Discussant of A Randomized Multicenter Clinical Trial of Renal Artery Stenting in Preventing Cardiovascular and Renal Events: Results of the CORAL Study

A Study Which had to Fail!
My Disclosures:

Advisory Board:
Medtronic, Invatec, Gore, Angioslide, MEDRAD, Medtronic-Ardian, Covedian-ev3, Abbott Vascular

Consulting Fees/Honoraria:
Sanofi-Aventis, C.R. Bard, J&J Cordis, ev3, Boston Scientific, Straub Medical, Invatec, Biotronik, Optimed, Medrad

Research Grants:
Cook, Krauth Medical, Pathway Medical, Abbott Vascular, J&J Cordis, Angioslide, Ardian, Biotronik, Invatec, InnoRa
Anatomical Inclusion Criteria without Proof of Hemodynamic Relevance

Renal Artery Stenosis:

• Angiographic: $\geq 60\%$ and $< 100\%$, OR
  – Hemodynamical relevance $>75\%$

• Duplex: systolic velocity of $>300$ cm/sec, OR
  – Arbitrary cut-off value

• Core lab approved MRA, OR
  – Overestimates degree of stenosis

• Core lab approved CTA
  – One plane only, no proximal reference
Determination of Significance of RAS is not Trivial!

Pressure gradient

• De Bruyne et al JACC 2006

Resistance index

• Zeller et al. CCI 2008

Renal Frame Count

• Mahmud E et al. JACC Cardiovasc Int. 2008;1:286
## CORAL
### Major Study Limitations

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Stent + Medical</th>
<th>Medical</th>
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<tbody>
<tr>
<td>Angiography</td>
<td></td>
<td></td>
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<tr>
<td>% stenosis <em>(core lab)</em></td>
<td>67.3 ± 11.4</td>
<td>66.9 ± 11.9</td>
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<tr>
<td>% stenosis <em>(investigator)</em></td>
<td>72.5 ± 14.6</td>
<td>74.3 ± 13.1</td>
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</tbody>
</table>

![Graph showing event-free survival](image)

- Stent + Medical Therapy 35.1%
- Medical Therapy 35.8%
- HR 0.94 [0.76-1.17], p =0.58
Discussion of CORAL
Summary

• CORAL confirms the findings of the ASTRAL trial that stent-angioplasty of - in the majority - moderate lesions is not superior to medical treatment
  – Identical combined clinical event endpoint
  – Identical improvement of BP control
• Hemodynamics are an essential prerequisite needed before indicating a renal artery revascularization procedure
• The outcome of CORAL can’t be transferred to other etiologies of RAS such as FMD and arteritis.
RADAR Study
Primary Endpoint - Details

Difference between treatments in change of estimated glomerular filtration rate (eGFR) over 12 month

BMT+ Stenting

Calculated changes of eGFR (patients with bilateral RAS: 15% to 20%) at 1 year:

\[ \Delta e\text{GFR} \approx 5.5 \text{ ml/min} \]

\[ \Delta e\text{GFR} \text{ BMT group:} \]

-1.0 ml/min at 1 yr. FU

Estimated \( \Delta e\text{GFR} \) stent vs. BMT:

\[ \approx 6.5 \text{ ml/min} \]
Primary Endpoint

Absolute $\Delta$ eGFR over 12 Months

Power Calculation: Estimated $\Delta$eGFR stent vs. BMT: $\approx 6.5$ml/min

• In conclusion, the challenge of conducting a properly designed comparative trial between medical therapy and revascularization of atherosclerotic RAS is hampered by the fear of potentially harming the patient by withholding revascularization in patients with high risk for end organ damage in case of randomization to the conservative treatment arm. By this patients with the highest probability of treatment effect are frequently excluded from randomized trials. This underlines the need – besides well designed randomized controlled trials - for properly controlled real world registries.
Case Example

Single Kidney (Nephrectomy Left Kidney)