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In Practice

Renal Artery Stenosis: Prevalence of, Risk Factors for, and Management of In-Stent Stenosis

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Atherosclerotic renal artery stenosis is common and is associated with hypertension and chronic kidney disease. More frequent use of percutaneous renal artery stent placement for the treatment of renal artery stenosis during the past 2 decades has increased the number of patients with implanted stents. In-stent stenosis is a serious problem, occurring more frequently than earlier reports suggest and potentially resulting in late complications. Currently, there are no guidelines covering the approach to restenosis after renal artery stent placement. This article reviews data on the prevalence of and risk factors for the development of in-stent stenosis and the clinical manifestations, evaluation, and treatment of in-stent stenosis and suggests a strategy for the management of patients after percutaneous renal artery stent placement.
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INDEX WORDS: Renal artery stent; in-stent stenosis; renal artery stenosis; secondary hypertension.

CASE PRESENTATION

A 74-year-old woman with coronary artery disease and dyslipidemia presented with hypertensive urgency in October 2005. A computed tomography angiogram (CTA) showed bilateral atherosclerotic renal artery stenosis, a 4.75-cm infrarenal abdominal aortic aneurysm, and iliac occlusive disease. Angiography showed mild proximal left renal artery stenosis and right renal artery high-grade proximal stenosis in a 5-mm diameter vessel; this lesion was treated with percutaneous renal artery stent placement using an Express SD bare-metal stent (Boston Scientific, www.bostonscientific.com). After this procedure, the patient remained on treatment with 4 antihypertensive agents, including an angiotensin-converting enzyme (ACE) inhibitor, with good blood pressure control and stable serum creatinine level of 1.5 mg/dL (132 μmol/L; estimated glomerular filtration rate [eGFR] of 34 mL/min/1.73 m^2 using the CKD-EPI [Chronic Kidney Disease Epidemiology Collaboration] standardized serum creatinine equation). One year later, aortobifemoral bypass surgery was performed after a magnetic resonance angiogram showed progression of aortoiliac disease. On these images, the stented portion of the right renal artery was obscured by signal gap artifact. Two years later, she developed worsening kidney function and blood pressure. Renal angiography was repeated and showed both severe left renal artery stenosis and right renal artery in-stent stenosis. Angioplasty of the right renal artery in-stent stenosis and percutaneous renal artery stent placement in the left renal artery stenosis using a 5×15-mm Express SD stent were performed. Blood pressure and kidney function improved.

Seventeen months later, hypertension worsened and creatinine level increased to 4 mg/dL (353.6 μmol/L; eGFR, 10.3 mL/min/1.73 m^2). Duplex ultrasonography showed peak systolic velocity in the aorta and proximal, mid, and distal left renal artery of 97, 416, 248, and 179 cm/s, respectively. The right renal artery could not be interrogated due to bowel gas. Angiography showed an occluded right renal artery stent not amenable to intervention and severe left in-stent stenosis. The lesion in the left renal artery stent was treated with angioplasty, with serum creatinine level subsequently decreasing to 1.1 mg/dL (97.2 μmol/L; eGFR, 49.4 mL/min/1.73 m^2) postprocedure. Within 6 months, the patient developed recurrent acute kidney injury. Despite discontinuation of the ACE inhibitor, creatinine level remained at 4.5 mg/dL (397.8 μmol/L; eGFR, 8.8 mL/min/1.73 m^2). Angiography showed severe left in-stent stenosis with an 81–mm Hg systolic pressure gradient (Fig 1). An Express SD 5 × 19-mm stent was placed within the pre-existing stent, followed by improvement in serum creatinine level to 1.4 mg/dL (123.8 μmol/L; eGFR, 36.9 mL/min/1.73 m^2 [Fig 2]).

INTRODUCTION

Renal artery stenosis occurs in >40% of patients with peripheral vascular disease and is noted in 10%-14% of patients undergoing coronary catheterization. More than 20,000 percutaneous renal artery stent placement procedures are performed annually in the United States.[1] Currently, there are no guidelines for the follow-up of patients who have undergone percutaneous renal artery stent placement. The purpose of this article is to review the available data regarding the incidence of and risk factors for the development of in-stent stenosis after percutaneous renal artery stent placement, along with screening and treatment options for in-stent stenosis. Finally, we discuss one approach to the management of patients with renal artery stents.

HISTORY OF RENAL ARTERY STENTS

Surgical renal revascularization, first performed in 1962, preceded the development of endovascular techniques for the treatment of atherosclerotic renal artery

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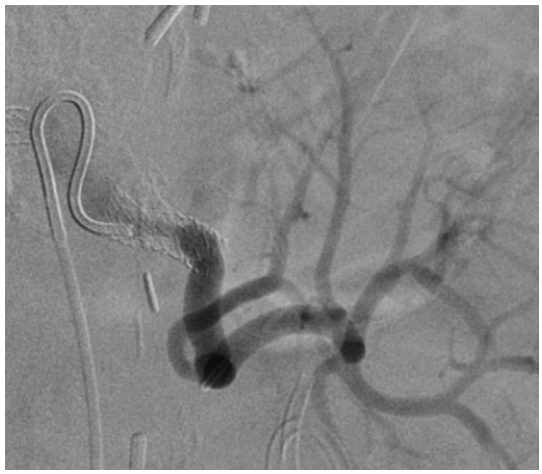

Figure 1. Angiogram showing renal artery in-stent stenosis.

stenosis. Percutaneous renal artery angioplasty, introduced in 1978, provided excellent short-term results but unacceptably high restenosis rates, particularly for ostial lesions, leading to application of stents for the treatment of renal artery stenosis. An early 2-arm prospective study comparing angioplasty with percutaneous renal artery stent placement in patients with renal artery stenosis reported 6-month primary patency rates of 75% for the stent group versus 29% after angioplasty alone.[2] Similarly, early meta-analyses suggested low restenosis rates post–percutaneous renal artery stent placement, with an overall rate of 17%.[3] Accordingly, percutaneous renal artery stent placement has become the standard treatment of atherosclerotic renal artery stenosis and, depending on the institution, is performed by interventional radiologists, cardiologists, and vascular surgeons.

THE CONTROVERSY OVER RENAL ARTERY STENT PLACEMENT

Indications for percutaneous renal artery stent placement in patients with renal artery stenosis were delineated by the American Heart Association to include resistant hypertension, unstable cardiac syndromes, and decreased kidney function attributed to reduced glomerular capillary pressure.[4] However, prospective randomized trials have been unable to demonstrate the superiority of percutaneous renal artery stent placement over medical therapy with respect to clinical outcomes.[5] This failure has been attributed to limitations in study design, suboptimal medical therapy, inclusion of patients with non–hemodynamically significant renal artery stenosis, high crossover rates, and inadequate surveillance for in-stent stenosis, among other reasons. In 2009, ASTRAL (Angioplasty and Stenting for Renal Artery Lesions) investigators published results of a randomized trial enrolling 806 patients with renal artery stenosis in the United Kingdom, Australia, and New Zealand to medical therapy versus percutaneous renal artery stent placement. They reported no benefit associated with percutaneous renal artery stent placement on the primary outcome of slope of the reciprocal of serum creatinine during a mean follow-up of 34 months. The trial has been criticized for its inclusion criteria, which specifically limited enrollment to patients whose physicians were "uncertain [that the patient] would have a worthwhile clinical benefit from revascularization."[6(p1954)] A smaller study (STAR [The Benefit of Stent Placement and Blood Pressure and Lipid-Lowering for the Prevention of Progression of Renal Dysfunction Caused by Atherosclerotic Ostial Stenosis of the Renal Artery]) also found no benefit of percutaneous renal artery stent placement over medical therapy on change in kidney function as defined by at least a 20% decrease in estimated creatinine clearance.[7] The CORAL (Cardiovascular Outcomes in Renal Atherosclerotic Lesions) Study recently has completed data collection for the largest group of patients with renal artery stenosis randomly assigned to percutaneous renal artery stent placement versus optimal medical therapy.[8] This trial used an angiographic core laboratory to ensure the hemodynamic significance of renal artery stenosis, included a duplex ultrasonography substudy tracking patency, and required blockade of the renin-angiotensin system. Results are expected in late 2012 or 2013.

COMPLICATIONS OF RENAL ARTERY STENT PLACEMENT

Complication rates related to percutaneous renal artery stent placement range from 1%-20%. Minor complications include groin hematomas, other bleeding, and contrast nephrotoxicity. Major complications occur in up to 9.4% and include atheroembolism, renal artery thrombosis or dissection, perinephric he-

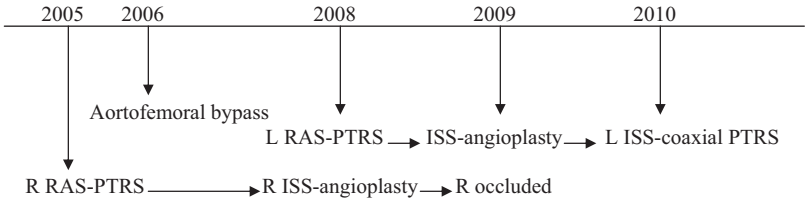

Figure 2. Case timeline of in-stent stenosis (ISS) and interventions. Abbreviations: L, left renal artery; PTRS, percutaneous renal artery stent placement; R, right renal artery; RAS, renal artery stenosis.