Distal embolic protection during renal artery angioplasty and stenting

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Background: **Percutaneous renal artery angioplasty and/or stenting (RA-PTAS) is increasingly being used as an alternative to surgery for renal artery revascularization. Unfortunately, renal function responses after RA-PTAS appear to be inferior to those observed after surgical revascularization both in terms of improving and preventing deterioration of renal function postintervention. Atheroembolism during RA-PTAS has been postulated as a potential cause for the disparate results. Strategies to limit the occurrence of atheroembolism, such as the use of distal embolic protection (DEP) systems, may result in improved outcomes after RA-PTAS.**

Methods: **All RA-PTAS procedures performed with DEP (using a commercially available temporary balloon occlusion and aspiration catheter) between October 2003 and July 2005 were reviewed. Glomerular filtration rate (eGFR) was estimated preintervention and 4 to 6 weeks postintervention using the abbreviated Modification of Diet in Renal Disease formula. Renal function and hypertension response rates as well as procedural data were classified and reported according to American Heart Association guidelines. Renal function improvement and deterioration were defined as a 20% increase and decrease in eGFR, respectively, compared with preoperative values. Continuous and categoric data were analyzed using paired *t* tests and repeated measures linear models.**

Results: **DEP was used in 32 RA-PTAS procedures in 15 women and 11 men with a mean age of 71 years. All patients were hypertensive, 24 (92%) had renal insufficiency, and the mean preintervention degree of renal artery stenosis was 79%. Immediate technical success was achieved in 100% of RA-PTAS cases. Mean pre- and postintervention serum creatinine and eGFR values were 1.9 vs 1.6 mg/dL ($P < .001$) and 37 vs 43 mL/min/1.73 m^2 ($P < .001$), respectively. Renal function was defined as improved after 17 (53%) of 32 procedures and worsened in none (0%).**

Conclusions: **RA-PTAS using DEP resulted in 4- to 6-week postintervention renal function results approximating those of surgical revascularization. These data suggest that DEP use may prevent renal function harm during RA-PTAS as a result of atheroembolism and warrant further investigation. (J Vasc Surg 2006;44:128-35.)**

Atherosclerotic renovascular disease (RVD) is increasingly recognized as a cause of severe secondary hypertension, excretory renal insufficiency, and end-stage renal disease by reducing renal blood flow. RVD represents an important public health problem, as all of these associated conditions have been demonstrated to increase cardiovascular and all-cause mortality.[1-5] Percutaneous transluminal angioplasty and stenting of the renal artery (RA-PTAS) as well as open surgical revascularization can be used to restore perfusion to affected kidneys. RA-PTAS has become the more frequently used treatment method in most centers and has demonstrated beneficial effects in improving control of renovascular hypertension in selected patients.[6-10] However, reported results have been less favorable in improving associated renal insufficiency,[6-10] which is the major determinant of subsequent cardiovascular morbidity and mortality as well as dialysis-dependence.[11-13]

We hypothesize that atheroembolization of the renal parenchyma is a major, preventable factor limiting the benefits derived from RA-PTAS. This hypothesis is supported by recent ex vivo data from RA-PTAS procedures performed on aortorenal endarterectomy specimens.[14] Distal embolic protection (DEP) devices, balloon or expandable filter-tipped guidewires that can be positioned distal to the lesion selected for treatment, have been recently developed and approved for use in the coronary and cerebral circulations to prevent distal passage of liberated debris. Use of such devices in the performance of RA-PTAS may increase the rate of beneficial clinical responses after revascularization. This report details a single-center experience with the use of a commercially available temporary distal balloon occlusion and aspiration DEP system during RA-PTAS.

METHODS

Patient population. This investigation was conducted with approval from the Wake Forest University Health Sciences Institutional Review Board. All RA-PTAS procedures performed between October 2003 and July 2005 were identified through an institutional registry. RA-PTAS was performed only in patients with hemodynamically significant atherosclerotic RVD (≥60% diameter-reducing steno-

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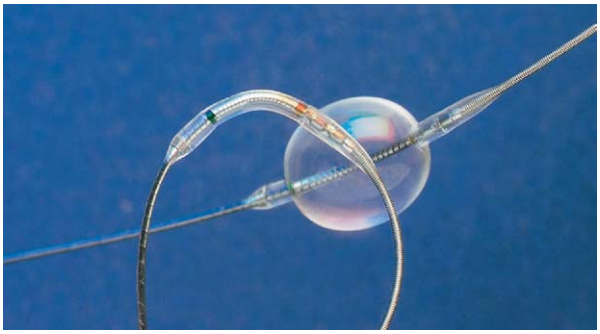

Fig 1. Photograph of the Medtronic Guardwire temporary balloon occlusion distal embolic protection system. (Used with permission from Medtronic AVE, Minneapolis Minn.)

sis confirmed by renal duplex sonography and angiography) and severe hypertension, with or without associated excretory renal insufficiency. Case records for all individuals undergoing RA-PTAS with attempted DEP use were selected for review. Only those individuals with ≥4 weeks of follow-up were included in this report.

Materials reviewed. All outpatient clinic, hospital, noninvasive vascular laboratory, and endovascular operating suite records were reviewed. Collected data included information regarding preoperative demographics, anthropometrics, and medical comorbidities as well as indication for revascularization, procedural specifics, complications, postoperative status, and postoperative renal artery patency/restenosis. The percentage of renal artery stenosis was calculated from angiographic images in a fashion congruent with that described in the Asymptomatic Carotid Atherosclerosis Study.[15] All collected data were entered into an electronic database.

Operative management. Patients were admitted on the day before RA-PTAS to a 23-hour day hospital for hydration and oral administration of 600 mg of N-acetylcysteine every 12 hours. RA-PTAS procedures were performed in an endovascularly equipped operating suite. Only one renal artery lesion was treated at any given procedural setting. Bilateral lesions were treated in a staged fashion, with interventions performed at least 4 weeks apart to minimize the volume administered and nephrotoxic effects of iodinated contrast and avoid the potential for bilateral ischemic renal complications.

Femoral sheath access was used for all procedures reported here, and intravenous heparin was administered (50 to 100 U/kg per surgeon preference) once access was secured. Iodinated and non-iodinated (carbon dioxide) contrast materials were used. In patients with severe renal insufficiency, carbon dioxide was used to initially localize and cannulate the renal artery, followed by hand injection of dilute (half-strength) iodinated contrast for treatment planning once selective cannulation was achieved.

Selective cannulation of the renal arteries was accomplished using a minimal contact technique of ostial engagement with an angled guiding catheter telescoped through a 10-cm 6F sheath. The lesion to be treated was not crossed with the guide catheter. Guidewire crossing of the lesion was performed using a commercially available temporary balloon occlusion and aspiration 0.014-inch DEP guidewire system (Guardwire, Medtronic AVE, Minneapolis Minn) (Fig 1). The Guardwire was chosen because of its ability to completely occlude the renal artery and, hopefully, prevent the passage of debris too small for retention by existing filter designs that currently have a porosity of no less than 100 μm. Preintervention pressure gradients were not measured to minimize manipulations across the lesion.

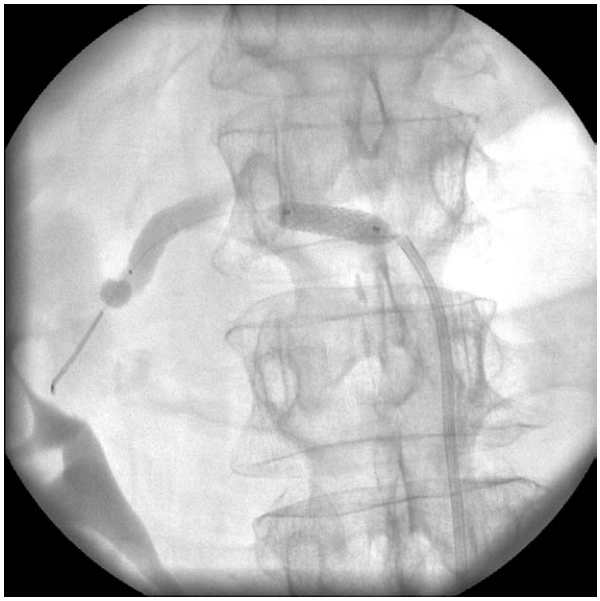

Fig 2. Hand injection angiogram demonstrates complete renal artery occlusion using the distal embolic protection system before stent placement.

The distal occlusion balloon was inflated in the distal main renal artery immediately after crossing the lesion, and occlusion was confirmed by hand injection of contrast (Fig 2). RA-PTAS was then performed using angioplasty balloons, balloon-mounted stents (Genesis, Cordis, Miami Lakes, Fla; Express, Boston Scientific, Natick, Mass; and Racer, Medtronic), or self-expanding stents (Wallstent, Boston Scientific) of operator choice sized to match the distal, normal appearing renal artery.

Predilation angioplasty was performed at the discretion of the operating surgeon. All predilation angioplasty was performed with the Guardwire in place and inflated. Stents were positioned to extend 1 to 2 mm into the aortic lumen while completely covering the lesion to be treated. After stent deployment, the static column of blood proximal to the temporary occlusion balloon was evacuated using a rapid exchange Export aspiration catheter (Medtronic AVE) (Fig 3). After 60 mL of blood was aspirated, the aspiration catheter was used to inject at least 20 mL of heparinized, injectable, sterile 0.9% saline to flush any residual debris from the renal artery.

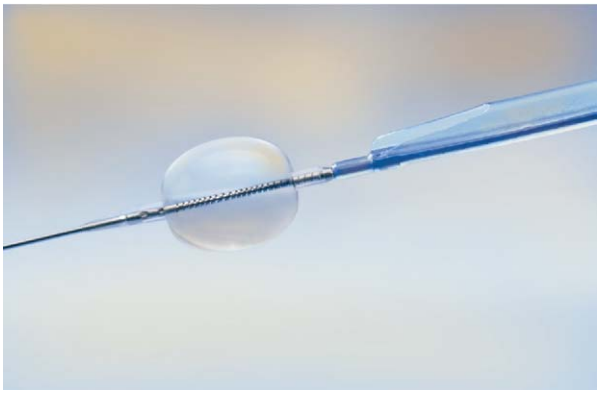

Fig 3. Photograph of the Medtronic Export catheter for aspiration of atheroembolic debris. (Used with permission from Medtronic AVE, Minneapolis, Minn.)

The temporary occlusion balloon was then deflated and completion renal arteriography performed. Pull-back pressure gradients or intraoperative duplex scans, or both, were performed in all cases to assess the hemodynamic effects of the procedure.

Routine follow-up included clinic visits at 4 weeks, 3 months, 6 months, and 1 year to assess clinical response and revascularization durability. Studies obtained at each visit included renal duplex sonography and measurement of serum creatinine levels.

Outcome measures and reporting. All outcome measures were reported in accordance with consensus reporting guidelines.[16] Renal function was evaluated using the abbreviated Modification of Diet in Renal Disease formula[17] for estimated glomerular filtration rate (eGFR) calculated from preoperative and postoperative serum creatinine concentration: $eGFR/1.73\ m^2 = 186 \times (\text{serum creatinine})^{-1.154} \times (\text{age})^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if African American})$.[17]

Post revascularization renal function was assessed at the 4- to 6-week follow-up to allow for the effects of perioperative volume expansion and contrast administration to resolve. This follow-up time point was chosen due to its coincidence with routinely scheduled follow-up used by our group. Renal function was considered improved if a ≥20% increase in eGFR was observed after RA-PTAS and worsened if a ≥20% decrease in eGFR was observed. Renal function was defined as unchanged if the criteria for improved or worsened function were not met. Renal function responses were reported on both a per-patient (considering bilateral staged interventions as a single treatment) and per-procedure basis.

Blood pressure response was also assessed at the 4- to 6-week follow-up using the highest measured brachial blood pressure pre- and postoperatively taken in a sitting position. Blood pressure response was defined as follows: cured—diastolic blood pressure (DBP) <90 mm Hg and systolic blood pressure (SBP) <140 mm Hg off all antihypertensive medications; improved—DBP <90 mm Hg or SBP <140 mm Hg, or both, on the same or reduced number of medications *or* a reduction in DBP of ≥15 mm Hg on the same or a reduced number of medications; failed—no change or inability to meet the criteria for cure or improvement. Blood pressure responses were also reported on both a per-patient and per-procedure basis.

Renal artery patency was evaluated using renal duplex sonography. Renal artery patency was defined as the absence of occlusion (defined as lack of a Doppler shifted signal from an imaged renal artery) on follow-up examination. Primary and primary-assisted patencies were examined. Restenosis during follow-up was defined as renal duplex sonography evidence of recurrent hemodynamically significant renal artery stenosis (defined as renal artery peak systolic velocity of 1.8 m/s or more[18]) on surveillance duplex sonography. Freedom from hemodynamically significant restenosis was also examined.

Statistical methods. Descriptive statistics (means ± standard deviations of continuous variables, frequencies and relative frequencies of categoric variables) were computed. Analyses of pre- to postoperative changes in patient-based responses (considering staged interventions as a single treatment) were performed using paired *t* tests. Procedure-based analyses of pre- to postoperative changes in responses were analyzed using maximum-likelihood repeated measures linear models assuming compound symmetry covariance structure.[19] Postoperative renal artery patency rates were estimated using product-limit methods.

RESULTS

Study group. During the study period, 27 individuals underwent RA-PTAS with DEP for atherosclerotic RVD. One patient was lost to follow-up. The resultant study group consisted of 15 women and 11 men with a mean age of 71 years. The mean preoperative serum creatinine value was 1.9 mg/dL, and eGFR was 37 mL/min/1.73 m^2. Moderate-to-severe preoperative renal insufficiency was present in 24 patients (92%) (eGFR ≤60 mL/min/1.73 m^2), including 9 (35%) with eGFR ≤30 mL/min/1.73 m^2. No patient was dialysis-dependent. All patients were hypertensive (mean preoperative SBP of 175 mm Hg and DBP of 81 mm Hg) with a mean antihypertensive agent usage of 3.4 medications. Demographics and medical comorbidity data for the 26 study group patients are summarized in Table I.

Procedural data. The 32 RA-PTAS procedures performed during the study period included 29 stent procedures and three primary angioplasty procedures (including two for restenosis). Treated were 25 primary atherosclerotic lesions and seven restenotic lesions (five from prior RA-PTAS procedures, one stenotic renal artery bypass, and one stenosis following renal artery endarterectomy). Renal artery lesions were located at the ostium in 26 cases and in the main renal artery in six (including five cases of in-stent restenosis). Mean renal artery diameter pretreatment was 5.8 mm (range, 4.3 to 7.5 mm).

Eighteen patients were treated for unilateral disease and four patients for bilateral disease, including one patient

Table I. Descriptive statistics for the study group patients (n = 26)

	n (%)	*Mean ± SD*	*Minimum*	*Maximum*
Demographics				
Age (years)		70.7 ± 9.1	48	84
Caucasian race	24 (92)			
Female gender	15 (58)			
Preoperative medical data				
SBP (mm Hg)		175 ± 23	126	222
DBP (mm Hg)		81 ± 12	65	111
Antihypertensive agents		3.3 ± 0.9	1	5
Serum creatinine (mg/dL)		1.9 ± 0.7	1.1	4
eGFR (mL/min/1.73 m^2)		37 ± 14	16	68
Moderate renal insufficiency	15 (57)			
Severe renal insufficiency	9 (35)			
Coronary artery disease	13 (50)			
Diabetes mellitus	9 (35)			
COPD	2 (8)			

SBP, Systolic blood pressure; *DBP,* diastolic blood pressure; *eGFR,* estimated glomerular filtration rate; *COPD,* chronic obstructive pulmonary disease.

Table II. Descriptive statistics for all renal artery angioplasty or stenting procedures performed using distal embolic protection

	n (%)	*Mean ± SD*	*Minimum*	*Maximum*
Demographics				
Preoperative stenosis		79 ± 12	60	95
Postoperative stenosis		1 ± 4	0	20
Contralateral stenosis		54 ± 43	0	100
Significant contralateral RVD	14 (54)			
Predilation necessary	8 (25)			
Stent diameter (mm)		5.6 ± 0.8	4	8
4 mm	2 (7)			
5 mm	8 (28)			
6 mm	18 (62)			
8 mm	1 (3)			
Stent length (mm)		16.0 ± 3.3	12	24
Stent type				
Genesis	19			
Racer	6			
Express	2			
Wallstent	1			
Fluoroscopy time (min)		10.8 ± 7.5	4.8	30.6
Iodinated contrast used (mL)		84 ± 36	10	156

RVD, Renovascular disease.

treated for a unilateral lesion to a solitary kidney. Four patients demonstrated contralateral renal artery occlusions, and 10 demonstrated contralateral stenosis >60%.

Iodinated non-ionic contrast was used in all cases (mean volume administered, 84 mL), and carbon dioxide was an adjunct in four. The mean degree of pre- and postoperative stenosis was 79% and 1%. Temporary balloon occlusion was complete in 28 cases (88%), and visible debris was noted in the aspirated blood in 14 (44%). Immediate technical success, in terms of lesion revascularization, was achieved in all cases. Procedural data for all 32 RA-PTAS procedures are summarized in Table II.

Complications. A significant complication, a femoral pseudoaneurysm that required thrombin injection, occurred in one patient (3%). No complications specifically related to use of the DEP device were observed.

Renal function response at 4 to 6 weeks. Pre- and postoperative serum creatinine and eGFR data are summarized in Table III. A significant decrease in the serum creatinine value and a significant increase in eGFR were observed. Renal function response at the 4- to 6-week follow-up was defined as improved in 13 patients (50%) and after 17 RA-PTAS procedures (53%), and unchanged in 13 patients (50%) and after 15 RA-PTAS procedures (47%). In no patient or after any procedure was renal function observed to be worsened. Among seven restenotic lesions treated with DEP, four demonstrated improved renal function after RA-PTAS. All 13 patients with renal function improvement post-RA-PTAS demonstrated moderate-to-severe preoperative renal insufficiency. In total, 13 (54%) of 24 patients with preoperative renal insufficiency demonstrated improved renal function after RA-PTAS using DEP.

Table III. Renal function and blood pressure responses after 32 renal artery angioplasty or stenting procedures performed with distal embolic protection

	Pre-op value	*Post-op value*	*Difference*	P
Renal function				
Serum creatinine (mg/dL)	1.9 ± 0.1	1.6 ± 0.1	−0.3	<.001
eGFR (mL/min/1.73 m^2)	37 ± 3	43 ± 3	6.6	<.001
Blood pressure				
SBP (mm Hg)	175 ± 23	159 ± 25	−15	.004
DBP (mm Hg)	81 ± 12	75 ± 11	−5.1	.018
Antihypertensive medications (n)	3.4 ± 0.2	3.1 ± 0.2	−0.3	.045

eGFR, Estimated glomerular filtration rate; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure.

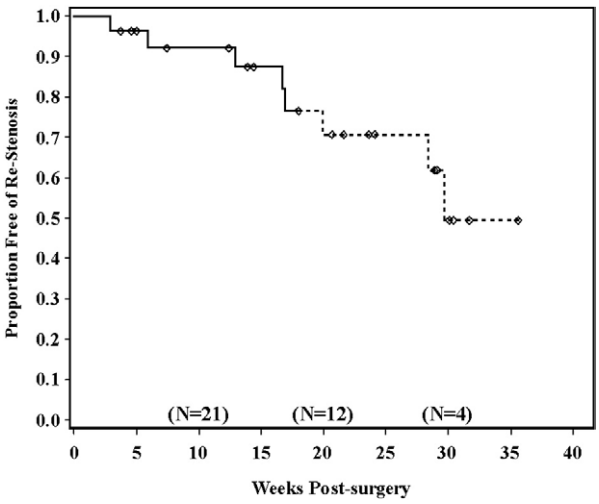

Fig 4. Estimated freedom from restenosis during follow-up.

Blood pressure response at 4 to 6 weeks. Pre- and postoperative blood pressure and antihypertensive medication use data are summarized in Table III. Significant decreases in SBP, DBP, and in the number of antihypertensive medications were observed. At the 4- to 6-week follow-up, blood pressure cure was observed in no patients (0%), improvement in nine (35%), and no change in 17 (65%).

Renal artery patency. Mean follow-up was 25.4 weeks. No renal artery occlusions were observed during follow-up. At 6 months, estimated primary and primary assisted renal artery patencies were 100%. Seven cases of restenosis were observed in six patients, with a mean time to detection of 17 weeks. Four of the restenotic lesions were confirmed angiographically with repeat treatment (three with repeat RA-PTAS and one with bypass). Mean renal artery and initial stent size in these cases were 5.5 mm (range, 4.3 mm to 7.1 mm) and 5.2 mm (range, 4 mm to 6 mm), respectively. Estimated 6-month freedom from restenosis was 71% (Fig 4). All cases involved in-stent restenosis, and in no case was the restenotic lesion observed in the distal main renal artery at the site of DEP balloon inflation.

Follow-up renal function response. Among those patients with improved renal function post-RA-PTAS, four (31%) had deterioration of renal function response to baseline or beyond observed during follow-up. Three of these patients had renal artery restenosis, the fourth had severe proteinuria and suspected intrinsic renal parenchymal disease. Two patients with restenosis and loss of beneficial renal function response achieved repeat improvement of renal function after additional RA-PTAS. The third patient refused further RA-PTAS.

DISCUSSION

This investigation examined a single center experience with RA-PTAS using a temporary balloon occlusion and aspiration DEP system, with the goal of decreasing or eliminating procedural related atheroembolization and maximizing beneficial renal function responses. At the 4- to 6-week follow-up, a significant decrease in serum creatinine values and an increase in eGFR were observed for the study group as a whole. Most of the patients with preoperative renal insufficiency demonstrated a ≥20% increase in eGFR, and no patient exhibited a short-term deterioration in renal function.

These results represent a marked improvement in short-term renal function response rates after percutaneous renal artery revascularization compared with previously published experiences and approximate the short-term results reported after open surgical revascularization. These data are intriguing, especially when considered in context of the population disease burden, changes in treatment patterns, and renal function effects associated with RVD.

We hypothesize that the renal function effects of RA-PTAS are strongly affected by atheroembolization that may occur at the time of procedure. Such atheroembolization may limit functional recovery in patients with renal insufficiency or lead to diminished function in individuals regardless of preoperative renal function. This hypothesis was initially tested using an ex vivo preparation of aortorenal endarterectomy specimens treated with RA-PTAS.[14] Thousands of liberated particles were observed, with an inverse relationship between particle size and number.

This hypothesis has also been examined indirectly in two published experiences of RA-PTAS performed with DEP that reported similar responses in terms of protection from short-term renal function deterioration.[20,21] In these series, renal function improvement rates approximating 40% were observed, and no acute renal function decline

was noted. Debris was collected in 65% and 100% of cases in these two reports in which the Guardwire and Angioguard (Cordis) were used. In this experience, 44% of cases had debris at the time of aspirated blood examination. We suspect that this is a conservative estimate of significant debris release, given that only visible debris was noted, with inability to appreciate the smaller fragments that would appear to be more likely given the ex vivo data.

Recent prevalence estimates indicate that atherosclerotic RVD is present in approximately 7% of the general elderly population[22] and in up to 40% of individuals with coronary or peripheral vascular disease.[23-25] These prevalence estimates translate into a current at-risk population of >3 million Americans. RVD is an increasingly recognized contributor to severe secondary hypertension and excretory renal insufficiency[25-29]and is the suspected cause in 10% to 20% of incident cases of dialysis-dependence among individuals aged >50 years.[26,28] In addition to the quality-of-life issues associated with the progression to dialysis-dependence, excretory renal insufficiency is an increasingly recognized risk factor for subsequent cardiovascular morbidity and mortality.[2,4,5] Reduction of risk for future adverse cardiovascular events and progression of renal insufficiency is the ultimate goal of any renal artery revascularization procedure.

RA-PTAS is increasingly being used to improve renal perfusion in hopes of ameliorating these problems despite the lack of any level I evidence supporting its use.[30] This increase in utilization is likely secondary to increased physician awareness of RVD as a potentially causative factor in severe hypertension and renal insufficiency as well as the perception of minimal morbidity associated with RA-PTAS. Several authors have demonstrated a shift away from open surgical renal artery revascularization and an increase in RA-PTAS, with a net total increase in the number of renal artery interventions performed.[30,31] This shift in utilization patterns and increase in RA-PTAS could be harmful to patients if RVD treated in this fashion demonstrates a worse natural history than RVD treated surgically or medically, a distinct possibility in the era of highly efficacious antihypertensive agents such as angiotensin-receptor blockers and converting-enzyme inhibitors. This latter possibility is currently being investigated by the ongoing Cardiovascular Outcomes in Renal Atherosclerotic Lesions (CORAL) trial, which will provide critical information to define appropriate treatment in the future.

Until those results are available, however, existing data must guide contemporary treatment. Recent reports concerning RA-PTAS[6-10] have observed short-term renal function improvement in 15% to 34% of patients and nearly identical rates of short-term deterioration (range, 8% to 27%). These data are similar to those published in a recent meta-analysis,[32] and they compare poorly with the reported results of surgical revascularization where short-term renal function improvement has been observed in 45% to 55% of patients and deterioration in 5% to 8% of patients.[11,13,33,34]

Short-term renal function response is an extremely important outcome, one that has been repeatedly demonstrated as a robust predictor of post-revascularization survival if improved, and subsequent death or progression to dialysis, or both, if diminished.[11-13,33,34] Changes in eGFR may be small in absolute terms, especially in patients with renal insufficiency, but relatively large in terms of overall residual function. In a report previously published by our group,[11] renal function improved and worsened by ≥20% following renal revascularization significantly and independently improved and worsened, respectively, dialysis-free survival across all strata of preoperative renal function.

Renal function unchanged (or "stabilized") had differing effects, however, according to the level of preoperative renal function. In individuals with severe preoperative renal insufficiency, unchanged renal function predicted a risk of death or progression to dialysis similar to that observed with renal function worsened. In individuals with more normal preoperative renal function, unchanged renal function predicted similar dialysis-free survival to that observed with renal function improved.

These results strongly suggest that renal function worsened after revascularization is an adverse outcome in all patients, regardless of the level of preoperative renal function. These results also question whether the concept of stabilized renal function is valid in patients with preoperative renal insufficiency and underscore the potential importance of the observations we have reported here that use of DEP was associated with no occurrence of short-term renal function deterioration.

Observed blood pressure responses, though, were less promising in this series, with only 35% of patients demonstrating improvement by American Heart Association guideline definitions. Several explanations exist for this observation, including follow-up too short to allow for detection of improvement, or coexisting severe essential hypertension or lack of downregulation of the renin-angiotensin system due to inadequate RA-PTAS results, or both. Review of our data did not demonstrate improvement of hypertension over longer follow-up, and all procedures used either post-RA-PTAS measurement of pressure gradients or renal duplex sonography with remediation of any observed residual lesions.

We speculate that these observations relate to the referral source for these patients, primarily nephrologists, and because almost all of the interventions were performed for ischemic nephropathy. Patients were well managed with effective agents upon presentation, and this patient group has a high prevalence of severe essential hypertension. Significant reductions in systolic and diastolic blood pressure as well as medication usage were observed, but the changes met guideline definitions in only 35% of individuals.

Follow-up renal function was promising but did demonstrate reason for concern. Of patients exhibiting improvement in renal function at 4 to 6 weeks, nearly one third returned to baseline during follow-up. Restenosis appeared to be a likely culprit in this process, affecting 75% of these individuals. Two of the three patients with restenosis demonstrated prompt return to their improved state after repeat RA-PTAS, and the third refused further treat-

ment. Issues of functional response durability are important and deserving of further investigation.

Although these results are promising and intriguing, this investigation has numerous limitations. Primary renal function outcomes were measured according to estimated glomerular filtration equations that have not been previously validated in individuals with RVD. Ideally, direct measures of renal function effect would be employed.

Another weakness is that most patients demonstrated bilateral RVD, but most of the interventions were unilateral. Several patients had planned second interventions that were performed after the time of data accumulation for this review; however, most had clinical responses that were significant and precluded contralateral intervention based upon our usual clinical indications. This may have led to an underestimation of the renal function effects of routine DEP use.

Conversely, the relatively small number of patients detailed in this investigation limited the expected number of adverse events observed and potentially increased the chance of a spurious observation of positive results. A similar limitation may have been present in the number of restenotic lesions included, as they may possess a lower atheroembolic potential than primary atherosclerotic lesions.

Patient numbers may also have limited the occurrence of anatomy not amenable to the use of the Guardwire. The design of the Guardwire precludes its use in individuals with long renal artery lesions or early renal artery bifurcations that will not allow for its deployment and in cases where the distal renal artery is >6 mm in diameter. Such anatomy was not observed in this series, but it is certain to occur with widespread use.

It is also possible that the beneficial renal function responses observed were partly or totally secondary to improvements in periprocedural renal protective measures such as hydration and N-acetylcysteine administration.

The most important limitation to this study, though, is that this report is a retrospective review of clinical practice and not a prospective, randomized clinical trial. Rigorous exam of this concept with a non-DEP comparison group is mandatory before widespread recommendation of DEP use can be made.

CONCLUSION

These limitations notwithstanding, this investigation presents promising results that deserve further investigation. We hope all of these limitations will be addressed, and the overriding question concerning the utility of DEP in renal artery PTAS will be answered by a well-designed randomized, clinical trial.

AUTHOR CONTRIBUTIONS

Conception and design: MSE, KJH, JA, RLG
Analysis and interpretation: MSE, KJH, KJS, BLC, JS
Data collection: MSE, KJS, BLC
Writing the article: MSE, JS
Critical revision of the article: MSE, KJH, JS
Final approval of the article: MSE, BLC, JS, JA, KJS, KJH, RLG
Statistical analysis: MSE, JS
Obtained funding: Not applicable
Overall responsibility: MSE

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