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EDITORIAL COMMENT

Renal Artery Revascularization

Is There a Rationale to Perform?*

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Renal artery stenosis is a common finding in patients with atherosclerotic vascular disease (1). Among patients with renal artery stenosis, more than 90% are atherosclerotic in nature, which typically involves the ostium and the proximal portion of the main renal artery with plaque extending into the peri-renal aorta (1). The prevalence of atherosclerotic renal artery stenosis (ARAS) increases with age, presence of diabetes, peripheral arterial disease, coronary artery disease, hypertension, and dyslipidemia. Fibromuscular dysplasia, a distant second in the etiology of renal artery stenosis accounts for <10% of cases and is typically seen in young and middle-aged women. As opposed to ARAS, fibromuscular dysplasia usually affects the distal two-thirds of the main renal artery with a characteristic beaded angiographic appearance. Based on epidemiological data, ARAS appears to be a relatively common clinical finding and is present in ~6.8% of patients over the age of 65 years (2) and in >50% of patients with atherosclerosis elsewhere such as abdominal aortic aneurysm, aorto-occlusive disease, or lower extremity occlusive disease (3).

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The goal for either pharmacological or revascularization therapy of ARAS should be normalization of blood pressure, preservation of renal function, and reduction of the risk of cardiovascular events. Among those with chronic renal disease or established nephropathy, one of the more meaningful end points is the rate of progression to renal replacement therapy or dialysis. The availability of safe and effective pharmacological agents in the contemporary era has made the control of blood pressure relatively easier with drugs than even a few years ago. At the same time, the improvements in interventional technology have increased the technical success rate of renal artery revascularization to >98% in most series. Since, optimal therapy in patients with ARAS should include optimal blood pressure control with pharmacological agents, modification of cardiovascular risk factors, the appropriate use of antiplatelet therapy, and lipid-lowering therapy, the clinically relevant question then becomes which patients are likely to benefit from renal artery revascularization and who should be targeted for such therapies.

In this issue of the *Journal*, Safian and Madder (4) and Textor et al. (5) offer perspective on the optimal role or lack of role for renal artery revascularization in patients with ARAS. Since the initial description of renal artery stenting by Gruntzig in 1978, there have been several contrasting studies on the efficacy of percutaneous revascularization for renal artery stenosis with absence of a consistent benefit. Several parameters have been suggested to predict clinical improvement after renal artery stenting such as the renal artery resistance index (6,7), renal size, and renal vein renin measurement, but the predictive value of such indexes has not been consistent. Despite the lack of a consistent benefit, the number of renal artery stenting procedures has quadrupled in the last decade (8). It, therefore, would be logical to try and understand the rationale for these procedures and try and define the patient cohort most likely to benefit from renal artery stenting. To this end, Safian and Madder (4) offer a new classification for ARAS stratifying patients into those with and without nephropathy (type 1/2) and those with and without renal ischemia (type A/B). Based on this classification, the authors suggest that for patients with no nephropathy and normal renal blood flow (type 1A), they would intensify the antihypertensive regimen and follow patients clinically for the development of vital organ injury. They further suggest that the best candidates for revascularization are those with minimal or no nephropathy and evidence of renal ischemia (type 1B), and the worst candidates are those with advanced nephropathy (type 2), especially if renal ischemia is absent (type 2A). It should be noted that the predictive ability of tests currently used for assessment of renal ischemia have not been well studied and will need further objective testing based on clinical hard end points to validate this approach. The authors contention that patients with severe bilateral ARAS, minimal or no nephropathy, renal ischemia (type 1B), and cardiovascular injury are ideal candidates for renal revascularization is consistent with current American College of Cardiology (ACC)/American Heart Association guidelines for the management of patients with peripheral arterial disease (2). These guidelines state that ARAS and unexplained pulmonary edema and/or recurrent heart failure are the only class I recommendations for renal artery revascularization.

Textor et al. (5) appropriately point out the lack of evidence of benefit with renal artery stenting and further enumerate the limitation of the studies to date including visual estimates of the degree of stenosis, significant crossover to the interventional arm, lack of standardized methods to assess the status of the intrarenal microcirculation, and renal hemodynamic and functional reserve. They also de-

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scribe the intrinsic differences between the coronary and peripheral circulation and the renal circulation. Unlike blood vessels supplying the heart or brain, the vessels to the kidney deliver a vast excess of oxygenated blood, far more than needed for basal metabolic demands, and the kidneys may be less susceptible to moderate changes in blood flow compared with other organs.

Both Safian and Madder (4) and Textor et al. (5) suggest the need for appropriately designed randomized clinical trials to further define the role of renal artery revascularization and identify the cohort likely to benefit after renal artery revascularization. The ongoing CORAL (Cardiovascular Outcomes in Renal Atherosclerotic Lesions) study will compare the effect of optimal medical therapy alone to stenting with optimal medical therapy, on a composite of cardiovascular and renal end points: cardiovascular or renal death, myocardial infarction, hospitalization for congestive heart failure, stroke, doubling of serum creatinine level, and need for renal replacement therapy in 1,080 patients. This trial has the potential to help us understand any incremental benefits of renal artery revascularization on clinical end points above and beyond contemporary optimal medical therapy. Two recent trials, the STAR (Stenting in Renal Dysfunction Caused by Atherosclerotic Renal Artery Stenosis) study and the ASTRAL (Angioplasty and Stent for Renal Artery Lesions) study have attempted to assess the effect of revascularization on the progression of chronic kidney disease. The ASTRAL trial presented at the Society for Cardiovascular Angiography Interventions-ACC i2 Summit/ACC 2008 reported that renal revascularization did not improve serum creatinine, systolic blood pressure, renal events (such as acute renal failure or dialysis), mortality, or overall vascular events (9). The results of the STAR study have not been reported.

Based on the reviews by Safian and Madder (4) and Textor et al. (5) and available data, several observations can be made regarding renal artery revascularization. First, the majority of patients with ARAS do not have renovascular hypertension explaining the low cure rate of hypertension after technically successful renal artery revascularization; secondly, all patients with ARAS should be treated with evidence-based secondary preventative therapies such as antiplatelet agents, statins, and optimal blood-pressure-lowering agents; thirdly, only a subset of patients with ARAS likely benefit from renal artery stenting, and identification of this cohort is paramount to long-term benefits from renal artery revascularization, and, finally, trials such as the CORAL study will likely help define the role of renal artery revascularization in the future. At this point, it seems prudent to select patients carefully for renal revascularization based on objective evidence of renal ischemia without evidence of significant parenchymal renal disease or nephropathy. The current ACC/American Heart Association guidelines are a reasonable reference point for which patients to assess for ARAS and those likely to benefit from revascularization. As stated before, it is imperative that these patients receive optimal secondary preventative therapy to reduce future cardiovascular events (10). A national registry that collects data on all patients undergoing renal artery intervention possibly under the auspices of ACC-National Cardiovascular Data Registry may prevent overuse of renal artery revascularization and at the same time help us learn in the "real world" setting which patients benefits and who may actually do worse after these procedures. Given the lack of benefit in most cases, physicians may serve themselves and their patients well by exercising appropriate caution before proceeding with renal artery stenting.

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Key Words: renal artery stenosis ■ angioplasty ■ stenting ■ renal revascularization.