A Randomized Sham-Controlled Trial of Renal Sympathetic Denervation in *Mild* Resistant Hypertension

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Disclosure Statement of Financial Interest

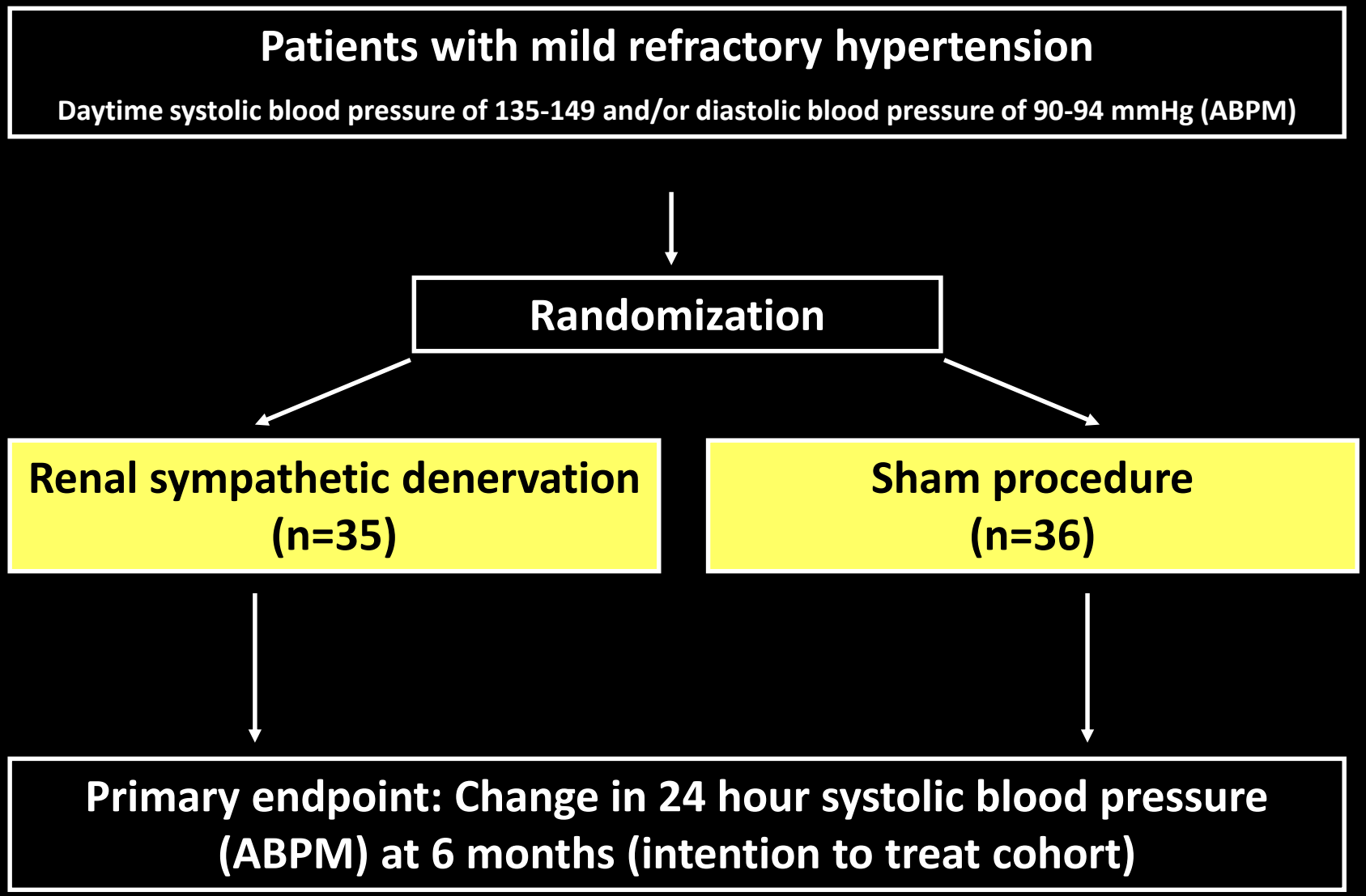
I, Steffen Desch, DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

Background

Percutaneous renal sympathetic denervation (RSD) might reduce blood pressure (BP) in patients with resistant hypertension.

Few data have been available with regard to the effectiveness of RSD in patients with resistant hypertension *yet only mildly elevated BP.*

Design: Overview



Inclusion and exclusion criteria

Inclusion criteria

- ✓ Mean daytime systolic BP on 24-hour ambulatory blood pressure measurement (ABPM) between 135 and 149 mmHg and/or mean daytime diastolic BP between 90 and 94 mmg
- ✓ Stable antihypertensive drug regimen of ≥3 agents of different classes including a diuretic at optimal dosage without change in the 4 weeks preceding randomization
- ✓ Age ≥18 to ≤75

Exclusion criteria

- ✓ ABPM values below or above predefined ranges above
- ✓ Unsuitable anatomy for RSD
- ✓ GFR <45 mL/min/1.73 m^2
- ✓ Change in BP medication in the 4 weeks preceding randomization
- ✓ Unwillingness to adhere to unchanging BP medication during study period

Procedures

RSD

Symplicity Flex Catheter (Medtronic)

4 to 6 circumferential ablation runs of 2 minutes for each renal artery from distal to proximal

Experienced interventionalists

>20 supervised procedures before treatment of study patients

Sham

Invasive examination

angiography of renal arteries and simulated RSD procedure guided by acoustic signals

Room setup as in regular RSD procedures.

Saline infusion to simulate administration of iv pain medication

BP medication and measurement

BP medication

- No change in BP medication in the previous 4 weeks before randomization
- Prospective recording of daily antihypertensive medication in the 2 weeks preceding randomization
- Patients and general practitioners were asked not to alter BP medication during study period

BP measurement

- ABPM (oscillometric device Spacelabs 90207)
- No office BP measurements
- 30 minutes intervals throughout 24 hours recording period
- Daytime interval 7:00 am to 10:00 pm
- Minimum of 75% valid readings, no more than 2 consecutive hours of missing data

Statistics

Sample size

- ASSUMPTION: ≥6 mmHg difference in primary endpoint

=75% of treatment effect observed in Symplicity HTN-2

- Anticipated standard deviation 8 mmHg, power 80%, two-sided test, α=0.05

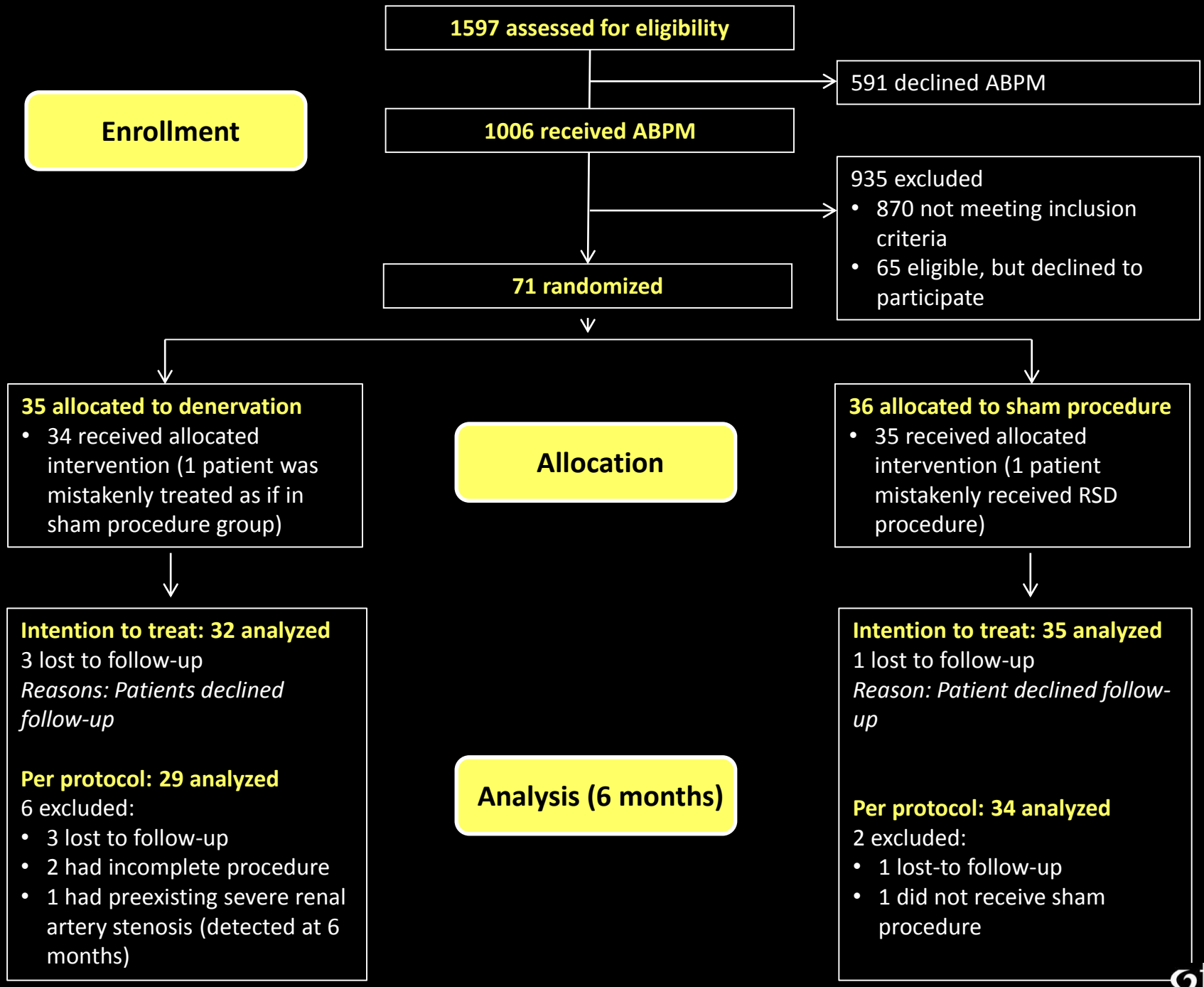
→ *29 analyzable patients needed per treatment arm. To account for dropouts/non-analyzable ABPM recordings, an additional 20% of patients were randomized in each arm.*

Statistical analysis

- 2-tailed independent samples t-test to compare BP changes between baseline and follow-up between groups

- Analysis for both intention to treat and per protocol population

ITT: Patients who underwent randomization irrespective of treatment actually received or protocol adherence.
Per protocol: Patients who completed entire trial according to rules outlined in study protocol.


1597 assessed for eligibility
591 declined ABPM
Enrollment
1006 received ABPM
935 excluded
• 870 not meeting inclusion criteria
• 65 eligible, but declined to participate
71 randomized
35 allocated to denervation
• 34 received allocated intervention (1 patient was mistakenly treated as if in sham procedure group)
Allocation
36 allocated to sham procedure
• 35 received allocated intervention (1 patient mistakenly received RSD procedure)
Intention to treat: 32 analyzed
3 lost to follow-up
Reasons: Patients declined follow-up
Per protocol: 29 analyzed
6 excluded:
• 3 lost to follow-up
• 2 had incomplete procedure
• 1 had preexisting severe renal artery stenosis (detected at 6 months)
Analysis (6 months)
Intention to treat: 35 analyzed
1 lost to follow-up
Reason: Patient declined follow-up
Per protocol: 34 analyzed
2 excluded:
• 1 lost-to follow-up
• 1 did not receive sham procedure

Results: Patient characteristics

	RSD (n=35)	Sham (n=36)	p
Systolic daytime BP (mmHg)	144.4 ± 4.8	143.0 ± 4.7	0.22
Age (yrs)	64.5 ± 7.6	57.4 ± 8.6	<0.001
Male, n (%)	27 (77)	25 (69)	0.59
Caucasian, n (%)	35 (100)	36 (100)	-
Current smoking, n (%)	6 (17)	4 (11)	0.51
History of stroke/TIA, n (%)	2 (6)	3 (8)	1.0
Coronary artery disease, n (%)	21 (60)	17 (47)	0.34
Peripheral arterial disease, n (%)	4 (11)	2 (6)	0.43
Diabetes mellitus, n (%)	19 (54)	13 (36)	0.16
Body mass index	31.9 ± 4.4	31.2 ± 4.6	0.57
Heart rate (bpm)	67 ± 11	68 ± 12	0.53
Glomerular filtration rate (ml/min/1.73 m^2)	79 ± 20	84 ± 20	0.27

Results: Baseline medication

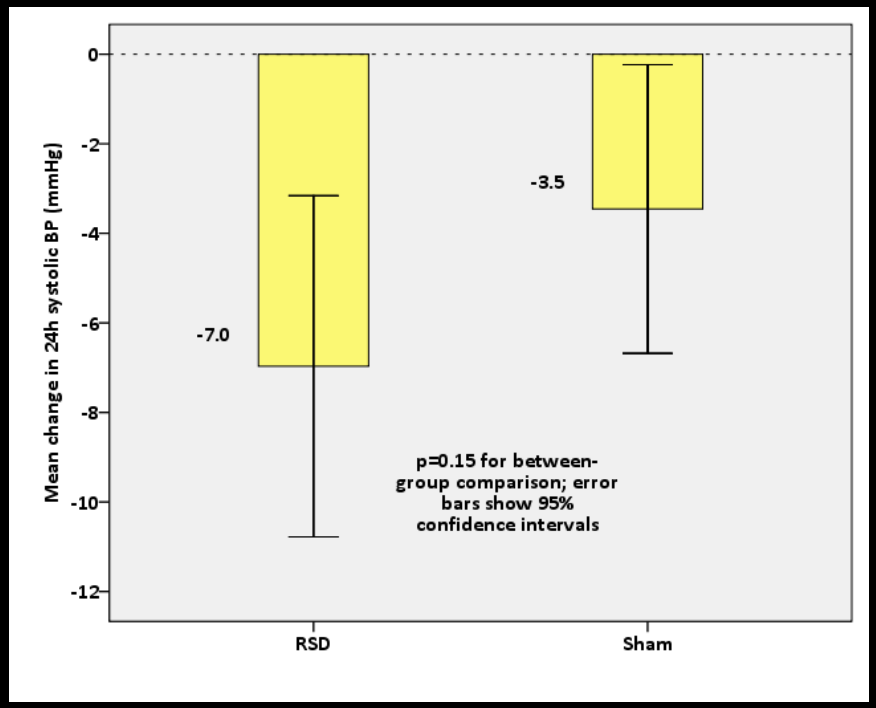
	RSD (n=35)	Sham (n=36)	p
Antihypertensive medication, n (%)			
Beta blocker	32 (91)	34 (94)	0.67
ACE inhibitor	18 (51)	20 (56)	0.81
Angiotensin receptor blocker	16 (46)	17 (47)	1.0
Direct renin inhibitor	1 (3)	3 (8)	0.61
Diuretic	35 (100)	33 (92)	0.24
Calcium channel blocker	24 (69)	23 (64)	0.80
Aldosterone antagonist	1 (3)	2 (6)	1.0
Vasodilator	2 (6)	4 (11)	0.67
Alpha blocker	7 (21)	5 (14)	0.54
Sympatholytic agent	9 (26)	10 (28)	1.00
Number of antihypertensive agents	4.4 $\pm$ 1.3	4.3 $\pm$ 1.3	0.84
≥5 antihypertensive agents, n (%)	14 (40)	14 (39)	1.0

Results: Primary endpoint

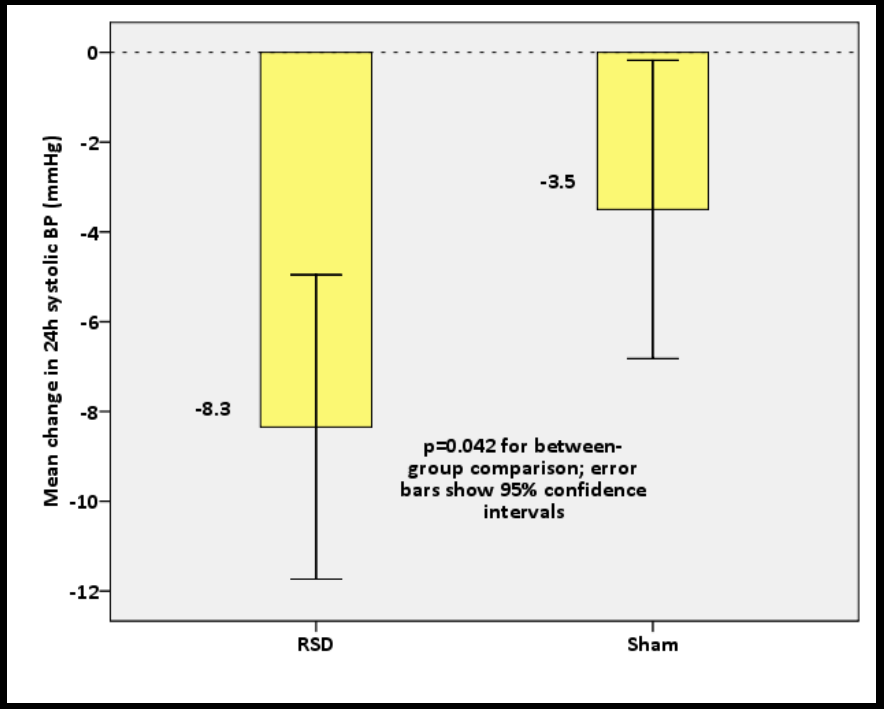
Mean change in 24h systolic BP from baseline to 6 months

Intention to treat

Primary endpoint



Per protocol



Limitations

Small sample size

No urine analysis to assess medication adherence

No objective assessment of success of blinding procedure (e.g. by dedicated questionnaire)

Summary

First randomized sham-controlled study to study a possible antihypertensive effect of RSD in patients with resistant hypertension *yet only mildly elevated BP.*

ABPM primary endpoint.

Significant reduction in 24h systolic BP at 6 months following RSD in per protocol cohort, however not in intention to treat population.