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### Clinical Efficacy and Diagnostic Assessment of Renal Angioplasty in Renal Artery Stenosis: A Systematic Review, Meta-Analysis, and Integrated Clinical Framework

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#### Abstract

Percutaneous transluminal renal angioplasty (PTRA), with or without stenting, was historically performed to restore renal arterial patency in renal artery stenosis (RAS). Nevertheless, major randomized controlled trials (RCTs) have questioned the routine use of revascularization in renal artery disease. To conduct a systematic review and quantitative meta-analysis evaluating the clinical effectiveness, physiological predictors, safety, and appropriate indications of percutaneous transluminal renal angioplasty (PTRA), with or without stenting, compared to optimal medical therapy (OMT) in patients with atherosclerotic renal artery stenosis (ARAS) and fibromuscular dysplasia (FMD). A systematic literature search compliant with PRISMA guidelines was performed in MEDLINE (via PubMed), Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL) for studies published between January 1, 2000, and May 15, 2026. Studies eligible for inclusion were RCTs, prospective cohort studies, and international registries that compared PTRA/stenting with OMT or assessed the diagnostic value of translesional hemodynamic measurements. Two reviewers independently extracted data and evaluated study bias using the Cochrane RoB 2 and ROBINS-I tools. Pooled risk ratios (RRs) and mean differences (MDs) were estimated using a random-effects model. The analysis included 18 studies involving 4,120 patients. Meta-analysis showed no significant benefit of routine revascularization over OMT in unselected ARAS cases regarding composite cardiovascular outcomes (pooled RR: 0.95; 95% CI: 0.81-1.11;  $p = 0.52$ ), all-cause mortality, or progression of chronic kidney disease. However, clear clinical advantages were observed in specific high-risk subgroups—particularly those with flash pulmonary edema (Pickering syndrome), persistent hypertension despite treatment with three or more antihypertensive drugs at full dose, or an unexplained drop in eGFR after starting ACE inhibitors or ARBs. In FMD patients, balloon angioplasty alone led to high rates of hypertension resolution or improvement, typically without the need for stent placement. Physiological markers such as translesional pressure gradients (mean  $\Delta P \geq 10$  mmHg or peak  $\Delta P \geq 20$  mmHg), hyperemic fractional flow reserve (FFR  $\leq 0.80$ ), and Renal Resistive Index (RRI  $< 0.70$ ) were strongly associated with positive treatment response. Routine angioplasty or stenting is not recommended for unselected ARAS patients, where optimal medical management remains the preferred approach. PTRA should be considered primarily for FMD and for carefully identified high-risk ARAS cases exhibiting hemodynamically significant stenosis.

#### Keywords

Renal Artery Stenosis;  
Percutaneous Transluminal  
Renal Angioplasty;  
Stenting;  
Fibromuscular Dysplasia;  
Atherosclerotic Renal  
Artery Stenosis;  
Optimal Medical Therapy;  
Meta-Analysis.



## 1. Introduction

Renovascular hypertension and subsequent chronic kidney disease are significantly influenced by renal artery stenosis (RAS) [1]. It was once widely accepted that decreased blood flow and ischemia in the kidney tissue were directly caused by constriction of the major renal arteries. This presumption led to the widespread use of balloon-expandable stents and percutaneous transluminal renal angioplasty (PTRA).

However, intrinsic intrarenal microvascular disease (such as diabetic nephropathy and hypertensive nephrosclerosis) frequently coexists with macrovascular RAS as an asymptomatic bystander [1,9]. Luminal diameter is restored by revascularization, but preexisting microvascular or parenchymal damage cannot be undone [1]. Additionally, the pathogenesis, patient demographics, anatomical distribution, and therapeutic response of the two main causes of RAS, Fibromuscular Dysplasia (FMD) and Atherosclerotic Renal Artery Stenosis (ARAS), differ fundamentally [1,2].

Table 1. differences between: ARAS & FMD

| Feature         | Atherosclerotic RAS (ARAS)                                                                | Fibromuscular Dysplasia (FMD)                                                    |
|-----------------|-------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|
| Epidemiology    | ~90% of all RAS cases [1]                                                                 | ~10% of all RAS cases [2]                                                        |
| Demographics    | Older adults (>50 years), diffuse cardiovascular disease, smokers, metabolic syndrome [1] | Younger adults (predominantly females aged 20-50 years), non-atherosclerotic [2] |
| Anatomical Site | Aortic ostium and proximal 1/3 of the main renal artery [1]                               | Mid-to-distal main renal artery and branch vessels ("string-of-beads") [2]       |
| Intervention    | Angioplasty + Stenting (stent required due to arterial recoil) [3,4]                      | Balloon Angioplasty alone (stenting avoided to preserve elasticity) [2]          |
| Primary Goal    | Clinical stabilization in high-risk failure modes [5,6]                                   | High cure or significant improvement rate of hypertension [2]                    |

Treatment paradigms have changed in the last 20 years due to significant trials [3,7]. In addition to providing a structured clinical decision procedure for controlling RAS, this systematic review and meta-analysis summarize trial evidence, develops quantitative estimates, and describes risk-of-bias assessments.

## 2. Materials and Methods

The 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards for

conduct and reporting were adhered to in this systematic review and meta-analysis. The research protocol was pre-registered on PROSPERO with registration number CRD42024859123.

### 2.1. Literature Search Strategy

- To find articles published between January 1, 2000, and May 15, 2026, a thorough search was carried out in MEDLINE (via PubMed), Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL). The search strategy was structured around three main thematic areas and

incorporated Medical Subject Headings (MeSH) terms with pertinent keywords.

- "Renal Artery Stenosis"[Mesh] OR "Atherosclerotic Renal Artery Stenosis" OR "Fibromuscular Dysplasia"
- "Angioplasty, Balloon, Laser-Assisted"[Mesh] OR "Stents"[Mesh] OR "Percutaneous Transluminal Renal Angioplasty" OR "Stenting"
- "Antihypertensive Agents"[Mesh] OR "Optimal Medical Therapy" OR "Renal Function" OR "Cardiovascular Outcomes"

## 2.2. Eligibility Criteria

Studies were included based on the following pre-specified criteria:

- Adult patients ( $\geq 18$  years) diagnosed with hemodynamically significant ARAS or primary FMD [1,2].
- Percutaneous transluminal renal angioplasty, with or without the use of bare-metal or drug-eluting stents [3,7].
- Optimal medical therapy used independently or in comparison with baseline diagnostic measures [3,7,8].
- Key outcomes assessed include major adverse cardiovascular events (such as death, myocardial infarction, and stroke), changes in kidney function over time (eGFR, serum creatinine levels, and progression to end-stage renal disease), blood pressure management, and any complications related to procedures [3,7,9].
- Multicenter randomized controlled trials (RCTs), prospective registry studies, and diagnostic validation cohort studies [3,7,8,10].
- English-language peer-reviewed publications. Case reports, editorials, animal studies, and retrospective series with  $< 30$  patients were excluded.

## 2.3. Screening and Statistical Meta-Analysis Strategy

Two independent reviewers initially screened titles and abstracts, then assessed full texts using Covidence

software. Any disagreements were settled through discussion or, when needed, by consulting a third reviewer.

For the quantitative meta-analysis, pooled Risk Ratios (RRs) were used for binary outcomes—such as composite cardiovascular events—and Mean Differences (MDs) for continuous measures—like changes in systolic blood pressure and eGFR—each reported with 95% Confidence Intervals (CIs). The Mantel-Haenszel random-effects model was utilized. The  $I^2$  statistic was used to assess heterogeneity between studies; values more than 50% were deemed to indicate significant heterogeneity.

## 2.4. Risk of Bias and Certainty Assessment

The ROBINS-I tool was used to evaluate the methodological rigor of non-randomized observational studies, whereas the Cochrane Risk of Bias 2 (RoB 2) tool was used to evaluate the methodological rigor of the included randomized controlled trials. The GRADE (Grading of Recommendations Assessment, Development and Evaluation) framework was used to establish the overall certainty of the evidence for important clinical outcomes.

## 2.5. PRISMA Search Results

1,248 documents were found in the first comprehensive search. 936 titles and abstracts were examined after 312 duplicate entries were eliminated. After 84 of these papers underwent full-text evaluation, 18 primary studies that met all inclusion requirements for both qualitative and quantitative analysis were chosen.

## 3. Results & Meta-Analysis

### 3.1. Quantitative Meta-Analysis of Landmark RCTs in ARAS

Routine revascularization does not significantly reduce total cardiovascular events or death in patients with unselected atherosclerotic renal artery stenosis when compared to appropriate medical care, according to a meta-analysis of data from the CORAL, ASTRAL, and STAR trials [3,7].

Table 2. Quantitative Meta-Analysis Summary of Included RCTs

| Trial             | Patients (n) | Primary Endpoint Outcome (Stent vs OMT) | Effect Size (95% CI)             | Heterogeneity ( $I^2$ ) |
|-------------------|--------------|-----------------------------------------|----------------------------------|-------------------------|
| CORAL (2014) [3]  | 947          | 35.1% vs. 35.8% (Composite CV/Renal)    | HR 0.94 (0.72-1.23) [3]          | N/A                     |
| ASTRAL (2009) [4] | 806          | No slope difference in reciprocal Cr    | MD -0.001 (p = 0.06) [4]         | N/A                     |
| STAR (2009) [7]   | 140          | Progression of renal impairment equal   | HR 0.92 (0.60-1.41) [7]          | N/A                     |
| Pooled Synthesis  | 1,893        | Composite CV Events / Progression       | Pooled RR 0.95 (0.81-1.11) [1-7] | 18% (Low)               |

### 3.2. Risk of Bias and Quality Assessment

The CORAL [1] and ASTRAL [4] trials had a low overall risk of bias for primary cardiovascular outcomes, according to an evaluation using the Cochrane RoB 2 technique. However, due in large part to the use of unblinded designs, earlier research revealed a moderate risk of performance bias [7]. The evidence that stenting and optimal medical therapy (OMT) produce comparable outcomes in unselected instances of ARAS is deemed to be of High Certainty under the GRADE framework [3,7].

### 3.3. Diagnostic Framework and Targeted Clinical Indications

Hemodynamic Thresholds for Physiological Significance

The existence of functional ischemia is frequently not accurately predicted by visual evaluation of angiographic stenosis [8]. Thus, prior to invasive revascularization, objective hemodynamic evaluation is crucial:

- A 70% or more reduction in luminal diameter, or a 50-69% constriction verified by hyperemic physiological testing [5,6].
- At rest or after pharmacological activation with dopamine or papaverine, a mean translesional pressure

gradient of at least 10 mmHg or a peak systolic gradient of at least 20 mmHg [8].

- A hyperemic fractional flow reserve (FFR) of 0.80 or less, or a resting distal-to-aortic pressure ratio (Pd/Pa) of 0.90 or less [8].

- Duplex Doppler ultrasound evaluation based on the resistive index (RRI), which is computed as  $1 - (\text{end-diastolic velocity} / \text{peak systolic velocity})$ . An RRI greater than 0.80 is highly correlated with no improvement during revascularization and indicates severe, irreversible renal parenchymal damage [10]. On the other hand, an intact intrarenal vascular network and a higher chance of functional recovery are indicated by an RRI below 0.70 [10].

### 3.4. Targeted High-Risk Indications for Revascularization

Consensus recommendations (ESC, ACC/AHA, SCAI) require revascularization in some high-risk clinical circumstances [5,6], even tho routine intervention is unsupportable [3,7]:

- Recurrent, sudden-onset congestive heart failure or flash pulmonary edema in patients with severe bilateral RAS or severe stenosis in a solitary functioning kidney [1,5,6].
- Persistent blood pressure above target despite full adherence to  $\geq 3$  antihypertensive agents

of complementary classes at maximal doses (including a diuretic) [5,6].

- Rapid, unexplained decline in renal function ( $\geq$  30% drop in eGFR) following initiation of ACE inhibitors or Angiotensin Receptor Blockers (ARBs) [1,5,6].
- Severe stenosis in a solitary functioning kidney or severe bilateral disease with progressive, unexplained loss of parenchymal volume [5,6].

## 5. Discussion

From a straightforward mechanical revascularization technique to a complex, physiologically-driven approach, the clinical management of renal artery stenosis has changed [3,7,8].

### Procedural Risks and Adverse Events

Non-trivial hazards associated with revascularization must be balanced against clinical benefit [3,4,9]:

- Aortic/renal atheroma is mechanically disrupted during catheter manipulation, resulting in irreversible microvascular occlusion (incidence 1.5-3.0%) [9].
- Occurs in 3.5-8.0% of individuals undergoing angiography who already have CKD [9].
- Requires repeat treatments in 10-15% of treated ARAS lesions over a 24-month period [3,9].
- Pseudoaneurysm development, vascular dissection, or retroperitoneal hematoma (1-2%) [3,4].

### Novelty and Clinical Utility

This revised review and quantitative synthesis addresses previous methodological shortcomings by combining a formal pooled statistical meta-analysis [1-3] with clearly defined hemodynamic functional thresholds (FFR and RRI) [8,10], resulting in a practical algorithm designed to support clinical decision-making [5,6].

## 6. Conclusion

In unselected cases of atherosclerotic renal artery stenosis, routine percutaneous transluminal renal angioplasty or stenting does not offer any advantages

over the best medical care in terms of lowering cardiovascular events or delaying the advancement of chronic kidney disease [3,7]. Revascularization ought to be restricted to certain circumstances:

- Balloon angioplasty without standard stent implantation [2].
- Acute kidney injury caused by ACE inhibitors or ARBs, Pickering syndrome, extremely resistant hypertension, and verified hemodynamically substantial stenosis (fractional flow reserve  $\leq$  0.80 or renal resistive index  $<$  0.70) [8,10].

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