CLINICAL REVIEW

Technical Considerations for Renal Artery Stenting

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Abstract
Renal artery stenosis (RAS) is the most common secondary cause of hypertension. It is associated with progressive renal failure. Percutaneous transluminal renal angioplasty and stenting (PTRAS) is associated with improved blood pressure control and preservation of renal function. PTRAS is associated with a high technical success rate and an acceptable adverse event and restenosis rate. Embolization and restenosis limit the benefit of this procedure, and are areas of future clinical research. After PTRAS, patients should be followed clinically and with duplex ultrasonography.

Key words: angioplasty, ischemic nephropathy, renal artery stenosis, peripheral vascular disease

Renal artery stenosis is the most common secondary cause of hypertension (HTN). It affects 5% of the 50 million people with HTN in the United States. Renovascular disease leads to malignant HTN in 10–45% of patients. In patients older than 50 years, it is responsible for 5–15% of the renal failure population, and 10–20% of the end-stage renal disease population. The prevalence of RAS, greater than 60%, has been reported to be 6.8% in patients older than 65 years of age.

Percutaneous transluminal renal angioplasty (PTRA) was introduced as an alternative to surgery by Gruentzig in 1978. Until the early 1990’s, surgical renal artery revascularization was primarily performed for RAS. In 1993, secondary patency, reduction in blood pressure and improvement in renal function were found to be similar with surgery or PTRA. PTRA was associated with a decreased number of complications. Currently, surgical revascularization is rarely performed solely for RAS.

In 1998, PTRA was demonstrated to provide a significant decrease in systolic pressure as compared to medical therapy in patients with bilateral RAS. In patients with unilateral RAS, PTRA, with stenting if necessary, has been associated with the need for fewer medications to provide a similar reduction of blood pressure compared to medical therapy. The Dutch RAS interventional cooperative trial randomized patients with greater than 50% stenosis and diastolic hypertension despite treatment with 2 anti-hypertensive medications to medical therapy versus PTRA without stenting. By 3 months, 44% of the medical group had failed medical therapy and crossed over to the intervention group. At 3 and 12 months, the extent of blood pressure lowering was similar. However, the number and dose of antihypertensive medications was lower in the PTRA group. Recent data from the RENAISSANCE trial demonstrated a significant improvement in systolic hypertension 9 months after percutaneous transluminal renal angioplasty and stenting (PTRAS).

In a non-randomized study, PTRA improved renal function in 41–43% of patients. Harden reported improvement or stabilization of renal function in 69% of stented renal arteries. In 2000, Watson demonstrated that renal artery stent placement was associated with a positive slope of the reciprocal of serum creatinine 72% of the time and a less negative slope 78% of the time.

The effect of renal artery angioplasty on renal function was elegantly demonstrated by La Batide-Alanore in 2001. After following 32 patients who underwent PTRA for a mean of 6 months, split renal function was derived using captopril renal scintography. The renal function of the treated kidney was found to improve significantly after PTRA. This suggests that PTRA improves the renal function in patients with unilateral RAS.
Plaque recoil with angioplasty alone leads to restenosis and limits patency. In 1999, 85 patients with greater than 50% RAS were randomized to treatment with PTRA versus PTRAS. PTRAS was associated with a significant improvement in primary and secondary patency rates and reduced restenosis without an increase in complications.12 In a meta-analysis of 14 studies involving 678 patients, RAS was associated with a 98% technical success rate. Hypertension was cured in 20% and improved in 49%. In patients with renal impairment, renal function was improved in 30% and stabilized in 38%. Most recently, Rocha-Singh, et al. reported results of the first prospective RAS trial in which the results were monitored by an independent core laboratory. Renal artery stenting for failed PTRA was associated with a significant lowering of systolic and diastolic blood pressure and a reduction in the number of antihypertensive agents.14

### Indications for Renal Artery Revascularization

Reductions greater than 60% are associated with a significant trans-lesional gradient.13 In a comparison of pressure gradient to renal artery vessel diameter, a vessel stenosis of approximately 50% corresponded to a 20 mm Hg pressure gradient. Beyond this severity of stenosis, there was a rapid increase in trans-lesional pressure gradients.14 Translesional pressure gradients are often measured using end-hole catheters. This technique may overestimate the gradient secondary to pressure damping. To measure pressure gradients associated with RAS, 0.014" pressure wires may be used.15 Pressure wires have been used in combination with papavarine to evaluate renal artery fractional flow reserve (FFR) in arteries with moderate (50–90%) stenosis. Subramanian, et al. demonstrated that maximal hyperemia can be achieved with papavarine, and that baseline pressure gradients correlated with FFR. They found a poor correlation between the visual angiographic estimation and hemodynamic measures of lesion severity. Furthermore, the visually estimated lesion severity was 74.9% ± 11.5%, while the quantitative vascular angiographic lesion severity was 56.6% ± 10.8%.16

These results suggest that interventionalists may overestimate renal artery lesion severity. This may lead to interventions on hemodynamically insignificant stenosis. Percutaneous renal artery revascularization should be reserved for patients with an angiographic RAS severity of 70% or greater, and a translesional gradient of greater than 20 mmHg. It is our recommendation that the hemodynamic significance of a lesion’s severity, using either renal arterial duplex or pressure wire, be confirmed prior to proceeding with intervention. This may decrease the number of PTRAS procedures performed without associated clinical benefit.

The newly released American College of Cardiology/American Heart Association Guidelines for the Management of Patients with Peripheral Arterial Disease defines the indications for percutaneous renal artery revascularization (Table 1). Surgery for RAS is indicated for patients with clinical indications who have fibromuscular dysplasia (FMD) that extends into the segmental arteries and patients with FMD and macro aneurysms, early primary branching of the main renal artery and in combination with pararenal aortic reconstruction.

Prospectively identifying patients who are likely to derive a benefit from renal artery revascularization is a challenge in treating patients with RAS. Zelar et al. reported that diabetes mellitus and nephrosclerosis do not define sets of patients in whom we cannot expect improvement of renal function. They found that elevated serum creatinine and impaired left ventricular function were independent predictors of improved renal function. Female sex, preserved parenchymal thickness and baseline mean arterial blood pressure predicted improved blood pressure control.17

### Intervention

Periprocedural anti-platelet therapy varies among studies. Presumably due to the high flow and low resistance within the renal arteries, treatment with aspirin alone has been associated with good outcomes. In A study to evaluate the safety and effectiveness of the Palmaz balloon expandable stent In the REnal artery after

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<tr>
<th>Indication</th>
<th>Classification of Recommendation</th>
<th>Level of Evidence</th>
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<tr>
<td>Asymptomatic bilateral or solitary viable kidney</td>
<td>IIB</td>
<td>C</td>
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<tr>
<td>Accelerated hypertension</td>
<td>IIA</td>
<td>B</td>
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<tr>
<td>Resistant hypertension</td>
<td>IIA</td>
<td>B</td>
</tr>
<tr>
<td>Hypertension and unexplained unilateral small kidney</td>
<td>IIA</td>
<td>B</td>
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<tr>
<td>Hypertension with intolerance to medication</td>
<td>IIA</td>
<td>B</td>
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<tr>
<td>Progressive kidney disease and bilateral RAS or RAS to a solitary functioning kidney</td>
<td>IIA</td>
<td>B</td>
</tr>
<tr>
<td>Chronic renal insufficiency and unilateral RAS</td>
<td>IIB</td>
<td>C</td>
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<tr>
<td>Recurrent, unexplained CHF or sudden unstable angina</td>
<td>I</td>
<td>B</td>
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**Recommendation Evidence**
failed angioplasty (ASPIRE-2), aspirin 81–500 mg was administered at least one day prior to the procedure and at the operator’s discretion post-procedurally. The stent thrombosis rate in this study was 1%. Despite the lack of evidence supporting its use, it has become our habit to treat these patients with clopidogrel, in addition to aspirin, for 30 days after stent implantation. Aspirin is usually continued indefinitely. Procedural anticoagulation is usually accomplished with heparin. Although unstudied with PTRAS, some operators utilize bivalirudin based on its reliable anticoagulation and decreased bleeding events. The procedural use of glycoprotein IIb/IIIa inhibitors is currently under investigation. There is currently no indication for their routine use.

In most cases, arterial access is obtained from either common femoral artery via a retrograde approach. In cases with severe bilateral aortoiliac disease, downward orientation of the renal artery or when an abdominal aortic aneurysm is present, an antegrade approach via the brachial artery may be preferable.

Renal artery revascularization may be performed using 6-Fr guiding catheters. The choice of guide catheter not only depends on the angle in which the renal artery arises from the aorta, but also the location of the stenosis, the anatomy of the peri-renal aorta and operator preference. Most commonly, internal mammary artery, renal standard curve, renal double curve and hockey stick guides are used.

The goal of renal artery intervention is to achieve an optimal angiographic and hemodynamic result, with minimal manipulation of the renal artery in an effort to reduce atheroembolic complications. The “no-touch” technique may be used to minimize atheroembolization. In this technique a 0.035-inch guide wire is advanced in the abdominal aorta superior to the renal arteries. Over this wire, the guide catheter is advanced in proximity to the renal artery (Figure 1). The 0.035-inch wire is then retracted to the soft portion of the wire so that the guide catheter begins to assume its shape and approach the ostium of the renal artery. From this position, a 0.014-inch wire is directed through the guide and into the distal renal artery (Figure 2). The 0.035-inch wire is then removed and the guide catheter is then allowed to gently engage the ostium of the renal artery. Alternatively, the “telescoping technique” uses a diagnostic catheter introduced through a guide catheter to engage the renal artery. The guide catheter may then be advanced over the diagnostic catheter for atraumatic engagement.

The average diameter of a renal artery is 5–7 mm. This may vary depending on the presence of accessory renal arteries. Predilatation is generally performed with an angioplasty balloon smaller than the reference vessel diameter. Inflation is performed to full expansion of the balloon. Flank pain is a concerning occurrence, indicating stretching of the renal artery adventitia. Higher pressure inflations should be avoided as further dilation may result in rupture. Atherosclerotic renal artery lesions are usually associated with significant recoil, and require intra-arterial stent placement. FMD lesions usually respond to balloon angioplasty alone. Stenting of FMD lesions is reserved for “bail out” situations.

Balloon-expandable stents are typically utilized for renal arteries. Closed cell stent designs may be preferred, as they provide more radial strength at the renal ostium. Care should be taken so that 1–2 mm of the stent is within the aorta in order to assure that the ostium of the renal artery is covered (Figure 3). Orthogonal views should be employed to confirm proper stent placement. Improper placement of the
stent with the ostium uncovered may contribute to restenosis or even stent embolization (Figure 4). It is our practice to retract the stent deployment balloon proximally and reinflate the balloon to a higher pressure, in an effort to flare the ostium of the stent in the aorta. Once this is achieved, the guide catheter can be advanced over the deflating balloon within the lumen of the stent for final angiography.

**Embolic Protection**

Despite careful technique, renal function worsens in 8–32% of patients after PTRAS\(^1\),\(^2\),\(^3\),\(^4\). In the ASPIRE-2 study, major embolic events occurred in 6.3% of the procedures\(^4\). Hiramoto demonstrated that angioplasty and stenting of ex-vivo aorto-renal atheroma specimens using a 0.018-inch guidewire system was associated with thousands of atheroemboli\(^5\). Each manipulation, including guidewire manipulation, was associated with atheroemboli. Hopefully, with the development of lower profile devices, which utilize smaller guide catheters and 0.014-inch wires, distal embolization, leading to a decline in renal functioning, will decrease.

An intriguing application of distal embolic protection is in conjunction with PTRAS (Figure 5). Although this is an exciting adjunct to this procedure, distal protection devices do not prevent emboli from reaching the kidney during initial catheter manipulation or during angiography. It is important that a careful technique be used as earlier described.

Henry utilized the PercuSurge GuardWire\(^\text{®}\) device (Medtronic Vascular, Santa Rosa, California) during PTRAS of 32 atherosclerotic RAS lesions in 28 patients. Visible debris was recovered in all patients\(^2\). In a subsequent study, Henry was able to retrieve visible debris after PTRAS in 100% of patients when using a GuardWire occlusion balloon, and in 80% of patients when using a EPI filterwire\(^\text{™}\) (Boston Scientific Corp., Maple Grove, Minnesota) or AngioGuard\(^\text{™}\) (Cordis Corporation, Miami Lakes, Florida).\(^2\) Holden retrieved embolic material in 65% of patients when using an AngioGuard during PTRAS.\(^2\) Deterioration in renal function was observed in 5.3% of patients at 3 years, and 5% of patients at 12.5 months by Henry and Holden, respectively. These results appear to be better than what is commonly reported in the literature and are thought to be due to a decrease in the amount of renal atheroembolization.

The use of distal embolic protection devices may be limited by the renal artery anatomy and the lack of devices dedicated for this application. In the case of early renal artery branching, it is often necessary to choose the larger and presumably more important branch for embolic protection. Devices specifically designed for this application may lead to a decrease in the occurrence of post-procedural renal insufficiency and an improvement in the outcome of PTRAS.

In our lab, outside of clinical trials, distal protection use depends on operator preference. Distal protection should be considered in patients who are at high risk for embolization (Table 2). It is sometimes helpful to first place a more supportive “buddy wire” in the renal artery before attempting to cross the lesion with a filter device (Figure 5). A slow or no-flow observed when using a filter distal protection device is due to a clogged filter. When this occurs, there is a stagnant column of blood proximal to the filter. Simply recapturing the filter will result in embolization to the kidney. Aspiration proximal to the filter should be performed prior to recapturing the device. The Export (Medtronic), Pronto (Vascular Solutions, Inc., Minneapolis, Minnesota) or the Diver (Invatec, Roncadelle, Italy) catheters are well-suited for this application.

**Table 2. Indications for Renal Artery Distal Protection Use**

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<tr>
<th>Elderly patients</th>
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<tr>
<td>Renal dysfunction</td>
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<td>Bilateral disease</td>
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<tr>
<td>Diseased aorta</td>
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Restenosis

Restenosis with RAS is approximately 40% for arteries less than 4 mm in diameter, 14–18% for arteries 5.5 mm, and less than 10% for arteries greater than 6 mm in diameter. The overall restenosis rate for RAS is 17% (Figure 6). Restenosis following angioplasty of FMD lesions is usually less than 10%. Restenotic FMD lesions respond well to repeat balloon angioplasty. The mainstay for treatment of in-stent restenosis has been balloon angioplasty. The use of endovascular brachytherapy as an adjunct to angioplasty has also been reported. Although there are no data supporting the use for RAS, peripheral-size Cutting Balloons (Boston Scientific Corp.) provide an alternative to routine angioplasty for the treatment of in-stent restenosis. This requires the use of an 8-Fr guide, which poses a concern. It is occasionally necessary to place a second stent for a suboptimal angioplasty result.

Drug-eluting Stents

The success of drug-eluting stents in the coronary circulation has provided an impetus to evaluate the concept within renal arteries. The GREAT (Palmaz® Genesis® peripheral stainless steel balloon-expandable stent in REnal Artery Treatment) trial seeks to evaluate the effect of sirolimus-coated stents within renal arteries. Fifty-three patients were randomized to receive a sirolimus-eluting Palmaz Genesis stent (Cordis Corporation), while 52 patients received a bare Palmaz Genesis stent. The primary endpoint is the mean in-stent diameter stenosis at 6 months. At 6 months, there was a non-significant difference in the restenosis (> 50%) rate, with 6.7% in the sirolimus stent group compared to 14.3% with the bare metal stent. This translated into a decrease in target lesion revascularization (TLR) rate from 7.7% to 3.8%.

Complications

The majority of complications associated with percutaneous renal artery revascularization are related to arterial access, including hematoma, retroperitoneal hemorrhage, pseudoaneurysm, arterio-venous fistula and infection. Renal artery spasm (Figure 4) and wire-straightening pseudo-lesions are not uncommon occurrences and should be recognized and treated appropriately. Spasm responds to vasodilators, and pseudo-lesions will resolve when the wire is retracted, allowing a tortuous artery to assume its normal shape. Renal artery dissection is treated with intraarterial stent placement (Figure 7). Distal wire perforation may resolve spontaneously with reversal of anticoagulation or require coil embolization. Renal artery perforation may respond to prolonged balloon inflation with reversal anticoagulation, or may require the placement of an intraarterial stent graft (Figure 8). However, if these techniques are unsuccessful, emergent nephrectomy or aorto-renal bypass may be necessary. Atheroembolization to the kidneys, bowel or lower extremities may result in renal failure, ischemic bowel or digital ischemia, respectively.

The major adverse event rate at 2 years in the ASPIRE-2 study was 19.7%, including 14.4% TLR. A major embolic event occurred 6.3% of the time. Other serious adverse clinical events, including stent thrombosis, major hemorrhage and access site complications occurred in 1%, 1.4% and 4.8% of the patients, respectively.

Follow-up

It is our practice to perform surveillance duplex ultrasonography every 6 months after renal artery stent placement. After PTRAS, worsening of hypertension or renal function is an indication for reevaluation of the renal artery. In the RENAISSANCE trial, a renal-to-aortic ratio within the stent of > 3.5, or a peak velocity within
the stent of ≥ 225 cm/sec was felt to represent ≥ 60% restenosis. Subsequent angiography demonstrated an 87% concordance with ≥ 50% angiographic restenosis. 7

The incidental finding of renal artery in-stent restenosis in a patient with stable renal function and controlled hypertension poses a difficult therapeutic dilemma. In these situations, the original indication for renal artery intervention must be revisited and reevaluated.

References