Medical therapy for atherosclerotic renal artery stenosis

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Atherosclerotic renal artery stenosis (ARAS) is a common manifestation of generalized atherosclerosis (ATS) and is the most common disorder of the renal arterial circulation [1–3]. Furthermore, ARAS typically occurs in patients at high risk of cardiovascular disease with coexistent vascular disease at nonrenal sites. Indeed, the prevalence of ARAS in a population-based study of people aged 65 years or over is 7%. Prevalence rates for ARAS is 18% in patients with hypertension, 20% in patients with diabetes mellitus and hypertension, 25% in patients with peripheral vascular disease and 33% in those with abdominal aortic aneurysm [4].

Patients affected by ARAS are likely to have more complications and more extensive target-organ damage than patients without ARAS. Indeed, hemodynamically significant ARAS (stenosis >70%) leads to a fall in poststenosis pressure, and if perfusion pressure falls below the limit of renal autoregulation, the glomerular filtration rate decreases. The renin–angiotensin–aldosterone system (RAAS) is activated by the decrease in renal perfusion with increased production of angiotensin II, whose action led to an increase in hemodynamic resistance and systemic blood pressure. Its other nonhemodynamic effects play an important role in structural changes in the ischemic kidney [5]. Recent experimental evidence suggests that ARAS is associated with the activation of intrarenal fibrogenic and inflammatory pathways, oxidative stress and microvascular remodeling, and blocking these mechanisms can improve renal hemodynamics and function. As recent evidence indicates, the relationship between renal artery stenosis and ATS is complex, and mediators implicated in the pathophysiology of atherosclerotic renovascular disease may also contribute to the progression of cardiovascular damage.

The therapeutic options to date include revascularization usually by percutaneous transluminal renal angioplasty (PTRA) with or without stenting and/or medical treatment. However, although the angiographic results after PTRA are often remarkable, clinical results are rarely satisfactory regarding hypertension, renal function and survival [6–11]. It is of note that these studies usually concern patients with stable clinical conditions and, in many cases, only moderate ARAS lesions. Recognizing these limitations, the conclusions drawn from these trials are that, compared with best medical management, PTRA with stenting has a very small role in the management of ARAS ... there was no difference in the change in renal function and overall cardiovascular mortality.

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In this issue of *Clinical Investigation*, WR Colyer Jr and CJ Cooper review the current medical therapy that should be used in case of ARAS [12]. The authors have carefully evaluated the various strategies of medical therapy and risk factor modification for all patients with ARAS. They have sharply displayed that although optimal therapy was not defined by ARAS trials, data existed to support the use of several pharmacologic agents among this high-risk population for renal dysfunction and cardiovascular disease. The management of patients with ARAS should aim to reduce cardiovascular mortality, prevent cardiovascular and renal events, and improve or stabilize renal function and blood pressure control.

Unfortunately, the effect of PTRA on the natural history of diffuse atherosclerotic disease has not shown its superiority over medical treatment in ARAS. In addition, angioplasty may have serious adverse events since it has been reported to exhibit complications in 7–15% of cases, including a rapid deterioration of renal function or even patients’ death. Any ARAS requires effective drug therapy to slow the progression of local and systemic atherosclerotic disease. In all cases, medical treatment includes careful control of blood pressure by blocking the RAAS and the fight against other cardiovascular risk factors. In general measures for prevention of atherosclerotic disease, a lipid-lowering therapy with statins and antiplatelet aggregation (aspirin with or without clopidogrel) remain indispensable. As most of the adverse outcomes for patients with ARAS derive from nonrenal vascular complications, the medical therapy should include proven cardiovascular protector agents such as angiotensin-converting enzyme inhibitor or an angiotensin-receptor blocker (ARB) [13]. Indeed, control of blood pressure during ARAS is a mandatory but delicate measure. Apart from angiotensin-converting enzyme inhibitor and ARB, other treatments such as calcium channel blockers, diuretics and β blockers may also be associated primarily to control blood pressure values as pointed out by Colyer Jr WR and Cooper CJ [12]. Furthermore, additional therapies may be required and need to be individualized to a given patient based upon comorbid conditions [12].

The indications for revascularization decreased with age, which remains a limit to invasive treatment. In addition, many elderly patients with ARAS have a normal or borderline blood pressure and renal function. They should not, in principle, be exposed to the risk of a complication related to the revascularization procedure. To try to answer these questions, the ongoing CORAL trial [10] was designed to determine the occurrence of cardiovascular and renal events in hypertensive patients with ARAS, treated with either PTRA with stenting or optimal medication alone [14]. This latter includes a statin and an ARB. This prospective trial should determine the exact role of the medical regimen alone or in combination with PTRA and stenting, to limit ATS effects.

In conclusion, ARAS can be managed with medical therapy to limit ATS, maintain kidney function and reduce blood pressure. The available results, which were mostly obtained from patients with stable clinical conditions and, in many cases, only moderate ARAS lesions, favor a conservative approach for most patients with ARAS. Beyond medical therapy, the management of ARAS should be considered individually in the prospect of prolonged survival of the patient or the free period before starting dialysis and/or prevention of any cardiovascular or cerebrovascular event. Moreover, different selection criteria must be taken into account in therapeutic choice. They include the patient’s age, the other widespread arterial lesions and the overall traditional or nontraditional (e.g., proteinuria) cardiovascular risk factors and the basal renal function. In this respect, the extensive review of [12] may allow using strategies to reduce these event rates in this high-risk population [12].

**Bibliography**

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Website
101 CORAL trial
www.coralclinicaltrial.org