Role of Distal Protection in Percutaneous Renal Intervention for Atherosclerotic Renovascular Disease

By Nicolas W. Shammas, MD, MS, FACC, FSCAI
From the Midwest Cardiovascular Research Foundation

ABSTRACT: Percutaneous renal intervention (PRI) for atherosclerotic obstructive renovascular disease is associated with worsening renal function in approximately 25% to 30% of patients. This is partially attributable to distal embolization of atherothrombotic debris that occurs during each step of the procedure. Proximal and distal protection has been shown to reduce embolic debris during PRI. Observational data support the use of embolic protection to prevent deterioration in glomerular filtration rate (GFR). Randomized data, however, has been disappointing. In the RESIST trial, the use of embolic filter protection or abciximab alone was associated with worsening of GFR compared to preprocedure baseline. The combination, however, showed neither worsening nor improvement in GFR compared to preprocedure baseline but did show an improvement in GFR compared to control PRI with no embolic protection. Dedicated renal embolic protection devices are not available in the United States. Also, cost-effectiveness data for routine use of these filters during PRI is lacking and therefore their use should be reserved at this time to high-risk patients and/or lesions.

Key words: embolic filter protection, embolic debris, renal intervention, renal insufficiency, indications

Treatment of atherosclerotic renovascular disease (Figure 1A) is indicated for patients with resistant hypertension and/or worsening renal insufficiency or in patients with unstable angina or flash pulmonary edema.1 Following percutaneous renal interventions (PRI) (Figure 1B) glomerular filtration rate (GFR) remains stable in about 45% to 50% of patients, improves in 25% to 30% of patients, and worsens in 25% to 30% of patients.2-4 The overall benefit seems to be offset by a subgroup of patients with continued progressive renal deterioration. It is unclear why chronic renal insufficiency (CRI) worsens in those patients despite improved renal blood flow post intervention.5 Speculations include a natural progression of CRI, radiocontrast nephropathy, reperfusion injury, and atheroembolization.

The rate of radiocontrast nephropathy can be partially reduced with hydration before and after the procedure. Atheroembolization, on the other hand, is a universal problem in any percutaneous intervention of atherosclerotic lesions of the renal, carotids, coronaries, bypass grafts, or lower extremity interventions6-10 and requires an understanding of its predictors and available mitigating interventions. It has been well documented that in every step of a percutaneous arterial intervention, from insertion of the arterial access sheath to closure of the arteriotomy site, atheroembolization may occur and does so to various degrees.11-12

In patients with already impaired renal function and significantly reduced GFR, even a small additional reduction in GFR secondary to distal embolization could raise creatinine sharply and precipitate severe renal dysfunction. Edwards et al7 have shown that embolic debris occurs in the thousands in patients undergoing renal artery stenting with balloon occlusive distal embolic protection. Change in GFR was negatively associated with captured particle counts larger than 60 micrometers ($P=.015$).

Krishnamurthi et al13 evaluated the effect of atheroembolic renal disease on morbidity and survival after surgical revascularization for renal artery obstructive disease. In 44 patients who underwent surgical revascularization for atherosclerotic renal artery stenosis, concomitant intraoperative renal biopsy was done to evaluate for the presence of atheroemboli. Postoperative patient
survival was evaluated at a median 6.2 years after revascularization. Distal embolization was found in 36% of patients. The 5-year survival in patients who had embolization was 54% vs 85% for those who did not have embolization.

PROXIMAL PROTECTION

Analysis of embolic debris following PRI consists of atheroma and platelet-rich debris. It is clear that these debris can be generated from disruption of atheroma present in the aortic wall, scraping the debris into the diagnostic or guiding catheters and inadvertently injecting them into the renal arteries. Debris also are generated from manipulation of the plaque itself by guide catheter entry into the artery or secondary to a range of maneuvers such as crossing the lesion with a wire to final treatment with stenting.

Walker et al demonstrated embolic debris during placement of guide catheters, sheaths, or diagnostic catheters before engaging the renal artery. They have used an aggressive aspiration of these catheters before engaging the renal artery, which yielded large (1 mm to 3 mm) particles in 41.7% of patients. Feldman and colleagues have promoted the concept of the “no touch technique” to avoid proximal embolization from touching the stenotic lesion with the guide catheter. A J-tip 0.035” wire is placed beyond the tip of the guide catheter to keep it away from touching the ostium of the renal artery and the aortic wall. The guide is then oriented toward the ostium of the renal artery and the vessel is engaged with a 0.014” or 0.018” wire. Proximal protection by avoiding embolization from the aortic

**Figure 1.** Atherosclerotic aorto-ostial renal disease (A). Post stent placement in the ostium of the renal artery (B).

**Figure 2.** Embolic filters more frequently used in the renal artery during percutaneous renal intervention. A=Angioguard, B=FilterWire, C=FiberNet, D=SpiderFX.
wall or from the guide catheters is of paramount importance to prevent large embolic debris and cholesterol embolization into the renal arteries and the distal arterial circulation.

**DISTAL PROTECTION**

Distal protection, on the other hand, is protecting the kidney from debris during PRI with the use of embolic protection devices distal to the lesion. Proximal embolic protection devices are not feasible during treatment of the renal arteries because the majority of lesions are aorto-ostial in nature. In an ex-vivo study by Hiramoto et al., debris ranging from less than 10 micrometers to more than 1 mm have been demonstrated during treatment of renal atherosclerotic disease. In 33 intact aortorenal atheroma specimens removed surgically from 17 patients with renal artery occlusive disease undergoing renal artery endarterectomy, excised plaque with aortic ring were fitted with a PTFE “adventitia” and underwent ex-vivo angioplasty and stenting with 0.018” wires and 3.0 mm and 5.0 mm angioplasty balloons. The Wallstent (Boston Scientific) was used for stenting. Released fragments during the angioplasty procedures were in the 100 to 10,000 range from larger (60 micrometers to 100 micrometers) to smaller sizes (<10 micrometers) respectively. Debris larger than 1 mm were also recovered. This experiment illustrates the large amount of debris released during PRI with large enough sizes to obliterate the glomerular arterioles and initiate parenchymal renal damage and worsening renal function.

With the advent of embolic protection, protecting the renal artery appears to have merit considering the evidence that large debris inevitably occurs during PRI.

Distal protection can be accomplished with distal interruption of renal blood flow with balloon occlusion or by the placement of distal embolic filters during PRI. Distal balloon occlusion such as the PercuSurge GuardWire (Medtronic Corporation) has the advantage of capturing small debris that typically escape embolic filters. Henry et al. reported visible debris from 100% of all patients who underwent PRI with GuardWire protection. The average size of the debris was 201.2 micrometers +/- 76.0 micrometers (range 38 micrometers to 6,206 micrometers) and the mean renal occlusion time was 6.55 minutes (range 2.29 minutes to 13.21 minutes). At 6 months follow-up they reported no deterioration of renal function in any of the patients.

It remains unclear, however, whether prolonged complete flow interruption with occlusive balloons would lead to ischemic parenchymal injury with longer follow-up and in patients with already significantly impaired renal function at baseline. Embolic filters have been used more frequently as they are relatively easier to use and do not interrupt blood flow to the kidney during the procedure.

In 63 consecutive patients with progressive ischemic nephropathy over the past 6 months and documented severe renal artery stenosis (83 renal arteries) by magnetic resonance angiography, Holden et al. performed complete revascularization with primary stenting under embolic filter protection. All patients had a “primary filter passage” and 8 arteries required “buddy wire” placement. The primary endpoint of the study was serum creatinine at 1 day and 6 months post stenting. Using the Kidney Disease Outcome Quality initiative classification (K-DOQI), 97% of patients had an improvement or stabilization of their kidney function at 6 months and 3% had deterioration or no change in the course of their CRI worsening (increase in serum creatinine by over 20% above baseline). Of interest, patients with debris captured in the filter had a significantly better outcome than those with no debris captured (P= .01).

The Embolic Protection and Platelet Inhibition During Renal Artery Stenting (RESIST) trial is the only randomized study comparing renal artery stenting with or without distal protection to evaluate the impact of the Angioguard XP short tip embolic protection filter (Cordis Corporation) and the glycoprotein GP IIb/IIIa inhibitor abciximab on GFR post PRI. In this 2x2 factorial design study, patients were randomized to control, Angioguard, abciximab, and combination of abciximab and Angioguard. Patients

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**Table 1. Ideal properties of a renal embolic filter.**

<table>
<thead>
<tr>
<th>Feature</th>
<th>Description</th>
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<tbody>
<tr>
<td>Mounted on a stiffer .014-inch or .018-inch wire</td>
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<tr>
<td>Short radiopaque tip</td>
<td></td>
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<tr>
<td>2.4 mm deflecting tip</td>
<td></td>
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<tr>
<td>Shorter landing zone</td>
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<tr>
<td>Low profile</td>
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<tr>
<td>Available in a variety of diameters or expansion compatible with target renal anatomy</td>
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<tr>
<td>Filter pore size to allow capture of small debris</td>
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<tr>
<td>Volume capacity to allow larger amount of debris capture</td>
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needed to have renal artery stenosis over 50%. 390 patients were screened and 100 patients were randomized. At 1 month follow-up there were 91 patients in the study (control 26, Angioguard 21, abciximab 21, and both therapies 23). The percentage change in mean Modification in Diet in Renal Disease GFR rate from baseline to 1 month showed a decline in GFR in all groups by about 10% each. The combination of abciximab and Angioguard, however, showed an improvement in mean GFR when compared to control but no statistical change in GFR compared to pretreatment baseline.

This study was somewhat disappointing as it failed to show that embolic filter protection or abciximab offer an improvement in renal function post stent of the renal artery. At best, the combination kept renal function unchanged post treatment. One criticism of this study is the inclusion of patients with 50% or more renal artery stenosis. No functional assessment was required to determine the true severity of moderate disease (50% to 70%).

It remains unclear in this study why the interaction of a filter and abciximab was more effective than either one alone in preserving GFR to pretreatment levels. Haller et al15 have shown that higher levels of sCD40L at baseline preprocedure are found in patients who embolized platelet-rich debris post PPI. sCD40L is produced by activated platelets. It is proinflammatory and may induce fibrosis. Levels of sCD40L are reduced with abciximab. It is speculated that patients with Angioguard protection only has layered activated platelets on the filter during treatment, releasing significant amount of sCD40L that can be injurious to the kidney.

**EMBOLIC FILTERS**

None of the current embolic filters are approved in the United States for use during PRI. The most commonly used filters off label are the Angioguard (Cordis Corporation), Filterwire (Boston Scientific), Spider filter (ev3) and recently the FiberNet (Lumen Biomedical). The Spider filter has, however, the lowest capture efficiency in an experimental model (143 micrometers: 1.50%; 200 micrometers: 19.34%)21 with little data available on its effectiveness in PRI. The FiberNet filter appears promising and more likely easier to adapt to PRI.22-24 Early experience in a limited number of patients was positive with overall good outcome. The filter is able to capture small debris (30 micrometers to 40 micrometers), has small landing zone (1.5 cm), and excellent crossing profile (1.7 mm to 2.9 mm). The filter can also be deployed in vessel size up to 7 mm.

Current filters are not designed to be used during PRI. Many of these filters have a long tip guidewire and are longer than the length of the main renal artery, which is about 40 mm in length. In addition, some of these filters are not kink resistant when transitioning the sharp angulation from the aorta into the renal arteries. Properties of an ideal renal filter are shown in Table 1.25 Integrated stent-embolic filters, such as the Vanguard (Contego Medical), during PRI are currently investigational and may be of particular interest to the interventionist. Integration of both stent and filter may reduce intraprocedural time and contrast use and simplify the procedural steps.

**CONCLUSION**

Embolization occurs during PRI and consists of both atherosclerotic and thrombotic debris. Distal embolization appears to be associated with worsening of renal function and a poor patient outcome.

The combined use of Angioguard and abciximab appears to preserve GFR whereas abciximab or the filter alone is associated with worse GFR compared to preprocedure baseline. A baseline elevated sCD40L seems to be a predictor of worse outcome and correlates with platelet-rich debris captured in the filters. At this time, embolic filter protection during PRI may be considered selectively and in patients who are at a particularly high risk for worsening GFR (Table 2). Dedicated renal filters are currently needed.

**Editor’s Note:** Disclosure: The authors have completed and returned the

**Table 2. Patient selection for distal embolic protection during percutaneous renal intervention.**

<table>
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<th>Baseline chronic renal insufficiency</th>
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<tr>
<td>Recent decline in renal function</td>
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<tr>
<td>Bilateral severe renal artery stenosis</td>
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<tr>
<td>Unilateral functioning kidney with severe renal artery stenosis</td>
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<tr>
<td>Unfavorable anatomy with complex ulcerated lesion</td>
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<tr>
<td>Anatomy suitable for embolic filter deployment</td>
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<tr>
<td>Consider in diabetic and elderly with likely impaired baseline renal function</td>
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<tr>
<td>Consider in conjunction with abciximab in patients with high sCD40L at baseline</td>
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*sCD40L is not a routinely available test.*
REFERENCES


