Renal PEI: critical appraisal

On Topaz  M.D., F.A.C.C.,F.S.V.M.

Professor of Medicine & Pathology
Director, Interventional Cardiology
McGuire Veterans Medical Center
Virginia Commonwealth University
Richmond, VA, USA

TCT Asia-Pacific, 2009
Seoul, Republic of Korea
• CKD is now widely recognized as a major risk factor for CVD.

• Elevated CV risk occurs early in the development of CKD.

Radbill et al. Mayo Clinic Proc
Dec. 2008; 83: 1373-1381
Outcome of pts. with heart failure and preserved LV function.

Figure 2  Predictors of death by Cox regression analysis. LVF = left ventricular function; CI = confidence interval.
Impact of Optimal Medical Therapy and Revascularization on Outcome of Patients With Chronic Kidney Disease and on Dialysis Who Presented With Acute Coronary Syndrome

Laurent Bonello, MD, Axel De Labriolle, MD, Probal Roy, MBBS, Daniel H. Stemberg, MD, Teruo Okabe, MD, Tina L. Pinto Slottow, MD, Zhenyi Xue, MS, Rebecca Torguson, MPH, William O. Suddath, MD, Lowell F. Satler, MD, Kenneth M. Kent, MD, PhD, Augusto D. Pichard, MD, Joseph Lindsay, MD, and Ron Waksman, MD*

Coronary artery disease is the main cause of death in patients with chronic kidney disease (CKD). The poor prognosis associated with acute coronary syndrome (ACS) in these patients has been related to therapeutic nihilism. This study included 2,357 patients with ACS who had percutaneous coronary intervention. According to their creatinine clearance and medical history, they were divided into 3 groups: dialysis (n = 73); CKD (n= 293); and control (n= 1,991). Rates of cardiovascular events were recorded during a 1-year follow-up period. Patients in all groups received similar contemporary therapy for ACS, including percutaneous coronary intervention and optimal medial therapy. On admission, patients with CKD and patients on dialysis more often presented with cardiogenic shock (p = 0.05 and 0.02, respectively). A graded increase in the rate of major adverse cardiovascular events at 1 year was observed with decreasing renal function (control 13%, CKD 22.9%, dialysis 45.2%, p <0.001 for all comparisons). In multivariate analysis, patients with CKD and on dialysis were significantly associated with 1-year major adverse cardiac events with adjusted hazard ratios of, respectively, 1.5 (95% confidence interval 1.1 to 2.1; p = 0.009) and 2.7 (95% confidence interval 1.7 to 4.1; p <0.001). In conclusion, despite optimal contemporary medical therapy and revascularization, the prognosis of patients with CKD and, in particular, of patients undergoing dialysis, remains poor.

Am J Cardiol 2008;102:535-540

In patients with Renal Insufficiency “therapeutic nihilism” creates a putative bias, leading to sub-optimal medical therapy and coronary revascularization.
RAS – clinical presentation

RAS clinically presents in 1 of 5 ways:

• HTN
• Acute or chronic renal failure
• CHF, flash pulm. edema - beware of “diastolic heart dysfunction”
• Unstable angina
• “Incidental” discovery
“Incidental” critical RAS

52 YO male, S/P CABGS x3V, LVEF = 50%

Repeat NTSEMI & episodes of severe angina associated with HTN & occasional SOB

EKG: ischemic T-waves in lateral leads
Cardiac Cath: 100% stenosis of native coronary arteries, SVGs occluded.
LIMA – patent to LAD, but diseased diagonal.
Normal renal function & kidney size
Management options for this case:
PCI of the diagonal artery ???

Of note:

- **If kidney size and/or function are normal – RAS could still be present!**
- **There is no “angina renalis”!!!**
- **The kidney dies silently !!!**
Gradient = 45 mmHg
0.9 mm X-80 excimer laser
## Etiology of Renal Artery Disease

<table>
<thead>
<tr>
<th>Condition</th>
<th>Affected Segment</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atherosclerosis</td>
<td>Ostial and proximal portion</td>
<td>85 – 90%</td>
</tr>
<tr>
<td>Fibromuscular disease</td>
<td>Main artery and / or branches</td>
<td>10 – 15%</td>
</tr>
<tr>
<td>Neurofibromatosis</td>
<td>Ostial and proximal portion</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>Rheumatoid Arthritis</td>
<td>All portions</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>Takayasu's Disease</td>
<td>Ostial and proximal portion</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>Radiation Injury</td>
<td>All portions</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>Trauma</td>
<td>All portions</td>
<td>&lt; 1</td>
</tr>
<tr>
<td>Congenital</td>
<td>Main Artery</td>
<td>&lt; 1</td>
</tr>
</tbody>
</table>

Predictors of RAS:
HTN, Renal Insufficiency, multivessel CAD

Cardiac cath in CAD pts.:
RAS >50% stenosis in 15%
RAS >75% stenosis in 5% - Duke
Cardiac cath in HTN pts.:

unilateral RAS > 50% in 26%

bilateral RAS > 50% in 4% - Mayo

Pts. with PAD: significant RAS in 22% – 59%

BP 200/110 mmHg
Gradient = 165 mmHg
Gradient = 55 mmHg
2 mm eccentric excimer laser
Final
BP = 158/94 mmHg
Gradient = 0 mmHg
Figure 21-2. Relationship between radiological evident vessel stenosis and measured pressure gradient in atherosclerotic renal artery disease. These data indicate that minor stenosis has minimal hemodynamic effect, but that more severe stenosis is associated with a precipitous rise in pressure gradients across the lesion. SPG: systolic pressure gradient.
RAS – Natural History

If initial renal angiography > 75% stenosis:

39% will progress to total occlusion !!!

RAS and Renal Atrophy

Prospective study: 122 pts. (204 kidneys) with known RAS
- f/u renal U/S for a mean 33 months -

development of renal atrophy:

1. atrophy at baseline without RAS: 5.5% of pts.
2. if baseline RAS <60%: atrophy will occur in 12%
3. if baseline RAS >60%: atrophy will develop in 21% (p=0.009) !!!

Caps et al. Kidney Inter 1998; 53: 735-742
RAS Natural History

2 yr. Survival:
- 96% among pts. with unilateral RAS
- 74% with bilateral RAS
- 47% in stenosis or occlusion of a solitary kidney.

RAS progression to end–stage CKD & dialysis:
- Median survival only 25 months
- 5 yr. survival only 18%.

FIGURE 22-2. Four-year survival rates in 1235 patients undergoing abdominal aortography at the time of cardiac catheterization based on the presence or absence of renal artery stenosis (RAS). In those patients with less than 75% stenosis, the 4-year survival rate was 89%; in patients with greater than 75% stenosis, the 4-year survival rate was only 57%. (From Conlon P, O’Riordan E, Kalaria P: New insights into the epidemiologic and clinical manifestations of atherosclerotic renovascular disease. Am J Kidney Dis 35:573, 2000.)
PEI for RAS: Indications


1. At least 70% stenosis of one or both renal arteries AND
   a. Uncontrolled HTN
   b. CRF not related to another cause; bilateral RAS or solitary functioning kidney with RAS
   c. Gradient > 20 mmHg

2. Dialysis-dependant renal failure – no other cause of end-stage renal disease - presence of bilateral RAS or a single kidney RAS

3. Recurrent CHF or “flash” pulmonary edema

A new indication for pts. in the Veterans Administration system: enable long-term treatment with ACE – I !!!
BP 180/100
Gradient = 75 mmHg
Predictors of Improved Renal Function After Percutaneous Stent-Supported Angioplasty of Severe Atherosclerotic Ostial Renal Artery Stenosis

Thomas Zeller, MD et al

**Background**—Percutaneous stent-supported angioplasty is a treatment option for atherosclerotic ostial renal artery stenosis. Improvement of renal function by such intervention, however, is controversial and thought to be limited to specific subsets, such as nondiabetic patients and bilateral stenoses. In this prospective study, we investigated predictors for improvement of renal function and blood pressure after renal artery stent placement.

**Methods and Results**—The study included 215 consecutive patients with ostial renal artery stenosis of >70% diameter stenosis undergoing stent-supported angioplasty. The primary end point was decrease in serum creatinine concentration at 1 year; the secondary end point, decrease in average mean arterial blood pressure assessed by 24-hour monitoring. One-year follow-up was complete in 191 surviving patients. In 52% (99/191) of the patients, serum creatinine concentration decreased during 1-year follow-up. Median serum creatinine concentration dropped significantly from 1.21 mg/dL (quartiles: 0.92, 1.60 mg/dL) at baseline to 1.10 mg/dL (quartiles: 0.88, 1.50 mg/dL) at 1 year (P=0.047). On average, mean arterial blood pressure decreased significantly, from 102 ± 12 mm Hg (mean±SD) at baseline to 92 ± 10 mm Hg at 1 year (P<0.001). Significant independent predictors of improved renal function were baseline serum creatinine (odds ratio [95% CI], 2.58 [1.35 to 4.94], P=0.004) and left ventricular function (OR 1.51 [1.04 to 2.21], /=0.032). Female sex, high baseline mean blood pressure, and normal renal parenchymal thickness were independent predictors for decreased mean blood pressure.

**Conclusions**—Stent-supported angioplasty for severe ostial renal artery stenosis improves renal function and blood pressure in a broader spectrum of patients than previously thought.

Abstract 1785: Renal Artery Angioplasty Improves Diastolic Cardiac Function In Patients With heart failure Possessing Renal Artery Stenosis.

Eisei Yamamoto, et al

In RAS patients with either overt or latent HF, renal artery angioplasty not only decreases arterial blood pressure but also improves diastolic cardiac function in parallel with the reduction of BNP level.

RAS critical appraisal: a lesson to learn -
Management of ischemic nephropathy:
Dialysis-free survival after surgical repair

232 pts. with HTN & atherosclerotic renovascular disease

**Pre-op:** Cr. 1.8 mg/dl or more
**Post-op:**

- 58% pts. improved renal function (EGFR > 20%):
- 27 pts. (12%) recovered from dialysis dependence
- 35% unchanged
- 7% worsened

**Conclusion:**
REVASCULARIZATION CAN RETREIVE EXCRETORY RENAL FUNCTION
IN SELECTED HTN PTS. WITH ISCHEMIC NEPHROPATHY.

Surgical management of dialysis-dependent ischemic nephropathy

Purpose: This retrospective review describes surgical management of dialysis-dependent ischemic nephropathy.

Methods: From February 1987 through September 1993, 340 patients underwent operative renal artery (RA) reconstruction at our center. A subgroup of 20 patients (6 women; 14 men; mean age 66 years) dependent on hemodialysis immediately before RA repair form the basis of this report. Glomerular filtration rates (EGFR) were estimated from at least three serum creatinine measurements obtained 26 weeks before and after operation. A linear regression model was used to estimate the mean rate of change of EGFR before and after RA repair. Comparative analysis of kidney status and change in EGFR were performed. The influence of function response on follow-up survival was determined by the product-limit method.

Results: Hemodialysis was discontinued in 16 of 20 patients (80%). For these 16 patients, postoperative EGFR ranged from 9.0 to 56.1 ml/min/1.73 m² (mean 32.4 ml/min/1.73 m²). Two of 16 patients resumed hemodialysis 4 and 6 months after surgery. Discontinuation of dialysis was more likely after bilateral or complete RA repair (15 of 16 patients) versus unilateral repair (one of four patients; \( p = 0.01 \)). Permanent discontinuation of dialysis was associated with a rapid preoperative rate of decline in EGFR (mean slope log., EGFR: -0.1393 ± 0.0340 without dialysis; -0.0188 ± 0.0464 with dialysis; \( p = 0.04 \), but NS after controlling for multiple comparisons). Immediate increase in EGFR after operation was inversely correlated with the severity of nephrosclerosis (rank correlation: -0.57; 95% confidence interval [-0.83, -0.10]). Follow-up death was associated with dialysis dependence; two deaths occurred among 14 patients not receiving dialysis, whereas five of six patients dependent on dialysis died \( (p < 0.01) \).

Conclusion: Surgical correction of ischemic nephropathy can retrieve renal function in selected patients dependent on dialysis characterized by a rapid decline in preoperative EGFR in combination with global renal ischemia treated by complete or bilateral renal revascularization. After RA repair, discontinuation of dialysis may be associated with improved survival rates when compared with continued dialysis dependence.

FIGURE 23-4. Patterns of change in renal function, before and after renal revascularization, using reciprocal serum creatinine concentrations. In all three patterns, serum creatinine rises over time before revascularization. After revascularization, pattern A shows improvement in renal function, manifested by a progressive fall in creatinine, and a positive slope in reciprocal creatinine. In pattern B, renal function stabilizes (does not improve or deteriorate), and the slope of the reciprocal serum creatinine relationship is zero. In pattern C, renal function continues to deteriorate, but the rate of decline may be slower than before revascularization.

Fig 23-4 from Creager, Dzau, Loscalzo;
VASCULAR MEDICINE; SAUNDERS 2006: p.355
### A. Complications Associated with Renal Artery Stent Implantation *

<table>
<thead>
<tr>
<th>Complication</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal failure</td>
<td>4.3</td>
</tr>
<tr>
<td>Segmental renal infarction</td>
<td>1.1</td>
</tr>
<tr>
<td>Perinephric hematoma</td>
<td>1.1</td>
</tr>
<tr>
<td>Renal artery thrombosis or occlusion</td>
<td>0.8</td>
</tr>
<tr>
<td>Stent misplacement</td>
<td>0.6</td>
</tr>
<tr>
<td>Brachial arterial occlusion</td>
<td>0.1</td>
</tr>
<tr>
<td>Mismatch of stent and vessel</td>
<td>0.1</td>
</tr>
<tr>
<td>Cholesterol embolism to lower extremities</td>
<td>0.1</td>
</tr>
<tr>
<td>Dissection of iliac artery</td>
<td>0.1</td>
</tr>
<tr>
<td>Brachial artery bleeding</td>
<td>0.1</td>
</tr>
<tr>
<td>Total major complications</td>
<td>8.9</td>
</tr>
<tr>
<td>Hematoma and access site complications</td>
<td>5.0</td>
</tr>
<tr>
<td>Total minor complications</td>
<td>5.0</td>
</tr>
</tbody>
</table>

* n = 678 patients, 799 treated arteries; mortality rate was 1.0% (95% confidence interval 0–2).

**Figure 4-43.** Complications associated with renal artery stent implantation. A. Common complications that occurred most frequently were contrast-induced acute renal failure and hematoma at the access site. Potentially devastating complications include atheromatous embolization to the kidneys (B), bowel and lower extremities, acute renal artery or stent thrombosis, and renal artery dissection. An experienced operator can limit many of these serious complications. Pseudoaneurysm at the access site can be treated with ultrasound-guided thrombin injection. (Panel A adapted from Leertouwer et al. [95].)

From Creager MA, ATLAS OF VASCULAR DISEASE, 2nd Ed, Current Medicine 2003, p. 106
Case Against Angioplasty and Stenting of Atherosclerotic Renal Artery Stenosis
Lance D. Dworkin, MD et al

Conclusions:
In summary, published randomized clinical trials provide little support for the notion that angioplasty with stenting significantly improves blood pressure, preserves kidney function, or reduces episodes of congestive heart failure in patients with atherosclerotic RAS. Whether revascularization reduces the incidence of adverse cardiovascular events such as sudden death, myocardial infarction, or stroke is also unknown. In contrast, advances in medical therapy continue to improve outcomes for patients with hypertension and vascular disease with aggressive medical management of diabetes, chronic renal disease, antiplatelet therapy, more effective antismoking interventions, and new lower targets for blood pressure and low-density lipoprotein cholesterol, it is quite possible that revascularization, no matter how well performed, will provide little additional benefit to most patients. Therefore, physicians should be conservative in recommending angioplasty and stenting. Given the current uncertainty, practitioners may wish to consider referring patients into one of the large clinical trials that are examining the effects of revascularization versus medical therapy on clinical outcomes in patients with RAS. Circulation. 2007; 15: 271-276
Embolic Protection and Platelet Inhibition During Renal Artery Stenting

**Background**—Preservation of renal function is an important objective of renal artery stent procedures. Although atheroembolization can cause renal dysfunction during renal stent procedures, whether adjunctive use of embolic protection devices or glycoprotein IIb/IIIa inhibitors improves renal function is unknown.

**Methods and Results**—One hundred patients undergoing renal artery stenting at 7 centers were randomly assigned to an open-label embolic protection device, Angioguard, or double-blind use of a platelet glycoprotein IIb/IIIa inhibitor, abciximab, in a 2X2 factorial design. The main effects of treatments and their interaction were assessed on percentage change in Modification in Diet in Renal Disease-derived glomerular filtration rate from baseline to 1 month using centrally analyzed creatinine. Filter devices were analyzed for the presence of platelet-rich thrombus. With stenting alone, stenting and embolic protection, and stenting with abciximab alone, glomerular filtration rate declined (P<0.05), but with combination therapy, it did not decline and was superior to the other allocations in the 2X2 design (P<0.01). The main effects of treatment demonstrated no overall improvement in glomerular filtration rate; although abciximab was superior to placebo (0±27% versus -10±20%; P<0.05), embolic protection was not (-1±28% versus -10±20%; />=0.08). An interaction was observed between abciximab and embolic protection (P<0.05), favoring combination treatment. Abciximab reduced the occurrence of platelet-rich emboli in the filters from 42% to 77c (P<0.01).

**Conclusions**—Renal artery stenting alone, stenting with embolic protection, and stenting with abciximab were associated with a decline in glomerular filtration rate. An unanticipated interaction between Angioguard and abciximab was seen, with combination therapy better than no treatment or either treatment alone.

Cooper et al Circulation. 2008;117:2752-2760
Refining the Approach to Renal Artery Revascularization
Safian RD, Madder RD JACC CV INTERVEN 2009: 2: 161-174

The Uncertain Value of Renal Artery Interventions – Where Are We Now?
Textor SC, Lerman L, McKusick M JACC CV INTERVEN 2009: 2: 175-182

Renal Artery Revascularization – Is There a Rationale to Perform?
Mukherjee D JACC CV INTERVEN 2009: 2: 183-184
Summary:

1. Stop traditional “therapeutic nihilism” regarding RAS!!

2. RAS & renal PEI should be considered during evaluation & management of pts. with CAD, PAD, HTN, diastolic heart dysfunction & CKD.

3. Further utilization of imaging modalities will increase accurate detection and improve management of RAS.

4. PEI techniques – more debulking, less balloon induced vessel trauma – are warranted.
Renal PEI: critical appraisal

TCT Asia-Pacific, 2009

Seoul, Republic of Korea
Figure 7.5  Color duplex image of a 60–99% right renal artery stenosis. Note that the Doppler angle is 60° and parallel to the direction of arterial flow. There is a dramatic increase in the peak systolic
Unilateral Renal Artery Stenosis

Reduced renal perfusion

→ ↑ Renin-angiotensin system (RAS)
→ ↑ Renin
→ ↑ Angiotensin II
→ ↑ Aldosterone

Angiotensin II-dependent hypertension

Increased renal perfusion

→ Supressed RAS
→ Increased Na⁺ excretion (pressure natriuresis)

Effect of blockade of RAS
- Reduced arterial pressure
- Enhanced lateralization of diagnostic tests
- Glomerular filtration rate (GFR) in stenotic kidney may fall

Diagnostic tests
- Plasma renin activity elevated
- Laterlized features (e.g., renin levels in renal veins, captopril-enhanced renography)
Bilateral Renal Artery Stenosis

Bilateral

Stenosis of solitary kidney

Reduced renal perfusion

↑ Renin-angiotensin system (RAS)
↑ Renin
↑ Angiotensin II
↑ Aldosterone

Inhibit RAS

Impaired Na⁺ and water excretion

Volume expansion

Increased arterial pressure

Normal or low angiotensin II

Effect of blockade of RAS
Reduced arterial pressure only after volume depletion
May lower GFR

Diagnostic tests
Plasma renin activity normal or low
Lateralized features: none

Fig 21-5 from Creager, Dzau, Loscalzo; VASCULAR MEDICINE; SAUNDERS 2006: p.328