Research Square

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Percutaneous Revascularization for Atherosclerotic Renal Artery Stenosis: a Meta-analysis

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Abstract

Objective: This study aimed to investigate whether percutaneous revascularization (PR) was as effective and safe as medication therapy alone in patients with atherosclerotic renal artery stenosis (ARAS).

Methods: We searched Embase, PubMed, and the Cochrane Library databases from their inception to July 31, 2021. We included randomized controlled trials (RCTs) reporting PR for ARAS. RevMan 5.3 was employed to conduct the analysis.

Results: Of 469 screened studies, 9 were included in our study. A total of 2433 patients with ARAS were recorded. The results demonstrated that PR and medication had a similar antihypertensive effect on both systolic [mean difference (MD)= 0.37, 95% CI: -1.37 to 2.11, p= 0.68] and diastolic blood pressure (MD= -0.75, 95% CI: -2.84 to 1.34, p= 0.48). Meanwhile, there were no differences in all-cause mortality [risk ratio (RR) = 0.90, 95% CI: 0.74-1.10, p=0.31)], stroke (RR = 0.81, 95% CI: 0.53-1.98, p=0.32), congestive heart failure (RR = 0.89, 95% CI: 0.70-1.14, p= 0.36), and periprocedural complications (RR = 0.89, 95% CI: 0.72-1.10, p=0.28).

Conclusions: The results revealed that PR was as effective and safe as medication therapy alone in patients with ARAS.

Introduction

Atherosclerotic renal artery stenosis (ARAS) was a common problem in patients with peripheral vascular atherosclerosis [1, 2] and was recognized as a cause of secondary hypertension [3]. Meanwhile, it was a contributing factor to cardiovascular disease development [4]. Treatment options for ARAS mainly included percutaneous revascularization (PR) and medication therapy alone [5–8].

PR with or without stenting has gained growing interest from vascular surgeons for treating ARAS [9, 10]. Some studies revealed that it could lead a better blood pressure control and a reduction in the number of antihypertensive agents [11–15]. The American College of Cardiology/American Heart Association (ACC/AHA) guidelines strongly recommend PR for patients with hemodynamically significant ARAS regardless of whether they have resistant hypertension or progressing kidney disease [16]. Additionally, several studies demonstrated that PR was a safe treatment for ARAS [17, 18]. However, few investigations compared the efficacy and safety between PR and medication therapy alone. As a result, this meta-analysis was conducted to evaluate the efficacy and safety of PR in patients with ARAS.

Methods

Search strategy

From inception to July 31, 2021, we performed keyword search in Embase, PubMed, and the Cochrane Library using the following terms: (“Atherosclerotic Renal Artery Stenosis” OR "ARAS”) AND (“Percutaneous revascularization” OR “PR” OR “Stenting” OR "angioplasty”). Meanwhile, we screened references of other meta-analyses to identify additional trials. Publication language was confined to Chinese and English.

Inclusion and exclusion criteria

The following selection criteria were employed to perform the analysis according to Patient-Intervention-Comparison-Outcome-study (PICOS) principles. Participants (P): patients who were diagnosed as ARAS. Intervention (I): percutaneous revascularization (PR). Comparison (C): medication therapy. Outcomes (O): (1) effectiveness: reduction of systolic blood pressure (SBP) and diastolic blood pressure (DBP); (2) safety: all-cause mortality, stroke, congestive

heart failure, and periprocedural complications. Study design (S): randomized controlled trials (RCTs). Meanwhile, reviews, editorials, letters, case reports, cell and animal studies, or expert opinions were excluded.

Data extraction and synthesis

Reduction of SBP and DBP by the end of follow-up period were calculated to determine PR effectiveness compared with medication therapy alone. The data about all-cause mortality, stroke, congestive heart failure, and periprocedural complications were recorded to determine whether PR was as safe as medication therapy alone. Moreover, several characteristics of included studies were extracted and summarized into simple standard forms, including the following contents: study title and publication year, study design, sample size, gender, mean age, history of diabetes mellitus, and smoking (Table 1). Continuous variables were expressed as mean differences with 95% confidence interval (CI). Risk ratio (RR) and mean difference (MD) were calculated to combine categorical and continuous variables, respectively [19–21]. This analysis was performed using RevMan software version 5.3.

Literature quality assessment

Two reviewers independently screened the studies and evaluated the quality of included studies. Any discrepancies were resolved through a discussion, and a third researcher would make a decision if necessary. The Cochrane tool was utilized to evaluate the quality of included studies. Meanwhile, the scores of each study were presented in Table 2. For pooled study results, Cochran's Q test and the degree of inconsistency (I^2) were employed to assess heterogeneity. I^2 statistic values of <25%, 25%-50%, and >50% were considered as low, moderate, and high heterogeneity, respectively. A fixed-effects model was utilized if I^2 was less than 50%; otherwise, a random-effects model would be applied. Publication bias was estimated from a funnel plot (Figure 3). A roughly symmetrical funnel plot could indicate an insignificant publication bias.

Table 2
The Cochrane risk of bias tool for assessing the quality of randomized controlled trials included in meta-analysis.

RCTs	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting	Other Biases
STAR,2009 [23]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
DRASTIC,2000 [24]	Un-report	Un-report	Un-report	Un-report	Low risk	Low risk	Low risk
ARSTRAL,2009 [17]	Low risk	Low risk	High risk	Un-report	Low risk	Low risk	Low risk
Webster,1998 [18]	Low risk	Low risk	High risk	Un-report	Low risk	Low risk	Low risk
EMMA,1998 [25]	Low risk	Low risk	Un-report	Un-report	Low risk	Low risk	Low risk
CORAL,2014 [26]	Low risk	Low risk	Un-report	Un-report	Low risk	Low risk	Low risk
RADAR,2017 [27]	Low risk	Un-report	Low risk	Un-report	Low risk	Low risk	Low risk
Krijnen,2005 [28]	Low risk	High risk	Un-report	High risk	Low risk	Low risk	Low risk
NITER,2009 [29]	Low risk	Low risk	High risk	Un-report	Low risk	Low risk	Low risk

Ethical approval was not required for this work. The following article has been reported in line with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Guideline [22].

Results

Search results

A total of 469 articles met inclusion and exclusion criteria, of which 149 were duplicates. After reading the titles and abstracts of 298 publications, we excluded them due to their different research types; the full texts of the remaining 22 articles were evaluated. Eight and one studies were excluded because of the type of included studies and repeated published data, respectively. Meanwhile, four studies were excluded because of other reasons. Ultimately, nine articles [17, 18, 23–29] comprising 2433 patients were included in the current meta-analysis. Of nine included studies, six were RCTs, and three were prospective randomized studies (PRS). A flow diagram of selection process was depicted in Figure 1.

Characteristics of included studies

Characteristics of all included studies were summarized in Table 1. All included articles were published between 1998 and 2017. Most studies were conducted in Europe, while one study was performed in USA. The sample size in this analysis ranged from 49 to 947. This meta-analysis comprised 2433 patients, including 1203 patients with a stenotic

renal artery undergoing percutaneous revascularization and 1230 patients treated with medication therapy alone. The results of methodological quality assessment of included studies were displayed in Table 2. All studies were of similar high quality.

Efficacy and safety of PR for ARAS

First, eight studies reported data about SBP [17, 23–29], and seven reported on DBP [17, 23–25, 27–29]. The pooled results revealed no significant differences between PR and medication therapy alone regarding reduction of SBP (MD = 0.37, 95% CI: -1.37 to 2.11, p=0.68) and DBP (MD =-0.75, 95% CI: -2.84 to 1.34, p=0.48) (Figure 2A). Second, five [17, 18, 23, 26, 27], four [17, 18, 23, 26], five [17, 18, 23, 26, 27] and six [17, 18, 23–26] studies reported data on all-cause mortality, stroke, congestive heart failure, and periprocedural complications. Additionally, the results revealed no significant differences between PR and medication therapy in all-cause mortality (RR = 0.90, 95% CI: 0.74-1.10, p=0.31), stroke (RR = 0.81, 95% CI: 0.53-1.98, p=0.32), congestive heart failure (RR = 0.89, 95% CI: 0.70-1.14, p=0.36), and periprocedural complications (RR = 0.89, 95% CI: 0.72-1.10; p=0.28), consistent with the results above (Figure 2B). A funnel plot representing publication bias of studies was presented in Figure 3; the funnel plot was symmetrical, indicating a slight publication bias.

Discussion

This meta-analysis identified nine RCTs investigating the efficacy and safety of PR for ARAS. The results indicated that PR had a similar impact on efficacy (reduction of SBP and DBP) and safety (mortality, stroke, congestive heart failure, and periprocedural complications) compared with medication therapy alone in ARAS patients, consistent with those from published studies [30–32].

PR was one of the common treatments for ARAS. However, it seems counterintuitive that treating with PR was not associated with reduced blood pressure and complications.

ARAS could result in ischemic nephropathy, which was defined as a reduction in glomerular filtration rate (GFR). Ultimately, it could result in resistant secondary hypertension [33]. However, secondary hypertension caused by ischemic nephropathy was not only caused by renal artery stenosis. Because renal metabolism minimally requires less than 10% blood flow, a decrease in blood flow alone cannot account for secondary hypertension and a decline in kidney function [34]. Numerous studies had demonstrated that kidney with insufficient blood supply could activate renin-angiotensin-aldosterone (RAS) pathway [35, 36]. Additionally, this may be the major cause of secondary hypertension in ARAS patients. In addition, RAS pathway could activate inflammatory and profibrogenic pathways and produce reactive oxygen species, resulting in irreversible glomerular damage [37, 38, 39]. Therefore, renal artery dilation may be ineffective in these situations.

Several investigations had attempted to elucidate the mechanism and pathways of irreversible kidney injury [40]. However, similar studies were scarce. Therefore, we believe that future studies should focus on elucidating the pathways of irreversible kidney injury from ARAS.

Limitations

We acknowledged the limitations of our study. First, the data remained limited with small sample size, although all included studies were RCTs. Second, some subgroups may be excluded due to the limited number of studies. Finally, most studies were performed at a single center. Therefore, multicenter studies with a larger sample size should be conducted to validate the findings. Therefore, the conclusions must be interpreted in the context of individual studies.

Conclusions

In conclusion, our meta-analysis demonstrated that PR had a similar impact on efficacy (reduction of SBP and DBP) and safety (mortality, stroke, congestive heart failure, and periprocedural complications) compared with medication therapy alone in ARAS patients. Moreover, well-designed and larger sample studies were required.

Declarations

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Availability of data and materials: All data generated or analysed during this study are included in this published article.

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Author contributions: (I) Conception and design: Shijun Cui, Tao Luo; (II) Administrative support: Linzhong Zhu, Tao Luo; (III) Provision of study materials or patients: Yu Li, Wenhao Cui, Jipeng Song, Jukun Wang; (IV) Collection and assembly of data: Yu Li, Wenhao Cui, Jipeng Song, Jukun Wang; (V) Data analysis and interpretation: Yu Li. Xin Chen, Chao Zhang; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

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Table

Due to technical limitations, table 1 docx is only available as a download in the Supplemental Files section.

Figures

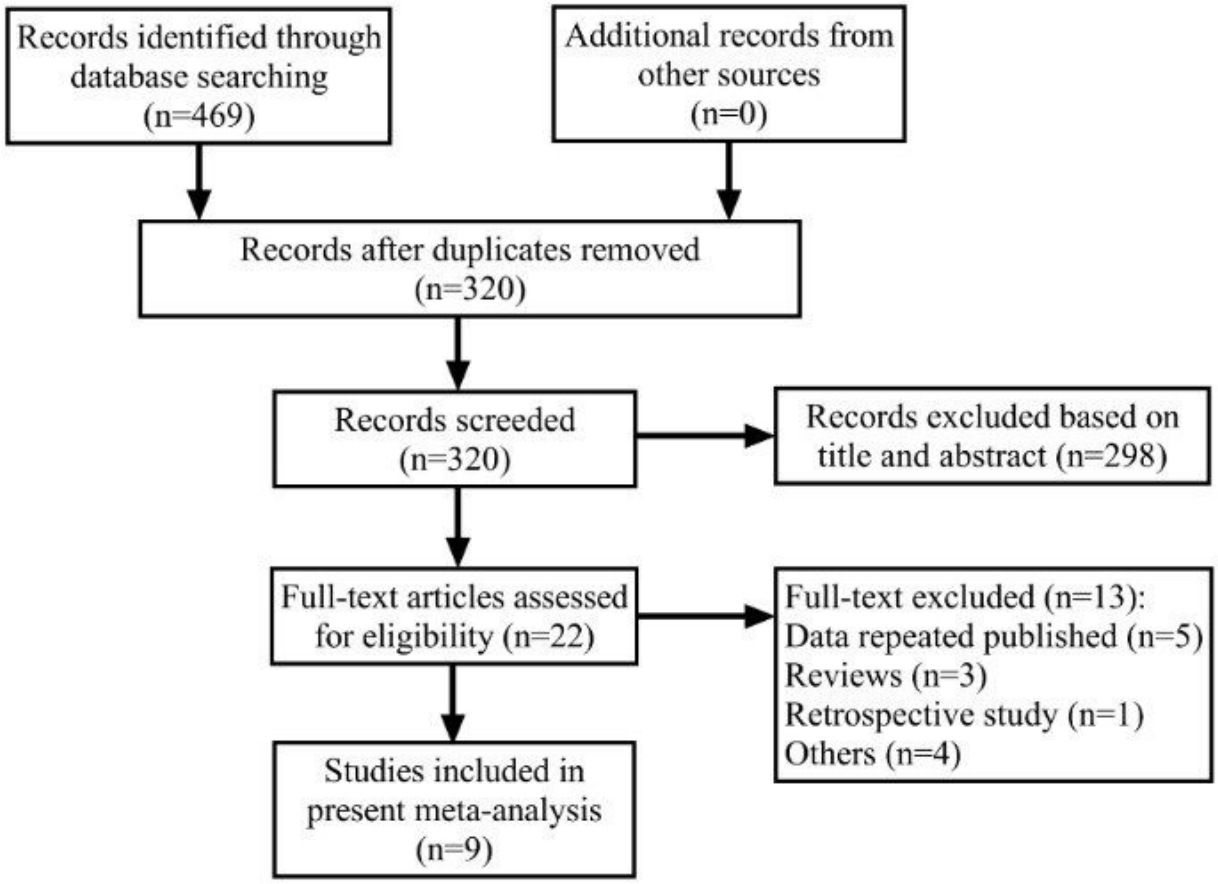

Figure 1

Flow chart of literature screening and selection process.

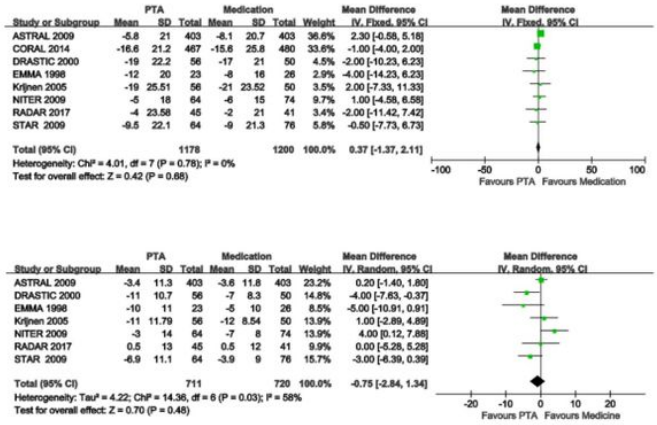

Figure 2A

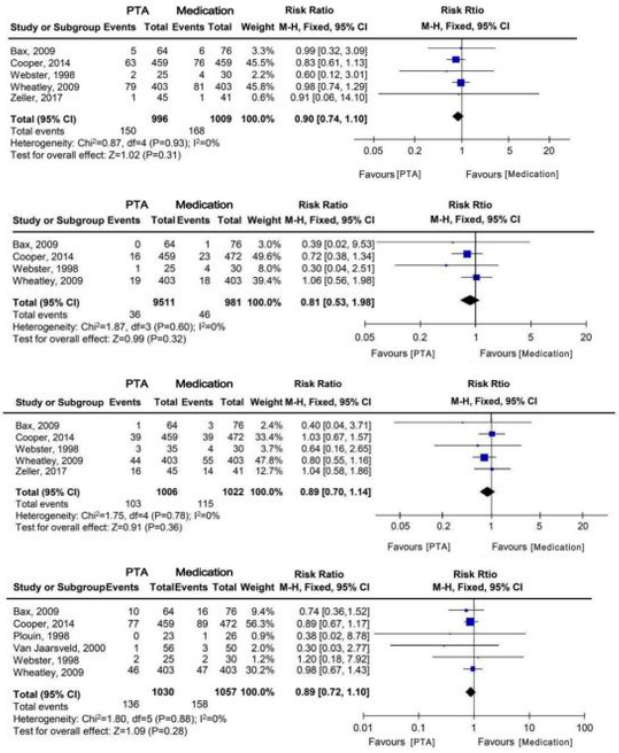

Figure 2B

Figure 2

A. Meta-analysis of reduction of systolic and diastolic blood pressure. B. Meta-analysis of PTA for all-cause mortality, stroke, congestive heart failure, and periprocedural complications.

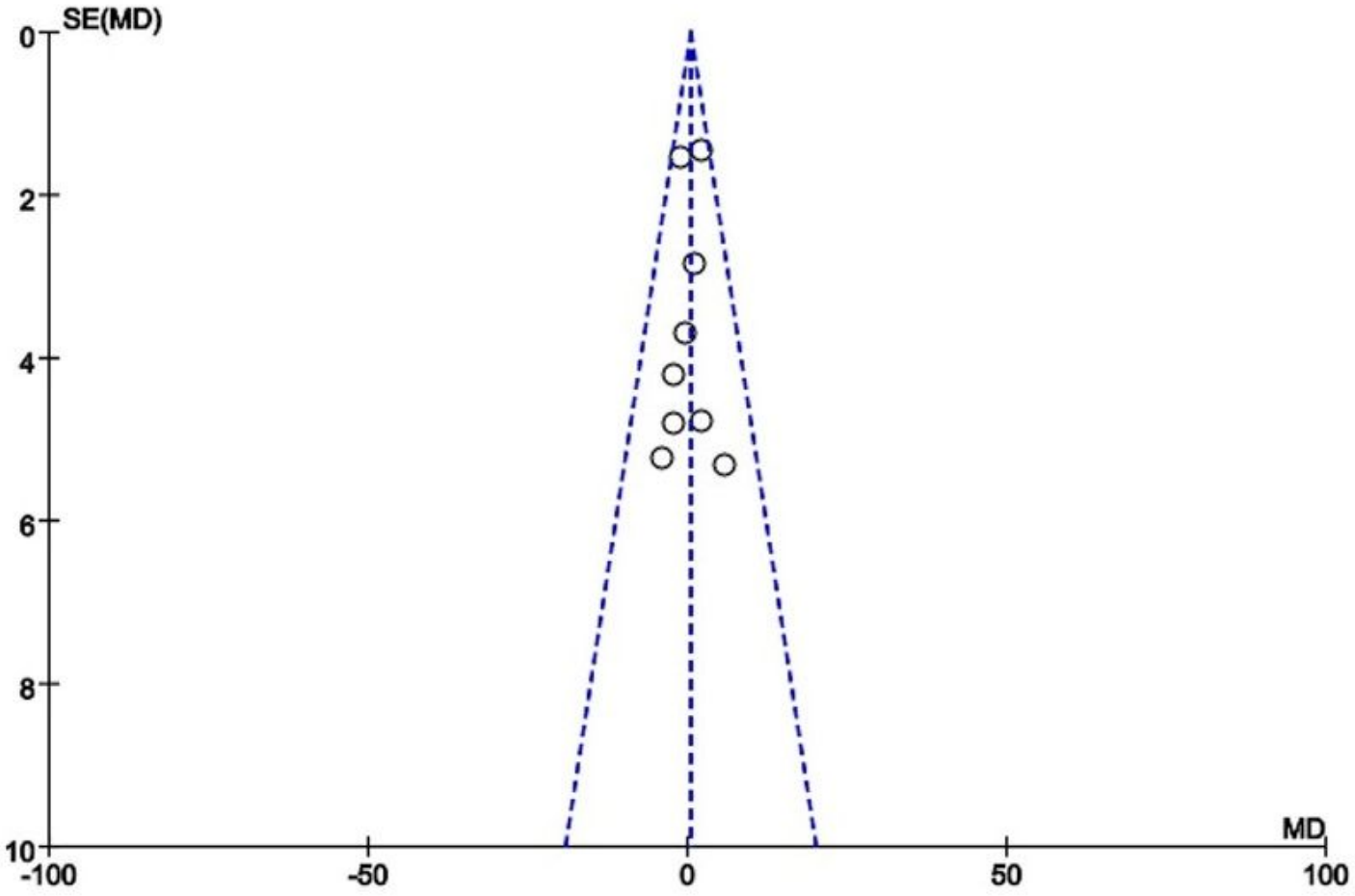

Figure 3

Funnel plot of meta-analysis.

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