Renal Artery Stenting 2017: Where do We Stand?

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Conflicts of Interest

Not Relevant to Renal Artery Interventions

proctor for:
- Abbott Vascular
- St Jude Medical
- Endologix
- Toray

I speak for:
- Abbott Vascular
- Angiovac
“COGNITIVE MISMATCH”

Interventionalist
Renal Stenting

"Open arteries are better than closed arteries"
INDICATIONS FOR

- **Hypertension (Class IIa)**
  - ★ Accellerated, refractory, & malignant.
  - ★ Unable to tolerate medicines.

- **Atherosclerotic nephropathy**
  - ★ Class IIa bilateral or solitary
  - ★ Class IIb for unilateral.

- **Cardiac destabilization**
  - ★ Flash pulmonary edema/CHF (Class I)
  - ★ Unstable angina (Class IIa)

Anatomic Criteria

- **Moderate lesion**: 50%–70% stenosis
  - ≥ 20 mmHg peak translesional gradient
  - ≥ 10 mmHg mean translesional gradient
  - FFR < 0.80
- **Severe lesion**: >70% stenosis.

Gradients are best measured with non-occlusive catheter/guidewire.

Hypertension Response to Renal Stenting

A Meta-Analysis of Renal Stenting

Wilms  Kuhn  Rees  Henry  Blum  Boisclair

Percent

Cured  Improved

~70%

Leertouwer TC et al. Radiology 2000; 216:78-85
★ Technical success of renal stent 95%.

★ Clinical success of renal stent for HTN = 70%.

★ Clinical success of renal stent for CKD = 75%.

Treating non-obstructive lesions.

Symptoms not related to RAS.

Over-estimate diameter stenosis.

Mild RAS and essential HTN.
Reality Testing

Is this a significant stenosis?

BEST PRACTICE

★ Hemodynamic gradients for moderate stenosis.

Does it “need” to be fixed?
• Fifteen years ago, Topol and Nissen described the oculostenotic reflex as an “irresistible temptation ... to perform angioplasty on any significant residual stenosis,” highlighting a widely held misperception that an angiographically severe stenosis must cause ischemia and that revascularization results in clinical benefit.
Angiographic RAS Assessment

- Perhaps the single weakest link renal stent.
- Visual estimation is not accurate.

Lack of correlation with hemodynamic parameters.

FFR as a Predictor of Lesion Severity and BP Response in Renal Stenting

Angiographic stenosis does not correlate with FFR

Mean BP gradient does correlate with FFR

FFR as a Predictor of BP Response in Renal Stenting

Improvement: BP < 140/90 mmHg, or a decrease of DBP by 15 mm Hg on the same or reduced # of medications

Pos Pred Value 77%
Neg Pred Value 86%
9 mmHg  
P = 0.008

23 mmHg  
P = 0.003

20 mmHg  
P = 0.001

Baseline Mean Gradient

Papaverine Mean Gradient

Dopamine Mean Gradient

Revascularization versus Medical Therapy for Renal-Artery Stenosis

Two RCT’s finding ...“no benefit” for Renal Stents ......... published in reputable journals.

Stent Placement in Patients With Atherosclerotic Renal Artery Stenosis and Impaired Renal Function
A Randomized Trial

STAR

STent placement and blood pressure and lipid-lowering for the prevention of progression of renal dysfunction caused by Atherosclerotic ostial stenosis of the Renal artery

Entry Criteria: eGFR < 80
RAS ≥ 50% diameter stenosis
BP controlled on meds (<140/90)

18/64 (30%) did not receive allocated stent.
12/64 (18%) stent patients had < 50% stenosis.
4/46 (9%) renal artery perforation !!!
Conclusion:
“We found substantial risks but no evidence of a worthwhile clinical benefit from revascularization in patients with atherosclerotic renovascular disease.”
### Table 1. (Continued.)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Revascularization (N=403)</th>
<th>Medical Therapy (N=403)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal physiology</td>
<td></td>
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<tr>
<td>Stenosis ¶</td>
<td></td>
<td></td>
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<tr>
<td>Mean (range) — %</td>
<td>76 (40–100)</td>
<td></td>
<td>75 (20–99)</td>
</tr>
<tr>
<td>Severity — no. (%)</td>
<td></td>
<td></td>
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<tr>
<td>&lt;50%</td>
<td>2 (&lt;1)</td>
<td>4 (1)</td>
<td>0.68</td>
</tr>
<tr>
<td>50–70%</td>
<td>159 (39)</td>
<td>164 (41)</td>
<td></td>
</tr>
<tr>
<td>&gt;70%</td>
<td>242 (60)</td>
<td>235 (58)</td>
<td></td>
</tr>
<tr>
<td>Mean length of kidney (range) — cm</td>
<td>9.7 (6–14)</td>
<td>9.8 (6–20)**</td>
<td>0.44</td>
</tr>
</tbody>
</table>

**MILD LESIONS?**

- How were stenoses assessed?
  - Core Lab Oversight
  - IVUS
  - Pressure Gradient

ASTRAL PROBLEMS

- Why are they randomizing “uncertain” patients?
- Angiography is not an accurate method to discriminate “borderline” stenosis.
- Their complication rate of 9% is way out of line with other contemporary studies (2%).
- 65% of all participating centers randomized fewer than 1 patient per year.

TAKE HOME MESSAGE

- Angiography is an inadequate method to select mild-moderate lesions for PTAS.

STAR & ASTRAL
“Guilty of intellectual crimes against medicine”

NEJM & Annals Editors
“Indicted as co-conspirators”
Kiss My Astral: One Seriously Flawed Study of Renal Stenting After Another

Christopher J. White,* MD
Editor-in-Chief, Catheterization and Cardiovascular Interventions

This week, the Angioplasty and STenting for Renal Artery Lesions (ASTRAL) trial was published [1]. This study offers students of clinical trials a remarkable opportunity to learn from the mistakes made by the ASTRAL group. The authors are to be congratulated on completing and publishing this study, as it takes a certain amount of courage to publish a trial this poorly conceived. I am sure they took comfort in knowing that they are not alone in reporting data that underestimate the benefits of renal artery stenting [2–4].
Stenting and Medical Therapy for Atherosclerotic Renal-Artery Stenosis

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., 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., for the CORAL Investigators*
Inclusion Criteria

Clinical Syndrome:
- Hypertension $\geq 2$ anti-hypertensive medications, OR
- Renal dysfunction defined $\geq$ Stage 3 CKD

-AND-

Atherosclerotic Renal Artery Stenosis:
- Angiographic: $\geq 60\%$ and $< 100\%$, OR
- Duplex: systolic velocity of $>300$ cm/sec, OR
- Core lab approved MRA, OR
- Core lab approved CTA

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

Primary Endpoint

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

Results: Secondary Endpoints

CV + Renal Death

P=ns

Stroke

P=ns

Myocardial Infarction

P=ns

Heart Failure

P=ns

Progressive Renal Insufficiency

P=ns

Renal Replacement

P=ns

Results: Systolic Blood Pressure

\[ P = 0.03 \]
Conclusion

- Renal artery stenting did not confer a benefit to the prevention of clinical events when added to comprehensive, multi-factorial medical therapy in people with atherosclerotic renal artery stenosis and HTN or CKD.

Cooper C, et al. NEJM 2014;370:1,13-22
Baseline Characteristics

- No significant differences in clinical and angiography characteristics
- Approximately 20% global ischemia
- Stenosis severity similar to FDA approval trials 1-3

Baseline Characteristics of the Study Population According to Treatment Group

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Stent + Medical</th>
<th>Medical</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 459</td>
<td>N = 472</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>69.3 ± 9.4</td>
<td>69.0 ± 9.0</td>
</tr>
<tr>
<td>Male gender (%)</td>
<td>51.0</td>
<td>48.9</td>
</tr>
<tr>
<td>White race (%)</td>
<td>91.5</td>
<td>90.9</td>
</tr>
<tr>
<td>Black race (%)</td>
<td>7.0</td>
<td>7.0</td>
</tr>
<tr>
<td>Body mass index (kg/m2)</td>
<td>28.2 ± 5.3</td>
<td>28.7 ± 5.7</td>
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<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>149 ± 23.2</td>
<td>150.4 ± 23.0</td>
</tr>
<tr>
<td>Estimate GFR (ml/minute)</td>
<td>58.0 ± 23.4</td>
<td>57.4 ± 21.7</td>
</tr>
<tr>
<td>Medical history and risk factors (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>32.4</td>
<td>34.3</td>
</tr>
<tr>
<td>Prior myocardial infarction</td>
<td>26.5</td>
<td>30.2</td>
</tr>
<tr>
<td>History of heart failure</td>
<td>12.0</td>
<td>15.1</td>
</tr>
<tr>
<td>Smoking in past year</td>
<td>28.0</td>
<td>32.2</td>
</tr>
<tr>
<td>Angiography</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% stenosis (core lab)</td>
<td>67.3 ± 11.4</td>
<td>66.9 ± 11.9</td>
</tr>
<tr>
<td>% stenosis (investigator)</td>
<td>72.5 ± 14.6</td>
<td>74.3 ± 13.1</td>
</tr>
<tr>
<td>Global ischemia (%)</td>
<td>20.0</td>
<td>16.2</td>
</tr>
<tr>
<td>Bilateral disease (%)</td>
<td>22.0</td>
<td>18.1</td>
</tr>
</tbody>
</table>

And now a shameless plug:
NO RCT’s For

- Parachutes.
- Bullet proof vests.
- Bicycle helmets.

Why for Renal Stents?

Parachute RCT

• Jumping off of the front porch (5 ft)?
• Jumping out of a second story window (15 ft)?
• Jumping out of an airplane (1,000 ft)?

Need level of uncertainty, equipoise.
Renal RCT

- ≤ 50% renal artery stenosis?
- 50% – 70% renal artery stenosis?
- 99% renal artery stenosis?

Need level of uncertainty, equipoise.
Would you be willing to “randomize” this patient to... best medical therapy?
THANK YOU

John Ochsner Heart & Vascular Institute