Atherosclerotic Ischemic Renal Vascular Disease: Do Published Outcomes Justify the Overzealous Diagnostic Approaches?

By Lionel U. Mailloux

Atherosclerotic renal vascular disease is being recognized more frequently in an elderly patient population with chronic kidney disease. It also is much easier to diagnose and treat, at this time, because of the wide availability of coronary angiography and other radiologic imaging studies. In general, patients with atherosclerotic ischemic renal vascular disease are much sicker than the usual ESRD patient with more cardiac comorbidity and higher mortality rates. It is important to determine whether the lesions in the renal artery are physiologically significant before performing an intervention. The interventions are often risky with significant morbidity. Nephrologists should guide their colleagues to follow prudent courses of action. There are no evidence-based guidelines in this area.

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ATHEROSCLEROTIC ISCHEMIC RENAL vascular disease (AIRVD) has become a very popular clinical diagnosis. This is in the setting of new epidemiologic data from the US Renal Data System (USRDS) showing that it is an increasingly frequent cause of end-stage renal disease (ESRD), ranging anywhere from 5% to 22% of incident ESRD patients (Fig 1).[1-8] There is widespread belief that intervention is simple, safe, and most beneficial to the majority of patients. As a result, there is a tendency by internists, nephrologists, and cardiologists to pursue this diagnosis at the slightest possibility of its existence, whether or not there is any clinical relevance to the diagnosis. AIRVD also has become the center of clinical controversy in view of the ease with which it can be diagnosed and radiologically corrected by interventional means (ie, balloon angioplasty with stenting either by interventional radiologists, interventional nephrologists, or interventional cardiologists).[6,8-12] Clinicians have a tendency to intervene either radiologically, cardiologically, or surgically to correct any anatomic lesion, although its hemodynamic and physiologic significance may not be clear, especially if there is any degree of renal insufficiency.

The patients with AIRVD have a significant number of associated comorbidities, leading to higher mortality rates in general and especially after initiating dialysis.[1,2,5] Based on USRDS data, patients with AIRVD causing ESRD had statistically significant more congestive heart failure, coronary heart disease, myocardial infarctions, and peripheral vascular disease.[5] High mortality rates and some progression into renal failure have been shown in patients with known unilateral atherosclerotic renal artery occlusion and renal insufficiency, but not necessarily from occlusion of the remaining renal artery.[13] AIRVD is being recognized with increasing frequency in patients undergoing angiography for coronary artery disease or peripheral vascular disease, in as many as 20% of the patients undergoing coronary angiography.[13-17] The identification of a significant renal artery lesion during another imaging procedure has made it more difficult to ignore these abnormalities. Whether or not they are hemodynamically and physiologically significant is difficult to decide. The usual clinical indications for intervention include resistant hypertension, progressive renal insufficiency, or prevention of renal insufficiency (Table 1). In a recent, prospective, population-based study in North Carolina using duplex ultrasound for diagnosis, approximately 7% of 834 patients greater than 60 years of age had significant AIRVD, its presence correlating well with increasing age and systolic blood pressure.[7]

This article reviews the current literature through September 2002 in an attempt to answer

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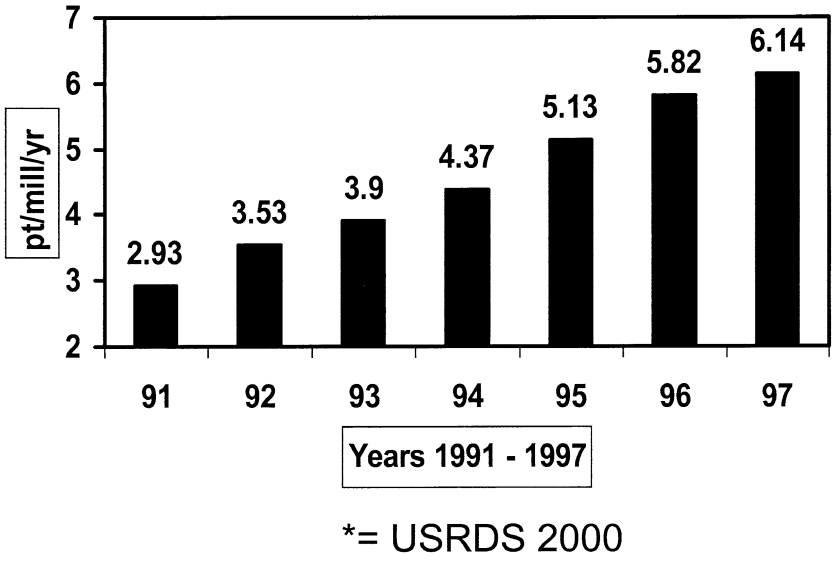

Fig 1. The changing incidence rate of atherosclerotic ischemic renal vascular disease. From the USRDS database and Fatica et al.[2]

the question, Do published outcomes justify the overzealous approach to diagnosis and therapy of atherosclerotic ischemic renal vascular disease?

DIAGNOSIS, THERAPY, AND OUTCOMES

The decision to be more invasive and subject the patient to either surgery or stent placement should be based largely on the clinical acumen of the physician using sound judgment to come to the conclusion that it is necessary to intervene. Certainly if the patient has anatomic renal artery stenosis and is able to tolerate angiotensin-converting enzyme (ACE) inhibitors without renal functional deterioration in the setting of good blood pressure control, it is highly unlikely that the lesions are hemodynamically significant.

Evidence-based protocols do not exist at this time to guide the clinician. AIRVD should be suspected in some particular clinical settings with severe or refractory hypertension, recurrent episodes of flash pulmonary edema in patients with normal left ventricular systolic function, or an increase in the plasma creatinine concentration after the administration of an ACE inhibitor or angiotensin-receptor blocking agents (ARB) (Table 2). Hypertension is present in the majority of these patients. Based on retrospective arteriographic studies, rates of progression of renal artery stenosis have been estimated to range from 36% to 53%.[18,19] In more recent studies using duplex Doppler ultrasound in patients followed-up for nearly 3 years, there was an overall progression in 18% to 49% of the patients related to the original degree of stenosis for renal arteries initially classified as being normal, less than 60% stenosis and 60% or greater stenosis, respectively, *P* less than .03 log rank test, with only 9 renal artery occlusions.[19,20] Similarly, there was a 21% incidence of significant decrease in kidney size, which was as-

Table 1. Indications for Intervention

Resistant hypertension
Recurrent pulmonary edema
Progressive azotemia
Progressive ↓ creatinine clearance on ACE inhibitors or ARBs
Need for ACE inhibitors in other underlying renal situations (eg, diabetic nephropathy, congestive heart failure with need for peripheral vascular unloading)

Table 2. AIRVD: Suspicious Clinical Settings

Elderly patient with refractory or severe hypertension on ≥ 3 or 4 agents
Asymmetry in kidney size or unilateral decrease in solitary kidney size
Recurrent flash pulmonary edema
White race, smoking history, and age >50 years
Increase in serum creatinine after use of ACE inhibitors, or angiotensin receptor blockers
Recurrent episodes of flash pulmonary edema with normal ventricular hemodynamics
Bland urinary sediment with little to moderate amounts of protein

sociated with increasing systolic blood pressures and increases in the serum creatinine levels.[21] These data would suggest there is an inevitable but slow progression of AIRVD in the susceptible patients. In a recent editorial by Zierler, the absolute risk for developing ESRD was stated as a cumulative 5-year incidence of 11.8%.[22]

Table 3 lists the potential benefits and hazards of any intervention. The older literature clearly has shown the benefit of surgical intervention in patients with flash pulmonary edema and hypertension with renal insufficiency.[23-25] More recent data show that a large number of patients benefited from bypass surgery and many are able to be removed from dialysis.[26-28] The most recent data from North Carolina where there appears to be a significant incidence of AIRVD leading to ESRD, especially in the white smoking patient population, is very encouraging. In their study of 626 patients, 28 were removed from dialysis; blood pressure control improved in 85% of the group, renal function was unchanged in 42% of the patients, and worse in 10%.[27] Surgical and in-hospital mortality is about 7% in this patient population.

The invasive cardiologists, interventional nephrologists, and interventional radiologists usually visually can correct the stenosis in about 95% to 99% of cases with deployment of the stent. However, one must differentiate an anatomic result from a functional one. More recent data would suggest that the detection of elevated intrarenal resistive indices, especially in the contralateral kidney, would predict failure of the intervention.[29] If these initial data can be duplicated in diverse populations this may provide a quasifunctional test to determine patterns of intrarenal hemodynamics in patients with underlying renal vascular disease. ACE inhibitors could be prescribed with close monitoring of renal function; if there is no change in creatinine level or clearance then the renal artery lesions are probably not hemodynamically significant.[30]

Table 3. Benefits and Hazards of Nonsurgical Intervention

Medical management with careful clinical monitoring
Percutaneous renal artery angioplasty with stenting
Surgical revascularization
  Endarterectomy versus bypass

Alleged Benefits	Real Risks
Improved blood pressure control	Contrast nephropathy
Improve renal function	Atheroembolic issue
Reverse dialysis dependency	Interventional risks Dissection Bleeding Hematomas Aortic rupture
Delay progressive chronic kidney disease	Fluid overload/congestive heart failure

Table 4. Generally Accepted Contraindications to Intervention

Small kidneys (? $<$ 9.0 cm versus $<$ 8.0 cm)
Significantly increased serum creatinine level
Nephrotic syndrome
Contraindication to possible surgery

The initial success rate of stenting is usually greater than 95%. A few randomized trials comparing medical therapy with intervention are available, showing no significant differences in renal function. As stated by Yutan et al,[31] "there is immediate clinical benefit for most patients...but, within 5 years the benefit is not maintained." In the study by vanJaarsvald, follow-up angiography showed total renal artery occlusion in 9% of patients by 12 months in those treated with medications.[35] Overall, after intervention and stent deployment, one can estimate that blood pressure control will improve in 50% to 70% of patients and renal function will improve slightly or remain unchanged in 65% to 70% of patients (Table 4). One should be aware of contraindications to intervention; these are usually patients who would not gain any benefit from a procedure (Table 5).

CONCLUSION

Although the published literature strongly supports the ability of surgeons and interventionalists to correct atherosclerotic renal artery stenosis, the clinical outcomes do not uniformly show significant improvement in the patients' renal insufficiency or hypertension. There is a short-term improvement in blood pressure control but 5-year data suggest no difference between medical therapy and interventional therapy except in the surgical series, which seem to have better outcomes.[31]

As a result the physicians must use their best clinical judgment before embarking on a diagnostic and therapeutic course that clearly has hazards,

Table 5. Results From Selected Studies

Author	Patients	Comments
Lederman[32]	300	BP ↓ in 70%, ↓ creatinine level in 27%, ↑ creatinine level in 19%, 10% mortality
Leertouwer[33]	678 meta-analysis	BP ↓ 70%, BP ↑ 6%, complications in 11%, ↓ creatinine level 32%
Rodriguez-Lopez[34]	108	BP ↓ 68%, BP ↑ 6%, 2% ↓ dialysis, complications in 7%
VanJaarsveld[35]	106 56-PTRA	No change in renal function, but 9% total renal artery occlusion in medications group
Yutan[31]	76	5% mortality, 49% mortality at 5 y, 37% restenosis, decreased creatinine level in 88% initially but decreased in 25% at 5 y
Webster[36]	55 (25 medication only)	No difference in creatinine level in either group
Plouin[37]	49	No difference in renal function
Van de Ven[38]	84 (42 medication)	24-month follow-up, Increased creatinine level in 15% of patients in both groups

Abbreviations: BP, blood pressure; ↓, decreased; ↑, increased.

with a significant portion of patients developing complications from these procedures. This is in the setting of an unknown natural history of the disease process.

Watchful waiting in stable patients certainly is safe provided renal anatomy (can be followed by appropriate noninvasive imaging technique), renal function, and blood pressure control can be monitored if the patient does not experience any bouts of heart failure or severe uncontrolled hypertension and the same course can be monitored. Although of concern, perhaps a trial of either ACE inhibitors or ARBs could be prescribed while further monitoring renal function more closely.[30] Also, renal arterial Dopplers with resistive indices may be of prognostic help in determining a course of action.[39]

There is a well-documented increase in the incidence of atherosclerotic renal artery disease as a cause of ESRD based on national and regional data. These patients present with more comorbidity and increased mortality rates. There are no large prospective medical versus intervention data on which to base a rational clinical decision. Incidental atherosclerotic renal artery stenosis also is found in as many as 20% of patients undergoing angiography for other purposes.

There is a need for a multicentered, prospective, randomized, clinical trial comparing surgical therapy with interventional radiology with aggressive medical therapies in the patients with diffuse atherosclerosis and ischemic nephropathy. Unless faced with acute processes or a significant change in blood pressure control, a prudent watchful course quite likely is safe: monitoring blood pressure control, cardiovascular disease risk factor control, use of ACE inhibitors and ARBs, monitoring renal size and vascular anatomy. Should there be any change in these parameters then the patient should be offered more invasive evaluation and therapy.

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