Renal Intervention: Does no one ever talk about it anymore?

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Boston
History

• 90 y.o. M in ED with unstable angina, associated w/severe HTN. Second presentation in 2 weeks
• CAD s/p CABG & PCI SVG  EF 65%
• PAD/Claudication; AAA 3.1x3.0
• Meds
  – Toprol 75/d
  – Diovan 160 bid
  – HCTZ 25
• CKD – creat 2.3; GFR 31cc
• BP – labile: 140 to 190 (200 at cath)
Non-invasive testing

- Renal artery Duplex
  - Lt kidney atrophic (5.5cm)
  - Rt kidney normal size (12cm); severe RAS
- Coronary and graft angio
  - Prior PCI sites open
  - Diffuse moderate disease
Renal Angio at time of cath for increasing angina

AP view

LAO 12 Caudal 1
Management

- Would you Rx medically?
- Will Renal intervention “work”?
- Indicated in a 90 y.o. man? (Indicated in anyone nowadays??)
- Anything that would compel intervention?
- Addl information necessary to justify RAS?
  - Pressure gradient?
  - FFR?
Renal Artery Intervention

Initial

Final
Post-procedure Course

- BP 130-140 on multiple office visits
- Creat 2.3
- Angina resolved

WHAT WOULD CORAL HAVE SAID?
Does Renal Intervention Work???

YES! No question about it. Open artery is better than a closed one, BUT:

…with caveats:

• We are not good at predicting those patients who will benefit vs those who will not

• Complications will offset benefit very quickly
Study Overview

- Patient-level data from 901 patients (117 centers) in 5 prospective multicenter FDA-approved IDE studies of renal artery stent revascularization was pooled
- Associations of BP reduction were determined by logistic regression

### Included studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Device</th>
<th>Number of Subjects</th>
<th>Selected Inclusion Criteria</th>
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<tbody>
<tr>
<td>HERCULES</td>
<td>RX Herculink Elite</td>
<td>202</td>
<td>Uncontrolled BP and suboptimal PTA</td>
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<tr>
<td>SOAR</td>
<td>Bridge™ balloon expandable stent</td>
<td>186</td>
<td>Uncontrolled BP and failed PTA</td>
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<tr>
<td>RENAISSANCE</td>
<td>Express ® SD Renal Premounted Stent System</td>
<td>100</td>
<td>Uncontrolled BP and suboptimal PTA, renal dysfunction (Cre&lt;3.0 mg/dL), recurrent “flash” pulmonary edema, or any combination thereof</td>
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<tr>
<td>RESTORE</td>
<td>ParaMount™ XS DoubleStrut™ Balloon Expandable Stent</td>
<td>205</td>
<td>Severe HTN</td>
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<tr>
<td>ASPIRE</td>
<td>Palmaz Balloon expandable stent</td>
<td>208</td>
<td>Uncontrolled BP and suboptimal PTA</td>
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</table>

Catheter Cardiovasc Intervent 2014;83:603–9
Blood Pressure Response (logistical regression)

[Graph showing blood pressure response with P<0.0001 for both systolic and diastolic blood pressure.]

Catheter Cardiovasc Intervent 2014;83:603–9
A Randomized Multicenter Clinical Trial of Renal Artery Stenting in Preventing Cardiovascular and Renal Events: Results of the CORAL Study

Christopher J. Cooper, M.D., Timothy P. Murphy, M.D., Donald E. Cutlip, M.D., Kenneth Jamerson, M.D., William Henrich, M.D., Diane M. Reid, M.D., David J. Cohen, M.D., M.Sc., Alan H. Matsumoto, M.D., Michael Steffes, M.D., Michael R. Jaff, D.O., Martin R. Prince, M.D., Ph.D., Eldrin F. Lewis, M.D., Katherine R. Tuttle, M.D., Joseph I. Shapiro, M.D., M.P.H., John H. Rundback, M.D., Joseph M. Massaro, Ph.D., Ralph B. D’Agostino, Sr., Ph.D., and Lance D. Dworkin, M.D.,
Primary Endpoint

- Composite of major cardiovascular or renal events:
  - Cardiovascular or Renal Death
  - Stroke
  - Myocardial Infarction
  - Heart Failure Hospitalization
  - Progressive Renal Insufficiency
  - Permanent Renal Replacement Therapy

Inclusion Criteria

Clinical syndrome:
- Hypertension ≥2 anti-hypertensive medications, OR
- Renal dysfunction defined as Stage 3 or greater CKD

AND

Atherosclerotic renal artery stenosis:
- Angiographic: ≥60% and <100%, OR
- Duplex: systolic velocity of >300 cm/sec, OR
- Core lab approved MRA, OR
- Core lab approved CTA

Results: Primary Endpoint

Clinical Events

Stent plus medical therapy

Medical therapy

Stent + Medical Therapy 35.1%, 3-years
Medical Therapy 35.8%, 3-years
HR 0.94 [0.76-1.17], p = 0.58

Results: Systolic Blood Pressure

Group
- Medical Therapy (N=472)
- Stent (N=459)

Test for group by visit interaction p-value=0.876
Test for group p-value=0.030

P = 0.03
ASTRAL Results…

Clinical impact?

MORTALITY

TIME TO FIRST CV EVENT

SYSTOLIC BP

CREAT
Issue: Case selection

- Trials (CORAL, ASTRAL) did an inadequate job of pre-selecting patients
- Possibly excluded many of the very patients who were most likely to benefit
Selection Bias

Tip of the iceberg… Many not even screened!

Screened Patients (N=5322)

Not Randomized (N=4375)

Randomized (N=947)

Stent Plus Medical Therapy (N=467)
- Received Stent (N=434, 94.6%)
- Not Attempted (N=9, 1.9%)
- False + Non-Invasive Study (N=13, 2.8%)
- Failed Stent (N=3, 0.9%)

Medical Therapy Only (N=480)
- Cross Over to Stent before Endpoint (N=12, 2.5%)

Excluded for Scientific Integrity (N=8)

Included in Primary Analysis (N=459)

Patient Refusal (N=801)
- Physician Preference (N=210)
- Anatomic Exclusion (N=1866)
- Clinical Exclusion (N=628)
- Other Reasons (N=870)

Excluded for Scientific Integrity (N=8)

Included in Primary Analysis (N=472)
Recruitment
- 806 patients randomized from 58 centers over 7 years = approx 2 pts per center per year!

What happened to all the rest of the patients with RAS at these 58 study sites?

**Trial Schema:**
- ARAS, uni or bilat No contraindication
- Uncertain whether to revascularize: Randomization
- Revasc – PTRA+/– Stent Plus Medical Rx
- MD convinced of benefit of RAR
- No Revasc – Medical Rx only
Challenging times for Renal Intervention

*Where do we go from here??*

- CORAL, ASTRAL
  - Negative trials for intervention
  - Compromised due to selection bias
  - Generalizable to all with RAS?
- RAR can truly benefit well-selected subsets of patients → significant role still
- Need to define better which patients and how to confirm benefit
Renal Stenting
Case Selection

Require careful assessment of...

- Clinical indications
- Degree of stenosis (angiographic / physiologic)
- Anatomical factors
- Alternative therapies available
- Patient substrate
  - Expected benefit
  - Expected risk
So, Now What?

Catheterization and Cardiovascular Interventions 00:00–00 (2014)

Core Curriculum

SCAI Expert Consensus Statement for Renal Artery Stenting Appropriate Use

Sahil A. Parikh, MD, FACC, FSCAI, Mehdi H. Shishehbor, DO, MPH, FACC, FSCAI, Bruce H. Gray, DO, FSCAI, Christopher J. White, MD, FACC, FSCAI, and Michael R. Jaff, DO, FACC, FSCAI

Parikh, S. et al, CCI, 84:1163-1171; Dec 1, 2014
SCAI Expert Consensus Guidelines
Appropriate Care

- **Cardiac Disturbance Syndromes** (Flash Pulmonary Edema or acute coronary syndrome (ACS)) with severe hypertension

- **Resistant HTN** (Uncontrolled hypertension with failure of maximally tolerated doses of at least 3 antihypertensive agents, one of which is a diuretic, or intolerance to medications)

- **Ischemic nephropathy** with chronic kidney disease (CKD) including unilateral significant RAS with a solitary kidney or bilateral significant RAS with eGFR < 45 cc/min.

Parikh, S. et al, CCI, 84:1163-1171; Dec 1, 2014
SCAI Expert Consensus Guidelines
May Be Appropriate

- **Unilateral RAS** with:
  - **CKD** (eGFR $\leq$ 45 cc/min)
  - prior **heart failure** (Stage C)

- Anatomically challenging or high risk lesion (early bifurcation, small vessel, severe concentric calcification, and severe aortic atheroma or mural thrombus)

*Parikh, S. et al, CCI, 84:1163-1171; Dec 1, 2014*
SCAI Expert Consensus Guidelines

Rarely Appropriate

• Unilateral, Solitary, or Bilateral RAS with:
  • controlled BP and normal renal function
  • chronic end stage renal disease on hemodialysis > 3 months

• Unilateral, Solitary, or Bilateral renal artery chronic total occlusion

Parikh, S. et al, CCI, 84:1163-1171; Dec 1, 2014
A Randomized Trial of Intensive versus Standard Blood-Pressure Control

The SPRINT Research Group

November 9, 2015
SPRINT – BP Control

![Graph showing systolic blood pressure over years for standard and intensive treatment groups. The graph includes a table with data points for each treatment group. The table includes the number of participants with data and the mean number of medications.]

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<thead>
<tr>
<th>Years</th>
<th>Standard treatment</th>
<th>Intensive treatment</th>
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<tr>
<td></td>
<td>4683</td>
<td>4345</td>
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<table>
<thead>
<tr>
<th>Mean No. of Medications</th>
<th>Standard treatment</th>
<th>Intensive treatment</th>
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<tbody>
<tr>
<td></td>
<td>1.9</td>
<td>1.8</td>
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<tr>
<td></td>
<td>2.3</td>
<td>2.7</td>
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</table>
Primary outcome

Death from any cause
Summary

• Renal intervention does work, but….
• Appropriate case selection critical
• Clinical, angiographic, and physiologic parameters can help define appropriateness
• Complications mitigate the benefit
• Even when all parameters indicate “green light”, benefit still not guaranteed
• Better evidence base…could it happen?