Meta-Analysis of Revascularization Versus Medical Therapy for Atherosclerotic Renal Artery Stenosis

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The aim of the study was to compare the efficacy of revascularization versus medical therapy in patients with atherosclerotic renal artery stenosis (ARAS). ARAS is the most common cause of secondary hypertension and is associated with several complications, such as renal failure, coronary artery disease, cardiac destabilization, and stroke. Medical therapy is the cornerstone for management of ARAS; however, numerous trials have compared medical therapy with revascularization in the form of percutaneous renal artery angioplasty (PTRA) or percutaneous renal artery angioplasty with stent placement (PTRAS). Medline (PubMed and Ovid SP), Embase, Cochrane Central Register of Controlled Clinical Trials (CENTRAL), and Cochrane Database of Systematic Review (CDSR) were searched till present (November 2013) to identify clinical trials where medical therapy was compared with revascularization (PTRA or PTRAS). We performed a meta-analysis using a random effects model. The heterogeneity was assessed using I^2 values. The initial database search identified 540 studies and 7 randomized controlled trials, and 2,139 patients were included in the final analysis. Angioplasty with or without stenting was not superior to medical therapy with respect to any outcome. The incidence of nonfatal myocardial infarction was 6.74% in both the stenting and medical therapy group (odds ratio = 0.998, 95% confidence interval 0.698 to 1.427, p = 0.992), and incidence of renal events in stenting population was found to be 19.58% versus 20.53% in medical therapy (odds ratio = 0.945, 95% confidence interval 0.755 to 1.182, p = 0.620). In conclusion, PTRA or PTRAS does not improve outcomes compared with medical therapy in patients with ARAS. Future studies should investigate to identify patient subgroups that may benefit from such an intervention. Published by Elsevier Inc. (Am J Cardiol 2014;114:1116−1123)

Atherosclerotic renal artery stenosis (ARAS) is the most common cause of secondary hypertension accounting for up to 5% of all cases.[1] The prevalence increases with age and the presence of multiple atherosclerotic risk factors.[2,3] Furthermore, evidence suggests that ARAS is a significant cause of chronic renal failure[4,5] and is associated with several other long-term complications, such as coronary artery disease, stroke, peripheral vascular disease, and cardiac destabilization.[6–8] Medical therapy has been the cornerstone of treatment for patients with ARAS. The data from animal studies[9,10] and early uncontrolled human studies[11,12] suggested that revascularization with or without stenting leads to better blood pressure control and decreases in using antihypertensive medications. This led to rapid adoption of this procedure in clinical practice. The associated costs and complications warrant robust evidence to support ARAS as a first-line therapy. The 2005 ACC/AHA guidelines strongly recommend percutaneous revascularization for patients with hemodynamically significant ARAS, recurrent unexplained congestive heart failure (CHF), or sudden pulmonary edema and may also be reasonable in patients with hemodynamically significant ARAS and resistant hypertension or progressive chronic kidney disease.[13] Several randomized controlled trials have been undertaken to identify if and which patients would benefit by undergoing therapeutic revascularization with percutaneous renal artery angioplasty (PTRA) or percutaneous renal artery angioplasty with stent placement (PTRAS). The individual trials are limited by several factors, such as sample size, duration of follow-up, methodological issues, heterogeneous end points, lack of clinical end points, and varying degrees of stenosis of the renal artery. The aim of this systematic review was to identify randomized controlled trials comparing revascularization strategies (PTRA and PTRAS) versus medical therapy looking at clinical outcomes (deaths and nonfatal myocardial infarction [MI], CHF, changes in systolic blood pressure from baseline, stroke, and deterioration in renal function).

Methods

Literature search was conducted using methods described in the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement.[14] Medline (PubMed and Ovid SP), Embase, Cochrane Central Register of Controlled Clinical Trials (CENTRAL), and Cochrane Database of

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See page 1122 for disclosure information.

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Table 1
Baseline characteristics of the patients

Study	Mean Age* (Years)	Patients Enrolled*	DBP (mm Hg)	CC (ml/min)	ARAS (% Stenosis)	Primary Outcome Measures	Duration of follow-up (Months)
Plouin et al	59.2 vs. 59.5	49 (23 vs. 26)	≥95	≥50	—	↓SBP	6
Jaarsveld et al	61 vs. 59	106 (56 vs. 50)	≥95	—	—	Renal function	12
Bax et al	66 vs. 67	140 (64 vs. 76)	—	<80	≥50	Renal function	1, 3, 24
Webster et al	59.4 vs. 62.6	135 (55 25 vs. 30)	≥95	—	—	↓SBP	1, 3, 6 and every 6 there after
ASTRAL Investigators	70 vs. 71	806 (403 vs. 403)	—	—	—	Renal function	60
CORAL study	69.3 vs. 69.	947 (459 vs. 472)	—	—	≥60	Clinical end points†	43 (median)

ARAS = atherosclerotic renal artery stenosis; CC = creatinine clearance; DBP = diastolic blood pressure; SBP = systolic blood pressure.
* Reported as intervention versus control group.
† Mortality, nonfatal MI, stroke, renal function, and hospitalization for CHF.

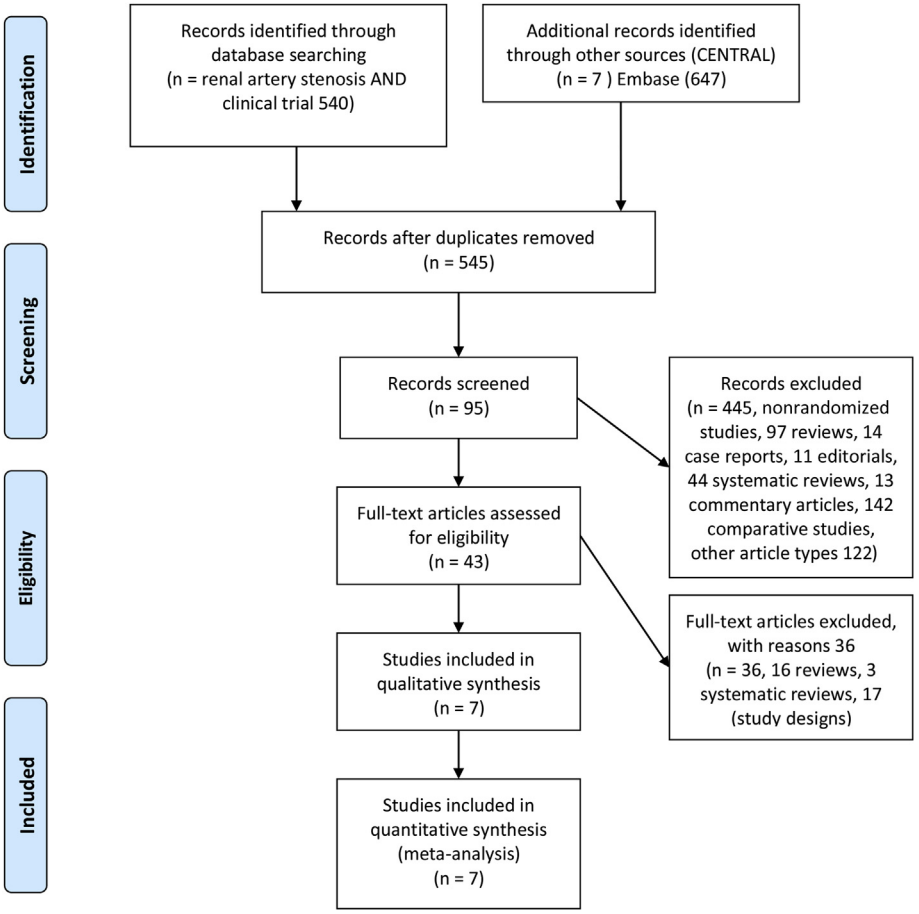

Figure 1. PRISMA flow sheet describing literature search strategy.

Systematic Review (CDSR) were searched from the inception of these databases till present (November 2013). We used "renal artery stenosis," "randomized controlled trials," "angioplasty," "surgical intervention," and "medical therapy" as the search terms. No limits of language were applied, and references of the included studies were hand searched to ensure that the eligible studies were not missed.

Only randomized controlled trials where medical therapy was compared with angioplasty and stenting were included in the study. Nonrandomized comparisons, observational studies, and other article types such as editorials were excluded.

Two researchers independently abstracted data in an excel sheet using a structured template. The extracted variables included baseline demographics, clinical characteristics, and outcomes (Table 1). Discrepancies were resolved through mutual consensus.

The Cochrane Collaboration tool[15] was used to ascertain the risk of bias in the included studies. The following domains were assessed: randomization, concealment to treatment allocation, avoidance of co-interventions, similarity of groups at baseline, eligibility criteria, blinding, and intention to treat analysis. Funnel plot was constructed to assess for publication bias.