followup. The prospective study was deemed low risk of bias.
	Surgical revascularization, Key Question 1: Effects of interventions (noncomparative)
Mortality	In 4 studies, mortality ranged from 26 to 36% after about 5 years of followup.
RRT	In 2 studies, incident RRT (or combined renal failure outcomes) occurred in 38 and 74% of patients at about 5 years of followup.

Table A. Summary of findings by intervention comparisons and Key Questions (continued)

	Surgical revascularization, Key Question 1: Effects of interventions (noncomparative) (continued)
Cardiovascular outcomes	One study reported new-onset angina in 10% of patients and coronary revascularization in 8% after a mean of 10 years; 6% of patients suffered an MI and 4% a stroke.
Kidney function	Two studies reported on kidney function; in 1, 43% of patients had improved kidney function, 10% had worsened kidney function, and 70% of those who were on RRT prior to surgery discontinued dialysis. Mean GFR increased by 7 mL/min after about 5 years (1 study), but mean SCr increased by 0.1 mg/dL at 4 years (in the second study).
BP control	In 4 studies, improved or cured HTN occurred in 53 to 82% of patients. Two studies found large improvements in SBP (−53 and −31 mmHg) at 4 to 5 years, but 1 found a large improvement in DBP (−23 mmHg) and the other study a small, not statistically significant improvement (−8 mmHg).
Adverse events	Three studies reported surgery-related adverse events, including postoperative mortality, bleeding, arterial occlusion or thrombosis, infection, and distal embolization.
	Surgical revascularization, Key Question 2: Patient factors predicting effects (noncomparative)
Patient factors	Two studies reported on patient-level predictors of clinical outcomes. Both studies found that patients who had a history of cardiovascular disease, diabetes, or worse kidney function, or who were older were at increased risk of all-cause death, cardiovascular death, or either death or RRT. In 1 study each, those with higher SBP were at lower risk of combined death or RRT but not all-cause death alone, preoperative angina was associated with cardiovascular mortality, and resistive index >0.8 was associated with all-cause death. Race, sex, DBP, and number of antihypertensive medications were not associated with outcomes.
	Surgical revascularization, Key Question 3: Treatment factors predicting effects (noncomparative)
Treatment factors	One study addressed differences in treatment factors as predictors of outcomes. Bilateral repair and whether renal artery repair was combined with aortic repair were not associated with death in adjusted analyses.
	Acute decompensation case reports, Key Question 1: Effects of interventions (noncomparative)
Outcomes	Twenty case reports of patients with acute decompensation of their RAS universally presented patients who, after revascularization (by PTRAS or surgery), improved symptomatically and with improved kidney function and/or BP control. Two case reports presented patients who, after an episode of acute decompensation, continued medical therapy alone for 10 months in 1 case and 5 years in the other, but who subsequently had a second episode of decompensation that resulted in clinical improvement. All 8 cases who required acute hemodialysis no longer required RRT after revascularization.

Abbreviations: ACEi = angiotensin converting enzyme inhibitor, ARAS = atherosclerotic renal artery stenosis, ARB = angiotensin receptor blocker, BP = blood pressure, CHF = congestive heart failure, DBP = diastolic blood pressure, GFR = glomerular filtration rate, HTN = hypertension, MCID = minimal clinically important difference, MI = myocardial infarction, NRCS = nonrandomized comparative study, PTRAS = percutaneous transluminal renal angioplasty with stent placement, RCT = randomized controlled trial, RRT = renal replacement therapy, SBP = systolic blood pressure, SCr = serum creatinine.

Full Report

This executive summary is part of the following document: Balk EM, Raman G, Adam GP, Halladay CW, Langberg VN, Azodo IA, Trikalinos TA. Renal Artery Stenosis Management Strategies: An Updated Comparative Effectiveness Review. Comparative Effectiveness Review No. 179. (Prepared by the Brown Evidence-based Practice Center under Contract No. 290-2015-00002-I.) AHRQ Publication No. 16-EHC026-EF. Rockville, MD: Agency for Healthcare Research and Quality; August 2016. www.effectivehealthcare.ahrq.gov/reports/final.cfm.

AHRQ Pub. No.16-EHC026-1-EF
August 2016