Renal Artery Stenting

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RAS is Common

- 1-5% of hypertensives
  - 2,000,000-4,000,000 cases in US
- Prevalence at autopsy increases with age
  
<table>
<thead>
<tr>
<th>Age</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤64</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>65-74</td>
<td>18%</td>
</tr>
<tr>
<td>≥75</td>
<td>42%</td>
</tr>
</tbody>
</table>

- CAD: 11-40%  
  Am J Card 1997
- PVD: 14-42% 
  Greco. AJKD, 1997
Renal Artery Stenosis
Sites and Characteristics

• 65-90% of all renovascular lesions are caused by atherosclerosis\(^1\)

• Common stenotic sites
  – Proximal 2 cm of the renal artery\(^1,2\)
  – Renal artery bifurcation sites\(^1\)

• Distal arterial or branch involvement is uncommon\(^1\)

• Bilateral disease is common in patients >50 years\(^3\)

RAS and SURVIVAL

- 3,987 abdominal aortograms
- Graded effect of stenosis severity on survival
  - Causal?
  - Confounding?
    Advanced Atherosclerosis
    Risk Factors: DM, HTN…


4-Year Survival

1235 cath lab patients screened for RAS > 50%
Progression Of RAS

Disease progression is associated with a decline in renal function

Patients with normal renal arteries at baseline

Crowley JJ et al Am Heart Journal 1998;136:913
Causes of Ischemic Renal Disease

- Atherosclerotic Renal Artery Stenosis
- Fibromuscular dysplasia
- Nephroangiosclerosis (HTN injury)
- Diabetic nephropathy (small vessels)
- Renal thromboembolic disease
- Atheroembolic renal disease
- Aortorenal dissection
- Post renal transplant RAS
- Renal artery vasculitis
- Trauma
- Neurofibromatosis
- Thromboangiitis obliterans
- Scleroderma

#1 Renal Artery Stenosis
#2 Fibromuscular Dysplasia
Renal Artery Stenosis

• Clues to diagnosis of Renovascular Disease
  – Onset of diastolic hypertension after age 55
  – Exacerbation of previously well-controlled HTN
  – Malignant HTN
  – Resistant HTN
  – Epigastric bruit (systolic/diastolic)
  – Unexplained azotemia
  – Azotemia while receiving Ace Inhibitors
  – Atrophic kidney or discrepancy in size between the kidneys
  – Atherosclerosis elsewhere

*Olin JW, Novich AC Chap. 18 Renovascular Disease in Peripheral Vascular Disease 2nd Ed*
Renal Artery Stenosis
Clinical Symptoms

• Uncontrolled hypertension\(^1\)
• Steady decline in renal function\(^1\)
• Cardiac dysfunction: flash pulmonary edema, CHF or unstable angina\(^2\)

1. Rosenfeld K., Isner J, Disease of Peripheral Vessels, Textbook of Cardiovascular Medicine, 1998
Atherosclerotic Renal Artery Stenosis

- Majority are ostial narrowings attributed to extension of aortic plaque
- Often occur in the setting of highly diseased aorta
- May be unilateral, bilateral, or involving a solitary functioning kidney
Making the Diagnosis of RAS: Imaging Requirements

1. Identify main and accessory renal arteries
2. Localize site of stenosis or disease
3. Provide hemodynamic significance of disease
4. Identify associated pathology
Renal Arteriography

- **Advantages**
  - Meets all 4 criteria
  - Can size RA and intervene at the same time of diagnosis
  - Sensitivity and Specificity are Gold Standard

- **Disadvantages**
  - Expense
  - Risks: Atheroembolism, CIN
  - Oculostenotic
Renal Arteriography

- Abdominal Aortogram: identification of ostia of the renal arteries and accessory renal arteries (25% of population)
- Arteriography should include both the arterial phase and the nephrographic phase
- Disease involving renal bifurcations require cranial or caudal angulation to open out the lesion
- Evidence of aortic atheroma: technique of no-touch angiography is recommended

IVUS provides a further method of renal artery evaluation for indeterminate lesions
Hemodynamic Assessment

• Hemodynamic Assessment confirms visual estimate

• 60% stenosis diameter stenosis correlates with 84% CSA reduction to create a pressure drop

• Magic number is 20 mm Hg

Does Renal Artery Stenting Further Reduce CV-Renal Events in Patients with RAS?
Renal Artery Angioplasty: Stats

• Approximately 20,000 renal artery interventional procedures/year
  – 1% of prevalence
• *Too few or too many?*
Fibromuscular Dysplasia (FMD)

- Unknown etiology
- Second most common cause of RAS
- Affects middle-aged women
- More common in first-degree relatives and in the presence of the ACE-I allele.
- Renal artery involvement is seen in 60% of cases - frequently bilateral compromise.
- Progressive renal stenosis is seen in 37% of cases and loss of renal mass in 63%
A. Classic “string of beads” appearance of fibromuscular dysplasia.
B. Intravascular ultrasound (IVUS) with a 40-MHz catheter demonstrating multiple fine fibrous bands and foci of interband aneurysmal dilatation.
C. Translesional gradient measured between a 6Fr guide catheter placed in the aorta and a 4F glide catheter placed in the distal renal artery. A 60-mm Hg resting gradient is demonstrated.
Fibromuscular Dysplasia (FMD) Treatment

- Balloon angioplasty alone: FMD localized within the main renal artery or its primary branches
- Stenting: Reserved for failure or complications of balloon angioplasty
- Surgery: FMD that involves multiple branch vessels or is associated with aneurysmal disease
D. Post-balloon angioplasty with a 4.5mm diameter balloon demonstrating improvement in the angiographic appearance.
E. Intravascular ultrasound (IVUS) confirms the postangioplasty improvement
F. Postprocedure IVUS demonstrates fracture of the fibrous bands, resulting in resolution of the gradient seen before the procedure.
Femoral Approach

- Renal artery angioplasty and stenting are usually performed via retrograde femoral approach.
- When the real artery origin is oriented horizontally or caudally with respect to the aorta, femoral approach is preferred.
Renal Artery Stent Placement

Ostial atheroma

Stent with protrusion into aortic lumen

2 mm into aorta

Ostial atheroma
Renal Intervention

- Pre-procedure
- Post-procedure
Brachial Approach

- For renal arteries that are oriented cephalad.
- When the aorta is occluded distally or the renal artery takeoff is severely angulated.
- Proximal renal artery segment initially courses inferiorly and posteriorly; braquial approach allows more coaxial alignment.
- Greater incidence of vascular site complications.
Complications Of Percutaneous Renal Revascularization

- Atheroembolism into the renal or peripheral vascular bed (cholesterol embolization)
- Dissection of renal artery or the wall of the aorta
- Acute or delayed thrombosis
- Infection
- Rupture of renal artery
- Renal perforation
A, Baseline selective renal angiogram showing tight ostial stenosis with normal filling of the renal arteries to the cortex

B, Poststent angiogram with poor filling of the distal renal arteries caused by embolization
What is the cause of deterioration in renal function after revascularization?

- Iodinated contrast?
- Atheroembolization?
- Something else?
Renal Artery Stenosis

• PTRA with Stenting
  – Associated with cumulative primary patency rate at 5 years of 84%\(^1\)
  – Procedure mortality 0%\(^1\)
  – Large body of experience demonstrating excellent results.\(^2\)

# Renal Stent Restenosis

<table>
<thead>
<tr>
<th>Author</th>
<th>Date</th>
<th>Arterie</th>
<th>Restenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Henry M.</td>
<td>1999</td>
<td>209</td>
<td>11.4</td>
</tr>
<tr>
<td>Blum U.</td>
<td>1997</td>
<td>74</td>
<td>11.0</td>
</tr>
<tr>
<td>van de Ven</td>
<td>1999</td>
<td>43</td>
<td>14.0</td>
</tr>
<tr>
<td>Tuttle</td>
<td>1998</td>
<td>148</td>
<td>14.0</td>
</tr>
<tr>
<td>K-Singh</td>
<td>1999</td>
<td>180</td>
<td>12.0</td>
</tr>
</tbody>
</table>

- **Restenosis Rate at 6 Mos ≤ 15%**
- **Restenosis after 1 Year is Unusual**
Renal Revascularization?

- Hypertensive Control
  - Reasonable Likelihood of Improvement
    - Refractory, accelerated or malignant HTN
- Renal Salvage
  - Unexplained Azotemia or ACE induced
  - Loss of renal mass over time
  - Progression of RAS
  - Renal transplant arterial stenosis or bypass stenosis producing hypertension, azotemia or both
- Cardiac disturbance
  - USA, “Flash Pulmonary Edema”, CHF
• In a clinical trial, 806 patients with renovascular disease were randomly assigned either to undergo percutaneous revascularization with medical therapy or to receive medical therapy alone.

• At a median follow-up of 34 months, the rate of decline in renal function (the primary end point) did not differ significantly between the two groups.

• Serious complications of revascularization in 23 patients.
MEAN CHANGE IN SYSTOLIC BP

Revascularisation: 384 330 315 274 216 137 83
Medical: 388 341 327 290 211 127 81
TIME TO FIRST OF MI, STROKE, VASCULAR DEATH OR HOSPITALISATION FOR ANGINA, FLUID OVERLOAD OR CARDIAC FAILURE

HR=0.90,

95% CI=0.66 to 1.15

2P = 0.3

At risk:
Revasc 403 246 159 104 54
Medical 403 251 158 94 50
MORTALITY

HR = 0.92,
95% CI = 0.68 to 1.26

68% 67%

Revasc  Medical
403  403
79  81
82.2  77.8

At risk:
Revasc  Medical
403  403
286  284
195  194
127  123
72  67

2P = 0.6

NorthShore University HealthSystem
Cardiovascular Outcomes in Renal Atherosclerotic Lesions (CORAL)

Enrollment: April 2004 – March 2010

Patients with
RAS >60% and hypertension

1:1 Randomization to:

Optimal medical therapy alone vs stenting with optimum medical therapy

Composite cardiovascular and renal endpoint:
Cardiovascular or renal death, MI, hospitalization for CHF, stroke, doubling of serum creatinine level, need for renal replacement therapy
INCLUSION CRITERIA

• Hx of systolic BP $\geq$ 155 mmHg
  – on $\geq$ 2 or more anti-hypertensives
• $\geq$ 1 Atherosclerotic stenosis
  ➢ $\geq$ 60% and $<$ 80% with 20 mmHg systolic gradient, or
  ➢ $\geq$ 80% and $<$ 100% by angiography
## Optimal Medical Therapy

### Required Therapies
- BP to target
  - ARB (Candesartan) based
  - $<140/90$
  - $<130/80$ with DM
- LDL to goal
  - Currently $<100$ mg/dl
- Diabetes Management
  - HbA1c to target, $<7$
- Smoking Cessation

### Monitoring
Summarized in Score Card
- Compliance
  - Candesartan
- BP Quarterly
- LDL annually
- HbA1c annually
- Document smoking status and education
Hazard ratio with stenting, 0.94 (95% CI, 0.76–1.17)
P=0.58 by log-rank test

### No. at Risk
- **Medical therapy alone**: 472, 371, 314, 214, 115, 40
- **Stent plus medical therapy**: 459, 362, 318, 224, 131, 59
## Coral Results - Clinical End Points

### Table 2. Clinical End Points. *

<table>
<thead>
<tr>
<th>End Point</th>
<th>Stenting plus Medical Therapy (N=459)</th>
<th>Medical Therapy Only (N=472)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary end point: death from cardiovascular or renal causes, stroke, myocardial infarction, hospitalization for congestive heart failure, progressive renal insufficiency, or permanent renal-replacement therapy †</td>
<td>161 (35.1)</td>
<td>169 (35.8)</td>
<td>0.94 (0.76–1.17)</td>
<td>0.58</td>
</tr>
<tr>
<td>Components of primary end point ‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death from cardiovascular or renal causes</td>
<td>20 (4.4)</td>
<td>20 (4.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>12 (2.6)</td>
<td>16 (3.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>30 (6.5)</td>
<td>27 (5.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospitalization for congestive heart failure</td>
<td>27 (5.9)</td>
<td>26 (5.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Progressive renal insufficiency</td>
<td>68 (14.8)</td>
<td>77 (16.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Permanent renal-replacement therapy</td>
<td>4 (0.9)</td>
<td>3 (0.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary clinical end points §</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death from any cause</td>
<td>63 (13.7)</td>
<td>76 (16.1)</td>
<td>0.80 (0.58–1.12)</td>
<td>0.20</td>
</tr>
<tr>
<td>Death from cardiovascular causes</td>
<td>41 (8.9)</td>
<td>45 (9.5)</td>
<td>0.89 (0.58–1.36)</td>
<td>0.60</td>
</tr>
<tr>
<td>Death from renal causes</td>
<td>2 (0.4)</td>
<td>1 (0.2)</td>
<td>1.89 (0.17–20.85)</td>
<td>0.60</td>
</tr>
<tr>
<td>Stroke</td>
<td>16 (3.5)</td>
<td>23 (4.9)</td>
<td>0.68 (0.36–1.28)</td>
<td>0.23</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>40 (8.7)</td>
<td>37 (7.8)</td>
<td>1.09 (0.70–1.71)</td>
<td>0.70</td>
</tr>
<tr>
<td>Hospitalization for congestive heart failure</td>
<td>39 (8.5)</td>
<td>39 (8.3)</td>
<td>1.00 (0.64–1.56)</td>
<td>0.99</td>
</tr>
<tr>
<td>Progressive renal insufficiency</td>
<td>77 (16.8)</td>
<td>89 (18.9)</td>
<td>0.86 (0.64–1.17)</td>
<td>0.34</td>
</tr>
<tr>
<td>Permanent renal-replacement therapy</td>
<td>16 (3.5)</td>
<td>8 (1.7)</td>
<td>1.98 (0.85–4.62)</td>
<td>0.11</td>
</tr>
</tbody>
</table>

* The hazard ratios were calculated with the use of multivariable proportional-hazards regression. P values were calculated with the use of the log-rank statistic.
† Only the first event per participant is included in the composite.
‡ Components of the composite are included only if it was the first event contributing to the primary end point.
§ The first event for each component of the primary composite end point is included as a secondary end point.
# Coral - Treatment Effects within Subgroups

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Stent plus Medical Therapy</th>
<th>Medical Therapy Alone</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value for Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>161/459 (35.1)</td>
<td>169/472 (35.8)</td>
<td>0.94 (0.76–1.17)</td>
<td>0.09</td>
</tr>
<tr>
<td>Creatinine level</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>&gt;1.6 mg/dl</td>
<td>43/84 (51.2)</td>
<td>34/87 (39.1)</td>
<td>0.69 (0.45–1.03)</td>
<td></td>
</tr>
<tr>
<td>≤1.6 mg/dl</td>
<td>112/352 (31.8)</td>
<td>128/367 (34.9)</td>
<td>0.87 (0.67–1.12)</td>
<td></td>
</tr>
<tr>
<td>Estimated GFR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥45 ml/min/1.73 m²</td>
<td>91/288 (31.6)</td>
<td>105/311 (33.8)</td>
<td>0.93 (0.70–1.23)</td>
<td>0.80</td>
</tr>
<tr>
<td>&lt;45 ml/min/1.73 m²</td>
<td>64/148 (43.2)</td>
<td>57/143 (39.9)</td>
<td>0.98 (0.68–1.40)</td>
<td></td>
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<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
<td>0.17</td>
</tr>
<tr>
<td>Yes</td>
<td>69/148 (46.6)</td>
<td>66/162 (40.7)</td>
<td>1.15 (0.82–1.61)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>92/309 (29.8)</td>
<td>101/310 (32.2)</td>
<td>0.84 (0.64–1.12)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td>0.64</td>
</tr>
<tr>
<td>Male</td>
<td>75/234 (32.1)</td>
<td>78/231 (33.8)</td>
<td>0.89 (0.65–1.22)</td>
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<tr>
<td>Female</td>
<td>86/225 (38.2)</td>
<td>91/241 (37.8)</td>
<td>0.99 (0.74–1.33)</td>
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<tr>
<td>Global ischaemia</td>
<td></td>
<td></td>
<td></td>
<td>0.22</td>
</tr>
<tr>
<td>Yes</td>
<td>39/89 (43.8)</td>
<td>20/51 (39.2)</td>
<td>1.07 (0.82–1.33)</td>
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<tr>
<td>No</td>
<td>119/356 (33.4)</td>
<td>106/264 (40.2)</td>
<td>0.78 (0.60–1.01)</td>
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<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td>0.62</td>
</tr>
<tr>
<td>Black</td>
<td>11/29 (37.9)</td>
<td>10/30 (33.3)</td>
<td>1.01 (0.42–2.43)</td>
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<tr>
<td>Other</td>
<td>126/356 (35.4)</td>
<td>126/357 (38.1)</td>
<td>0.88 (0.69–1.13)</td>
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<tr>
<td>Baseline systolic blood pressure</td>
<td></td>
<td></td>
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<td>0.55</td>
</tr>
<tr>
<td>&gt;160 mm Hg</td>
<td>66/148 (44.6)</td>
<td>58/139 (41.7)</td>
<td>1.02 (0.71–1.45)</td>
<td></td>
</tr>
<tr>
<td>≤160 mm Hg</td>
<td>95/309 (30.7)</td>
<td>108/328 (32.9)</td>
<td>0.90 (0.68–1.18)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td>0.56</td>
</tr>
<tr>
<td>&gt;70 yr</td>
<td>91/226 (40.3)</td>
<td>94/220 (42.7)</td>
<td>0.87 (0.65–1.16)</td>
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<tr>
<td>≤70 yr</td>
<td>70/231 (30.0)</td>
<td>75/252 (29.8)</td>
<td>1.00 (0.72–1.39)</td>
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<tr>
<td>U.S. sites</td>
<td></td>
<td></td>
<td></td>
<td>0.38</td>
</tr>
<tr>
<td>Yes</td>
<td>137/385 (35.6)</td>
<td>146/387 (37.7)</td>
<td>0.90 (0.71–1.14)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>24/74 (32.4)</td>
<td>23/85 (27.1)</td>
<td>1.22 (0.69–2.16)</td>
<td></td>
</tr>
<tr>
<td>Maximal diameter stenosis</td>
<td></td>
<td></td>
<td></td>
<td>0.66</td>
</tr>
<tr>
<td>≥80%</td>
<td>77/198 (38.9)</td>
<td>64/166 (38.6)</td>
<td>0.93 (0.67–1.30)</td>
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<tr>
<td>&lt;80%</td>
<td>77/231 (33.3)</td>
<td>79/208 (38.0)</td>
<td>0.84 (0.61–1.14)</td>
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</tr>
</tbody>
</table>
Case Selection: Should You?

- BP 148/94
- 2 Antihypertensive Meds
- 12 mm Hg gradient

NO!
Case Selection

• “Drive-by Aortogram”
• BP 148/94
• Atenolol only
• Creatinine 1.9
What about the Very Tight RAS?
Normal BP, No Meds, Normal GFR

No.
Case Selection: Should You?

- 28 y/o nurse
- BP 209/119 mm Hg
- Meds: None
- Creat 0.9
- LRA normal
Case Selection

BP 196/104
Prinivil, HCTZ, Metoprolol

71 mmHg gradient
Unfavorable Predictors

- Renal atrophy demonstrated by kidney length <7.5 cm on ultrasound
- High renal resistance index detected by duplex ultrasound
- Proteinuria > 1gm/day
- Hyperuricemia
- Creatinine clearance <40 mL/minute
Favorable Predictors
Successful Outcome For Control Of Hypertension

- Rapid acceleration of hypertension over the prior weeks or months
- Presence of “malignant” hypertension
- Hypertension in association with flash pulmonary edema
- Contemporaneous rise in serum creatinine
- Development of azotemia in response to ACE inhibitors administered for control of hypertension.
Summary

• Renal ischemia causes hypertension, ischemic nephropathy
• Nephropathy is strongly associated with CV events and mortality
• Routine RAS in moderate to severe lesions is not recommended (ASTRAL, STAR, CORAL)
• Severe stenotic lesions (>80%) in specific clinical settings may benefit from RAS
  – Discuss with Team
• Serious questions persist:
  – Is routine revascularization effective in lesions >80% for:
    • BP control?
    • Preservation of renal function?
    • Prevention of CV or Renal events?