Comparative Effectiveness Review
Number 179

Renal Artery Stenosis Management Strategies: An Updated Comparative Effectiveness Review

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This report is based on research conducted by the Brown Evidence-based Practice Center (EPC) under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. 290-2015-00002-I). The findings and conclusions in this document are those of the authors, who are responsible for its contents; the findings and conclusions do not necessarily represent the views of AHRQ. Therefore, no statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

The information in this report is intended to help health care decisionmakers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of health care services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

This report may periodically be assessed for the currency of conclusions. If an assessment is done, the resulting surveillance report describing the methodology and findings will be found on the Effective Health Care Program Web site at www.effectivehealthcare.ahrq.gov. Search on the title of the report.

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of systematic reviews to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. These reviews provide comprehensive, science-based information on common, costly medical conditions, and new health care technologies and strategies.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews can help clarify whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about AHRQ EPC systematic reviews, see www.effectivehealthcare.ahrq.gov/reference/purpose.cfm.

AHRQ expects that these systematic reviews will be helpful to health plans, providers, purchasers, government programs, and the health care system as a whole. Transparency and stakeholder input are essential to the Effective Health Care Program. Please visit the Web site (www.effectivehealthcare.ahrq.gov) to see draft research questions and reports or to join an email list to learn about new program products and opportunities for input.

If you have comments on this systematic review, they may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to epc@ahrq.hhs.gov.

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Technical Expert Panel

In designing the study questions and methodology at the outset of this report, the EPC consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicted opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodologic approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts.

Technical Experts must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

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Peer Reviewers

Prior to publication of the final evidence report, EPCs sought input from independent Peer Reviewers without financial conflicts of interest. However, the conclusions and synthesis of the scientific literature presented in this report do not necessarily represent the views of individual reviewers.

Peer Reviewers must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential nonfinancial conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential nonfinancial conflicts of interest identified.

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Renal Artery Stenosis Management Strategies: An Updated Comparative Effectiveness Review

Structured Abstract

Background. Treatment options for atherosclerotic renal artery stenosis (ARAS) include medical therapy alone or renal artery revascularization with continued medical therapy, most commonly by percutaneous transluminal renal angioplasty with stent placement (PTRAS). This review updates a prior Comparative Effectiveness Review of management strategies for ARAS from 2006, which was updated in 2007.

Objectives. Compare the effectiveness and safety of PTRAS versus medical therapy, and also versus surgical revascularization, to treat ARAS. Identify predictors of outcomes by intervention.

Data sources. MEDLINE®, Embase®, the Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews from inception to March 16, 2016; eligible studies from the original reports and other relevant existing systematic reviews; and other sources.

Review methods. We included studies comparing ARAS interventions, single-group prospective PTRAS and medical therapy studies, and prospective or retrospective surgery studies. We also included 20 recent case reports of patients with acute ARAS decompensation. Outcomes included all-cause and cardiovascular mortality, cardiovascular events, renal replacement therapy (RRT), other kidney events and function, hypertension events, blood pressure (BP), medication use, and adverse events.

Results. From 1,454 citations, we included 78 studies and 20 case reports. We included 9 randomized controlled trials (RCTs), 11 nonrandomized comparative studies, 67 cohorts (in 63 studies) of PTRAS; 20 cohorts (in 17 studies) of medical therapy alone; and 4 cohorts of surgery. For the primary comparison of PTRAS versus medical therapy, seven RCTs found no difference in mortality, RRT, cardiovascular events, or pulmonary edema. They mostly found no difference in kidney function or BP control after PTRAS. Procedural adverse events were rare but medication-related adverse events were not reported. The nonrandomized studies were more variable than the RCTs and found no significant difference in mortality, but heterogeneous effects on kidney function and BP control after PTRAS. All 20 case reports describe patients with successful clinical and symptomologic improvement after revascularization. In subgroup analyses, two RCTs found no patient characteristics associated with outcomes between PTRAS and medical therapy. In one retrospective comparative study, patients with flash pulmonary edema or both rapidly declining kidney function and refractory hypertension had decreased mortality with PTRAS (vs. medical therapy). Single-intervention studies found that various factors predicted outcomes.

Conclusions. There is a low strength of evidence of no statistically significant or minimal clinically important differences in important clinical outcomes (death, cardiovascular events, RRT) or BP control between PTRAS and medical therapy alone, and that kidney function may improve with PTRAS. Clinically important adverse events related to PTRAS are rare; however, studies generally did not report medication-related adverse events. Based on the evidence,

subsets of patients benefit from revascularization, but the evidence does not clearly define who these patients are, except that case reports demonstrate that some patients with acute decompensation benefit from revascularization. Evidence is limited regarding differences in outcomes based on different PTRAS-related treatments. The RCTs had limited applicability to many patients for whom PTRAS is recommended, particularly those who present with pulmonary edema or rapidly declining kidney function. All nonrandomized trials were inadequately adjusted to account for underlying differences between patients undergoing different interventions. New studies or reanalyses of data in existing studies are needed to better understand the comparative effectiveness of PTRAS versus medical therapy.

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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.

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 ($N \geq 30$), medical therapy alone ($N \geq 10$), and surgery ($N \geq 10$ if prospective, $N \geq 100$ 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.

Variable	Topic /Findings
	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.
	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.

Variable	Topic /Findings
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.
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.

Variable	Topic /Findings
	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.
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.

Variable	Topic /Findings
	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.

Introduction

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 and usually involves the ostium and proximal third of the main renal artery and the perirenal aorta.[1] Atherosclerotic RAS (ARAS) is a progressive disease that may occur alone or in combination with hypertension (HTN) and ischemic kidney disease. ARAS is becoming increasingly common because of atherosclerosis in an aging population with increasing prevalence of diabetes, obesity, hyperlipidemia, aortoiliac occlusive disease, coronary artery disease, and HTN. Based on a recent systematic review,[2] the prevalence of RAS among the general hypertensive population is unknown, but among people with clinical characteristics of renovascular HTN—including severe HTN, therapy-resistant HTN, HTN-onset at a young age, recent onset of HTN, or presence of an abdominal bruit—RAS prevalence (generally defined as stenosis ≥50%) is 14.1 percent (95% confidence interval [CI] 12.7 to 15.8%).[2] Among people with diabetes mellitus and HTN, the prevalence is 20.0 percent (95% CI 15.4 to 25.5%) and among people undergoing coronary angiography, the prevalence is 10.5 percent (95% CI 9.8 to 11.2%). In the United States, 11 to 14 percent of new patients entering dialysis programs were found to have ARAS from 1996 to 2001.[3]

Optimal strategies for evaluating patients suspected of having RAS remain unclear. Patients with moderate to high risk atherovascular diseases who present with uncontrolled HTN or unexplained abnormal kidney function tests are generally evaluated for RAS.[1, 4, 5] A reduction in estimated glomerular filtration rate of at least 30 percent from baseline following the introduction of angiotensin converting enzyme inhibitor (ACEi) or angiotensin-receptor blocker (ARB) therapy is a clinical clue suggestive of RAS.[6] However, it is important to note that the primary reason for diagnosing ARAS is to set the patient up for revascularization, since medical management of ARAS is identical to medical management of other patients with difficult to control HTN who are at increased risk of cardiovascular events and kidney damage. A variety of physiological studies to assess the renin-angiotensin system and perfusion studies to assess renal blood flow are available. However, the clinical clues can be nonspecific and physiologic studies have limited usefulness in ARAS, especially among the elderly. Initial evaluation often relies on imaging techniques such as duplex ultrasonography, magnetic resonance angiography, computed tomographic angiography, and radionuclide renal scanning. However, magnetic resonance and computed tomographic angiography may also be contraindicated in patients with kidney insufficiency and can be compromised by the presence of metallic implants such as aortic endografts. The value of ultrasonography may depend on operator's experience, body habitus, the presence of bowel gas, and may be less reliable in visualizing distal segments of renal arteries. Currently, catheter angiography remains the *de facto* reference standard for evaluating the degree of stenosis in RAS, but carries risk of contrast-induced nephropathy and the risks of any invasive vascular procedure. However, angiography is not a true reference standard since it intrinsically has measurement error that may vary by equipment and operator. The accuracy of angiography to measure degree of stenosis has not been compared to autopsy or pathology confirmation of the lesion. Furthermore, the link between angiographic stenosis and translesional pressure drop, the more direct measure of the hemodynamic significance of the stenosis.

The goals of therapy are improvement in uncontrolled HTN, preservation or salvage of kidney function, prevention or treatment of cardiac syndromes such as pulmonary edema or unstable angina, and ultimately improved survival. Combination therapy with multiple

antihypertensive agents, typically including ACEi or ARBs, calcium channel blockers, and/or beta blockers, are frequently prescribed with a goal of normalizing blood pressure (BP). Statins are commonly prescribed to lower low density lipoprotein cholesterol, and antiplatelet agents, such as aspirin or clopidogrel, are prescribed to reduce thrombosis. This "triple therapy" (antihypertensive, antilipid, and antiplatelet medications) approach is much more intensive than is typically prescribed for patients with primary HTN. Among patients treated with medical therapy alone, there might be a risk for deterioration of kidney function since the treatments do not reduce the stenosis and thus cannot substantially improve blood flow to the kidneys. Based on studies found for this review, as described in more detail in the Results, about 10 percent or more of patients with RAS treated medically require renal replacement therapy (RRT) within about 5 years. RAS patients treated medically also appear to be at relatively high risk for cardiovascular disease (e.g., one study reported that 12 percent of patients had a new cardiovascular event at about 3 years[7]). ACEi and ARBs are effective in controlling renovascular HTN in 86 to 92 percent of these patients, but a loss of kidney function due to reduction in transcapillary filtration pressure might, in some patients, result in acute or chronic kidney disease.[1] Thus, both treatment options (percutaneous transluminal renal angioplasty with stent placement [PTRAS] and medical therapy alone) have risks. Whether loss of kidney function and other clinical outcomes differ based on treatment choice is a question of interest.

Indications for and timing of revascularization for ARAS are topics of considerable debate. The American Heart Association lists three clinical criteria for revascularization: 1) HTN (accelerated, refractory, or malignant [HTN with coexistent end-organ damage]), 2) preservation of kidney function, and 3) cardiac syndromes (recurrent "flash" pulmonary edema or unstable angina with significant RAS).[8] By one prospective study's estimate, at diagnosis of ARAS about half of people meet at least one of these criteria (refractory HTN, rapid kidney function decline, or flash pulmonary edema).[9] The decision to proceed with revascularization must be weighed against the morbidity and mortality risks of the invasive procedures. Per expert opinion, the Society for Cardiovascular Angiography and Interventions also includes "hemodynamically significant" stenoses to warrant consideration for revascularization, including angiographic stenosis of 50 to 70 percent—only with an abnormal translesional pressure gradient—or stenosis greater than 70 percent.[10] Renal artery revascularization may provide immediate improvement in kidney function and BP; however, as with all invasive interventions, it may also result in procedural complications of bleeding, dissection, or embolization in some patients.

The current standard for revascularization in most patients is PTRAS across the stenosis. Angioplasty without stent placement is rarely employed due to the high rate of restenosis. Placement of renal artery stents can also resolve dissections, minimize stenosis recoil and restenosis, and correct translesional pressure gradients. Most patients undergoing renal artery revascularization have been exposed to many years of relative kidney ischemia and poorly controlled HTN. Thus, revascularization may not have substantial long-term clinical benefit due to prior kidney and cardiovascular damage and ongoing atherosclerotic processes that requires continuation of medical management.

Even after revascularization, patients generally continue triple therapy with antihypertensive agents, antiplatelet agents, and statins, though fewer (or lower dose) antihypertensive agents may be necessary to control BP. Furthermore, patients may be better able to tolerate ACEi or ARBs after revascularization. Particularly for patients with diabetes or with congestive heart failure (CHF), the ability to use ACEi or ARBs can be renoprotective and reduce cardiovascular disease.

Revascularization by surgical reconstruction is generally reserved for patients with complicated renal artery anatomy or who require pararenal aortic reconstructions for aortic aneurysms or severe aortoiliac occlusive disease. The percentage of patients undergoing surgical revascularization has dropped precipitously over time. In the U.S. Medicare population, among people having renal revascularization, 33 percent had surgical revascularization in 1992; by 2004, this had dropped to 1.5 percent.[11] The total number of PTRAS performed in the outpatient setting remained stable from 2005 to 2009 ((3.8 and 3.7 per 100,000, respectively). The number of inpatient PTRAS procedures for the management of RAS has decreased significantly after 2006. (7.9 per 100,000 in 2006 to 4.2 per 100,000 in 2009).[12]

The Tufts Evidence-based Practice Center (EPC) conducted a Comparative Effectiveness Review of management strategies for RAS in 2006 (with an update in 2007).[13, 14] The review evaluated medical therapies (without revascularization), angioplasty (with or without stent, but focusing primarily on with stent), surgical revascularization, and natural history studies. The review included 68 studies, but none of the studies evaluated the principal question of interest—namely, the relative effects of intensive medical therapy and PTRAS. 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 whether any clinical or intervention characteristics affect outcomes.

Since the original EPC review, the two major then-ongoing trials of PTRAS versus medical therapy alone, the Cardiovascular Outcomes in Renal Atherosclerotic Lesions (CORAL) and the Angioplasty and Stenting for Renal Artery Lesions (ASTRAL) trials, have been published. These trials have influenced clinical decisionmaking regarding management of ARAS. Without clear benefit on BP or kidney function in these trials, indications for interventional treatment have been interpreted to be limited. The trials also failed to identify specific subpopulations that may benefit from revascularization. As a result, since their publication, fewer patients are referred for procedures, and medical therapy alone, using antihypertensive agents, antiplatelet agents, and statins, has become the standard of care. Importantly though, the trials had difficulties recruiting patients, mostly because clinicians and patients often had strong preferences for or against undergoing revascularization that precluded their enrollment for randomized treatment. Therefore, questions remain about the applicability of these trials and the true value of PTRAS for patients who have (or whose clinicians have) a strong preference for PTRAS.

A subset of patients effectively excluded from the trials includes patients with acute decompensation related to ARAS. These patients have rapidly declining kidney function with possible oliguria or anuria, flash pulmonary edema, and/or intractable malignant HTN. It is generally understood that these patients usually benefit from rapid revascularization, which must be undertaken before the kidneys are permanently injured. However, less well understood is which patients may or may not benefit from revascularization.

Thus, controversy remains regarding optimal strategies for evaluation and management of patients with ARAS. In particular, a fuller understanding in needed of which patients are most likely to benefit from revascularization and for which continued aggressive medical therapy alone may be most appropriate.

Scope and Key Questions

This report summarizes the evidence evaluating the comparative effectiveness and safety of PTRAS, surgical revascularization, and medical therapy in the treatment of ARAS,

particularly after long-term followup. Key Questions addressed in this report remain unchanged from the original reviews and are as follows:

1. For patients with ARAS in the modern management era (i.e., since JNC-5 in 1993), what is the evidence on the effects of aggressive medical therapy (i.e., antihypertensive, antiplatelet, and antilipid treatment) compared to PTRAS on long-term clinical outcomes (at least 6 months) including BP 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 PTRAS?

2. What clinical, imaging, laboratory and anatomic characteristics are associated with improved or worse outcomes when treating with either aggressive medical therapy alone or PTRAS?

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

Note: The Fifth Joint National Committee (JNC-5) on Detection, Evaluation, and Treatment of High Blood Pressure guidelines (1993) marked a substantial change from previous guidelines in treatment recommendations for HTN, including more aggressive BP targets. This time point also marks when ACEi began to be used more routinely for patients with severe HTN.

Analytic Framework

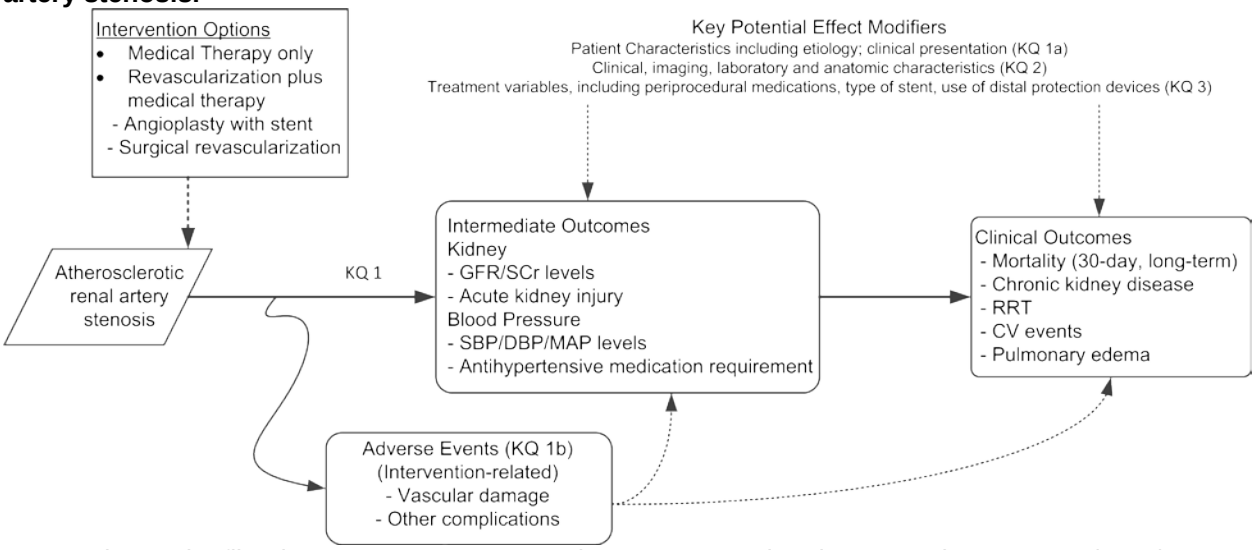
We applied the analytic framework depicted in Figure 1 to answer the Key Questions in the evaluation of the treatment modalities for ARAS. This framework addressed relevant clinical outcomes. It also examined clinical predictors that affected treatment outcomes. While evidence from high quality randomized controlled trials (RCT) was preferred, these data were rare, so nonrandomized and uncontrolled studies were used to augment the evidence.

Types of Participants

The population of interest for this report is adults with ARAS that is of sufficient severity to warrant aggressive management, either due to resistant HTN, evidence of reduced kidney function, or the high likelihood of poor outcomes based on such factors as CHF severity or frequency, threatened renal mass, diastolic dysfunction. Because of the variety of techniques used to diagnose and define RAS, the definitions used by study authors were accepted. Patients with ARAS commonly also have aortic disease, which must be treated simultaneously. The original 2006 report was restricted to studies that performed only renal artery procedures. However, it is increasingly common that subclinical aortic disease is treated at the same time as

the renal artery lesion in a single invasive intervention. Therefore, this report aims to include studies of all ARAS treatments, regardless of whether an aortic procedure was also conducted, as long as the primary indication for the intervention was the ARAS. Studies of patients with severe aortic disease requiring surgery who also had a concomitant renal artery stent placed were excluded since the ARAS was not the primary indication for the intervention.

Figure 1. Analytic framework for evaluating the effectiveness and safety of treatments for renal artery stenosis.



GFR = glomerular filtration rate; KQ = Key Question; RRT = renal replacement therapy; SBP/DBP/MAP = systolic, diastolic, and mean arterial pressures; SCr = serum creatinine.
* Usually a combination of antihypertensive medications, antilipid medications (statins), and antiplatelet medications.

Types of Interventions

The primary interventions of interest are aggressive medical therapy, PTRAS, and open vascular repairs. However, this review covers any medical (noninvasive) intervention, PTRAS, and any open vascular surgery whose primary indication is amelioration of RAS. This review does not update the literature on angioplasty without stent or natural history studies.

Types of Outcome Measures

The primary outcomes of interest include long-term (6 months or more) mortality, kidney function, HTN, cardiovascular disease, and related outcomes, in addition to adverse events and complications (including 30-day mortality).

Types of Studies

The ideal study to answer the Key Questions would be a RCT directly comparing the primary interventions of interest. However, given the paucity of RCTs and of nonrandomized comparative studies, this review evaluates studies of cohorts of patients who received one treatment (or one set of treatments) without a control group.

Case Reports

Due to concerns that the trial and observational studies do not adequately address outcomes in patients with ARAS who have acute decompensation, this review also includes a summary of the more recent case reports of patients treated for acute decompensation, including malignant HTN or acutely uncontrollable HTN, flash pulmonary edema, acute kidney injury, and recent-onset end-stage renal disease requiring dialysis.

Methods

Technical Expert Panel

This report on the comparison of aggressive medical therapy, percutaneous transluminal renal angioplasty with stent placement (PTRAS), and surgical revascularization for the management of atherosclerotic renal artery stenosis (ARAS)is based on a systematic review of the literature. We convened a Technical Expert Panel (TEP), which included nephrologists, invasive cardiologists and radiologists with expertise in RAS, vascular surgeons, the medical officer from the CORAL study (in the Division of Cardiovascular Sciences at NHLBI), and an FDA representative (in the Division of Cardiovascular Devices). The TEP includes experts nominated by the Society of Interventional Radiology, the Kidney and Urology Foundation of America, the National Kidney Foundation, and the American College of Cardiology Foundation/American Heart Association. The TEP provided input to help refine the protocol, identify important issues, and define parameters for the review of evidence. The TEP was also asked to suggest additional studies for evaluation by the Evidence-based Practice Center (EPC).

Search Strategy

A comprehensive search of the scientific literature was conducted to identify relevant studies addressing the Key Questions that have been published since the original RAS reports, which had a final search date of April 23, 2007. We searched MEDLINE®, the Cochrane Central Trials Registry® and Cochrane Database of Systematic Reviews®, and Embase (2007 – March 16, 2016). The reference lists of existing systematic reviews were hand-searched, and the TEP was asked to identify additional studies. With the dual goals of increasing the sensitivity of the search and of assessing the risk of potential publication bias, we searched the "grey literature" for relevant completed studies in the FDA database (with assistance from our FDA TEP representative), clinicaltrials.gov, the World Health Organization International Clinical Trials Registry Platform (ICTRP) (http://apps.who.int/trialsearch/default.aspx), and conference proceedings from 2012 through 2014 for the National Kidney Foundation, the American Society of Nephrology, the Kidney and Urology Foundation, the American Urological Association, and the Society of Vascular Surgery. In our searches, we combined terms for renal artery stenosis, renal hypertension, and renal vascular disease, limited to adult humans and relevant research designs, including case reports and series (see Appendix A for the complete search strategies). Furthermore, we solicited studies via Scientific Information Packets from manufacturers (one study was sent to us, which was already known to us).

Study Selection

We assessed titles and/or abstracts of citations identified from literature searches for inclusion, using the criteria described below. Full-text articles of potentially relevant abstracts were retrieved and a second review for inclusion was conducted by reapplying the inclusion criteria. Both abstract and full-text screening was conducted in duplicate with conflicts resolved by reconciliation with the whole research team. All rejected full-text articles were confirmed by the project lead.

Studies included in the original reports were reassessed for inclusion based on the current eligibility criteria. Those that remain eligible are fully included in the current update.

Population and Condition of Interest

We included studies of adults (≥18 years) with ARAS, as defined by the study authors, whether unilateral, bilateral, or in patients with a solitary functioning kidney. We excluded studies in which >20 percent of patients had fibromuscular dysplasia, arteritis-associated RAS, embolic or thrombotic stenosis, or other nonatherosclerotic stenosis. We excluded studies of patients with previous surgical or angioplasty interventions for RAS (i.e., with restenosis or in-stent stenosis) or with RAS in the setting of a transplanted kidney, renal artery aneurysms (requiring repair), or concurrent cancer (including renal cell carcinoma). We allowed studies that performed simultaneous repair of aortic disease (e.g., aneurysm) only if the RAS was the primary indication for surgery and the aortic disease surgery was incidental.

Interventions of Interest

The primary interventions of interest were "aggressive medical therapy"—defined as antihypertensive drugs, antilipid (lipid lowering) drugs, and antiplatelet drugs—and PTRAS. However, the review covers a broader range of interventions that are currently used in practice, including a range of medical therapies alone, PTRAS, and open surgical revascularization.

Specifically, we included studies of any medical intervention or set of medical interventions in patients who did not have revascularization. In particular, use (and tolerance) of ACEi or ARB was of interest.

We included studies of PTRAS (where ≥80% of patients had stent placement). We excluded "drive-by" angioplasty—renal artery angioplasty done at the time of coronary angiography (or angioplasty) in patients who do not have previously known RAS. There was consensus among the TEP members that the currently accepted invasive intervention for ARAS in the large majority of patients in the United States is PTRAS. In contrast with the original reports, given advances in revascularization interventions, studies of angioplasty without stent placement are not included.

We included studies of any renal artery revascularization, with the caveats about concomitant aortic surgery noted above. We excluded studies that used endografts or endarterectomy that included the renal arteries to prevent or repair renal artery damage due to the aortic surgery.

We excluded "natural history" studies that did not evaluate a specific intervention, but instead followed patients regardless of treatment. This restriction is in contrast with the original reports.

Comparators of Interest

Given the known paucity of comparative studies, we included both noncomparative (single group) studies and comparative studies that compared any of the three interventions of interest.

Outcomes of Interest

With the TEP, we identified clinical and surrogate outcomes of greatest interest regarding the comparison of medical and revascularization interventions. It was agreed that given the chronicity of the disease process, only long-term clinical outcomes were of interest, along with adverse effects at any time. For the purposes of this report, "long-term" was defined as at least 6 months, but results at 12 months or more are of greater interest.

Outcomes of interest included:

- Mortality, all cause
- Kidney function
    - Event (e.g., need for renal replacement therapy)
    - Categorical (e.g., better/worse)
    - Continuous (i.e., glomerular filtration rate, creatinine clearance, serum creatinine [SCr])
- Blood pressure (BP)
    - Event (e.g., hypertensive crisis)
    - Categorical (e.g., better/worse)
    - Continuous BP
    - Medication need (e.g., number of antihypertensive drugs used)
    - Angiotensin converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB) tolerance
- Congestive heart failure (CHF) events, including flash pulmonary edema (including hospitalization)
- Other cardiovascular events (cardiac, cerebrovascular, peripheral vascular)
- Adverse events (e.g., postprocedure in-hospital or 30-day deaths, peri- and postprocedure events, drug reactions)

For Key Questions 2 and 3, we also included subgroup and regression analyses that compared preintervention patient and intervention characteristics and outcomes of interest. These included, but were not limited to, patient demographics; clinical, imaging, laboratory, and anatomic characteristics of the RAS; and treatment variables, such as periprocedural medications, type of stent, use of distal protection devices, or other adjunct techniques. We extracted details from studies that reported analyses on the likelihood of outcomes based on the presence of patient or procedure related variables (e.g., that compared death rates among patients with high or low kidney function). We did not extract data related to comparisons of average values of the variables in patients with dichotomized outcomes (e.g., that reported mean age of those who lived and those who died). These latter analyses were not considered to be sufficiently helpful for a clinician making a decision of which intervention to recommend to a given patient.

When outcomes were reported at multiple time points, we included those that occurred at 6 months, 12 months, and each subsequent year, so long as there were at least 10 subjects being evaluated.

Years of Intervention of Interest

The original report restricted studies to those in which patients were treated after publication of the Fifth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-5) in 1993, when emphasis was placed on attempting to achieve lower BP levels than earlier sets of recommendations, together with recommendations for use of antilipid and antiplatelet treatments, and increasing use of ACEi and ARB. The current update maintains this time period for when patients were evaluated and treated.

Study Designs of Interest

The basic parameters were maintained for intervention-specific study design eligibility criteria are the same as in the previous report.

Comparative Studies

For studies that compared two or more of the three intervention categories (medical therapy, PTRAS, surgical), we included studies of any study design, whether prospective or retrospective, as long as at least 10 subjects were evaluated in each group. Any comparative study that failed to meet eligibility criteria (e.g., angioplasty without stent versus comparator) was also examined to determine whether individual groups of subjects were eligible for review (e.g., the medical therapy arm).

Medical Therapy Only Studies

For single-group medical intervention studies, we included only prospective studies of antihypertensive, antilipid, or antiplatelet medications with at least 10 subjects who received treatment.

Angioplasty With Stenting Studies

For single-group PTRAS studies, we included only prospective studies with at least 30 subjects who received treatment. The majority of available articles on ARAS have reported on groups of subjects who received PTRAS; therefore a higher sample size threshold was used. Furthermore, it was known from the original EPC reports and from an early screen of the literature that there is a large volume of PTRAS cohort studies. Therefore, it was agreed to restrict the review to the (theoretically) less biased prospective studies.

Surgical Revascularization Studies

For single-group surgical studies, we included prospective or retrospective studies. We included prospective studies with at least 10 subjects who had surgery. Because there are relatively few prospective surgical studies, we also included retrospective studies with at least 100 subjects.

Case Reports

To address the issue of patients excluded from essentially all comparative and almost all single group studies because they have acute decompensation (and, therefore, “require” revascularization), we included case reports and case series of patients with acute decompensation as defined by acute symptoms with acute worsening of kidney function, new-onset flash pulmonary edema, CHF, or peripheral edema, and/or recent-onset uncontrollable HTN. We selected the 20 most recently published eligible case reports (through March 2015, prior to submission of the draft report), regardless of the intervention(s) employed.

Data Extraction

Data extraction was conducted into customized forms in the Systematic Review Data Repository (SRDR) online system (http://srdr.ahrq.gov) designed to capture all elements relevant

to the Key Questions. These included population characteristics, including description of patients' RAS, descriptions of the interventions analyzed, descriptions of relevant outcomes, enrolled and analyzed sample sizes, study design features, funding sources, results (including adverse events), and risk of bias assessment. We captured methodological descriptions and results of subgroup or predictor (regression) analyses for any preintervention factor. Analyses based on postintervention factors (such as stent restenosis or followup BP) were excluded. When multiple models were reported, the most adjusted model was extracted. The forms were tested on several studies and revised as necessary.

All eligible studies from the original reports were entered into SRDR based on the original completed data extraction forms and, when necessary, the full-text articles.

Risk of Bias Assessment

We based the methodological quality of each study on predefined criteria. We used the Cochrane risk of bias tool for randomized controlled trials (RCT)[15]—which asks about risk of selection bias, performance bias, detection bias, attrition bias, reporting bias, and other potential biases—and selected questions from the Newcastle Ottawa Scale[16] about comparability of cohorts, representativeness of the population, and adjustment for different lengths of followup. All eligible studies from the original reports were reevaluated for methodological quality in the same way as new studies.

Data Synthesis

All included studies were summarized in narrative form and in summary tables that tabulate the important features of the study populations, design, intervention, outcomes, and results. Meta-analysis was considered, but given the large clinical and study design heterogeneity of the randomized and observational comparative studies (primarily in terms of indications for intervention) and the large heterogeneity in outcome definitions and results of the single arm studies, meta-analysis was not deemed to be appropriate. Studies are summarized semiquantitatively and, for PTRAS and medical therapy studies, graphically.

The report uses the same basic structure as the original reports. Namely, it is organized by study design first (comparative studies, each of the single intervention analyses, and case reports), then by Key Question and outcome, within each study design section. Studies are summarized semiquantitatively and, for PTRAS and medical therapy studies, graphically.

Minimal Clinically Important Differences

The concept of minimal clinically important difference (MCID) was considered to help users of this report to determine the comparative value of treatments. However, no useful guidance for determining thresholds for MCID was found. Several members of the TEP were sceptical about the concept in regards to RAS management given the current state of knowledge about RAS management and the complexity of RAS and its interactions with concurrent diseases (including cardiac disease and chronic kidney disease). MCIDs for individual patients require contextualization for their particular circumstances, medical history, and preferences. The TEP did not suggest MCIDs for outcomes of interest, except possibly statistically significant differences (i.e., an MCID of 0). We sought guidance from the Agency for healthcare and Research Quality (AHRQ) staff, other EPC review leads, AHRQ reports and guidance

documents, clinical practice guidelines, PubMed and internet searches. Guidelines for kidney disease (www.kdigo.org, www.kdoqi.org) and hypertension (JNC-8[5]) do not consider or suggest MCID for continuous or categorical outcomes. Two publications were illuminating on the subject. In a critique, Madeline King commented "There is no universal [MCID], despite the appeal of the notion. Indeed, for a particular patient-reported outcome instrument or scale, the [MCID] is not an immutable characteristic, but may vary by population and context. At both the group and individual level, the [MCID] may depend on the clinical context and decision at hand, the baseline from which the patient starts, and whether they are improving or deteriorating."[17] In a survey of Canadian physicians and patients with HTN, median MCIDs for major cardiovascular events ranged from 1 to 6 percent (absolute risk reduction), depending on predicted risk, with up to one-quarter of patients stating a preference for an MCID of 0 (they would want treatment "even if there was no benefit").[18] Notably, patients expressed a statistically significantly larger MCID than physicians; patients were less likely to want treatment given a risk scenario.

The CORAL study used a 25 percent reduction in a composite of cardiovascular and kidney events for their power calculation. The researchers' opinion was that "this threshold of effect size (25%) is a clinically reasonable goal for an expensive and invasive treatment. A smaller effect on a composite outcome, with an expensive and invasive therapy, is unlikely to be sufficiently compelling to justify such treatment."[19] This implies that the hazard ratio (HR) should be ≤ 0.75 to be clinically important. The ASTRAL "was designed to detect a reduction of 20 percent in the mean slope of [1/SCr]."[20] However, few studies reported slope in change in kidney function and the trials reported heterogeneous kidney function measures (slope of kidney function change, with various measures; absolute kidney function change, with various measures; categorical changes, variously defined).

With these various considerations in mind, the decision was made to use an arbitrarily determined MCID of 25 percent (translating into $HR \leq 0.75$) for clinical outcomes. No MCID was used for kidney function and BP measures. The MCIDs were considered in summary conclusions about comparative effectiveness and in strength of evidence determination (see next).

Grading the Strength of Evidence

As per the AHRQ Methods Guide,[21] we assigned an overall grade describing the body of evidence for each Key Question that was based the number of studies, their study designs, the study limitations (i.e., risk of bias), the directness of the evidence to the Key Questions, the consistency of study results, the precision of any estimates of effect (taking into account MCID), the likelihood of reporting bias, other limitations, and the overall findings across studies. Limitations in any of these factors downgraded the strength of evidence among the categories high, moderate, or low, or we made a determination that there was insufficient evidence to estimate an effect. The grading was done by the team as a whole. RCTs and well-adjusted comparative observational studies were deemed to provide stronger evidence than poorly- or unadjusted comparative studies, which in turn provided stronger evidence than noncomparative studies. Issues related to the domains of study limitations, directness, consistency, reporting bias, and other limitations could decrease the strength of evidence, as described in the Methods Guide.

Peer Review

A draft version of this report was reviewed by a panel of invited expert reviewers and the general public. The reviewers included experts in nephrology, cardiology, interventional

radiology, and vascular surgery. These experts were either directly invited by the EPC or offered comments through a public review process. Revisions of the draft were made, where appropriate, based on their comments. The draft and final reports were also reviewed by the Task Order Officer and an Associate Editor from another EPC. However, the findings and conclusions are those of the authors, who are responsible for the contents of the report.

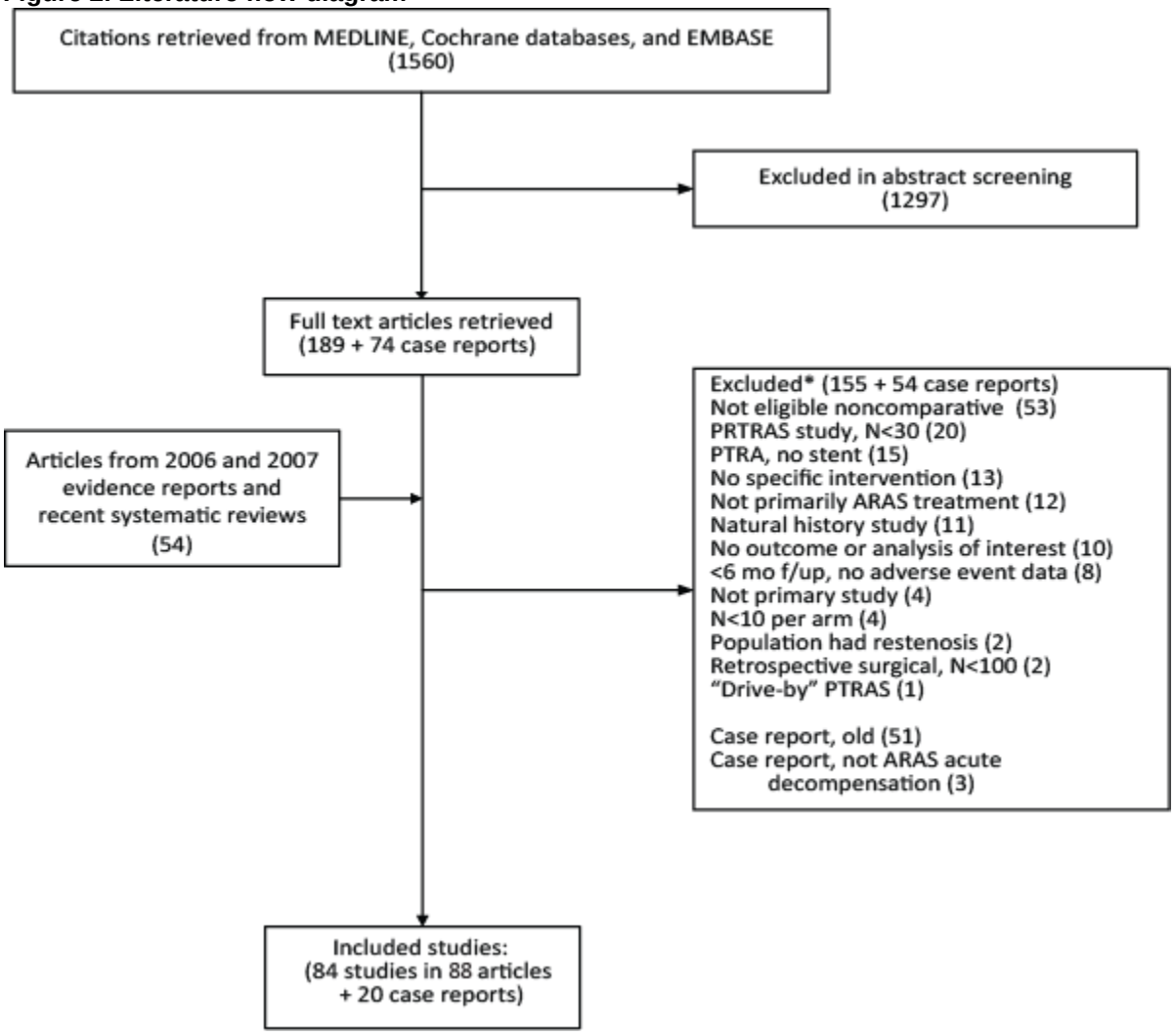
Results

The literature search yielded 1560 citations (Figure 2). We identified 189 of these as potentially relevant full studies plus 74 case reports of potential interest. These were retrieved for further evaluation. We also rescreened the 50 studies included in the 2006 and 2007 reports to determine their eligibility for this update, plus 4 additional articles found in other existing systematic reviews. Overall, 209 full-text articles and case reports did not meet eligibility criteria (see Appendix B for a list of rejected articles along with reasons for rejection); thus 84 comparative and noncomparative studies (in 88 articles) are included in this report, and an additional 20 case reports were selected for inclusion.

The "grey literature" search for unpublished trials, done to assess publication bias, in the FDA database, clinicaltrials.gov, the WHO International Clinical Trials Registry Platform, and conference proceedings, did not find any trials with results that were not already included in the report.

The strength of evidence for all Key Questions, with summaries of the evidence, is presented at the end of this chapter under Strength of Evidence Across Study Designs.

Figure 2. Literature flow diagram



* Excluded list does not include studies that were screened and excluded for the 2006 report.

Comparative Studies

We identified 20 studies (with a total of 4526 patients, 2279 in randomized controlled trials [RCT]s and 2247 in nonrandomized comparative studies [NRCS]) that assessed the comparative effectiveness of treatment strategies for the treatment of atherosclerotic renal artery stenosis (ARAS) and reported data on clinical outcomes.[9, 19, 20, 22-36] Of these, 15 studies compared percutaneous transluminal renal angioplasty with stent placement (PTRAS) with medical therapy in 3887 patients,[9, 19, 20, 22, 24, 25, 28-33, 34b, 35] seven of which were RCTs;[19, 20, 24, 32, 32b, 34b, 35] one RCT compared surgical revascularization with medical therapy only in 52 patients.[34] Four studies compared PTRAS with surgical therapy in 468 patients,[23, 26, 27, 36] one of which was a RCT.[23] The studies followed patients from 1 to 8 years.

Most (14/20) comparative studies did not report their funding source, including three of the seven RCTs comparing PTRAS with medical therapy (Ziakka 2008[35] and the two conference abstracts, Scarpioni 2009[32b] and Zeller 2013[34b]) and the RCTs of surgical revascularization versus medical therapy (Uzzo 2002[34]) and PTRAS versus surgical therapy (Balzer 2009[23]). The remaining comparative studies were funded by government, academic or hospital centers, or nonprofit organizations, except that two RCTs of PTRAS versus medical therapy were partially funded by industry (ASTRAL [Wheatley 2009[20]] and STAR [Bax 2009[24]]). The industry-funded trials had similar findings as the other comparable trials.

PTRAS Versus Medical Therapy

Key Points

- Seven RCTs and eight 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 one 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.
- **Mortality**: Four RCTs and five NRCS found no statistically significant difference or MCID between interventions, but no study was adequately powered for mortality.
- **Renal replacement therapy (RRT)**: Four RCTs and five NRCSs had wide differences in rates of RRT across studies. Imprecise estimates found no statistically significant differences or minimal clinically important difference (MCID) in incident RRT between interventions.
- **Cardiovascular outcomes**: Four RCTs and three 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 congestive heart failure (CHF). No statistically significant differences or MCID between interventions were found.

- **Kidney function**: Six RCTs and five 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 (glomerular filtration rate [GFR] or serum creatinine [SCr]). In contrast, about half the NRCSs found that patients' kidney function was more likely to improve (or less likely to worsen) after PTRAS than with medical therapy alone; however, these analyses were not adjusted for underlying differences between the cohorts.
- **Blood pressure (BP) control**: Seven RCTs and six NRCSs reported on BP control. One RCT found no difference in improvement (or worsening) of BP control; one found that hypertension (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 one 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 six NRCSs reported highly heterogeneous results, except that all but one found no difference in changes in number of antihypertensive medications.
- **Adverse events**: Five RCTs and four NRCSs reported on adverse events, but only related to PTRAS. PTRAS-associated adverse events included periprocedural 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.
- **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); One 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.
- **Treatment factors**: No comparative studies addressed differences in treatment factors as a predictor of outcomes in the comparison of PTRAS versus medical therapy.

Key Question 1. Effects of Intervention on Outcomes

Randomized Controlled Trials (PTRAS vs. Medical Therapy)

Seven RCTs compared PTRAS with medical therapy only.[19, 20, 24, 32, 32b, 34b, 35] The median mean age across the RCTs was 69 years. Enrolled patients had uncontrolled HTN while on two or more medications, with or without mild to moderate chronic kidney disease. About one-third of included patients had diabetes. Coronary artery disease among included patients ranged from 26 to 50 percent. Analyzed studies typically included more men (median 63% male) than women. The definitions of ARAS varied across studies, as described for each study, below (Appendix Tables C.1 and C.3). Only CORAL measured stenosis severity with translesional pressure gradients. Of note, the trials excluded patients with acute decompensation. By contrast, a recent, prospective study found that 106 of 467 patients (23%) presenting with ARAS had flash pulmonary edema (8%) or rapidly declining kidney function (18%), or both.[9] A recent literature review reported that the overall weighted prevalence of acute flash pulmonary edema in ARAS was 3.5 percent in those with unilateral ARAS and 14.3 percent among those with bilateral ARAS, although it was unclear what studies these patients came from or exactly who they were.[37]

Three of seven of the RCTs were of high or unclear risk of bias for blinding of outcome assessment or detection bias (1 high; 2 unclear), five for incomplete outcome data (attrition bias) (3 high; 2 unclear), and four for sample representing the entire population (1 high, 3 unclear). In the two conference abstracts selective reporting bias was high (Appendix Table D.1).

The CORAL trial (Cooper 2014) was conducted at more than 100 international (>80% U.S.) medical centers that were vetted for their PTRAS experience and expertise.[19] Due to difficulties enrolling patients, the eligibility criteria changed during enrollment. Initially, eligible patients had systolic BP (SBP) ≥155 mmHg on at least two antihypertensive medications and had >80 percent stenosis with a systolic pressure gradient ≥20 mmHg. Patients with stenosis as low as 60 percent who met other imaging criteria were also included. The measurement of translesional pressure gradients were at the discretion of the operators if stenosis measured at 60 to 80 percent; those with <20 mmHg systolic pressure gradient were excluded. The threshold for SBP was subsequently removed, but if patients did not have systolic HTN, they had to have chronic kidney disease defined as GFR <60 mL/min per 1.73 m^2 not due to a nonischemic cause. The CORAL trial used an angiographic core lab which standardized readings of angiographic stenosis (core lab estimates of stenosis severity were generally lower than investigator "visual estimates). This was the only study to standardize stenosis severity measurement. Patients were randomized to PTRAS with medical therapy or medical therapy alone, consisting of candesartan (an ARB) with or without hydrochlorothiazide (a diuretic), an amlodipine (calcium channel blocker)-atorvastatin (statin) combination pill, and antiplatelet therapy, all as tolerated. PTRAS was conducted with a distal protection device at the discretion of investigators, and the Genesis™ stent was employed. Periprocedural prophylaxis was given with combination regimens of heparin with ticlopidine, clopidogrel, or aspirin. The trial was funded in part by government grants but many principal investigators disclosed industry connections. The trial analyzed 931 patients (90 percent power would have required 1080 patients). The primary end point was the occurrence of a composite outcome of major cardiovascular or kidney-related event. These included a composite of death from cardiovascular or kidney-related cause, stroke, myocardial infarction, hospitalization for CHF, progressive kidney disease, or the need for permanent kidney-replacement therapy. Secondary clinical end points included the individual components of the primary end point (with death from cardiovascular causes and death from renal causes as separate end points), as well as all-cause mortality. Overall, after a mean followup of 43 months, there were no significant differences in primary or secondary outcomes and no significant interactions were found in a predefined list of subgroups. PTRAS-related complications were rare and did not result in death or dialysis in any patient.

The ASTRAL trial (Wheatley 2009) was conducted in 57 hospitals primarily in the UK.[20] Patients with poorly controlled HTN or unexplained kidney disease were screened. Patients were enrolled if they had "substantial anatomical atherosclerotic stenosis…that was considered suitable" for PTRAS and "if the patient's doctor was uncertain that the patient would definitely have a worthwhile clinical benefit from revascularization." Almost all patients had at least 50 percent stenosis and 60 percent had at least 70 percent stenosis. Angioplasty without stenting was allowed, but 95 percent had a stent. No distal protection devices were used. Only 83 percent of patients assigned to angioplasty had the procedure. Medical therapy varied according to local protocols, but "typically" consisted of "optimal BP control," statins, and antiplatelet drugs. The study was funded in part by industry. The study analyzed 806 patients (80 percent power was calculated to be achieved with 700 patients). The primary outcome was change in kidney function, measured as the mean slope of 1/SCr level over time. Secondary outcomes assessed

were BP, the time to the first renal event, the time to the first major cardiovascular event, and mortality. Overall, during a median 34 month followup, no significant differences were found in the primary or secondary outcomes; however, the rate of progression of renal impairment, measured by the slope of 1/SCr was slower after PTRAS than with medical therapy alone (P=0.06). Serious complications associated with PTRAS occurred in 23 patients (6%), including cardiac death within 1 month, pulmonary edema, myocardial infarction, rehospitalization for hemorrhage, acute kidney injury, and peripheral amputations due to cholesterol embolisms.

The STAR trial (Bax 2009) was conducted in 10 medical centers in the Netherlands and France.[24] This study included 140 patients with GFR 15 to 80 mL/min per 1.73 m^2, 50 percent or greater stenosis, and controlled BP on a stable medication dosage. Patients who had diabetes with proteinuria or malignant HTN were excluded. The STAR trial was the only trial to explicitly include patients with CHF (about 10%). Patients were randomized to PTRAS with medical therapy or medical therapy alone, consisting of antihypertensive treatment (with a target BP of <140/90 mmHg), a statin, and aspirin (and smoking cessation counseling). Multiple stents were used and patients were given periprocedural aspirin. The trial was funded in part by industry. The primary outcome was worsening of kidney function, as assessed on two repeated measurements by a ≥20 percent decrease in estimated creatinine clearance as compared with baseline. Secondary outcomes were procedural complications, changes in BP, incidence of refractory or malignant HTN and pulmonary edema, cardiovascular morbidity and mortality, and total mortality. Overall, after 2 years of followup, no significant differences were found in primary or secondary outcomes between the two groups; however, only 46 of 64 patients (71%) assigned to PTRAS had the procedure (12 patients were found have stenosis <50 percent at angiography). Four of these 64 patients had serious procedure related complications, including death and dialysis related to a cholesterol embolism.

The RASCAD trial (Marcantoni 2012) randomized 84 patients to PTRAS or medical therapy at a single institution in Italy.[32] The study enrolled patients who were undergoing nonemergent coronary angiography, who were screened for ARAS by renal arteriography, and who were found to have >50 percent and ≤80 percent stenosis but not a single functioning kidney and elevated serum creatinine (>4 mg/dL) or an aortic aneurysm requiring surgery. All patients were treated with antihypertensive drugs, statins, and antiplatelet drugs. The study was funded by the hospital with no reported industry funding. The trial analyzed 84 patients who were followed for 1 year. The primary outcome was change in echocardiographic left ventricular myocardial index. Secondary outcomes included left ventricular systolic dysfunction, cardiovascular mortality and morbidity, progression of kidney disease, and BP. Overall, there were no significant differences in primary or secondary outcomes. No serious PTRAS-related complications were reported.

The Ziakka 2008 trial was conducted in one institution in Greece.[35] They enrolled 82 patients with ARAS that was not specifically defined. Mean stenosis was 74 percent, using angiographic criteria, but no minimum criteria were reported. All patients had HTN. No medication regimen was specified, but patients were treated with different classes of drugs and "some of them" were taking statins. No mention is made of antiplatelet drugs. The funding sources were not reported, but the authors declared that none had a conflict of interest. Patients were followed for a mean of 48 months. The primary or secondary outcomes were not specified in this trial. Compared to medical therapy alone, after PTRAS, significantly more patients had cured HTN (diastolic BP [DBP] <90 mmHg off treatment, 11% vs. 0%) and improved kidney

function (SCr decreased >20%, 31% vs. 0%), but similar numbers started dialysis. Other clinical outcomes were not reported. PTRAS-related complications were not reported.

The RADAR trial (Zeller 2013) aimed to randomize 300 patients with ≥70 percent stenosis, GFR >10 mL/min, and at least mild HTN in a multicenter trial.[34a, 34b] However, the trial was terminated early after 89 patients were enrolled. An analysis of 67 patients randomized in Germany was presented in a conference abstract. BP and GFR were not significantly different after 12 months of followup.

The NITER trial (Scarpioni 2009) randomized 52 patients in Italy to PTRAS or medical therapy.[32a, 32b] Patients had ARAS with ≥70 percent stenosis diagnosed by Doppler duplex and confirmed by magnetic resonance, kidney failure, and HTN. The study results have been reported only in a conference abstract. BP and cardiovascular event-free survival were similar in both groups at a mean of 27 months of followup.Nonrandomized Comparative Studies (PTRAS Vs. Medical Therapy)

Eight NRCSs compared PTRAS with medical therapy in a total of 1828 patients.[9, 22, 25, 28-31, 33] The average patient age was 70 years. All NRCSs included patients with uncontrolled HTN while on two or more medications, as well as those with or without mild to moderate chronic kidney disease (CKD). Four studies included patients with decompensating conditions, such as acute flash pulmonary edema and acute kidney injury.[9, 29, 30, 33] Between 30 and 80 percent of patients had coronary artery disease. NRCSs typically included more males (mean: 58% male) than females. See Appendix Table C.3.

The definitions of renal artery stenosis (RAS) varied across NRCSs. Two included patients with over 50 percent stenosis,[9, 30] one with over 60 percent,[22] and three with over 70 percent stenosis.[28, 31, 33] ARAS was diagnosed in the preoperative period by renal angiography alone in two NRCSs,[29, 33] but was diagnosed using additional diagnostic methods, such as magnetic resonance or computed tomographic angiography or duplex ultrasonography, in the remaining six NRCSs. None of the studies reported using translesional pressure gradients to diagnose RAS. The median average SBP was 155 mmHg and DBP 82 mmHg. The median average GFR or creatinine clearance (CrCl) in five NRCSs was 37.8 mL/min/1.73 m^2. See Appendix Table C.1.

Two of eight NRCSs reported using bare-metal stents,[28, 30] but the remaining studies provided no information. Preprocedural and procedural prophylaxis against thrombosis was reported in four NRCSs with varying regimens: one used combination regimens of heparin with ticlopidine, clopidogrel, or aspirin;[30] two studies reported aspirin only;[29, 33] and one used heparin only.[31] The remaining studies provided no details of antiplatelet therapy. See Appendix Table C.2.1. However, as noted below, no studies reported acute thrombotic adverse events, regardless of periprocedural prophylaxis (or lack thereof).

These studies were evenly divided between high and low risk of bias for selection bias (4 high; 3 low), incomplete outcome data (attrition bias) (3 high; 1 unclear; 1 low), and selective reporting bias (3 unclear; 2 high; 2 low). In all studies except one, the sample representing the entire population was rated as having low risk of bias (6 low; 1 unclear) (Risk of Bias Description Appendix Table D.2).

Mortality (Study Duration 6 Months or Greater)

Randomized Trials

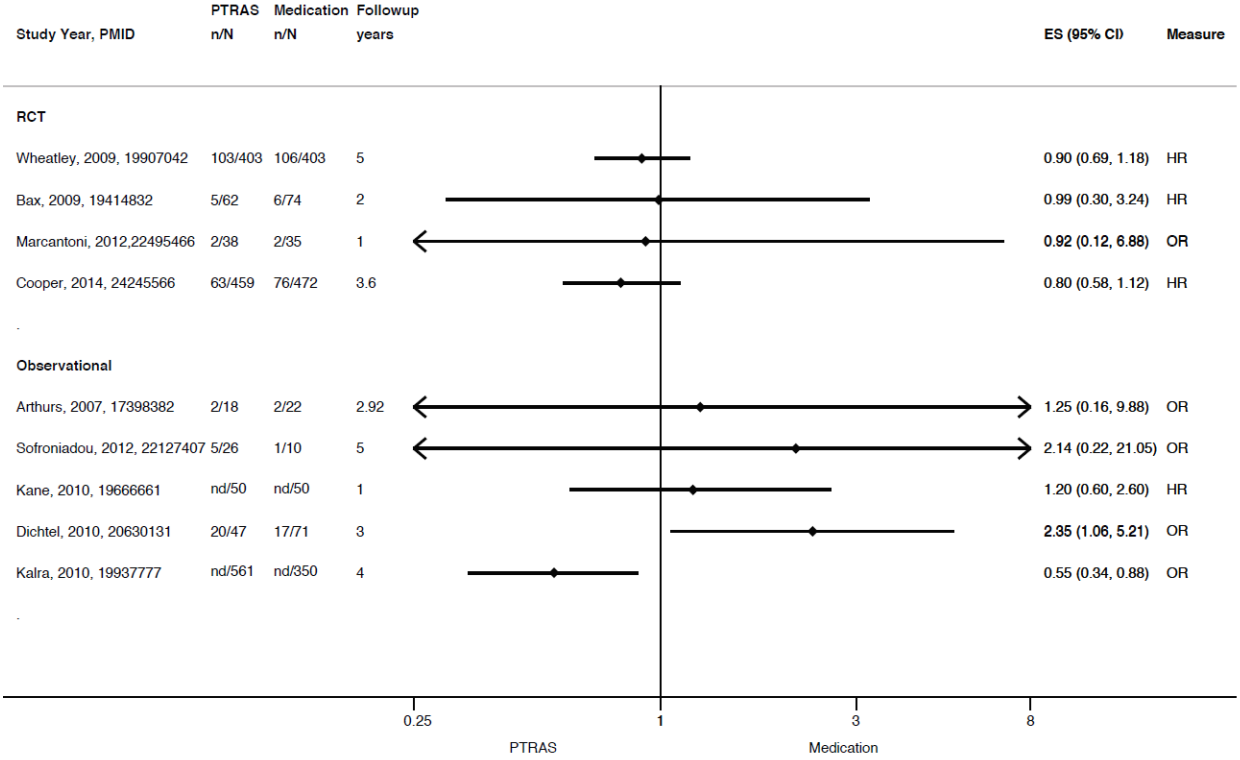
No study was reported to be adequately powered to detect a difference between interventions for mortality. See Appendix Table C.4.1.

Four RCTs reported mortality data for 1 to 5 years followup duration (Figure 3).[19, 20, 24, 32] The number and time frame of deaths were similar in all four RCTs. The STAR trial found no difference in all-cause death (crude hazard ratio [HR] 0.99; 95% confidence interval [CI] 0.30 to 3.24) and cardiovascular death (crude HR 0.59; 95% CI 0.11to 3.25) after 2 years between 62 patients who received PTRAS intervention and 74 who were treated medically.[24] Similarly, no statistically significant differences were found in the CORAL trial for the outcomes of all-cause death (adjusted HR 0.80; 95% CI 0.58 to 1.12), cardiovascular death (adjusted HR 0.89; 95% CI 0.58 to 1.36), and death due to renal causes (adjusted HR 1.89; 95% CI 0.17 to 20.85) after 3.6 years between the 459 patients who received PTRAS intervention and the 472 who were treated medically. In this RCT, there was no difference in mortality by Kaplan-Meier curve analysis up to 5 years after either PTRAS (n=459) or of medical therapy (n=472).[19] (Of note, while not statistically significant, the HR estimate for all-cause death [0.80] just reaches this review's arbitrary threshold for MCID, however, not the CORAL study's MCID [0.75 for its primary outcome]). Of the 806 patients who were enrolled in the ASTRAL trial, 103 in the PTRAS group and 106 in the medical-therapy group died during the 5-year study period (HR 0.90; 95% CI 0.69 to 1.18).[20] In the RASCAD trial, there was no significant difference between two comparison groups (2 deaths occurred in both arms; odds ratio (OR) 0.92; 95% CI 0.12 to 6.88).[32]

Nonrandomized Studies

Five NRCSs comparing PTRAS with medical therapy reported mortality data. Except for one study that found significantly reduced the risk of death by 45 percent in the combined overall groups from UK and Germany,[30] none found a statistically significant difference in all-cause death (Figure 3).[22, 28, 30, 31, 33] Notably, 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. No study was reported to be adequately powered to assess mortality. Only one NRCS provided adjusted analysis, having matched patients for age and sex;[31] none of the studies conducted propensity score matched analyses. Effect sizes ranged from 0.55 to 2.35, with no clear explanation for the heterogeneity. See Appendix Table C.4.1.

Figure 3. Death: PTRAS versus medical therapy alone



Point estimates of odds ratios (OR) or hazard ratio (HR) and 95% confidence intervals (CI) from individual studies. ES = effect size, n/N = number of events/total, nd = no data, PMID = PubMed Identifier, PTRAS = percutaneous transluminal renal angioplasty with stent placement, RCT = randomized controlled trials.

Renal Replacement Therapy

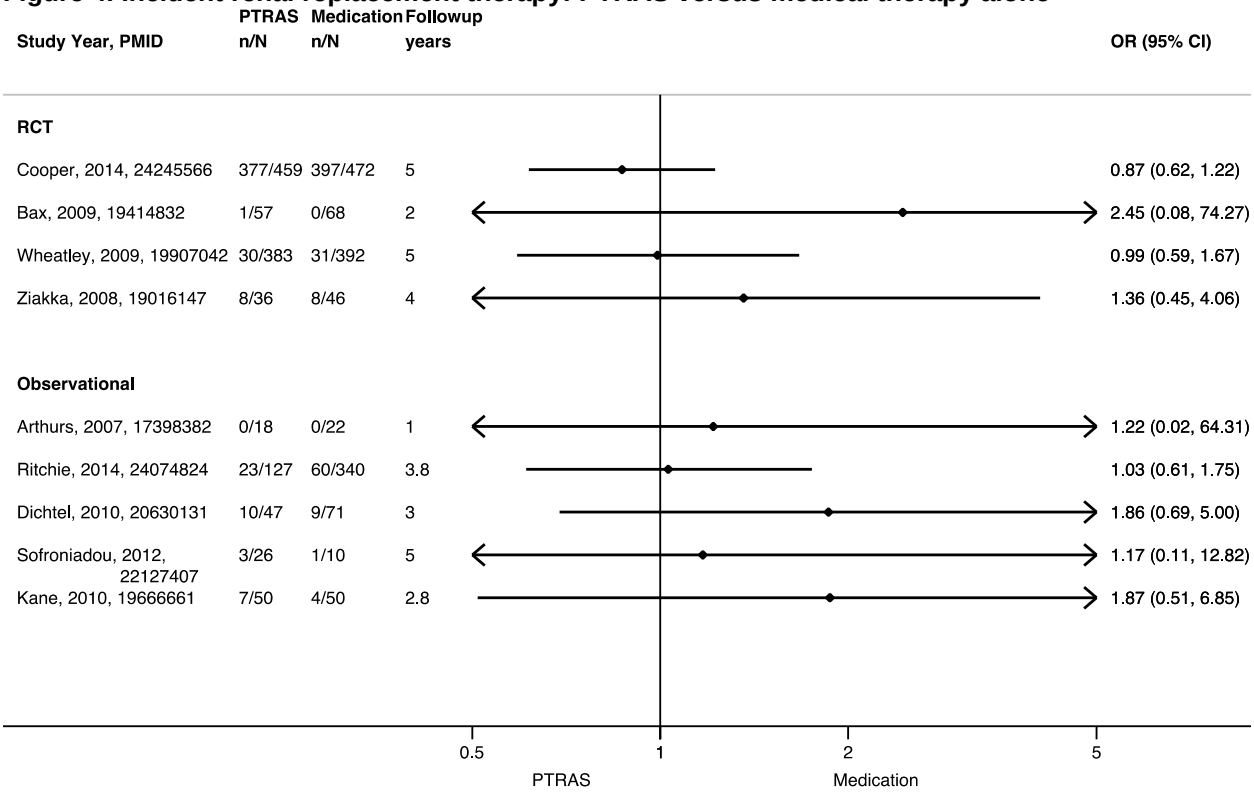
Randomized Trials

Four of the RCTs reported on RRT.[19, 20, 24, 35] The overall rates of dialysis varied from 0.7 percent at 2 years to 10 percent at a mean of 4 years of followup (Figure 4). However, no statistically significant differences were found between PTRAS and medical therapy for all trials, with ORs ranging from 1.0 to 2.0, with wide confidence intervals. See Appendix Table C.4.6.

Nonrandomized Studies

Five studies reported data on patients progressing to end stage renal disease (ESRD) (Figure 4).[9, 22, 28, 31, 33] One study explicitly reported that no patients started dialysis. In the remaining four studies, for patients progressing to ESRD, three found no statistically significant difference between comparison groups, with ORs ranging from 1.03 to 7.94 and wide confidence intervals, across all studies. No analysis was adjusted for baseline differences or patient characteristics. See Appendix Table C.4.6.

Figure 4. Incident renal replacement therapy: PTRAS versus medical therapy alone



Point estimates of odds ratios (OR) and 95% confidence intervals (CI) from individual studies. n/N = number of events/total, PMID = PubMed Identifier, PTRAS = percutaneous transluminal renal angioplasty with stent placement, RCT = randomized controlled trials.

Cardiovascular Outcomes

Randomized Trials

Four RCTs[19, 20, 24, 32b] reported similar cardiovascular event rates in both treatment groups, including myocardial infarction (MI); stroke; newly diagnosed coronary artery, peripheral artery, or cerebrovascular disease; cardiovascular event-free survival, and cardiovascular mortality. See Appendix Table C.4.12.

Nonrandomized Studies

Three NRCSs[22, 31, 33] reported on different cardiovascular outcomes in each study. Stroke, angina, and abdominal aortic aneurysm rupture each occurred in no or one patient per study. In one study, myocardial infarctions occurred in 17 percent of patients 2 years after PTRAS and 4.5 percent of patients who remained on medical therapy alone, yielding a nonsignificant unadjusted hazard ratio of 3.0 (0.60, 14). In a second study, 14 percent of patients required coronary revascularization within a mean of 2.8 years after PTRAS compared with 22 percent in the medical therapy group (unadjusted OR = 0.58 [0.20, 1.64]). See Appendix Table C.4.17.

Pulmonary Edema

In three RCTs (STAR, CORAL, RASCAD),[19, 24, 32] episodes of pulmonary edema or CHF were uncommon (1% to 6%) and did not significantly differ between treatment groups. See Appendix Tables C.4.17 and C.4.18. None of the NRCSs reported on pulmonary edema.

Kidney Function

Randomized Trials

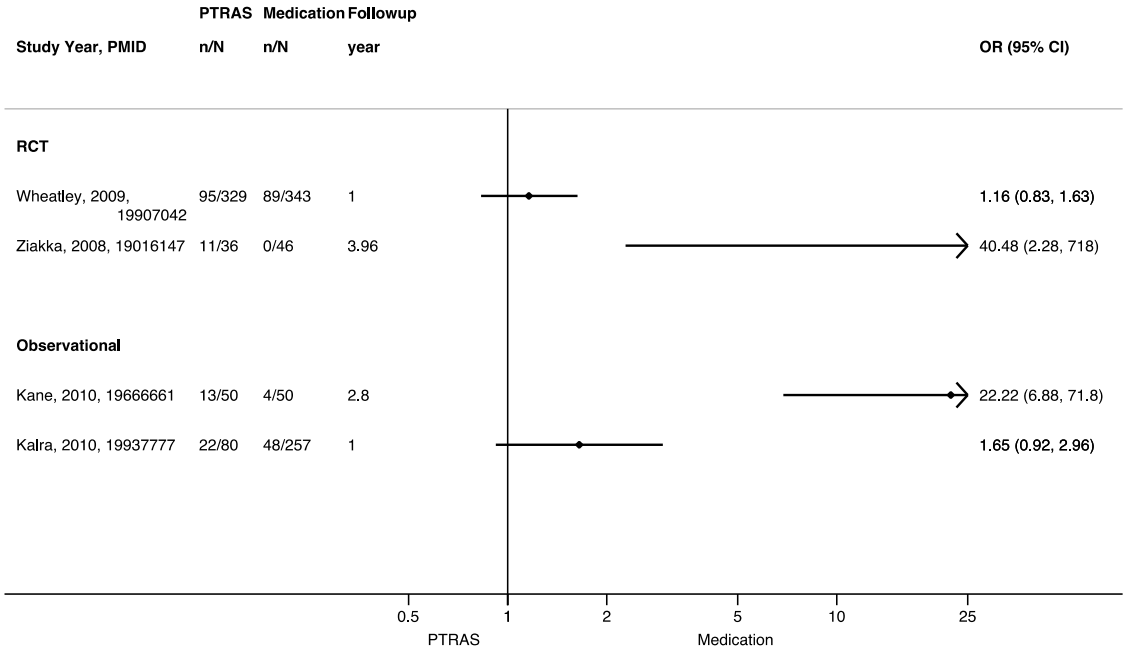
Six RCTs reported on changes in kidney function.[19, 20, 24, 32, 34b, 35] In CORAL, SCr was measured in local labs and any doubling was confirmed by the core lab; other trials did not report on SCr measurement methods. No differences were found in the CORAL trial for the outcomes of progressive renal insufficiency (adjusted HR 0.86; 95% CI 0.64 to 1.17).[19] In the ASTRAL trial, the two study groups had similar rates of renal events (HR 0.97; 95% CI 0.67 to 1.40).[20] In RASCAD, GFR (MDRD equation)[38] remained stable for 1 year in both treatment arms and no significant difference was found.[32] The STAR trial found no significant difference in SCr or creatinine clearance (Cockcroft-Gault) at 2 years.[24] In ASTRAL, the mean slope of 1/SCr revealed a trend towards less decline (p=0.06) but the mean slope of SCr did not (p=0.11). In RADAR, GFR rose over 12 months after PTRAS and fell in the medical therapy arm, but the difference was not statistically significant (p=0.23).[34b] Only in Ziakka 2008 was a significant difference found; kidney function improved (SCr decreased >20 percent) in 30.5 percent or patients and worsened (SCr increased >20 percent) in 36.2 percent of patients in PTRAS arm, whereas in the medical therapy arm kidney function remained stable in 69.8 percent of patients and worsened in 30.2 percent (P<0.001) (Figure 5).[35] See Appendix Tables C.4.2, C.4.3, C.4.5, C.4.6, and C.4.7.

Nonrandomized Studies

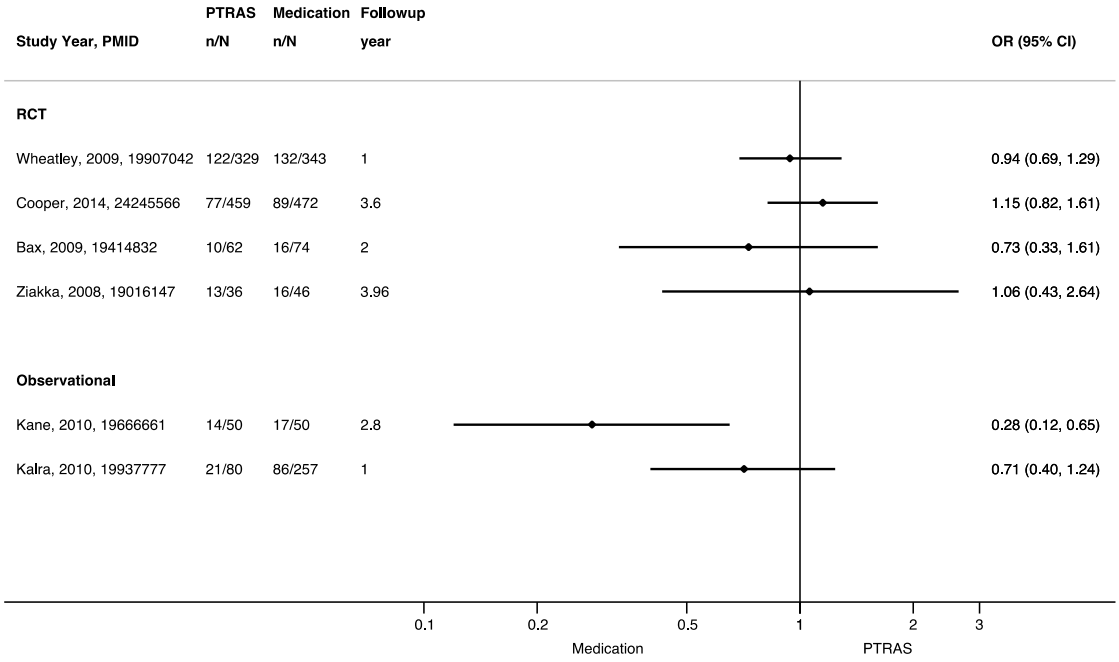
Of the five studies that reported on kidney function outcomes, none reported specific methods for measuring SCr; to measure GFR, four used the MDRD equation[28, 30, 31, 33] and one iothalamate clearance.[29] Three NRCSs reported ordinal outcomes for renal improvement (Figure 5, top).[29-31] Kidney function improved in 7 to 25 percent of patients in PTRAS group, as compared with 6 to 8 percent improvement in the medical therapy alone group. Five NRCSs reported higher GFR in the PTRAS group, as compared with the medical therapy group in kidney function.[28-31, 33] These studies reported a median 0.1 mL/min change in GFR in PTRAS, as compared with a median −0.4 mL/min change in GFR in medical therapy only group. See Appendix Tables C.4.2, C.4.3, C.4.5, C.4.6, and C.4.7.

Figure 5. Kidney function improvement (panel A) and worsening (panel B): PTRAS versus medical therapy alone

Panel A: Improvement (or cure)



Panel B: Worsening



Point estimates of odds ratios (OR) and 95% confidence intervals (CI) from individual studies. n/N = number of events/total, PMID = PubMed Identifier, PTRAS = percutaneous transluminal renal angioplasty with stent placement, RCT = randomized controlled trials.

Blood Pressure Control

Randomized Trials

The STAR trial, Ziakka 2008, and the NITER trial reported BP related events (as categorical/ordinal outcomes).[24, 32b, 35] In STAR, refractory HTN continued in 0 percent in the PTRAS arm, as compared with 4 percent in medical therapy alone;[24] the percentage of patients with target BP (<140/90 mmHg) was similar in both arms (32% vs. 29%, P=0.95). In Ziakka 2008, BP was cured in 11.1 percent, improved in 66.6 percent, and failed to improve in 22.3 percent of patients in PTRAS arm, whereas in the medical therapy arm HTN was cured in 0 percent of patients, improved in 71.4 percent, and failed to improve in 28.6 percent (P<0.001).[35] The NITER abstract reported no BP "cures".[32b]. See Appendix Tables C.4.12 and C.4.13.

Across four RCTs[19, 20, 24, 32, 32b, 34b] comparing PTRAS versus medical therapy with detailed BP results, there was a reduction in SBP that ranged from −6 to −17 mmHg in PTRAS arms, as compared with a range of −5.5 to −16 mmHg reduction in SBP in the medical therapy arms. In their longitudinal analysis, the CORAL trial reported a significant difference in SBP (measured in the clinic) favoring PTRAS (−2.3 mm Hg; 95% CI, −4.4 to −0.2; P = 0.03), as compared with medical therapy.[19] In contrast, the other five trials (ASTRAL, RASCAD, STAR, NITER, RADAR)[20, 24, 32, 32b, 34b] found no significant between-group difference in SBP or DBP (measured in the clinic in STAR; not reported other trials). The CORAL trial did not report data on DBP (Figure 6). See Appendix Tables C.4.8, C.4.9, and C.4.11.

Changes in number of antihypertensive medications were reported for the CORAL and ASTRAL trials.[19, 20] Both found that after PTRAS, patients on average were prescribed 0.2 fewer antihypertensive medications than those who remained on medical therapy only; this difference was statistically significant in CORAL (difference = −0.2 [−0.397, −0.003], P=0.046), but untested (no confidence intervals reported) in ASTRAL (Appendix Table C.4.14).

Nonrandomized Studies

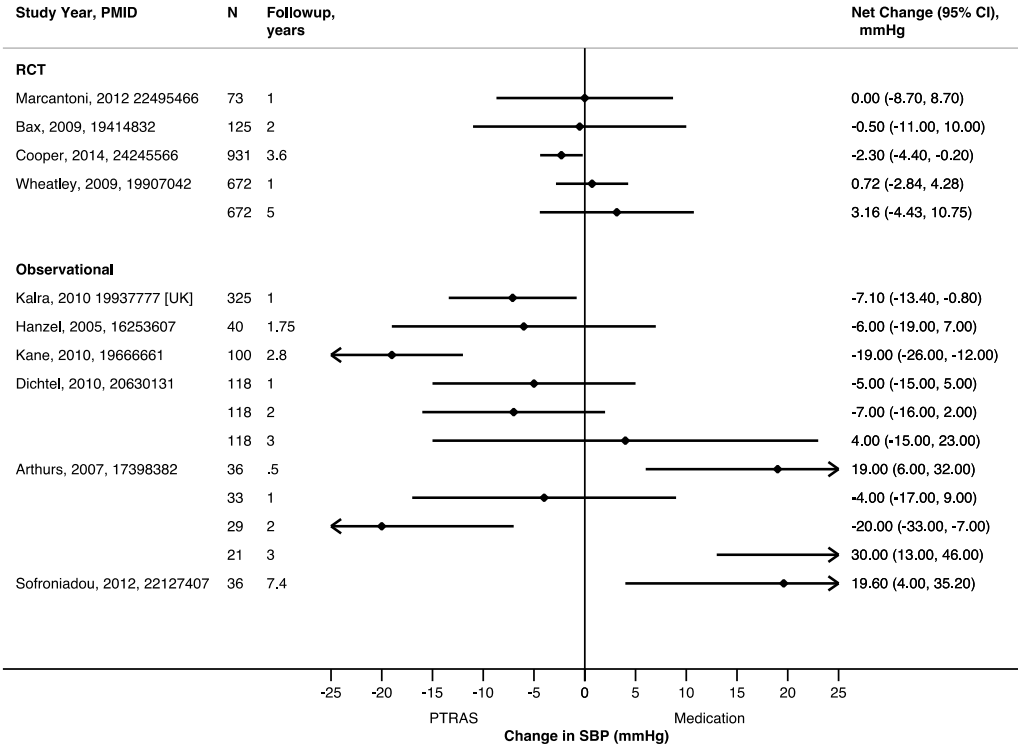
One NRCS reported ordinal outcomes for BP improvement.[29] Both groups observed a significant decrease in BP, but the magnitude of effect was greater in the PTRAS, as compared with medical therapy (9% SBP decrease in PTRAS vs. 5% decrease in medical therapy only; p=0.016).[29] See Appendix Table C.4.13.

The six NRCSs that reported on changes in BP were highly heterogeneous (Figure 6)[22, 28-31, 33]; three of these studies reported measuring clinic BP,[22, 28, 31] one measured clinic BP at one center and 24 hour ambulatory BP at another center.[30] Two studies found statistically significant net reductions in SBP favoring PTRAS by 7 or 19 mmHg,[11, 31] and, in Kalra 2010, significant net reduction in DBP also favoring PTRAS by 4 mmHg (Kane 2010 did not report DBP).[30] But Sofroniadou 2010 found significantly higher SBP (20 mmHg) and DBP (9 mmHg) in patients who had PTRAS.[33] Two studies found no significant difference for either SBP or DBP.[28, 29] Arthurs reported data that allowed calculations of net change BP, with highly variable differences between PTRAS and medical therapy at different time points from 6 months to 4 years (4 year data omitted from figure because sample size appeared to be about 4 or 5 individuals in each group at that time point).[22] See Appendix Tables C.4.8, C.4.9, C.4.11.

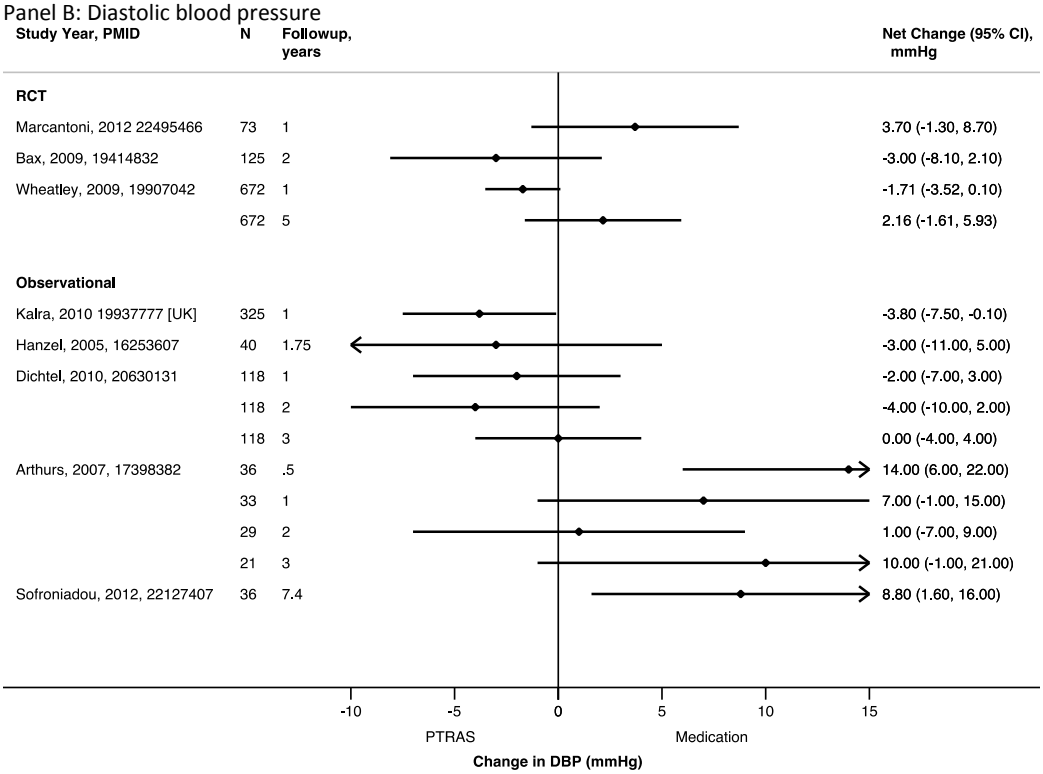
Changes in number of antihypertensive medications were reported five NRCSs.[22, 28, 29, 31, 33] Only one reported a statistically significant difference between groups.[31] See Appendix Table C.4.14.

Figure 6. Blood pressure, net change: PTRAS versus medical therapy alone

Panel A: Systolic blood pressure



Panel B: Diastolic blood pressure



Point estimates of net change blood pressure and 95% confidence intervals (CI) from individual studies. DBP = diastolic blood pressure, N = total sample size, PMID = Pubmed identifier, PTRAS = percutaneous transluminal renal angioplasty with stent placement, RCT = randomized controlled trials, SBP = systolic blood pressure, UK = study cohorts from the UK.

Adverse Events (Including 30-Day Mortality)

Randomized Trials

Five trials reported on adverse events related to PTRAS; adverse events related to medications were not reported.[19, 20, 23, 24, 32] Two trials reported that 2/280 (0.7%)[20] and 2/64 (3%)[24] died within 30 days of the procedure due to complications following renal artery perforation or cardiac events. CORAL, the largest trial, had no periprocedural deaths.[19] Across all four trials 4 of 848 patients who received PTRAS (including those assigned to medical therapy who crossed over to receive PTRAS) died (0.5%). Of note, the CORAL trial reported that 1 of 478 patients assigned to medical therapy had a fatal stroke on the day of randomization.[19] Other serious adverse events reported included, in CORAL, only angiographic complications (implicitly without long-term consequence) including dissections (11/495, 2.2%), vessel occlusions (6/495, 1.2%), distal embolization (6/495, 1.2%), and in one patient each, wire perforation, vessel rupture, and pseudoaneurysm.[19] In ASTRAL, 12 serious events in 11 patients occurred in 280 patients, including four with groin hematomas or hemorrhages requiring hospitalization, five with clinically significant acute kidney injury, and one with renal-artery occlusion.[20] In addition to the procedure-related deaths, STAR reported two patients with femoral artery false aneurysms and one patient who eventually required permanent dialysis after cholesterol embolization.[24] The only serious adverse event in RASCAD was that 1/41 patients (2.5%) required a blood transfusion and rehospitalization from a groin hematoma.[32] Balzer 2009 reported 5 periprocedural events in 49 patients, including stent dislocation, local dissection, and postoperative occlusion.[23] Appendix Tables C.4.19 and C.4.20.

Nonrandomized Studies

Four NRCSs reported periprocedural complications.[9, 22, 29, 33] No study reported on medication-related adverse events. Three reported no major complications (renal failure or death in one study;[29] acute thrombosis, dissection, renal failure, rapid kidney function decline, hemorrhage, or death in one study;[22] undefined in one study[33]). In contrast, Ritchie 2014 reported a 4.8 percent major complication rate (undefined).[9] No study reported episodes of acute thrombosis, regardless of use of prophylaxis. See Appendix Tables C.4.19 and C.4.20.

Key Question 2. Association of Patient Factors With Outcomes

The CORAL trial tested for interaction terms with their composite outcome (cardiovascular or renal death, stroke, myocardial infarction, CHF hospitalization, GFR decrease by at least 30%, or RRT).[19] None of the prespecified terms (sex, black race, global kidney ischemia, or diabetes) interacted with (altered the comparative effectiveness between) the interventions (PTRAS versus medical therapy alone). They also found no interactions with other tested factors—SCr >1.6 mg/dL, GFR <45 mL/min, SBP >160 mmHg, age >70 years, or site-reported renal artery stenosis ≥80 percent.

In the ASTRAL trial, subgroup analyses were performed for the analysis of the slope of 1/SCr (a proxy for GFR) over 5 years.[20] No differences in effect were reported among the prespecified subgroups (baseline SCr and GFR, percent stenosis, kidney length, and prior renal impairment progression) or bilateral versus unilateral severe (>70%) stenosis.

Ritchie 2014, in a retrospective observational study that compared PTRAS to medical therapy only, ran analyses adjusted for age, sex, kidney function, proteinuria, BP, renal artery patency, diabetes, and use of angiotensin converting enzyme inhibitor (ACEi) / angiotensin-receptor blocker (ARB) in different subgroups of patients, comparing PTRAS and medical

therapy.[9] In patients presenting with flash pulmonary edema, those who received PTRAS had a reduced relative rate of death (0.36; 95% CI 0.16 to 0.80) compared with those treated medically. Similarly, those presenting with both rapidly declining kidney function (SCr increased 20% or by 1.14 mg/dL in 6 months) and refractory HTN (BP >140/90 mmHg on at least three medications) who received PTRAS had a reduced relative rate of death (0.14; 95% CI 0.01 to 0.99) compared with those treated medically. In contrast, those who presented with either rapidly declining kidney function or refractory HTN alone had statistically similar rates of death regardless of treatment choice. In all risk groups, rates of cardiovascular events and RRT were similar between those who received PTRAS or medical therapy.

Key Question 3. Association of Treatment Factors With Outcomes

No comparative study addressed this question.

Surgery Versus Medical Therapy

One RCT (but no NRCS) compared open surgical revascularization with medical therapy alone.

Key Points

- One RCT only compared surgery and medical therapy. The study was of low (or unclear) risk of bias.
- **Outcomes**: No statistically significant differences or MCID were found between interventions for death, dialysis-free survival, or BP control. Adverse events were not reported.
- **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.
- **Treatment factors**: No comparative studies addressed differences in treatment factors as a predictor of outcomes in the comparison of surgery versus medical therapy.

Key Question 1. Effects of Intervention on Outcomes

Randomized Controlled Trial (Surgery Vs. Medical Therapy)

Uzzo 2002 randomized 52 patients with bilateral ARAS (or ARAS in a solitary kidney) or unilateral disease with chronic kidney disease (SCR >1.5 mg/dL or GFR <70 mL/min).[34] Patients had >75 percent stenosis; it was not reported whether translesional pressure gradients were used to define stenosis severity. Excluded were patients with SCr >4.0 mg/dL, DBP >100 despite "adequate medical management" or comorbid conditions precluding surgical revascularization. Medical management was not described (but was under the direction of a single nephrologist). Surgery included aortorenal bypass (6/25 patients), splenorenal bypass (3/25), hepatorenal bypass (8/25), ileorenal bypass (6/25), endarterectomy (1/25), and aortic replacement with renal artery reimplantation (1/25). See Appendix Tables C.1, C.2.2, C.3).

This RCT was rated as having low risk of bias for outcome assessment (detection bias), attrition bias, and selective reporting (reporting bias). For all other items, including detection bias and sample representativeness of the entire population, it was unclear. See Appendix Table D1.

Median follow-up time was 74 months. Overall, there were no statistically significant differences or MCID in outcomes or times to outcomes, including death (approximately 60% at 7 years in both groups, P=0.31), time to death (surgery 69 months vs. medical 62 months; P=0.75), dialysis-free survival (P=0.64), or BP control (undefined, P=0.20). See Appendix Tables C.4.1, C.4.6, C.4.12.

Adverse events were not reported.

Key Question 2. Association of Patient Factors With Outcomes

Uzzo 2002 reported that patients with baseline elevated SCr (2 to 4 mg/dL) were less likely to die or have uncontrollable HTN if surgically revascularized than if treated medically (P=0.11),[34] in contrast with no significant difference in effect for the total cohort, who also included patients lower SCr. However, by multivariable analysis, no interactions were found between treatment choice and baseline demographic factors.

Key Question 3. Association of Treatment Factors With Outcomes

No comparative study addressed this question.

Surgery Versus PTRAS

One RCT and three NRCSs compared surgery to PTRAS.

Key Points

- One RCT and three 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.
- **Outcomes**: The 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 the three 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.
- **Patient factors**: One of two 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.
- **Treatment factors**: No comparative studies addressed differences in treatment factors as a predictor of outcomes in the comparison of surgery versus PTRAS.

Key Question 1. Effects of Intervention on Outcomes

Randomized Controlled Trial (Surgery Vs. PTRAS)

Balzer 2009 randomized patients with >70 percent ostial ARAS with HTN to either surgical revascularization (thromboendarterectomy or aortorenal bypass) or angioplasty (with or

without stent).[23] It was not reported whether translesional pressure gradients were used to define stenosis severity. In 27 patients, thromboendarterectomy was performed in 45 renal arteries and aortorenal bypass grafting in four renal arteries. In the 22 patients who had angioplasty, stents were placed in 22 of 28 renal arteries receiving treatment. Among the patients, 63 percent were male, mean age was 64 years, 18 percent had diabetes, 78 percent hyperlipidemia, and 53 percent coronary artery disease. Notably, 60 percent of patients who had surgical revascularization had >20 pack-years of smoking history, in contrast with 9 percent of those who had PTRAS; analyses were not adjusted for this baseline difference.[23] See Appendix C.1, C.2.3, C.3.

This RCT was rated as having low risk of bias for attrition bias and selective reporting (reporting bias). For all other items, including sample representativeness of the entire population, selection bias, performance bias, and detection bias, it was unclear. See Appendix Table D.1.

During a mean 54 months of follow-up, deaths were not statistically significantly different (surgery 26% [7/27] vs. PTRAS 18% [4/22], P=0.80); although the OR of 0.63 (95% CI 0.16, to 2.53) meets this review's MCID threshold, ignoring statistical significance (Appendix Table C.4.1). RRT or cardiovascular events were not reported. Four years after surgery, SCr levels stabilized after surgery (no data on how SCr was measured), and there was a significant improvement in PTRAS compared to baseline levels (P=0.04). However, there was no difference between groups (Appendix Tables C.4.2, C.4.4, C.4.5). Also at 4 years, there was significant improvement in clinic-measured SBP and DBP in both groups compared to baseline levels, but the difference was not significant between the two groups (P=0.73 for SBP and P=0.49 for DBP) (Appendix Tables C.4.8, C.4.10, C.4.11).[23] This RCT also reported ordinal outcomes for BP improvement or cure and found no difference between groups (P=0.72) (Appendix Table C.4.13). Two patients in each group no longer required antihypertensive treatment to control their HTN. There were no periprocedural deaths. After surgery, one patient required PTRAS due to local dissection after endarterectomy. After PTRAS, two patients required surgery due to dislocated stents (Appendix Table C.4.20)

Nonrandomized Comparative Studies (Surgery Vs. PTRAS)

Three retrospective NRCSs compared patients who had open surgery and those who had PTRAS.[26, 27, 36] None of the studies reported whether translesional pressure gradients were used to define stenosis severity. The studies were of unclear or high risk of bias for selection bias regarding the similarity of the compared groups. Two of the studies were of high risk of bias for incomplete outcome data (attrition bias) (Risk of Bias Description Appendix Table D.2).

In de Donato 2007,[27] patients were included with ≥80 percent stenosis and HTN requiring at least three medications. Of note, 15 percent of patients had fibromuscular dysplasia. Patients had a mean age of 62 years, and 81 percent were male. The study included 83 patients who had 97 renal arteries treated. It was not reported how many patients received each intervention, but 15 renal arteries had surgical revascularization (11 endarterectomy, 4 aortorenal bypass) and 82 arteries had angioplasty (68, 81% with stent). There were no major periprocedural complications (including death) with either procedure. After 1 year, there was no significant difference in whether patients had HTN improvement or cure (however, this was analyzed by renal artery not patient). No other outcomes were compared between interventions. See Appendix Tables C.1, C.2.3, C.3, C.4.20; Risk of bias, Appendix Table D.2.

In Crutchley 2009, 56 patients had surgical revascularization because they had HTN requiring multiple medications, a history of flash pulmonary edema or malignant HTN, or ischemic nephropathy (not defined) with bilateral disease or a solitary kidney. Among these

patients, 17 had bypass, 22 had endarterectomy, and 17 had combined aortic and renal artery procedures. In contrast, 30 patients had angioplasty (26, 87% with stent) for a variety of unreported reasons. Patients' mean age was 68 years and 46 percent were male. No outcome of interest was explicitly compared between interventions, but the article implied no significant difference in mortality during a mean of 58 months of followup.[26] See Appendix Tables C.1, C.2.3, C.3, C.4.1; Risk of bias, Appendix Table D.2.

Patel 2009 retrospectively compared 203 patients who had PTRAS and 47 who had open surgery for ARAS with at least 75 percent stenosis.[36] Patients were excluded if renal artery revascularization was conducted in the context of concomitant aortic reconstruction without specific indications for renal artery revascularization, but one-third (15/47) did have concomitant aortic surgery. Among the open surgeries, 21 (47%) were endarterectomies and 26 (53%) were bypasses, of which 17 were aortorenal, 6 were hepatorenal, 2 were splenorenal, and 1 was iliorenal. Few details were reported regarding the PTRAS procedures. Patients' mean age was 71 years, and 58 percent were men. Fifty-one percent had "chronic renal insufficiency," 13 percent acute renal failure, and for 49 percent the reason for the intervention was renal salvage. Almost all patients (94%) had HTN, and for 51 percent this was the indication for the intervention. All-cause death (28% at 3 years) and incident RRT (~30% at 3 years) rates were similar between groups (P=0.9 and 0.7, respectively) across 3 years. At 1 year, statistically significantly more patients had improved kidney function after open surgery than PTRAS (52% vs. 24%, P=0.009); this difference persisted beyond 1 year but was not statistically significant (43% vs. 19%, P=0.1). At all time points, nonsignificantly more patients had cure or improvement in BP control (e.g., open 89% vs. PTRAS 74% at 1 year, P=0.2). SCr, SBP, and DBP were all similar at and after 1 year of followup (P>0.6); details about how SCr and BP were measured were not reported. Perioperative complications were significantly more common with open surgery (23%) than with PTRAS (12%, P=0.001), including death (1/47 vs. 1/203).

Key Question 2. Association of Patient Factors With Outcomes

Crutchley 2009 found that a renal resistive index ≥0.8 (vs. <0.8) predicted all-cause mortality among patients who had PTRAS (HR 5.7, 95% CI 1.1 to 28) or surgical revascularization (HR 4.8; 95% CI 1.6 to 14).[26] However, no statistical analysis of an interaction between renal resistive index and revascularization approach was reported.

Patel 2009 found that patients with HTN as their indication for intervention were significantly more likely to have BP control cure or improvement and kidney function improvement at 1 year after open surgery than PTRAS patients (100% vs. 73%, P=0.04; 50% vs. 8%, P=0.01, respectively), but no significant differences by intervention if renal salvage was their indication.[36] However, the differences in effects between indication subgroups and revascularization approach were not statistically analyzed.

Key Question 3. Association of Treatment Factors With Outcomes

No comparative study addressed this question.

Single-Group Studies

Eligibility criteria for single-group studies varied based on the expected volume of evidence for each intervention. For PTRAS, we include prospective studies with at least 100 patients. For medical therapy, we include prospective studies with at least 10 patients. For

surgery, we include both prospective studies with at least 10 patients and retrospective studies with at least 100 patients. These studies include both true single-group studies (in which the whole study comprised a cohort of patients receiving a single intervention), comparisons of different cohorts of patients all receiving the same overarching intervention (PTRAS, medical therapy alone, or surgery), and relevant cohorts from RCTs and NRCSs. Note that not all cohorts from the comparative studies are included here. For example, the single groups from a retrospective comparison of PTRAS versus medical therapy do not meet criteria for analysis of single-group studies.

Angioplasty With Stenting

Key Points

- 67 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.
- **Mortality**: In 31 studies, mortality ranged from 0 to 53 percent after 6 months to 5 years of followup (one 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 seven studies, incident RRT occurred in 2.3 to 23 percent 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 four studies 2 to 82 percent of patients had episodes of acute kidney injury. In 21 studies, kidney function improved in 12 to 82 percent and worsened in 4 to 37 percent of patients. 21 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 two studies 0 and 4 percent of patients had new-onset HTN. In 19 studies, BP improved in 4 to 69 percent and stabilized or worsened in 7 to 67 percent 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 post-operative death, RRT, and acute renal failure; and severe bleeding, dissection, unplanned surgery, and thrombosis.
- **Patient factors**: 20 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 three 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 one of four or five 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 one of either three or four studies.

- **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.

Key Question 1. Effects of Intervention on Outcomes

In 63 articles,[9, 19, 20, 23-25, 27, 29, 30, 32, 33, 35, 39-89] we identified 67 cohorts of patients who were treated with PTRAS (a total of 8286 patients) in prospective studies. Among the studies, 48 cohorts[41-45, 47-66, 70-75, 77-82, 84-88] assessed the effectiveness of PTRAS on outcomes in single cohorts of patients (or compared different cohorts of patients receiving PTRAS), and 19 cohorts[9, 19, 20, 23-25, 27, 29, 30, 32, 33, 35, 46, 67-69, 76, 83] were from studies comparing PTRAS to medical therapy or surgery.

Analyzed studies typically included more males than females (the median study population was 57% male [range 36-83%]). Three-quarters of included studies included patients with a mean age of 70 years and above (range 59-77 years). Two studies reported a mean HTN duration of 13.5 years. [61, 87] See Appendix Table C.3.

The most common reason for angioplasty was HTN or renal insufficiency without prior treatment (42 studies).[19, 20, 24, 25, 27, 29, 30, 35, 42, 44-49, 52, 54, 56-58, 64-68, 70-73, 76-85, 87] Uncontrolled HTN while on two or more medications was another common indication for angioplasty (9 studies)[19, 42, 49, 64, 72, 79, 84, 85, 89] [53, 64, 70, 73, 77] Seventeen of the studies used translesional pressure gradient measurements to determine eligibility for PTRAS, mostly using a threshold of 20 mmHg (10 studies[19, 39, 42, 47, 53, 55, 57, 78, 79, 89]); one study used a threshold of 15 mmHg,[75] two studies used 30 mmHg,[45, 51] one 40 mmHg,[41] and three did not report their threshold.[58, 72, 85] Five studies included only patients with cardiovascular disease or flash pulmonary edema.[53, 64, 70, 73, 77] Across studies, the median average BP was 162/83 mmHg (range 110-196/73-105 mmHg); the median average GFR was 52 mL/min (range 31.5-67.2 mL/min), and median average SCr was 1.5 mg/dL (range 1.1-3 mg/dL) before PTRAS. See Appendix Table C.1.

Forty-five included studies reported on patients with a history or current cardiovascular disease. [9, 19, 20, 23, 24, 30, 32, 33, 41, 43, 45-49, 52-58, 61, 64, 66-68, 70-73, 75-81, 85-88] These 45 studies reported medians of 63 percent of patients who had coronary artery disease, 32 percent myocardial infarction, and 32 percent coronary revascularization. Medians of 22.5 percent of patients had CHF, and 29 percent left ventricular hypertrophy. Medians of 7 percent of patients had an abdominal aortic aneurysm, 39 percent cerebrovascular disease, and 16.5 percent a history of stroke. Lastly, a median of 44 percent of patients had a history of peripheral artery disease. See Appendix Table C.3.

The definitions of RAS varied across studies. Two studies included patients with over 80 percent stenosis,[19, 27] 23 over 70 percent stenosis,[19, 23, 29, 32, 33, 41, 43, 45, 46, 51, 53, 56, 59-61, 63, 65, 66, 70, 71, 73, 76-81, 85-87] 10 over 60 percent,[19, 30, 41, 46, 55, 75, 80, 85, 87, 89] and 21 over 50 percent. [9, 24, 30, 32, 42-46, 50,

[52, 54, 58, 67-69, 72, 74, 78, 81, 85] The minimum percent stenosis was not stated in 9 studies.[20, 25, 35, 48, 49, 57, 62, 64, 79]

In 43 studies that reported data, bilateral stenting was present among a median of 28 (range 0-100%) percent of patients.[19, 23-25, 29, 33, 41-46, 51-55, 57, 59-62, 64, 66, 70-80, 82-84, 86-88]

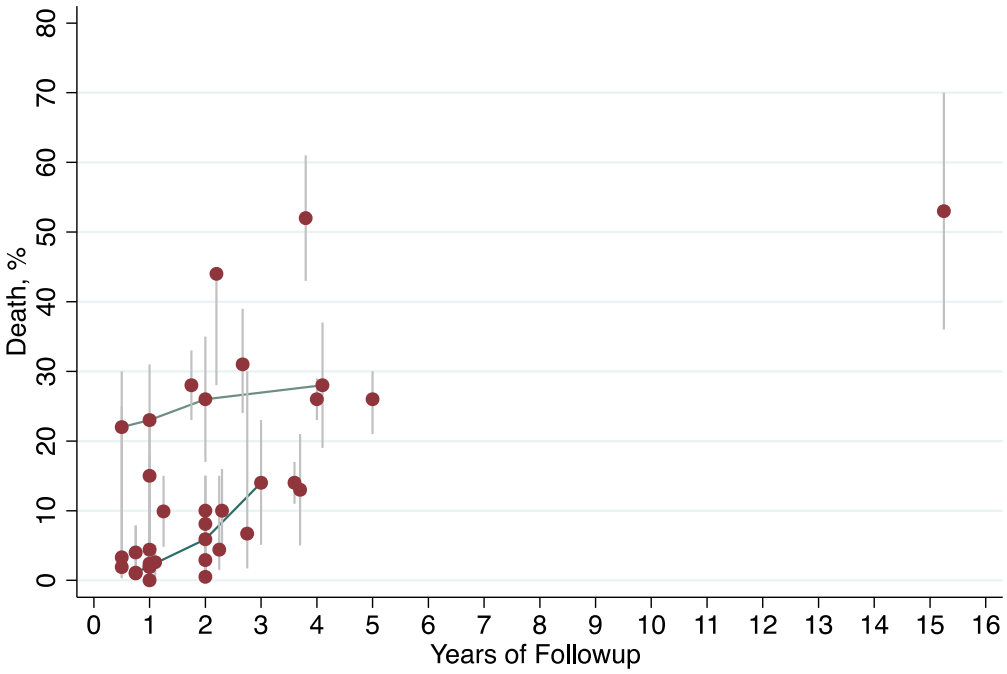
Palmaz stents were used in 25 studies,[23, 24, 41-44, 46-53, 55, 57-60, 63, 67, 78, 79, 81, 88] 20 studies (21 cohorts) used non-Palmaz stents or did not report stent brand information,[19, 25, 30, 39, 54, 56, 62, 66, 68, 70, 71, 73-76, 83, 85-87, 89] and 18 studies (19 cohorts) did not report data on the type of stent used.[9, 20, 27, 29, 32, 33, 35, 39, 45, 61, 64, 65, 69, 72, 77, 80, 82, 84] Twenty-five studies (26 cohorts) reported utilizing a distal protection device.[19, 20, 24, 25, 30, 42, 44, 48, 49, 54, 57, 58, 61-63, 67, 68, 70, 74-76, 85-88] See Appendix Tables C.2.1, C.2.3 C.2.4

In general, across risk of bias questions, between 10 and 43 percent of studies were considered to be of high risk of bias, and between 57 and 90 percent were considered low risk of bias (Appendix Figure D.3). Twenty-five studies were judged high risk of bias for failing to adjust for different lengths of followup, 21 high risk of bias for incomplete outcome data (attrition bias), and 14 for selective outcome reporting. The samples were considered to be representative of the entire population from which they were recruited in 48 studies.

Mortality (Study Duration 6 Months or Greater)

Data on mortality long-term mortality after PTRAS was reported in 31 studies (Figure 7).[9, 19, 20, 24, 39, 41-43, 45, 47-50, 52, 55-57, 64, 67, 70-76, 78, 82, 83, 86, 88] The mean followup time for reporting mortality was 2.4 years, with the longest followup at 15 years. The mortality rates ranged from 0 to 53 percent, with a median of 10 percent. Most studies reported mortality between 0 and 31 percent, but there are four included studies that reported mortality above 40 percent. These four studies reported that the intervention did not significantly reduce the risk of kidney failure and cardiac events. At 1 year, in about a third of the studies (10 of 31), 2.6 percent of patients had died (range 0% to 23%); at 2 years, in most studies (7 of 31), 8.1 percent of patients had died (range 0.5% to 44%). Other than a general trend toward increased death with longer-term followup, there was no clear explanation across studies for the difference in mortality. The most common cause of mortality reported was cardiovascular-related deaths (12 studies).[19, 20, 24, 44, 53, 54, 60, 64, 73, 74, 76, 80] Renal- and stroke-related deaths were reported in four[19, 20, 64, 74] and two[19, 24] studies, respectively. See Appendix Table C.4.1.

Figure 7. Death after PTRAS, percent of patients

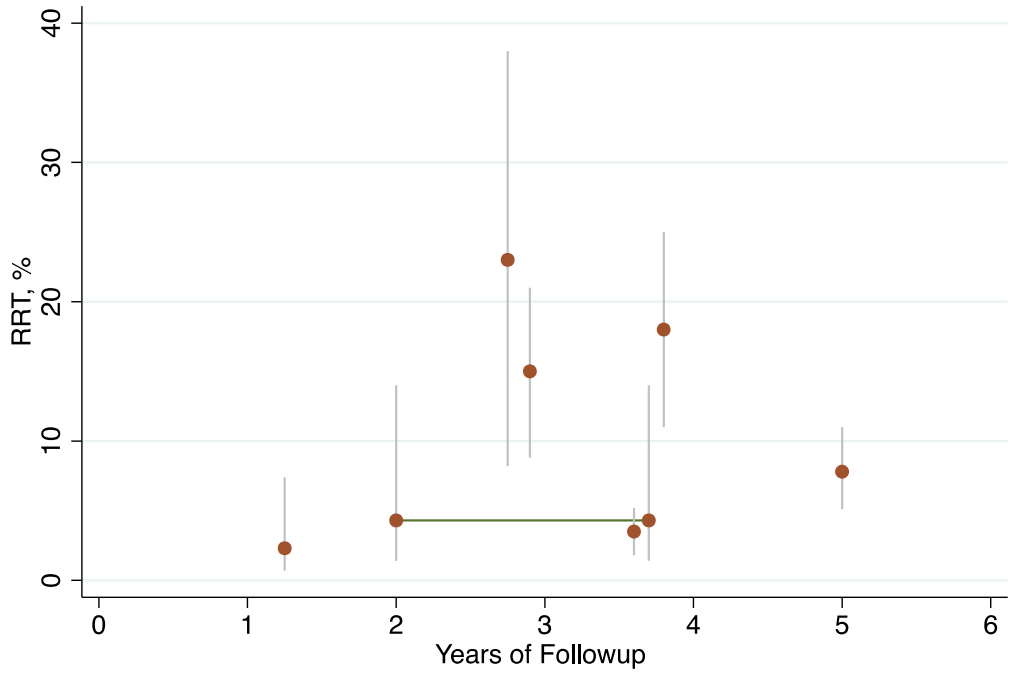


Point estimates and 95% confidence intervals from individual studies. Lines connecting points indicate data coming from the same study (or cohort) at different time points. PTRAS= percutaneous transluminal renal angioplasty with stent.

Renal Replacement Therapy

Seven studies[9, 19, 20, 48, 76, 82, 83] reported that RRT occurred in 2.3 to 23 percent of patients between 1.25 and 5 years (Figure 8). In three of the studies, RRT occurred in at least 15 percent of patients. Additionally, three studies reported RRT occurred in less than 5 percent of patients. There was no clear explanation across studies for the wide heterogeneity in RRT occurrence, including length of followup. See Appendix Table C.4.6.

Figure 8. Renal replacement therapy after PTRAS, percent of patients



Point estimates and 95% confidence intervals from individual studies. Lines connecting points indicate data coming from the same study (or cohort) at different time points. PTRAS= percutaneous transluminal renal angioplasty with stent, RRT = renal replacement therapy.

Cardiovascular Outcomes

Twelve studies[9, 19, 20, 24, 39, 48, 55, 65, 67, 76, 78, 80] reported cardiovascular event rates, indicating that patients remain at increased risk of cardiovascular disease after PTRAS. CHF was reported in four studies (0 to 83%). Other cardiovascular events included angina in 7.5 percent (one study)[20], MI in 1 to 82 percent (eight studies)[19, 20, 48, 55, 67, 76, 78, 80], stroke in 1.2 to 19 percent (six studies),[19, 20, 39, 55, 76, 80] coronary revascularization in 3.8 to 3.9 percent (two studies),[20, 48] and composite cardiovascular events in 0 to 37 percent (four studies).[9, 20, 65, 80] See Appendix Tables C.4.17 and C.4.18.

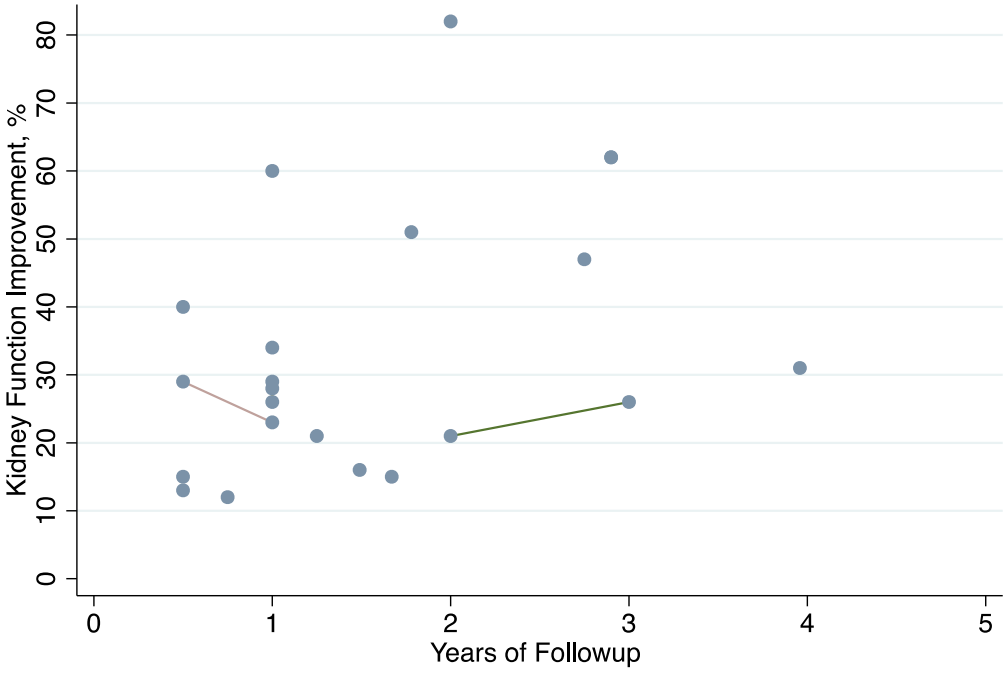
Kidney Function

The studies were highly heterogeneous regarding which kidney function measures were analyzed, in particular for definitions of ordinal (categorical) outcomes such as kidney function improvement. The definitions used by studies are in the summary tables in Appendix Table C.4. Among 20 studies that reported CKD at baseline, some included only patients without CKD, some only those with CKD. A median of 47.5 percent had CKD.

Four studies[20, 80, 86, 88] reported that between 1.9 and 82 percent of patients had episodes of acute kidney injury at 1 to 3 years. Twenty-two studies reported ordinal outcomes for kidney function improvement (Figure 9).[19, 20, 30, 43, 46, 48, 53, 54, 58, 60-62, 65, 67, 71, 74, 75, 82-84, 86, 88] Kidney function improved in 12 to 82 percent of patients (14 studies),[20, 30, 46, 48, 54, 61, 62, 65, 71, 74, 83, 86, 88]; did not change in 3.2 to 72 percent (11 studies),[20, 30, 46, 48, 54, 61, 62, 71, 83, 88] stabilized in 33 to 59 percent (two studies),[62, 74] and worsened in 3.8 to 37 percent (15 studies).[20, 30, 40, 46, 48, 54, 58, 61, 65,

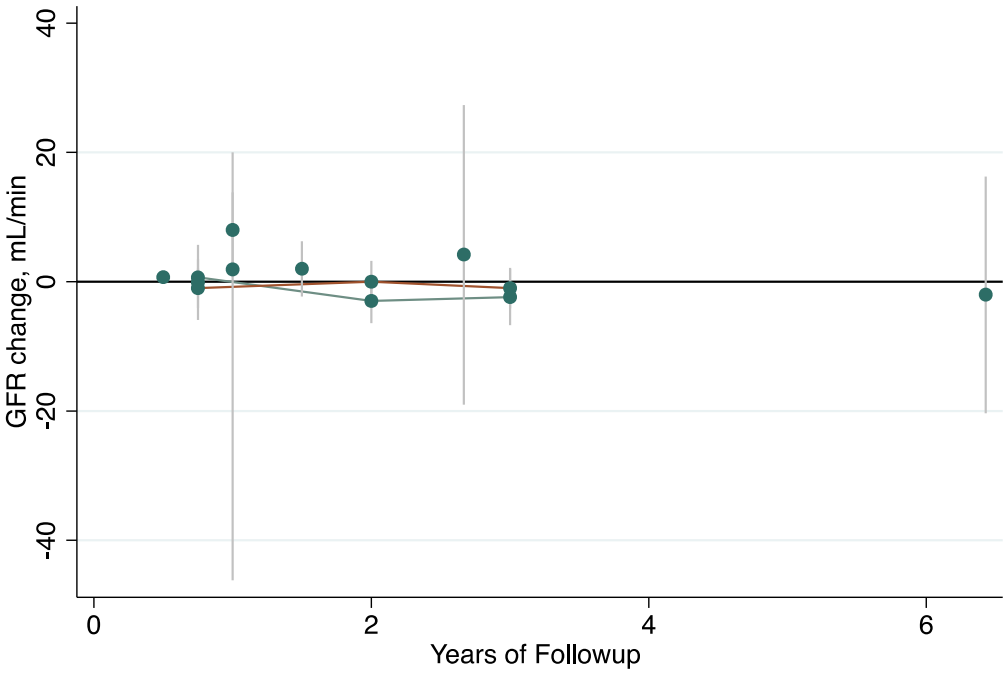
[71, 74, 83, 86, 88] Twenty-one studies reported a median 0 mL/min change in GFR (range −9 to 10 mL/mL); eight estimated GFR with the MDRD equation, five used Cockcroft-Gault, and the rest did not report how kidney function was estimated (Figure 10).[20, 30, 32, 51, 60, 61, 63, 64, 69-71, 74, 76, 78, 80, 82, 85-87, 89] Twenty-seven studies reported a median −0.1 mg/dL change in SCr (range −0.8 to 1.7 mg/dL).[20, 25, 42, 45-47, 49, 51, 52, 54, 57, 58, 61-65, 67, 69-72, 76, 77, 81, 84, 86] There was no clear explanation across studies for the wide heterogeneity in change in kidney function. For details, see Appendix Tables C.4.2, C.4.6, and C.4.7.

Figure 9. Kidney function improvement after PTRAS, percent of patients



Point estimates and 95% confidence intervals from individual studies. Lines connecting points indicate data coming from the same study (or cohort) at different time points. PTRAS= percutaneous transluminal renal angioplasty with stent.

Figure 10. GFR change (in mL/min) after PTRAS



Point estimates and 95% confidence intervals from individual studies. Lines connecting points indicate data coming from the same study (or cohort) at different time points. GFR = glomerular filtration rate, PTRAS= percutaneous transluminal renal angioplasty with stent.

Blood Pressure Control

The studies were highly heterogeneous regarding which BP measures were analyzed, in particular for definitions of ordinal (categorical) outcomes such as BP improvement. The definitions used by studies are in the summary tables in Appendix Table C.4.

New-onset HTN was reported in 0 to 3.9 percent (two studies).[24, 55] Ordinal outcomes for BP improvement were reported in 19 studies (Figure 11). In these studies, BP improved in 4.2 to 69 percent (15 studies),[41, 42, 45, 46, 58, 65, 67, 71, 72, 74, 75, 77, 80] did not change in 9.1 to 54 percent (10 studies),[41, 42, 45, 65, 67, 71, 77, 80] and stabilized or worsened in 7.4 to 67 percent (5 studies).[40, 41, 46, 58, 80]

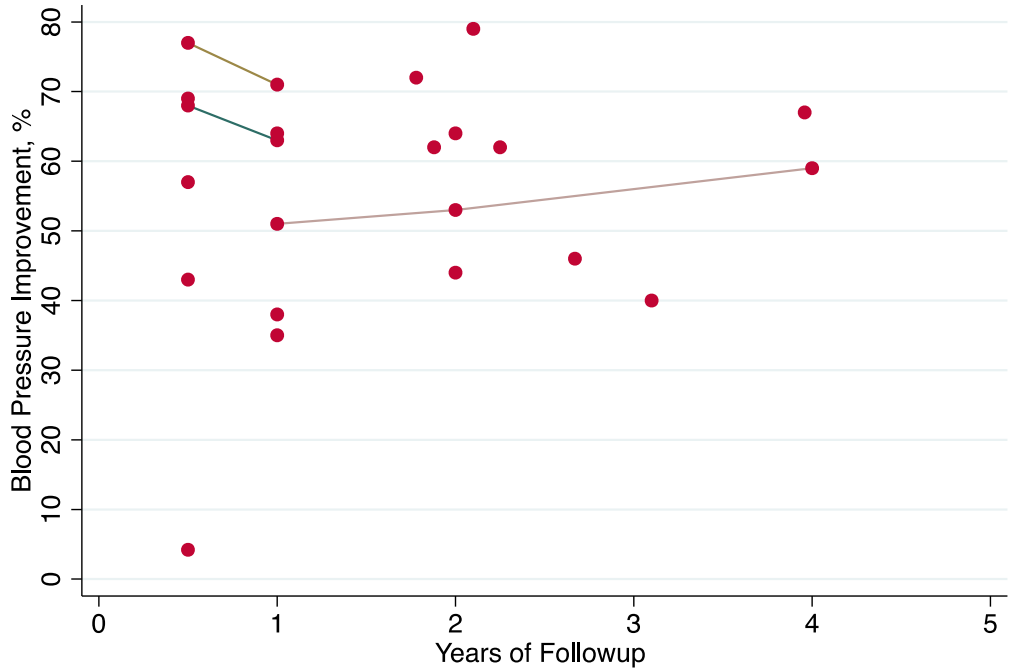
Changes in BP were reported in 36 studies[19, 20, 25, 30, 32, 41, 42, 44-47, 49-52, 56-58, 60, 61, 63-65, 67, 70-72, 74, 76-78, 80, 81, 85-87, 89] (Figure 12); BP was measured in the clinic in 15 studies, by 24 hour ambulatory measurements in 4 studies, by self-measured BP in one study, and extracted from the medical record in 2 studies; other studies did not explicitly define BP measurement. Of these, 33 studies reported a −17 mmHg median change in SBP (range −51 to 28 mmHg),[19, 20, 30, 32, 41, 44-46, 49-52, 57, 58, 60, 61, 63-65, 67, 70-72, 74, 76-78, 80, 81, 85-87, 89] 31 studies reported a −6 mmHg median change in DBP (range −30 to 5 mmHg),[20, 30, 32, 41, 44-46, 49-52, 57, 58, 60, 61, 63-65, 67, 70-72, 74, 77, 78, 80, 81, 85-87, 89] and five studies reported a −13.7 mmHg median change in mean arterial pressure (range −29 to 6 mmHg).[42, 45, 47, 56, 78] See Appendix Tables C.4.8, C.4.10, and C.4.11.

Changes in number of antihypertensive medications were reported in 30 studies (Figure 13).[19, 41, 43, 44, 46-50, 53-57, 60, 61, 63-65, 67, 71, 72, 75-80, 86, 87] These studies reported a median −0.3 change

in the number of antihypertensive medications (1.4 decrease to 1.2 increase). For details, see Appendix Tables C.4.8, C.4.14.

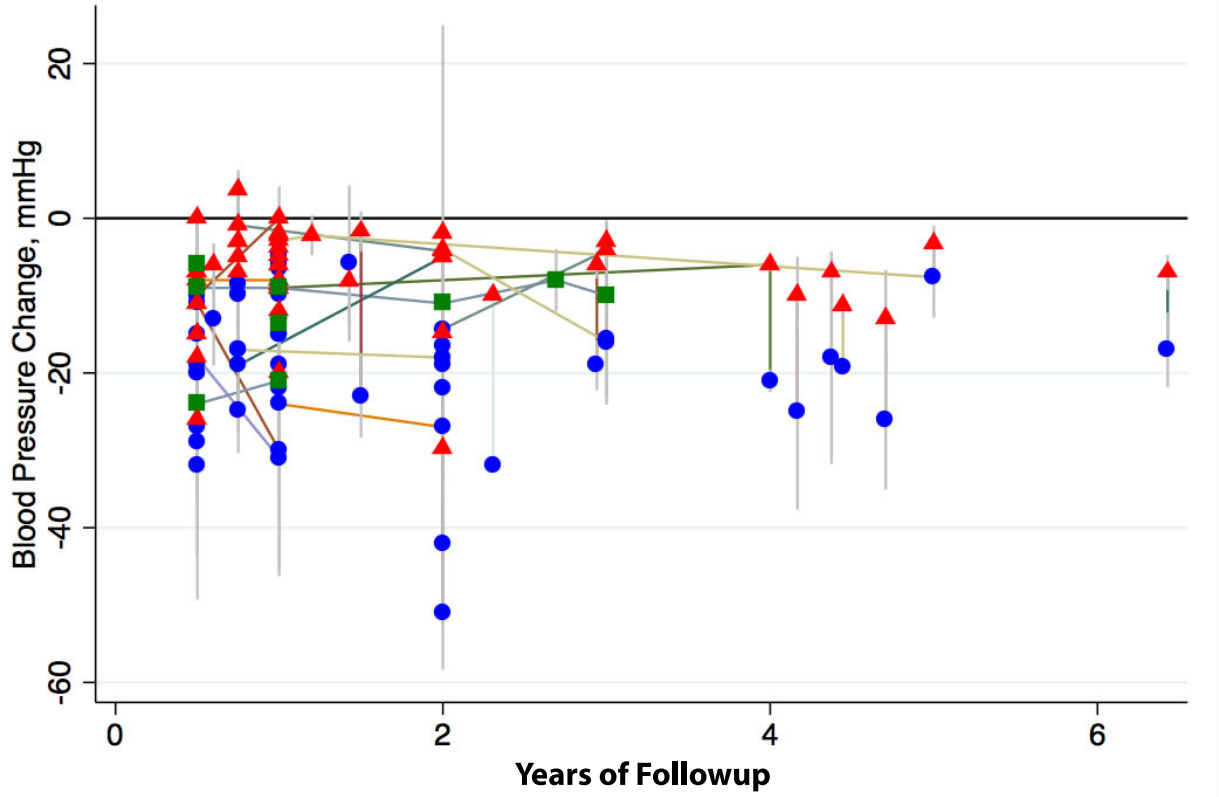
For all BP outcomes, there were no clear explanations for the wide heterogeneity across studies in outcomes after stent.

Figure 11. Blood pressure improvement after PTRAS, percent of patients



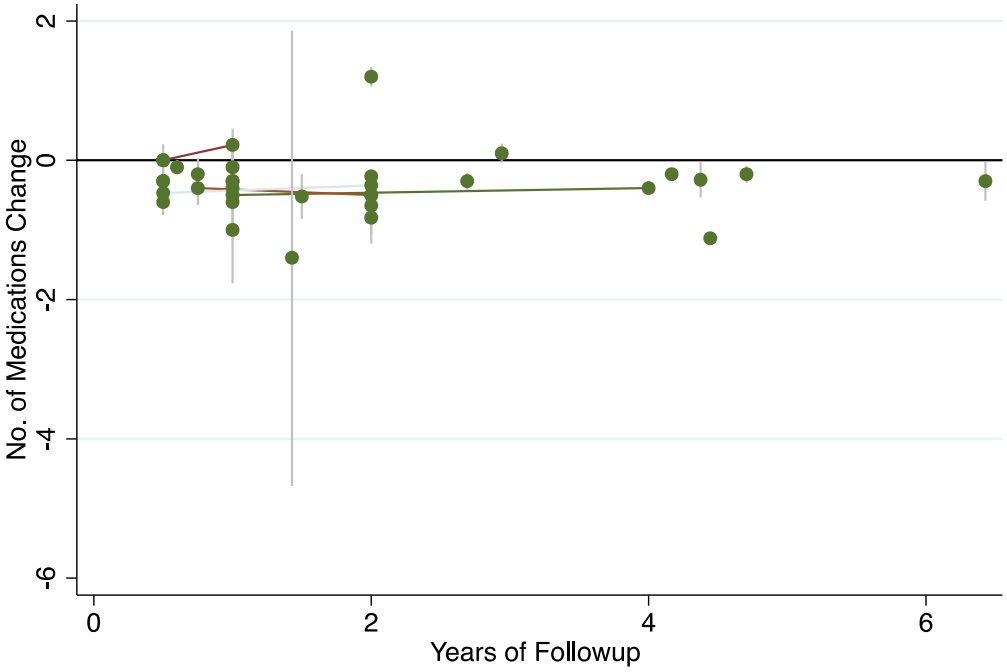
Point estimates and 95% confidence intervals from individual studies. Lines connecting points indicate data coming from the same study (or cohort) at different time points. PTRAS= percutaneous transluminal renal angioplasty with stent.

Figure 12. Blood pressure change (in mmHg) after PTRAS



Point estimates and 95% confidence intervals from individual studies. Blue circles = systolic blood pressure; red triangles = diastolic blood pressure; green squares = mean arterial pressure. Lines connecting points indicate data coming from the same study (or cohort) at different time points. PTRAS= percutaneous transluminal renal angioplasty with stent.

Figure 13. Change in number of antihypertensive medications after PTRAS



Point estimates and 95% confidence intervals from individual studies. Lines connecting points indicate data coming from the same study (or cohort) at different time points. PTRAS= percutaneous transluminal renal angioplasty with stent.

Adverse Events (Including 30-Day Mortality)

A total of 19 studies reported adverse events immediately following PTRAS.[20, 42-46, 48, 51, 52, 54, 58, 59, 61, 62, 67, 72, 75, 76, 80] The 30-day mortality was reported in 9 studies and ranged from 0 to 15 percent.[39, 41, 45, 50, 71-73, 86, 88] Other reported adverse events included RRT 1.5 to 3.1 percent (two studies),[48, 82] acute renal failure 2.3 to 11 percent (two studies),[20, 75] severe bleeding 1.6 to 31 percent (nine studies),[41, 43, 51, 59, 64, 68, 72, 75, 80] dissection 2.2 to 3.9 percent (two studies),[65, 75] unplanned surgery 0 to 6 percent (one study),[48]and thrombosis 0 to 12 percent (three studies).[20, 46, 75] See Appendix Tables C.4.19 and C.4.20.

Key Question 2. Association of Patient Factors With Outcomes

Twenty studies of PTRAS[22, 26, 31, 47, 50, 51, 55, 56, 60-62, 72, 74-76, 78, 80, 82-84] reported analyses of patient-level (or disease characteristic) factors associated with outcomes of interest (Tables 1 and 2). An additional study pooled data from three eligible studies, [57, 70, 85] together with two ineligible studies.[90]

Three studies evaluated subgroups of patients as predictors of requiring RRT (Table 1). Kane 2010 found that patients with CHF were significantly more likely to develop RRT (risk ratio [RR] 2.3; 95% CI 1.1 to 5.0), adjusted for sex, age, and SCr.[31] Both Mannarino 2012 and Valluri 2012 found no difference between patients with bilateral or unilateral stenosis.[82, 83] Valluri 2012 also found no difference between those patients with relatively rapid kidney function decline prior to PTRAS compared to other patients.[82]

Eleven studies evaluated a variety of potential predictors for long-term kidney function (Table 1). Six of eight studies found that patients with *worse* pre-PTRAS kidney function were more likely to have improved kidney function after PTRAS than other patients; the other two found no significant association. Three studies each found that patients with bilateral stenosis either had greater improvement than those with unilateral stenosis or there was no significant association. No other factors potentially predicting kidney function were evaluated by more than three studies.

Eight studies evaluated predictors of long-term BP outcomes (Table 1); an additional pooled meta-analysis of three eligible studies (and two ineligible studies) also evaluated predictors of BP response.[90] Four of six studies found that patients with higher pre-PTRAS BP were more likely to have BP improvement than other patients; the other two studies found no association. Five found no association between pre-PTRAS kidney function and BP, but two found that patients with worse kidney function (GFR <40 or 50 mL/min) were significantly less likely to have BP improvement. Only one of four studies found that patients with bilateral disease were more likely to have BP improvement; the other three found no association. Four studies found no association with diabetes. No other factors potentially predicting kidney function were evaluated by more than three studies.

Five studies evaluated predictors of all-cause death (Table 2). Three of four studies found that patients with worse pre-PTRAS kidney function were significantly more likely to die; the fourth found no association. Three found no association with a history of coronary artery disease, but one of these did find that significantly more patients who had had a myocardial infarction died. This study also found that patients with bilateral stenosis were more likely to die, but two other studies found no association.

Three studies evaluated composite outcomes that included all-cause or cardiovascular death, various cardiovascular events, and in some instances RRT, acute kidney injury, CHF, uncontrolled HTN, or revascularization (Table 2). All three tested histories of various cardiovascular diseases. Rzeznik 2011 found that coronary artery disease severity (which was not defined) increased the risk of the composite outcome. However, Kennedy 2003 and Trani 2010 found that coronary artery disease, myocardial infarction, and peripheral vascular disease were not associated with outcomes. All four also evaluated pre-PTRAS left ventricular function; two studies found increase risk of outcomes with a history of CHF, but two found no associations with left ventricular mass or ejection fraction.

Key Question 3. Association of Treatment Factors With Outcomes

In a subgroup analysis of a retrospective study, Beck 2010 found that neither use of gold-coated stents or embolic protection were associated with BP at 1.5 years.[75]

In an observational comparative study, Zahringer 2007 found no differences at 2 years in BP, HTN cure, the number of antihypertensive medications, SCr, or kidney function worsening between patients who had angioplasty with either sirolimus eluting or bare stents.[67]

In a RCT, Lekston 2008 found no difference in 10 month SCr between those who received or did not receive intraluminal brachytherapy during stenting.[69]

Table 1. Independent predictors of kidney and blood pressure outcomes after angioplasty with stent

Outcome Study	**Mean F/up (Metric)**	**CKD**	**Pre-Stent ΔGFR**	**Bilat**	**Stenosis Grade**	**CAD**	**Sex**	**BP**	**Age**	**Misc**	**Other NS**
RRT											
Kane 2010**	5 y (RR)									CHF: 2.3 (1.1, 5.0)	
Mannarino 2012	2.75 y (%)			NS*							
Valluri 2012	2.9 y (%)		Fast vs. Slow: NS*	NS*							
Kidney Function											
Arthurs 2007	1.25 y (SCr slope)	SCr ≥1.5: −0.03/mo SCr <1.5: 0.03/mo P<0.05*		NS*							RI >0.8*
Holden 2006	1.3 y (Imp)	Stage NS*									
Leesar 2009	1 y (SCr)										HSG*
Mannarino 2012	2.75 y (GFR/mo)		Fast: 0.01 Slow: −0.14 P=0.04*	Bilat: 0.02 Unilat: −0.16 P=0.02*							Proteinuria*
	2.75 y (GFR imp, OR)		16 (1.5, 166)	NS							
Ramos 2003	1 y (GFR)	GFR<50: 20.7 GFR≥50: −4.8 P sig, implied*									
Rivolta 2005	1.67 y (1/SCr slope)	SCr NS									Kidney diameter
Sapoval 2010	1 y (GFR imp, %)	CKD 1/2: 3.5% CKD 3: 23% CKD 4: 50% P nd*									

Outcome Study	**Mean F/up (Metric)**	**CKD**	**Pre-Stent ΔGFR**	**Bilat**	**Stenosis Grade**	**CAD**	**Sex**	**BP**	**Age**	**Misc**	**Other NS**
	1 y (GFR)	CKD 1/2: −25 CKD 3: 1 CKD 4: 13 CKD 5: 24 P nd*									
Trani 2013	6 mo (SCr imp, OR)	SCr, per quartile 2.5 (1.3, 4.7)		NS	NS†		NS		NS	CRP per quartile 0.39 (0.19, 0.82)	LVEF, Statins, ACEi/ARB, DM
Tsao 2005	6 mo (GFR)	NS*		Bilat: 5 Unilat: −10 P<0.001*							
	6 mo (SCr imp, %)	SCr >1.5: 24% SCr ≤1.5: 0% P nd*			NS (≥90%)*						HTN duration*
Valluri 2012	2.9 y (GFR slope imp)			NS*			NS*				
Zeller 2004	2.67 y (SCr)	SCr (>3.0 vs. <1.2 mg/dL): −0.9 (−1.3, −0.6) P<0.001 SCr (1.21-3.0 vs <1.2 mg/dL): −0.2 (−0.3, 0) P<0.009*′‡		NS*′‡							RI*′‡, DM*′‡
	2.67 y (SCr imp, OR)	SCr† 2.57 (1.55, 4.25)		2.04 (1.01, 4.21)	1.05 (1.04, 1.09)†	3v: 0.39 (0.17, 0.91)					
Blood Pressure											
Beck 2010	1.5 y (no imp, OR)	GFR<40: 1.6 (1.0, 2.9)		NS		NS	F: 1.3 (1.0, 2.1)	SBP>180 NS DBP>90 NS	>70 NS		AAA, DM, COPD, Dyslipidemia, Smoking
Leesar 2009	1 y (imp, OR)							NS		HSG ≥21 mmHg: 1.32 (1.05, 1.65)	Other renal artery measures§
Ramos 2003	1 y (mmHg)	GFR<50: −10/−4 GFR ≥50: −21/−10 P nd*									

Outcome Study	**Mean F/up (Metric)**	**CKD**	**Pre-Stent ΔGFR**	**Bilat**	**Stenosis Grade**	**CAD**	**Sex**	**BP**	**Age**	**Misc**	**Other NS**
Rocha-Singh 1999	13 mo (response#, OR)	SCr>1.4 NS		4.6, P=0.009		NS	NS	MAP >110: 2.9, P=0.003	NS		DM, Ostial lesion, Solitary kidney
Rzeznik 2011	1 y (imp, RR)	NS		NS	1.28 (1.08, 1.51)†	NS		DBP: 1.74 (1.47, 2.06)† SBP NS			Echocardiography measures
Staub 2010	6 mo (imp, OR)	NS					NS	MAP per mmHg 1.05 (1.01, 1.20)	Per y, 0.95 (0.89, 0.99)	BNP >50: 4.0 (1.2, 13.2)	RI
Tsao 2005	6 mo (mmHg)	NS									
Zeller 2004	2.67 y (imp, OR)			NS						No. Rx† 1.81 (1.38, 2.36)	DM, RI
Weinberg 2014††	9 mo (imp, OR)	SCr>1.5 NS				NS	NS	SBP per 10 mmHg: 1.76 (1.53, 2.03) DBP per 10 mmHg: NS	NS		No. Rx, DM, Smoking
BP or SCr¶											
Gill-Leertouwer, 2002	1 y (imp, OR)	GFR per mL/min 0.92 (0.85, 0.998)			NS						Other renal artery measures||
No. Rx											
Leesar 2009	1 y (mean number)									HSG ≥21: 2.3 HSG <21: 3.4 P<0.01*	
Tsao 2005	6 mo (mean number)	NS*									

* Univariate

† Categorization not defined; implied that worse severity associated with improvement.

‡ Estimated based on reported data.

§ Intravascular ultrasound measures (mean lumen area, area stenosis, minimum lumen diameter, plaque plus media area), pressure guidewire measures (fractional flow reserve, hyperemic mean gradient, resting systolic gradient, renal angiography measures (minimum lumen diameter, diameter stenosis).

DBP ≤90 mmHg with no change in medications or decrease in ≥1 medications; or DBP 90-100 mmHg and decrease in MAP ≥5 mmHg and no change in medications.

¶ DBP decrease ≥10 mmHg or SCr decrease ≥20% depending on indication

|| Intravascular ultrasound measures, renal scintigraphy measure.

** Kane 2010 was a retrospective comparative study of angioplasty with stent to medical therapy.[31] Therefore, this studies did not meet eligibility criteria for Key Question 1 for PTRAS cohorts and was not included there.

†† Weinberg 2014.[90] Pooled meta-analysis of Rocha Singh 2005,[57] Rocha Singh 2008,[70] Jaff 2012,[85] a study that did not meet eligibility criteria because it included patients with ostial restenosis requiring repeat angioplasty,[91] and an unpublished study whose data are not available.

3v = 3 vessel coronary artery disease, AAA = abdominal aortic aneurysm, ACEi/ARB = angiotensin converting enzyme inhibitor or angiotensin receptor blockers, Bilat = bilateral stenosis, BNP = brain natriuretic protein (in pg/mL), BP = blood pressure, CAD = coronary artery disease, CHF = congestive heart failure, CKD = chronic kidney disease, COPD = chronic obstructive pulmonary disease, CRP = C reactive protein, DBP = diastolic blood pressure (in mmHg), DM = diabetes mellitus, F = female, F/up = followup, Fast = fast progressor (more than −0.25 mL/mo preprocedure), GFR = glomerular filtration rate (unit used in regression not reported), HSG = Pressure guidewire-measured hyperemic systolic gradient, HTN = hypertension, imp = improvement, LVEF = left ventricular ejection fraction, MAP = mean arterial pressure, Misc = miscellaneous, nd = no data, No. Rx = number of antihypertensive medications, NS = no significant association, OR = odds ratio, Other NS = nonsignificant predictors not otherwise listed, RI = resistance index, RR = risk ratio, SBP = systolic blood pressure, SCr = serum creatinine (in mg/dL), sig = significant, Slow = slow progressor (less than −0.25 mL/mo preprocedure), Unilat = unilateral stenosis, ΔGFR = rapid kidney function decline (>80th percentile preprocedure) or fast progressor (more than −0.25 mL/mo preprocedure).

Table 2. Independent predictors of clinical event outcomes after angioplasty with stent

Outcome Study	Mean F/up (Metric)	CKD	BP	Bilat	CVD	CHF	Age	DM	Smoking	Misc	Other NS
Death											
Crutchley 2009*	4.8 y (HR)									RI>0.8: 6.7† (2.6, 17)	
Kane 2010**	5 y (RR)	SCr, per mg/dL: 2.7 (1.1, 6.6)			CAD NS	3.4 (2.0, 5.7)		NS			HTN
Kennedy 2003	1.75 y (%)	SCr (higher) P=0.001		32% v 25% P<0.01	MI 36% v 24% P<0.05‡ CAD NS	56% v 15% P<0.001‡		NS	NS		Sex, Race
Mannarino 2012	2.75 y (%)			NS‡							
Valluri 2012	2.9 y (%)	Rapid decline NS‡		NS‡							
Death, CV or Renal											
Kennedy 2003	1.75 y (%)	SCr (higher) P=0.001			CAD NS						
Composite											
CV death, RRT or SCr increase >30%, MI, Stroke, CHF, Uncontrolled HTN											
Kennedy 2003	1.75 y (%)			48% v 30% P<0.01‡	CAD NS‡ MI NS‡	53% v 30% P<0.01‡		51% v 31% P<0.01‡	NS		Sex, Race
CV death, MI, Stroke, Revascularization											
Rzeznik 2011	1 y (RR)	GFR NS		NS	CAD severity§ 1.27 (1.04, 1.56)	LVM NS			1.29 (1.05, 1.57)		BP, Stenosis grade
CV death, RRT, MI, Stroke											
Trani 2010	2 y (OR)	SCr per mg/dL 2.20 (1.11, 4.38)		7.32 (1.53, 35.1)	PVD NS	LVEF NS	NS	NS			Sex, Stenosis grade
Myocardial Infarction											
Kennedy 2003	1.75 y (%)	SCr (higher) P=0.001			CAD NS						
Congestive Heart Failure											
Kennedy 2003	1.75 y (%)	SCr (higher) P=0.001			CAD NS						

* Crutchley 2004 was a retrospective comparative study of surgery vs. angioplasty with stent with <100 participants in the surgical arm.[26] Therefore, this studies did not meet eligibility criteria for Key Question 1 for surgical cohorts and was not included there.

† HR for combined surgery and angioplasty with stent groups, described in text and graphically as similar results for both intervention groups.
‡ Univariate analysis.
§ Categorization not defined
** Kane 2010 was a retrospective comparative study of angioplasty with stent to medical therapy.[31] Therefore, this studies did not meet eligibility criteria for Key Question 1 for PTRAS cohorts and was not included there.

Bilat = bilateral stenosis, BP = blood pressure, CAD = coronary artery disease, CHF = congestive heart failure, CKD = chronic kidney disease, CV = cardiovascular, CVD = cardiovascular diseases, DM = diabetes mellitus, F/up = followup, GFR = glomerular filtration rate (in mL/min), HR = hazard ratio, HTN = hypertension, LVEF = left ventricular ejection fraction, LVM = left ventricle mass, MI = myocardial infarction, Misc = miscellaneous, NS = nonsignificant association, OR = odds ratio, Other NS = nonsignificant predictors not otherwise listed, PVD = peripheral vascular disease, RI = resistance index, RR = risk ratio, RRT = renal replacement therapy, SCr = serum creatinine (in mg/dL).

Medical Therapy Only

Key Points

- 20 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.
- **Mortality**: In 10 studies, mortality ranged from 9 to 56 percent 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.
- **RRT**: In seven studies, incident RRT occurred in 2 to 18 percent of patients between 3 and 5 years, but with no clear explanation of the heterogeneity across studies, including length of followup.
- **Cardiovascular outcomes**: In nine 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**: 10 studies reported on kidney function outcomes. Kidney function improvement occurred in 0 to 26 percent of patients and deteriorated in 19 to 38 percent of patients (4 studies). In three 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 four studies 2 to 82 percent of patients had episodes of acute kidney injury. In 21 studies, kidney function improved in 12 to 82 percent and worsened in 4 to 37 percent of patients. 21 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**: 12 studies reported on BP outcomes. In one study 4 percent of patients became newly hypertensive and none 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 percent 1 year in one study and from 38 to 43 percent in the other.
- **Adverse events**: No study reported on adverse events related to medication use.
- **Patient factors**: Two studies reported on patient-level predictors of clinical outcomes. In one study each, statistically significant associations were found between flash pulmonary edema and both death and cardiovascular events, between lower GFR and RRT, and a near significant association between proteinuria and RRT. No associations were found between flash pulmonary edema and RRT, lower GFR and death, or between rapid kidney function deterioration, refractory HTN, sex, or history of coronary artery disease and clinical outcomes.
- **Treatment factors**: 2 studies addressed differences in treatment factors as predictors of outcomes. One study found no association between beta blockers or angiotensin inhibitors and death or RRT, but the second study found that angiotensin inhibitor use was associated

with reduced cardiovascular events and statin use was associated with reduced cardiorenal events, death and RRT.

Key Question 1. Effects of Intervention on Outcomes

In 17 articles, [7, 9, 19, 20, 24, 25, 29, 30, 32, 33, 35, 50, 92-97] we identified 20 cohorts of patients who were treated with medical therapy only (a total of 7778 patients) in prospective studies. Among the studies, nine cohorts assessed the effectiveness of medical therapy on outcomes in single cohorts of patients (or compared different cohorts of patients receiving medical therapy) and 12 cohorts were from studies comparing medical therapy to PTRAS; one study provided analyses relevant only to Key Question 3.[96, 97]

Only Hackam 2011 explicitly reported consecutive enrollment of patients.[97] Four studies reported the presence of HTN as an additional inclusion criterion.[19, 25, 93, 95] One study required that patients be over 65 years of age.[97] One study specifically included patients with chronic kidney disease.[19] The studies mostly included men, with a median average of 64 percent male (range 43-96%). The median average age across the studies was 69.5 years old (range 60.9-78 years). The percentage of patients with bilateral ARAS ranged from 18 to 55 percent. The median average baseline BP across studies was 154/79 mmHg (range 131-175.4/74-95 mmHg). The median average baseline GFR was 40 mL/min (range 33-66.2 mL/min), and SCr was 1.8 mg/dL (range 1-2.29 mg/dL).

The definitions of ARAS varied across studies. Six studies included patients with over 50 percent stenosis[9, 24, 32, 92, 93, 95] (one of which required that patients had less than 80% stenosis [32]), one with over 60 percent stenosis,[7] three with over 70 percent or 75 percent stenosis,[29, 33, 34] and two with over 80 percent stenosis.[19, 94] The percent stenosis was not reported in four studies. One study was multicenter and had different definitions at the two centers. [30] None of the studies reported using translesional pressure gradients to define stenosis severity. See Appendix Table C.1 for eligibility criteria and Table C.2.2 for arm details.

None of the studies reported on the patients' history of coronary artery revascularization or concomitant aortic disease; however, one study reported that 26.5 percent of patients had concomitant cerebrovascular disease.[30] In four studies, between 36 and 60 percent of patients had concomitant peripheral vascular disease,[9, 20, 33, 94] and in two studies 19 and 40 percent of patients had a history of stroke.[20, 33] One study reported that 36 percent of patients had peripheral artery disease,[93] and another reported 50 percent of patients had carotid stenosis.[33] See Appendix Table C.3 for full baseline data.

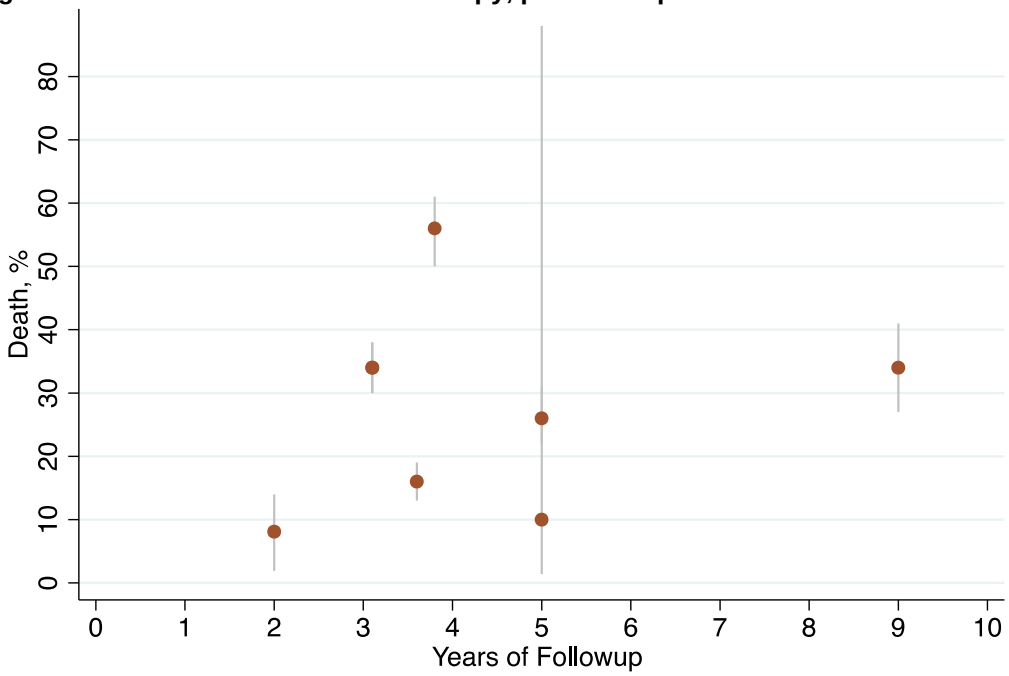
Among the 17 studies, only three are newly published since the 2006 and 2007 reports. The risk of bias for all studies is summarized in Appendix Figure D.4. About half the studies were of high risk of bias for adjusting for different lengths of patient followup and for incomplete outcome data (attrition bias). All studies were of low risk of bias for sample representing the entire population. About half the studies were deemed to be at low risk of selective reporting bias and the other half unclear risk of bias.

Mortality (Study Duration 6 Months or Greater)

Data on long-term mortality was reported in ten studies (Figure 14). All-cause death was reported in 9 to 56 percent of patients (seven studies)[7, 9, 19, 20, 24, 33, 93] followed for 2 to 9 years; higher death rates were generally found in longer followup studies. Death as a result of stroke occurred in 5.4 to 85 percent of patients (two studies)[19, 24] followed for 2 to 5 years,

cardiovascular related deaths occurred in 5.4 to 16 percent of patients (four studies)[19, 24, 33, 94] followed for 2 to 7 years, and renal related deaths occurred in 4.2 percent of patients (one study)[20] followed for 5 years. For details, see Appendix Table C.4.1.

Figure 14. Death while on medical therapy, percent of patients

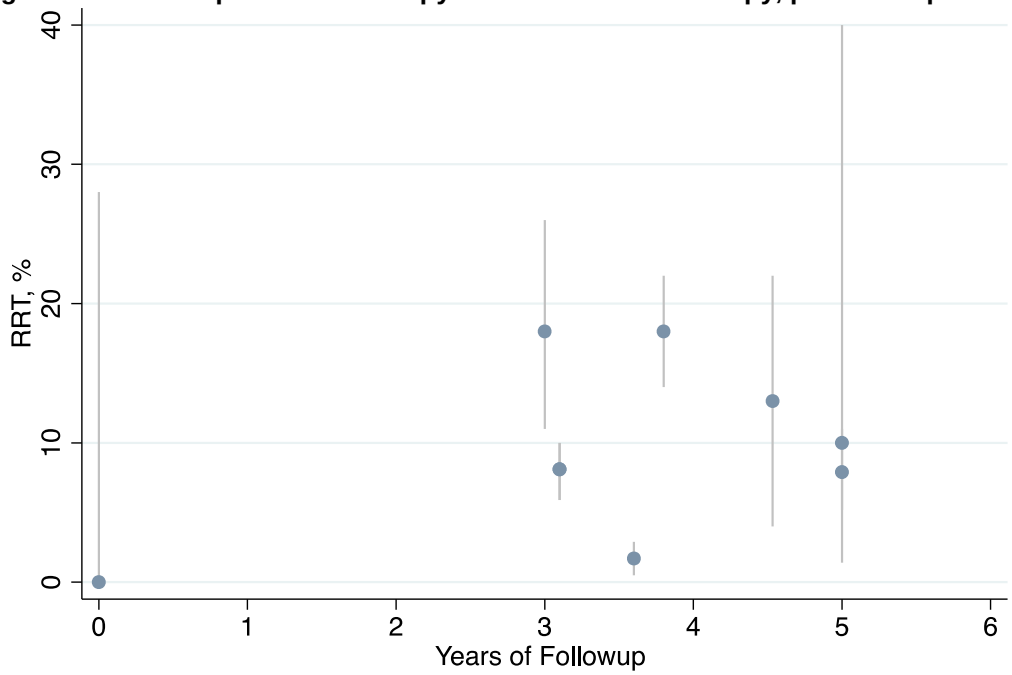


Point estimates and 95% confidence intervals from individual studies.

Renal Replacement Therapy

Among seven studies that reported 3 to 5 year followup, between 2 and 18 percent of patients required RRT, with a median of 10 percent (Figure 15).[9, 19, 20, 33, 92, 94, 95] There is no clear explanation for the wide range of rates of RRT. See Appendix Table C.4.6.

Figure 15. Renal replacement therapy while on medical therapy, percent of patients



Point estimates and 95% confidence intervals from individual studies. RRT = renal replacement therapy

Cardiovascular Outcomes

Overall, nine studies reported on cardiovascular outcomes. Three studies reported data on CHF events.[20, 24, 33] Followup times ranged from 3 months to 7.4 years, and incidence ranged from 1.4 to 13 percent. One study reported a 1.4 percent incidence of flash pulmonary edema at 2-year followup.[24] A second study reported a 10 percent incidence of abdominal aortic aneurysm rupture at 7.4-year followup.[33] The third study reported an incidence of 8.6 percent of angina resulting in hospitalization at 5-year followup.[20] This latter study reported that 4.1 percent of patients followed for 5 years required a coronary artery procedure.[20]

Four studies reported on incidence of MI, one of which reported that no patients experienced MI during followup.[33] Incidence in the other three studies ranged from 2.5 to 83 percent in patients who were observed from 1.75 to 5 years.[19, 20, 29] Data on incidence of stroke was reported in 5 studies, one of which reported that no patients had a stroke during followup.[22] Incidence of stroke in the other four studies ranged from 2.5 to 23 percent in patients who were observed from 1.75 to 5 years.[19, 20, 29, 95]

One study reported that 12 percent of patients had a new cardiovascular event (new onset angina, ischemic heart disease, myocardial infarction, revascularization, CHF hospitalization, peripheral vascular disease, or stroke or transient ischemic attack) at a median of 3.1 years.[7] In addition, 42 percent had a composite outcome that also included death and RRT. Another study reported that 57 percent had a composite cardiorenal outcome that included death, cardiovascular event (myocardial infarction, stroke, CHF), and RRT or acute kidney injury at a mean of 3.3 years.[97] See Appendix Tables C.4.17 and C.4.18.

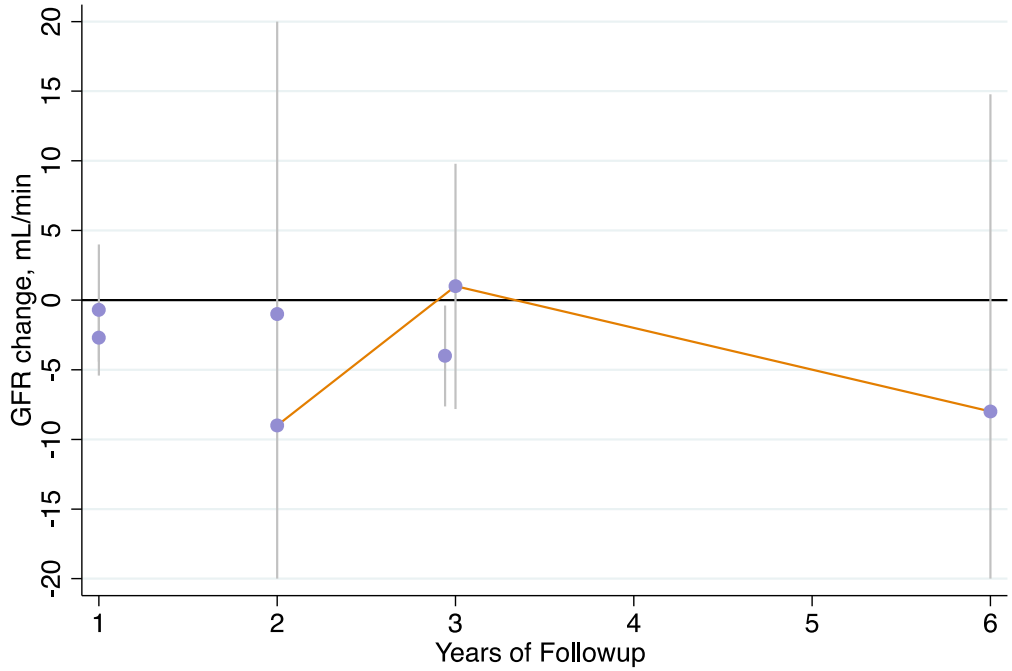
Kidney Function

Overall, 10 studies reported on kidney function outcomes; none reported on the percent of patients with CKD at baseline. Three studies reported data on improvement of kidney

function. In two of the studies, improvements occurred in 19 and 26 percent of patients who were observed for 1 year;[20, 30] in one study no patients improved at 4-year followup.[35] The studies reported no change in kidney function in 35 to 65 percent of patients. A fourth study only reported on the percentage of patients whose kidney function deteriorated.[19] Across the four studies, 19 to 38 percent of patients experienced deterioration in kidney function. In one study, at 5-year followup, 5.9 percent of patients had experienced acute kidney injury.[20]

Four studies reported a decrease of between 0.7 and 8 mL/min in MDRD-estimated GFR at between 1 and 6 years of followup (Figure 16).[30, 32, 33, 94] One study reported an average decrease in 1/SCr of 0.012 dL/mg per year over 5 years.[20] Four studies reported a change in SCr of between −0.1 and 1.3 mg/dL at between 1 and 5 years of followup.[20, 25, 29, 92] For details, see Appendix Tables C.4.3, C.4.6, and C.4.7.

Figure 16. GFR change (in mL/min) while on medical therapy



Point estimates and 95% confidence intervals from individual studies. The line connecting points indicate data coming from the same study (or cohort) at different time points. GFR = glomerular filtration rate.

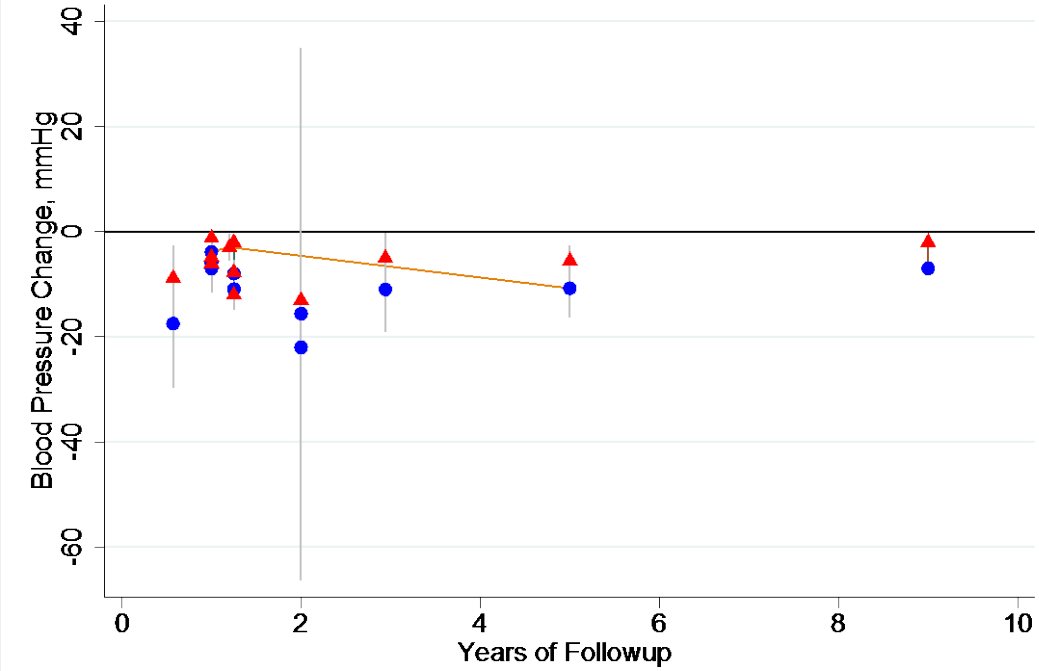
Blood Pressure Control

Only one study reported data on incidence of HTN and hypertensive crises.[24] At 2-year followup, 4.1 percent of patients became newly hypertensive, while none experienced a hypertensive crisis.[24] Data on change in SBP was reported in 11 studies (Figure 17), which found decreases in SBP between 6 and 22 mmHg in patients who were observed from 1 to 9 years (one cohort in one study measured 24 hour ambulatory BP; other studies reported clinic BP or did not define how BP was measured).[19, 20, 25, 29, 30, 32, 33, 92-95] Nine studies reported data on change in DBP, with decreases ranging from 1 to 13 mmHg in patients who were observed from 1 to 9 years. [20, 29, 30, 32, 33, 92-95]

Two studies reported data on the change in number of antihypertensive medications from baseline to maximum followup (Figure 18). One study reported no change in the average number of medications at 1.75-year followup,[29] while the other reported an increase of 1.4 medications

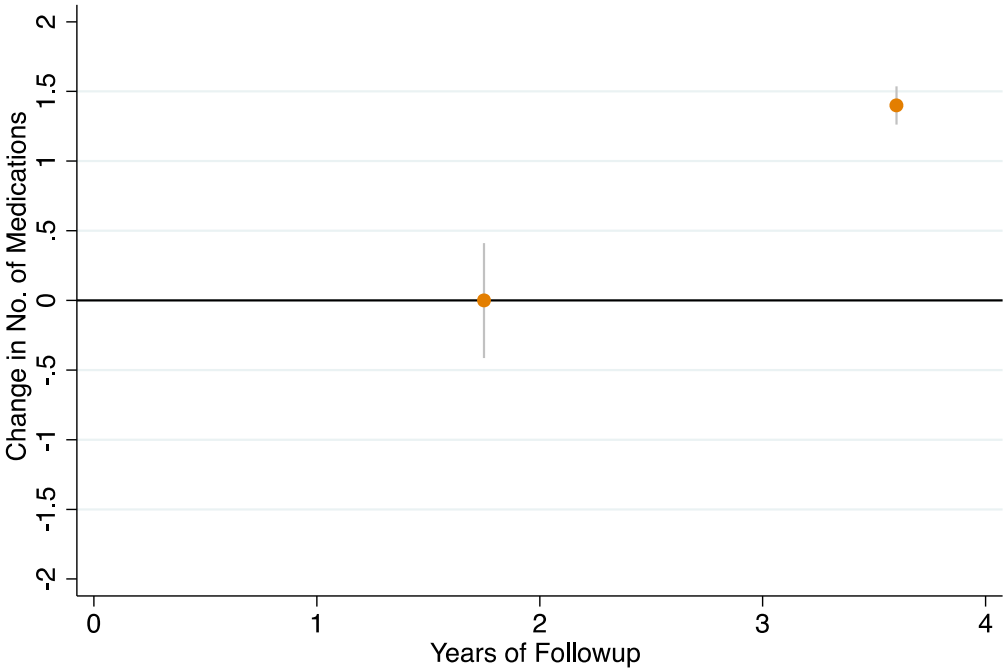
for patients who were observed for 3.6 years.[19] For details, see Appendix Tables C.4.9, C.4.12, and C.4.14.

Figure 17. Blood pressure change (in mmHg) while on medical therapy



Point estimates and 95% confidence intervals from individual studies. Blue circles = systolic blood pressure; red triangles = diastolic blood pressure; green squares = mean arterial pressure. The line connecting points indicate data coming from the same study (or cohort) at different time points.

Figure 18. Change in number of antihypertensive medications while on medical therapy



Point estimates and 95% confidence intervals from individual studies.

ACEi/ARB Use

Two studies reported data on ACEi/ARB use. Both found an increase in the percentage of patients on the drugs from baseline to 1 year. RASCAD reported that 79 percent of patients were using ACEi/ARBs at baseline compared to 83 percent at 1 year.[32] Wheatley 2009 reported that 38 percent of patients were using ACEi/ARBs at baseline, while 43 percent were using the drugs at 1 year.[20] See Appendix Tables C.4.14, C.4.15 and C.4.16.

Adverse Events

No study reported adverse events related to medication use.

Key Question 2. Association of Patient Factors With Outcomes

Three studies reported analyses of patient-level predictors of clinical outcomes (Table 3). Ritchie 2014,[9] in univariate analyses, found that patients with flash pulmonary edema were significantly more likely to die or, in a separate analysis, to have a cardiovascular event (see Table 3 for list of events), but were not likely to require RRT. Neither rapid kidney function deterioration nor refractory HTN predicted outcomes (see Table 3 for definitions of predictors).

Silva 2008 found that lower GFR was significantly associated with RRT but not death.[94] Proteinuria was a near-significant predictor of RRT, but not death. Sex and history of coronary artery disease were not associated with outcomes.

Key Question 3. Association of Treatment Factors With Outcomes

Three analyses in two studies examined the association between specific medication treatments and clinical outcomes (Table 3). Silva 2008, in multivariable analyses, found that use of beta blockers or angiotensin inhibitors (ACEi or ARB) were not associated with likelihood of death or RRT.[94] In contrast, Hackam et al. in two overlapping analyses of four (Hackam 2008)[96] or six (Hackam 2011)[97] administrative databases, found that angiotensin inhibitor use was associated with reduced cardiovascular events and statin use was associated with reduced cardiorenal events, death and RRT.

Table 3. Independent predictors of selected clinical outcomes in patients receiving medical therapy only

Outcome Study	**Mean F/up (Metric)**	**GFR**	**FPE**	**Prot**	**Statins**	**ACEi/ARB**	**Other NS**
Death							
Ritchie 2014	3.8 y (HR)		2.19* (1.39, 3.47)				Rapid ΔGFR*, Refractory HTN*
Silva 2008	3 y (HR)	0.97 (0.94, 1.002)		NS	0.13 (0.04, 0.44)	NS	Sex, CAD, BB
RRT							
Ritchie 2014†	3.8 y (HR)		NS*				Rapid ΔGFR*, Refractory HTN*
Silva 2008	3 y (HR)	0.92 (0.88, 0.97)		1.16 (0.99, 1.37)	0.21 (0.07, 0.64)	NS	Sex, CAD, BB
CV Event‡							
Ritchie 2014	3.8 y (HR)		3.07* (1.71, 5.51)				Rapid ΔGFR*, Refractory HTN*
Hackam 2008§						0.75 (0.62, 0.91)	
Cardiorenal Event¶							
Hackam 2008/2011§	3.3 y (HR)				0.60 (0.53, 0.69)		

*Univariate

† or serum creatinine doubling

‡ Ritchie 2014: Myocardial infarction, acute coronary syndrome, flash pulmonary edema hospitalization, arrhythmia hospitalization, stroke, transient ischemic attack, new onset angina, or coronary revascularization

Hackam 2008: Death, myocardial infarction, or stroke

§ Overlapping studies with data from four (Hackam 2008) or six (Hackam 2011) administrative databases

¶ Myocardial infarction, stroke, heart failure, acute renal failure, dialysis or death

ACEi/ARB = angiotensin converting enzyme inhibitor or angiotensin receptor blockers, BB = beta blocker, CAD = coronary artery disease, CV = cardiovascular, F/up = followup, FPE = flash pulmonary edema, GFR = glomerular filtration rate, HR = hazard ratio, HTN = hypertension, NS = no significant association, Other NS = nonsignificant predictors not otherwise listed, Prot = proteinuria, Rapid ΔGFR = rapid kidney function decline (serum creatinine increase by 20% or 1.14 mg/dL increase in 6 months), Refractory HTN = refractory hypertension (BP >140/90 mmHg on ≥3 medications), RRT = renal replacement therapy.

Surgical Revascularization

Key Points

- 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.
- **Mortality**: In four studies, mortality ranged from 26 to 36 percent after about 5 years of followup.
- **RRT**: In two studies, incident RRT (or combined renal failure outcomes) occurred in 38 and 74 percent of patients at about 5 years of followup.
- **Cardiovascular outcomes**: One study reported new-onset angina in 10 percent of patients and coronary revascularization in 8 percent after a mean of 10 years; 6 percent of patients suffered an MI and 4 percent a stroke.
- **Kidney function**: Two studies reported on kidney function; in one, 43 percent of patients had improved kidney function, 10 percent 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 four studies, improved or cured HTN occurred in 53 to 82 percent of patients. Two studies found large improvements in SBP (−53 and −31 mmHg) at 4 to 5 years, but one 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.
- **Patient factors**: Two studies reported on patient-level predictors of clinical outcomes. Both studies found that found that patients with a history of cardiovascular disease, diabetes, worse kidney function, or who were older were at increased risk of all-cause death, cardiovascular death, or either death or RRT. In one study each, 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.
- **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.

Key Question 1. Effects of Intervention on Outcomes

Four studies reported on primary surgical revascularization for ARAS,[23, 98-100] three of which were used in the previous update. There were three retrospective, nonrandomized comparative studies of surgery with PTRAS[98-100] and one RCT (versus PTRAS).[23] In total, 880

patients were included. The mean durations of followup ranged from 3.1 to 4.7 years (or up to 5 or 10 years). An additional study reported only significance of differences in outcomes between surgical revascularization and PTRAS and is not included in this section.[34]

Study inclusion criteria incorporated patients with at least 60 percent ARAS,[100] but frequently participants had 70 to 80 percent stenosis or more, by ultrasound or angiography imaging. Inclusion criteria based on degree of stenosis were incomplete or not reported in two studies.[26, 98] No study reported using translesional pressure gradients to define stenosis severity. The sex distribution varied widely from 43 percent males in Galaria 2005 to 65 percent males in Alhadad 2004. The mean age of the surgical cohorts ranged from 62 to 76 years. Patients with fibromuscular dysplasia were either specifically excluded or accounted for a small fraction (<10%) of the total study population. See Appendix Table C.1 for study eligibility criteria and designs.

The indications for operative intervention were to treat ARAS that was causing derangements in BP or kidney function. cardiovascular disease was present in 53 and 90 percent of patients in the two studies that reported it.[99, 100] All baseline SBP measurements were elevated and ranged from a mean of 171 to 200 mmHg. Mean DBP measurements were between 82 and 104 mmHg. The mean serum Cr values were between 1.3 and 2.6 mg/dL See Appendix Tables C.1 and C.3.

Surgical approaches varied according to revascularization needs and available vessels or conduits. Procedures included renal endarterectomy, renal and aortic endarterectomy, and mesenteric (i.e., splenorenal, hepatorenal, iliorenal) or aortorenal bypass procedures. Bypass procedures used native saphenous vein, PTFE (polytetrefluoroethylene), and Dacron grafts to construct the conduits when the native renal artery was not reimplanted. The choice and use of prosthetic grafts were at the surgeon's discretion. In all studies, some patients (9 to 56%) required combined aortic procedures, some of which were done to facilitate the renal bypass, and others were due to concomitant aortoiliac atherosclerotic disease. In one study, secondary operations performed for prior failed endoluminal repairs were included and comprised 10 percent of the total cohort.[100] Specific medication adjuncts used during operative procedures included alprostadil[23] when mentioned. See Appendix Table C.2.6.

The one RCT (Balzer 2009)[23] was of low risk of bias for all Cochrane risk of bias questions. The two retrospective NRCSs (Alhadad 2004 and Galaria 2005)[98, 99] were both adequately representative, but one each were high risk of bias for high attrition, selective outcome reporting, and different lengths of follow-up for different study arms. The prospective study (Cherr 2002)[99] was low risk of bias for all items;

Mortality (Study Duration 6 Months or Greater)

In four studies, mortality and long-term survival rates were described after open revascularization.[23, 98-100] In one study, a mortality rate of 26 percent was reported after a mean followup period of 4.5 years.[23] In the other three studies, mortality rates ranged from 26 to 36 percent after a mean followup of 5 years. The majority of late deaths were related to cardiovascular disease in two studies.[98, 99] For details, see Appendix Table C.4.1.

Renal Replacement Therapy

Progression to ESRD or new requirement for hemodialysis was defined as an endpoint in 2 studies.[99, 100] After a mean follow-up of 4.7 years in one study, 38 percent of survivors required RRT.[99] At 5 years in the second study, the cumulative freedom from RRT or recurrent renal

insufficiency (Cr > 1.5 mg/dL), reported as renal disease-related mortality, was 74 percent (SD 7 percent). [100] See Appendix Table C.4.6.

Cardiovascular Outcomes

Only a single study reported long-term cardiovascular outcomes. Cherr 2002 reported new-onset angina in 9.8 percent of patients and coronary revascularization in 8.3 percent after a mean of 10 years; 5.8 percent of patients suffered an MI and 4.4 percent a stroke.[99] See Appendix Table C.4.17.

Kidney Function

In the two studies reporting kidney function outcomes, 4 and 12 percent had CKD at baseline.[26, 100] In one study, 43 percent of patients had improved kidney function (including 28 of 40, 70%, who discontinued dialysis), 47 percent had no clinically significant change, and 10 percent had worsened kidney function.[99] In this same study, mean CrCl (estimated by Cockcroft-Gault) increased by 7 mL/min (95% CI 3.5 to 10.7) at a mean of 4.7 years. In another study, mean SCr increased by 0.1 mg/dL (95% CI −0.2 to 0.35) at both 1 and 4 years of followup.[23] See Appendix Tables C.4.4, C.4.6, and C.4.7.

Blood Pressure Control

Improved or cured HTN was reported in four studies and occurred in 53 to 82 percent of patients.[23, 98-100] Cherr 2002 found decreases in SBP/DBP at a mean of 4.7 years of −53 mmHg (95% CI −80 to −26) / −23 mmHg (−35 to −11).[99] Balzer 2009 found statistically significant decreases in clinic SBP at 1 and 4 years: at 1 year −21 mmHg (95% CI −38 to −4); at 4 years −31 mmHg (95% CI −49 to −13). But they found nonsignificant changes in DBP at 1 year (−4 mmHg; 95% CI −14 to 6) and 4 years (−8 mmHg; 95% CI −18 to 2).[23] See Appendix Tables C.4.10, C.4.12, and C.4.13.

Adverse Events (Including 30-Day Mortality)

In three studies, 30-day or in-hospital median mortality was 7 percent (range 0% to 9%).[98-100] Major reported adverse operative events at 30 days included bleeding (8%),[98] arterial occlusion or thrombosis (3.7% and 6.0%),[23, 98] infection (3%),[98] and distal embolization (2%).[98] Immediate reoperations occurred in 4 and 28 percent in two studies.[98, 100] Major nontechnical morbidity events were acute kidney injury (1% to 12%),[98, 99] cerebrovascular events (1%),[98, 99] cardiovascular events (4% to 14%),[98-100] and septicemia (1%).[98, 100] See Appendix Tables C.4.19 and C.4.20.

Key Question 2. Association of Patient Factors With Outcomes

Two studies reported analyses of patient-level predictors of clinical outcomes.[26, 99] Between the two studies, they found that patients with a history of cardiovascular disease, diabetes, and those with worse kidney function or who were older were at increased risk of all-cause death, cardiovascular death, or either death or RRT (Table 4). Specifically, Cherr 2002 found that the HRs for both all-cause death and combined death or RRT were increased independently in patients with lower GFR, and histories of diabetes, myocardial infarction, stroke, and severe aortic occlusive disease.[99] For both outcomes, patients with prior myocardial revascularization were at significantly decreased risk. Older patients were at increased risk of all-cause death, but not combined death or RRT. Those with higher SBP were at lower risk of

combined death or RRT, but not all-cause death alone. Race, sex, DBP, and number of antihypertensive medications were not independently associated with these outcomes. In this study, only the presence of preoperative angina was associated with the risk of cardiovascular mortality (HR 2.18; 95% CI 1.25 to 3.84). Crutchley 2009 found that resistive index >0.8 was an independent predictor of all-cause death.[26]

Key Question 3. Association of Treatment Factors With Outcomes

Cherr 2002 found that bilateral repair did not independently predict death and that perioperative mortality was higher in patients with combined aortic and bilateral repair (6.9%) compared to isolated renal artery repair (0.8%; P=0.01, univariate), but after adjustment for age and clinical CHF, this difference was not statistically significant. [99]

Table 4. Independent predictors of selected clinical outcomes after surgical renal artery repair

Outcome Study	**Mean F/up (Metric)**	**Age**	**GFR**	**RI ≥0.8**	**SBP**	**DM**	**CorRevasc**	**Stroke**	**MI**	**Aortic Dz**	**Other NS**
Death											
Cherr 2002	4.7 y (HR)	1.22 (1.02, 1.46)	0.60 (0.49, 0.74)		NS	1.75 (1.18, 2.60)	0.60 (0.38, 0.96)	1.52 (1.00, 2.29)	1.48 (1.06, 2.07)	1.49 (1.06, 2.10)	Race, Sex, DBP, Rx
Crutchley 2009*	4.8 y (HR)			6.7† (2.6, 17)							
Death or RRT											
Cherr 2002	4.7 y (HR)	NS	0.43 (0.34, 0.54)		0.79 (0.67, 0.94)	2.14 (1.15, 3.97)	0.69 (0.45, 1.06)	1.50 (1.02, 2.22)	1.36 (0.99, 1.88)	1.66 (1.19, 2.31)	Race, Sex, DBP, Rx

* Crutchley 2004 was a retrospective comparative study of surgery vs. angioplasty with stent with <100 participants in the surgical arm.[26] Therefore, this studies did not meet eligibility criteria for Key Question 1 for surgical cohorts and was not included there.

† HR for combined surgery and angioplasty with stent groups, described in text and graphically as similar results for both intervention groups.

Aortic Dz = Severe aortic occlusive disease, CHF = congestive heart failure, CorRevasc = coronary revascularization, DBP = diastolic blood pressure, DM = diabetes mellitus, F/up = followup, GFR = glomerular filtration rate (unit used in regression not reported), HR = hazard ratio, LVEF = left ventricular ejection fraction, MI = myocardial infarction, NS = no significant association, Other NS = nonsignificant predictors not otherwise listed, RI = resistance index, RRT = renal replacement therapy, Rx = number of antihypertensive medications, SBP = systolic blood pressure (unit used in regression not reported).

Acute Decompensation Case Reports

Key Points

- 20 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 one case and 5 year in the other, but who subsequently had a second episode of decompensation that resulted in clinical improvement. All eight cases who required acute hemodialysis no longer required RRT after revascularization.

Key Question 1. Effects of Intervention on Outcomes

None of the comparative or single group studies focused on or explicitly included patients with acute decompensation who have rapidly declining kidney function with possible oliguria or anuria, flash pulmonary edema, and/or intractable malignant HTN. To partially overcome this deficiency, we summarized the 20 most recent case reports of such patients, published between 2006 and 2014 (Table 5).[101-120]

The patients ranged in age from 49 to 83 years old (median 69.5); 13 were women. Most commonly, patients (n=13) had new onset dyspnea, orthopnea, CHF or flash pulmonary edema symptoms. Nine patients were described as having difficult to control, rapidly accelerating, or malignant HTN. Seven patients had acute renal failure or rapid rises in SCr or falls in GFR; four described oliguria or anuria; and eight of the patients required hemodialysis at some point. Other presenting symptoms included angina, chest pain, or acute myocardial infarction, peripheral edema, nausea and vomiting, malaise and other nonspecific symptoms. Among the six patients with reported data, presentation GFR ranged from 17 to 45 mL/min. Among 19 patients, the presentation SCr ranged from 1.1 to 9.3 mg/dL; in seven cases, there was a description of a rapid rise in SCr over the proceeding days, which usually led to hemodialysis. Presentation BP was substantially elevated in all but one case (and one additional case whose BP was not reported), ranging from 170/90 mmHg on one antihypertensive drug to 220/100 mmHg on 11 drugs. Five patients were on no or one antihypertensive drug at presentation. The lowest presentation BP was 120/70 mmHg on three drugs (in a patient who was being medically treated for RAS and presented requiring hemodialysis).

All but one patient were found to have high grade stenosis (of at least 80% or described as critical or some other term) in at least one renal artery. High grade stenosis in both renal arteries (or equivalent) was reported in 10 of 18 patients.

Two of the 10 patients refused PTRAS on first presentation and were treated medically. One of these cases (reported by Li 2012) remained stable for 4 or 5 years but after a second episode of decompensation had bilateral PTRAS.[108] The second case (Islam 2009) did not have true RAS decompensation at first presentation since her rapid rise in SCr was secondary to ramipril treatment.[110] However, 10 months later, the patient decompensated and suffered a myocardial infarction and required hemodialysis. She also then had PTRAS. All other patients had PTRAS or surgical revascularization (2 cases) within one or two weeks of initial decompensation.

Followup after revascularization occurred from hospital discharge to 5 years (median 5 months). Only seven of the cases reported outcomes 1 year or more after revascularization. Among the 18 cases that reported followup kidney function, all patients had improved (or stable, one patient) kidney function. All eight cases who required acute hemodialysis no longer required RRT after revascularization. Among 16 cases with followup data, BP was improved in 15; in one case[108] (Li 2012), SBP was increased compared with presentation but DBP was stable; the number of medications the patient was on was not reported. In seven of eight cases with data on the number of antihypertensive medications at presentation and followup, the number of drugs was reduced or the same (one case) at followup with a lower BP. One patient was on one drug at presentation and had controlled BP at 6 week followup on three drugs. One case report (Alonso 2013) did not report kidney or BP followup but reported only that the patients pulmonary edema symptoms had fully resolved at 3 months.[104] For all cases who presented with flash pulmonary edema, CHF, or dyspnea, it was stated or implied that symptoms were fully resolved without recurrence at followup.

In summary, a review of the 20 most recently published case reports of management of patients with ARAS with acute decompensation—as manifested by rapid worsening of kidney function, recent severe or difficult to control HTN, flash pulmonary edema, or related symptoms—found that all patients improved after revascularization, almost always with PTRAS. One of the case reports described a patient who refused recommended revascularization for her acute RAS decompensation. She was managed successfully for 5 years until she had a second decompensation at which point she was treated with PTRAS. Overall, the case reports all report clinically successful revascularizations in patients with acute decompensation.

Table 5. Case reports
Each row = individual patient

Study, Year PMID	Decompensation Description	Comorbidities	Acuity (Time)	o Age, y (Sex) • % Stenosis	Pre-Tx ▪ GFR [SCr] ❖ Pulm Ed?	Pre-Tx ➢BP ● No. Rx	Intervention	Followup Time	Response ▪ GFR [SCr] ❖ Pulm Ed?	Response ➢BP ● No. Rx
Komatsu, 2014 None	RI, HTN	DM, PVD		o 65 y (M) • L 90%	▪ [1.10] ❖	➢156/98 ●	PTRAS L	In-hospital	▪ [0.97] ❖	➢122/73 ●
Demming, 2013 23673780	Acute chest pain and progressive dyspnea	DCM, MR, MetS, COLD	7 d	o 83 y (F) • L "high-grade"; R hypoplasia	▪ 23 [2.2] ❖ Yes	➢220/100 ● 11 Rx	PTRAS L	1.5 y	▪ 34 [1.55] ❖	➢ ● 5 Rx
Ishida, 2013 23473081	Severe HTN, rapidly worsening RI	CRF		o 69 y (M) • R 99%	▪ [6.94] ❖ Severe LE edema	➢180/90 ● 5 Rx	PTRAS R	1 mo	▪ [4.0] ❖ Edema ameliorated	➢135/70 ● 3 Rx
								1 y	▪ [3.8] ❖	➢135/65 ● 1 Rx
Alonso, 2013 22944546	Sudden acute dyspnea	HTN, DM, no CAD	2 (FPE x 3 in 6 mo)	o 73 y (F) • B critical	▪ ❖ Yes	➢194/115 ● 4 Rx	PTRAS B	3 mo	▪ ❖ None	➢ ●
Chrysochou, 2013 22262735	FPE x 3, poorly controlled HTN	LVH, claudication, no CAD	12 mo	o 65 y (F) • B 85%	▪ 26 [] ❖ Yes (NYHA II)	➢161/80 (ABPM) ● 6 Rx	PTRAS	2 wk	▪ ❖ No (2 flights*)	➢101/57 ● 4 Rx
								4 mo	▪ 34 ❖	➢ ● 1 Rx
								1 y	▪ ❖	➢129/71 ● 3 Rx
Noce 2012 23427756	Refractory HTN, ARF	No HTN	Recent ()	o 51 y (M) • R 85%; L 75%	▪ 28 [5.78] ❖ No (LVH, no edema)	➢190-220 / 100-130 ● 2 Rx	PTRAS B	30 d	▪ [2.8] ❖	➢150/85 ● 2 Rx
								5 y	▪ 65 [1.5] ❖	➢120/80 ● 1 Rx
Li, 2012 21558176	FPE, ACS (in 2002)			o 73 y (F) • R 82% L 87%	▪ 17 [2.9] ❖ Yes	➢ ● 0 Rx (implied)	Medical (refused PTRAS)	4 y	▪ [1.8-2.0] ❖ No	➢154/69 ● 3 Rx
	FPE, ARF (in 2007), RRT †			o ~78 • B "tight"	▪ HD ❖ Yes	➢120/70 ● 3 Rx (implied)	PTRAS B	3.5 y	▪ 30 [1.7] Off RRT ❖ AFib/CHF	➢140/72 ●

Study, Year PMID	Decompensation Description	Comorbidities	Acuity (Time)	○ Age, y (Sex) • % Stenosis	Pre-Tx ▪ GFR [SCr] ❖ Pulm Ed?	Pre-Tx ➢BP ● No. Rx	Intervention	Followup Time	Response ▪ GFR [SCr] ❖ Pulm Ed?	Response ➢BP ● No. Rx
Navaravong, 2011 21855421	CHF Sx, ARF, Uncontrolled HTN	L occluded, R 70%, CAD, CKD IV (SCr 1.6), HTN, AAA		○ 79 y (M) • R 99%; L 100%	▪ [5.4], anuric ❖ Yes	➢170/90 ● 1 Rx	PTRAS R	4 d	▪ [1.5] ❖ Yes	➢Improved ●
George, 2011 21566313	Rest angina, acute LVF & FPE, uncontrolled HTN		>2 d	○ 70 y (F) • (bilat)	▪ 45 [3.0] ❖ Yes	➢210/110 ● 4 Rx	PTRAS R	D/C	▪ 63 [1.6] ❖	➢"well-controlled ● 2 Rx
								2 mo	▪ [1.3] ❖	➢ ●
Kindo 2011 21118836	FPE	CHF, PAD, Heart transplant, HTN		○ 60 y (M) • (L no function)	▪ [2.5] ❖ Yes	➢190/100 ●	Hepatorenal bypass R	5 d	▪ [2.0] ❖	➢Controlled ●
								3 y	▪ [1.6] ❖ No	➢ ●
Islam, 2009 19808722	SCr rise on ramipril	(SCr 1.2)	Acute	○ ~59 (F) • B Severe	▪ [2.0] ❖	➢ ●	Medical (refused PTRAS)	10 mo	▪ (1.5-2.5) ❖ Yes	➢ ●
	SOB, FPE, AMI, RRT (10 mo later)‡	Uncontrolled HTN, Acute CHF‡	10 d	○ 60 y • 100% (bilat)	▪ [4.0→7.6, HD] ❖ Yes	➢180/92 ● 5 Rx	PTRAS B	3 d	▪ [2.1] Off RRT ❖ "no recurrence in followup"	➢ ●
Kanamori, 2009 19726830	Dizziness, Severe HTN, ARF, RRT		30 d	○ 72 y (F) • R 100%; L 90%	▪ [1.2→6.7, HD] ❖ Yes	➢190/100 ● 1 Rx (implied)	PTRAS B		▪ [0.8] Off RRT ❖ No	➢140/90 ●
Dippel, 2009 19652259	Accelerated HTN	CAD, TIA		○ 74 (F) • R 40-50% L 80%	▪ 30 [1.3] ❖ No	➢200/100 ● 3 Rx	PTRAS L (with DEP)	30 d	▪ ❖	➢90/46 ● 2 Rx
								1 y	▪ ❖	➢100/60 ● 2 Rx
Dziemianko, 2009 19379457	ARF, RRT, HTN crisis, Dyspnea, LE edema	None		○ 53 y (M) • R 75%; L 95%	▪ [3.6→HD] ❖ Yes	➢260/150 ● 0 Rx (implied)	PTRAS L#	6 mo#	▪ [1.5] Off RRT ❖ No	➢144/91 (ABPM) ●

Study, Year PMID	Decompensation Description	Comorbidities	Acuity (Time)	o Age, y (Sex) • % Stenosis	Pre-Tx ▪ GFR [SCr] ❖ Pulm Ed?	Pre-Tx ➢BP ● No. Rx	Intervention	Followup Time	Response ▪ GFR [SCr] ❖ Pulm Ed?	Response ➢BP ● No. Rx
Chrysochou, 2009 18045711	Oligoanuria, RRT, malaise, breathlessness	RAS (50-75% L), DM, HTN (199/89)	3 d	o 73 y (F) • R 100%, L >95%	▪ [8.0→HD] ❖ Yes	➢221/80 ● 5 Rx	PTRAS L	3 d	▪ [2.6] Off RRT ❖	➢ ●
								8 mo	▪ 26 [2.0] ❖	➢ ●
Campbell, 2008 18335782	N/V/D, Low back pain, anuria, RRT	HTN	5 d	o 49 y (F) • R ≥60% • L <60%	▪ [9.3→HD] ❖ No	➢188/76 ● 1 Rx	Aortorenal artery bypass R	6 d	▪ [1.8] Off RRT ❖ No	➢ ●
								6 wk	▪ [1.5] ❖ No	➢Controlled ● 3 Rx
Wykrzykowska, 2008 18174627	FPE (ventilation)	Giant cell arteritis, HTN, PVD		o 81 y (F) • R mild; L severe	▪ [2.7] ❖	➢200/ ● 5 Rx	PTRAS L	5 mo	▪ [1.4] ❖ No	➢160/ ●
	CHF, Severe HTN (6 mo later)§			o 81 or 82 y • R severe; L patent	▪ ❖ Yes	➢Severe ●	PTRAS R		▪ ❖ No	➢Improved ●
Kuznetsov, 2007 17703833	Weakness, dyspnea, chest discomfort, N/V→Anuria, RRT	HTN, CVA, CAD, CHF, Aortic stenosis (SCr 1.5)	2 wk	o 75 y (F) • B critical	▪ [2.8→6.5→HD] ❖ Yes	➢210/110 ● 3 Rx	PTRAS B (with DEP)	D/C	▪ [1.9] Off RRT ❖ No	➢115-147/ 53-72 ● 3 Rx
								4 mo	▪ [1.7] ❖	➢ ●
Kumar, 2006 16941797	Recurrent breathlessness, FPE x 4	CAD, No HTN	1 mo	o 58 y (M) • L 99% R 90%	▪ [1.7] ❖ Yes	➢160-170 / 100-110 ● 2 Rx	PTRAS B	3 mo	▪ [1.2] ❖ No	➢ ●
George, 2006 16521653	Dyspnea, oliguria, RRT, anasarca, orthopnea	Aortoarteritis, L nephrectomy (occluded RA)	2 wk	o 51 y (F) • R 100%	▪ [3.6→HD] ❖ Yes	➢190/110 ●	PTRAS R	2 d	▪ [1.0] Off RRT ❖ No	➢ ● 2 Rx
								3 wk	▪ Stable ❖	➢Stable ● 2 Rx

* Exercise tolerance improved to ~50 yards and she was able to climb 2 flights of stairs before needing to stop.
† Second acute episode in same woman about 5 years later.
‡ Second episode 10 months later
# R PTRAS placed at 6 months. 6 months subsequently "kidney function remained normal and blood pressure normalized."
§ Second episode 6 months later

AAA = abdominal aortic aneurysm, ABPM = 24 hour ambulatory blood pressure monitoring, ACS = acute coronary syndrome, AFib = atrial fibrillation, AMI = acute myocardial infarction, B = bilateral, BP = blood pressure (in mmHg), CHF = congestive heart failure, CKD IV = chronic kidney disease stage IV, COPD = chronic obstructive pulmonary disease, CRF = chronic renal failure, D/C = hospital discharge, DCM = dilated cardiomyopathy, DEP = distal embolic protection device, DM = diabetes mellitus, FPE = flash pulmonary edema, GFR = glomerular filtration rate (in mL/min/m^2), HD = hemodialysis, HTN = hypertension, K = potassium (in mg/dL), L = left renal artery, LE = lower extremity, LVF = left ventricular failure, M/F = male or female, MetS = metabolic syndrome, MR = mitral regurgitation, N/V/D = nausea vomiting and diarrhea, nd = no data, NYHA = New York Heart Association class, PAD = peripheral artery disease, Plasty = angioplasty, Pre-Tx = pre-treatment (during acute decompensation), PTRAS = percutaneous transluminal renal angioplasty with stent, Pulm Ed = flash pulmonary edema, PVD = peripheral vascular disease (not including renal artery disease), R = right renal artery, RA = renal artery, RCA = right coronary artery stenosis, RI = “renal impairment”, RRT = renal replacement therapy (dialysis) [required], Rx = antihypertensive medications required, SCr = serum creatinine (in mg/dL), Sx = symptoms, TIA = transient ischemic attack.

Strength of Evidence Across Study Designs

As summarized in Table 6, for all outcomes, the strength of evidence is low regarding the relative benefit of *PTRAS versus medical therapy alone* for patients with ARAS, across both comparative and noncomparative studies.

Overall, there is a low strength of evidence of no difference in clinically important outcomes (death, cardiovascular events, RRT) either in terms of statistically significant differences or the arbitrary MCID of HR≤0.80. This conclusion is most applicable to those patients for whom there is clinical equipoise between the two treatments (patients for whom no clear benefit of revascularization is perceived). The RCTs generally found no clear differences in rates of clinically important outcomes but had the important limitation of low applicability to typical patients for whom PTRAS is being recommended, since these patients were excluded from the trials either by design or because of difficulty recruiting them into trials that might disallow revascularization. The NRCSs were less consistent, but provided less reliable estimates of comparative effectiveness due to inadequate adjustment for fundamental differences in patients who are chosen for revascularization and those who remain on medical therapy. For these reasons, the NRCSs were deemed to not provide sufficiently strong evidence to upgrade the strength of evidence derived from the RCTs. Likewise, the single-intervention cohorts are highly heterogeneous across studies in their patient populations and their estimates of outcome rates. It is highly unlikely that the patients in the PTRAS studies are comparable to those in the (many fewer) medical therapy studies.

Overall, there is low strength of evidence that kidney function may be improved in patients who undergo PTRAS, based on comparative studies and the indirect comparison between cohorts of patients who had PTRAS or continued medical therapy; although the RCTs generally found no difference in effect.

Overall, there is low strength of evidence that BP control is similar in patients who undergo PTRAS and those who remain on medical therapy alone. The RCTs mostly found no significant difference, but the NRCS had inconstant, heterogeneous findings.

Likewise, overall, there is low strength of evidence that clinically important adverse events are more common, though rare, related to PTRAS than medical therapy alone; however, studies generally failed to report medication-related adverse events.

As summarized in Table 7, for all outcomes, evidence is insufficient to determine the strength of evidence regarding the relative benefit of *open surgery versus medical therapy alone* for patients with ARAS, across both comparative and noncomparative studies. Only a single comparative study of open surgery versus medical therapy and few single-group studies of surgery exist. These did not provide sufficient evidence to adequately assess the relative difference in outcomes between the interventions.

As summarized in Table 8, for each outcomes, the strength of evidence is insufficient or low regarding the relative benefit of *PTRAS versus surgery* for patients with ARAS, across both comparative and noncomparative studies. A single RCT and three poorly reported NRCS evaluated this comparison. There is low strength of evidence of no difference in mortality or BP control between the two revascularization approaches, but inadequate evidence for other outcomes of interest.

Table 6. Angioplasty with stent versus medical therapy alone for the treatment of ARAS: Strength of evidence

Outcome	Strength of Evidence	Design No. Studies	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Other Issues	Finding
Death	Low	RCT: 4 NRCS: 5	Moderate	RCT: Direct Other: Indirect	RCT: inconsistent All: inconsistent	Imprecise	Undetected	Important*	Comparative studies: No evidence of a difference
RRT/ESRD	Low	RCT: 4 NRCS: 5 Case report: 18	Moderate	RCT: Direct Other: Indirect	RCT: consistent All: consistent	Imprecise	Undetected	Important*	Comparative: No evidence of a difference Case reports: RRT averted with revascularization
Cardiovascular event	Low	RCT: 5 NRCS: 3 Case report: 18†	Moderate	RCT: Direct Other: Indirect	RCT: consistent All: consistent	Imprecise	Undetected	Important*	Comparative: No evidence of a difference Case reports: Cardiovascular symptoms resolved immediately with revascularization
Kidney function	Low	RCT 6 NRCS: 7 Case report: 18	Moderate	RCT: Direct Other: Indirect	RCT: consistent All: inconsistent	Imprecise	Undetected	Important*	RCT: No evidence of a difference NRCS: Heterogeneous effect on kidney function after PTRAS, favoring PTRAS Case reports: Improvement with revascularization
BP control	Low	RCT: 6 NRCS: 6 Case report: 18	Moderate	RCT: Direct Other: Indirect	Comparative: inconsistent All: consistent	Imprecise	Undetected	Important*	Comparative: Inconsistent Case reports: Improvement with revascularization
Adverse events	Low	RCT: 4 NRCS: 4 Cohort PTRAS: 34 Cohort Rx: 0	Moderate	RCT: Direct Other: Indirect	Consistent	Imprecise	Suspected	Important‡	Severe adverse events rare, but reported only in PTRAS studies.

AE = adverse events, ARAS = atherosclerotic renal artery stenosis, BP = blood pressure, Case = case reports, CV = cardiovascular, MCID = minimum clinically important difference, N = number of study participants, No. = number, NRCS = nonrandomized comparative studies, PTRAS = percutaneous transluminal renal angioplasty with stent placement, RCT = randomized controlled trials, RRT = renal replacement therapy, Rx = medical therapy alone, SoE = strength of evidence.

* RCTs of limited applicability to typical patients choosing PTRAS. NRCSs inadequately adjusted. Single arm studies analyzed poorly comparable cohorts of patients.
† Congestive heart failure / pulmonary edema symptoms and angina
‡ Noncomparable adverse events between PTRAS and medical therapy. Poorly reported.

Table 7. Surgery versus medical therapy alone for the treatment of ARAS: Strength of evidence

Outcome	SoE Grade	Design No. Studies	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Other Issues	Finding
Death	Insufficient	RCT: 1 NRCS: 0 Cohort Surgery: 4 Cohort Rx: 10	Low	RCT: Direct Other: Indirect	Single comparative study	Imprecise	Undetected	Important*	Comparative study: No statistically significant difference or MCID Single arm studies: Broadly similar
RRT	Insufficient	RCT: 1 NRCS: 0 Cohort Surgery: 2 Cohort Rx: 10 Case: 2	Low	RCT: Direct Other: Indirect	Single comparative study	Imprecise	Undetected	Important*	RCT: No statistically significant difference or MCID Single arm studies: Broadly similar Case: RRT averted with revascularization
CV event	Insufficient	RCT: 0 NRCS: 0 Cohort Surgery: 1 Cohort Rx: 10 Case: 2	Low	RCT: none Other: indirect	No comparative studies	Imprecise	Undetected	Important*	RCT: No data Single arm studies: Unclear Case: CV symptoms resolved immediately with revascularization
Kidney function	Insufficient	RCT: 1 NRCS: 0 Cohort Surgery: 1 Cohort Rx: 10 Case: 2	Low	RCT: Direct Other: Indirect	Single comparative study	Imprecise	Undetected	Important*	RCT: No difference Single arm studies: PTRAS better Case: Improvement with revascularization
BP control	Insufficient	RCT: 1 NRCS: 0 Cohort Surgery: 4 Cohort Rx: 10 Case: 2	Low	RCT: Direct Other: Indirect	Single comparative study	Imprecise	Undetected	Important*	RCT: No difference Single arm studies: PTRAS better Case: Improvement with revascularization
Adverse events	Insufficient	RCT: 1 NRCS: 0 Cohort Surgery: 3 Cohort Rx: 10 Case: 2	Low	RCT: Direct Other: Indirect	Single comparative study	Imprecise	Suspected	Important‡	RCT: No data Single arm studies: reported only in surgery studies

AE = adverse events, ARAS = atherosclerotic renal artery stenosis, BP = blood pressure, Case = case reports, CV = cardiovascular, MCID = minimum clinically important difference, N = number of study participants, No. = number, NRCS = nonrandomized comparative studies, PTRAS = percutaneous transluminal renal angioplasty with stent placement, RCT = randomized controlled trials, RRT = renal replacement therapy, Rx = medical therapy alone, SoE = strength of evidence.

* RCT of limited applicability to typical patients choosing PTRAS. Single comparative study only. Single arm studies analyzed poorly comparable cohorts of patients.
‡ Noncomparable adverse events between surgery and medical therapy. Poorly reported.

Table 8. Angioplasty with stent versus surgery for the treatment of ARAS: Strength of evidence

Outcome	SoE Grade	Design No. Studies	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Other Issues	Finding
Death	Low	RCT: 1 NRCS: 2 Cohort PTRAS: 31 Cohort Surgery: 4	Low	RCT: Direct Other: Indirect	RCT: consistent All: consistent	Imprecise	Undetected	Important*	Comparative studies: No statistically significant difference, but MCID in RCT (OR=0.63; 95% CI 0.16, 2.53) Single arm studies: Broadly similar
RRT	Low	RCT: 0 NRCS: 1 Cohort PTRAS: 31 Cohort Surgery: 2 Case: 20	Low	RCT: Direct Other: Indirect	RCT: no data All: consistent	Imprecise	Undetected	Important*	Comparative: No difference Single arm studies: Broadly similar Case: Similar outcomes
CV event	Low	RCT: 0 NRCS: 0 Cohort PTRAS: 31 Cohort Surgery: 1 Case: 20	Low	RCT: none Other: Indirect	RCT: no data All: inadequate data	Imprecise	Undetected	Important*	Comparative: No difference Single arm studies: Unclear Case: Similar outcomes
Kidney function	Low	RCT: 1 NRCS: 1 Cohort PTRAS: 31 Cohort Surgery: 1 Case: 20	Low	RCT: Direct Other: Indirect	RCT: consistent All: inconsistent	Imprecise	Undetected	Important*	Comparative: No difference Single arm studies: PTRAS better Case: Similar improvement
BP control	Low	RCT: 1 NRCS: 2 Cohort PTRAS: 31 Cohort Surgery: 4 Case: 20	Low	RCT: Direct Other: Indirect	RCT: consistent All: inconsistent	Imprecise	Undetected	Important*	Comparative: No difference Single arm studies: PTRAS better Case: Similar improvement
Adverse events	Low	RCT: 1 NRCS: 1 Cohort PTRAS: 31 Cohort Surgery: 3	Low	RCT: Direct Other: Indirect	Consistent	Imprecise	Suspected	Important‡	Severe AE rare with both interventions, requiring additional procedures.

AE = adverse events, ARAS = atherosclerotic renal artery stenosis, BP = blood pressure, Case = case reports, CV = cardiovascular, MCID = minimum clinically important difference, N = number of study participants, No. = number, NRCS = nonrandomized comparative studies, PTRAS = percutaneous transluminal renal angioplasty with stent placement, RCT = randomized controlled trials, RRT = renal replacement therapy, Rx = medical therapy alone, SoE = strength of evidence.

* RCTs of limited applicability to typical patients choosing PTRAS. NRCSs inadequately adjusted. Single arm studies analyzed poorly comparable cohorts of patients.

† Congestive heart failure / pulmonary edema symptoms and angina

‡ Noncomparable adverse events between PTRAS and medical therapy. Poorly reported.

Discussion

This review included 76 studies that evaluated medical therapy, percutaneous transluminal renal angioplasty with stent placement (PTRAS), or surgical revascularization since approximately 1995 in patients with atherosclerotic renal artery stenosis (ARAS), in addition to the 20 most recent case reports of revascularization in patients with acute decompensation related to ARAS. The review was restricted to primary treatment of patients being treated principally for ARAS, thus, excluding studies of treatment of restenosis or of patients with a transplanted kidney, and revascularization procedures not done primarily for ARAS (e.g., done during endovascular aortic aneurysm or dissection repairs). Among the eligible studies, only five randomized controlled trials (RCT)compared the two most common interventions in current practice, namely PTRAS (with continued medical therapy) and medical therapy alone. However, in only three of these (CORAL, RASCAD, and STAR)[19, 24, 32] were all patients treated with "aggressive" or "optimal" medical therapy, namely antihypertensives, a statin, and an antiplatelet drug.

Summary

The trials of PTRAS versus medical therapy found no difference in long-term outcomes in patients for whom there was equipoise between the two interventions. These results generalize to patients who are similar to those enrolled in the RCTs—patients with a moderate degree of stenosis (e.g., 50-70%), medically controlled hypertension (HTN), relatively stable kidney function, without symptoms such as pulmonary edema, for whom revascularization is an option but not considered necessary in current clinical practice (since the patients and their clinicians had to agree to the possibility of not having PTRAS)—but possibly not to many patients undergoing PTRAS, since, in clinical practice, there is often a strong belief that PTRAS is superior to continued medical therapy alone. Many patients presenting with ARAS would not have qualified for, and thus would not have been enrolled in, the RCTs. In one of the recent prospective studies of PTRAS, 23 percent of patients presenting with ARAS had flash pulmonary edema or rapidly declining kidney function, which would have excluded them from most of the trials. It remains unclear whether PTRAS (with continuation of medical therapy) offers a clinical benefit to patients currently indicated to have PTRAS compared with remaining on medical therapy alone. The relative effectiveness of PTRAS versus continued medical therapy in patients with a high degree of stenosis (e.g., >80%) or commonly used indications for revascularization (refractory HTN, rapid kidney deterioration, or recurrent pulmonary edema) remains unclear. Among the single group (noncomparative) studies, after PTRAS, on average, glomerular filtration rate did not improve, but blood pressure (BP) generally decreased by about 10 to 30 mmHg at the same time that the number of antihypertensive medications used decreased by about 0.5 drugs. In different cohorts of patients, those remaining on medical therapy alone generally had BP decreases by an average of about 5 to 10 mmHg without significant changes in the number of antihypertensive medications used. These differences were not seen in the comparative studies and do not appear to correlate with improvement in clinical outcomes or prevention of cardiovascular events. This apparent discordance may highlight the noncomparability between patient enrolled in RCTs (for whom there is clinical equipoise) or included in single group studies of PTRAS (who are deemed to need revascularization) and medical therapy(who are deemed to not need revascularization).

For the clinical outcomes, there is little suspicion of publication bias. The grey literature search did not reveal any unpublished comparative studies or study results. The recent, larger RCTs powered for clinical outcomes have fully published their findings, per their protocols. Furthermore, the commonly reported "negative" or "null" findings argues against the likelihood that studies or results have not been published because they did not show benefit.

Arguably, given the results of the RCTs, an important question is which factors predict patient response to each intervention. In populations such as those included in the RCTs, some patients may benefit more from medical therapy only and some from PTRAS plus medical therapy, resulting in no difference overall. More generally, for all patients it is important to know which factors would predict better outcomes with PTRAS than medical therapy.

We analyzed noncomparative studies, wherein everyone received a single treatment option (medical therapy alone, PTRAS, or open surgery). We evaluated these studies primarily to gather information about typical responses upon followup (e.g., change in BP or incidence of clinical events) and to evaluate possible predictors of outcomes. These studies generally found a wide range of outcomes among patients who, in separate studies, were treated with medical therapy, PTRAS, or open surgical revascularization. As examples, all-cause death was reported between 9 and 56 percent of patients on medical therapy, between 0 and 53 percent of patients after PTRAS, and in 26 to 36 percent of patients after surgical revascularization. Similarly glomerular filtration rate and SBP changes on medical therapy ranged from −8 to −0.7 mL/min and −22 to −6 mmHg; after PTRAS these outcomes ranged from −9 to 10 mL/min and −51 to 28 mmHg. These wide ranges suggest that there were underlying large differences across noncomparative studies in patient populations included in each study. Examples of such differences include different severity of renal artery stenosis (RAS), baseline BP and kidney function, concomitant cardiovascular disease and other comorbidities. Furthermore, particularly for these studies, it would be flawed to compare outcomes across the three sets of studies (by intervention) since the patients in each study type are even more noncomparable than patients in each study of a particular intervention may be to each other. Noncomparative studies of medical therapy included all patients who had not had an invasive intervention, including immediately after diagnosis. In contrast, noncomparative studies of PTRAS and open surgery for the most part included patients who had failed medical therapy alone, since medical therapy is standard of care regardless of other treatments and if they were doing well on medical therapy alone, no further intervention would have been necessary. Furthermore, patients receiving open surgery generally have some other indication for surgery, even if not well described in the studies, that precluded use of PTRAS.

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. The relative rarity of reporting of adverse events raises suspicion that adverse events were not captured by study researchers and/or that they were not reported in publications.

Subgroup and Predictor Analyses

Nevertheless, there is clearly a subset of patients who have improved kidney function and improved BP control after PTRAS compared to their kidney and BP status while on medical therapy alone (pre-PTRAS). There is a strong indication of heterogeneity of treatment effect occurring, such that some patients benefit but others fail to. After PTRAS, in most studies,

between 10 and 20 percent of patients have kidney function improvement and about 40 to 80 percent have BP improvement.

The case reports of patients who presented with acute decompensation of their ARAS—namely rapidly developing uncontrollable HTN, acute kidney injury, new onset dialysis, flash pulmonary edema, or other signs of decompensating congestive heart failure—provide anecdotal evidence that this subset of patients can benefit from renal artery revascularization. Certainly, these case reports are not an unbiased sample of such patients. It is striking that all case reports were patients who had successful outcomes, but it is highly unlikely that all patients with acute decompensation benefit from revascularization; particularly those already on dialysis. Descriptions of patients who failed to benefit would be interesting and could potentially yield some insights to predict who may not benefit. Better, a study that includes an unbiased sample of these patients is needed.

Analyses of predictors of outcomes after PTRAS yielded generally inconsistent or not particularly illuminating findings. The trials (CORAL and ASTRAL)[19, 20] failed to find factors that describe a putative subset of patients who benefited from PTRAS. The one observational study that reported an analysis of predictors with terms describing the interaction between the predictor factors and intervention (Ritchie 2014) found that patients presenting with flash pulmonary edema with both rapidly declining kidney function and refractory HTN (but not either of the latter conditions alone) had reduced relative rates of death compared with those treated medically.[9] This finding comports with the generally good outcomes seen in case reports of patients with acute decompensation. In the observational studies of PTRAS, the most consistent, though not universal, finding was that patients with worse kidney function or BP were most likely to have improvement in those outcomes after PTRAS; though to what degree this is due to regression to the mean is unclear. Studies were not consistent regarding whether patients with bilateral stenosis had significantly different effects on kidney function or BP than patients with unilateral disease. Regarding clinical event outcomes, the most consistent finding was that people with worse cardiovascular risk factors or history of cardiovascular disease were more likely to die or have future cardiovascular events, consistent with what would be found in the general population regardless of treatment.

Across all studies, most patients were elderly (≥65 years), with mean or median ages generally between about 60 and 80 years old. The CORAL trial found no difference in their composite cardiovascular and renal outcome between study participants above and below age 70 years.[19] One angioplasty cohort study found no significant difference by age in a similar composite cardiovascular-renal outcome.[75] None of the medication alone cohort studies reported on age as an outcome predictor.

The data on whether different intervention techniques (such as different stent types or use of brachytherapy or embolization protection devices) improve outcomes remains sparse, but does not support any specific PTRAS-related technique.

Future publications are expected from the CORAL study that may shed further light on patient-level predictors of outcomes (and of relative effectiveness between PTRAS and medical therapy) and of the relative effect of differences in treatment, such as the use of embolic protection devices or whether translesional pressure gradients were measured, both of which were at the discretion of operators. Of note, SPRINT, a recent multicenter RCT conducted in a general population of adults with hypertension has reported that medical therapy with an systolic BP (SBP) target of 120 mmHg decreased the risk of cardiovascular events by about one-third and mortality by about one-quarter compared to the more-typical target of 140 mmHg. Subgroup

analyses, including among patients with cardiovascular disease and with chronic kidney disease have not yet been reported. While this trial suggests that more intensive medical therapy might be clinically beneficial, which would lessen any relative benefit of revascularization, it would be highly speculative to conclude that using a treatment goal of 120 mmHg would be safe or effective in patients with RAS. The medical therapy studies found an average reduction in SBP of only about 5 mmHg; more intensive medical therapy may not succeed in further lowering BP but may increase treatment-related adverse events. Even if SBP were successfully lowered to under 120 mmHg, it is possible that such low BP may be harmful to patients with systemic atherosclerosis and comorbid conditions.

Comparison With Prior Comparative Effectiveness Review

Since 2007, the comparative study evidence has improved sufficiently to allow us to focus on PTRAS versus medical therapy (and surgery). In the 2006 and 2007 reports, because of limited evidence, studies of PTRA (without stenting) or of either PTRAS or PTRA were included as proxies for evaluation of PTRAS. With the publication of trials of PTRAS specifically, we were able to exclude these studies. Thus, of the two RCTs and eight nonrandomized comparative studies of PTRAS or PTRA included in the 2006 review, only one reported on an analysis of interest to the current review.[29] The evidence regarding the principal comparison of interest—PTRAS versus medical therapy—is, therefore, based on almost all recently published studies. Due to the limitations of the new studies, though, the conclusions about the relative benefits and harms of the interventions remain weak. It might be noted that, in contrast with the current review, the strength of evidence in the original reports was graded as "acceptable" for some outcomes. The apparent downgrading of the evidence can be explained by application of the more rigorous, current methodology for evaluating strength of evidence than was used in 2006 and 2007. Similarly, only one of the other comparative studies (of surgery vs. medical therapy[34]) was included in the original reviews.

The evidence from single-group studies was also mostly from newly published studies since 2007. This includes 35 of 63 single-group studies of PTRAS, 13 of 17 single-group studies of medical therapy, and one of four surgical single-group studies. Similarly, among studies providing evidence for Key Questions 2 and 3 (patient and treatment characteristics as predictors of outcomes) from single intervention groups, 12 of 20 PTRAS studies, both medical therapy studies, and one of the two surgical studies are newly published. While there is currently more evidence about more predictors and outcomes, the studies still do not provide conclusive evidence to support which patients should (or should not) have revascularization over continued medical therapy alone.

Comparison With Current Clinical Practice Guidelines

The current evidence is in concordance with current clinical practice guidelines, specifically the 2005 American College of Cardiology Foundation / American Heart Association (ACCF/AHA) guideline for the management of patients with peripheral artery disease (including RAS),[121] the 2011 ACCF/AHA guideline update (which did not change the original 2005 guideline),[122, 123] and the 2014 Society for Cardiovascular Angiography and Interventions (SCAI) expert consensus statement.[10]

Although this review did not address the comparative effectiveness of different antihypertensive medications and few studies evaluated only a single class of antihypertensive medications or compared effectiveness in patients with unilateral versus bilateral disease, the

evidence supports the conclusion that antihypertensive medications reduce BP in most patients with RAS.

The 2011 ACCF/AHA update occurred after publication of the ASTRAL study, but before publication of the CORAL study. The 2014 SCAI consensus statement was able to fully consider both studies. Consistent with the evidence, both guidelines recommend against PTRAS in patients who do not have hemodynamically significant RAS or who do not have signs or symptoms of decompensation. Both guidelines note the limitations regarding the applicability of the patients included in ASTRAL or CORAL. Taking into account the limitations of the evidence, both guidelines state that PTRAS may be an appropriate option for patients with hemodynamically significant RAS. The SCAI consensus statement is more cautious, though, limiting their recommendation to "carefully selected patients."[10] This review found only a low strength of evidence, hampered by imprecision and few RCTs, of possibly no difference in clinical outcomes between PTRAS and medication treatment, but possibly better kidney function and BP control after PTRAS.

Both guidelines recommend revascularization in patients with decompensation. These patients have rarely been included in the RCTs and were not specifically analyzed in the nonrandomized comparative studies. However, the case reports provide anecdotal evidence that these patients may benefit from revascularization.

The guidelines recommend consideration of open surgery for selected patients receiving revascularization, primarily based on anatomy or concomitant aortic disease. The review found low strength of evidence of no difference in mortality or BP control between the two revascularization approaches and inadequate evidence for other outcomes of interest. However, the review does not directly address the types of patients for whom open surgery is recommended. The review also excluded studies of patients receiving concomitant aortic surgery.

In agreement with this review, the SCAI consensus statement found insufficient evidence to make a recommendation regarding use of embolic protection devices during PTRAS. This review did not evaluate glycoprotein IIb/IIIa inhibitors, for which the guideline also stated there is insufficient evidence.

Possible Reasons for Inconclusive Evidence, Including Study Limitations

There are several plausible reasons why renal artery revascularization may not substantially improve clinical outcomes in individual patients. Primarily, there is substantial overlap in the etiologic factors of aortorenal vascular disease, parenchymal kidney disease, and cardiac and cerebral vascular diseases. While diabetes mellitus, dyslipidemia, and elevated BP are associated with atherosclerotic narrowing of the renal arteries and consequent worsening of BP and kidney function, they are also independently associated with direct kidney injury. Overcoming the renal artery lesion may fail to improve HTN or kidney function, which may be mediated not only by ARAS but also by underlying kidney disease (due to parenchymal disease or prior irreversible damage from ARAS). The underlying pathophysiology and atherosclerotic milieu present in individuals with ARAS is unchanged by PTRAS. Therefore, continuation of aggressive medical therapy (antihypertensives, statins, and antilipid drugs) is still necessary after PTRAS to minimize risk of cardiovascular events (including cardiac, stroke, kidney, aortic aneurysm, and peripheral vascular disease outcomes). Theoretically, some reduction in antihypertensive medication dose or number of drugs may be feasible after PTRAS due to better

BP control, but this is not borne out by the limited evidence. However, the complexity in how antihypertensive drug regimens are varied in response to changes in BP (and kidney function in regards to ARBs) in the setting of patients with atherosclerotic disease may make it unrealistic to find a common pattern in changes in drug doses or numbers with treatment.

A number of issues complicate the process of making decisions both for individual patients and for populations of patients. For one, the exact definition of ARAS varies depending on which diagnostic test is used, what threshold for stenosis is preferred, what degree of either resistant HTN or of kidney damage is required, and whether other evidence of atherosclerotic disease is present. Furthermore, the definition and relative importance of these items have been and continue to change as new diagnostic tests are used or existing tests are refined, as definitions of chronic kidney disease change, as treatments for HTN improve, and as techniques and modalities of surgical and percutaneous interventions change and, presumably, improve. In addition, for individual patients, the evaluation of RAS may be complicated by the risks, difficulties, and expense of the diagnostic tests, including acute kidney injury due to contrast dye. In clinical practice, the primary indication for performing renal angiography or other testing to diagnose ARAS is to determine whether a given patient should have revascularization. Patients who are not candidates for revascularization will not benefit from testing since medical therapy—antihypertensives as tolerated, antilipid drugs, and antiplatelet drugs—is identical with or without confirmation of the diagnosis. With the exception of the CORAL trial, which used an angiographic core lab, studies did not implement standardized methods for assessing the degree of artery stenosis to confirm whether they met criteria for PTRAS. The CORAL trial found that the standardized core lab measures of stenosis severity was generally lower than estimates made by individual investigators. The CORAL trial was also the only comparative study that explicitly incorporated translesional pressure gradient measurements into its eligibility criteria and assessment of stenosis severity. Patients with moderate percent stenosis (60-80%) also had to have translesional pressure gradient of >20 mmHg. If PTRAS studies inadvertently included patients with "nonsevere" stenosis (due to poor estimation of percent stenosis or inclusion of people without hemodynamic compromise, as estimated by translesional pressure gradient,[124] the studies may be biased to the null, since one would not expect revascularization to be more effective than medical therapy alone in these patients.

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. Few studies used standard definitions of BP or kidney function improvement or worsening; for the most part, each used an *ad hoc* definition that varied across studies. Conclusions across studies are therefore limited about incidence and relative rates of these outcomes. 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 following, for example, PTRAS. However, we did not discern a relationship between average baseline kidney function or BP and outcomes.

For individual patients and their clinicians, the question of what the preferred treatment for ARAS may be is fraught with difficulties largely related to the frequent frailty of these patients and the known complications from any of the interventions. These patients are generally elderly, often with severe cardiovascular disease, including atherosclerosis and diastolic left

ventricular dysfunction, often with moderate or severe chronic kidney disease, and with diabetes. Each of the antihypertensive agents carries substantial risks of bothersome and dangerous adverse events, which may be more likely or serious when multiple drugs are used. These drugs in general need to be taken lifelong and may only prevent further worsening of cardiovascular or kidney disease, as opposed to reducing the severity of existing disease. Invasive interventions, whether open or percutaneous, however, also carry risks of immediate death, cardiovascular events, acute and permanent kidney injury, and pain or other effects on quality of life. Also, the procedure may not carry any noticeable benefit to patients, in that they are likely to continue to require antihypertensive medications and may have no survival benefit or lessened risk of cardiovascular events or renal replacement therapy (RRT). Thus the relative overall effectiveness of angioplasty and continued aggressive medical therapy for most patients with ARAS remains unclear. For some patients with acutely worsening kidney or cardiovascular function, anecdotal evidence strongly suggests a benefit from revascularization.

Another limiting issue was that adverse event reporting was generally sparse and not reported in a consistent manner. In particular for adverse events, reporting was different for different interventions. Across all studies, both comparative and single arm, studies reported on adverse events related to PTRAS but not medical therapy. Revascularization studies tended to focus exclusively on periprocedure complications, without considering any RAS-related drug adverse events.

Future Research

Given the limitation of who could be recruited into trials of PTRAS versus medical therapy, well-analyzed, high-quality observational studies could yield some better insights into whether patients who receive PTRAS based on standards of practice actually do better because of the intervention. Such studies would have to be multicenter and from practices that have different thresholds or criteria for which patients have PTRAS to allow for an overlap across the centers in patients who likely would have continued medical therapy alone at more conservative centers but would have had PTRAS at more aggressive centers. A registry of all patients being considered for revascularization (that, ideally, includes a representative sample of ARAS patients not being considered for revascularization) could provide the basis for future studies that could allow for more generalizable, stronger evidence. In addition, a set of future studies should focus specifically on patients who are proven to have hemodynamically significant RAS, based on a combination of determination of severe percent stenosis (>75-80% thresholds have been used by existing studies) and abnormal translesional pressure gradients (e.g., >20 mmHg systolic gradient) in patients with moderate percent stenosis (e.g., 60-80%).[19, 124] Conceptually, it is appropriate to consider invasive treatment only for those people with clinically (or hemodynamically) significant disease. In studies, it is only in these patients that that one would expect a clinical effect of treatment.

It can be argued that nonrandomized comparative studies should be analyzed by propensity score adjustment, where the outcomes are adjusted for each patient's likelihood of having received PTRAS. Such an analysis could better account for differences between groups due to fundamental differences in treatment assignment (who gets which treatment) and may come close to estimating the associations that theoretically could be found in a RCT in patients who are commonly thought to "require" PTRAS.[125-127] However, none of the comparative observational studies performed such an analysis or even sufficiently adjusted their analyses to overcome the inherent clinical differences in patients who go ahead with invasive

revascularization and those who continue with medical therapy alone. Therefore, the studies continue to provide an inadequate evaluation of whether the general population of patients for whom PTRAS is thought to be indicated truly benefit from the procedure in terms of the most important patient-centered outcomes of death, RRT, and cardiovascular events. Future, well-conducted, well-analyzed (preferably prospective) observational studies are warranted. The design and implementation of such studies, while not simple, should be easier to implement and less resource intensive than the larger, well-conducted, and complex recent RCTs. Existing larger studies could be reanalyzed both to better compare interventions and to further evaluate potential subgroup differences or predictors of outcomes (e.g., based on stenosis severity or cointerventions)

There have been suggestions to create a national registry of all PTRAS, as discussed at the 2007 MEDCAC Panel discussion of RAS.[128] However, there is not consensus that a registry would be of sufficient value to mandate, or if one were created, who specifically should be included. Among the concerns was that a national registry would preclude enrollment of patients into then-ongoing randomized trials. However, now that those trials are complete, this may no longer be a major concern. The main advantages of a national registry of patients undergoing PTRAS would be to better understand who is undergoing the procedure, what their outcomes are, and, most importantly, to better answer Key Questions 2 and 3, namely, what patient and treatment factors predict outcomes. There remains a need for evidence to better define which patients would most (or least) benefit from revascularization. A registry, however, would not be able to compare PTRAS to continued medical therapy, unless somehow a registry were created of patients diagnosed with sufficiently severe RAS who did not undergo revascularization.

As recommended by the Institute of Medicine report on guideline implementation, "[guideline] developers [and guideline] implementers… should collaborate in an effort to align their needs with one another" to best support unbiased guidance.[129] Thus, future guidelines on ARAS management would benefit not only on reliance on this and related comprehensive systematic reviews, but also from collaboration among nephrologists, interventional radiologists, interventional cardiologists, vascular surgeons, and other stakeholders.

Conclusions

Overall, the evidence suggests that PTRAS does not provide a benefit over medical therapy alone in patients for whom there is equipoise between the two intervention approaches. Observational studies suggest that patients with greater indications for PTRAS—specifically worse kidney function (variously defined), higher BP (also variously defined), or flash pulmonary edema—may be more likely to have improved kidney function and BP with PTRAS. Nevertheless, it still remains unknown whether these "high risk" patients have benefits in survival and avoiding cardiovascular events and RRT, compared to remaining on medical therapy. Anecdotal evidence confirms that some patients with acute decompensation due to ARAS benefit clinically from revascularization. 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)". Future studies or reanalyses of data in existing studies are needed to determine the relative effectiveness of PTRAS and medical therapy in patients for whom PTRAS is currently commonly recommended. Since patients who receive PTRAS are generally different in their health status

from those who remain on medical therapy alone, propensity score adjustment of large observational datasets may allow for relatively unbiased analyses of these patients by properly accounting for these differences.

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Abbreviations

AAA	abdominal aortic aneurysm
ABPM	24 hour ambulatory blood pressure monitoring
ACCF	American College of Cardiology Foundation
ACEi	angiotensin converting enzyme inhibitor
ACS	acute coronary syndrome
AE	adverse events
AFib	atrial fibrillation
AHA	American Heart Association
AHRQ	Agency for Healthcare Research and Quality
AMI	acute myocardial infarction
ARAS	atherosclerotic renal artery stenosis
ARB	angiotensin-receptor blocker
ASTRAL	Angioplasty and Stenting for Renal Artery Lesions
BNP	brain natriuretic protein
BP	blood pressure
CAD	coronary artery disease
CHF	congestive heart failure
CI	confidence interval
CKD	chronic kidney disease
COPD	chronic obstructive pulmonary disease
CORAL	Cardiovascular Outcomes in Renal Atherosclerotic Lesions
CrCl	creatinine clearance
CRF	chronic renal failure
CRP	C reactive protein
CT	computed tomography
CV	cardiovascular
DBP	diastolic blood pressure
DCM	dilated cardiomyopathy
DEP	distal embolic protection device
DM	diabetes mellitus
EPC	Evidence-based Practice Centers
ESRD	end stage renal disease
FPE	flash pulmonary edema
GFR	glomerular filtration rate
HR	hazard ratio
HTN	hypertension
ICTRP	International Clinical Trials Registry Platform
LDL	low density lipoprotein
LVEF	left ventricular ejection fraction
LVF	left ventricular failure
MAP	mean arterial pressure
MetS	metabolic syndrome
MI	myocardial infarction
MR	mitral regurgitation
MRI	magnetic resonance imaging
NRCS	nonrandomized comparative studies
NYHA	New York Heart Association class
OR	odds ratio
PAD	peripheral artery disease

PFTE	polytetrefluoroethylene
PTRA	percutaneous transluminal renal angioplasty (without stent placement)
PTRAS	percutaneous transluminal renal angioplasty with stent placement
PVD	peripheral vascular disease
RA	renal artery
RAS	renal artery stenosis
RCA	right coronary artery stenosis
RCT	randomized controlled trial
RI	resistance index
RR	Risk ratio
RRT	renal replacement therapy
SBP	systolic blood pressure
SCAI	Society for Cardiovascular Angiography and Interventions
SCr	serum creatinine
SoE	strength of evidence
SRDR	Systematic Review Data Repository
TEP	technical expert panel
TIA	transient ischemic attack

Appendixes

Appendix A. Search Strategy

The search from the 2006 report was updated and run in MEDLINE, Cochrane, and Embase on July 21, 2014, December 31, 2014, March 20, 2015, and March 16, 2016:

1. exp Hypertension, Renal/
2. exp Renal Artery Obstruction/
3. renal arter$ stenosis.tw.
4. renal arter$ dis$.tw.
5. renovascular dis$.tw.
6. reno vascular dis$.tw.
7. renal vascular dis$.tw.
8. (arvd or "atherosclerotic renovascular dis$").tw.
9. renal steno$.tw.
10. steno$ kidney.tw.
11. renovascular steno$.tw.
12. or/1-11
13. limit 12 to humans
14. limit 13 to english language
15. limit 14 to (addresses or bibliography or biography or case reports or congresses or consensus development conference or consensus development conference, nih or dictionary or directory or editorial or festschrift or government publications or interview or lectures or legal cases or legislation or letter or news or newspaper article or patient education haout or periodical index or "review of reported cases")
16. 14 not 15
17. limit 16 to "all adult (19 plus years)"
18. 16 not 17
19. limit 18 to "all child (0 to 18 years)"
20. 16 not 19
21. limit 20 to (guideline or practice guideline or "review" or review, academic or "review literature" or review, multicase or review, tutorial)
22. limit 20 to meta analysis
23. 20 not (21 or 22)
24. follow-up studies/
25. (follow-up or followup).tw.
26. exp Case-Control Studies/
27. (case adj20 control).tw.
28. exp Longitudinal Studies/
29. longitudinal.tw.
30. exp Cohort Studies/
31. cohort.tw.
32. (Random$ or rct).tw.
33. exp Randomized Controlled Trials/
34. exp Random allocation/
35. exp Double-Blind Method/
36. exp Single-Blind Method/
37. randomized controlled trial.pt.

38. clinical trial.pt.
39. controlled clinical trial.pt.
40. (clin$ adj trial$).tw.
41. ((singl$ or doubl$ or trebl$ or tripl$) adj (bli$ or mask$)).tw.
42. exp PLACEBOS/
43. placebo$.tw.
44. exp Research Design/
45. exp Evaluation Studies/
46. exp Prospective Studies/
47. exp Comparative Study/
48. or/24-47
49. 23 and 48
50. (2007$ or 2008$ or 2009$ or 2010$ or 2011$ or 2012$ or 2013$ or 2014$).ed.
51. 49 and 50

At the suggestion of the Technical Expert Panel, we ran a separate search for a selection of case studies of more severe patients, who were likely to benefit from stenting and would have been excluded from the RCTs. This search was run only in MEDLINE on August 14, 2014.

1. exp Hypertension, Renal/
2. exp Renal Artery Obstruction/
3. renal arter$ stenosis.af.
4. renal arter$ dis$.af.
5. renovascular dis$.af.
6. reno vascular dis$.af.
7. renal vascular dis$.af.
8. (arvd or "atherosclerotic renovascular dis$").af.
9. renal steno$.af.
10. steno$ kidney.af.
11. renovascular steno$.af.
12. or/1-11
13. High risk.af.
14. Critical stenosis.af.
15. Critical lesion.af.
16. exp Acute Kidney Injury/
17. (Subacute and (renal failure or renal insufficiency or kidney failure)).af.
18. (Renovascular and crisis).af.
19. exp Kidney Failure, Chronic/
20. (Acute and ischemic nephropathy).af.
21. (Acute and (renal failure or renal insufficiency or kidney failure)).af.
22. ((chronic kidney disease or CKD) and (stage IV or stage V)).af.
23. Rescue.af. and (RRT.af. or exp renal replacement therapy/ or renal replacement therapy.af. or dialysis.af.)
24. Flash pulmonary edema.af.
25. (Acute adj diastolic dysfunction).af.

26. exp Heart Failure/
27. Acute heart failure.af.
28. Hypertensive crisis.af.
29. exp Hypertension, Malignant/
30. exp Hypertensive encephalopathy/
31. (Hospitalization adj10 hypertension).af.
32. (Bilateral and severe).af.
33. (Single and functioning and kidney).af.
34. hypertensive emergency.af.
35. or/13-34
36. 12 and 35
37. limit 36 to english language
38. limit 37 to humans
39. case.af.
40. 38 and 39

Appendix B. Excluded Studies

Table B. Excluded studies with rejection reasons

Rejection Reason	PMID	Authors	Title	Journal	Note
P: Not primarily ARAS treatment	9408615	Harjai	Effect of Geer on Outcomes Following Renal Artery Stent Placement for Renovascular Hypertension		Original report
P: Not primarily ARAS treatment	10658941	Johansson	Increased cardiovascular mortality in hypertensive patients with renal artery stenosis. Relation to sympathetic activation, renal function and treatment regimens.		Original report
P: Not primarily ARAS treatment	18472384	Modrall JG Rosero EB Smith ST Arko FR 3rd Valentine RJ Clagett GP Timaran CH	Operative mortality for renal artery bypass in the United States: Results from the National Inpatient Sample	Journal of Vascular Surgery	New
P: Not primarily ARAS treatment	19233600	Mohabbat W Greenberg RK Mastracci TM Cury M Morales JP Hernaez AV	Revised duplex criteria and outcomes for renal stents and stent grafts following endovascular repair of juxtarenal and thoracoabdominal aneurysms	Journal of Vascular Surgery	New
P: Not primarily ARAS treatment	19853403	Patel R Conrad MF Paruchuri V Kwolek CJ Cambria RP Comment in: J Vasc Surg. 2010 Feb;51(2):315-6; PMID: 20141955	Balloon expandable stents facilitate right renal artery reconstruction during complex open aortic aneurysm repair	Journal of Vascular Surgery	New
P: Not primarily ARAS treatment	22104341	Reed NR Kalra M Bower TC Oderich GS McKusick M Duncan AA Schleck CD Gloviczki P	Efficacy of combined renal and mesenteric revascularization	Journal of Vascular Surgery	New
P: Not primarily ARAS treatment	no PMID	Marone	Revascularization for renal function retrieval: which patients will benefit?	Pers Vasc Surg Endovasc Ther	Original report
Other: Restenosis	23538936	HS Itani	First use of a drug-eluting balloon in the treatment of acute renal artery occlusion and in-stent restenosis		New
Other: RCT protocol	19229814	Marcantoni C Zanoli L Rastelli S Tripepi G Matalone M Di Laro D Scaura S Tamburino C Zoccali C Castellino P	Stenting of renal artery stenosis in coronary artery disease (RAS-CAD) study: a prospective, randomized trial	Journal of Nephrology	New

Other: Protocol	19635148	Schwarzwalder U Hauk M Zeller T	RADAR - A randomized, multi-centre, prospective study comparing best medical treatment versus best medical treatment plus renal artery stenting in patients with haemodynamically relevant atherosclerotic renal artery stenosis	Trials [Electronic Resource]	New
Other: Not primary study	18670376	Henry M Henry I Polydorou A Hugel M	Embolic protection for renal artery stenting	Journal of Cardiovascular Surgery	New
Other: Not primary study	no PMID		Revascularization versus medical therapy for renal-artery stenosis. The ASTRAL investigators. The New Engla Journal of Medicine 2009; 361: 1953-1962	Vascular Medicine	New
Other: Not ARAS	17349328	Grigoryants V Henke PK Watson NC Upchurch GR Jr Wakefield TW Stanley JC	Iliorenal bypass: indications and outcomes following 41 reconstructions	Annals of Vascular Surgery	New
Other: Not ARAS	17453127	Lanzer P Weser R Prettin C	Intentional single-stage revascularization of two different vascular beds in patients with vascular multimorbidity; a feasibility study	Clinical Research in Cardiology	New
Other: Not ARAS	18760724	Cai S Ouyang YS Li JC Dai Q Tan L Xia Y Xu ZH Li HJ Jiang YX	Evaluation of acute renal artery thrombosis or embolism with color Doppler sonography		New
Other: Not an analysis of interest (CORAL)	no PMID	David A Folt1; Kaleigh L Evans1; Sravya Brahmaam1; Wencan He1; Pamela Brewster1; Timothy P Murphy2; Donald E Cutlip3; Lance Dworkin4; Kenneth Jamerson5; William Henrich6; Diane Reid7; Christopher J Cooper1	Abstract 14746: Region and physician specialty influence medical management of atherosclerotic renal artery stenosis	Circulation	New
Other: No new primary data (PMID 18490527)	no PMID	He W, Chen J, Zhang D et al	Abstract 14283: Time depeant changes in systolic blood pressure after renal artery stenting: Role of stenosis severity	Circulation	New
Other: No new primary data (ASTRAL abstract plus commentary)	no PMID		Should revascularisation be recommended for atherosclerotic renal artery stenosis?	Journal of the Royal College of Physicians of Edinburgh	New
Other: Natural Hx	8254782	Fergany	Management of atherosclerotic renal artery disease in younger patients		Original report

Other: Natural Hx	9507221	Caps	Risk of atrophy in kidneys with atherosclerotic renal artery stenosis.		Original report
Other: Natural Hx	11099684	Iglesias	The Natural History of Incidental Renal Artery Stenosis in Patients with Aortoiliac Vascular Disease		Original report
Other: Natural Hx	11576364	Conlon	Severity of renal vascular disease predicts mortality in patients undergoing coronary angiography		Original report
Other: Natural Hx	11752032	Cheung	Epidemiology of Renal Dysfunction and Patient Outcome in Atherosclerotic Renal Artery Occlusion		Original report
Other: Natural Hx	12027983	Pillay	Prospective multicentre study of the natural history of atherosclerotic renal artery stenosis in patients with peripheral vascular disease.		Original report
Other: Natural Hx	12358138	Uzu	Prevalence and outcome of renal artery stenosis in atherosclerotic patients with renal dysfunction.		Original report
Other: Natural Hx	15161949	Houston	Spiral laminar flow in the abdominal aorta: a predictor of renal impairment deterioration in patients with renal artery stenosis?		Original report
Other: Natural Hx	17713349	Cheung CM Patel A Shaheen N Cain S Eddington H Hegarty J Middleton RJ Cowie A Mamtora H Kalra PA	The effects of statins on the progression of atherosclerotic renovascular disease	Nephron	New
Other: Natural Hx	19667039	Wright JR Shurrab AE Cooper A Kalra PR Foley RN Kalra PA	Progression of cardiac dysfunction in patients with atherosclerotic renovascular disease	Qjm	New
Other: Natural Hx	25150754	Aboyans V and Tanguy and B. and Desormais and I. and Bonnet and V. and Chonchol and M. and Laskar and M. and Mohty and D. and Lacroix and P.	Prevalence of renal artery disease and its prognostic significance in patients undergoing coronary bypass grafting	American Journal of Cardiology	New
Other: Drive by stent	19952777	Rimoldi SF de Marchi SF Wiecker S Meier B Allemann Y	Screening renal artery angiography in hypertensive patients undergoing coronary angiography a 6-month follow-up after ad hoc percutaneous revascularization	Journal of Hypertension	New

Other: Case, not ARAS	17003541	Rehan A and Almanaseer and Yassar and Desai and Devang M. and Ali and Arshad and Yamasaki and Hiroshi	Complete resolution of acute renal failure after left renal artery angioplasty and stent placement for total renal artery occlusion		New
Other: Case, not acute decompensation	17022392	Mannebach PC and Dieter and Robert S. and Marks and David Scott	Use of gadolinium-based angiography for renal artery stenting in a patient with renal insufficiency: A case report	Angiology	New
Other: Case, not acute decompensation	17712213	Adriaenssens T and Kastrati and Adnan and Schomig and Albert	Successful stenting of bilateral multiple renal arteries in a patient with renovascular hypertension	Journal of Invasive Cardiology	New
O: No outcome of interest	17723005	Puchner S Stadler A Minar E Lammer J Bucek RA	Multidetector CT angiography in the follow-up of patients treated with renal artery stents: value of different reformation techniques compared with axial source images	Journal of Endovascular Therapy	New
O: No outcome of interest	18386125	Parenti GC Palmarini D Bilzoni M Campioni P Mannella P Ginevra A	Role of color-Doppler sonography in the follow-up of renal artery stenting	Radiologia Medica	New
O: No outcome of interest	18712043	Tanemoto M Abe M Uruno A Abe T Ito S	Angiographic index for angioplasty-treatable atheromatous renal artery stenosis	Hypertension Research - Clinical & Experimental	New
O: No outcome of interest	18922676	Giles H Lesar C Erdoes L Sprouse R Myers S	Balloon-expandable covered stent therapy of complex endovascular pathology	Annals of Vascular Surgery	New
O: No outcome of interest	20675902	Thalhammer C Ferriani V Husmann M Rufibach K Meier T Amann-Vesti BR	Predictive value of duplex ultrasound for restenosis after renal artery stenting	Clinical Hemorheology & Microcirculation	New
O: No outcome of interest	24746646	Crimmins JM	Validity of estimated glomerular filtration rates for assessment of renal function after renal artery stenting in patients with atherosclerotic renal artery stenosis	Jacc: Cardiovascular Interventions	New
O: No outcome of interest	no PMID		Determinants of angiotensin converting enzyme inhibitor/angiotensin receptor blocker use in patients with atherosclerotic renal artery stenosis and effects on blood pressure	Circulation	New

I: No specific intervention(s)	16892443	Jones NJ Bates ER Chetcuti SJ Lederman RJ Grossman PM	Usefulness of translesional pressure gradient and pharmacological provocation for the assessment of intermediate renal artery disease	Catheterization & Cardiovascular Interventions	New
I: No specific intervention(s)	17631082	de Silva R Loh H Rigby AS Nikitin NP Witte KK Goode K Bhaari S Nicholson A Clark AL Clela JG	Epidemiology, associated factors, and prognostic outcomes of renal artery stenosis in chronic heart failure assessed by magnetic resonance angiography	American Journal of Cardiology	New
I: No specific intervention(s)	17891347	Komea P Zalunardo N Burnett S Love J Buller C Taylor P Duncan J Djurdjev O Levin A	Conservative outpatient renoprotective protocol in patients with low GFR undergoing contrast angiography: a case series	Clinical & Experimental Nephrology	New
I: No specific intervention(s)	18569908	Onuigbo MA Onuigbo NT	Renal failure and concurrent RAAS blockade in older CKD patients with renal artery stenosis: an exteed Mayo Clinic prospective 63-month experience	Renal Failure	New
I: No specific intervention(s)	18670374	Bergqvist D Bjorck M Lugren F Troeng T	Invasive treatment for renovascular disease. A twenty year experience from a population based registry	Journal of Cardiovascular Surgery	New
I: No specific intervention(s)	18692990	Davies MG Saad WE Peden EK Mohiuddin IT Naoum JJ Lumsden AB	Implications of acute functional injury following percutaneous renal artery intervention	Annals of Vascular Surgery	New
I: No specific intervention(s)	19098012	Esteban C Perez P Fernaez-Llamazares J Surinach JM Camafort M Martorell A Monreal M Comment in: Angiology. 2010 May;61(4):415-6; PMID: 20483812	Clinical outcome in patients with peripheral artery disease and renal artery stenosis	Angiology	New
I: No specific intervention(s)	19754857	Dechering DG Kruis HM Adiyaman A Thien T Postma CT	Clinical significance of low-grade renal artery stenosis	Journal of Internal Medicine	New
I: No specific intervention(s)	21133827	Andersen UB Borglykke A Jorgensen T	Prevalence of renal artery stenosis in subjects with moderate hypertension. A population-based study	Blood Pressure	New

I: No specific intervention(s)	22771675	A. Eirin and Gloviczki and Monika L. and Tang and Hui and Gossl and Mario and Jordan and Kyra L. and Woollard and John R. and Lerman and Amir and Grae and Joseph P. and Textor and Stephen C. and Lerman and Lilach O.	Inflammatory and injury signals released from the post-stenotic human kidney		New
I: No specific intervention(s)	no PMID		Severity of renal artery lesions in patients enrolled into the CORAL trial	Journal of Vascular and Interventional Radiology	New
I: No specific intervention(s)	2150435	Khangura KK and A.; Kane and G. C.; Misra and S.; Textor and S. C.; Lerman and A.; Lerman and L. O.; Khangura and Kirandeep K.; Eirin and Alfonso; Kane and Garvan C.; Misra and Sanjay; Textor and Stephen C.; Lerman and Amir; Lerman and Lilach O.	Extrarenal atherosclerotic disease blunts renal recovery in patients with renovascular hypertension	Journal of Hypertension	New
I: Angioplasty w/o stent (≥80%)	2939491	L. G. Martin and Casarella and W. J. and Alspaugh and J. P. and Chuang and V. P.	Renal artery angioplasty: increased technical success and decreased complications in the seco 100 patients		New
I: Angioplasty w/o stent (≥80%)	10924577	Baumgartner	Stent Placement in Ostial and Nonostial Atherosclerotic Renal Arterial Stenoses: A Prospective Follow-up Study		Original report
I: Angioplasty w/o stent (≥80%)	11172177	Radermacher	Use of Doppler ultrasonography to predict the outcome of therapy for renal-artery stenosis		Original report
I: Angioplasty w/o stent (≥80%)	12469977	Ziakka	Percutaneous transluminal renal artery angioplasty: who benefits most?		Original report
I: Angioplasty w/o stent (≥80%)	16897141	Lanzer P Weser R Prettin C	Coronary-like revascularization for atherosclerotic renal artery stenosis--results in 181 consecutive patients	Clinical Research in Cardiology	New
I: Angioplasty w/o stent (≥80%)	17491539	Mak G Tan CY Ben Khiaron O McEniff N Feely J	An evaluation of the effects of renal artery stenting in renovascular hypertension	Irish Medical Journal	New

I: Angioplasty w/o stent (≥80%)	18580055	Zalunardo N Rose C Starovoytov A Djurdjev O Fox R Taylor P Duncan JA Buller CE Levin A	Incidental atherosclerotic renal artery stenosis diagnosed at cardiac catheterization: no difference in kidney function with or without stenting	American Journal of Nephrology	New
I: Angioplasty w/o stent (≥80%)	18772602	Lekston A Chudek J Gasior M Wilczek K Wiecek A Kokot F Gierlotka M Niklewski T Fijalkowski M Szygula-Jurkiewicz B Wojnicz R Bialas B Osuch M Maciejewski B Polonski L	Angiographic and intravascular ultrasound assessment of immediate and 9-month efficacy of percutaneous transluminal renal artery balloon angioplasty with subsequent brachytherapy in patients with renovascular hypertension	Kidney & Blood Pressure Research	New
I: Angioplasty w/o stent (≥80%)	19217744	Davies MG Saad WE Bismuth JX Naoum JJ Peden EK Lumsden AB	Endovascular revascularization of renal artery stenosis in the solitary functioning kidney	Journal of Vascular Surgery	New
I: Angioplasty w/o stent (≥80%)	19337882	Jensen G Annerstedt M Klingenstierna H Herlitz H Aurell M Hellstrom M Comment in: Sca J Urol Nephrol. 2010 Feb;44(1):62-3; author reply 64; PMID: 19958074	Survival and quality of life after renal angioplasty: a five-year follow-up study	Scainavian Journal of Urology & Nephrology	New
I: Angioplasty w/o stent (≥80%)	19367240	Alhadad A Mattiasson I Ivancev K Liblad B Gottsater A	Predictors of long-term beneficial effects on blood pressure after percutaneous transluminal renal angioplasty in atherosclerotic renal artery stenosis	International Angiology	New
I: Angioplasty w/o stent (≥80%)	19413179	Lekston A Niklewski T Gasior M Chudek J Wilczek K Wiecek A Kokot F Fijalkowski M Gierlotka M Osuch M Maciejewski B Polonski L	Effects of short- and long-term efficacy of percutaneous transluminal renal angioplasty with or without intravascular brachytherapy on regression of left ventricular hypertrophy in patients with renovascular hypertension	Polskie Archiwum Medycyny Wewnetrznej	New

I: Angioplasty w/o stent (≥80%)	19950087	Lekston A Chudek J Wilczek K Gasior M Wiecek A Kokot F Fijalkowski M Gierlotka M Szygula-Jurkiewicz B Wojnicz R Bialas B Osuch M Maciejewski B Polonski L	Comparison of early and late efficacy of percutaneous transluminal renal angioplasty with or without subsequent brachytherapy: the effect on blood pressure in patients with renovascular hypertension	Cardiology Journal	New
I: Angioplasty w/o stent (≥80%)	19955827	Duranay M Kanbay M Akay H Unverdi S Surer H Altay M Kirbas I Covic A Zoccali C	Nebivolol improves renal function in patients who underwent angioplasty due to renal artery stenosis: a pilot study	Nephron	New
I: Angioplasty w/o stent (≥80%)	21613792	Nowakowska Fortuna E Herlitz H Saeed A Attman PO Jensen G Alaupovic P Guron G	Lipoprotein abnormalities in patients with atherosclerotic renovascular disease	Kidney & Blood Pressure Research	New
D: Surg retro cohort N<100	21636929	Kumar B Sinha PK Unnikrishnan M	Anesthetic management of patients undergoing extra-anatomic renal bypass surgery for renovascular hypertension	Annals of Cardiac Anaesthesia	New
D: Surg retro cohort N<100	21821380	Ghanami RJ, Rana H, Craven TE, Hoyle J, Edwards MS, Hansen KJ.	Diastolic function predicts survival after renal revascularization.	Journal of Vascular Surgery	New
D: Plasty/Rx cohort, retrospective	19631505	Corriere MA Hoyle JR Craven TE D'Agostino RB Jr Edwards MS Moore PS Hansen KJ	Changes in left ventricular structure and function following renal artery revascularization	Annals of Vascular Surgery	New
D: Plasty/Rx cohort, retrospective	2939491	Martin LG and Casarella and W. J. and Alspaugh and J. P. and Chuang and V. P.	Renal artery angioplasty: increased technical success and decreased complications in the seco 100 patients		New
D: Plasty/Rx cohort, retrospective	9774123	Tuttle	Treatment of Atherosclerotic Ostial Renal Artery Stenosis With the Intravascular Stent		Original report
D: Plasty/Rx cohort, retrospective	11479472	Lederman	Primary renal artery stenting: Characteristics and outcomes after 363 procedures		Original report
D: Plasty/Rx cohort, retrospective	14718831	Pizzolo	Renovascular disease: Effect of ACE gene deletion polymorphism and endovascular revascularization		Original report
D: Plasty/Rx cohort, retrospective	14743583	Bucek	Long-term follow-up after renal artery stenting		Original report
D: Plasty/Rx cohort, retrospective	17042665	Bates MC Rashid M Campbell JE Stone PA Broce M Lavigne PS	Factors influencing the need for target vessel revascularization after renal artery stenting	Journal of Endovascular Therapy	New

D: Plasty/Rx cohort, retrospective	17192944	Silva JA Potluri S White CJ Collins TJ Jenkins JS Subramanian R Ramee SR Comment in: Catheter Cardiovasc Interv. 2007 May 1;69(6):908-9; PMID: 17427206	Diabetes mellitus does not preclude stabilization or improvement of renal function after stent revascularization in patients with kidney insufficiency and renal artery stenosis	Catheterization & Cardiovascular Interventions	New
D: Plasty/Rx cohort, retrospective	17210392	Kashyap VS Sepulveda RN Bena JF Nally JV Poggio ED Greenberg RK Yadav JS Ouriel K	The management of renal artery atherosclerosis for renal salvage: does stenting help?	Journal of Vascular Surgery	New
D: Plasty/Rx cohort, retrospective	17400563	Tan J Filobbos R Raghunathan G Nicholson T Fowler R Wright M Eadington D	Efficacy of renal artery angioplasty and stenting in a solitary functioning kidney	Nephrology Dialysis Transplantation	New
D: Plasty/Rx cohort, retrospective	17488176	Zeller T Rastan A Schwarzwalder U Muller C Frank U Burgelin K Sixt S Schwarz T Noory E Neumann FJ	Regression of left ventricular hypertrophy following stenting of renal artery stenosis	Journal of Endovascular Therapy	New
D: Plasty/Rx cohort, retrospective	17525962	Bates MC Campbell JE Stone PA Jaff MR Broce M Lavigne PS Comment in: Catheter Cardiovasc Interv. 2007 Jun 1;69(7):1046-7; PMID: 17525963 Comment in: Catheter Cardiovasc Interv. 2007 Jun 1;69(7):1044-5; PMID: 17525995 Comment in: Catheter Cardiovasc Interv. 2007 Jun 1;69(7):1048-9; PMID: 17525964	Factors affecting long-term survival following renal artery stenting	Catheterization & Cardiovascular Interventions	New
D: Plasty/Rx cohort, retrospective	17606122	Edwards MS Corriere MA Craven TE Pan XM Rapp JH Pearce JD Mertaugh NB Hansen KJ	Atheroembolism during percutaneous renal artery revascularization	Journal of Vascular Surgery	New
D: Plasty/Rx cohort, retrospective	17673882	Tagle R Acevedo M Xu M Pohl M Vidt D	Use of endovascular stents in atherosclerotic renovascular stenosis: blood pressure and renal function changes in hypertensive patients	Journal of Clinical Hypertension	New
D: Plasty/Rx cohort, retrospective	17934918	Ovrehus KA Aersen PE Jacobsen IA Comment in: Blood Press. 2007;16(5):288-90; PMID: 17934915	Treatment of renovascular hypertension by transluminal angioplasty--13 years experience in a single centre	Blood Pressure	New

D: Plasty/Rx cohort, retrospective	18238866	Bates MC Campbell JE Broce M Lavigne PS Riley MA	Serum creatinine stabilization following renal artery stenting	Vascular & Endovascular Surgery	New
D: Plasty/Rx cohort, retrospective	18256017	Kane GC Stanson AW Kalnicka D Rosenthal DW Lee CU Textor SC Garovic VD	Comparison between gadolinium and iodine contrast for percutaneous intervention in atherosclerotic renal artery stenosis: clinical outcomes	Nephrology Dialysis Transplantation	New
D: Plasty/Rx cohort, retrospective	18620111	Suliman A Imhoff L Greenberg JI Angle N	Renal stenting for incidentally discovered renal artery stenosis: is there any outcome benefit?	Annals of Vascular Surgery	New
D: Plasty/Rx cohort, retrospective	18727962	Corriere MA Pearce JD Edwards MS Stafford JM Hansen KJ Comment in: Perspect Vasc Surg Endovasc Ther. 2009 Sep;21(3):201-2; PMID: 19602506	Endovascular management of atherosclerotic renovascular disease: early results following primary intervention	Journal of Vascular Surgery	New
D: Plasty/Rx cohort, retrospective	18760140	Hackam DG Duong-Hua ML Mamdani M Li P Tobe SW Spence JD Garg AX	Angiotensin inhibition in renovascular disease: a population-based cohort study	American Heart Journal	New
D: Plasty/Rx cohort, retrospective	18789723	Misra S Gomes MT Mathew V Barsness GW Textor SC Bjarnason H McKusick MA	Embolic protection devices in patients with renal artery stenosis with chronic renal insufficiency: a clinical study	Journal of Vascular & Interventional Radiology	New
D: Plasty/Rx cohort, retrospective	18829238	Klonaris C Katsargyris A Alexarou A Tsigris C Giannopoulos A Bastounis E	Efficacy of protected renal artery primary stenting in the solitary functioning kidney	Journal of Vascular Surgery	New
D: Plasty/Rx cohort, retrospective	19128271	Singer GM Setaro JF Curtis JP Remetz MS	Distal embolic protection during renal artery stenting: impact on hypertensive patients with renal dysfunction	Journal of Clinical Hypertension	New
D: Plasty/Rx cohort, retrospective	19172426	Eklof H Bergqvist D Hagg A Nyman R	Outcome after endovascular revascularization of atherosclerotic renal artery stenosis	Acta Radiologica	New
D: Plasty/Rx cohort, retrospective	19202165	Chrysochou C Cheung CM Durow M Middleton RJ Solomon LR Craig A Venning M Kalra PA	Proteinuria as a predictor of renal functional outcome after revascularization in atherosclerotic renovascular disease (ARVD)	Qjm	New
D: Plasty/Rx cohort, retrospective	19217748	Davies MG Saad WA Bismuth JX Peden EK Naoum JJ Lumsden AB	Outcomes of eoluminal reintervention for restenosis after percutaneous renal angioplasty and stenting	Journal of Vascular Surgery	New

D: Plasty/Rx cohort, retrospective	19328725	Thatipelli MR Misra S Sanikommu SR Schainfeld RM Sharma SK Soukas PA	Embolic protection device use in renal artery stent placement	Journal of Vascular & Interventional Radiology	New
D: Plasty/Rx cohort, retrospective	19595532	Corriere MA Edwards MS Pearce JD Arews JS Geary RL Hansen KJ	Restenosis after renal artery angioplasty and stenting: incidence and risk factors	Journal of Vascular Surgery	New
D: Plasty/Rx cohort, retrospective	19625262	Padigala KK Hartle JE Kirchner HL Schultz MF	Renal cortical thickness as a predictor of renal function and blood pressure status post renal artery stenting	Angiology	New
D: Plasty/Rx cohort, retrospective	19699353	Dieter RS Darki A Nanjuappa A Chhokar VS Khadim G Morshedi-Meibodi A Freihage JH Steen L Lewis B Leya F	Usefulness of wide pulse pressure as a predictor of poor outcome after renal artery angioplasty and stenting	American Journal of Cardiology	New
D: Plasty/Rx cohort, retrospective	19759030	Albertal M Nau G Padilla LT Cura FA Thierer J Belardi JA	Do men and women respo differently to percutaneous renal artery interventions?	Angiology	New
D: Plasty/Rx cohort, retrospective	19878369	Singer GM Remetz MS Curtis JP Setaro JF	Impact of baseline renal function on outcomes of renal artery stenting in hypertensive patients	Journal of Clinical Hypertension	New
D: Plasty/Rx cohort, retrospective	20022208	Davies MG Saad WE Bismuth J Naoum JJ Peden EK Lumsden AB	Impact of metabolic syndrome on the outcomes of percutaneous renal angioplasty and stenting	Journal of Vascular Surgery	New
D: Plasty/Rx cohort, retrospective	20150008	Dervisoglu E Ciftci E Selek A Sarisoy HT Kaleer B Yilmaz A Comment in: Anadolu Kardiyol Derg. 2010 Feb;10(1):66-8; PMID: 20150009	Percutaneous renal artery stenting reduces arterial blood pressure, but what about renal function? A single-center experience	Anadolu Kardiyoloji Dergisi	New
D: Plasty/Rx cohort, retrospective	20201707	Chang JH Kim BS Oh HJ Yoo TH Kang SW Lee HY Choi D Shim WH Choi KH	Effect of baseline glomerular filtration rate on renal function following stenting for atherosclerotic renal artery stenosis	Scainavian Journal of Urology & Nephrology	New
D: Plasty/Rx cohort, retrospective	20410427	Bommart S Cliche A Therasse E Giroux MF Vidal V Oliva VL Soulez G	Renal artery revascularization: predictive value of kidney length and volume weighted by resistive iex	AJR. American Journal of Roentgenology	New
D: Plasty/Rx cohort, retrospective	20619585	Fleming SH Davis RP Craven TE Deonanan JK Godshall CJ Hansen KJ	Accuracy of duplex sonography scans after renal artery stenting	Journal of Vascular Surgery	New
D: Plasty/Rx cohort, retrospective	21034349	A. Pelta and Aersen and Ulrik B. and Just and Sven and Baekgaard and Niels	Flash pulmonary edema in patients with renal artery stenosis--the Pickering Syndrome		New

D: Plasty/Rx cohort, retrospective	21316901	Modrall JG Rosero EB Leonard D Timaran CH Anthony T Arko FA 3rd Valentine RJ Clagett GP Trimmer C	Clinical and kidney morphologic predictors of outcome for renal artery stenting: data to inform patient selection	Journal of Vascular Surgery	New
D: Plasty/Rx cohort, retrospective	21803522	Modrall JG Timaran CH Rosero EB Chung J Arko FA 3rd Valentine RJ Clagett GP Trimmer C	Predictors of outcome for renal artery stenting performed for salvage of renal function	Journal of Vascular Surgery	New
D: Plasty/Rx cohort, retrospective	21992685	Hegde U Rajapurkar M Gang S Khanapet M Durugkar S Gohel K Aghor N Ganju A Dabhi M Comment in: Semin Dial. 2012 Jan-Feb;25(1):105-7; PMID: 21917001	Fifteen years' experience of treating atherosclerotic renal artery stenosis by interventional nephrologists in India	Seminars in Dialysis	New
D: Plasty/Rx cohort, retrospective	22097232	Wolak T Belkin A Ginsburg V Greenberg G Mayzler O Bolotin A Paran E Szero G	Does percutaneous transluminal renal artery angioplasty improve blood pressure control and renal function in patients with atherosclerotic renal artery stenosis?	Israel Medical Association Journal: Imaj	New
D: Plasty/Rx cohort, retrospective	22133456	Modrall JG Rosero EB Timaran CH Anthony T Chung J Valentine RJ Trimmer C	Assessing outcomes to determine whether symptoms related to hypertension justify renal artery stenting	Journal of Vascular Surgery	New
D: Plasty/Rx cohort, retrospective	22264697	Modrall JG Timaran CH Rosero EB Chung J Plummer M Valentine RJ Trimmer C	Longitudinal changes in kidney parenchymal volume associated with renal artery stenting	Journal of Vascular Surgery	New
D: Plasty/Rx cohort, retrospective	22613636	Liao CJ Yang BZ Wang ZG	Percutaneous transluminal renal angioplasty with stent is effective for blood pressure control and renal function improvement in atherosclerotic renal artery stenosis patients	Chinese Medical Journal	New
D: Plasty/Rx cohort, retrospective	22692467	Khosla A Misra S Greene EL Pflueger A Textor SC Bjarnason H McKusick MA	Clinical outcomes in patients with renal artery stenosis treated with stent placement with embolic protection compared with those treated with stent alone	Vascular & Endovascular Surgery	New
D: Plasty/Rx cohort, retrospective	23043033	Yuksel UC Anabtawi AG Cam A Poddar K Agarwal S Goel S Kim E Bajzer C Gornik HL Shishehbor MH Tuzcu EM Kapadia SR	Predictive value of renal resistive index in percutaneous renal interventions for atherosclerotic renal artery stenosis	Journal of Invasive Cardiology	New

D: Plasty/Rx cohort, retrospective	23057705	He Y Liu Y Wang M Sun Y Dong D Yuan H Wu X Chong Z Jin X	Clinical effect of endovascular treatment on blood pressure and kidney function for hypertensive patients with renal artery stenosis	Clinical & Experimental Hypertension (New York)	New
D: Plasty/Rx cohort, retrospective	23091375	Zhao J Cheng Q Zhang X Li M Liu S Wang X	Efficacy of percutaneous transluminal renal angioplasty with stent in elderly male patients with atherosclerotic renal artery stenosis	Clinical Interventions In Aging	New
D: Plasty/Rx cohort, retrospective	23645044	Su CS Liu TJ Tsau CR Liang KW Chang WC Ting CT Lee WL	The feasibility, safety, and mid-term outcomes of concomitant percutaneous transluminal renal artery stenting in acute coronary syndrome patients at high clinical risk of renal artery stenosis	Journal of Invasive Cardiology	New
D: Plasty/Rx cohort, retrospective	23688626	Simone TA Brooke BS Goodney PP Walsh DB Stone DH Powell RJ Cronenwett JL Nolan BW	Clinical effectiveness of secondary interventions for restenosis after renal artery stenting	Journal of Vascular Surgery	New
D: Plasty/Rx cohort, retrospective	23863797	Ginzburg V Volak T Grinberg G Maiizler O Leitsin A Saro G	Angioplasty and stenting of renal arteries: in search for prognostic criteria	AngiologIndia i Sosudistaia KhirurgIndia/Angiology & Vascular Surgery	New
D: Plasty/Rx cohort, retrospective	24502495	Kawarada O and Yokoi and Y. and Sakamoto and S. and Harada and K. and Ishihara and M. and Yasuda and S. and Ogawa and H.	Impact of aortorenal morphology on renal artery stent procedures: significance of aortic tortuosity and renal artery derivation	Journal of Endovascular Therapy	New
D: Plasty/Rx cohort, retrospective	25327064	Sathyamurthy I and Sudhakar and K. and Jayanthi and K. and Subramanyan and K. and Ramachandran and P. and Mao and R. and Samuel and K. M.	Renal artery stenting: one year outcome on BP control and antihypertensive medication	Journal of the Association of Physicians of India	New
D: Plasty/Rx cohort, retrospective	no PMID	Nau	Long-term outcome of atherosclerotic renovascular disease in patients treated with angioplasty	Revista Argentina de Cardiologia	New
D: Plasty cohort N<30	2996342	Franklin	Comparison of effects of enalapril plus hydrochlorothiazide versus standard triple therapy on renal function in renovascular hypertension.		Original report
D: Plasty cohort N<30	3018602	Franklin	A comparison of enalapril plus hydrochlorothiazide with standard triple therapy in renovascular hypertension		Original report
D: Plasty cohort N<30	6100883	Tillman	Enalapril in hypertension with renal artery stenosis: long-term follow-up and effects on renal function.		Original report

D: Plasty cohort N<30	12603580	S. Prasad and Bannister and K. and Taylor and J.	Is magnetic resonance angiography useful in renovascular disease?		New
D: Plasty cohort N<30	17351955	Mitchell JA Subramanian R White CJ Soukas PA Almagor Y Stewart RE Rosenfield K	Predicting blood pressure improvement in hypertensive patients after renal artery stent placement: renal fractional flow reserve	Catheterization & Cardiovascular Interventions	New
D: Plasty cohort N<30	18341947	Urbano J Manzarbetia F Caramelo C	Cholesterol embolism evaluated by polarized light microscopy after primary renal artery stent placement with filter protection	Journal of Vascular & Interventional Radiology	New
D: Plasty cohort N<30	18471677	Wierema TK Yaqoob MM	Renal artery stenosis in chronic renal failure: caution is advised for percutaneous revascularization	European Journal of Internal Medicine	New
D: Plasty cohort N<30	18954765	Thatipelli M Misra S Johnson CM Arews JC Stanson AW Bjarnason H McKusick MA	Renal artery stent placement for restoration of renal function in hemodialysis recipients with renal artery stenosis	Journal of Vascular & Interventional Radiology	New
D: Plasty cohort N<30	19084431	Brountzos EN Tavernaraki K Gouliamos AD Degiannis D Chaidaroglou A Panagiotou I Arsenis G Kelekis D Vlahakos D	Systemic inflammatory response to renal artery percutaneous angioplasty with stent placement and the risk for restenosis: a pilot study	Journal of Vascular & Interventional Radiology	New
D: Plasty cohort N<30	19463314	Mahmud E Smith TW Palakodeti V Zaidi O Ang L Mitchell CR Zafar N Bromberg-Marin G Keramati S Tsimikas S Comment in: JACC Cardiovasc Interv. 2008 Jun;1(3):293-4; PMID: 19463315	Renal frame count and renal blush grade: quantitative measures that predict the success of renal stenting in hypertensive patients with renal artery stenosis	Jacc: Cardiovascular Interventions	New
D: Plasty cohort N<30	19493475	Li CJ Wu Z Yan HB Wang J Zhao HJ	Safety and efficacy of coronary drug eluting stent for atherosclerotic stenosis of the small renal artery	Chinese Medical Journal	New
D: Plasty cohort N<30	19647181	Pellerin O Garcon P Beyssen B Raynaud A Rossignol P Jacquot C Plouin PF Sapoval M	Spontaneous renal artery dissection: long-term outcomes after endovascular stent placement	Journal of Vascular & Interventional Radiology	New
D: Plasty cohort N<30	21805607	Laird JR Tehrani F Soukas P Joye JD Ansel GM Rocha-Singh K Comment in: Catheter Cardiovasc Interv. 2012 Feb 15;79(3):437-8; PMID: 22328234	Feasibility of FiberNet embolic protection system in patients undergoing angioplasty for atherosclerotic renal artery stenosis	Catheterization & Cardiovascular Interventions	New

D: Plasty cohort N<30	22134935	Takumi T Mathew V Barsness GW Kataoka T Rubinshtein R Rihal CS Gulati R Eeckhout E Lennon RJ Lerman LO Lerman A	The association between renal atherosclerotic plaque characteristics and renal function before and after renal artery intervention	Mayo Clinic Proceedings	New
D: Plasty cohort N<30	22785108	Koivuviita N Liukko K Kudomi N Oikonen V Tertti R Manner I Vahlberg T Nuutila P Metsarinne K	The effect of revascularization of renal artery stenosis on renal perfusion in patients with atherosclerotic renovascular disease	Nephrology Dialysis Transplantation	New
D: Plasty cohort N<30	23207915	Kok HK Leong S Goveer P Browne R Torreggiani WC	Percutaneous renal artery angioplasty and stenting: indications, technique and results	Irish Journal of Medical Science	New
D: Plasty cohort N<30	24434389	Labidi J Touat D Abdelghanim K Ajili F Ariba YB Abdelhafidh NB Louzir B Othmani S	Renovascular hypertension: a report of 21 cases	Saudi Journal of Kidney Diseases & Transplantation	New
D: Plasty cohort N<30	No PMID	Adel SMH	Clinical efficacy of percutaneous renal revascularization with stent placement in hypertension among patients with atherosclerotic renovascular diseases	Journal	New
D: No analysis of interest	no PMID	Yu MSM and A. H.; Pencina and K.; Tuttle and K.; He and W.; Evans and K.; Ren and K.; Folt and D. A.; Brewster and P. S.; Murphy and T. P.; Cutlip and D. E.; Dworkin and L. D.; Jaff and M. R.; Steffes and M.; Shapiro and J. I.; Henrich and W.; Cooper and C. J.	Stenosis severity and kidney function in atherosclerotic renal artery stenosis	Circulation	New
D: No analysis of interest	no PMID	He WE and K. L.; Ren and K.; Folt and D. A.; Brewster and P. S.; Murphy and T. P.; Cutlip and D. E.; Dworkin and L. D.; Shapiro and J. I.; Henrich and W.; Cooper and C. J.; Steffes and M.; Jaff and M. R.	Albuminuria determines event-free survival in atherosclerotic renal-artery stenosis	Circulation	New

D: Comparative N<10/arm	18375475	Onuigbo MA Onuigbo NT	Worsening renal failure in older chronic kidney disease patients with renal artery stenosis concurrently on renin angiotensin aldosterone system blockade: a prospective 50-month Mayo-Health-System clinic analysis	Qjm	New
D: Comparative N<10/arm	18503896	Misra S Thatipelli MR Howe PW Hunt C Mathew V Barsness GW Pflueger A Textor SC Bjarnason H McKusick MA	Preliminary study of the use of drug-eluting stents in atherosclerotic renal artery stenoses 4 mm in diameter or smaller	Journal of Vascular & Interventional Radiology	New
D: Comparative N<10/arm	22134468	Mazza A Rigatelli G Piva M Rampin L Cardaioli P Giordan M Roncon L Zattoni L Zuin M Al-Nahhas A Rubello D Ramazzina E Ravenni R Casiglia E	In high risk hypertensive subjects with incidental and unilateral renal artery stenosis percutaneous revascularization with stent improves blood pressure control but not glomerular filtration rate	Minerva Cardioangiologica	New
D: <6 mo follow-up (and no AE/comp)	no PMID	Kanjwal K, Haller S. Steffes M. Virmani R. Shapiro J. I. Burket M. W. Cooper C. J. Colyer W. R.	Complete versus partial distal embolic protection during renal artery stenting	Catheterization and cardiovascular interventions	New
D: <6 mo follow-up (a no AE/comp)	2009147	Ogihara	Clinical evaluation of delapril in Japan. Report from the Japan Study Group on Delapril.		Original report
D: <6 mo follow-up (a no AE/comp)	19261820	Tanemoto M Suzuki T Abe M Abe T Ito S	Hemodynamic index of atheromatous renal artery stenosis for angioplasty	Clinical Journal of The American Society of Nephrology: CJASN	New
D: <6 mo follow-up (a no AE/comp)	20209644	Kanjwal K Cooper CJ Virmani R Haller S Shapiro JI Burket MW Steffes M Brewster P Zhang H Colyer WR Jr Comment in: Catheter Cardiovasc Interv. 2010 Jul 1;76(1):24-5; PMID: 20578189	Predictors of embolization during protected renal artery angioplasty and stenting: Role of antiplatelet therapy	Catheterization & Cardiovascular Interventions	New
D: <6 mo follow-up (a no AE/comp)	21078879	Mangiacapra F Trana C Sarno G Davidavicius G Protasiewicz M Muller O Ntalianis A Misonis N Van Vlem B Heyrickx GR De Bruyne B Comment in: Circ Cardiovasc Interv. 2010 Dec;3(6):526-7; PMID: 21078878	Translesional pressure gradients to predict blood pressure response after renal artery stenting in patients with renovascular hypertension	Circulation: Cardiovascular Interventions	New

D: <6 mo follow-up (a no AE/comp)	21389959	Pokrovskii AV Kokov LS Suntsov DS	[Surgical management of atherosclerotic-aetiology vasorenal hypertension]	AngiologIndia i Sosudistaia KhirurgIndia/Angiology & Vascular Surgery	New
D: <6 mo follow-up (a no AE/comp)	22407515	Paul TK Lee JH White CJ Comment in: Catheter Cardiovasc Interv. 2012 Nov 15;80(6):1023-4; PMID: 23166103	Renal embolic protection devices improve blood flow after stenting for atherosclerotic renal artery stenosis	Catheterization & Cardiovascular Interventions	New
D: <6 mo follow-up (a no AE/comp)	23853222	McBride J Schueler B Oderich G Misra S	An analysis of the factors influencing radiation dose and fluoroscopic time during renal artery stent placement	Vascular & Endovascular Surgery	New
D: <6 mo follow-up (a no AE/comp)	24135303	Protasiewicz M Kadziela J Poczatek K Poreba R Podgorski M Derkacz A Prejbisz A Mysiak A Januszewicz A Witkowski A	Renal artery stenosis in patients with resistant hypertension	American Journal of Cardiology	New
Case report, old	424606	B. T. Katzen and Chang and J. and Lukowsky and G. H. and Abramson and E. G.	Percutaneous transluminal angioplasty for treatment of renovascular hypertension	Radiology	Case report
Case report, old	496100	M. H. Weinberger and Yune and H. Y. and Grim and C. E. and Luft and F. C. and Klatte and E. C. and Donohue and J. P.	Percutaneous transluminal angioplasty for renal artery stenosis in a solitary functioning kidney	Annals of Internal Medicine	Case report
Case report, old	786649	N. Serrallach and Sole-Balcells and F. and de Torres and J. A. and de Blas and A. and Serrate and R. and Brulles and A.	Severe renal insufficiency and renovascular hypertension	European Urology	Case report
Case report, old	839607	B. Jackson and Clarkson and A. R. and Jamieson and G. G. and Marshall and V. R. and Seymour and A. E.	Persistent acute renal failure with renal artery stenosis: cure following reconstructive arterial operation	Journal of Urology	Case report
Case report, old	856104	D. Heaney and Kupor and L. R. and Noon and G. P. and Suki and W. N.	Bilateral renal artery stenosis causing acute oliguric renal failure. Report of a case corrected by renovascular surgery	Archives of Surgery	Case report
Case report, old	946990	A. Besarab and Brown and R. S. and Rubin and N. T. and Salzman and E. and Wirthlin and L. and Steinman and T. and Atlia and R. R. and Skillman and J. J.	Reversible renal failure following bilateral renal artery occlusive disease. Clinical features, pathology, and the role of surgical revascularization	JAMA	Case report

Case report, old	1463668	J. R. Schneider and Wright and A. and Mitchell and R. S.	Successful percutaneous balloon catheter treatment of renal artery occlusion and anuria	Annals of Vascular Surgery	Case report
Case report, old	1865575	T. Koga and Okuda and S. and Takishita and S. and Shigematsu and A. and Komota and T. and Fujishima and M. and Matsukuma and A.	Renal failure due to cholesterol embolization following percutaneous transluminal renal angioplasty	Japanese Journal of Medicine	Case report
Case report, old	2234255	M. K. O'Donohoe and Donohoe and J. and Corrigan and T. P.	Acute renal failure of renovascular origin: cure by aortorenal reconstruction after 25 days of anuria	Nephron	Case report
Case report, old	2398582	R. A. McCready and Siderys and H. and Foster and P. R. and Goens and B. M.	Combined coronary artery bypass grafting and bilateral renal revascularization for unstable angina and impeding renal failure	Journal of Vascular Surgery	Case report
Case report, old	2523265	J. E. Scoble and Maher and E. R. and Hamilton and G. and Dick and R. and Sweny and P. and Moorhead and J. F.	Atherosclerotic renovascular disease causing renal impairment--a case for treatment	Clinical Nephrology	Case report
Case report, old	2532661	J. J. Beraud and Calvet and B. and Dura and A. and Mimran and A.	Reversal of acute renal failure following percutaneous transluminal recanalization of an atherosclerotic renal artery occlusion	Journal of Hypertension	Case report
Case report, old	3158624	D. Modai and Cohen and N. and Weissgarten and J. and Segal and B. and Pik and A.	Symptomatic renal artery stenosis superimposed on chronic glomerulonephritis	Israel Journal of Medical Sciences	Case report
Case report, old	3218663	A. Cases and Campistol and J. M. and Abad and C. and Botey and A. and Torras and A. and Revert and L.	Reversal of renal failure after revascularization in atheromatous renovascular disease. Report of two cases	American Journal of Nephrology	Case report
Case report, old	3336930	R. D. MacMillan and Uldall and R. and Lipton and I. H.	Simultaneous aortic and renal artery reconstruction for acute arterial occlusion in solitary kidney	Urology	Case report
Case report, old	3688666	B. A. Perler	Emergency gastroduodenal-renal artery bypass. An extra-anatomic approach for salvage of the solitary kidney	American Surgeon	Case report

Case report, old	6223006	J. P. Sheehan	Percutaneous transluminal renal artery angioplasty (PTRA) in hypertensive encephalopathy	Irish Medical Journal	Case report
Case report, old	6368463	F. Mosca and Brai and L. S. and Carmellini and M. and Ferrari and M. and Cei and A. and Giulianotti and P. C. and Medi and F.	Successful treatment of recurrent renovascular hypertension by solitary kidney autotransplantation	Italian Journal of Surgical Sciences	Case report
Case report, old	6650591	A. G. Ramsay and D'Agati and V. and Dietz and P. A. and Svahn and D. S. and Pirani and C. L.	Renal functional recovery 47 days after renal artery occlusion	American Journal of Nephrology	Case report
Case report, old	6986478	J. Stessman and Drukker and A. and Dolberg and M. and Pfau and A. and Merin and G.	Orthotopic renal autotransplantation in the treatment of renovascular hypertension	Journal of Urology	Case report
Case report, old	7015851	N. E. Madias and Ball and J. T. and Millan and V. G.	Percutaneous transluminal renal angioplasty in the treatment of unilateral atherosclerotic renovascular hypertension	American Journal of Medicine	Case report
Case report, old	7035691	J. Kawamura and Okada and Y. and Nishibuchi and S. and Yoshida and O.	Transient anuria following administration of angiotensin I-converting enzyme inhibitor (SQ 14225) in a patient with renal artery stenosis of the solitary kidney successfully treated with renal autotransplantation	Journal of Urology	Case report
Case report, old	7469726	R. J. Manly and Belzer and F. O.	Spontaneous reversal of renal failure by renal artery recanalization	Archives of Surgery	Case report
Case report, old	7629207	M. Wengrovitz and Healy and D. A. and Diamo and J. R. and Atnip and R. G.	Renal revascularization in patients on dialysis	Journal of Cardiovascular Surgery	Case report
Case report, old	7703578	C. P. Harker and Steed and M. and Althaus and S. J. and Coldwell and D.	Flash pulmonary edema: an acute and unusual complication of renal angioplasty	Journal of Vascular & Interventional Radiology	Case report
Case report, old	8099389	C. G. Missouris and Buckenham and T. and Vallance and P. J. and MacGregor and G. A.	Renal artery stenosis masqunderading as congestive heart failure	Lancet	Case report
Case report, old	8238011	Z. Roche and Rutecki and G. and Cox and J. and Whittier and F. C.	Reversible acute renal failure as an atypical presentation of ischemic nephropathy	American Journal of Kidney Diseases	Case report

Case report, old	8264029	E. Ascer and Gennaro and M. and Rogers and D.	Unilateral renal artery revascularization can salvage renal function and terminate dialysis in selected patients with uremia	Journal of Vascular Surgery	Case report
Case report, old	8285186	L. E. Schlanger and Haire and H. M. and Zuckerman and A. M. and Loscalzo and C. E. and Mitch and W. E.	Reversible renal failure in an elderly woman with renal artery stenosis	American Journal of Kidney Diseases	Case report
Case report, old	8596600		Case records of the Massachusetts General Hospital. Weekly Clinicopathological Exercises. Case 11-1996. A 69-year-old man with progressive renal failure and the abrupt onset of dyspnea	New Engla Journal of Medicine	Case report
Case report, old	8862385	J. M. Reilly and Rubin and B. G. and Thompson and R. W. and Allen and B. T. and Flye and M. W. and Aerson and C. B. and Sicard and G. A.	Revascularization of the solitary kidney: a challenging problem in a high risk population	Surgery	Case report
Case report, old	9230557	D. M. Little and Burke and P. E. and O'Callaghan and J. and Vella and J. and Donoghue and J. and Sami and T. and Hickey and D. P.	Renal revascularisation by gastroduodenal-renal bypass as treatment of renal artery stenosis	Irish Medical Journal	Case report
Case report, old	9247781	D. Ducloux and Jamali and M. and Chalopin and J. M.	Chronic congestive heart failure associated with bilateral renal artery stenosis	Clinical Nephrology	Case report
Case report, old	9497208	T. M. Sullivan and Hertzer and N. R.	Stenting of the renal artery to improve renal function prior to thoracoabdominal aneurysm repair	Journal of Endovascular Surgery	Case report
Case report, old	9507232	S. C. Textor	Revascularization in atherosclerotic renal artery disease	Kidney International	Case report
Case report, old	9713602	D. J. Goldsmith and Hamilton and G.	Hypertension and renal failure	Postgraduate Medical Journal	Case report
Case report, old	10648486	C. G. Missouris and Belli and A. M. and MacGregor and G. A.	Apparent heart failure: a syndrome caused by renal artery stenoses	Heart	Case report
Case report, old	10742424	D. Eton and Terramani and T. T. and Katz and M.	Staged thoracic and abdominal aortic aneurysm repair using stent graft technology and surgery in a patient with acute renal failure	Annals of Vascular Surgery	Case report

Case report, old	11032259	R. L. Yue and Collins and T. J. and Sternbergh and W. C. and 3rd and Ramee and S. R. and White and C. J.	Acute renal failure after redo thoracoabdominal aortic aneurysm repair in a patient with a solitary kidney: successful percutaneous treatment	Journal of Endovascular Therapy	Case report
Case report, old	11136196	D. L. Cohen and Townse and R. R. and Kobrin and S. and Genega and E. M. and Tomaszewski and J. E. and Fairman and R.	Dramatic recovery of renal function after 6 months of dialysis depeence following surgical correction of total renal artery occlusion in a solitary functioning kidney	American Journal of Kidney Diseases	Case report
Case report, old	11274271	J. R. Wright and Duggal and A. and Thomas and R. and Reeve and R. and Roberts and I. S. and Kalra and P. A.	Clinicopathological correlation in biopsy-proven atherosclerotic nephropathy: implications for renal functional outcome in atherosclerotic renovascular disease	Nephrology Dialysis Transplantation	Case report
Case report, old	12025924	H. Takakuwa and Shimizu and Kazuaki and Izumiya and Yoshiaki and Kato and Tamayo and Yokoyama and Hitoshi and Kobayashi and Ken-ichi and Matsui and Osamu and Ise and Takuyuki	Unilateral stent implantation for renal function in bilateral atherosclerotic renovascular hypertension--a case report	Angiology	Case report
Case report, old	12082500	B. Agroyannis and Chatziioannou and A. and Mourikis and D. and Patsakis and N. and Katsenis and K. and Kalliafas and S. and Dimakakos and P. and Vlachos and L.	Abdominal aortic aneurysm and renal artery stenosis: renal function and blood pressure before and after endovascular treatment	Journal of Human Hypertension	Case report
Case report, old	12087578	K. M. Dwyer and Vrazas and John I. and Lodge and Robert S. and Humphery and Timothy J. and Schlicht and Stephen M. and Murphy and Brean F. and Mossop and Peter J. and Goodman and David J.	Treatment of acute renal failure caused by renal artery occlusion with renal artery angioplasty	American Journal of Kidney Diseases	Case report
Case report, old	12611127	G. Tarantini and Romano and Silvia and Cardaioli and Paolo and Ramoo and Angelo	Effect of renal artery stenting on the progression of renovascular renal failure: a case of intravascular ultrasound-confirmed renovascular disease	Italian Heart Journal: Official Journal of the Italian Federation of Cardiology	Case report

Case report, old	12943603	D. C. Choo and Fisher and Daniel Z.	Renal artery stenosis: when to intervene?	Cardiology in Review	Case report
Case report, old	14685757	A. A. Kiykim and Boz and Murat and Ozer and Caner and Camsari and Ahmet and Yildiz and Altan	Two episodes of anuria and acute pulmonary edema in a losartan-treated patient with solitary kidney	Heart & Vessels	Case report
Case report, old	14989566	M. Rajacharan and Altin and Robert	The Goldblatt kidney revisited	Vascular Medicine	Case report
Case report, old	15065618	R. J. Cook and Young and Timothy J. and McDonald and Furman S.	81-year-old woman with nausea, fatigue, and shortness of breath	Mayo Clinic Proceedings	Case report
Case report, old	15150371	B. G. Han and Kim and Jang Young and Choi and Jong Uk and Lee and Seung Hwan and Choi and Seung Ok	An acute renal failure patient successfully stented for bilateral renal artery occlusion with a distal embolism protection device	Nephrology Dialysis Transplantation	Case report
Case report, old	15960152	E. Svarstad and Urheim and L. and Iversen and B. M.	Critical renal artery stenoses may cause a spectrum of cardiorenal failure and associated thromboembolic events	Clinical Nephrology	Case report

Appendix C. Summary Tables

Table C.1. Study design

Author, date PMID country study dates	Study Design	Funding source	Eligibility Criteria	Inclusion criteria: % stenosis	Inclusion criteria: Other	Exclusion criteria
Alhadad, 2004 14718896 Sweden 1987-1996	nRCS, retrospective	nd	ARAS undefined undergoing any revascularization	Surgical or endovascular procedures		
Arthurs, 2007 17398382 US 1/2001-6/2006	nRCS, retrospective	nd	≥60% ostial ARAS with >6 mo HTN >140/90 and CKD≥1.5	Duplex ultrasound evidence of renal artery stenosis	hypertension requiring multiple medications or worsening renal function. [5/40 had previous angioplasty; 1 in RAS arm and 4 in medication arm]	
Balzer, 2009 19135837 Germany 1/1998-12/2004	RCT	nd	>70% ostial ARAS with HTN	>70% diameter reduction in angiography		fibromuscular dysplasia, dissection or stenosis in combination with renal artery aneurysms, as well as simultaneous reconstructions for aortic aneurysm or aorto/mesenteric/iliac occlusive disease
Baril, 2007 17391902 US 1/1999-12/2005	Single arm, prospective	nd	>70% stenosis ARAS with HTN and CKD or >90% asymptomatic ARAS undergoing EVAR for AAA	>70% renal artery stenosis on selective arteriography	clinical hypertension or renal insufficiency	

Author, date PMID country study dates	Study Design	Funding source	Eligibility Criteria	Inclusion criteria: % stenosis	Inclusion criteria: Other	Exclusion criteria
Bax, 2009 19414832 Netherlands, France 6/2000-12/2005	RCT	industry, Society, nonprofit	>50% ostial ARAS with CKD CrCl<80	Ostial ARAS was defined as a reduction in the luminal diameter of the renal artery of 50% or more within 1 cm of the aortic wall in the presence of atherosclerotic changes in the aorta, detected by computed tomographic angiography, magnetic resonance angiography, or digital subtraction angiography performed as part of routine clinical care by the patients physicians.	Impaired renal function was defined as an estimated creatinine clearance less than 80 mL/min per 1.73 m2 according to the Cockcroft and Gault formula, based on the mean of 2 fasting serum creatinine values measured within 1 month of each other.	
Beck, 2010 19939607 US 2001-2007	Single arm, prospective	nd	>60% ARAS and refractory RVH with or without CKD	>60%	Stenosis 60% or a pressure gradient 15 mm Hg, or both, was considered an indication for intervention.	There were no specific guidelines for exclusion from intervention. General considerations included evidence of a nonviable or minimally functioning kidney on the preprocedural work-up or an elevated renal parenchymal resistive index 0.8. No patient in this database was treated for asymptomatic renal artery stenosis, and patients with purely ischemic nephropathy without concomitant hypertension were excluded.

Author, date PMID country study dates	Study Design	Funding source	Eligibility Criteria	Inclusion criteria: % stenosis	Inclusion criteria: Other	Exclusion criteria
Bersin, 2013 22581488 US 2/2008-5/2009	Single arm, prospective	academic/hospital, industry	>70% ostial denovo or restenotic (after PTRA) ARAS excluding high renal risk patients	de novo or restenotic atherosclerotic ostial renal artery lesions with a stenosis >70%	Stent were placed (in the same setting) after suboptimal PTRA result was defined as either >=50% residual stenosis by visual angiographic assessment, and translesional pressure gradient >=20 mm Hg systolic or >=10 mm Hg mean utilizing a> =4 Fr catheter or pressure wire, or by the presence of a flow-limiting dissection	The major exclusion criteria included: occlusion of the target or contralateral renal artery, previous stenting of the target lesion, lesions within or beyond a bypass graft, lesions that extend into the arterial branches, multiple ipsilateral lesions, fibromuscular dysplasia, and previous kidney transplant, one functioning kidney or past nephrectomy, pole-to-pole length of the affected kidney =8 cm, serum creatinine (SCr) =3.0 mg/dl, or hemodialysis or chronic peritoneal dialysis.
Blum, 1997 9017938 Germany 3/1989-3/1996	Single arm, prospective	nd	>50% ostial denovo or restenotic (after PTRA) ARAS	Stenoses of 50% of the diameter of the renal artery, caused by atherosclerosis (by color duplex sonogram or intraarterial angiography and transstenotic pressure gradient >20 mm Hg)	Failure of balloon angioplasty (see comments to description of intervention) Ostial lesion within 5 mm of the aortic lumen. Received conventional balloon angioplasty. All patients had a history of sustained hypertension resistant to intensive antihypertensive treatment.	

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Bruno, 2014, 24555729 Italy 1990-2008	Single arm, prospective	nd	>60% unilateral ARAS; HTN and with or without CKD (stages 1-4)	Unilateral atherosclerotic renal artery stenosis >60% defined by a renal to aortic ratio greater than 3.5 at duplex ultrasound examination, confirmed by angio-magnetic resonance or spiral computed tomography as recommended	Diagnosis of arterial hypertension according to current Guidelines, with or without chronic kidney disease	fibromuscolar dysplasia; bilateral renal artery stenosis; age > 80 years; KDOQI stage 5 chronic kidney disease (glomerular filtration rate <15 ml/min or dialysis); history of severe adverse reaction to iodinated contrast; technical limitations to revascularization procedure; severe comorbidities that contraindicated the intervention according to clinical judgment
Cherr, 2002 11854720 US 1987-1999	Single arm, retrospective	nd	≥80% ostial ARAS with severe HTN and with or without CKD	80% ostial stenosis or occlusion	Surgical repair, Severe or uncontrolled hypertension	
Christie, 2012 23083664 US 9/2003-7/2010	Single arm, prospective	government	>60% ostial ARAS with HTN and CKD	60% stenosis on arteriography	All patients had the indication of severe multidrug hypertension or observed decreases in renal function manifested by decreasing estimated glomerular filtration rate or increasing creatinine. Each ostial stenosis was treated with primary endoluminal stenting.	Patients with RA-PTAS performed for nonostial stenosis, restenosis of previously stented atherosclerotic disease or for treatment of fibromuscular dysplasia.
Chrysant, 2014 24909590 US no dates given	Single arm, prospective	nd	≥60% ostial denovo or restenotic (after PTRA) ARAS with uncontrolled HTN and CKD<2.5 mg/dL	>= 60% stenosis	Eligible patients included those with uncontrolled HTN defined as systolic BP (SBP) 140 mm Hg or diastolic BP (DBP) 90 mm Hg despite maximal doses of at least 2 antihypertensive agents in appropriate combinations	

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Chrysochou, 2012 21993376 UK 1999-2009	Single arm, prospective	nd	% stenosis nd, ARAS	RAS < 60%, significant RAS > 60%	unilateral or bilateral renovascular disease	
Cianci, 2011 20547539 Italy 2004-2009	nRCS, prospective	nd	% stenosis nd, PWV >250 cm/s with uncontrolled HTN and CKD		Revascularization was decided in the presence of peak wave velocity >250 cm/s and uncontrolled hypertension with drugs or an increase in serum creatinine after starting reninangiotensin- aldosterone system (RAAS) blockers. Patients were assigned to medical therapy if the peak wave velocity was < 250 cm/s or >250 cm/s in the presence of drugcontrolled blood pressure (BP) or unchanged serum creatinine after starting RAAS blockers.	
Cianci, 2013 23467950 Italy 2007 -12/2009	Single arm, prospective	nd	≥70% stenosis ARAS and without diabetes	at least 70%) atherosclerotic, mono or bilateral, RAS to undergo RPTAs	-	non significant stenosis (< 70%), non atherosclerotic or dysplastic stenosis and restenosis. Diabetic patients were not selected for this study to exclude other causes of proteinuria. Patients with atrial fibrillation, aortic valve insufficiency, nephritis, and other diseases

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Cooper, 2008 18490527 US no dates given	RCT	industry	≥50% to <100% ARAS with HTN, CKD, CHF, or angina + HTN	The presence of 1 renal artery stenoses 50% and <100% treatable with the embolic protection device.	History of hypertension, renal insufficiency, heart failure, or angina with poorly controlled hypertension.	age <18 years, pregnancy, life expectancy 6 months, dialysis, kidney transplant, stenosis not amenable to stent, allergy to study agents, unrelated renal disease, untreated aortic aneurysm, kidney size 8 cm, restenosis, vessel dimensions out of range for study devices, treatment of a side branch or distal stenosis, active bleeding, stroke within 2 years or with a significant residual neurological deficit, INR >1.2 times control, thrombocytopenia, major surgery or trauma within 6 weeks, intracranial neoplasm, arteriovenous malformation or aneurysm, vasculitis, or a nonstudy procedure within 24 hours.
Cooper, 2014 24245566 US 5/2005-1/2010	RCT	government	≥60% ARAS with uncontrolled HTN and CKD GFR<60	angiographic stenosis >= 80% to < 100% of the diameter or stenosis of >= 60% to <80% of the diameter of an artery, with a systolic pressure gradient of at least 20 mm Hg and criteria for diagnosis varied by the use of duplex ultrasonography, magnetic resonance angiography, or computed tomographic angiography.	Adults diagnosed with severe HTN with a systolic BP >= 155 mm Hg while receiving two or more antihypertensive medications or CKD with GFR <60 mL/min/m2	fibromuscular dysplasia, CKD from a cause other than ischemic nephropathy or associated with a SCr level > 4.0 mg per dL (354 mol per liter), kidney length < 7 cm, an index lesion that cannot be treated with the use of a single stent (>18 mm in length), h/o stroke within 6 mo; pregnant women; untreated aneurysm of the abdominal aorta >5.0 cm;

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Crutchley, 2009 18951751 US 1997-2005	nRCS, retrospective	nd	% stenosis nd, FPE, uncontrolled HTN, CKD		Selection criteria for renal artery intervention in the open repair group included (1) patients with severe hypertension taking multiple medications, (2) hypertension complicated by flash pulmonary edema or malignant hypertension, and (3) patients with ischemic nephropathy in the setting of bilateral RVD or RVD in a solitary kidney. In contrast, all percutaneous interventions were performed by nonsurgeons reflect patient selection criteria particular to those physician groups. Doppler derived data were available for analysis.	
Dangas, 2001 11491257 US no dates given	Single arm, prospective	nd	% stenosis nd, ARAS, with DM, HTN, CKD/ESRD	Established by renal artery angiography or results of non invasive imaging studies	Consecutive patients who underwent renal artery stenting over a 2 yr period and referred by their primary physicians. Included pts with DM, HTN, scr >1.5 mg/dL, dialysis (HD, PD), hyperlipidemia if treated medically or if sr cholesterol >240 mg/dL	
de Donato, 2007 17653002 Italy 1/1998-7/2006	nRCS, retrospective	nd	>=80% stenosis with uncontrolled HTN>140/90	>80%	renovascular hypertension, at least three medications including a diuretic at near-maximum doses	

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Dichtel, 2010 20630131 US 1/1999-6/2007	nRCS, retrospective	government	>75% stenosis	> 75% stenosis by magnetic resonance angiography or by renal aortic ratio > 3.5 on duplex ultrasound	chronic kidney disease (defined as eGFR 15-60 ml/min/1.73m^2)	
Dorros, 2002 11835644 US 1990-1997	Single arm, prospective	Foundation, nonprofit	ARAS with >50 years of age onset HTN uncontrolled or malignant, and CKD≥1.5		Patients with RAS had hypertension and/or chronic renal insufficiency and met one or more of the following inclusion criteria: onset of hypertension after age 50 years; accelerated, severe, or malignant hypertension; inadequate response to appropriate antihypertensive therapy; poorly controlled hypertension; declining renal function after blood pressure control with pharmacologic agents; and stenosis of one or both main renal arteries. Patients who underwent the procedure to reserve renal function had a documented serum creatinine 1.5 mg/dl on two separate measurements.	No patient had fibromuscular dysplasia or longitudinal kidney length of <7.0 cm (as measured by ultrasound or renal laminography)
Galaria, 2005 15735947 US 1/1984-1/2004	nRCS, retrospective	nd	≥60% ARAS with HTN or CKD		Presence of clinical criteria defined by Ruback et al and a >= 60% stenosis on US or MRA or a positive renal scan, angiography was performed	Patients with hypertension and/or elevated serum creatinine levels had a diagnostic study to identify the presence of RAS.

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Gill, 2003 12601202 UK 6/1993-7/1999	Single arm, prospective	nd	>50% ARAS with HTN or CKD	>50% stenosis (intervention limited to these stenoses) Subjects had severe HTN resistant to multiple medications (n=25); CKD, SCr>130 mcmol/L (n=50); resistant HTN and CKD (n=25)	Angiographically proven ARAS referred to Radiology Dept for endovascular treatment.	
Gill-Leertouwer, 2002 12466252 Netherlands 9/1996-12/1998	Single arm, prospective	nd	>50% ARAS	>50% atherosclerotic stenosis		
Girndt, 2007 17164562 Germany 5/1997-11/2002	Single arm, retrospective	nd	>70% ARAS	angiographically proven stenosis > 70%		patients with stenosis of artery of a renal transplant
Gonçalves, 2007 17364124 Brazil 5/1999-10/2003	Single arm, prospective	nd	≥70% ARAS with uncontrolled HTN or CKD<6 mo	Atherosclerotic stenosis of one or both renal arteries ≥70% occlusion and/or systolic gradient >20 mmHg in the lesion	High blood pressure of difficult management (or refractory hypertension) and presenting recent deterioration (< 6 months) of renal function. ARAS identified during coronary angiography and followed at the study recruitment center.	Valve diseases, neoplastic diseases, degenerative diseases (diseases of the connective tissue), patients with CKD with severe renal atrophy (kidney size <7 cm), non-atherosclerotic RAS (fibromuscular dysplasia, arteritis), ARAS < 50% identifiable with renal arteriography, or lesion <50% a gradient <20 mmHg, and patients on dialysis.

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Gray, 2002 12710843 US 1991-1997	Single arm, prospective	nd	>70% ARAS with CHF and FPE	Definition of severe RAS: >70% diameter reduction with pressure gradient > 20 mm Hg. Unclear if all patients had severe RAS.	Must have recurrent CHF and/or flash pulmonary edema preop to be included in this report.	
Gross, 1998 9736342 Germany no dates given	Single arm, prospective	nd	>50% ostial ARAS with HTN or CKD	Ostial lesions were defined as stenoses of more than 50% of diameter of the renal artery within 5 mm of the aortic lumen. A lesion was designated atherosclerotic if it did not demonstrate the characteristic appearance of fibromuscular dysplasia	All patients had been referred to the Franz Volhard Clinic because of known or suspected CAD. The authors routinely search for renal artery stenoses in patients with a history of hypertension with or without serum creatinine level above the normal range.	Patients with stenoses of the renal artery distal to the ostium were excluded from evaluation and were treated separately.
Hackam, 2011 21156722 Canada 7/1994-7/2007	nRCS, retrospective	government, Foundation, nonprofit	% stenosis nd ARAS		We included consecutive patients older than 65 years with codes identifying renal artery stenosis or RVD in the CIHI-DAD, CIHI-SDS, and OHIP databases	
Hanzel, 2005 16253607 US no dates given	nRCS, prospective	nd	≥70% ostial ARAS with non-proteinuric CKD scr≤2.0 mg/dL	angiographically confirmed unilateral or bilateral atherosclerotic RAS (diameter stenosis ≥ 70%)	RAS involving the ostium or proximal 2 cm of the main renal artery and baseline serum creatinine 2.0 mg/dl.	Patients were excluded if there was known renal parenchymal disease, proteinuria 1.0 g in 24 hours, severe peripheral arterial disease precluding safe access to the central arterial circulation, or anticipated life expectancy 2 years.

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Harden, 1997 9113012 UK 04/1992-12/1995	Single arm, prospective	nd	>50% ostial ARAS or flow-limiting dissection or occlusion	Patients who had hemodynamically significant (>50% diametric narrowing) ostial stenoses, restenoses (>50%) after percutaneous renal-artery angioplasty (PTRA), or flow-limiting dissection or occlusion underwent renal-stent placement.		
Henry, 2003 14571477 France, India, and Greece 1/1999-11/2002	Single arm, prospective	nd	>50% ostial ARAS with HTN	ostial lesion with stenosis > 50% within 5 mm of the aortic lumen by arteriography	All have HTN; all have atherosclerotic RAS	Renal artery diameter > 6 mm excluded for occlusion balloon; diameter > 5.5 mm excluded for filters; bifurcated or trifurcated renal arteries in which the lesion was positioned < 2 cm from the division also excluded
Holden, 2006 16837918 New Zealand no dates given	Single arm, prospective	nd	% stenosis nd ARAS with high risk patients or CKD		High risk patients with ischemic nephropathy	
Iannone, 1996 8974797 US 8/1992-12/1993	Single arm, prospective	nd	≥60% ARAS	60% stenosis or atherosclerotic with 40 mm Hg transtenotic gradient, by angiography	RAS, receiving angioplasty	

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Jaff, 2012 22511402 US 8/2007-10/2009	Single arm, prospective	nd	≥60% ARAS with uncontrolled HTN ≥140/90	>=50% residual stenosis, persistent translesional pressure gradient, flow limiting dissection, or thrombolysis in myocardial infarction (TIMI) flow <3.	Eligible patients included those with uncontrolled HTN defined as systolic blood pressure (SBP) >=140 mm Hg or diastolic blood pressure >=90 mm Hg, despite maximal doses of at least two antihypertensive agents in appropriate combinations in association with renal artery stenosis >=60% via angiographic visual estimate a suboptimal PTA result	Patients who underwent successful primary renal artery stent deployment or successful PTA were not eligible.
Jokhi, 2009 19668788 Canada 6/2000 - 3/2007	Single arm, prospective	nd	≥70% ARAS with uncontrolled or severe HTN or CKD or FPE	>70% ARAS inpatients	identified from iividuals with with iividuals with resistant or severe hypertension, unexplained renal dysfunction (or induced by angiotensin-converting enzyme [ACE] inhibitors or angiotensin receptor blockers [ARBs]), pulmonary edema with preserved systolic function; or the presence of clinically evident atherosclerosis in two vascular territories	-

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Kalra, 2010 19937777 UK and Germany 1995-2007	nRCS, prospective	nd	>50% ARAS with a subset with decompensation	UK: > 60% (or 50 60% if there was evidence of poststenotic dilatation or dephasing (MRA)) Germany: significant RAS indicated by renal-aortic flow velocity ratio > 3.5 a, in unilateral RAS, when the difference in resistance index between the two main renal arteries was > 0.05; in cases of bilateral RAS an acceleration time > 0.07 sec was required for diagnosis of hemodynamic significance	UK: renal artery revascularization after enrolment into the multicenter ASTRAL trial	UK: patients with insignificant disease (RAS < 50%), those with bilateral RAO and all patients who had undergone previous revascularization. Germany: no ARVD patients excluded.
Kane, 2010 19666661 US no dates given	nRCS, retrospective / Single arm, retrospective	academic/hospital	>70% stenosis and uncontrolled HTN or CKD	Presence of a high-grade (>70%) stenosis of at least one renal artery on magnetic resonance angiography or conventional angiography	accelerated or medically resistant systemic hypertension and/or ischaemic nephropathy stage 3 5 chronic, non-dialysis depeent, kidney disease	

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Kawarada, 2010 20884436 Japan no dates given	Single arm, prospective	nd	% stenosis nd and uncontrolled HTN or CKD or CAD or CHF		patients satisfied at least one of the following: suboptimal control of hypertension by at least two antihypertensive agents, renal impairment, renal atrophy, cardiac symptoms including "unstable coronary syndrome" or "congestive heart failure."	
Kennedy, 2003 14582036 US 7/1993-11/2001	Single arm, prospective	nd	≥60% and/or a translesional systolic pressure gradient of ≥20 mm Hg.	>=60% diameter stenosis and/or a translesional systolic pressure gradient of >= 20 mm Hg. By digital caliper.	-	-
Kobo, 2010 20684176 Israel 2001-2007	Single arm, prospective	nd	≥70% ARAS with CVD or uncontrolled HTN or CKD or FPE	>=70%	Patients undergoing coronary angiography were selected for renal angiography if they also had at least one of the following predetermined criteria: Multiple atherosclerotic diseases: at least two of the following: Coronary artery disease, Peripheral vascular disease, Carotid diseases; Hypertension resistant to medical therapy or controlled by multiple (3) drugs, Chronic renal failure (serum creatinine levels > 1.5 mg/dl), Flash pulmonary edema. Bilateral selective renal angiography was performed in patients selected as described above. Patients with significant renal artery stenosis were referred for renal artery stenting.	

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Leesar, 2009 19539148 US 12/2004-08/2006	Single arm, prospective	nd	50% to 90% unilateral ARAS with uncontrolled HTN ≥140/90 mmHg with or without CKD <3.0 mg/dL	A diameter stenosis of 50% to 90% by visual estimation	Hypertension was defined as systolic blood pressure 140 mm Hg and/or diastolic blood pressure 90 mm Hg. Patients with accelerated or refractory hypertension on 2 or 3 antihypertensive medications, respectively, were enrolled into the study. Unilateral RAS.	Exclusion criteria were severe renal dysfunction as evidenced by serum creatinine 3.0 mg/dl or kidney length 8.0 cm, and presence of accessory renal arteries.
Lekston, 2008 19006027 Poland no dates given	RCT	nd	≥50% ARAS with uncontrolled HTN or progressive CKD	50%stenosis 2/2 ARAS and clinical signs suggesting RVH refractory to medical therapy, patients at risk for renal failure development due to progressive ischaemia with diameter of stenotic artery 3 mm were selected.	-	contraindications to angiography
Losito, 2005 15870215 Italy 1992-2000	nRCS, prospective	nd	>50% ARAS	ARAS >50%, by arteriogram		
Mannarino, 2012 22260219 Italy 1/2003-12/2008	nRCS, prospective	nd	>70% ARAS with CKD stage 3 or 4.	>70% assessed by visual angiographic estimation	CKD stages 3 4, patients selected for stent placement: Kidney size 9 cm plus Normal or near normal cortical echogenicity plus PSV >300 cm/s or RAR >3.8 or intrarenal tardus parvus pattern plus Intrarenal resistive index <0.80	less than 6 months followup, instent restenosis

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Marcantoni, 2012 22495466 Italy 2006-2009	RCT	academic/hospital.	>50% and ≤80% ARAS with CKD ≤4 mg/dL and incident IHD, but without AMI	Patients with renal artery stenosis >50% and =<80% in at least one renal artery were considered eligible for the study	-	Patients were not eligible if they had any of the following conditions: (1) renal artery stenosis >80%, (2) acute myocardial infarction (AMI), (3) a single functioning kidney and serum creatinine level >4 mg/dL, (4) severe aortic valve stenosis, (5) neoplastic disease, (6) aortic aneurysm necessitating surgery, or (7) renal artery stenosis secondary to fibromuscular dysplasia. Patients with renal artery stenosis >80% were excluded because at the time the study was designed, authoritative reviews held that although the benefits of renal revascularization in patients with severe renal artery stenosis still remained to be tested in specific clinical trials, a protective effect of renal revascularization seemed fairly probable.
Murphy, 2014, 24325931 US 3/2005-11/2009	Single arm, prospective	nd	>60% ARAS with uncontrolled HTN with SBP ≥160 mmHg with or without CKD < 60 mL/min/1.73 m^2	>60% stenosis	Either a systolic blood pressure of at least 160 mm Hg while receiving two blood pressure medications from different classes of drugs or chronic kidney disease with an estimated glomerular filtration rate (eGFR) rate of < 60 mL/min/1.73 m^2. Roll-in enrollment inclusion criteria included patients with an atherosclerotic renal artery stenosis o 2 cm in length, with the reference artery being 3.5–8 mm.	

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Patel, 2009, 9497511 US 1/2002-12/2006	nRCS, retrospective	nd	≥75% ARAS and underwent revascularization either due to uncontrolled HTN with CKD ≥ 1.5 mg/dL or due to severe stenosis with single functioning kidney	≥ 75% stenosis	Underwent PTRAS or OR. Indications for revascularization included hypertension (HTN) in patients with uncontrolled blood pressure in the setting of multiple antihypertensive agents or escalating blood pressure in the setting of previously controlled hypertension on three or more agents. The indication for renal revascularization was RS in the setting of ischemic nephropathy with Cr >= 1.5 mg/dL or significant stenosis to a single functioning kidney or if revascularization was required to the entire functioning renal mass irrespective of baseline renal function. Indications for revascularization vary and in many instances include a combination of HTN and RS, however we defined the indication as HTN or RS depending on the more pressing clinical indication at the time of revascularization or as defined by the operative note.	Secondary interventions for previously treated vessels were excluded from analysis. In the OR group, patients undergoing renal artery revascularization in the context of concomitant aortic reconstruction or aortic de-branching procedures and without specific indications for renal artery revascularization were excluded.
Ramos, 2003 12472793 Argentina no dates given	Single arm, prospective	academic/hospital	≥70% stenosis with technical success and at least 3 mo followup	≥ 70% stenosis	Follow-up at least 100 days; only pts with primary technical success were included	

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Rastan, 2008 19110785 Germany 6/2005-6/2006	Single arm, prospective	industry	≥70% bilateral or ≥50% unilateral ARAS with HTN and/or CKD and a baseline Scr<4.0 mg/dL	≥70% stenosis confirmed by angiography, and reference target vessel diameter of 4.0-7.0 mm	HTN and/or CKD and a baseline scr<4.0 mg/dL	non-ARAS, RAS<70% stenosis and scr >=4.0 mg/dL
Ritchie, 2014 24074824 UK 1995-7/2011	nRCS, prospective	nd	>50% unilateral ARAS without occlusion	baseline data and a minimum 50% unilateral renal artery stenosis	-	unilateral occlusion and insignificant contralateral stenosis were excluded
Rivolta, 2005 16358234 Italy 1997-2004	Single arm, prospective	nd	≥50% to <100% ARAS with or without FPE, AKI, and refractory HTN	>70% luminal diameter established by angiography	All patients with ARAS presenting to nephrology and radiology clinic with CKD (scr >1.5 mg/dL)	
Rocha-Singh, 1999 10376497 US 1/1993-12/1995	Single arm, prospective	industry	≥75% ARAS and transstenotic peak-to-peak gradient ≥ 20mmHg	Angiographic documentation of visually estimated ≥75% atherosclerotic renal artery stenosis with an associated transstenotic peak-to-peak gradient ≥ 20mmHg	Patients with clinically suspected renovascular hypertension referred by family practitioners, internists, nephrologists, and general cardiologists for screening renal angiography	

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Rocha-Singh, 2005 16139124 US 12/1997-5/1999	Single arm, prospective	industry	≥70% de novo or restenotic ARAS with uncontrolled HTN and CKD (≤ 3.0 mg/dL) and and persistent peak-to peak translesional pressure gradient of ≥20 mm Hg	Unilateral or bilateral stenoses within 10 mm of the aorto-renal border	Patients enrolled had uncontrolled hypertension, serum creatinine concentrations 3.0 mg/dl, 70% de novo or restenotic renal artery atherosclerotic stenoses, and persistent peak-to-peak translesional pressure gradient of 20 mm Hg, flow-limiting dissections, or residual 50% stenoses after PTRAattempts.	a successful renal angioplasty, sequential stenoses in a single renal artery, a renal artery diameter <4 mm or >8 mm, an occluded renal artery, the need for more than two stents, a major vascular complication after PTRA, stenosis of a transplant or bypass graft anastomosis, non-atherosclerotic disease, serum creatinine 3.0 mg/dl, kidney length <8.0 cm, intolerance to aspirin, a life expectancy of fewer than two years, known hemorrhagic diathesis or hypercoagulable state, contraindication to receiving heparin, myocardial infarction within 30 days, an abdominal aortic aneurysm measuring >4.0 cm in diameter, current pregnancy, inability to grant informed consent, or patient refusal to undergo surgery to repair the renal artery or vascular access site in the event of a complication.

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Rocha-Singh, 2008 19006254 US 1/2004-8/2004	Single arm, prospective	industry	≥70% de novo or restenotic ARAS with uncontrolled HTN and CKD (≤ 3.0 mg/dL)	≥ 70% by angiographic visual estimate	Patients were eligible for inclusion if they had a de novo or restenotic lesion [Prior renal percutaneous intervention 4.0% (4/99); Percutaneous transluminal renal artery angioplasty (PTRA) 1.0% (1/96); Stenting 4.0% (4/99)] in the ostium of the renal artery. Lesions were required to be 15 mm in length, and between 4.0 mm and 7.0 mm in diameter. In addition, patients were required to have hypertension, renal dysfunction, recurrent flash pulmonary edema, or any combination thereof. Unilateral or bilateral renal artery stenoses were eligible for inclusion.	Accessory (polar) renal arteries were excluded. Patients with an occluded renal artery, a requirement for more than two stents, patients with stenosis in a transplant renal artery or bypass graft anastomosis, nonatherosclerotic etiologies (i.e., fibromuscular dysplasia), serum creatinine 3.0 mg/dl, renal hypoplasia (with a pole-pole renal length 8.0 cm), intolerance to aspirin, or with known bleeding or thrombotic disorders.
Rocha-Singh, 2011 21648052 US no dates given	Single arm, prospective	nd	≥50% ARAS with uncontrolled HTN (SBP ≥ 155 mmHg)	≥ 50% stenosis	hypertensive patients (≥ 155 mm Hg)	
Ruchin, 2007 17317314 Australia 9/1997-12/2003	Single arm, prospective	nd	% stenosis nd with uncontrolled HTN or FPE, ARF with ACEIs or ARBs	Patients referred for stenting of one or both renal arteries	Uncontrolled hypertension or intolerance of multiple antihypertensive agents, flash pulmonary edema or unexplained renal failure, especially associated with the use of ACEIs or ARBs.	
Rzeznik, 2011 21129903 Poland 1/2005-5/2009	Single arm, prospective	nd	>60% ARAS with HTN	> 60% lumen reduction	hypertension (5/84 had balloon angioplasty alone for fibromuscular dysplasia)	

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Safak, 2013 23321402 Germany 1995-2010	Single arm, prospective	nd	>50% ARAS with HTN	>50% diameter stenosis in semiquantitative vascular analysis in at least one renal artery	hypertensive patients referred for elective coronary catheterization to our institution beginning	

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Sapoval, 2005 16151060 multi-center Europe 2001-2002	Single arm, prospective	nd	>50% ARAS with clinical indications for renal revascularization and CKD (Scr <5.0 mg/dL)	Clinical indication for renal artery revascularization of atherosclerotic renal artery stenosis 50% as measured by operator or estimated original vessel diameter, based on healthy vessel segment and contralateral side	Age over 30 years; If female patient with child bearing potential, must have a documented negative pregnancy test within 3 days prior to inclusion; The reference vessel renal artery must be 4mm and 8 mm by visual estimate; The patient must have a baseline serum creatinine of 5.0 mg/dL; Patient is willing and able to comply with the specified follow-up evaluation; The patient or legally authorized representative must provide written informed consent prior to the procedure.	More than one index lesion in a renal artery, including tandem lesions; however, bilateral artery stenosis are allowed (If the patient requires treatment of the contralateral renal artery, this is allowed during the same procedure, as long as this is done prior to the index procedure, and with a successful outcome.); Total occlusion of the renal artery; Lesions that would require more than two stents; Any known complication (eg, guide wire perforation) following balloon angioplasty; Lesions which are in arteries to transplanted or bypassed kidneys; Any patient allergic or intolerant to aspirin and/or sirolimus (Rapamycin); Any patient with a co-existing condition with a life expectancy of less than 2 years; Patients with a known bleeding or hypercoagulation disorder; Absolute contraindication to administration of intravenous contrast material, heparin, or known allergy to 316 L stainless steel or any of its components; bdominal aortic aneurysm > 4 cm in diameter; Major surgical or interventional procedures within 30 days prior to this study or planned surgical or interventional procedures within 30 days of entry into this study; Patients with ASA classification 4; Life expectancy of less than 2 years or factors making clinical follow-up difficult; Imprisoned persons; Patients enrolled in this or other clinical trial or anticipated to be included into a trial which may interfere with this study, or patients already enrolled in this trial before.

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Sapoval, 2010 19908091 Many 2/2005-2/2007	Single arm, prospective	industry	>50% ARAS with clinical indications for renal revascularization	Patients, at least 18 years old, with atherosclerotic renal artery stenosis of more than 50%, judged by the clinicians as indicated for renal revascularizatio n, were enrolled in the study.		Excluded were patients with fibromuscular dysplasia, total occlusion, spontaneous dissection or in-stent restenosis of renal artery, stenosis of a transplant or bypass graft anastomosis, aneurysm of abdominal aorta larger than 45 mm in diameter, current pregnancy, a contraindication to contrast media, aspirin, thienopyridines, heparin or any other therapy as required for elective intervention.
Scarpioni, 2009 Conference abstract Italy No dates reported	RCT	nd	Stenosis ≥70%, renal failure, HTN	≥70% by Doppler duplex and confirmed by magnetic resonance	HTN on ≤5 medications	
Silva, 2008 18670414 Brazil 1/1996-3/2007	nRCS, retrospective	nd	≥80% ARAS	≥80%	angiographically confirmed ARD causing at least a 60% reduction in renal artery diameter, which corresponds to an 80% stenosis of the lumen of one or both main arteries	
Sofroniadou, 2012 22127407 UK 6/1997-2/2003	nRCS, prospective	nd	>70% unilateral ARAS and/or FPE, AKI, and refractory HTN were eligible for PTRAS >50% unilateral ARAS with or without HTN and without AKI or FPE were eligible for medical therapy	>70% stenosis ARAS unilaterally	Single functional kidney, acute kidney injury (AKI), flash pulmonary oedema (FPO) and untreatable hypertension were the indications for renal arterial intervention. Unilateral ARAS between 50 and 95%, with or without HTN underwent medical therapy.	-

Author, date PMID country study dates	Study Design	Funding source	Eligibility Criteria	Inclusion criteria: % stenosis	Inclusion criteria: Other	Exclusion criteria
Staub, 2010 20739200 Switzerland 8/2004-12/2007	Single arm, prospective	government, industry	≥50% unilateral or bilateral ARAS with HTN ≥140/90 mmHg	unilateral or bilateral RAS 50% and arterial hypertension (systolic BP >=140 mmHg and/or diastolic BP >=90 mmHg or on any anti-hypertensive drug therapy).	RAS was classified as haemodynamically relevant if the renal/ aortal velocity ratio was >=2.5. unilateral RAS, the side- to-side difference in intrarenal resistance index (RI Z 1 e (e-diastolic velocity/peak systolic velocity)) between the two kidneys >0.05 was also used to classify haemodynamically relevant RAS	-
Trani, 2010 20578190 Italy 6/2002-6/2007	nRCS, prospective	nd	≥70% ARAS with uncontrolled HTN or CKD (SCr >1.2 mg/dL) but not on hemodialysis	≥70% stenosis (angiographic, visual estimation)	Stenosis suspected at noninvasive testing or due to severe HTN and/or renal insufficiency at time of coronary angiography. Chronic ischemic heart disease (previous AMI or coronary stenosis >=50% or inducible ischemia at noninvasive testing). Severe HTN (grade 2 or 3) or renal insufficiency (SCr >1.2 mg/dL)	Hemodialysis, interventions on chronically occluded arteries, kidney size <7 cm longitudinally.
Trani, 2013 22503569 Italy 6/2002-6/2007	Single arm, prospective	nd	>70% ARAS with CKD stage ≥3, but not on hemodialysis and/or uncontrolled HTN	>70%	Main inclusion criteria were CKD stage 3 according to the NKF DOQUI classification and/or severe hypertension (defined as hypertension not controlled despite administration of 3 antihypertensive drugs). CKD staging was based on estimated glomerular filtration rate (eGFR) according to the simplified MDRD method.	Patients who had been on a hemodialysis program and those who did not provide informed consent to participate were excluded. Our institutional ethics committee approved the study.

Author, date PMID country study dates	Study Design	Funding source	Eligibility Criteria	Inclusion criteria: % stenosis	Inclusion criteria: Other	Exclusion criteria
Tsao, 2005 16394602 Taiwan 6/2001-1/2004	Single arm, prospective	nd	≥70% ARAS and eligible for PTRAS with CKD <4.0 mg/dL	70% stenosis.	Primarily admitted for PTRA and treated during admission for severe RAS. Suitable for PTRAS	Second session PTRAS & the first session attempt failed recently. ≥200 mL contrast medium administered for other causes within 3 days Lesion <70% stenotic or signs of renal irreversibililty (SCr≥4.0 mg/dL, renal size <7 cm, no late phase nephrogram, severely impaired cortical blood flow, seriously abnormal intrarenal arteries) PTRAS performed by an inexperienced operator or improvisational intervention
Uzzo, 2002 12009679 US no dates given (over an 8 yr period)	RCT	nd	>75% ARAS with CKD>1.5 to <=4 mg/dL and without uncontrolled HTN	Bilateral RAS involving >75% of the luminal diameter, high-grade (>75%) disease involving a solitary kidney, or unilateral high grade (>75%) stenosis	Angiographically confirmed RAS and those with azotemia (scr >1.5mg/dL and GFR <70 ml/min	Patients were considered ineligible if their baseline serum creatinine was >4.0 mg/dL, if their blood pressure was poorly controlled despite adequate medical management [diastolic blood pressure (DBP) > 100 mm Hg] or if they had comorbid conditions that would prohibit their ability to tolerate surgical revascularization.
Valluri, 2012 21765186 UK 2003-2007	Single arm, prospective	nd	≥70% ARAS referred for renal revascularization	Angiographically significant stenosis (70 to 90%) with >7 8 cm kidney length	Referred for renal revascularization and had primary stent placement with satisfactory angiographic result	Those who underwent revascularization as part of the ASTRAL protocol (n = 10)

Author, date PMID country study dates	Study Design	Funding source	Eligibility Criteria	Inclusion criteria: % stenosis	Inclusion criteria: Other	Exclusion criteria
van de Ven, 1999 9929021 Netherlands 12/1993-3/1997	RCT	Foundation, nonprofit	50% ostial ARAS with HTN >160 / 95 mmHg with or without medication	Ostial RAS: reduction 50% in luminal diameter within the first 10 mm of the aortic lumen as shown in angiography in association with atherosclerotic changes of the abdominal aorta	HTN (BP>160 / 95 mmHg with or without medication); stenosis shown to affect renal function by positive captopril renography or by an increase 20% in SCr during standardized use of an ACE inhibitor	Hx cholesterol embolism; pole to pole distance of affected kidney 8 cm on US plus 25% renal function in renography; renal tumor
Webster, 1998 9655655 UK no dates given	RCT	academic/hospital	50% ARAS with HTN (DBP 95 mm Hg on 2 drugs) or CKD <5.6 mg/dL and without recent stroke or MI	50% stenosis	DBP 95 mm Hg on 2 drugs	< 40 yo > 75 yo sCr > 500 mcmol/L (5.6 mg/dL) Stroke or MI within 3 months
Wheatley, 2009 19907042 UK 9/2000-10/2007	RCT	government, industry	% stenosis nd, ARAS with uncontrolled HTN or unexplained CKD	substantial anatomical atherosclerotic stenosis in at least one renal artery that is suitable for balloon angioplasty and/or stent	uncontrolled or refractory hypertension or unexplained renal dysfunction; not previously undergone and revascularization procedure for ARVD; and decision based on medical team	A partial nephrectomy to treat renal carcinoma was excluded from analysis
White, 1997 9362400 US 6/1992-12/1994	Single arm, prospective	nd	>50% ARAS with uncontrolled HTN (SBP >150 mmHg or DBP >90 mmHg or both)	>50% diameter stenosis by angiographic visual estimation of renal aorto-ostial lesion or restenosis (8%) or after a suboptimal PTA	Consecutive series of all patients treated with stents for poorly controlled HTN (SBP >150 mmHg or DBP >90 mmHg or both)	

Author, date PMID country study dates	Study Design	Funding source	Eligibility Criteria	Inclusion criteria: % stenosis	Inclusion criteria: Other	Exclusion criteria
Zahringer, 2007 17696619 Germany 11/2001-6/2003	nRCS, prospective	industry	>50% ARAS with HTN or CKD ≤5.0 mg/dL	>50% by visual estimation	Consecutive patients with hypertension or renal insufficiency and concomitant renovascular disease	Excluded from the trial were patients with totally occluded renal arteries, lesions requiring >2 stents, lesions located in arteries to transplanted kidneys, or arteries already bypassed by surgical grafts and those with severe renal insufficiency (serum creatinine .5.0 mg/dL).
Zeller, 2004 15056029 Germany 10/1996-11/2002	Single arm, prospective	nd	70% unilateral or bilateral ostial ARAS with HTN and CKD (men Scr >1.2 mg/dL, in women >1.1 mg/dL)	Unilateral or bilateral RAS and ostial RAS 70% diameter by duplex ultrasound and confirmed by angiography	Consecutive patients undergoing stent placement for ARAS lesion located within 1 cm of the ostium. Pts had hemodynamically sig RAS+HTN and/or impaired kidney fuxn (men scr >1.2 mg/dL, in women >1.1 mg/dL)	
Zeller, 2005 16212462 Germany 7/2002-7/2004	Single arm, prospective	nd	70% ARAS	70% by Doppler and subsequent angiogram	Radix carbofilm-coated or Palmaz-Genesis bare stent used	
Zeller, 2013 Conference abstract Germany 2008-2010	RCT	nd	De novo ≥70% stenosis, HTN	≥70%	≥18 years, at least mild HTN,	Renal failure (GFR ≤10 mL/min), renal atrophy, prior revascularization of RAS, associated with aortic aneurysm
Ziakka, 2008 19016147 Greece no dates given	RCT	nd	Mean stenosis 74% ARAS		We enrolled 82 patients who had atherosclerotic renal artery stenosis demonstrated by an angiogram (average lumen narrowing 74.2 17.4%). Angiograms of all patients were reviewed by two radiology consultants and were assessed for lumen narrowing and sites of stenosis (right or left renal artery; ostial, proximal or distal; unilateral or bilateral).	

Table C.2.1. Arm details: Comparative studies, PTRAS versus medication only

Author, date PMID country study dates	Medication: Anti-hypertensive (% in medication only cohort) {mean number of Anti HTN meds} [ACEi/ARB (% in medication only cohort)]; BP goal	Medication: Statins (%) [other anti-lipids]	Medication: Clopidogrel [other anti-platelet]	Other Medication (%) [Aspirin dose (%)]	Stent, %	Stent: Stent description	Stent: Distal protection device, type (%)	Stent: Peri-procedure medications	Stent: Other (%)
Arthurs, 2007 17398382 US 1/2001-6/2006	beta-blocker (73) diuretic (68) {4} [(ACE (59); ARB(43)]				100	transluminal			
Bax, 2009 19414832 Netherlands, France 6/2000-12/2005	Angiotensin II-receptor antagonists [yes]; < 140/90	Atorvastatin titrated 10 mg		[yes 75-100 mg/d]	100	A Palmaz- Corinthian IQ/Palmaz-Genesis stent (Johnson & Johnson Medical, Miami Lakes, Florida) was placed in every ostial stenosis, according to a standardized protocol (14).		Yes (aspirin, 75 to 100 mg/d, the day before admission.)	Truncal stenoses were treated by balloon angioplasty; Patients in the stent group received the same medical treatment as patients in the medication group

Author, date PMID country study dates	Medication: Anti-hypertensive (% in medication only cohort) {mean number of Anti HTN meds} [ACEi/ARB (% in medication only cohort)]; BP goal	Medication: Statins (%) [other anti-lipids]	Medication: Clopidogrel [other anti-platelet]	Other Medication (%) [Aspirin dose (%)]	Stent, %	Stent: Stent description	Stent: Distal protection device, type (%)	Stent: Peri-procedure medications	Stent: Other (%)
Cianci, 2011 20547539 Italy 2004-2009	alpha blockers, beta blockers (11) calcium channel blockers (49) [yes, (ACEis 23/53, ARBs 20/53)] < 140/90 mm Hg	Yes (25)	yes [yes]	[Yes (32)]	100	Express Vascular SD Monorail 5.5-6-15/20 mm premounted on a balloon catheter on Choice extra support 014 inch guide			In all patients who underwent revascularization, the renal artery was approached through the femoral artery. A 6F guiding catheter (Cobra or Bates) was used for selective renal artery angiography and for positioning the stent. All stenotic lesions were repaired using stainless stent. In these cases, primary stenting was performed. The procedure usually requires an injection of a 30-mL of 50-50 mixture of isotonic

Author, date PMID country study dates	Medication: Anti-hypertensive (% in medication only cohort) {mean number of Anti HTN meds} [ACEi/ARB (% in medication only cohort)]; BP goal	Medication: Statins (%) [other anti-lipids]	Medication: Clopidogrel [other anti-platelet]	Other Medication (%) [Aspirin dose (%)]	Stent, %	Stent: Stent description	Stent: Distal protection device, type (%)	Stent: Peri-procedure medications	Stent: Other (%)
Cooper, 2014 24245566 US 5/2005-1/2010	hydrochlorothiazide and amlodipine {2.1} [yes, caesartan]; <140/90 without coexisting conditions and < 130/80 mm Hg in patients with diabetes or CKD	atorvastatin			95	Genesis TM		325 mg of aspirin, and clopidogrel or ticlopidine in doses determined	Short-tip Angioguard device or a list of FDA approved devices listed in the protocol- N is at the discretion of operator
Dichtel, 2010 20630131 US 1/1999-6/2007 (nRCS					100	bare metal stents	Yes, used in a small number of cases at the discretion of the intervention alist		
Hackam, 2011 21156722 Canada 7/1994-7/2007	Yes								

Author, date PMID country study dates	Medication: Anti-hypertensive (% in medication only cohort) {mean number of Anti HTN meds} [ACEi/ARB (% in medication only cohort)]; BP goal	Medication: Statins (%) [other anti-lipids]	Medication: Clopidogrel [other anti-platelet]	Other Medication (%) [Aspirin dose (%)]	Stent, %	Stent: Stent description	Stent: Distal protection device, type (%)	Stent: Peri-procedure medications	Stent: Other (%)
Hanzel, 2005 16253607 US no dates given	As necessary {2.2} [yes]	to achieve a low-density lipoprotein cholesterol level <100 mg/dl		[yes 325 mg/day]	100			After intervention, patients received ticlopidine 250 mg twice daily or clopidogrel 75 mg/day for >= 30 days.	

Author, date PMID country study dates	Medication: Anti-hypertensive (% in medication only cohort) {mean number of Anti HTN meds} [ACEi/ARB (% in medication only cohort)]; BP goal	Medication: Statins (%) [other anti-lipids]	Medication: Clopidogrel [other anti-platelet]	Other Medication (%) [Aspirin dose (%)]	Stent, %	Stent: Stent description	Stent: Distal protection device, type (%)	Stent: Peri-procedure medications	Stent: Other (%)
Kalra, 2010 19937777 UK and Germany 1995-2007	[yes both 47.3%]	Yes (53%)			100	Various types of bare metal balloon expandable stents		UK: the majority of patients received antiplatelet therapy in the form of 75 mg aspirin. In both centers, statins were given to all patients who could tolerate them, and angiotensin converting enzyme inhibitors (ACE inhibitors) and/or angiotensin receptor blockers (ARB) used as tolerated; other antihypertensive medication was used if required. Germany: Antiplatelet therapy was started at least the day before intervention and routinely consisted of 75 mg of clopidogrel daily or ticlopidine 250 mg bid for 4 weeks, and then 100 mg of aspirin given indefinitely. Immediately before the intervention, and bolus dose of	

Author, date PMID country study dates	Medication: Anti-hypertensive (% in medication only cohort) {mean number of Anti HTN meds} [ACEi/ARB (% in medication only cohort)]; BP goal	Medication: Statins (%) [other anti-lipids]	Medication: Clopidogrel [other anti-platelet]	Other Medication (%) [Aspirin dose (%)]	Stent, %	Stent: Stent description	Stent: Distal protection device, type (%)	Stent: Peri-procedure medications	Stent: Other (%)
Kane, 2010 19666661 US no dates given	{3.4} [yes 60%]							Heparin infusion to keep clotting time at least 200 during stent placement	
Losito, 2005 15870215 Italy 1992-2000	beta-blockers, CCBs [yes]				100	A Palmaz (Cordis Corp., Warren, New Jersey) balloon expandable stent (P104, P154, P204)			Transfemoral or brachial approach
Marcantoni, 2012 22495466 Italy 2006-2009	beta blockers, alpha blockers, calcium channel blockers, diuretic [yes]	Yes		nitroglycerin	100			Diuretic, calcium channel blocker, beta blocker, ACEi, ARB, alpha blocker, antiplatelet drug, statin, nitroglycerin	
Ritchie, 2014 24074824 UK 1995-7/2011	[yes]	yes		yes					
Scarpioni, 2009 Conference abstract Italy No dates reported					100				
Sofroniadou, 2012 22127407 UK 6/1997-2/2003	[Yes ACEi (60) ARB (10)]; Yes < 140/80 mm Hg	same as ASTRAL (89%)		yes					2 from stent group also underwent surgical revascularization

Author, date PMID country study dates	Medication: Anti-hypertensive (% in medication only cohort) {mean number of Anti HTN meds} [ACEi/ARB (% in medication only cohort)]; BP goal	Medication: Statins (%) [other anti-lipids]	Medication: Clopidogrel [other anti-platelet]	Other Medication (%) [Aspirin dose (%)]	Stent, %	Stent: Stent description	Stent: Distal protection device, type (%)	Stent: Peri-procedure medications	Stent: Other (%)
Wheatley, 2009 19907042 UK 9/2000-10/2007	Any antihypertensive medication (99) diuretic (67); calcium channel blocker (68); beta-blocker (52); alpha blocker (37) [Yes (38)]; Yes "optimal BP"	yes (95) [any anti-lipid agent other than statin (80)]	[any anti-platelet (78)]	Warfarin (11) [Yes (93)]	95		distal protection devices were not used.		
Zeller, 2013 Conference abstract (19, 20) Germany 2008-2010	Optimal drug therapy for control of hypertension (blood pressure ≤ 125/80 mmHg)	Optimal drug therapy for control of hypercholesterolemia (LDL ≤ 100 mg/dL)		Optimal drug therapy for control of diabetes (HbA1c ≤ 6.5%).	100	Dynamic Renal stent			
Ziakka, 2008 19016147 Greece no dates given	beta blockers, alpha blockers, calcium channel blockers [yes]; DBP 90-110	yes			100				

Table C.2.2. Arm details: Comparative studies, surgery versus medication only

Author, date PMID country study dates	Medication: Anti-hypertensive (% in medication only cohort) {mean number of Anti HTN meds} [ACEi/ARB (% in medication only cohort)]; BP goal	Surgery: Description	Surgery: Aortic repair (%)
Uzzo, 2002 12009679 US no dates given (over an 8 yr period)	DBP < 100	Aortic replacement with renal artery reimplantation	Yes (100)

Table C.2.3. Arm details: Comparative studies, PTRAS versus surgery

Author, date PMID country study dates	Stent, %	Stent: Stent description	Stent: Distal protection device, type (%)	Stent: Peri-procedure medications	Surgery: Description	Surgery: Aortic repair (%)
Balzer, 2009 19135837 Germany 1/1998-12/2004	100	Palmaz-Stent, Johnson & Johnson, Langhorne, Pa, Wallstent, Boston Scientific, Natick, Mass, Jostent, Abbott, Abbott Park, Ill/Herkulink-Stent, Boston Scientific, Natick, Mass		Yes (hypertensive drugs)	22/27 bilateral reconstruction, 5/27 unilateral reconstruction (transaortic renal thromboendarterectomy with subsequent direct suture of the aorta was performed for reconstruction) periprocedureal medications: alprostadil)	
Crutchley, 2009 18951751 US 1997-2005	87				56 patients had open operative repair consisting of renal artery repair alone in 39 or renal artery repair combined with aortic procedures in 17. Renal artery repairs included anatomic in 15 and extra-anatomic renal artery bypass in 2, transaortic endarterectomy in 3, and renal endarterectomy in 19. Combined aortic procedures included renal artery bypass in 11 or endarterectomy in 7 in addition to aneurysm repair in 10, aortic endarterectomy in 4, and aortoiliac/aortofemoral bypass for occlusive disease in 3.	renal artery repair combined with aortic procedures (30)
de Donato, 2007 17653002 Italy 1/1998-	83			70 U/kg heparin, 100 mg/die acetylsalicylic acid, 75 mg/die clipidogrel or 500 mg/die ticlopidine for at least 4-5 days prior to admission	11/15 (73.3%) renal endarterectomies, 4/15(26.7%) aortorenal bypasses #of kidneys endarterectomy was performed for atherosclerotic ostial lesions, which bypass was performed for long or trunk lesions	abdominal aortic reconstruction due to aneurysm (67) or Leriche's Syndrome (33)
Patel, 2009, 9497511 US 1/2002-12/2006	97				Endarterectomy 21/47 (47%); Bypass 26/47 (53%): Aortorenal (17/26), Hepatorenal (6/26); Splenorenal (2/26); Iliorenal (1/26)	15/47 (32%)

Table C.2.4. Arm details: PTRAS single arm studies

Author, date PMID country study dates	Stent, %	Stent: Stent description	Stent: Distal protection device, type (%)	Stent: Other (%)	Stent periprocedural medications
Baril, 2007 17391902 US 1/1999-12/2005	100	Balloon-expandable stainless steel renal artery stents were used. Initially, the Corinthian 0.035-inch (Cordis/Johnson & Johnson, Warren, NJ) system was used, and later, the Genesis 0.014-inch (Cordis/Johnson and Johnson) system.			
Beck, 2010 19939607 US 2001-2007	100	Stent diameters were < 6mm in 52% and >= 6 mm in 48%, and stent size selection was based on the adjacent normal vessel diameter size.		Embolic protection devices, including the Guardwire (Medtronic, Minneapolis, MN) a Spider (ev3 Endovascular Inc, Plymouth, Minn) 20%	Patients with a creatinine level 1.3 mg/dL underwent pretreatment with N-Acetylcysteine (600 mg orally twice daily on the day before the procedure and for 48 hours after the procedure) along with periprocedural bicarbonate (150 mL bicarbonate in 850 mL of D5W at 3 mL/kg for 1 hour and then 1 mL/kg until 5 hours after completion of the procedure)
Bersin, 2013 22581488 US 2/2008-5/2009	100	FormulaTM balloon-expandable renal stent system consists of a low-profile 316L stainless steel stent premounted on a balloon catheter delivery system between two radiopaque marker bas. ... Hybrid open-closed cell design with alternating ring geometry with peak valley and peak connections			Clopidogrel or other thienopyridone 24 hr prior or loading dose day of surgery, continues for 30 days post-procedure
Blum, 1997 9017938 Germany 3/1989-3/1996	91	Palmaz stent 10 or 15 mm		4.8 F angioplasty balloon catheter (Olbert catheter), passed through a valved 8F introducer sheath with a femoral approach	Heparin 5000 IU, then for 2 days to PPT=60. ASA 100 mg or ticlopidine 250 mg daily
Bruno, 2014, 24555729 Italy 1990-2008	58			168/168 balloon catheters	
Christie, 2012 23083664 US 9/2003-7/2010	100	Balloon-mounted stents were used in all patients and sized to match the diameter of the distal, normal-caliber (RA) as measured by angiography at the time of treatment, while ensuring areas of poststenotic dilatation were not used for sizing			

Author, date PMID country study dates	Stent, %	Stent: Stent description	Stent: Distal protection device, type (%)	Stent: Other (%)	Stent periprocedural medications
Chrysant, 2014 24909590 US no dates given	100	RX Herculink Elite Renal Stent System [Abbott Vascular, Santa Clara, CA]			All patients received aspirin 325 mg orally once daily, and clopidogrel either 75 mg orally once daily for 4 days prior to the procedure, or as a single loading dose of 300 mg orally within 24 hours prior to the procedure. Heparin was used as the procedural anticoagulant agent. Following stent placement, aspirin 325 mg orally once daily was continued for a minimum of 12 months and clopidogrel 75 mg orally once daily for at least 4 weeks
Cianci, 2013 23467950 Italy 2007 -12/2009	100	stainless steel Palmaz-Schatz stents (AVE, Bard Saxx Palmaz 6-15/20, Miami Lakes, FL, USA) pre-mounted on a balloon catheter			Acetylsalicylic or ticlopidine + clopidogrel
Cooper, 2008 18490527 US no dates given (RCT of PTRAS)	100	Genesis stent	Angioguard (47)	A bolus of 0.25 mg/kg abciximab (or placebo) was administered 5 minutes before crossing the lesion (50)	Acetylcysteine, sodium bicarbonate, or other agents to prevent contrast nephropathy and study medication abciximab
Dangas, 2001 11491257 US no dates given	100	Palmaz stent (P104 or P154)		Hand-crimped on predilated balloon Guiding catheter Intra-arterial nitroglycerin; stent deployed at 10 to 12 atmospheres	Heparin 5000U IV Hydration if creatinine increased
Dorros, 2002 11835644 US 1990-1997	100	Palmaz or Palmaz-Schatz		The methodology of determining balloon diameter size used for stent deployment was made by comparing the angiographic catheter s diameter with the angiographic renal artery size; usually a 5 mm balloon was used for small arteries and the arteries of women and a 6 mm balloon was used for the vast majority of the arteries in men.	

Author, date PMID country study dates	Stent, %	Stent: Stent description	Stent: Distal protection device, type (%)	Stent: Other (%)	Stent periprocedural medications
Gill, 2003 12601202 UK 6/1993-7/1999	100	Balloon-mounted (Medtronic AVE) or Palmaz		Femoral approach (99), brachial approach (1)	Heparin 5000 IU intra-procedure, then ASA 75-300 mg qD
Gill-Leertouwer, 2002 12466252 Netherlands 9/1996-12/1998	100	Palmaz			5000 IU heparin & continued for 48 h after procedure; ASA 100 mg daily for the entire f/u period
Girndt, 2007 17164562 Germany 5/1997-11/2002	100	Among the 64 arteries, 63 were treated with balloon-expandable stainless steel stents (48 Herkulink, Guidant, I., USA; 12 Jo-Stent, JOMED, Rangeingen, Germany; 2 Palmaz and 1 Corinthian, both Johnson & Johnson Interventional Systems, Warren, N.J., USA) and 1 was treated with a self-expandable nitinol stent (Sinus-stent, Optimed, Karlsruhe, Germany). Tube length varied from 10 to 20 mm. After deployment a mean stent diameter of 5.9 8 0.7 (range 4.0 7.0, median 6.0) mm was reached		balloon expandable stents (94)	During the procedure, a bolus dose of 5,000 IU unfractionated heparin was administered intra-arterially. The post-interventional treatment included low molecular weight heparin in therapeutic doses for 2 days a low dose acetylsalicylic acid (100 mg/day) as a regular medication. Additional clopidogrel 75 mg/day for 6 weeks was given in 6 patients
Gonçalves, 2007 17364124 Brazil 5/1999-10/2003	100				
Gray, 2002 12710843 US 1991-1997	100	Palmaz			Heparin
Gross, 1998 9736342 Germany no dates given	100	PalmazTM stent (Johnson & Johnson, Warren, NJ) in 20 patients, an Inflow stent (InFlow Dynamics, Munich, Germany) in 13 patients, a Sito stent (Jomed, Rangeingen, Germany) in 8 patients, and a be-Stent (Medtronic, Minneapolis, MN) in 3 patients		Predilation and femoral approach	Heparin (10,000 U intra arterially) was given before the procedure and was then continued with low-molecular-weight heparin after removal of the sheaths until discharge of the patient. Because of the CAD of these patients, 100 mg of aspirin once daily was added
Harden, 1997 9113012 UK 04/1992-12/1995	100	Palmaz; Johnson & Johnson Interventional Systems, Warren, NJ, USA			All patients routinely received low-dose aspirin but no other anticoagulation after stent insertion
Henry, 2003 14571477 France, India, and Greece 1/1999-11/2002	100	Cordis P154, Corinthian, Genesis, M3, Medtronic AVE, NIR, Herculink, Biotronik, Stentec		GuardWire system (Medtronic), EPI Filter (Boston Scientific), Angioguard (Cordis)	Ticlopidine 500 mg or clopidogrel 75 mg/d and ASA 100 mg/d; IV bolus of 5,000 u of heparin and 3 mg of cefamaole; ASA 100 mg/d indefinitely and ticlopidine 250 mg/d or clopidogrel 75 mg/d for 1 mo

Author, date PMID country study dates	Stent, %	Stent: Stent description	Stent: Distal protection device, type (%)	Stent: Other (%)	Stent periprocedural medications
Holden, 2006 16837918 New Zealand no dates given	100	Balloon expandable stainless steel stent	Embolic filter		
Iannone, 1996 8974797 US 8/1992-12/1993		Palmaz-Schatz stents, 4-9 mm diameter, 10 or 15 mm length			
Jaff, 2012 22511402 US 8/2007-10/2009	100	The RX Herculink Elite Renal Stent System features a balloon expandable stent composed of L605 Cobalt Chromium. The stent design is based on a series of zig-zagging rings with multiple links per ring. The study stent included 12, 15, and 18 mm lengths with diameters ranging from 4 to 7 mm.			All patients received aspirin 325 mg orally once daily, and clopidogrel either 75 mg orally once daily for 4 days before the procedure, or as a single loading dose of 300 mg orally within 24 hr before the procedure. Heparin was used as the procedural Anticoagulant agent. Following stent placement, aspirin 325 mg orally once daily was continued for a minimum of 12 months and clopidogrel 75 mg orally once daily for at least 4 weeks
Jokhi, 2009 19668788 Canada 6/2000 - 3/2007	100	All bare metal stents - Express Biliary (Boston Scientific; 14.3%), Genesis (Cordis Corporation; 2.9%), Herculink (Guidant, USA; 20%), Racer (Medtronic, USA; 4.3%), Ross (evYsio Medical Devices, Canada [investigational stent used in the unpublished ROSSE study]; 32.9%), Tetra (Guidant Corporation, USA; 1.4%), Ultra (Abbott Laboratories, USA; 7.1%) or Liberte (Boston Scientific Corporation; 17.1%). Coronary stents used when estimated reference vessel diameter less than 5 mm.		Angio-Seal (St Jude Medical Inc, USA) and Perclose (Abbott) 6.5%	Acetylsalicylic acid (ASA) 325 mg and clopidogrel (300mg more than 6h or 600 mg more than 2h before the procedure). prehydrated for at least 6h w/ 1 mL/kg/h intravenous saline. N-actetyl cysteine at discretion of responsible physician
Kawarada, 2010 20884436 Japan no dates given	100	Use of a 5- to 6-mm x 15- to 18-mm Genesis or Palmaz stent was attempted.			Aspirin, clopidogrel, ticlopidine or ciloztazol was administered for a minimum of 2 days before the procedure (61/61)

Author, date PMID country study dates	Stent, %	Stent: Stent description	Stent: Distal protection device, type (%)	Stent: Other (%)	Stent periprocedural medications
Kennedy, 2003 14582036 US 7/1993-11/2001	100	Through 2/98*: Palmaz:94%; Palmaz-Schartz:5%; Wallstent:1%		IV hydration if renal insufficiency (CKD)); Through 2/98: Vessels >= 4 mm were treated with Palmaz stents; vessels < 4 mm were treated with Palmaz-Schatz stents	Heparin pre-procedure ASA 325 mg/d indefinitely Warfarin for 1 mo in procedures performed up to 09/94 (target INR:2)
Kobo, 2010 20684176 Israel 2001-2007	100			Predilatation before stent placement: (54)	Acetylcysteine 600 mg twice a day and 0.9% normal saline 2 L/day for 2 days before the procedure
Leesar, 2009 19539148 US 12/2004-08/2006	100				
Lekston, 2008 19006027 Poland no dates given (RCT of PTRAS)	88			brachytherapy; compatible self-centering PARIS catheter by the Guidant company, iridium source was approximately 10 C	Oral ASA (150mg) oral Ticlopidine (250 mg) 2 days prior to procedure. IV heparin 10, 000U immediately prior to procedure. Continued on anti-platelet agents.
Mannarino, 2012 22260219 Italy 1/2003-12/2008 (NRCS of PTRAS)	100	Transluminal			
Murphy, 2014, 24325931 US 3/2005-11/2009	100	Genesis	67		
Ramos, 2003 12472793 Argentina no dates given	100	Palmaz Schatz			
Rastan, 2008 19110785 Germany 6/2005-6/2006	100	The Hippocampus TM .014 Balloon Expanding Rapid Exchange Renal Stent System (Invatec Corp., Concesio Brescia, Italy)			Aspirin 100 mg/d for life; clopidogrel 75 mg/d x 4wks after a loading dose of 600 mg; heparin 2500 to 5000 IU
Rivolta, 2005 16358234 Italy 1997-2004	100	Palmaz stents; Corinthian or and Genesis premounted stent			Aspirin 325 mg/d
Rocha-Singh, 1999 10376497 US 1/1993-12/1995	100	Palmaz			Aspirin 325mg; shorter acting anti-HTN medications; warfarin (INR 2-3)

Author, date PMID country study dates	Stent, %	Stent: Stent description	Stent: Distal protection device, type (%)	Stent: Other (%)	Stent periprocedural medications
Rocha-Singh, 2005 16139124 US 12/1997-5/1999	100	A Palmaz (Cordis Corp., Warren, New Jersey) balloon expandable stent (P104, P154, P204)		Transfemoral or brachial approach	Aspirin 81 to 500 mg and intra-arterial heparin 3000 to 10000 U bolus before procedure
Rocha-Singh, 2008 19006254 US 1/2004-8/2004	100	The ExpressTM Renal Premounted Stent System consists of a stainless steel stent loaded on a monorail delivery balloon catheter. The stent is centered on a high-pressure balloon between two radiopaque marker bas to aid in positioning the system during the procedure and to ensure full expansion of the stent. The ExpressTM Renal Stent has an asymmetric design along its length, allowing for greater scaffolding and smaller cell area on the proximal e to counteract the greater recoil forces commonly noted with aortorenal ostial disease. The stent has a maximum length of 19 mm and a maximum diameter of 7.0 mm, and is intended to treat vessels 4.0 mm and 7.0 mm in diameter.			All patients received aspirin at a dosage of 81 mg at least one day prior to the index procedure. Aspirin use was required for 9 months after stent placement and recommended indefinitely thereafter. In addition, intravenous heparin was administered during the procedure at the discretion of the investigator
Rocha-Singh, 2011 21648052 US no dates given	100	(PalmazTM Stent, Cordis Corporation, New Brunswick, NJ [6]; Double StrutTM XS Stent (IDE #G990224), ev3, Inc. Plymouth [10]; BridgeTM Extra Support Stent (PMA #P020007), Medtronic, Inc. Santa Rosa, CA [8])			
Ruchin, 2007 17317314 Australia 9/1997-12/2003	100			Type of stents was at the discretion of the interventionalist	Prehydration with 0.9% Saline N-acetylcysteine 600mg orally; 5000 IU of unfractionated heparin intravenously or intra-arterially preprocedure; Post-procedure: aspirin 300mg x 3 months then 150mg indefinitely and clopidogrel 75mg daily x 1 month. Ticlopidine 250mg bd was used prior to the availability of clopidogrel
Rzeznik, 2011 21129903 Poland 1/2005-5/2009	94			Direct stenting (82%), predilation (18)	Yes, but no details given
Sapoval, 2005 16151060 multi-center Europe 2001-2002	100	Palmaz Genesis stent (Cordis) Low profile balloon expandable stent		Commonly femoral arterial route was used; occasional use of brachial artery when needed	

Author, date PMID country study dates	Stent, %	Stent: Stent description	Stent: Distal protection device, type (%)	Stent: Other (%)	Stent periprocedural medications
Sapoval, 2010 19908091 Multiple 2/2005-2/2007	100	Tsunami peripheral stent is a stainless-steel, laser cut, open-cells stent mounted on a rapid exchange delivery balloon catheter compatible with 0.01400 and 0.01800 guidewire. The stent design comprises 12 cells with a triple link in diameters 5 and 6 mm, and 14 cells with quadruple link in 7 mm diameter, with a strut thickness of 0.007100 (0.18 mm). All stents are compatible with 5 Fr long sheath or 6 Fr guiding catheter. Stents were available in diameters of 5, 6 and 7 mm and in lengths of 12 and 18 mm.			
Staub, 2010 20739200 Switzerland 8/2004-12/2007	100	as Hippocampus (Invatec), Dynamic renal (Biotronik) or Palmaz blue (J&J Cordis)			Anti-platelet therapy was started at least 1 day before the intervention and routinely consisted of 75 mg of clopidogrel daily for 4 weeks and 100 mg of aspirin indefinitely
Trani, 2010 20578190 Italy 6/2002-6/2007 (NRCS of PTRAS)	100	Coronary stent 22% (when stent <=5 mm required) [ML/Ultra 14, Express 4, Other 1], dedicated renal stent 78% [Hippocampus 23, Herculink 19, Radix 18, Other 7]		Adjuntive postdilation with a different balloon (14)	ASA 160 mg and (clopidogrel 75 mg or ticlopidine 500 mg), 48 pre & for at least 1 month. N-acetyl-cysteine 1200 mg 24 hr pre & for at least 48 hr; IV hydration (sodium bicarbonate)
Trani, 2013 22503569 Italy 6/2002-6/2007	100				
Tsao, 2005 16394602 Taiwan 6/2001-1/2004	100			Minimal amount of low-osmolality contrast medium and the least number of injections possible. PTRAS performed by qualified interventional cardiologist well experienced in PCI and familiar with PTRAS. Delicate PTRAS: efforts made to minimize trauma and exposure.	Aspirin plus ticlopidine or clopidogrel. clinically optimized including adequate hydration, no diuretics or nephrotoxic agents
Valluri, 2012 21765186 UK 2003-2007	100				

Author, date PMID country study dates	Stent, %	Stent: Stent description	Stent: Distal protection device, type (%)	Stent: Other (%)	Stent periprocedural medications
van de Ven, 1999 9929021 Netherlands 12/1993-3/1997 (RCT of PTRAS)	97	Palmaz			Heparin iv (5000 IU); warfarin pos
White, 1997 9362400 US 6/1992-12/1994	100	Palmaz (balloon mounted)		Predilation	Heparin 3000 to 5000 IU Aspirin 325 mg preop Warfarin 1-3 mo for an INR 2.0 to 2.5
Zahringer, 2007 17696619 Germany 11/2001-6/2003 (NRCS of PTRAS)	100	Palmaz-Genesis peripheral stent. Diameters of 5.0 and 6.0 mm and lengths of 15 or 18 mm. The SES were coated with an elastomeric copolymer of ,5 mm thickness bleed with sirolimus. The total sirolimus content was 210 mg for a 15-mm-long stent and 256 mg for an 18-mm-long stent.		Standard introducer sheaths, guiding catheters, and standard 0.018-inch guidewires were used during the index procedure.	The routine antithrombotic and antiplatelet drug regimen of each catheter laboratory was used in the trial without general standardization. Predilation, postdilation, and antihypertensive and general cardiac medication prescriptions were left to the discretion of the individual investigators according to the observational nature of the trial
Zeller, 2004 15056029 Germany 10/1996-11/2002	100	14 different stents (gold coated and non coated stents)	-	Ostial stenoses were treated with or without predilation.	One day before the intervention clopidogrel 75 mg/d until 4 wk; immediately before heparin bolus 2500- 10,000 IU, aspirin 100 mg indefinitely
Zeller, 2005 16212462 Germany 7/2002-7/2004	100	Radix carbofilm-coated or Palmaz-Genesis bare			Aspirin 100 mg/d Loading and postop dose clopidogrel

Table C.2.5. Arm details: Medication only single arm studies

Author, date PMID country study dates	Medication: Anti-hypertensive (% in medication only cohort) {mean number of Anti HTN meds} [ACEi/ARB (% in medication only cohort)]; BP goal	Medication: Statins (%) [other anti-lipids]	Medication: Clopidogrel [other anti-platelet]	Other Medication (%) [Aspirin dose (%)]
Chrysochou, 2012 21993376 UK 1999-2009	[yes]	yes (62)		[yes (52)]
Safak, 2013 23321402 Germany 1995-2010	Any antihypertensive drug (99) beta blockers (72) diuretics (58) calcium channel blockers (24) {3.2} [ACEi or AT1 receptor blockers]	yes		yes
Silva, 2008 18670414 Brazil 1/1996-3/2007 (NRCS of medication)	Antihypertensive drug classes, beta-blockers [yes (81)]	Yes (based BP and lipid profile, as recommended by guidelines.)	use of platelet antiaggregant	folic acid
Webster, 1998 9655655 UK no dates given (RCT of medication)	atenol, beroflumethiazide, CCB [no]			furosemide, methyldopa or prazosin (alternatives to ACEi)

Table C.2.6. Arm details: Surgical revascularization single arm studies

Author, date PMID country study dates	Surgery: Description	Surgery: Aortic repair (%)
Alhadad, 2004 14718896 Sweden 1987-1996 (NRCS of surgery)	Transverse arteriotomy, endartectomy and a patch closure if not aortic surgery was needed when a 5-6 mm dacron or PFTE by-pass with e-to-e anastomosis to the renal artery was used. The remainder underwent nephrectomy (11), division on the crus diaphragma (1) a correction of a venous malformation (1)	yes (31)
Cherr, 2002 11854720 US 1987-1999	Aortorenal bypass graft; splanchnorenal bypass graft; reimplantation; endarterectomy; nephrectomy (primary and contralateral)	Yes (41)
Galaria, 2005 15735947 US 1/1984-1/2004 (NRCS of surgery)	Aorto renal bypass; Hepatorenal bypass; Splenorenal bypass; Endarterectomy; Concomitant aortic aneurysm repair; Operations following failed endoluminal repair	Aorto renal bypass (56)

Table C.3. Baseline data

Author, date PMID	Arm	N	Arteries, N	Age*	Male, %	Stenosis, %*	Bilateral†, %	SBP, mm Hg*	DBP, mm Hg*	HTN, %	GFR/ CrCl, mL/ min*	SCr mean mg/dL*	Kidney disease, % (definition)	Post-PTRAS MLD (SD) [length (SD)]	CVD, %
Alhadad, 2004 14718896	Surgical	106		64 {9-84}	65		37	180 {160-202}	100 {90-110}						
Arthurs Z, 2007 17398382	Medication only	22	34	67 (13)			55	142 (21)	73 (13)			1	22 (CRI)		CAD 50; CeVD 27; PAD 36
	PTRAS	18	29	72 (9)			61	162 (17)	75 (13)			1.5	52 (CRI)		CAD 47; CeVD 29; PAD 35
Balzer, 2009 19135837	PTRAS	22	28	66 (9) {44-84}		{70-100}	73	169 {95% CI 161-178}	87 {95% CI 82-92}			1.6 {95% CI 1.4-1.8}			Aortic dz 55
	Surgical	27	49	62 (8) {49-77}		{70-100}	19	171 {95% CI 163-178}	88 {95% CI 84-92}			1.3 {95% CI 1.0-1.6}			Aortic dz 52
Baril 2007 17391902	PTRAS	56	62	77 (7)	79		11			63; 7 (uncontrolled)	53 (25)		38 (SCr > 1.5 mg/dL)		Aortic dz 100
Bax, 2009 19414832	Medication only	76		67 (9)	59		46	163 (26)	82 (12)			1.6 (0.6)			
	PTRAS	64		66 (8)	67		50	160 (25)	83 (13)			1.7 (0.7)			
Beck, 2010 19939607	PTRAS	129	179	68 (11)	53		30	161 (31)	80 (15)		46 (14)				CAD 52; AAA 29

Author, date PMID	Arm	N	Arteries, N	Age*	Male, %	Stenosis, %*	Bilateral†, %	SBP, mm Hg*	DBP, mm Hg*	HTN, %	GFR/ CrCl, mL/ min*	SCr mean mg/dL*	Kidney disease, % (definition)	Post-PTRAS MLD (SD) [length (SD)]	CVD, %
Bersin, 2013 22581488	PTRAS		114	72 (10)	44	100	100	150 (21) {102-202}	74 (13) {43-112}	31 (140-159/90-99); 52 (≥160/≥100)	61 (29)	1.3 (0.1) {0.5-2.9}	49 (CKD stage III); 10 (CKD stage IV)	2.2 (0.8) [7.7 (3.6)]	MI 30; LVH 28; CHF 26; PAD 56; CVA 18; TIA 11
Blum, 1997 9017938	PTRAS	68	82	60 (10)	65		9	188 (28)	105 (11)			1.2 (0.6)			
Bruno, 2014, 24555729	PTRAS	97		61 (11)	65			162 (21)	90 (14)		67.2 (29)	1.33 (0.61)			26
Cherr, 2002 11854720	Surgical	500	776	65 (9)	49		59	200 (35)	104 (21)	[Duration mean (SD) 10 (9); range 0-57 y]		2.6			CVD 90
Christie, 2012 23083664	PTRAS	83	91	70 (10)	41		8.4	196 (29)	100 (23)	[Duration mean (SD) 15 (15) y]	51 (24)	1.5 (0.6)		5.6 [15.7]	CAD 31; CHF 6; MI/angina 26; LVH 30; AAA 7
Chrysant, 2014 24909590	PTRAS	202	241	72		65.9 (11.4)		162 (19)	78 (12)		58 (21)	1.2 (0.4)		5.4 (1.1) [1.8 (0.7)]	

Author, date PMID	Arm	N	Arteries, N	Age*	Male, %	Stenosis, %*	Bilateral†, %	SBP, mm Hg*	DBP, mm Hg*	HTN, %	GFR/ CrCl, mL/ min*	SCr mean mg/dL*	Kidney disease, % (definition)	Post-PTRAS MLD (SD) [length (SD)]	CVD, %
Chrysochou, 2012 21993376	Medication only	621		71 (9) {40-92}	66			150 (27) {75-220}	78 (14) {33-130}	84	36 (18) {5-120}	2.3 (1.4) {0.4-9.7}}			CHF 14; FPE 4
Cianci R, 2013 23467950	PTRAS	55		66 (8)	62		15	170 (23)	89 (15)	98	42 (25)	2.0 (0.9)			PAD 64
Cianci, 2011 20547539	Medication only	40		70 {26-85}	43	{50-100}	20								
	PTRAS	53		64 {24-86}	58	{70-100}	28								
Cooper, 2008 18490527	PTRAS	100	139	73	44	67		159	74		59	1.2		2.0	CAD 25; AAA 0
Cooper, 2014 24245566	Medication only	480		69 (9)	49	66.9 (11.9)	18	150 (23)		75	57		50 (GFR<60 mL/min)		MI 30; CHF 15
	PTRAS	467	434	69 (9)	51	67.3 (11.4)	22	150 (23)		71	58		50 (GFR<60 mL/min)		MI 27; CHF 12
Crutchley, 2009 18951751	PTRAS	30		71 (11)	57		37	186 (31)	92 (17)		51 (23)	1.8 (1.3)	0 (RRT)		CAD 77; PAD 27
	Surgical	56		67 (9)	41		80	181 (31)	92 (17)		47 (33)	1.6 (0.8)	4 (RRT)		CAD 66; PAD 40

Author, date PMID	Arm	N	Arteries, N	Age*	Male, %	Stenosis, %*	Bilateral†, %	SBP, mm Hg*	DBP, mm Hg*	HTN, %	GFR/ CrCl, mL/ min*	SCr mean mg/dL*	Kidney disease, % (definition)	Post-PTRAS MLD (SD) [length (SD)]	CVD, %
Dangas, 2001 11491257	PTRAS	131	153	71	48	74 (10)		170 (25)	84 (14)	95		1.9 (1.3)	50 (SCr >1.5 mg/dL); 2 (RRT)		MI 55; Stroke 25; Angina 26; CABG 44; Aortic repair 46; PAD 60
de Donato, 2007 17653002	PTRAS		82												
	Surgical		15												AAA 67
	Total	83	97	62 (9)	84		14.3	165 (17)	92 (12)	100		1.4 (0.7)			CAD 39; CABG/PCI 0
Dichtel, 2010 20630131	Medication only	71	100	73 (8)	96		41	141 (20)	70 (10)		37 (11)				CAD 67; CHF 27; PAD 38
	PTRAS	47	74	73 (8)	100		57	145 (19)	75 (11)		38 (13)				CAD 46; CHF 13; PAD 26

Author, date PMID	Arm	N	Arteries, N	Age*	Male, %	Stenosis, %*	Bilateral†, %	SBP, mm Hg*	DBP, mm Hg*	HTN, %	GFR/ CrCl, mL/ min*	SCr mean mg/dL*	Kidney disease, % (definition)	Post-PTRAS MLD (SD) [length (SD)]	CVD, %
Dorros, 2002 11835644	PTRAS	1058		69 (10)	49			168 (27)	84 (15)	85 (poorly controlled)		1.7 (1.2)	41 (CRI)		CHF 15
Galaria, 2005 15735947	Surgical	109		66 (10)	43		19	171 (17)	82 (11)	34	51 (29)	1.7 (0.7)	12 (CRI)		CAD 53; CVD 26
Gill, 2003 12601202	PTRAS	100	120	68 {43-86}	60		51								Sxic CAD 47; Claudication 36; CeVD 25; CHF 25
Gill-Leertouwer, 2002 12466252	PTRAS	41		60 (9)	66			177 (21)	96 (11)	34			34 (CRI)		
Girndt, 2007 17164562	PTRAS	64	64	67 (9) {39-84}	61	{70-100}		155 (20)	83 (10)		57 (23) {25-23}	1.4 (0.5) {0.6-2.8}		5.5 (0.7) [range 10-20]	
Gonçalves, 2007 17364124	PTRAS	46		[59] {33-84}	57		33	177 (30) {124-248}	98 (17) {80-170}			2.3 (1.3) {1.0-6.1}			CAD 46; CHF 14
Gray, 2002 12710843	PTRAS	39		70 {50-85}	41		46	174 (32)	85 (23)						CABG 28
Gross, 1998 9736342	PTRAS	30	37	66 {45-85}	63	75 (15)	23	163 (30) {normal-230}	93 (18) {normal-130}			1.47 (0.7)			CAD 100; CHF 20; PAD 23

Author, date PMID	Arm	N	Arteries, N	Age*	Male, %	Stenosis, %*	Bilateral†, %	SBP, mm Hg*	DBP, mm Hg*	HTN, %	GFR/ CrCl, mL/ min*	SCr mean mg/dL*	Kidney disease, % (definition)	Post-PTRAS MLD (SD) [length (SD)]	CVD, %
Hackam, 2011 21156722	Medication only	2113													
Hanzel, 2005 16253607	Medication only	40		70 (9)			20	154 (5)	77 (3)		61 (4)	1.3 (0.6)			
	PTRAS	26		66 (9)			50	162 (4)	82 (3)		56 (3)	1.5 (0.1)			
Harden, 1997 9113012	PTRAS	32		67 {49-79}			78	[169] {153-175}	[95] {85-103}						CAD 70; CeVD 44; PAD 50
Henry, 2003 14571477	PTRAS	56		66 (12) {22-87}	57	84.5 (8.3)	14	169 (15)	104 (13)			1.3 (0.5)			CAD 35/56 (62.5 %); Aortic dz 66; CeVD 25; PAD 39
Holden, 2006 16837918	PTRAS	63	73	70	63		92	153	101	70		1.9	76 (CKD stage 3); 24 (CKD stage 4)		
Iannone, 1996 8974797	PTRAS	63	83	70 {51-83}	49	67 {23-94}	22	160	80	100		1.8 {0.1-6.1}	46 (SCr>1.5 mg/dL); 3 (RRT)		CHF 37%, CAD 94%; PAD 48
Jaff, 2012 22511402	PTRAS	202	241	72	62	{50-100}		162 (19)	78 (12)		58 (21)	1.2 (0.4)		5.5 [15]	Aortic dz 67

Author, date PMID	Arm	N	Arteries, N	Age*	Male, %	Stenosis, %*	Bilateral†, %	SBP, mm Hg*	DBP, mm Hg*	HTN, %	GFR/ CrCl, mL/ min*	SCr mean mg/dL*	Kidney disease, % (definition)	Post-PTRAS MLD (SD) [length (SD)]	CVD, %
Jokhi, 2009 19668788	PTRAS	106	108	72 (9) {38-91}	61		32	166 (28)	74 (14)	69 (uncontrolled)	47 (19)	1.6 (0.7)	61 (GFR<60 mL/min)	5.6 (0.7) [17.6 (2.8)]	CAD 93; PAD 37
Kalra, 2010 19937777	Medication only [UK]	347	347	71 (9) {40-90}	58			156 (27) {90-240}	80 (15) {33-134}		35 (19)		8 (CKD stage 1-2); 46 (CKD stage 3); 44 (CKD stage 4-5)		Angina 28; CAD 28; CeVD 27
	PTRAS [Germany]	472		67 (9) {33-90}	62			144 (19) {100-218}	78 (11) {49-134}		60 (26)		48 (CKD stage 1-2); 36 (CKD stage 3); 14 (CKD stage 4-5)		Angina 80; CAD 80; CeVD 51
	PTRAS [UK]	89	89	69 (7) {42-81}	62			157 (29) {95-220}	81 (14) {58-130}		34 (17)		8 (CKD stage 1-2); 47 (CKD stage 3); 44 (CKD stage 4-5)		Angina 40; CAD 38; CeVD 25
Kalra, 2010 19937777	Total	908		69 {33-90}	60			151 {90-240}	80 {33-134}		48		29 (CKD stage 1-2); 41 (CKD stage 3); 29 (CKD stage 4-5)		Angina 56; CAD 55; CeVD 39

Author, date PMID	Arm	N	Arteries, N	Age*	Male, %	Stenosis, %*	Bilateral†, %	SBP, mm Hg*	DBP, mm Hg*	HTN, %	GFR/ CrCl, mL/ min*	SCr mean mg/dL*	Kidney disease, % (definition)	Post-PTRAS MLD (SD) [length (SD)]	CVD, %
Kane, 2010 19666661	Medication only	50		78 (7)	54		38	148 (30)			37 (18)				CHF 84; CAD 78; NYHA III or IV 62; CeVD 48; PAD 52
	PTRAS (comparative)	50		74 (8)	54		53	154 (29)			40 (21)				CHF 94; CAD 74; NYHA III or IV 66; CeVD 54; PAD 36
	PTRAS (prevalence)	163		73	55		50	156				3.0			CAD 68; CHF 31
Kawarada, 2010 20884436	PTRAS	61	73	72 (7) {56-82}	59		21	152 (26) {96-224}	81 (12) {51-107}	97; 31 (resistant)		1.1 (0.5) {0.4-2.9}		5.5 [16.5]	
Kennedy, 2003 14582036	PTRAS	261		70	41	70	38	168	82		51				CAD 80; CHF 32; MI 34

Author, date PMID	Arm	N	Arteries, N	Age*	Male, %	Stenosis, %*	Bilateral†, %	SBP, mm Hg*	DBP, mm Hg*	HTN, %	GFR/ CrCl, mL/ min*	SCr mean mg/dL*	Kidney disease, % (definition)	Post-PTRAS MLD (SD) [length (SD)]	CVD, %
Kobo, 2010 20684176	PTRAS	41/ 41	49	70 (9)	36		20	164 (17)	82 13)	100		1.2 (0.2)	54 (RF)		CAD 72; Carotid dz 22; PAD 28
Leesar, 2009 19539148	PTRAS	62	62	62 (10)		61 (10)	0	170 (12)	91 (13)			1.2 (0.3)		2.4 (0.7)	CAD 48
Lekston, 2008 19006027	PTRAS	62		52 (8)	62							1.3			
Losito, 2005 15870215	Medication only	54		68	73	73.5 (SE 17.5)	26	160 (SE 17)	89 (SE 10)			1.7 (SE 0.8)			
Mannarino, 2012 22260219	PTRAS	30	37	73 (7)	70		57	156 (31)	89 (13)	96	34 (14)		100 (CKD stage 3- 4)		
Marcantoni, 2012 22495466	Medication only	41	41	69 (9)	66	58 (6)		131 (16)	74 (18)		58 (22)		24 (CKD)		
	PTRAS	43	43	69 (8)	53	60 (7)		133 (20)	73 (11)		65 (25)		12 (CKD)		
Murphy, 2014, 24325931	PTRAS	239		70 (9)	49		27	154 (24)			50 (21)	1.41 (0.51)	3.8 (CKD)		CAD 40; stroke 8
Patel, 2009, 9497511	PTRAS	203	247	72 (9)	58		22	150 (24)	75 (13)	95		1.8 (1)	50 (CKD)		CAD 51; PVD 38
Patel, 2009, 9497511	Surgical	47	67	65 (11)	55		43	155 (26)	77 (13)	94		2.2 (1.6)	51 (CKD)		CAD 64; PVD 75
Ramos, 2003 12472793	PTRAS	105		59 (10)	60		43	160 (26)	91 (12)	25 (uncontrolled)	54 (26)	1.7 (0.9)	51 (GFR<50 mL/min)		

Author, date PMID	Arm	N	Arteries, N	Age*	Male, %	Stenosis, %*	Bilateral†, %	SBP, mm Hg*	DBP, mm Hg*	HTN, %	GFR/ CrCl, mL/ min*	SCr mean mg/dL*	Kidney disease, % (definition)	Post-PTRAS MLD (SD) [length (SD)]	CVD, %
Rastan, 2008 19110785	PTRAS	50	55	66 (12) {41-88}	58	82 (9)	10	148 (17)	78 (10)		51 (26) {18-134}	1.4 (0.6) {0.6-3.2}	12 (CKD I); 34 (CKD II); 54 (CKD III)	6.0 (0.3) [13.3 (2.1)]	CAD 44; PAD 44; CVA 6
Ritchie, 2014 24074824	Medication only	340	0	71 (9)				155 (30)	79 (17)		35 (20)				Angina 34; MI 30; PAD 38
Ritchie, 2014 24074824	PTRAS	127	127	68 (9)				163 (30)	83 (16)		37 (21)				Angina 39; MI 39; PAD 43
Ritchie, 2014 24074824	Total	467	127												
Rivolta, 2005 16358234	PTRAS	52		69 (8)	58		37	161 (7)	86 (7)			2.9 (1.8)			
Rocha-Singh, 1999 10376497	PTRAS	150		67	44			MAP 110				1.5 (0.6)			CAD 73; CABG 32; PAD 49; CeVD 23
Rocha-Singh, 2005 16139124	PTRAS	208	208	70 {40-88}	37		21	168 (25)	82 (13)			1.4 (0.5)			CAD 63; CeVD 39; PAD 44

Author, date PMID	Arm	N	Arteries, N	Age*	Male, %	Stenosis, %*	Bilateral†, %	SBP, mm Hg*	DBP, mm Hg*	HTN, %	GFR/ CrCl, mL/ min*	SCr mean mg/dL*	Kidney disease, % (definition)	Post-PTRAS MLD (SD) [length (SD)]	CVD, %
Rocha-Singh, 2008 19006254	PTRAS	100	117	71 (9) {41-85}	48	68.4 (11) {46.4-93}	17	157 (21) {106-233}	75 (12) {43-109}	99	51 (21) {16-116}	1.4		4.7 (0.8)	CAD 73; MI 21; Unstable angina 3; PCI 37; CABG 37; PAD 9; CVA 4; TIA 4
Rocha-Singh, 2011 21648052	PTRAS	286	327	71 (9) {33-89}	47	68.1 (10.8) {50-100}		179 (19) {155-288}	83 (13) {49-131}			1.3 (0.5) {0.5-3.9}			Aortic dz 47; CeVD 47; PAD 23
Ruchin, 2007 17317314	PTRAS	89	102	70 (9) {37-86}	60	84.3 (10.8) {50-100}	16	162 (30) {110-270}	78 (14) {44-120}		50 (20) {11-110}	1.6 (0.7) {0.7-4.3}			CAD 62
Rzeznik, 2011 21129903	PTRAS	84	104	64	50		40	135 (19)	75 (11)	39 (HTN crisis)	58 (26)		57 (GFR<60)		CAD 63; FPE 6
Safak, 2013 23321402	Medication only	171		67 (9)	65			137	78		66 (28)				Angina 75%; CAD 80; PAD 36

Author, date PMID	Arm	N	Arteries, N	Age*	Male, %	Stenosis, %*	Bilateral†, %	SBP, mm Hg*	DBP, mm Hg*	HTN, %	GFR/ CrCl, mL/ min*	SCr mean mg/dL*	Kidney disease, % (definition)	Post-PTRAS MLD (SD) [length (SD)]	CVD, %
Sapoval, 2005 16151060	PTRAS	52		64	46	68.2		172 (25)	92 (15)	92		1.2 (0.1)	19 (CrCl <= 50)		PAD 39
Sapoval, 2010 19908091	PTRAS	251	276	70 (10)	57		11.2	171 (26)	89 (14)		54 (33)	1.7 (1.4)		5.9 (0.7) [14.9 (3.8)]	
Scarpioni, 2009 Conference abstract	Medication only	28		74.3 (6.1)	61		46	149.3 (10.1)	79.1 (9.1)	100	46 (18)	1.6 (0.6)			CAD 64%, PAD 43%, Supraortic vascular dz 29%, AAA 29%
	PTRAS	24		69.4 (9.2)	58		58	147.5 (14.5)	78.7 (10.3)	100	40 (14)	1.7 (0.5)			CAD 63%, PAD 50%, Supraortic vascular dz 33%, AAA 25%
Silva, 2008 18670414	Medication only	104	146	65	54		40	167	95		33 {14-56}				CAD 60%; Angina 36; CABG/PCI 35; PAD 60

Author, date PMID	Arm	N	Arteries, N	Age*	Male, %	Stenosis, %*	Bilateral†, %	SBP, mm Hg*	DBP, mm Hg*	HTN, %	GFR/ CrCl, mL/ min*	SCr mean mg/dL*	Kidney disease, % (definition)	Post-PTRAS MLD (SD) [length (SD)]	CVD, %
Sofroniadou, 2012 22127407	Medication only	10		72 (5)	90			146 (32)	77 (10)		42 (15)				CAD 70; Carotid dz 50; PAD 60; CVA 40
	PTRAS	26		68 (8)	58		77	177 (38)	90 (20)		32 (15)				CAD 65; Carotid dz 15; PAD 58; CVA 15
Staub, 2010 20739200	PTRAS	120		63 (13)	52	100	11	148 (17)	81 (13)		66 (28)		43 (GFR<60 mL/min)		CAD 37
Trani, 2010 20578190	PTRAS	70	86	70 (8)	39		28			96 (ESH/EHC Grade 2 or 3)			83 (SCr >1.2 mg/dL)	5.7 (0.9) [16.3 (3.9)]	CAD 100
Trani, 2013 22503569	PTRAS	57	69	69 (8)	58	84.9 (8.4)	21				51 (22)	[3.1] {IQR 2.9-7}	19 (CKD stage 4-5)	[17 (range 13-18)]	
Tsao, 2005 16394602	PTRAS	54		71	83	86	22	146	78	[Duration mean 12 y]	36	2.0	63 (SCr >1.6 mg/dL)	5.9 (0.3) [17 (1)]	Angina 24; CHF 19; CABG/PCI 15
Uzzo, 2002 12009679	Medication only	27													
	Surgical	25													

Author, date PMID	Arm	N	Arteries, N	Age*	Male, %	Stenosis, %*	Bilateral†, %	SBP, mm Hg*	DBP, mm Hg*	HTN, %	GFR/ CrCl, mL/ min*	SCr mean mg/dL*	Kidney disease, % (definition)	Post-PTRAS MLD (SD) [length (SD)]	CVD, %
Valluri, 2012 21765186	PTRAS	127	162	[74] {IQR 66-79}	46	77	31					1.8 {IQR 1.5-2.4}			
van de Ven, 1999 9929021	PTRAS	40		65 (8)	55	76 (15)	21	186 (24)	103 (12)			[1.6] {IQR 1.2-2.2}			CAD 39; CeVD 24; PAD 55
Webster, 1998 9655655	Medication only, bilateral (randomized)	81		63	50	{50-100}						1.8			
Wheatley, 2009 19907042	Medication only	403		71 {43-88}	63	75 {20-99}		152 {90-241}	76 {46-130}		40 {7-122}	2.0 {0.7-8.5}			CAD 48; PAD 40; CVA 19
	PTRAS	403	335	70 {42-86}	63	76 {40-100}		149 {87-270}	76 {45-120}		40 {5-125}	2.0 {0.7-6.2}			CAD 50; PAD 41; CVA 18
White, 1997 9362400	PTRAS	100	133	67 (10)	42		33	173 (25)	88 (17)	100		2.4 (1.6)	44 (CKD)		
Zahringer, 2007 17696619	PTRAS	105	105	66	50	68.9		166	89			1.4		5.5 [10.1]	PAD 55
Zeller, 2004 15056029	PTRAS	354		66 (10) {44-84}	66							1.5 (0.9)			CAD 83; PAD 68; CeVD 57

Author, date PMID	Arm	N	Arteries, N	Age*	Male, %	Stenosis, %*	Bilateral†, %	SBP, mm Hg*	DBP, mm Hg*	HTN, %	GFR/ CrCl, mL/ min*	SCr mean mg/dL*	Kidney disease, % (definition)	Post-PTRAS MLD (SD) [length (SD)]	CVD, %
Zeller, 2005 16212462	PTRAS	125		67 {42-90}	55	80	18			100					
Zeller, 2013 Conference abstract	Medication only	33		65.8 (12.3)	67					100					
	PTRAS	34		67.8 (8.5)	68					100					
Ziakka, 2008 19016147	Medication only	46	62	61 (14)	83		30	175 (32)	90 (18)			2.2 (1.8)			
	PTRAS	36	48	69 (8)	67		39	178 (27)	88 (17)			2.0 (1.1)			

CHF: congestive heart failure; PAD: peripheral artery disease; CeVD: cerebrovascular disease; CVA: stroke; CABG/PCI: coronary revascularization; CABG: CABG; dz: disease; AAA: AAA; MI: MI. † Bilateral or solitary kidney stenosis. * mean [median] (SD) {range}

Table C.4.1. Results: Mortality

Author, year, PMID	Outcome and description	Timepoint	Arm	n/N % (95% CI)	Between-Arm Comparison
PTRAS vs. Medication RCT					
Bax, 2009, 19414832	Death: All cause	2 years	Medication only	6/74 8.1 (1.9, 14)	
			PTRAS	5/62 8.1 (1.3, 15)	HR 0.99 (0.30, 3.24)
	Death: cerebrovascular disease	2 years	Medication only	1/74 1.4 (0.2, 9.9)	
			PTRAS	0/62 0 (0, 13)	--
	Death: coronary artery disease	2 years	Medication only	3/74 4.1 (1.3, 13)	
			PTRAS	3/62 4.8 (1.6, 16)	HR 1.16 (0.23, 5.73)
	Death: CV	2 years	Medication only	4/74 5.4 (0.3, 11)	
			PTRAS	2/62 3.2 (0.8, 14)	HR 0.59 (0.11, 3.25)
Cooper, 2014, 24245566	Death: All cause	3.6 years	Medication only	76/472 16 (13, 19)	
			PTRAS	63/459 14 (11, 17)	HR 0.80 (0.58, 1.12) P = 0.2
	Death: cerebrovascular disease	1 year	Medication only	45/472 9.5 (6.9, 12)	
		2 years		79/472 17 (13, 20)	
		3 years		193/472 41 (36, 45)	
		4 years		307/472 65 (61, 69)	
		5 years		399/472 85 (81, 88)	
		1 year	PTRAS	44/459 9.6 (6.9, 12)	
		2 years		68/459 15 (12, 18)	
		3 years		148/459 32 (28, 37)	
		4 years		266/459 58 (53, 62)	
		5 years		375/459 82 (78, 85)	
	Death: CV	3.6 years	Medication only	45/472 9.5 (6.9, 12)	
			PTRAS	41/459 8.9 (6.3, 12)	
	Death: renal	3.6 years	Medication only	1/472 0 (0, 1.5)	
			PTRAS	2/459 0 (0.1, 1.8)	HR 1.89 (0.60, 1.89)
Marcantoni, 2012, 22495466	Death: All cause	1 year	Medication only	2/35 5.7 (1.5, 25)	
			PTRAS	2/38 5.3 (1.3, 23)	OR 0.92 (0.12, 6.88)
Wheatley, 2009, 19907042	Death: All cause	5 years	Medication only	106/403 26 (22, 31)	
			PTRAS	103/403 26 (21, 30)	HR 0.90 (0.69, 1.18) P=0.46
	Death: CV	5 years	Medication only	45/403 11 (8.1, 14)	
			PTRAS	42/403 10 (7.4, 13)	OR 0.93 (0.59, 1.44)
	Death: renal	5 years	Medication only	17/383 4.4 (2.9, 7.6)	

Author, year, PMID	Outcome and description	Timepoint	Arm	n/N % (95% CI)	Between-Arm Comparison
			PTRAS	10/383 2.6 (1.4, 5.0)	OR 0.58 (0.26, 1.28)
PTRAS vs. Medication NRCS					
Arthurs, 2007, 17398382	Death: All cause	1 year	Medication only	0/22 0 (0, 0.4)	
		1.92 years		0/22 0 (0, 0.4)	
		2.92 years		2/22 9 (2.9, 54)	
		1 year	PTRAS	2/18 11 (2.9, 54)	
		1.92 years		2/18 11 (2.9, 54)	
		2.92 years		2/18 11 (2.9, 54)	HR 0.02 (0, 15.16) P=0.62 OR (calculated) 1.25 (0.16, 9.88)
Dichtel, 2010, 20630131	Death: All cause	3 years	Medication only	17/71 24 (14, 34)	
			PTRAS	20/47 43 (28, 57)	OR 2.35 (1.06, 5.21)
Kalra, 2010, 19937777	Death: All cause	4 years	PTRAS vs. Medication only	nd	OR 0.55 (0.34, 0.88) P = 0.013
Kane, 2010, 19666661	Death: All cause	1 year	PTRAS (comparative) vs. Medication only	nd	HR 1.2 (0.60, 2.60) P=0.60
Sofroniadou, 2012, 22127407	Death: All cause	5 years	Medication only	1/10 10 (1.4, 88)	
			PTRAS	5/26 19 (4.1, 34)	OR 2.14 (0.22, 21.05)
	Death: CV	7.4 years	Medication only	3/10 30 (1.6, 58)	
			PTRAS	6/26 23 (6.9, 39)	OR 0.70 (0.14, 3.58)
Surgery vs. Medication RCT					
Uzzo, 2002, 12009679	Death: All cause	6.17 years	Surgical vs. Medication only		P = 0.31
Surgery vs. PTRAS RCT					
Balzer, 2009, 19135837	Death: CV	4 years	PTRAS	4/22 18 (7.5, 66)	OR 0.63 (0.16, 2.53) P=0.80
			Surgical	7/27 26 (15, 83)	
Surgery vs. PTRAS NRCS					
Crutchley, 2009, 18951751	Death: All cause	1 year	PTRAS	1/30 3.3 (0.5, 25)	
		2 years		4/30 13 (1.2, 25)	
		3 years		5/30 17 (3.3, 30)	

Author, year, PMID	Outcome and description	Timepoint	Arm	n/N % (95% CI)	Between-Arm Comparison
		4 years		5/30 17 (3.3, 30)	
		5 years		6/30 20 (5.7, 34)	
		6 years		8/30 27 (11, 42)	OR 0.99 (0.36, 2.71)
		1 year	Surgical	2/56 3.6 (0.9, 15)	
		2 years		4/56 7.1 (0.4, 14)	
		3 years		8/56 14 (5.1, 23)	
		4 years		14/56 25 (14, 36)	
		5 years		15/56 27 (15, 38)	
		6 years		15/56 27 (15, 38)	
Patel, 2009, 9497511	Death: All cause	1 year	PTRAS	22/178 12 (9, 22)	
		2 years		31/178 17 (14, 31)	
		3 years		38/178 21 (19, 39)	OR 0.93 (0.41, 2.13) P=0.9
		1 year	Surgical	4/40 10 (4, 31)	
		2 years		7/40 17.5 (9, 48)	
		3 years		9/40 22.5 (14, 61)	
PTRAS only					
Beck, 2010, 19939607	Death: All cause	2 years	PTRAS	13/129 10 (4.9, 15)	
Bersin, 2013, 22581488	Death: All cause	9 months	PTRAS	4/100 4.0 (0.2, 7.8)	
Blum, 1997, 9017938	Death: All cause	2.25 years	PTRAS	3/68 4.4 (1.5, 15)	
Cianci, 2013, 23467950	Death: All cause	6 months	PTRAS	1/53 1.9 (0.3, 14)	
Dangas, 2001, 11491257	Death: All cause	1.25 years	PTRAS	13/131 9.9 (4.8, 15)	
Dorros, 2002, 11835644	Death: All cause	4 years	PTRAS	275/1058 26 (23, 29)	
Gill, 2003, 12601202	Death: All cause	0.5 years	PTRAS	22/100 22 (14, 30)	
		1 year		23/100 23 (15, 31)	
		2 years		26/100 26 (17, 35)	
		4.1 year		28/100 28 (19, 37)	
Gill-Leertouwer, 2002, 12223011	Death: All cause	1 year	PTRAS	1/41 2.4 (0.3, 18)	
Gray, 2002, 12710843	Death: CV	1 year	PTRAS	8/39 21 (7.8, 33)	
		1.78 years		9/31 29 (13, 45)	
Gross, 1998, 9736342	Death: All cause	0.5 years	PTRAS	1/30 3.3 (0.5, 25)	
Harden, 1997, 9113012	Death: All cause	15.25 years	PTRAS	17/32 53 (36, 70)	
Henry, 2003, 14571477	Death: CV [Death from MI]	0.5 years	PTRAS	2/56 3.4 (0.9, 15)	
		1 year		3/56 5.4 (1.8, 18)	

Author, year, PMID	Outcome and description	Timepoint	Arm	n/N % (95% CI)	Between-Arm Comparison
Iannone, 1996, 8974797	Death: All cause	1 year	PTRAS	9/61 15 (5.9, 24)	
Jokhi, 2009, 19668788	Death: All cause	12 months	PTRAS	2/106 1.9 (0.5, 7.8)	
Kane, 2010, 19666661	Death: All cause	1 year	PTRAS (prevalence)	76/163 46 (39, 54)	
Kennedy, 2003, 14582036	Death: All cause	21 months	PTRAS	73/261 28 (23, 33)	
Leesar, 2009, 19539148	Death: All cause	1 year	PTRAS	0/62 0 (0, 13)	
Mannarino, 2012, 22260219	Death: All cause	2.75 years	PTRAS	2/30 6.7 (1.7, 30)	
Murphy, 2014, 24325931	Death: All cause	9 months	PTRAS	1/181 0.6 (0.1, 4.0)	
Rastan, 2008, 19110785	Death: All cause	1 year	PTRAS	1/50 2.0 (0.3, 15)	
Ritchie, 2014, 24074824	Death: All cause	3.8 years	PTRAS	66/127 52 (43, 61)	
Rivolta, 2005, 16358234	Death: CV	0.5 years	PTRAS	2/52 3.8 (1.0, 16)	
Rocha-Singh, 1999, 10376497	Death: All cause	1.1 year	PTRAS	4/154 2.6 (0.1, 5.1)	
Rocha-Singh, 2005, 16139124	Death: All cause	2 years	PTRAS	1/208 0.5 (0.1, 3.4)	
Rocha-Singh, 2008, 19006254	Death: All cause	9 months	PTRAS	1/92 1.1 (0.2, 7.9)	
		2 years		5/85 5.9 (0.9, 11)	
		3 years		8/56 14 (5.1, 23)	
Ruchin, 2007, 17317314	Death: All cause	2.3 years	PTRAS	9/89 10 (3.8, 16)	
	Death: CV			3/89 3.4 (1.1, 11)	
	Death: renal			3/89 3.4 (1.1, 11)	
Rzeznik, 2011, 21129903	Death: CV	1 year	PTRAS	3/84 3.6 (1.2, 12)	
Sapoval, 2010, 19908091	Death: All cause	1 year	PTRAS	11/251 4.4 (1.8, 6.9)	
	Death: CV			4/251 1.6 (0, 3.1)	
	Death: renal			3/251 1.2 (0.4, 3.8)	
Staub, 2010, 20739200	Death: All cause	6 months	PTRAS	2/122 1.6 (0.4, 6.7)	
Trani, 2010, 20578190	Death: All cause	3.7 (mean) years	PTRAS	9/70 13 (5.0, 21)	

Author, year, PMID	Outcome and description	Timepoint	Arm	n/N % (95% CI)	Between-Arm Comparison
	Death: CV	3.7 (mean) years	PTRAS	7/70 10 (3.0, 17)	
Valluri, 2012, 21765186	Death: All cause	2.2 (median) years	PTRAS	46/127 44 (28, 45)	
White, 1997, 9362400	Death: CV	0.5 years	PTRAS	3/100 3.0 (1.0, 9.8)	
Zahringer, 2007, 17696619	Death: All cause	2 years	PTRAS	3/105 2.9 (0.9, 9.3)	
Zeller, 2004, 15056029	Death: All cause	2.67 (mean) years	PTRAS	44/140 31 (24, 39)	
Medication only					
Chrysochou, 2012, 21993376	Death: All cause	3.1 (median) years	Medication only	212/621 34 (30, 38)	
Ritchie, 2014, 24074824	Death: All cause	3.8 years	Medication only	189/340 56 (50, 61)	
Safak, 2013, 23321402	Death: All cause	9 years	Medication only	58/171 34 (27, 41)	
Silva, 2008, 18670414	Death: CV	3 years	Medication only	17/104 16 (9.2, 23)	
Surgery only					
Alhadad, 2004, 14718896	Death: All cause	5 years	Surgical	38/106 36 (27, 45)	
		10 years		30/36 83 (71, 96)	
Cherr, 2002, 11854720	Death: All cause	5 years	Surgical	146/500 29 (25, 33)	
		10 years		171/500 34 (30, 38)	

Table C.4.2. Results: Kidney function, within arm change, angioplasty with stent

Author, Year, PMID	N Baseline	Baseline SCr, Mean, mg/dL [GFR*]	Years	SCr Change (95% CI), mg/dL	GFR Change (95% CI), mL/min*
Arthurs, 2007, 17398382	18	[0.72, dL/mg (1/SCr)]	0.5		0 (nd) dL/mg
			1		0 (nd) dL/mg
			2		0.1 (nd) dL/mg
			4		-0.1 (nd) dL/mg
Balzer, 2009, 19135837	22	1.6	1	-0.2 (-0.5, 0.03)	
			4	-0.2 (-0.5, 0.02)	
Baril, 2007, 17391902	56	[53]	1.5 (mean)		4.2 (-19, 27)
Bax, 2009, 19414832	64	1.7 (0.68)	2	0.1 (-0.07, 0.35)	
Beck, 2010, 19939607	129	[46]	1.5 (mean)		-2 (-20, 16)
Bersin, 2013, 22581488	100	1.3 [61]	0.75	0 (-0.1, 0.1)	-0.1 (-5.9, 5.7)
Blum, 1997, 9017938	68	1.2	0.5	0.1 (-1.0, 1.2)	
			1	0.1 (-1.0, 1.1)	
			2	0 (-1.1, 1.0)	
			3	-0.1 (-1.2, 0.9)	
			4	-0.2 (-1.3, 0.9)	
			5	-0.1 (-1.2, 0.9)	
Christie, 2012, 23083664	83	[51]	2		4.1 (nd)
Chrysant, 2014, 24909590	202	[58]	0.75		-1 (-4.1, 2.0)
			2		0 (-3.2, 3.2)
			3		-1 (-4.1, 2.1)
Cianci, 2011, 20547539	53	1.5	1	-0.3 (-0.4, -0.1)	
Dichtel, 2010, 20630131	47	[38]	1		-1.4 (-4.4, 1.5)
			2		1.5 (-0.1, 3.1)
			3		0.1 (-2.3, 2.5)
Dorros, 2002, 11835644	1058	1.7	1	0 (-0.1, 0.1)	
			4	-0.4 (-0.5, -0.3)	

Author, Year, PMID	N Baseline	Baseline SCr, Mean, mg/dL [GFR*]	Years	SCr Change (95% CI), mg/dL	GFR Change (95% CI), mL/min*
Gill, 2003, 12601202	65	2.7	0.5	-0.1 ()	
			1.5	-0.3 ()	
			2	-0.6 ()	
			3	-0.7 ()	
Girndt, 2007, 17164562	64	1.4 [57]	1	0.4 (0.1, 0.6)	-3.6 (-9.7, 2.5)
Gonçalves, 2007, 17364124	39	2.3	2	-0.4 (-0.8, 0.04)	
Gray, 2002, 12710843	39	3.2	1.8 (mean)	-0.5 (-1.0, 0.02)	
Gross, 1998, 9736342	30	1.5	0.5	-0.1 (-0.1, -0.03)	
Hanzel, 2005, 16253607	26	1.5 [61]	1.75	0 (-0.2, 0.2)	-4.0 (-7.6, -0.4)
Henry, 2003, 14571477	56	1.3	0.5	-0.2 (-0.3, -0.1)	
			2	-0.2 (-0.3, -0.1)	
			3	-0.1 (-0.3, 0.1)	
Holden, 2006, 16837918	63	1.9	0.5	-0.1 (-0.1, -0.1)	
Jaff, 2012, 22511402	202	[58]	0.75		-1 (-3.2, 1.2)
Kalra, 2010, 19937777 [Germany]	472	[60]	1		0.7 (-1.0, 2.4)
Kalra, 2010, 19937777 [UK]	89	[34]	1		-1 (-4.1, 2.5)
Kane, 2010, 19666661	50	[40]	2.8 (median)		-9 (-9.8, -8.3)
Kawarada, 2010, 20884436	61	1.1	0.6 (mean)	0 ()	
Kennedy, 2003, 14582036	261	[37]	1.75		-2 (-4.8, 0.8)
Kobo, 2010, 20684176	41	1.2	2	-0.1 (-0.2, -0.04)	
Leesar, 2009, 19539148	62	1.2	0.5	0 (-0.2, 0.1)	
			1	-0.1 (-0.2, 0.04)	

Author, Year, PMID	N Baseline	Baseline SCr, Mean, mg/dL [GFR*]	Years	SCr Change (95% CI), mg/dL	GFR Change (95% CI), mL/min*
Lekston, 2008, 19006027 [w/o Brachytherapy]	29	1.3 [74]	1	-0.1 (-0.4, 0.2)	3 (0.1, 5.9)
Lekston, 2008, 19006027 [w/Brachytherapy]	32	1.3 [75]	1	-0.2 (-0.3, -0.1)	9 (3.6, 14.4)
Mannarino, 2012, 22260219	30	[37]	2.75		-15 (nd)
Marcantoni, 2012, 22495466	38	[68]	1		-2 (-7.7, 3.3)
Patel, 2009, 9497511	199	1.8	1	0 (-0.16, 0.16)	
			1.68	0.1 (-0.98, 0.298)	
Ramos, 2003, 12472793	105	1.7 [54]	1	-0.3 (-0.5, -0.1)	8 (2.2, 13.8)
Rastan, 2008, 19110785	50	1.4 [51]	1	-0.1 (-0.3, 0.03)	10 (2.5, 17.5)
Rivolta, 2005, 16358234	52	[-0.0008, dL/mg (1/SCr) per month]	1.7 (mean)		0.001 (-0.006, 0.008) dL/mg per month
Rocha-Singh, 1999, 10376497	132	1.5	1.1	0 (-0.1, 0.2)	
Rocha-Singh, 2005, 16139124	208	1.4	0.75	0.0 (-0.04, 0.1)	
			2	0.1 (0.00, 0.2)	
Rocha-Singh, 2008, 19006254	100	1.4 [51]	0.75	0.1 (-0.1, 0.2)	0.7 (-2.1, 3.5)
			2	0.09 (0.002, 0.18)	-3.0 (-6.4, 0.4)
			3	0.1 (-0.01, 0.2)	-2.4 (-6.7, 2.0)
Rocha-Singh, 2011, 21648052	241	1.3	0.75	0.1 (-0.03, 0.1)	
Ruchin, 2007, 17317314	89	1.6 [50]	2.3 (mean)	-0.1 (-0.2, 0.02)	2 (-2.3, 6.3)
Rzeznik, 2011, 21129903	84	[58]	1		2 (-46.2, 49.8)
Sapoval, 2005, 16151060	52	1.2	0.5	-0.1 (-0.2, 0.1)	
Sapoval, 2010, 19908091	248	[55]	0.5		1.7 (0.8, 2.5)

Author, Year, PMID	N Baseline	Baseline SCr, Mean, mg/dL [GFR*]	Years	SCr Change (95% CI), mg/dL	GFR Change (95% CI), mL/min*
			1		-5.3 (-8.0, -2.6)
Sofroniadou, 2012, 22127407	26	[37]	1 to 3		-4 (-6.9, -1.1)
			3 to 6		-5 (-8.5, -1.5)
			≥6		-6 (-10.7, -1.3)
Trani, 2010, 20578190	70	1.5	2	-0.1 (-0.3, 0.1)	
Trani, 2013, 22503569	57	1.4 (median)	0.5	-0.1 (chg median)	
Tsao, 2005, 16394602	54	1.9 [35.8]	0.5	-0.1 (-0.2, -0.02)	0.7 (0.1, 1.2)
Valluri, 2012, 21765186	127	[-0.044 dL/mg (1/SCr) per year (median)]	2.9 (mean)		0.042 dL/mg per year (chg median)
van de Ven, 1999, 9929021	40	1.8	0.5	-0.2 ()	
Wheatley, 2009, 19907042	403	2.0 [0.57, dL/mg (1/SCr)]	1	0.2 (0.1, 0.3)	
			5	0.3 (0.1, 0.6)	-0.006 (nd) dL/mg per year
Zahringer, 2007, 17696619	105	1.4	0.5	0 (-0.4, 0.4)	
			1	0 (-0.4, 0.3)	
			2	0 (-0.4, 0.3)	
Zeller, 2004, 15056029	330	1.5 [59]	2.7 (mean)	-0.1 (-0.2, 0.1)	3 (-1.2, 7.2)
Zeller, 2013 Conference abstract	34		1		4.0 (SD 16.8)

* Unless otherwise indicated

Table C.4.3. Results: Kidney function, within arm change, medication

Author, Year, PMID	N Baseline	Baseline SCr, Mean, mg/dL [GFR*]	Years	SCr Change (95% CI), mg/dL	GFR Change (95% CI), mL/min*
Arthurs, 2007, 17398382	22	[0.96, dL/mg (1/SCr)]	0.5		-0.1 (nd) dL/mg
			1		-0.1 (nd) dL/mg
			2		0.0 (nd) dL/mg
			3		0.1 (nd) dL/mg
			4		-0.3 (nd) dL/mg
Bax, 2009, 19414832	76	1.6 (0.58)	2	0.3 (0.14, 0.54)	
Cianci, 2011, 20547539	40	1.5	1	-0.1 (-0.2, -0.02)	
Dichtel, 2010, 20630131	71	[37]	1		-1.6 (-3.6, 0.4)
			2		-0.5 (-2.4, 1.4)
			3		-0.2 (-2.3, 1.9)
Hanzel, 2005, 16253607	40	1.3	1.75	0.1 (0.01, 0.2)	
Kalra, 2010, 19937777 [UK]	350	[35]	1		-2.7 (-4.4, -1.0)
Kane, 2010, 19666661	50	[37]	2.8 (median)		-7 (nd)
Losito, 2005, 15870215	54	1.7	4.5 (mean)	1.3 (0.6, 2.0)	
Marcantoni, 2012, 22495466	35	[60]	1		-0.7 (-5.4, 4.0)
Silva, 2008, 18670414	104	[33]	2		-1.0 (nd)
Sofroniadou, 2012, 22127407	10	[44]	1 to 3		1.0 (-7.8, 9.8)
			3 to 6		-9 (-50, 31)
			≥6		-8 (-31, 15)
Webster, 1998, 9655655 [Bilateral]	16	1.7	4.5	0 (-0.2, 0.3)	
Webster, 1998, 9655655 [Nonrandomized]	47	1.6	4.5	0 (-0.2, 0.3)	
Webster, 1998, 9655655 [Unilateral]	14	1.9	4.5	0 (-0.6, 0.6)	

Author, Year, PMID	N Baseline	Baseline SCr, Mean, mg/dL [GFR*]	Years	SCr Change (95% CI), mg/dL	GFR Change (95% CI), mL/min*
Wheatley, 2009, 19907042	403	2.0 [0.57, dL/mg (1/SCr)]	1	0.2 (0.04, 0.3)	
			5	0.1 (-0.2, 0.4)	-0.012 (nd) dL/mg per year
Zeller, 2013 Conference abstract	33		1		-2.0 (SD 14.4)

* Unless otherwise indicated

Table C.4.4. Results: Kidney function, within arm change, surgery

Author, Year, PMID	N Baseline	Baseline SCr, Mean, mg/dL [GFR*]	Years	SCr Change (95% CI), mg/dL	GFR Change (95% CI), mL/min*
Balzer, 2009, 19135837	27	1.3	1	0.1 (-0.2, 0.4)	
			4	0.1 (-0.2, 0.3)	
Cherr, 2002, 11854720	472	[41]	4.7 (mean)		7.1 (3.5, 10.7)
Patel, 2009, 9497511	45	2.2	1	-0.5 (-6.2, 5.2)	
			2.12	-0.5 (-0.926, -0.074)	

Table C.4.5. Results: Kidney function, between-arm differences

Author, Year, PMID	N Baseline	Years	SCr Net Change* [est, CI, P]	GFR Net Change*
PTRAS vs. Medication RCT				
Marcantoni, 2012 22495466	73	1		nd
Wheatley, 2009, 19907042	403	5	Mean slope: -3.05 mol/liter/year (-6.75, 0.65 P=0.11	Mean slope: 0.06 x 10^{-3} mol/liter/year (-0.002, 0.13) P=0.06
		1	3.53 (-12, 19.06) P=0.656	0 liter/mol (x1000) (-0.352, 0.352) P=1.0
		5	24.09 (-10.489, 58.669) P=0.172	
Zeller, 2013 Conference abstract	67	1		6.0 mL/min, P=0.228
PTRAS vs. Medication NRCS				
Dichtel, 2010, 20630131	118	1		P=0.137
		2		P=0.655
		3		P=0.548
Hanzel, 2005, 16253607	66		Nd	
Kalra, 2010 19937777	911			nd
Kane, 2010, 19666661	100	2.8		-2 (SE 3.55)
Sofroniadou, 2012 22127407	36			nd
PTRAS vs. Surgery RCT				
Balzer, 2009 19135837	49		Nd	
PTRAS vs. Surgery NRCS				
Patel, 2009, 9497511	262	1	P=0.6	Nd

Table C.4.6. Results: Kidney function, categorical outcomes, simple

Author, year, PMID	Outcome and description	Timepoint	Arm	N/N % (95% CI) n/N % (95% CI)	Between-Arm Comparison
PTRAS vs. Medication RCT					
Bax, 2009, 19414832	RRT	2 years	Medication only	0/68 0 (0, 12)	
			PTRAS	1/57 1.8 (0.2, 13)	
Cooper, 2014, 24245566	ESRD/RRT	1 year	Medication only	40/472 8.5 (6.0, 11)	
		2 years		73/472 15 (12, 19)	
		3 years		183/472 39 (34, 43)	
		3.6 years		8/472 1.7 (0.5, 2.9)	
		4 years		301/472 64 (59, 68)	
		5 years		397/472 84 (81, 87)	
		1 year	PTRAS	47/459 10 (7.5, 13)	
		2 years		69/459 15 (12, 18)	
		3 years		155/459 34 (29, 38)	
		3.6 years		16/459 3.5 (1.8, 5.2)	1.98 (0.85, 4.62) P=0.119
		4 years		271/459 59 (55, 64)	
		5 years		377/459 82 (79, 86)	
Wheatley, 2009, 19907042	Acute kidney failure	5 years	Medication only	23/392 5.9 (3.5, 8.2)	
			PTRAS	25/383 6.5 (4.1, 9.0)	OR 1.12 (0.62, 2.01) P=0.70
	ESRD/RRT	5 years	Medication only	31/392 7.9 (5.2, 11)	
			PTRAS	30/383 7.8 (5.1, 11)	OR 0.99 (0.59, 1.67)
Ziakka, 2008, 19016147	RRT	4 years	Medication only	8/46 17 (9.8, 45)	
			PTRAS	8/36 22 (13, 63)	OR 1.36 (0.45, 4.06)
PTRAS vs. Medication NRCS					

Author, year, PMID	Outcome and description	Timepoint	Arm	N/N % (95% CI) n/N % (95% CI)	Between-Arm Comparison
Dichtel, 2010, 20630131	ESRD/RRT	3 years	Medication only	9/71 13 (4.9, 20)	
			PTRAS	10/47 21 (9.6, 33)	OR 1.86 (0.69, 5.0)
Hanzel, 2005, 16253607	10% increase in total GFR	1.75	PTRAS vs. Medication only	nd	OR 7.94 (2.29, 27.6)
Kane, 2010, 19666661	ESRD/RRT [Progression to RRT]	2.8 years	Medication only	4/50 8.0 (0.5, 16)	
			PTRAS (comparative)	7/50 14 (4.4, 24)	OR 1.87 (0.51, 6.85) P=0.2
Ritchie, 2014, 24074824	ESRD/RRT	3.8 years	Medication only	60/340 18 (14, 22)	
			PTRAS	23/127 18 (11, 25)	OR 1.03 (0.61, 1.75)
Sofroniadou, 2012, 22127407	ESRD/RRT	5 years	Medication only	1/10 10 (1.4, 88)	
			PTRAS	3/26 12 (3.9, 43)	OR 1.17 (0.11, 12.82)
Arthurs, 2007, 17398382	Dialysis	15 months	Medication only	0/22 0 (0, 39)	
			PTRAS	0/18 0 (0, 48)	
Surgery vs. Medication RCT					
Uzzo, 2002, 12009679	Dialysis-free survival	6.2 years	Surgical vs. Medication only		P=0.64
PTRAS vs. Surgery NRCS					
Patel, 2009, 19497511	Dialysis	3 years	PTRAS	40/65 61 (49, 72)	OR 1.12 (0.38, 3.32) P=0.7
			surgical	10/17 59 (36, 78)	
PTRAS only					

Author, year, PMID	Outcome and description	Timepoint	Arm	N/N % (95% CI) n/N % (95% CI)	Between-Arm Comparison
Bersin, 2013, 22581488	Acute kidney failure [acute renal failure and worsening chronic kidney disease]	9 months	PTRAS	4/97 4.1 (0.2, 8.1)	
Cianci, 2013, 23467950	Acute kidney failure	1 year	PTRAS	1/53 1.9 (0.3, 14)	
Dangas, 2001, 11491257	ESRD/RRT	1.25 years	PTRAS	3/131 2.3 (0.7, 7.4)	
Kennedy, 2003, 14582036	Renal Event	21 months	PTRAS	32/230 14 (9.4, 18)	
Mannarino, 2012, 22260219	ESRD/RRT [ESRD]	2.75 years	PTRAS	7/30 23 (8.2, 38)	
Rzeznik, 2011, 21129903	Acute kidney failure [eGFR 60 mL/min]	0 years	PTRAS	48/84 57 (47, 68)	
		1 year	PTRAS	35/84 42 (31, 52)	
Trani, 2010, 20578190	ESRD/RRT	2 years	PTRAS	3/70 4.3 (1.4, 14)	
		3.7 years	PTRAS	3/70 4.3 (1.4, 14)	
Valluri, 2012, 21765186	ESRD/RRT [RRT]	2.9 years	PTRAS	19/127 15 (8.8, 21)	
Zeller, 2004, 15056029	RRT	2.7 years	PTRAS	4/330 1.2 (0.5, 3.3)	
	Rescue from RRT	2.7 years	PTRAS	8/nd	
Medication only					
Chrysochou, 2012, 21993376	ESRD/RRT	3.1 (median) years	Medication only	50/621 8.1 (5.9, 10)	
Losito, 2005, 15870215	ESRD/RRT	54.4 (mean) months	Medication only	7/54 13 (4.0, 22)	

Author, year, PMID	Outcome and description	Timepoint	Arm	N/N % (95% CI) n/N % (95% CI)	Between-Arm Comparison
Silva, 2008, 18670414	ESRD/RRT [ESRD or doubling creatinine]	3 years	Medication only	19/104 18 (11, 26)	
Webster, 1998, 9655655	ESRD/RRT	0 months	Medication only	0/30 0 (0, 28)	
		3-54 months	Medication only	2/30 6.7 (1.7, 30)	
Surgery only					
Cherr, 2002, 11854720	ESRD/RRT	4.67 years	Surgical	84/500 17 (14, 20)	

Table C.4.7. Results: Kidney function, categorical outcomes, multiple

Author, year, PMID	Time point	Arm	IMPROVED	NO CHANGE	STABILIZED	WORSE/ STABLE	WORSE	Between-Arm Comparison
PTRAS vs. Medication RCT								
Cooper, 2014, 24245566	3.6 years	Medication only				89/472 (19%)		
		PTRAS				77/459 (17%)		OR worse 1.15 (0.82, 1.61)
Wheatley, 2009, 19907042	1 year	Medication only	89/343 (26%)	121/343 (35%)			132/343 (38%)	
		PTRAS	95/329 (29%)	112/329 (34%)			122/329 (37%)	OR improved 1.16 (0.83, 1.63) OR worse 0.94 (0.69, 1.29)
Ziakka, 2008, 19016147	3.96 years	Medication only	0/46 (0%)	30/46 (65%)			16/46 (35%)	
		PTRAS	11/36 (31%)	12/36 (33%)			13/36 (36%)	OR worse 1.06 (0.43, 2.64)
Bax, 2009, 19414832	2 years	Medication only					16/74 (22%)	HR worse 0.73 (0.33, 1.61)
		PTRAS					10/62 (16%)	
PTRAS vs. Medication NRCS								
Kalra, 2010, 19937777	1 year	Medication only [UK]	48/257 (19%)	123/257 (48%)			86/257 (33%)	
		PTRAS [Germany]	91/348 (26%)	190/348 (55%)			67/348 (19%)	OR improved 1.54 (1.04, 2.29) OR worse 0.47 (0.33, 0.69)

Author, year, PMID	Time point	Arm	IMPROVED	NO CHANGE	STABILIZED	WORSE/ STABLE	WORSE	Between-Arm Comparison
		PTRAS [UK]	22/80 (28%)	37/80 (46%)			21/80 (26%)	OR improved 1.65 (0.92, 2.96) OR worse 0.71 (0.40, 1.24)
Kane, 2010, 19666661	2.8 years	Medication only	4/50 (8.0%)	29/50 (58%)			17/50 (34%)	
		PTRAS (comparative)	13/50 (26%)	23/50 (46%)			14/50 (28%)	OR improved 22.22 (6.88, 71.79) OR worse 0.28 (0.12, 0.65) P=NS
PTRAS vs. Surgery NRCS								
Patel, 2009, 9497511	1 year	PTRAS	35/147 (24%)	86/147 (59%)		26/147 (18%)		OR improved 0.29 (0.13, 0.66) OR worse 1.34 (0.43, 4.19) P=0.009
		Surgical	15/29 (52%)	10/29 (35%)		4/29 (14%)		
Patel, 2009, 9497511	1.68 years	PTRAS	17/90 (19%)	51/90 (57%)		22/90 (24%)		OR improved 0.31 (0.10, 1.01) OR worse 1.94 (0.40, 9.35) P=1.0
	2.12 years	Surgical	6/14 (43%)	6/14 (43%)		2/14 (14%)		
PTRAS only								
Beck, 2010, 19939607	1.5 years	PTRAS	21/129 (16%)	77/129 (60%)			31/129 (24%)	
Bruno, 2014, 24555729	1 year	PTRAS	89/97 (92%)			8/97 (8%)		
Cianci, 2013, 23467950	1 year	PTRAS	18/53 (34%)	18/53 (34%)			17/53 (32%)	
Dangas, 2001, 11491257	1.25 years	PTRAS	27/131 (21%)	80/131 (61%)			24/131 (18%)	
Gonçalves, 2007, 17364124	2 years	PTRAS	32/39 (82%) [improved or unchanged]				4/39 (10%)	
Gray, 2002, 12710843	1.78 years	PTRAS	20/39 (51%)	10/39 (26%)			9/39 (23%)	
Harden, 1997, 9113012	1.42 years	PTRAS			18/23 (78%)			
Holden, 2006, 16837918	0.5 years	PTRAS	25/63 (40%)	2/63 (3.2%)	36/63 (57%) [put together with No Change]			
Mannarino, 2012, 22260219	2.75 years	PTRAS	14/30 (47%)	6/30 (20%)			10/30 (33%)	

Author, year, PMID	Time point	Arm	IMPROVED	NO CHANGE	STABILIZED	WORSE/ STABLE	WORSE	Between-Arm Comparison
Rastan, 2008, 19110785	1 year	PTRAS	30/50 (60%)	11/50 (22%)			9/50 (19%)	
Sapoval, 2005, 16151060	0.5 years	PTRAS					2/48 (3.8%)	
Sapoval, 2010, 19908091	0.5 years	PTRAS	44/154 (29%)		87/154 (57%)		23/154 (15%)	
	1 year	PTRAS	22/97 (23%)		57/97 (59%)		18/97 (19%)	
Trani, 2013, 22503569	0.5 years	PTRAS				17/30 (57%)		
Valluri, 2012, 21765186	2.9 years	PTRAS	79/127 (62%)			48/127 (38%)		
Zahringer, 2007, 17696619	0.5 years	PTRAS				7/107 (6.5%)		
	2 years	PTRAS				6/105 (5.7%)		
van de Ven, 1999, 9929021	0.5 years	PTRAS	5/40 (13%)	26/40 (65%)			8/40 (20%)	
Rivolta, 2005, 16358234	1.67 years	PTRAS	8/52 (15.5%)	31/52 (59.5%)			13/52 (25%)	
Tsao, 2005, 16394602	0.5 years	PTRAS	8/53 (15%)	42/53 (79%)			3/53 (5.7%)	
Bersin, 2013, 22581488	9 months	PTRAS	10/84 (12%)				6/84 (7.1%)	
Henry, 2003, 14571477	2 years	PTRAS	6/28 (21%)	20/28 (71%)			2/28 (7.1%)	
	3 years	PTRAS	5/19 (26%)	12/19 (63%)			2/19 (11%)	
Surgery only								
Cherr, 2002, 11854720	4.67 years	Surgical	203/472 (43%)	222/472 (47%)			47/472 (10%)	

Table C.4.8. Results: Blood pressure, within-arm change, angioplasty with stent

Author, Year, PMID	N Baseline	Baseline SBP/DBP [MAP], Mean, mmHg	Followup, Years	SBP Change (95% CI), mmHg	DBP Change (95% CI), mmHg	MAP Change (95% CI), mmHg
Arthurs, 2007, 17398382	18	162/75	0.5	9 (-0.6, 18.5)	3 (-2.3, 8.2)	
			1	-10 (-19.3, -0.8)	3 (-2.3, 8.2)	
			2	-16 (-22.9, -9.1)	1 (-4.4, 6.4)	
			3	5 (-7.8, 17.7)	3 (-3.6, 9.6)	
			4	4 (-19, 27)	5 (-11, 20)	
Balzer, 2009, 19135837	22	170/88	1	-22 (-41, -3)	-5.1 (-14, 3.6)	
			4	-27 (-46, -8)	-10 (-19, -1.5)	
Bax, 2009, 19414832	64	160/83	2	-9 (-15, -2.1)	-6(-9.1, -2.8)	
Beck, 2010, 19939607	129	161/80	1.5 (mean)	-17 (-22, -12)	-7 (-9.3, -4.7)	
Bersin, 2013, 22581488	100	150/	0.75	-9.8 (-14.1, -5.6)	-2 (-3.9, -0.1)	
Blum, 1997, 9017938	68	[133]	0.5			-24 (-49, 1)
			1			-21 (-46, 4)
			2			-20 (-45, 5)
			3			-25 (-51, 1)
			4			-28 (-53, -3)
			5			-29 (-54, -4)
Christie, 2012, 23083664	83	196/100	2	-51 ()	-30 ()	
Chrysant, 2014, 24909590	202	162/78	0.75	-17 (-19.8, -14.2)	-3 (-4.7, -1.3)	
			2	-18 (-20.9, -15.1)	-4 (-5.7, -2.3)	
			3	-16 (-24.1, -7.9)	-3 (-5.5, -0.5)	
Cianci, 2011, 20547539	53	160/	1	-4.9 (-8.3, -1.5)		
Cooper, 2014, 24245566	459	150/	3.6 (mean)	-17 (-58, 25)		
Dangas, 2001, 11491257	131	170/84	1.25	-25 (-38, -12)	-10 (-15.1, -5.0)	
Dichtel, 2010, 20630131	47	145/75	1	-9 (-14.5, -3.6)	-3 (-6.4, 0.4)	

Author, Year, PMID	N Baseline	Baseline SBP/DBP [MAP], Mean, mmHg	Followup, Years	SBP Change (95% CI), mmHg	DBP Change (95% CI), mmHg	MAP Change (95% CI), mmHg
			2	-11 (-16.5, -5.6)	-4 (-7.2, -0.9)	
			3	-3 (-8.7, 2.7)	-1 (-4.4, 2.4)	
Dorros, 2002, 11835644	1058	168/84	1	-22 (-23.6, -20.5)	-9 (-9.8, -8.2)	
			4	-21 (-22.5, -19.5)	-6 (-6.8, -5.2)	
Gill-Leertouwer, 2002, 12223011	40	177/96	1	-19 (-27, -11)	-12 (-15.5, -8.5)	
Gill, 2003, 12601202	48	191/98	0.5	-26 (-46, -6)	-11 ()	
			1.5	-35 (-62, -8)	-15 ()	
			2	-27 (-48, -6)	-12 ()	
			3	-28 (-52, -4)	-16 ()	
			4	-39 (-69, -9)	-19 ()	
Girndt, 2007, 17164562	64	155/83	1	-13 (-17.8, -8.4)	-4.9 (-7.3, -2.5)	
Gonçalves, 2007, 17364124	44	177/98	2	-42 (-51, -33)	-15 (-19, -10)	
Gray, 2002, 12710843	39	174/85	1.8 (mean)	-26 (-35, -17)	-13 (-19.3, -6.7)	
Gross, 1998, 9736342	30	163/93 [117]	0.5	-18 (-23, -13)	-10 (-12.9, -7.1)	-18 (-22, -14)
Hanzel, 2005, 16253607	26	162/82	1.75	-15 (-26, -4)	-8 (-15.3, -0.8)	
Harden, 1997, 9113012	32	169/95	1.4 (mean)	-6 (-15.9, 4.3)	-8 (-13.9, -2.3)	
Henry, 2003, 14571477	56	169/104	1.9 (mean)	-19.3 (-20.0, -18.6)	-11 (-13, -10)	
Holden, 2006, 16837918	44	164/108	1.3 (mean)	-32 ()	-10 ()	
Iannone, 1996, 8974797	63	160/80	0.5	-10 (-19.1, -1.0)	0 ()	
			1	-15 (-25.3, -4.8)	0 ()	
Jaff, 2012, 22511402	202	162/78	0.75	-17 (-19.7, -14.3)	-3 (-6, 0)	

Author, Year, PMID	N Baseline	Baseline SBP/DBP [MAP], Mean, mmHg	Followup, Years	SBP Change (95% CI), mmHg	DBP Change (95% CI), mmHg	MAP Change (95% CI), mmHg
Kalra, 2010, 19937777 [Germany]	292	144/78	1	-9.9 (-12.2, -7.6)	-3.8 (-5.1, -2.5)	
Kalra, 2010, 19937777 [UK]	80	157/81	1	-13 (-20, -6)	-8.6 (-12.8, -4.4)	
Kane, 2010, 19666661	163	154/163	2.8 (median)	-28 (-35, -21)		
Kawarada, 2010, 20884436	61	152/81	0.6 (mean)	-13 (-19.0, -7.0)	-6 (-8.8, -3.2)	
Kennedy, 2003, 14582036	261	168/82	1.75	-19 (-22.2, -15.8)	-6 (-7.8, -4.2)	
Kobo, 2010, 20684176	41	164/82	2	-22 (-36, -8)	-5 (-8.7, -1.3)	
Leesar, 2009, 19539148	62	170/91	0.5	-32 (-36, -28)	-18 (-22, -14)	
			1	-31 (-36, -26)	-20 (-24, -16)	
Marcantoni, 2012, 22495466	38	134/74	1	-6 (-13.1, 1.1)	-2 (-5.3, 0.7)	
Patel, 2009, 9497511	217	150/74	1	-20 (-23.1, -16.8)	-5 (-6.7, -3.3)	
			1.68	-20 (-23.7, -16.2)	-5 (-7.1, -3.0)	
Ramos, 2003, 12472793	105	160/91	1	-15 (-23, -7)	-8 (-12.0, -4.0)	
Rastan, 2008, 19110785	50	148/78	1	-15 (-19, -11)	-6 (-8.7, -3.4)	
Rivolta, 2005, 16358234	52	161/86	1.7 (mean)	-18 (-32, -4)	-7 (-8.8, -5.2)	
Rocha-Singh, 1999, 10376497	127	[110]	1.1 (mean)			-14 (-22, -6)
Rocha-Singh, 2005, 16139124	208	168/82	0.75	-19 (-30, -8)	-5 (-8.0, -2.0)	
			2	-19 (-30, -8)	-5 (-8.0, -2.0)	

Author, Year, PMID	N Baseline	Baseline SBP/DBP [MAP], Mean, mmHg	Followup, Years	SBP Change (95% CI), mmHg	DBP Change (95% CI), mmHg	MAP Change (95% CI), mmHg
Rocha-Singh, 2008, 19006254	100	157/75	0.75	-8.6 (-13.4, -3.7)	-0.9 (-3.7, 1.9)	
			2	-14 (-20, -8)	-4.3 (-7.5, -1.0)	
			3	-16 (-23, -8)	-4.1 (-8.0, -0.3)	
Rocha-Singh, 2011, 21648052	248	179/83	0.75	-25 (-28, -22)	-7.0 (-8.5, -5.6)	
Ruchin, 2007, 17317314	89	162/78	2.3 (mean)	-23 (-28, -18)	-1.7 (-4.3, 0.9)	
Rzeznik, 2011, 21129903	84	135/	1	-6.6 (-11.4, -1.8)	-7.8 (-17.7, 2.1)	
Sapoval, 2005, 16151060	52	172/92	0.5	-20 (-27, -13)	-7 (-11.1, -2.9)	
Sapoval, 2010, 19908091	251	171/89	0.5	-29 (-44, -14)	-11 (-17, -5.5)	
			1	-30 (-45, -15)	-9 (-14, -4.5)	
Sofroniadou, 2012, 22127407	26	177/90	7.4 (mean)	-28 (-42, -13)	-13 (-20, -5)	
Staub, 2010, 20739200	120	148/81 [103]	0.5	-11 (-14.0, -8.0)	-26 (-28, -24)	-6 (-8.2, -3.8)
Tsao, 2005, 16394602	54	146/78	0.5	-15 (-17, -13)	-7 (-8.0, -6.0)	
van de Ven, 1999, 9929021	40	180/105	0.5	-20 ()	-15 ()	
Wheatley, 2009, 19907042	385	149/76	1	-3.1 (-5.6, -0.6)	-3 (-4.2, -1.7)	
			5	-7.6 (-12.8, -2.4)	-3 (-5.8, -0.9)	
White, 1997, 9362400	100	173/88	0.5	-27 (-37, -17)	-2 (-4.8, 0.4)	
Zahringer, 2007, 17696619	105	166/89	0.5	-19	-8	
			1	-24	-8	
			2	-27	-2	
Zeller, 2004, 15056029	340	[102]	0.5			-9 (-10.4, -7.6)

Author, Year, PMID	N Baseline	Baseline SBP/DBP [MAP], Mean, mmHg	Followup, Years	SBP Change (95% CI), mmHg	DBP Change (95% CI), mmHg	MAP Change (95% CI), mmHg
			1			-9 (-10.3, -7.7)
			2			-11 (-12.5, -9.5)
			3			-10 (-11.6, -8.4)
			2.7 (mean)			-8 (-12.0, -4.0)
Zeller, 2013 Conference abstract	34		1	141 (Final)	79 (Final)	

Table C.4.9. Results: Blood pressure, within-arm change, medication

Author, Year, PMID	N Baseline	Baseline SBP/DBP [MAP], Mean, mmHg	Followup, Years	SBP Change (95% CI), mmHg	DBP Change (95% CI), mmHg	MAP Change (95% CI), mmHg
Arthurs, 2007, 17398382	22	142/73	0.5	-10 (-18, -2.4)	-11 (-17, -5)	
			1	-6 (-14, 2)	-4 (-10, 2)	
			2	4 (-7, 15)	0 (-6, 6)	
			3	-25 (-33, -17)	-7 (-15, 0.7)	
			4	-5 (-38, 28)	5 (-20, 30)	
Bax, 2009, 19414832	76	163/82	2	-8 (-14, -2)	-3 (-5.6, -0.3)	
Cianci, 2011, 20547539	40	155/	1	-7 (-9, -5)		
Cooper, 2014, 24245566	472	150/	3.6 (mean)	-16 (-66, 35)		
Dichtel, 2010, 20630131	71	141/70	1	-4 (-10, 2.3)	-1 (-4, 2)	
			2	-4 (-9, 1)	0 (-3, 3)	
			3	-7 (-14, -0.3)	-1 (-4, 2)	
Hanzel, 2005, 16253607	40	154/77	1.75	-11 (-19, -2.9)	-5 (-9.7, -0.3)	
Kalra, 2010, 19937777 [UK]	245	156/80	1	-5.9 (-9.4, -2.4)	-4.8 (-6.6, -3.0)	
Kane, 2010, 19666661	163	148/163	2.8 (median)	-9 (-16, -1)		
Losito, 2005, 15870215	54	160/89	4.5 (mean)	-11 (-15, -7)	-7.7 (-10.0, -5.4)	

Author, Year, PMID	N Baseline	Baseline SBP/DBP [MAP], Mean, mmHg	Followup, Years	SBP Change (95% CI), mmHg	DBP Change (95% CI), mmHg	MAP Change (95% CI), mmHg
Marcantoni, 2012, 22495466	35	132/75	1	-6 (-12, -0.5)	-6 (-10, -2)	
Safak, 2013, 23321402	171	137/78	9	-7 ()	-2 ()	
Silva, 2008, 18670414	104	167/95	2	-22 (-31, -13)	-13 (-18, -8)	
Sofroniadou, 2012, 22127407	26	147/77	7.4 (mean)	-18 (-30, -5)	-9 (-15, -3)	
Webster, 1998, 9655655 [Bilateral]	16	179/93	4.5	-8 ()	-2 ()	
Webster, 1998, 9655655 [Unilateral]	79	175/98	4.5	-11 ()	-12 ()	
Wheatley, 2009, 19907042	388	152/76	1	-3.9 (-6.4, -1.3)	-1.2 (-2.5, 0.1)	
			5	-10.8 (-16.3, -5.2)	-5.5 (-8.4, -2.7)	
Zeller, 2013 Conference abstract	33		1	140 (Final)	75 (Final)	

Table C.4.10. Results: Blood pressure, within-arm change, surgery

Author, Year, PMID	N Baseline	Baseline SBP/DBP [MAP], Mean, mmHg	Followup, Years	SBP Change (95% CI), mmHg	DBP Change (95% CI), mmHg	MAP Change (95% CI), mmHg
Balzer, 2009, 19135837	27	169/87	1	-21 (-38, -4)	-3.0 (-5.5, -0.4)	
			4	-31 (-49, -13)	-4.0 (-13.8, 5.7)	
Cherr, 2002, 11854720	472	201/104	4.7 (mean)	-53 (-80, -26)	-23 (-35, -11)	
Patel, 2009, 9497511	45	160/77	1	-30 (-36.7, -23.3)	-7 (-10.7, -3.3)	
			2.12	-30 (-39, -21)	-12 (-16.2, -7.8)	

Table C.4.11. Results: Blood pressure, between-arm differences

Author, Year, PMID	N Baseline	Years	SBP Net Change* [est, CI, P]	DBP Net Change*	MAP Net Change*
PTRAS vs. Medication RCT					
Bax, 2009, 19414832	125	2	-0.5 (-11, 10) NS	-3.0 (-8.1, 2.1) NS	
Cooper, 2014, 24245566	931	3.6	-2.3 (-4.4, -0.2) P=0.03	nd	
Marcantoni, 2012 22495466	73	1	0 (-8.7, 8.7) NS	3.7 (-1.3, 8.7) NS	
Scarpioni, 2009 Conference abstract	52	3.6 (mean)	[P=0.53]	[P=0.22]	
Wheatley, 2009, 19907042	672	1	0.72 (-2.84, 4.28) P=0.69	-1.71 (-3.52, 0.10) P=0.064	
		5	3.16 (-4.43, 10.75) P=0.415	2.16 (-1.61, 5.93) P=0.261	
PTRAS vs. Medication NRCS					
Dichtel, 2010, 20630131	118	1	-5 (-15, 5) P=0.329	-2 (-7, 3) P=0.428	
		2	-7 (-16, 2) P=0.146	-4 (-10, 2) P=0.182	
		3	4 (-15, 23) P=0.682	0 (-4, 4) P=0.946	
Hanzel, 2005, 16253607	40	1.75	-6 (-19, 7) NS	-3 (--11, 5) NS	
Kalra, 2010 19937777 [UK cohorts]	325	1	-7.1 (-13.4, -0.8)	-3.8 (-7.5, -0.1)	
Kane, 2010, 19666661	100	2.8 (median)	-19 (-26, -12)	nd	
Sofroniadou, 2012 22127407	36	7.4	Final values: 19.6 (4.0, 35.2) P=0.014	Final values: 8.8 (1.6, 16.0) P=0.016	
Arthurs, 2007, 17398382	36	0.5	19 (6, 32)	14 (6, 22)	
	33	1	-4 (-17, 9)	7 (-1, 15)	
	29	2	-20 (-33, -7)	1 (-7, 9)	

Author, Year, PMID	N Baseline	Years	SBP Net Change* [est, CI, P]	DBP Net Change*	MAP Net Change*
	21	3	30 (13, 46)	10 (-1, 21)	
PTRAS vs. Surgery RCT					
Balzer, 2009 19135837	49	1 and 4	nd	nd	
PTRAS vs. Surgery NRCS					
Patel, 2009, 9497511	262	1	P=NS	nd	

Table C.4.12. Results: Blood pressure/hypertension, categorical outcomes, simple

Author, year, PMID	Outcome description	Timepoint	Arm	N/N % (95% CI)	Between-Arm Comparison
PTRAS vs. Medication RCT					
Bax, 2009, 19414832	HTN [Therapy-refractory hypertension]	2 years	Medication only	3/74 4.1 (1.3, 13)	
			PTRAS	0/62 0 (0, 13)	
	Malignant HTN/HTNsive crisis	2 years	Medication only	0/74 0 (0, 11)	
			PTRAS	0/62 0 (0, 13)	
Scarpioni, 2009 Conference abstract	HTN cure	3.6 years	Medication only	0/24 0 (0, 36)	
			PTRAS	0/28 0 (0, 30)	
Surgery vs. Medication RCT					
Uzzo, 2002, 12009679	Uncontrollable HTN	6.2 years	Surgical vs. Medication only		P=0.20
PTRAS only					
Kennedy, 2003, 14582036	HTN	21 months	PTRAS	9/230 3.9 (1.4, 6.4)	

Table C.4.13. Results: Blood pressure/hypertension, categorical outcomes, multiple

Author, year. PMID	Timepoint	Arm	CURED	IMPROVED	NO CHANGE	STABILIZED	WORSE/ STABLE	WORSE	Between-Arm Comparison
PTRAS vs. Medication RCT									
Ziakka, 2008, 19016147	4 years (mean)	Medication only	0/46 (0.0%)	33/46 (72%)			13/46 (28%)		
Ziakka, 2008, 19016147	4 years (mean)	PTRAS	4/36 (11%)	24/36 (67%)			8/36 (22%)		OR cured/improved 1.38 (0.31, 2.03) OR worse/stable 0.11 (0.04, 0.31)
Bax, 2009, 19414832	2 (years)	Medication only	20/68 (29%)						P=0.95
		PTRAS	18/57 (32%)						
Surgery vs. PTRAS RCT									
Balzer, 2009, 19135837	1 and 4 years	PTRAS	2/22 (9%)	14/22 (64%)			6/22 (27%)		OR cured/improved 0.61 (0.16, 2.34) OR worse/stable 1.65 (0.43, 6.37)
		Surgical	2/27 (7%)	20/27 (74%)			5/27 (19%)		
Surgery vs. PTRAS NRCS									
de Donato, 2007, 17653002	3.1 years	PTRAS	15/83 (18%)	33/83 (40%)	20/83 (25%)			14/83 (17%)	OR cured 0.88 (0.22, 3.52) OR worse 0.81 (0.20, 3.26) P=NS
		Surgical	3/15 (20%)	5/15 (33%)	4/15 (27%)			3/15 (20%)	
Patel, 2009, 9497511	1 year	PTRAS	12/138 (9%)	90/138 (65%)			36/138 (26%)		OR cured/improved 0.35 (0.12, 1.07) OR worse/stable 2.82 (0.93, 8.54)
		Surgical	3/36 (8%)	29/36 (81%)			4/36 (11%)		
	1.68 years	PTRAS	4/75 (5%)	51/75 (68%)			20/75 (27%)		OR cured/improved 0.37 (0.08, 1.75) OR worse/stable 2.73 (0.57, 13.0)
	2.12years	Surgical	0/17 (0%)	15/17 (88%)			2/17 (12%)		
PTRAS only									

Author, year. PMID	Timepoint	Arm	CURED	IMPROVED	NO CHANGE	STABILIZED	WORSE/ STABLE	WORSE	Between-Arm Comparison
Beck, 2010, 19939607	2 years	PTRAS		68/129 (53%)					
Beck, 2010, 19939607.	1 year	PTRAS		66/129 (51%)					
Beck, 2010, 19939607.	4 years	PTRAS		76/129 (59%)					
Blum, 1997, 9017938	2.25 years	PTRAS	11/68 (16%)	42/68 (62%)	15/68 (22%)				
Bruno, 2014, 24555729	1 year	PTRAS		32/97 (33%)			65/97 (67%)		
Gill, 2003, 12601202	2.1 year	PTRAS	2/48 (4.2%)	38/48 (79%)	8/48 (17%)				
Gonçalves, 2007, 17364124	2 years	PTRAS		19/44 (44%)	4/44 (9.1%)				
Gray, 2002, 12710843	1.78 years	PTRAS		28/39 (72%)				11/39 (28%)	
Gross, 1998, 9736342	0.5 years	PTRAS		20/29 (69%)	9/29 (31%)				
Henry, 2003, 14571477	1.88 years	PTRAS	10/56 (19%)	33/56 (62%)	13/56 (25%)				
Iannone, 1996, 8974797	1 year	PTRAS	2/54 (3.7%)	19/54 (35%)	29/54 (54%)			4/54 (7.4%)	
Kobo, 2010, 20684176	2 years	PTRAS	9/41 (22%)	27/41 (64%)	6/41 (14%)				
Leesar, 2009, 19539148	1 year	PTRAS		39/62 (63%)					
Leesar, 2009, 19539148	0.5 years	PTRAS		42/62 (68%)					
Rastan, 2008, 19110785	1 year	PTRAS		32/50 (64%)	17/50 (33%)				
Rzeznik, 2011 21129903	1 year	PTRAS		32/84 (38%)	40/84 (48%)			12/84 (14%)	
Sapoval, 2005, 16151060	6 months	PTRAS	29/48 (61%)	2/48 (4.2%)			16/48 (34%)		
Sapoval, 2010, 19908091	6 months	PTRAS	8/164 (4.9%)	127/164 (77.4%)					
	1 year	PTRAS	6/111 (5.7%)	79/111 (70.8%)					
Staub, 2010, 20739200	6 months	PTRAS		65/120 (54%)					

Author, year. PMID	Timepoint	Arm	CURED	IMPROVED	NO CHANGE	STABILIZED	WORSE/ STABLE	WORSE	Between-Arm Comparison
van de Ven, 1999, 9929021	0.5 years	PTRAS	6/40 (15%)	17/40 (43%)			17/40 (43%)		
Zahringer, 2007, 17696619	0.5 years	PTRAS	2/53 (3.8%)	28/53 (53%)	23/53 (43%)				
Zahringer, 2007, 17696619	0.5 years	PTRAS	3/52 (5.8%)	32/52 (61%)	17/52 (34%)				
Zahringer, 2007, 17696619	0.5 years	PTRAS	5/105 (4.8%)	60/105 (57%)	40/105 (38%)				
Zeller, 2004, 15056029	2.67 years (mean)	PTRAS		152/330 (46%)	142/330 (43%)			36/330 (11%)	

Table C.4.14. Results: Number of medications

Author, Year, PMID	Arm	N baseline	Mean baseline, No. Rx	Years	Within arm Change, No. Rx	Between arm Change, No. Rx
PTRAS vs. Medication RCT						
Cooper, 2014, 24245566	Medication only	472	2.1	3.6	1.4 (1.3, 1.5)	
	PTRAS	83	2.8	3.6	1.2 (1.1, 1.3)	-0.2 (-0.397, -0.003) P=0.046
Wheatley, 2009, 19907042	Medication only	403	2.8	1	0.17	
	PTRAS	403	2.79	1	-0.02	-0.19 (nd)
PTRAS vs. Medication NRCS						
Arthurs, 2007, 17398382	Medication only	22	4 (median)	1	1 (chg median)	
				2	2 (chg median)	
				3	3 (chg median)	
				4	4 (chg median)	
	PTRAS	18	3.5 (median)	0.5	-0.5 (chg median)	
				1	0.5 (chg median)	
				2	0.5 (chg median)	
				3	0.5 (chg median)	
				4	0.5 (chg median)	
Dichtel, 2010, 20630131	Medication only	71	4.7	1	-0.3 (-0.9, 0.3)	
				2	-0.1 (-0.8, 0.6)	
				3	-0.7 (-1.6, 0.2)	
	PTRAS	47	3.9	1	-0.2 (-0.9, 0.5)	P=0.048
				2	0.5 (-0.05, 1.0)	P=0.581
				3	1.2 (0.2, 2.2)	P=0.291
Hanzel, 2005, 16253607	Medication only	40	2.2	1.75	0 (-0.4, 0.4)	
	PTRAS	26	3.1	1.75	-0.4 (-0.9, 0.1)	
Kane, 2010, 19666661	Medication only	50	3.5	2.8	0.2 (0.01, 0.4)	
	PTRAS (comparative)	50	3.6	2.8	-0.6 (-0.9, -0.3)	P<0.01
PTRAS only						

Author, Year, PMID	Arm	N baseline	Mean baseline, No. Rx	Years	Within arm Change, No. Rx	Between arm Change, No. Rx
PTRAS vs. Medication RCT						
Cooper, 2014, 24245566	Medication only	472	2.1	3.6	1.4 (1.3, 1.5)	
	PTRAS	83	2.8	3.6	1.2 (1.1, 1.3)	-0.2 (-0.397, -0.003) P=0.046
Wheatley, 2009, 19907042	Medication only	403	2.8	1	0.17	
	PTRAS	403	2.79	1	-0.02	-0.19 (nd)
PTRAS vs. Medication NRCS						
Arthurs, 2007, 17398382	Medication only	22	4 (median)	1	1 (chg median)	
				2	2 (chg median)	
				3	3 (chg median)	
				4	4 (chg median)	
Beck, 2010, 19939607	PTRAS	129	3.1	1.49	-0.3 (-0.6, -0.02)	
Bersin, 2013, 22581488	PTRAS	100	2.5	0.75	-0.2 (-0.4, 0.03)	
Christie, 2012, 23083664	PTRAS	83	2.8	2	-0.2 (nd)	
Dangas, 2001, 11491257	PTRAS	131	2.2	1.25	-0.2 (-0.2, -0.2)	
Dorros, 2002, 11835644	PTRAS	1058	2.4	1	-0.5 (-0.6, -0.4)	
				4	-0.4 (-0.5, -0.3)	
Gill-Leertouwer, 2002, 12223011	PTRAS	40	3.4	1	-0.6 (-1.0, -0.2)	
Girndt, 2007, 17164562	PTRAS	64	2.6	1	-0.1 (-0.5, 0.3)	
Gonçalves, 2007, 17364124	PTRAS	40	3.075	2	-0.8 (-1.2, -0.5)	
Gray, 2002, 12710843	PTRAS	39	3.0	1.78	-0.2 (-0.3, -0.1)	
Gross, 1998, 9736342	PTRAS	30	3.2	0.5	-0.4 (-0.4, -0.4)	
Harden, 1997, 9113012	PTRAS	32	1.6	1.42	-1.4 (-4.7, 1.9)	
Henry, 2003, 14571477	PTRAS	56	2.31	1.88	-1.12 (-1.15, -1.09)	
Iannone, 1996, 8974797	PTRAS	63	2.5	1	-0.3 (-0.6, -0.04)	
Kawarada, 2010, 20884436	PTRAS	61	2.2	0.6	-0.1 (-0.2, 0.00)	
Kennedy, 2003, 14582036	PTRAS	261	2.3	1.75	0.1 (-0.04, 0.2)	

Author, Year, PMID	Arm	N baseline	Mean baseline, No. Rx	Years	Within arm Change, No. Rx	Between arm Change, No. Rx
PTRAS vs. Medication RCT						
Cooper, 2014, 24245566	Medication only	472	2.1	3.6	1.4 (1.3, 1.5)	
	PTRAS	83	2.8	3.6	1.2 (1.1, 1.3)	-0.2 (-0.397, -0.003) P=0.046
Wheatley, 2009, 19907042	Medication only	403	2.8	1	0.17	
	PTRAS	403	2.79	1	-0.02	-0.19 (nd)
PTRAS vs. Medication NRCS						
Arthurs, 2007, 17398382	Medication only	22	4 (median)	1	1 (chg median)	
				2	2 (chg median)	
				3	3 (chg median)	
				4	4 (chg median)	
Kobo, 2010, 20684176	PTRAS	41	3.0	2	-0.7 (-1.0, -0.3)	
Leesar, 2009, 19539148	PTRAS	62	2.76	0.5	0 (-0.2, 0.2)	
				1	0.2 (-0.01, 0.5)	
Rastan, 2008, 19110785	PTRAS	50	3.0	1	-0.3 (-0.7, 0.1)	
Rivolta, 2005, 16358234	PTRAS	52	2.28	1.67	-0.3 (-0.5, -0.03)	
Rocha-Singh, 1999, 10376497	PTRAS	140	2.9	1.1	-1.0 (-1.8, -0.2)	
Rocha-Singh, 2005, 16139124	PTRAS	208	2.8	0.75	-0.4 (-0.6, -0.2)	
				2	-0.5 (-0.8, -0.2)	
Ruchin, 2007, 17317314	PTRAS	89	3.14	2.3	-0.5 (-0.8, -0.2)	
Rzeznik, 2011, 21129903	PTRAS	84	3.2	1	-0.4 (-0.6, -0.2)	
Staub, 2010, 20739200	PTRAS	120	2.9	0.5	-0.3 (-0.5, -0.1)	
Trani, 2010, 20578190	PTRAS	70	2.2	2	-0.5 (-0.8, -0.2)	
Tsao, 2005, 16394602	PTRAS	54	2.8	0.5	0 (nd)	
van de Ven, 1999, 9929021	PTRAS	40	1.8	0.5	-0.3 (nd)	
White, 1997, 9362400	PTRAS	100	2.6	0.5	-0.6 (-0.8, -0.4)	
Zahringer, 2007, 17696619	PTRAS	105	2.06	0.5	-0.5 (nd)	

Author, Year, PMID	Arm	N baseline	Mean baseline, No. Rx	Years	Within arm Change, No. Rx	Between arm Change, No. Rx
PTRAS vs. Medication RCT						
Cooper, 2014, 24245566	Medication only	472	2.1	3.6	1.4 (1.3, 1.5)	
	PTRAS	83	2.8	3.6	1.2 (1.1, 1.3)	-0.2 (-0.397, -0.003) P=0.046
Wheatley, 2009, 19907042	Medication only	403	2.8	1	0.17	
	PTRAS	403	2.79	1	-0.02	-0.19 (nd)
PTRAS vs. Medication NRCS						
Arthurs, 2007, 17398382	Medication only	22	4 (median)	1	1 (chg median)	
				2	2 (chg median)	
				3	3 (chg median)	
				4	4 (chg median)	
				2	-0.4 (nd)	
Zeller, 2004, 15056029	PTRAS	340	3.06	2.67 (mean)	-0.3 (-0.4, -0.2)	

Table C.4.15. Results: Medications, categorical outcomes, simple

Author, year, PMID	Outcome and description	Timepoint	Arm	N/N % (95% CI)	Between-Arm Comparison
PTRAS vs. Medication RCT					
Marcantoni, 2012, 22495466	Rx: ACEi/ARB use	0 years	Medication only	33/42 79 (66, 91)	
		1 year		29/35 83 (70, 95)	
		0 years	PTRAS	34/43 79 (67, 91)	OR 1.03 (0.36, 2.92) P=0.9
		1 year		31/38 82 (69, 94)	OR 0.92 (0.28, 3.05) P=0.8
Wheatley, 2009, 19907042	Rx: ACEi/ARB dose	0 years	Medication only	146/383 38 (33, 43)	
		1 years		nd 43 (nd)	
		0 years	PTRAS	174/373 47 (42, 52)	P = 0.02
		1 year		nd 50 (nd)	P = 0.05
PTRAS only					
Chrysant, 2014, 24909590	Rx: >=3 Anti-HTN drugs	9 months	PTRAS	133/202 66 (59, 72)	
		3 years		138/202 68 (62, 75)	
		2 years		141/202 70 (63, 76)	
		0 months		143/202 71 (65, 77)	
	Rx: ACEi/ARB use	3 years		141/202 70 (63, 76)	
		2 years		150/202 74 (68, 80)	
		0 months		154/202 76 (70, 82)	
		9 months		154/202 76 (70, 82)	
Gray, 2002, 12710843	Rx: ACEi/ARB use	0 years	PTRAS	6/39 15 (4.1, 27)	
		1.78 years		19/39 49 (33, 64)	
Rzeznik, 2011, 21129903	Rx: ACEi/ARB use	0 years	PTRAS	52/84 62 (52, 72)	
		1 year		50/84 60 (49, 70)	

Table C.4.16. Results: Medications, categorical outcomes, multiple

Author, year. PMID	Time point	Arm	IMPROVED	NO CHANGE	STABILIZED	WORSE/ STABLE	WORSE
Dangas, 2001, 11491257	1.25 years	PTRAS	17/131 (13%)	30/131 (40%)			63/131 (48%)
Rzeznik, 2011, 21129903	1 year	PTRAS	6/84 (7.1%)				26/84 (31%)

Table C.4.17. Results: Cardiovascular events

Author, year, PMID	Outcome and description	Timepoint	Arm	N/N % (95% CI)	Between-Arm Comparison
PTRAS vs. Medication RCT					
Cooper, 2014, 24245566	MI	1 year	Medication only	47/472 10 (7.3, 13)	
		2 years		83/472 18 (14, 21)	
		3 years		187/472 40 (35, 44)	
		4 years		296/472 63 (58, 67)	
		5 years		391/472 83 (79, 86)	
		1 year	PTRAS	56/459 12 (9.2, 15)	
		2 years		82/459 18 (14, 21)	
		3 years		174/459 38 (33, 42)	
		4 years		283/459 62 (57, 66)	
		5 years		378/459 82 (79, 86)	OR 0.97 (0.69, 1.36)
	MI [presence of clinical symptoms or electrocardiographic changes and elevated cardiac markers]	3.6 years	Medication only	37/472 7.8 (5.4, 10)	
		3.6 years	PTRAS	40/459 8.7 (6.1, 11)	HR 1.09 (0.70, 1.71) P=0.7
	Stroke [focal neurological deficit defined by imaging or clinical characteristics]	1 year	Medication only	44/459 9.6 (6.9, 12)	
		2 years		24/459 5.2 (3.2, 7.3)	
		3 years		85/459 19 (15, 22)	
		3.6 years		16/459 3.5 (1.8, 5.2)	
		4 years		118/459 26 (22, 30)	

Author, year, PMID	Outcome and description	Timepoint	Arm	N/N % (95% CI)	Between-Arm Comparison
		5 years		105/459 23 (19, 27)	
		1 year	PTRAS	45/472 9.5 (6.9, 12)	
		2 years		34/472 7.2 (4.9, 9.5)	
		3 years		114/472 24 (20, 28)	
		3.6 years		23/472 4.9 (2.9, 6.8)	OR 0.71 (0.37, 1.35)
		4 years		114/472 24 (20, 28)	
		5 years		92/472 19 (16, 23)	
Wheatley, 2009, 19907042	Angina [Hospitalization]	5 years	Medication only	34/395 8.6 (5.8, 11)	
			PTRAS	29/386 7.5 (4.9, 10)	OR 0.86 (0.51, 1.45)
	Coronary artery procedure (e.g. CABG or PCTA)	5 years	Medication only	16/395 4.1 (2.1, 6.0)	
			PTRAS	15/386 3.9 (2.0, 5.8)	OR 0.96 (0.47, 1.97)
	MI	5 years	Medication only	37/395 9.4 (6.5, 12)	
			PTRAS	36/386 9.3 (6.4, 12)	OR 1.00 (0.61, 1.61)
	Stroke	5 years	Medication only	23/395 5.8 (3.5, 8.1)	
			PTRAS	24/386 6.2 (3.8, 8.6)	OR 1.07 (0.59, 1.93)
Scarpioni, 2009 Conference abstract	Cardiovascular event-free survival (not defined)	3.6 years year	Medication only	27 (SD 18) months	
			PTRAS	27 (SD 18) months	
PTRAS vs. Medication NRCS					
Arthurs, 2007, 17398382	Stroke	2 years	Medication only	0/22 0 (0, 39)	
			PTRAS	1/18 5.6 (0.8, 44)	
	MI	2 years	Medication only	1/22	
			PTRAS	3/18	HR 0.338 (0.069, 1.668) P=0.183
Kane, 2010, 19666661	Coronary revascularization	2.8 years	Medication only	11/50 22 (11, 33)	
			PTRAS (comparative)	7/50 14 (4.4, 24)	OR 0.58 (0.20, 1.64)
Sofroniadou, 2012, 22127407	Angina	7.4 years	Medication only	0/10 0 (0, 93)	

Author, year, PMID	Outcome and description	Timepoint	Arm	N/N % (95% CI)	Between-Arm Comparison
			PTRAS	1/26 3.8 (0.5, 30)	
	MI	7.4 years	Medication only	0/10 0 (0, 93)	
			PTRAS	2/26 7.7 (2.0, 35)	
	AAA rupture	7.4 years	Medication only	1/10 10 (1.4, 88)	
			PTRAS	0/26 0 (0, 33)	
PTRAS only					
Dangas, 2001, 11491257	Coronary artery procedure (e.g. CABG or PCTA) [CABG]	1.25 years	PTRAS	5/131 3.8 (0.5, 7.1)	
	MI	1.25 years	PTRAS	6/131 4.6 (1.0, 8.2)	
Hanzel, 2005, 16253607	MI	1.75 years	PTRAS	1/26 3.8 (0.5, 30)	
	Stroke	1.75 years	PTRAS	2/26 7.7 (2.0, 35)	
Kennedy, 2003, 14582036	MI	21 months	PTRAS	24/230 10 (6.5, 14)	
Kennedy, 2003, 14582036	Stroke	21 months	PTRAS	15/230 6.5 (3.3, 9.7)	
Murphy, 2014, 24325931	Stroke	9 months	PTRAS	1/181 0.6 (0.1, 4.0)	
Rzeznik, 2011, 21129903	MI	1 year	PTRAS	3/84 3.6 (1.2, 12)	
	Stroke	1 year	PTRAS	1/84 1.2 (0.2, 8.7)	
Staub, 2010, 20739200	MI	6 months	PTRAS	2/122 1.6 (0.4, 6.7)	
Trani, 2010, 20578190	MI	2 years	PTRAS	0/70 0 (0, 12)	
		3.7 mean years	PTRAS	2/70 2.9 (0.7, 12)	
	Stroke	2 years	PTRAS	0/70 0 (0, 12)	
		3.7 years	PTRAS	0/70 0 (0, 12)	
Zahringer, 2007, 17696619	MI	2 years	PTRAS	1/105 1.0 (0.1, 6.9)	
Medication only					
Hanzel, 2005, 16253607	MI	1.75 years	Medication only	1/40 2.5 (0.4, 19)	
	Stroke	1.75 years	Medication only	1/40 2.5 (0.4, 19)	

Author, year, PMID	Outcome and description	Timepoint	Arm	N/N % (95% CI)	Between-Arm Comparison
Webster, 1998, 9655655	Stroke	3-54 months	Medication only	4/30 13 (1.2, 25)	
Surgery only					
Alhadad, 2004, 14718896	Cardiac event	1 month years	Surgical	4/106 3.8 (0.1, 7.4)	
	Cardiac event	1 month years	Surgical	1/106 0.9 (0.1, 6.8)	
Cherr, 2002, 11854720	Angina	10 years	Surgical	49/500 9.8 (7.2, 12)	
	Coronary artery procedure (e.g. CABG or PCTA)	10 years	Surgical	41/500 8.2 (5.8, 11)	
	MI	10 years	Surgical	29/500 5.8 (3.8, 7.8)	
	Stroke	10 years	Surgical	22/500 4.4 (2.6, 6.2)	

Table C.4.18. Results: Congestive heart failure

Author, year, PMID	Outcome and description	Timepoint	Arm	N/N % (95% CI)	Between-Arm Comparison
PTRAS vs. Medication RCT					
Bax, 2009, 19414832	Flash pulmonary edema	2 years	Medication only	1/74 1.4 (0.2, 9.9)	
			PTRAS	0/62 0 (0, 13)	
Cooper, 2014, 24245566	CHF event	1 year	Medication only	50/472 11 (7.8, 13)	
		2 years		89/472 19 (15, 22)	
		3 years		195/472 41 (37, 46)	
		4 years		314/472 67 (62, 71)	
		5 years		406/472 86 (83, 89)	
		1 year	PTRAS	53/459 12 (8.6, 14)	
		2 years		79/459 17 (14, 21)	
		3 years		165/459 36 (32, 40)	
		4 years		282/459 61 (57, 66)	
		5 years		383/459 83 (80, 87)	OR 0.82 (0.57, 1.17)
	CHF: Hospitalization [if the patient was hospitalized for 12 hours or longer because of documented signs and symptoms of heart failure and received intravenous therapy (vasodilators, diuretics, or inotropes) during the hospital stay]	3.6 years	Medication only	39/459 8.5	
			PTRAS	39/472 8.3	OR 1.03 (0.64, 1.56) P=0.99
PTRAS vs. Medication NRCS					
Kane, 2010, 19666661	CHF Hospitalization	2.8 years	Medication only	23/50 46	
			PTRAS	11/50 22	OR 0.33 (0.14, 0.79) P<0.005
Sofroniadou, 2012, 22127407	CHF event	7.4 years	Medication only	1/10 10 (1.4, 88)	
			PTRAS	1/26 3.8 (0.5, 30)	OR 0.36 (0.02, 6.38)

Author, year, PMID	Outcome and description	Timepoint	Arm	N/N % (95% CI)	Between-Arm Comparison
PTRAS only					
Kennedy, 2003, 14582036	CHF event	21 months	PTRAS	46/230 20 (15, 25)	
Murphy, 2014, 24325931	CHF event	9 months	PTRAS	6/181 3.3 (1.5, 7.7)	
Medication only					
Webster, 1998, 9655655	CHF event	0 months	Medication only	0/30 0 (0, 28)	
		3-54 months	Medication only	4/30 13 (1.2, 25)	

Table C.4.19. Results: Composite major adverse events

Author, year, PMID	Outcome and description	Timepoint	Arm	N/N % (95% CI)	Between-Arm Comparison
PTRAS vs. Medication RCT					
Cooper, 2014, 24245566	Composite: MACE [Events from composite MAE]	1 year	Medication only	101/472 21 (18, 25)	
		2 years		158/472 33 (29, 38)	
		3 years		258/472 55 (50, 59)	
		4 years		357/472 76 (72, 80)	
		5 years		432/472 92 (89, 94)	
		1 year	PTRAS	97/459 21 (17, 25)	
		2 years		141/459 31 (26, 35)	
		3 years		235/459 51 (47, 56)	
		4 years		328/459 71 (67, 76)	
		5 years		400/459 87 (84, 90)	
	Composite: MACE [death from cardiovascular or renal causes, stroke, myocardial infarction, hospitalization for congestive heart failure, progressive renal insufficiency, or permanent renal-replacement therapy (Primary endpoint)]	3.6 years	Medication only	169/472 36 (31, 40)	
			PTRAS	161/459 35 (31, 39)	HR 0.94 (0.76, 1.17) P=0.58
Wheatley, 2009, 19907042	CVD: CV event (composite) [MI, stroke, CV death, hospitalization for angina, fluid overload or cardiac failure, coronary-artery revascularization, or another peripheral arterial procedure.]	5 years	Medication only	145/395 37 (32, 41)	
			PTRAS	141/386 37 (32, 41)	HR 0.94 (0.75, 1.19) P=0.61
PTRAS vs. Medication NRCS					
Ritchie, 2014, 24074824	CVD: CV event (composite)	3.8 years	Medication only	110/340 32 (27, 37)	
			PTRAS	45/127 35 (27, 44)	OR 1.15 (0.75, 1.76)
PTRAS only					
Bersin, 2013, 22581488	Composite: MACE [Death, Q-wave myocardial infarction, clinically-driven target lesion revascularization, significant embolic events]	1 months	PTRAS	0/100 0 (0, 8.1)	
		9 months	PTRAS	2/92 2.2 (0.5, 9.0)	

Author, year, PMID	Outcome and description	Timepoint	Arm	N/N % (95% CI)	Between-Arm Comparison
Gill-Leertouwer, 2002, 12223011	Overall: BP & SCr improvement [Clinical success defined as 1) normalization or a >= 10 mm decrease in DBP with the same or fewer defined daily doses of antihypertensive medication in pts treated for HTN, 2) normalization (<1.25 mg/dL) or a >= 20% decrease of serum creatinine in pts treated for renal function impairment, and 3) in pts treated for both HTN and renal impairment, normalization of or a >= 10 mm decrease in DBP with the same or fewer defined daily doses of antihypertensive medication and/or normalization (<1.25 mg/dL) or a >=20% decrease of serum creatinine in pts treated for renal function impairment]	1 year	PTRAS	27/40 68 (53, 82)	
Gonçalves, 2007, 17364124	CVD: any outcome	2 years	PTRAS	0/46 0 (0, 18)	
Murphy, 2014, 24325931	Composite: MAE	9 months	PTRAS	16/181 9 (6, 16)	
Rocha-Singh, 2005, 16139124	Composite: MAE	2 years	PTRAS	41/208 20 (14, 25)	
Rzeznik, 2011, 21129903	CVD: CV event (composite)	1 year	PTRAS	12/84 14 (6.8, 22)	
Sapoval, 2010, 19908091	Composite: MAE [Not defined]	1 year	PTRAS	16/251 6.4 (3.4, 9.4)	
Trani, 2010, 20578190	Composite MAE	3.7 mean years	PTRAS	11/70 16 (7.2, 24)	
		2 years	PTRAS	5/70 7.1 (1.1, 13)	
Medication only					
Chrysochou, 2012, 21993376	Composite: Death, CV event, RRT [ACE-I/ARB as time-varying covariate]	3.1 (median) years	Medication only	259/621 42 (38, 46)	
		3.1 (median) years	Medication only	259/621 42 (38, 46)	
	CVD: CV event (composite) [ACE-I/ARB as time-varying covariate]	3.1 (median) years	Medication only	73/621 12 (9.2, 14)	
		3.1 (median) years	Medication only	73/621 12 (9.2, 14)	
Webster, 1998, 9655655	Composite: Death, CV event, RRT [Death, MI, Dialysis]	3-54 months	Medication only	4/30 13 (1.2, 25)	
Surgery only					
Alhadad, 2004, 14718896	deterioration or death	1 month years	Surgical	19/106 18 (11, 25)	

Table C.4.20. Results: Periprocedural adverse events

Author, year, PMID	Outcome description	Timepoint	Arm	N/N % (95% CI)	Notes	Between-Arm Comparison
PTRAS vs. Medication RCT						
Bax, 2009, 19414832	Death	30 (within) (days)	Medication only	0/74 0 (0, 11)		
			PTRAS	2/62 3.2 (0.8, 14)		
	Major periprocedural event: femoral artery false aneurysms	30 (within) (days)	PTRAS	2/62 3.2 (0.8, 14)		
	Major periprocedural event: cholesterol embolization	30 (within) (days)	PTRAS	1/62 1.6 (0.2, 11.8)		
Cooper, 2008, 18490527	Bleed, major	1 month	PTRAS [4 arms of PTRAS]	28/91 31 (21, 40)		
Wheatley, 2009, 19907042	Major periprocedural event	1 month	PTRAS	30/280 11 (7.1, 14)		
	Major periprocedural event: Renal artery occlusion	1 month	PTRAS	1/280 0 (0.1, 2.6)		
	Major periprocedural event: Renal arterial thrombosis or occlusion	1 day	PTRAS	4/335 1.2 (0, 2.4)		
Surgery vs. PTRAS RCT						
Balzer, 2009, 19135837	Major periprocedural event [local dissection]	0 years	Surgical	1/27 3.7 (0.5, 28.3)		
	Major periprocedural event [stent dislocation]	0 years	PTRAS	2/22 9.1 (2.3, 42.8)		OR 2.60 (0.22, 30.75)
PTRAS vs. Medication NRCS						
Arthurs, 2007, 17398382	Death	0 years	Medication only	0/22 0 (0, 0.4)		
			PTRAS	2/18 11 (2.9, 54)		
Ritchie, 2014, 24074824	Major periprocedural complication	3.8 years	PTRAS	6/127 4.7 (1.0, 8.4)		

Author, year, PMID	Outcome description	Timepoint	Arm	N/N % (95% CI)	Notes	Between-Arm Comparison
Surgery vs. PTRAS NRCS						
de Donato, 2007, 17653002	Death	1 month	PTRAS	0/82 0 (0, 9.9)		
			Surgical	0/15 0 (0, 59)		
Patel, 2009, 19497511	Death	0 years	PTRAS	1/203 0.5 (0.1, 3.5)		OR 0.23 (0.01, 3.71)
			Surgical	1/47 2 (0.3, 15.8)		
Patel, 2009, 19497511	Major periprocedural event [Hematoma]	0 years	PTRAS	8/203 3.9 (2, 8)		OR 1.89 (0.23, 15.47)
			Surgical	1/47 2 (0.3, 15.8)		
Patel, 2009, 19497511	Major periprocedural event [Contrast nephropathy, Pseudoaneurysm]	0 years	PTRAS	12/203 6 (3, 11)		
	Major periprocedural event [Pneumonia, HIT, Re-exploration for bleeding, Wound infection]		Surgical	7/47 15 (8, 39)		
PTRAS only						
Beck, 2010, 19939607	Major periprocedural event [Acute renal insufficiency]	0 years	PTRAS	3/129 2.3 (0.8, 7.5)		
	Major periprocedural event [Acute thrombosis]	0 years	PTRAS	3/129 2.3 (0.8, 7.5)		
	Major periprocedural event [Renal artery dissection]	0 years	PTRAS	5/129 3.9 (0.5, 7.2)		
	Major periprocedural event: Renal hemorrhage	0 years	PTRAS	2/129 1.6 (0.4, 6.4)		
Blum, 1997, 9017938	Major periprocedural event	0 years	PTRAS	0/68 0 (0, 12)	No major complications	
Cianci, 2013, 23467950	Death	0 years	PTRAS	1/53 1.9 (0.3, 14)		
Dangas, 2001, 11491257	Major periprocedural event: Emergency Surgical	0 years	PTRAS	0/131 0 (0, 6.2)		

Author, year, PMID	Outcome description	Timepoint	Arm	N/N % (95% CI)	Notes	Between-Arm Comparison
	Post-procedure dialysis	0 years	PTRAS	2/131 1.5 (0.4, 6.3)		
	Death	0 years	PTRAS	1/131 0.8 (0.1, 5.5)	Had aortocoronary bypass during same hospitalization	
Gill, 2003, 12601202	Major periprocedural event: femoral artery false aneurysm requiring US guided compression (1) or surgery (1), acute on chronic kidney disease requiring 1 week of HD (1), removal of stent with femoral artery trauma requiring surgery (2), surgical retrieval of a migrating stent (1)	0 years	PTRAS	6/100 6.0 (1.3, 11)		
	Death	0 years	PTRAS	2/100 2.0 (0.5, 8.3)		
Gonçalves, 2007, 17364124	Major periprocedural event: renal artery dissection	2 years	PTRAS	1/46 2.2 (0.3, 16)		
Gross, 1998, 9736342	Major periprocedural event	0 years	PTRAS	3/30 10 (3.4, 37)	Dissection after predilatation	
Hanzel, 2005, 16253607	Bleed, major: blood transfusion	0 years	PTRAS	1/26 3.8 (0.5, 30)	blood transfusion was required in 1 patient	
Harden, 1997, 9113012	Major periprocedural event	0 years	PTRAS	0/32 0 (0, 26)	(3 femoral-artery pseudoaneurysms, which were successfully treated with ultrasound-guided compression)	
	Bleed, major	0 years	PTRAS	3/32 9.4 (3.2, 34)	hemorrhage, which required transfusion. Despite surgical intervention, 1 patient died 3 days after stent placement from circulatory collapse due to uncontrolled hemorrhage from a brachial puncture site.	
Henry, 2003, 14571477	Major periprocedural event	0 years	PTRAS	0/56 0 (0, 15)	(2 had arterial spasm at site of protection devices)	
	Death	3 days	PTRAS	1/56 1.8 (0.3, 13)		

Author, year, PMID	Outcome description	Timepoint	Arm	N/N % (95% CI)	Notes	Between-Arm Comparison
Holden, 2006, 16837918	Major periprocedural event	0 years	PTRAS	1/44 2.3 (0.3, 17)	One patient with mild CKD at baseline suffered acute deterioration of kidney function after the procedure. Partial response was seen after repeated boluses of NTG	
Iannone, 1996, 8974797	Bleed, major, requiring transfusion	0 years	PTRAS	10/63 16 (6.8, 25)		
	Major periprocedural event	0 years	PTRAS	21/63 33 (22, 45)	Bleed requiring transfusion (10), renal artery perforation (3), acute renal failure (8).	
	Death	0 years	PTRAS	2/63 3.2 (0.8, 13)	1 after heart surgery after stent; 1 temporary dialysis, perinephric bleed and multi-system organ failure	
Jokhi, 2009, 19668788	Death	0 years	PTRAS	0/106 0 (0, 7.7)		
	Major periprocedural complications	1 month	PTRAS	0/106 0 (0, 7.7)		
Leesar, 2009, 19539148	Bleed, major	0 years	PTRAS	2/62 3.2 (0.8, 14)	femoral artery pseudoaneurysm	
Murphy, 2014, 24325931	Dissection	9 months	PTRAS	11/239 4.6 (2.6, 8.8)		
	Embolus			9/239 4 (2, 8)		
	Occlusion			9/239 4 (2, 8)		
	pseudoaneurysm			1/239 0.4 (0.1, 3.0)		
	Thrombus			3/239 1.3 (0.4, 4)		
	Vessel rupture			2/239 0.8 (0.2, 3.4)		
Ramos, 2003, 12472793	Bleed, major	0 years	PTRAS	3/105 2.9 (0.9, 9.3)	2 cases of bleeding and 1 case of right peri-renal hematoma	
Rastan, 2008, 19110785	Major periprocedural event	1 month	PTRAS	0/50 0 (0, 16)		

Author, year, PMID	Outcome description	Timepoint	Arm	N/N % (95% CI)	Notes	Between-Arm Comparison
Rocha-Singh, 1999, 10376497	Major periprocedural event: Restenosis; renal parenchymal guidewire perforations; death(renal parenchymal; guidewire perforation); massive GI hemorrhage; contrast induced nephropathy	1.1 years	PTRAS	30/154 19 (13, 26)		
Rocha-Singh, 2008, 19006254	Death	1 month	PTRAS	0/100 0 (0, 8.1)		
Ruchin, 2007, 17317314	Bleed, major: periprocedural complication	0 years	PTRAS	2/89 2.2 (0.6, 9.3)		
	Major periprocedural complication	0 years	PTRAS	4/89 4.5 (0.2, 8.8)		
Rzeznik, 2011 21129903	Bleed, major	0 years	PTRAS	2/84 2.4 (0.6, 9.9)	Transfusion 1, renal hematoma 1	
	Emergency procedure	0 years	PTRAS	1/84 1.2 (0.2, 8.7)	acute lower limb ischemia requiring urgent surgery	
Sapoval, 2005, 16151060	Major periprocedural event	0 years	PTRAS	1/52 1.9 (0.3, 14)	cerebrovascular event	
Staub, 2010, 20739200	Major periprocedural event: procedural complications	0 years	PTRAS	4/122 3.3 (0.1, 6.4)		
Trani, 2010, 20578190	Major periprocedural event	0 years	PTRAS	0/70 0 (0, 12)		
Tsao, 2005, 16394602	Death	0 years	PTRAS	1/54 1.9 (0.3, 14)	One patient died of acute renal failure on day 3 due to contrast overdose	
Valluri, 2012, 21765186	Bleed, major: hematoma at the puncture site leading to infection and lower limb amputation	1 month	PTRAS	1/127 0.8 (0.1, 5.7)		
	Post-procedure dialysis	1 month	PTRAS	4/127 3.1 (0.1, 6.2)	AKI leading to permanent HD	
	Death	0 years	PTRAS	1/127 0.8 (0.1, 5.7)		

Author, year, PMID	Outcome description	Timepoint	Arm	N/N % (95% CI)	Notes	Between-Arm Comparison
van de Ven, 1999, 9929021	Major periprocedural event: Cholesterol embolism; femoral artery aneurysm (arteriovenous fistula); renal artery injury (dissection; occlusion / thrombosis); transient decrease in renal function due to radiography contrast agent	0 years	PTRAS	10/85 12 (4.9, 19)	Femoral artery aneurysm (arteriovenous fistula) (n=5); renal artery injury (dissection; occlusion / thrombosis) (n=5). Also minor: Cholesterol embolism (n=8); transient decrease in renal function due to radiography contrast agent (n=1)	
White, 1997, 9362400	Major periprocedural event	0 years	PTRAS	0/100 0 (0, 8.1)	In 1: Subacute stent thrombosis occurred 3 d after stent placement (but no clinical sequelae described)	
	Death, CV	2 days	PTRAS	1/100 1.0 (0.1, 7.2)	Sudden ischemic cardiac death 2 days after hospital discharge	
Zahringer, 2007, 17696619.	Major periprocedural event	0 years	PTRAS	1/105 1.0 (0.1, 6.9)	One patient in the SES group had a severe flow-obstructing renal artery dissection and lost his single functional kidney despite all reasonable interventional and surgical efforts to re-establish flow.	
Zeller, 2005, 16212462.	Bleed, major: large hematomas	0 years	PTRAS	2/125 1.6 (0.4, 6.6)		
	Death	0 years	PTRAS	1/125 0.8 (0.1, 5.8)	due to pulmonary embolism after immobilization for compression of false aneurysm	
Medication only						
Hanzel, 2005, 16253607	Bleed, major: blood transfusion	0 years	Medication only	0/40 0 (0, 21)		
Surgery only						
Alhadad, 2004, 14718896	Death	1 month	Surgical	10/106 9.4 (3.9, 15)		

Author, year, PMID	Outcome description	Timepoint	Arm	N/N % (95% CI)	Notes	Between-Arm Comparison
Cherr, 2002, 11854720	Major periprocedural event	0 years	Surgical	83/500 17 (13, 20)	Peri-operative morbidity: 16%, MI (15 pts), stroke (5 pts), significant arrhythmia (22 pts), pneumonia (36 pts). 5 pts had worsening renal function within 1 month that required permanent dialysis	
	Death	1 month	Surgical	23/500 4.6 (2.8, 6.4)		

Appendix D. Risk of Bias Assessment

Table D.1. Risk of bias: Randomized controlled trials

Author, Year, PMID	1a*	1c*	2a*	2b*	3b*	3c*	3d*	3e*	3f*	3g*	3h*	4a*
Balzer, 2009, 19135837	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
Bax, 2009, 19414832	Low	Low	Low	Low	Low	High	Low	High	Low	High	Low	Low
Cooper, 2014, 24245566	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	High (multiple protocol changes)
Marcantoni, 2012, 22495466	Unclear	Low	Low	Low	Low	Low	Low	High	Low	High	Low	Low
Scarpioni, 2009 Conference abstract	Unclear	High	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low	Low	High	High (incomplete conference abstract)
Uzzo, 2002, 12009679	Low	Low	Unclear	Unclear	Low	Low	Unclear	Low	Low	Low	Low	Low
Wheatley, 2009, 19907042	Low	Low	Low	Low	Low	Low	Low	High	Low	Low	Low	High (specific interventions at physician discretion)
Zeller,	Hig	Uncl	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low	Low	High	High (data

2013 Conference abstract	h	ear										from 1 of 4 countries, terminated trial, incomplete conference abstract)
Ziakka, 2008, 19016147	Uncl ear	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low

1a. Sampling: Were the subjects in the study representative of the entire population from which they were recruited?

1b. Sampling: Comparability of cohorts on the basis of the design or analysis

1c. Sampling: Group similarity at baseline (selection bias): Selection bias due to dissimilarity at baseline for the most important prognostic indicators

1d. Sampling: Selection of the comparator (Medicine) cohort

2a. Selection: Random sequence generation (selection bias): Selection bias (biased allocation to interventions) due to inadequate generation of a randomized sequence

2b. Selection: Allocation concealment (selection bias): Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment

3a. Measurement: Ascertainment of exposure

3b. Measurement: Co-interventions (performance bias): Performance bias because co-interventions were different across groups

3c. Measurement: Blinding of outcome assessor (detection bias): Detection bias due to knowledge of the allocated interventions by outcome assessors

3d. Measurement: Intention-to-treat-analysis: Bias due to incomplete reporting and analysis according to group allocation

3e. Measurement: Incomplete outcome data (attrition bias): Attrition bias due to amount, nature or handling of incomplete outcome data

3f. Measurement: Timing of outcome assessments (detection bias): Detection bias because important outcomes were not measured at the same time across groups

3g. Measurement: Do the analyses adjust for different lengths of follow-up of patients?

3h. Measurement: Selective Reporting (reporting bias): Reporting bias due to selective outcome reporting

4a. Additional Bias: Bias due to problems not covered elsewhere in the table.

Table D.2. Risk of bias: Nonrandomized comparative studies

Author, Year, PMID	Study Design	1a*	1b*	1c*	1d*	3a*	3b*	3c*	3e*	3f*	3g*	3h*	4a*
Arthurs, 2007, 17398382	Retrospective	Low	Low	High	Low	Low	Low	Low	High	Low	Low	Low	Low
Cianci, 2011, 20547539	Prospective	Low	High	Low	Low	N/A	Low	Low	Low	Low	Low	High	Low
Crutchley, 2009, 18951751	Retrospective	Unclear	High	Unclear	Low	Low	Unclear	Low	High	Low	Low	Unclear	Low
de Donato, 2007, 17653002	Prospective	Low	Low	Unclear	Low	Low	Low	High	Low	Low	Low	Low	Low
Dichtel, 2010, 20630131	Retrospective	Low	High	Low	Low	Low	Unclear	Low	Low	High	High	Low	Low
Hackam, 2011 21156722	Retrospective	Low	N/A	N/A	N/A	Low	N/A	N/A	Low	N/A	High	Low	Low
Hanzel, 2005, 16253607	Retrospective	Low	High	High	Low	N/A	Low	Low	Low	Low	Low	Low	Low
Kalra, 2010, 19937777	Prospective	Unclear	High	High	High	Low	High	Low	Low	Low	Low	Unclear	Low
Kane, 2010, 19666661	Retrospective	Low	Low	Low	Low	Low	Low	High	Low	Low	High	Low	Low

Author, Year, PMID	Study Design	1a*	1b*	1c*	1d*	3a*	3b*	3c*	3e*	3f*	3g*	3h*	4a*
Losito, 2005 15870215	Prospective	Low	Low	Low	Low	N/A	Unclear	Low	Low	Low	Low	Low	Low
Patel, 2009, 19497511	Retrospective	Low	Low	High	Low	Unclear	Unclear	Low	High	High	Low	Low	Low
Ritchie, 2014, 24074824	Prospective	Low	Low	High	Low	Low	Low	Low	High	Low	Low	High	Low
Sofroniadou, 2012, 22127407	Prospective	Low	High	High	Low	N/A	Low	Low	High	High	High	High	Low

1a. Sampling: Were the subjects in the study representative of the entire population from which they were recruited?

1b. Sampling: Comparability of cohorts on the basis of the design or analysis

1c. Sampling: Group similarity at baseline (selection bias): Selection bias due to dissimilarity at baseline for the most important prognostic indicators

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3a. Measurement: Ascertainment of exposure

3b. Measurement: Co-interventions (performance bias): Performance bias because co-interventions were different across groups

3c. Measurement: Blinding of outcome assessor (detection bias): Detection bias due to knowledge of the allocated interventions by outcome assessors

3d. Measurement: Intention-to-treat-analysis: Bias due to incomplete reporting and analysis according to group allocation

3e. Measurement: Incomplete outcome data (attrition bias): Attrition bias due to amount, nature or handling of incomplete outcome data

3f. Measurement: Timing of outcome assessments (detection bias): Detection bias because important outcomes were not measured at the same time across groups

3g. Measurement: Do the analyses adjust for different lengths of follow-up of patients?

3h. Measurement: Selective Reporting (reporting bias): Reporting bias due to selective outcome reporting

4a. Additional Bias: Bias due to problems not covered elsewhere in the table.

Table D.3. Risk of bias: Single-arm studies

Author, Year, PMID	Study Design	1a*	3e*	3g*	3h*	4a*
Alhadad, 2004, 14718896	NRCS of surgery	Low	Low	High	Low	Low
Baril, 2007, 17391902	Prospective	Low	Low	Low	Unclear	Low
Beck, 2010, 19939607	Retrospective	Low	Low	Low	Low	Low
Bersin, 2013, 22581488	Prospective	Low	Low	Low	Low	Low
Blum, 1997, 9017938	Prospective	Low	High	High	Low	Low
Bruno, 2014, 24555729	Prospective	Low	Low	Low	Low	Low
Cherr, 2002, 11854720	Prospective	Low	Low	Low	Low	Low
Christie, 2012, 23083664	Prospective	High	Low	Low	Unclear	Low
Chrysant, 2014, 24909590	Prospective	Low	Low	Low	Low	Low
Chrysochou, 2012, 21993376	Prospective	Low	High	Low	Low	Low

Author, Year, PMID	Study Design	1a*	3e*	3g*	3h*	4a*
Cianci, 2013, 23467950	Prospective	High	High	Low	High	Low
Cooper, 2008, 18490527	RCT of PTRAS	Low	Low	Low	Low	Low
Dangas, 2001, 11491257	Prospective	Low	High	High	High	Low
Dorros, 2002, 11835644	Prospective	Low	High	Low	High	Low
Galaria, 2005, 15735947	Retrospective NRCS of surgery	Low	High	Low	High	Low
Gill, 2003, 12601202	Prospective	Low	High	High	Low	Low
Gill-Leertouwer, 2002, 12466252	Prospective	Low	Low	Low	Low	Low
Girndt, 2007, 17164562	Prospective	High	High	High	Low	Low
Gonçalves, 2007, 17364124	Prospective	Low	High	High	High	High
Gray, 2002, 12710843	Prospective	Low	High	High	Unclear	Low

Author, Year, PMID	Study Design	1a*	3e*	3g*	3h*	4a*
Gross, 1998, 9736342	Prospective	Low	Low	Low	High	Low
Harden, 1997, 9113012	Prospective	Low	High	Low	Low	Low
Henry, 2003, 14571477	Prospective	Low	High	High	Low	Low
Holden, 2006, 16837918	Prospective	Low	Low	High	Low	Low
Iannone, 1996, 8974797	Prospective	Unclear	Low	High	Low	Low
Jaff, 2012, 22511402	Prospective	Low	Low	Low	Low	Low
Jokhi, 2009, 19668788	Prospective	Low	Unclear	Low	High	Low
Kawarada, 2010, 20884436	Prospective	Low	Low	High	Low	Low
Kennedy, 2003, 14582036	Prospective	Low	High	Low	Low	Low
Kobo, 2010, 20684176	Prospective	High	Low	Low	Low	Low

Author, Year, PMID	Study Design	1a*	3e*	3g*	3h*	4a*
Leesar, 2009, 19539148	Prospective	Unclear	Low	High	High	Low
Lekston, 2008, 19006027	RCT of PTRAS	Unclear	High	High	High	High
Mannarino, 2012, 22260219	Prospective NRCS of PTRAS	High	Low	High	Low	Low
Murphy, 2014, 24325931	Prospective	Low	High	Low	Low	High
Ramos, 2003, 12472793	Prospective	High	Low	Low	Low	Low
Rastan, 2008, 19110785	Prospective	Low	Low	High	Low	Low
Rivolta, 2005, 16358234	Prospective	Low	High	Low	High	Low
Rocha-Singh, 1999, 10376497	Prospective	Low	Low	Low	Low	Low
Rocha-Singh, 2005, 16139124	Prospective	Low	Low	High	Low	Low
Rocha-Singh, 2008, 19006254	Prospective	Low	High	Low	High	Low

Author, Year, PMID	Study Design	1a*	3e*	3g*	3h*	4a*
Rocha-Singh, 2011, 21648052	Prospective	Low	Low	High	Low	Low
Ruchin, 2007, 17317314	Retrospective	Low	Low	High	Low	Low
Rzeznik, 2011 21129903	Prospective	Low	Low	Low	Low	Low
Safak, 2013, 23321402	Prospective	Low	Low	High	Unclear	Low
Sapoval, 2005, 16151060	Prospective	Low	Low	Low	Low	Low
Sapoval, 2010, 19908091	Prospective	Low	High	High	Low	High
Silva, 2008, 18670414	Retrospective NRCS of medication	Low	Low	Low	Unclear	Low
Staub, 2010, 20739200	Prospective	Low	Low	Low	Low	Low
Trani, 2010, 20578190	Prospective NRCS of PTRAS	Low	Low	Low	Low	Low
Trani, 2013, 22503569	Prospective	Low	Low	Low	Low	Low

Author, Year, PMID	Study Design	1a*	3e*	3g*	3h*	4a*
Tsao, 2005, 16394602	Prospective	Low	Low	Low	High	Low
Valluri, 2012, 21765186	Prospective	High	Low	High	Low	Low
van de Ven, 1999, 9929021	RCT of PTRAS	Low	Low	Low	Low	Low
Webster, 1998, 9655655	RCT of medication	Low	High	High	Low	Low
White, 1997, 9362400	Prospective	Low	High	High	High	Low
Zahringer, 2007, 17696619	Prospective NRCS of PTRAS	Low	Low	Low	Low	High
Zeller, 2004, 15056029	Prospective	Low	High	High	Low	Low
Zeller, 2005, 16212462	Prospective	Low	Low	High	High	High

1a. Sampling: Were the subjects in the study representative of the entire population from which they were recruited?

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3g. Measurement: Do the analyses adjust for different lengths of follow-up of patients?

3h. Measurement: Selective Reporting (reporting bias): Reporting bias due to selective outcome reporting

4a. Additional Bias: Bias due to problems not covered elsewhere in the table.

Figure D.1. Risk of bias in RCTs

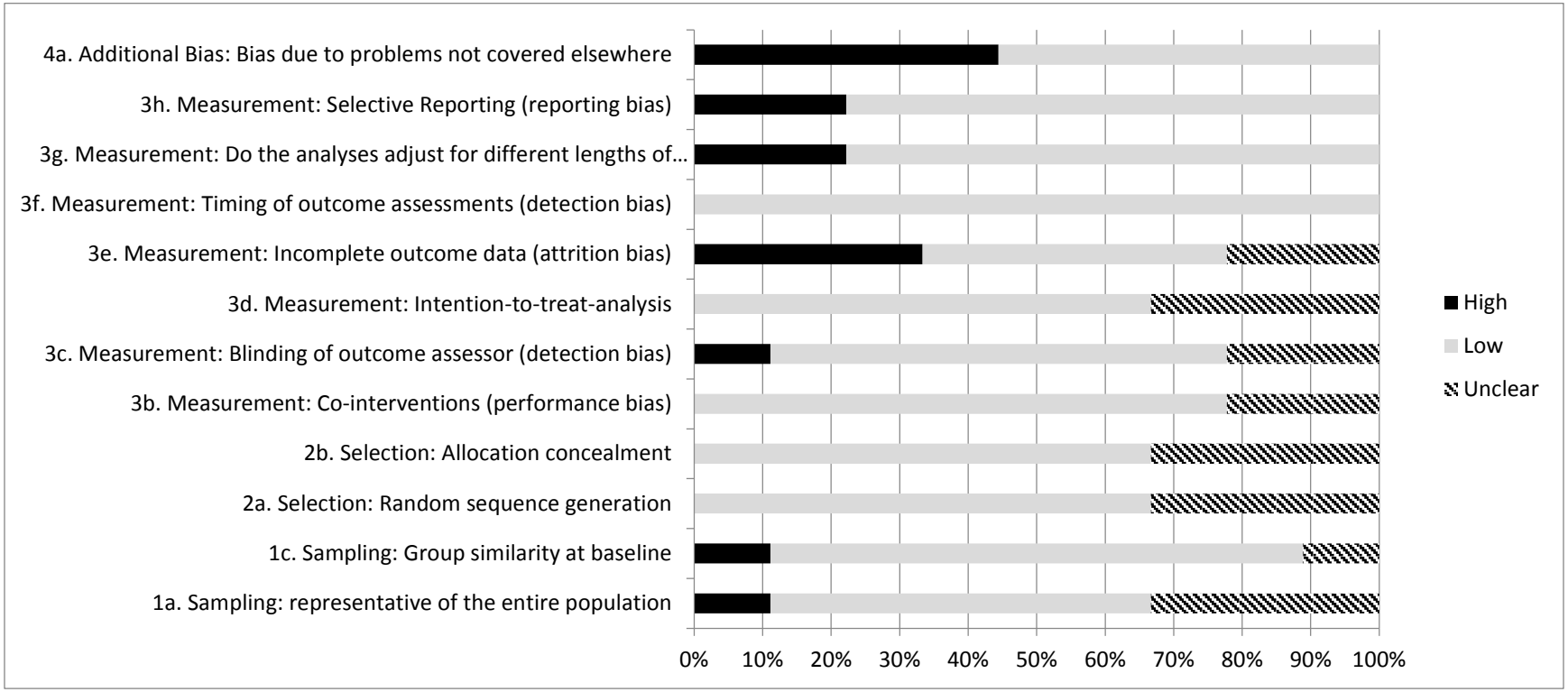

Figure D.2. Risk of bias in NRCS

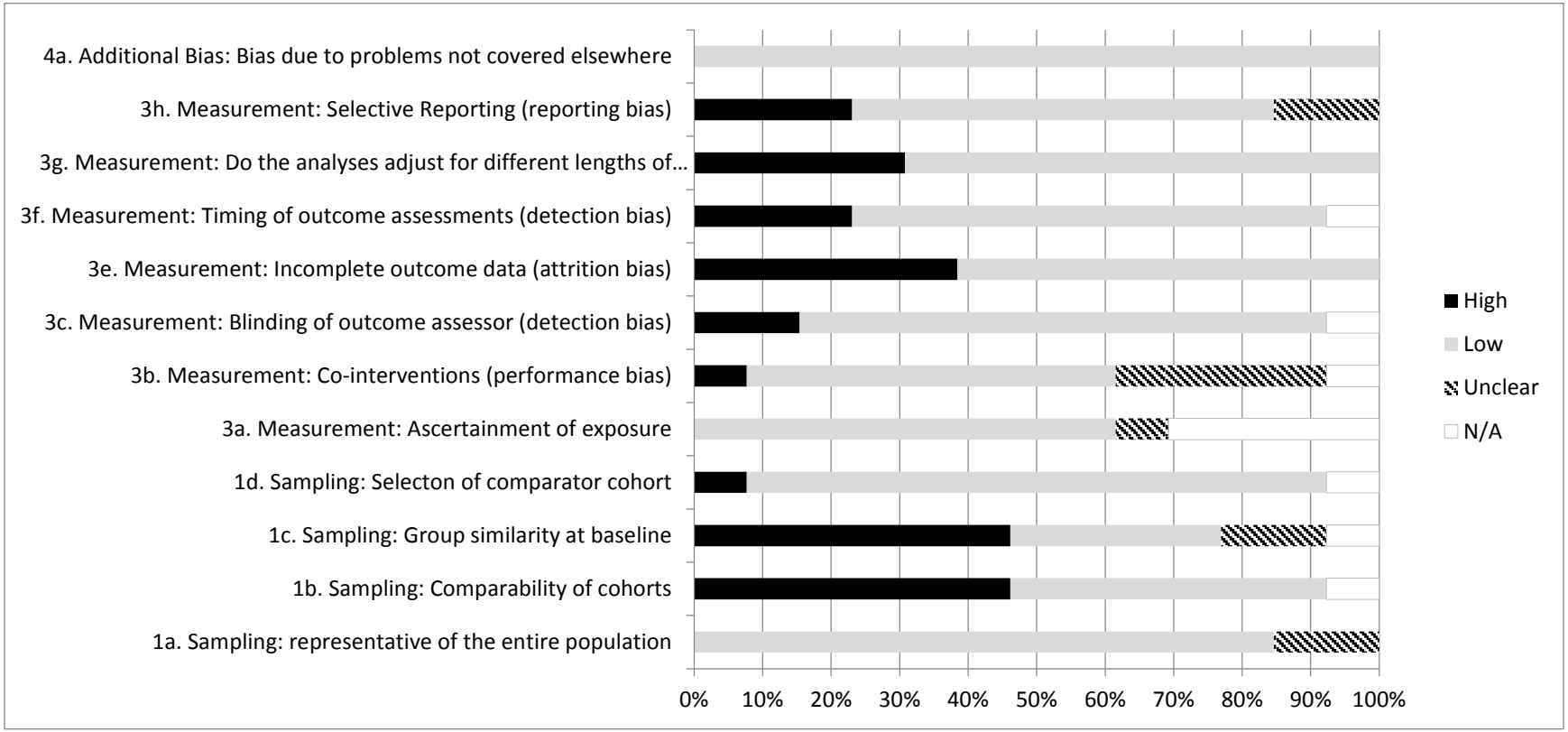

Figure D.3. Risk of bias in single arm studies of PTRAS

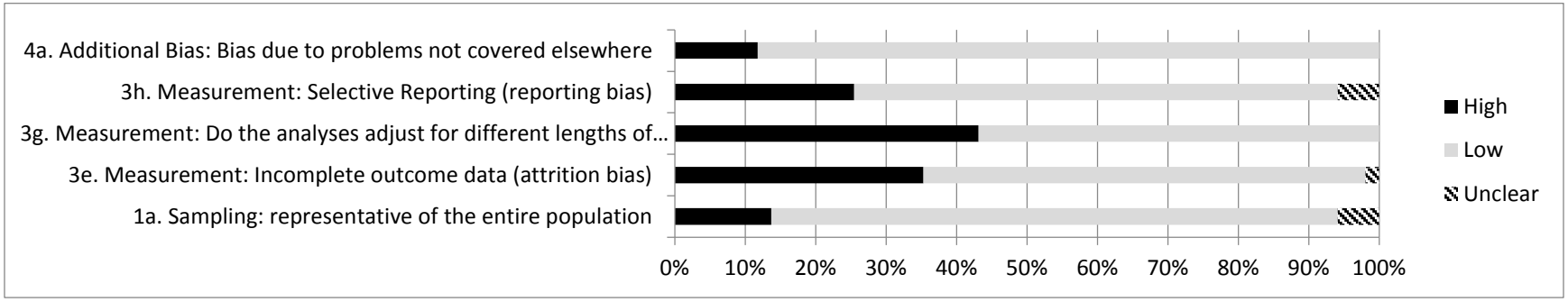

Figure D.4. Risk of bias in single arm studies of medication

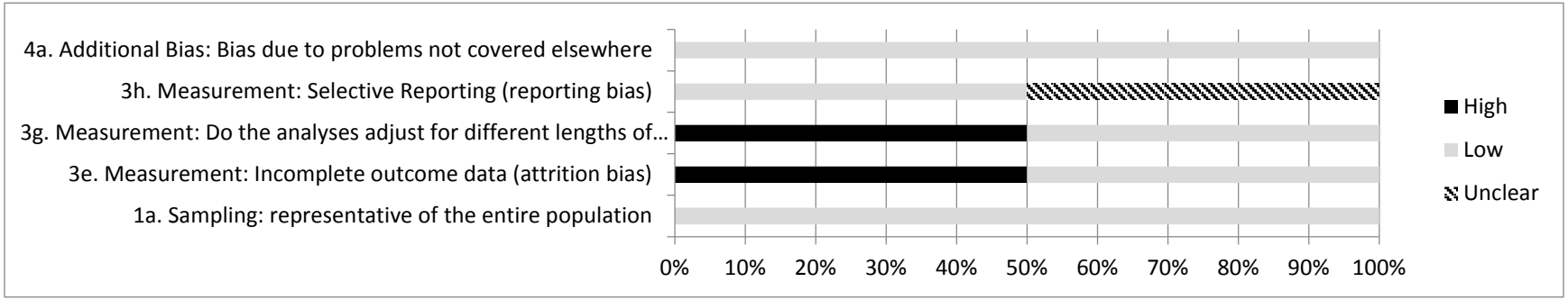

Figure D.5. Risk of bias in single arm studies of surgery