What is the future for renal denervation: What are its assets beyond lowering BP will it become a mainstream treatment?

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What is the future for RDN?

• A new world order since Symplicity HTN3 – and little RCT data to challenge the position
• However Dener HTN has shown that RDN does work*

Lessons for future trials

<table>
<thead>
<tr>
<th>Lessons</th>
<th>Associated with this feature</th>
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<tr>
<td>Hypertension prevalent among African American populations</td>
<td>Need to identify racial disparities in renal denervation outcomes</td>
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<td>Study site diversity</td>
<td>Need to include diverse populations</td>
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<td>Need to ensure adequate follow-up</td>
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BP is reduced after renal denervation is done properly!


Conflicts of interest

• Consultant to ROX Medical
• Speaker Bureau and Advisory boards St Jude Medical
• Educational grants from Medtronic


Markedly heterogeneous response to RDN defines responders/non-responders and reverse responders

Reasons for non-response to RDN

- Technical failure
  - Inefficient number of ablations
  - Unilateral ablation
  - Non-circumferential ablation
  - Energy modality-dependent factors*

- Renal SNS signalling not an important cause of hypertension
- Arterial stiffness


Does RF energy cause renal artery damage?

Short term injury to renal artery post-RF RDN visualised with OCT includes:
- Diffuse vasospasm
- Oedema
- Dissections
- Thrombus formation - role of antiplatelet therapy

Increasing reports of renovascular disorder post-RDN

Incidence of renovascular disorder following RDN with Vessix (Boston Scientific) system is ~ 30% at 2 sites in this study
25 cases of renal artery stenosis reported in the literature is a likely significant underestimate of the incidence post-RDN

Clues to reduced BP response to RDN in patients with isolated systolic hypertension (ISH)

- Renal denervation significantly reduced office SBP and DBP at 3, 6, & 12 months by 17/18 and 5/4/4 mm Hg in ISH and by 28/27/30 and 13/16/18 mm Hg in combined hypertension (CH), respectively.
- The non-responder rate (change in office SBP <10 mmHg) after 6 months was 37% in ISH and 21% in CH (P<0.001)

Non-responders to RDN demonstrate a substantial BP response to central iliac arteriovenous anastomosis

ROX Coupler Group

Control Group

Systolic BP

Diastolic BP

-30.5

-13.4

14.6

-30.5

-18.4

14.6

3.2

-4.6

1.0

2.2

p<0.005 for systolic and diastolic BP

p=NS for systolic and diastolic BP

Conclusions...

- Rigorous clinical evaluation of RDN across the varying modalities will be essential to determining whether or not it has a role in hypertension therapy
- The complexity of radiofrequency ablation therapy in the renal arterial wall needs to be better understood and it is possible that other ablation therapies e.g. external US may have an important role to play
- Radiofrequency ablation of the renal arteries injures the vessel wall and is associated with the development of renovascular complications
- After technical failure of ablation is excluded, arterial stiffness is likely to be an important cause of reduced/non-response to RDN