Editorial

Atherosclerotic renal artery stenosis

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Atherosclerotic renal artery stenosis (RAS) is a secondary cause of hypertension (1). RAS causes renal ischemia which leads to renin release from the juxtaglomerular cells of the kidneys (2). Renin release activates conversion of angiotensin I to angiotensin II and increases adrenal gland release of aldosterone (3). Angiotensin II causes vasoconstriction, and aldosterone causes increased retention of sodium and water, both leading to renovascular hypertension (RVHT) (3). RVHT occurs in 1% to 5% of persons with hypertension and in 20% to 40% of persons with severe refractory hypertension or persons having diagnostic coronary angiography (4). Atherosclerotic RAS is the most common cause of RVHT (5).

RAS should be suspected if an abdominal bruit is heard, if there is accelerated or resistant hypertension, or if there is unexplained deterioration in kidney function or electrolyte imbalance (1). RAS should also be suspected if there is worsening renal function after administration of an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) or if there is sudden, unexplained pulmonary edema (6). Atherosclerotic RAS usually occurs in older persons and in patients with multiple risk factors for atherosclerosis (5). Screening noninvasive imaging tests for RAS include spiral computed tomography (CT), magnetic resonance imaging (MRI), captopril scintigraphy, and duplex Doppler ultrasound (DUS) (4,7). Renal angiography is needed if RAS revascularization is considered (8).

The 2005 American College of Cardiology/American Heart Association (ACC/AHA) guidelines recommended percutaneous revascularization of hemodynamically significant atherosclerotic RAS with a class IIa recommendation for the following conditions: (I) accelerated hypertension, resistant hypertension, malignant hypertension, hypertension with an unexplained unilateral small kidney, and hypertension with intolerance to medication; (II) progressive chronic kidney disease with bilateral RAS, or a RAS to a solitary functioning kidney; (III) recurrent, unexplained congestive heart failure or sudden, unexplained pulmonary edema; or (IV) unstable angina pectoris (6).

Although uncontrolled studies suggested that renal artery angioplasty or stenting in persons with atherosclerotic RAS with hypertension caused significant lowering of blood pressure and stabilization of chronic kidney disease, randomized, controlled clinical trials of renal artery angioplasty or renal artery angioplasty with stent placement have failed to show a benefit of renal artery revascularization in lowering blood pressure (9-12).

The Angioplasty and Stent for Renal Artery Lesions (ASTRAL) trial randomized 806 persons with atherosclerotic renovascular disease to renal artery revascularization plus medical treatment or to receive medical treatment alone (9). At a median follow-up of 34 months, compared to medical treatment alone, the renal artery revascularization group had a similar systolic blood pressure, a smaller decrease in diastolic blood pressure, and similar rates of renal events (9). Serious complications caused by renal artery revascularization occurred in 23 patients, including two deaths and three amputations of toes or limbs (9). Renal artery revascularization did not improve blood pressure, renal events, cardiovascular events, or mortality in this study (9). In addition, patients with bilateral RAS or more than 70% stenosis in a single functioning kidney did not have a beneficial outcome (9).

Of 64 persons with atherosclerotic RAS and a creatinine clearance below 80 mL/min/1.73 m^2 randomized to stent placement plus medical treatment, 46 patients had the

procedure, and 76 similar persons were randomized to medical treatment alone (10). Stent placement had no effect on progression of impaired renal function. The stent placement group had 2 procedure-related deaths (4%), 1 late death caused by an infected hematoma (2%), and 1 patient who required dialysis secondary to cholesterol embolism (2%) (10).

The Cardiovascular Outcomes in Renal Atherosclerotic Lesions (CORAL) study randomized 947 participants with atherosclerotic RAS and either systolic hypertension receiving at least two antihypertensive drugs or chronic kidney disease to medical treatment plus renal artery stenting or to medical treatment alone (11). At a median follow-up of 43 months, the rates of the primary composite endpoint of death from cardiovascular or renal causes, myocardial infarction, stroke, hospitalization for congestive heart failure, progressive renal insufficiency, or the need for renal replacement therapy were similar in both treatment groups (11). There was no significant difference in the rates of the individual components of the primary endpoint or in all-cause mortality between both treatment groups. However, the renal artery stent plus medical treatment group had a 2.3 mmHg lower systolic blood pressure than the medical treatment alone group (11).

A meta-analysis of seven randomized controlled clinical trials investigating revascularization versus medical therapy alone for atherosclerotic RAS included 2,139 patients (12). This meta-analysis showed that renal artery revascularization by angioplasty with or without renal artery stenting was not better than medical treatment alone in improving any clinical outcome including change in systolic blood pressure, mortality, nonfatal myocardial infarction, renal events, hospitalization for congestive heart failure, or stroke (12).

These studies show that for the vast majority of patients with atherosclerotic RAS and either hypertension or chronic kidney disease, treatment of atherosclerotic RAS should be limited to medical management (13). At 1-year mean follow-up of 175 patients with hypertension due to RAS treated with percutaneous transluminal renal angioplasty (PTRA), 35 patients (20%) also developed restenosis (14). At 5.1-year mean follow-up of these patients, 56 patients (32%) developed restenosis (14). In the patients with atherosclerotic RAS (70% of the group) in this study, no significant reduction in systolic blood pressure was found (14).

Whether patients with severe atherosclerotic RAS to a single functioning kidney, severe RAS and acute kidney injury, patients presenting with flash pulmonary edema, patients with resistant hypertension, and patients with progressive reduction of renal function might benefit from renal artery revascularization remains to be demonstrated by randomized controlled clinical trials (13,15,16).

A retrospective analysis of 529 patients with atherosclerotic RAS showed that at 3.8-year median follow-up, use of antiplatelet drugs reduced mortality by 48% (17). Use of beta blockers reduced mortality by 55% and nonfatal cardiovascular events by 26% (17). The 2005 ACC/AHA guidelines recommended that patients with hypertension associated with atherosclerotic RAS should be treated for their hypertension with a class I indication with either an ACE inhibitor, ARB, calcium channel blocker (CCB), or beta blocker (6). These patients should also be treated with an antiplatelet drug, statins, smoking cessation, control of diabetes mellitus, and weight loss if obese to reduce progression of atherosclerosis. However, it should be pointed out that there are no randomized controlled clinical trial data showing the efficacy on outcomes of different medical regimens in treating patients with atherosclerotic RAS (5).

Finally, it is time for the ACC/AHA to update their guidelines for the indications for renal artery angioplasty with renal artery stenting for patients with atherosclerotic RAS. Expert medical opinion will be needed for these updated guidelines because we do not have randomized clinical controlled trial data to support the recommended indications for renal artery revascularization.

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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