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Atherosclerotic renal artery stenosis: how should we do?

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Atherosclerotic renal artery stenosis (ARAS) is a common form of renal vascular disease and progressive disease. It could lead to resistant hypertension and renal insufficiency. It is almost associated with ischemic nephropathy with progressive decline in renal function and cardiac complications including flash pulmonary edema. The presence of ARAS is also associated with an increased risk of cardiovascular death. Common therapeutic strategies for ARAS include medical therapy and angioplasty with stenting.

But current guidelines on ARAS revascularization have seen a major shift. The benefit of revascularization has been challenged since three large randomized controlled trials failed to demonstrate any improvement in clinical outcomes after endovascular revascularization.[1-3] Now, what should we do for ARAS?

Re-understanding for the Prevalence

ARAS is common in the elderly, patients with diabetics, patients with other types of atherosclerosis. For example, concurrent diagnosis of coronary artery disease among individuals with ARAS ranges from 11.3% to 39.0%.[4] The prevalence of ARAS is poorly defined. The majority of patients with ARAS are asymptomatic; therefore, the actual prevalence of renal disease may be much higher than the estimated prevalence.

Re-understanding for the Diagnosis

Renal artery angiography is still the gold standard for diagnosing ARAS. Previous studies reported the progression of worsening severity was 50% at 5 years.[5] A recent paper considered that patients with low-grade (<50%) ARAS have an excess risk for cardiovascular and renal complications.[6] Therefore, it used to be considered that early diagnosis of ARAS is of great value, but renal artery angiography is expensive and hazards with contrast agent. Finding safer and cheaper procedures to estimate ARAS earlier is very important. As well, simple, and typical clinical characteristics are more meaningful if ARAS is present.

Re-understanding for the Clinical Characteristics

Unfortunately, ARAS is frequently asymptomatic and has no characteristic clinical or laboratory manifestation. This makes its early diagnosis very difficult. There should be a high index of clinical suspicion for ARAS in the setting of epigastric bruit, pulse pressure, uncontrolled hypertension, or some risk factors such as diabetes, dyslipidemia, and smoking. But in our multi-regression analysis, we did not find smoking is a strong predicting factor for ARAS.[7] We established a simple model of scoring risk and predicted a high probability of ARAS. Meanwhile, Khatami *et al*[8] did some researches for a simple risk score model to predict ARAS. This model can be used for both clinical and research purposes.

Clinically, recurrent flash pulmonary edema may warn existing severe ARAS lesions. Also, ARAS is an important contributor to renal failure and aggravating hypertension. In addition, ARAS with chronic kidney disease poses a risk for exacerbation of cardiovascular disease and multiple long-term complications. Can timely therapy improve clinical outcomes?

Re-understanding for the Treatment Strategies

This topic is debatable. Currently, optimal medical therapy (OMT) is the first-line treatment for ARAS. Especially, three large randomized controlled trials suggested there was no difference between OMT and revascularization.[1-3] OMT is more important in a clinic. It is involved in the control of dyslipidemia and hypertension, platelet inhibition. The focus of OMT relies on controlling hypertension. These therapeutic options are only based

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on clinical experience. The mild lesion (<50%) can be controlled by OMT. Follow the degree of stenosis aggravated, the damage of renal function is difficult to reverse, the blood pressure is also difficult to control. Once the patients had refractory hypertension and pulmonary edema or recurrent heart failure, renal revascularization would be performed.

Due to the morbidity and mortality of open surgery, the approach of renal revascularization is renal artery stenting in the patients with ARAS, it replaced surgical revascularization over the past decade. Whether the treatment strategies are optimal, OMT plus renal artery stenting or OMT alone? The key point is how to obtain a benefit on renal revascularization.

Re-understanding for the Renal Revascularization

First, we should analyze these three randomized clinical trials again. Participants of these trials were those who mostly had a moderate degree of stenosis (50%–70% diameter reduction), moderately uncontrolled hypertension, relatively stable kidney function, and no pulmonary edema. So, the results were not fit for the global ARAS populations. However, subgroups had good outcomes after renal artery stenting, which included resistant hypertension, ischemic nephropathy, and cardiac destabilization syndrome.

Second, how to select a suitable patient for renal revascularization. Recent clinical trials in high-risk patients with ARAS have reported that blood pressure control was improved in up to 65% of patients and renal function was improved in approximately 30% to 40% of patients. Also, the estimated glomerular filtration rate was increased by at least 11 $mL \cdot min^{-1} \cdot 1.73\ m^{-2}$. This benefit was obtained after revascularization. Followed over 5 years, cardiovascular death or stroke risk was reduced.[9,10] Newer case report suggested a renal revascularization is an effective option for treating specific criteria of ARAS patients. The criteria are refractory hypertension, an atrophic kidney, chronic total renal artery occlusion, and recent blood pressure deterioration or the presence of collateral perfusion to the affected kidney.[11] So, the patients with severe lesions and unstable hemodynamics are suitable for renal revascularization.

Third, how to estimate middle lesion. The middle lesion with the degree of stenosis is 50% to 70%. It needs some measures to help delineate hemodynamic significance. Clinical experience suggests that resting or hyperemic translesional systolic gradient >20 mmHg, mean pressure gradient >10 mmHg hemodynamic, or renal fractional flow reserve of ≤0.8 will confirm hemodynamic significance. We should carefully evaluate the hemodynamic significance of patients with middle lesions before deciding whether or not revascularization.

Finally, how to evaluate the benefit of renal revascularization. Pulmonary edema or recurrent heart failure can be reversed by revascularization. This effect was confirmed.

Usually, uncontrolled blood pressure and renal insufficiency is a common clinical problem by ARAS causing. The main benefit of renal revascularization is possibly improvement of blood pressure and renal function. Revascularization can improve blood flow perfusion of the kidney. Kidney injury is often associated with blood pressure and dyslipidemia other factors. So, these benefit factors are involved in OMT.

Then, an evaluation of cardiovascular outcomes and renal events was observed. But, no study of medical treatment reported cardiovascular and other outcomes. The evidence regarding other outcomes is poor. Additionally, it needs to evaluate adverse events and restenosis rates after revascularization. Stent placement is currently most commonly used. No randomized trial evaluated revascularization technique with stent placement.

Latest meta-analysis shows that renal revascularization plus OMT reduces the incidence of refractory hypertension, but compared with OMT alone, the rates of stroke, renal events, cardiac events, cardiac mortality, and all-cause mortality do not improve.[12] Meanwhile, the author considered the low strength of the meta-analysis for these findings, if candidates for renal revascularization are carefully selected, renal revascularization will have more effect.

Clinicians must identify the responsive patients who would benefit from angioplasty through risk stratification and the prediction of outcomes. We should establish clinical scores or decision-making trees that would guide clinicians on patient selection either OMT or renal revascularization.

Future Direction

Newer therapeutic interventions are needed, such as new drugs, genes, and cell-based therapies. Renal revascularization can potentially cure or significantly improve blood pressure control, but the response to revascularization is hard to predict. Therefore, new diagnostic strategies are needed for optimal patient selection.

It addresses the challenges associated with clinical decision-making in patients with ARAS. Currently, we should develop a simple risk score model, especially for the asymptomatic patient, or decision-making trees to ARAS. We also should do some research to define appropriate patients for percutaneous transluminal renal angioplasty treatment.

Shortly, we expect that a safe non-invasive and accurate imaging method would be established. It would judge the degree of ARAS and blood perfusion, would allow screening of patients before intervention and prediction of the efficacy of an intervention, and would provide important guidance for clinicians.

Conflicts of interest

None.

References

1. Murphy TP, Cooper CJ, Pencina KM, D'Agostino R, Massaro J, Cutlip DE, *et al*. Relationship of albuminuria and renal artery stent outcomes: results from the CORAL randomized clinical trial (cardiovascular outcomes with renal artery lesions).

Hypertension 2016;68:1145–1152. doi: 10.1161/HYPERTENSIONAHA.116.07744.
2. Siddiqui EU, Murphy TP, Naeem SS, Siddique A, McEnteggart GE, Scarpioni R. Interaction between albuminuria and treatment group outcomes for patients with renal artery stenosis: the NITER study. J Vasc Interv Radiol 2018;29:966–970. doi: 10.1016/j.jvir.2018.03.003.
3. Zachrisson K, Krupic F, Svensson M, Wigelius A, Jonsson A, Dimopoulou A, *et al*. Results of renal artery revascularization in the post-ASTRAL era with 4 years mean follow-up. Blood Press 2020;29:285–290. doi: 10.1080/08037051.2020.1756740.
4. Zeller T. Renal artery stenosis: epidemiology, clinical manifestation, and percutaneous endovascular therapy. J Interv Cardiol 2005;18:497–506. doi: 10.1111/j.1540-8183.2005.00092.x.
5. Schreiber MJ, Pohl MA, Novick AC. The natural history of atherosclerotic and fibrous renal artery disease. Urol Clin North Am 1984;11:383–392.
6. de Leeuw PW, Postma CT, Spiering W, Kroon AA. Atherosclerotic renal artery stenosis: should we intervene earlier? Curr Hypertens Rep 2018;20:35. doi: 10.1007/s11906-018-0829-3.
7. Peng M, Jiang XJ, Dong H, Zou YB, Zhang HM, Song L, *et al*. Etiology of renal artery stenosis in 2047 patients: a single-center retrospective analysis during a 15-year period in China. J Hum Hypertens 2016;30:124–128. doi: 10.1038/jhh.2015.40.
8. Khatami MR, Jalali A, Zare E, Sadeghian S. Development of a simple risk score model to predict renal artery stenosis. Nephron 2018;140:257–264. doi: 10.1159/000492732.
9. Kim S, Kim MJ, Jeon J, Jang HR, Park KB, Huh W, *et al*. Effects of percutaneous angioplasty on kidney function and blood pressure in patients with atherosclerotic renal artery stenosis. Kidney Res Clin Pract 2019;38:336–346. doi: 10.23876/j.krcp.18.0148.
10. Iwashima Y, Fukuda T, Horio T, Kusunoki H, Hayashi SI, Kamide K, *et al*. Impact of percutaneous revascularization on left ventricular mass and its relationship to outcome in hypertensive patients with renal artery stenosis. Am J Hypertens 2020;33:570–580. doi: 10.1093/ajh/hpaa036.
11. Sasaki Y, Mishima E, Kikuchi K, Toyohara T, Suzuki T, Ota H, *et al*. Treatment of refractory hypertension with timely angioplasty in total renal artery occlusion with atrophic kidney. Intern Med 2021;60:287–292. doi: 10.2169/internalmedicine.5290-20.
12. Chen Y, Pan H, Luo G, Li P, Dai X. Use of percutaneous transluminal renal angioplasty in atherosclerotic renal artery stenosis: a systematic review and meta-analysis. J Int Med Res 2021;49:300060520983585. doi: 10.1177/0300060520983585.

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