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

Steffen Desch, Thomas Okon, Diana Heinemann, Konrad Kulle, Karoline Röhnert, Melanie Sonnabend, Martin Petzold, Ulrike Müller, Gerhard Schuler, Ingo Eitel, Holger Thiele, Philipp Lurz

Abstract—Few data are available with regard to the effectiveness of renal sympathetic denervation in patients with resistant hypertension yet only mildly elevated blood pressure (BP). Patients with resistant hypertension and slightly elevated BP (day-time systolic pressure, 135–149 and diastolic pressure, 90–94 mm Hg on 24-hour ambulatory measurement) were randomized in a 1:1 ratio to renal sympathetic denervation with the Symplicity Flex Catheter (Medtronic) or an invasive sham procedure. The primary efficacy end point was the change in 24-hour systolic BP at 6 months between groups in the intention to treat population. A total of 71 patients underwent randomization. Baseline day-time systolic BP was 144.4±4.8 mm Hg in patients assigned to denervation and 143.0±4.7 mm Hg in patients randomized to the sham procedure. The mean change in 24-hour systolic BP in the intention to treat cohort at 6 months was −7.0 mm Hg (95% confidence interval, −10.8 to −3.2) for patients undergoing denervation and −3.5 mm Hg (95% confidence interval, −6.7 to −0.2) in the sham group (P=0.15). In the per protocol population, the change in 24-hour systolic BP at 6 months was −8.3 mm Hg (95% confidence interval, −11.7 to −5.0) for patients undergoing denervation and −3.5 mm Hg (95% confidence interval, −6.8 to −0.2) in the sham group (P=0.042). In patients with mild resistant hypertension, renal sympathetic denervation failed to show a significant reduction in the primary end point of 24-hour systolic BP at 6 months between groups in the intention to treat analysis.

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Key Words: blood pressure ■ blood pressure monitoring, ambulatory ■ randomized controlled trial

Resistant hypertension is defined as a blood pressure (BP) of ≥140/90 mm Hg despite the intake of ≥3 antihypertensive drugs, including a diuretic at maximally tolerated doses. Its prevalence has been reported to be 12.8% in a US population. Sympathetic overactivity contributes to the development and perpetuation in a subset of patients with resistant hypertension. Its negative effects include sodium and water retention, increased renin release, and alterations of renal blood flow. Afferent and efferent sympathetic nerves that travel in the renal artery walls mediate pathological interactions between the central nervous system and the kidneys. Recently, catheter-based disruption of these renal sympathetic nerve fibers using radiofrequency energy has been introduced as a new treatment against resistant hypertension. Initial nonrandomized and randomized, nonblinded trials demonstrated a dramatic reduction in systolic and diastolic BP after renal sympathetic denervation (RSD). In contrast, in the recent sham-controlled Simplicity HTN-3 trial of patients with severe treatment-resistant hypertension, RSD led to no significant improvement in BP when compared with the sham group. Some think that the results of this trial with the so far most rigorous design commenced the beginning of the end of RSD for resistant hypertension. Proponents of RSD argue that the negative outcome is a consequence of inefficient denervation procedures and suboptimal selection of patients. One aspect that deserves further consideration is that patients recruited into the Simplicity HTN-3 study might represent a population at the most advanced spectrum of the disease with marked and in many cases long-standing hypertension. One could argue that in such patients, RSD might be less effective because of irreversible alterations of the anatomic structures and physiological processes supporting chronic BP elevations. The present trial was conducted to test the hypothesis that RSD is superior to a sham intervention in patients with only mild resistant arterial hypertension.

Methods

Design Overview

The trial’s main objective was to study a possible blood-pressure lowering effect of RSD in patients with resistant hypertension and mildly elevated BP. Eligible patients between 18 and 75 years of age were randomized to RSD or a sham procedure. Resistant hypertension with mildly elevated BP was defined as (1) a stable antihypertensive drug
regimen of ≥3 agents of different classes, including a diuretic (except when not tolerated/contraindicated) at optimal dosage without change in the 4 weeks preceding randomization and (2) mean daytime systolic BP on 24-hour ambulatory BP measurement (ABPM) between 135 and 149 mm Hg or mean daytime diastolic BP between 90 and 94 mm Hg. The primary efficacy end point was the change in 24-hour systolic BP at 6 months between groups in the intention to treat population. Exclusion criteria included ABPM values below or above the predefined ranges mentioned above, unsuitable anatomy for RSD, severe renal artery stenosis, estimated glomerular filtration rate <45 mL/min per 1.73 m² (modification of diet in renal disease formula), change in BP medication in the 4 weeks preceding randomization, unwillingness to adhere to unchanging BP medication during the study period of 6 months, pregnancy, and severe comorbidities with limited life expectancy.

The study was approved by the local Institutional Review Board and conducted in accordance with the principles of the Declaration of Helsinki. All patients provided written informed consent before randomization. Enrollment was completed in January 2014.

Randomization
Potentially eligible patients willing to take part in the study underwent ABPM. If the predefined BP criteria were met, patients were randomized in a 1:1 ratio to either RSD or an invasive sham procedure. Patients were assigned to the treatment groups by simple randomization via an internet-based system using a computer-generated list of random numbers. The randomization list was generated and maintained by an information technology expert who was not involved in the clinical conduct of the study.

Interventions and Blinding
RSD was performed with the Symplicity Flex Catheter (Medtronic) as described previously. Four to 6 ablation runs of 2 minutes for each renal artery were delivered circumferentially to the renal artery wall from distal to proximal according to the internal algorithm of the Symplicity generator which monitors and controls temperature, impedance, and power output to assure delivery of energy to each site. Participants in the active RSD group were given intravenous remifentanil to control visceral pain. All RSD procedures were performed by 3 experienced interventionists (>20 supervised procedures before treatment of study patients).

For patients in the sham group, the room setup was prepared as in regular RSD procedures. Patients received saline infusion to simulate administration of intraarterial pain medication and underwent invasive examination (including angiography of the renal arteries and a simulated RSD procedure with 4–6 sham runs for each renal artery guided by 2-minute acoustic signals similar to those of the Symplicity generator; overall procedure time was kept similar in both treatment arms).

Except for the physicians performing the invasive procedures, all investigators (including personnel responsible for BP assessment) were blinded to treatment assignment. Patients in neither group were informed about technical details or duration of the procedure. Treatment allocation was not disclosed until completion of the study.

BP medication and Measurements
Pre-existing BP medication remained unchanged at study entry. No change in BP medication in the previous 4 weeks before randomization was allowed. To control medication adherence, patients had to be on the same regimen of ≥3 agents of different classes, including a diuretic (except when not tolerated/contraindicated) at optimal dosage without change in the 4 weeks preceding randomization. Patients and general practitioners involved in the clinical conduct of the study.

Follow-Up and End Points
Patients underwent outpatient follow-up at 1, 3, and 6 months including ABPM. The primary end point was assessed at 6 months, and the trial was unblinded afterward. The primary efficacy end point was the change in 24-hour systolic BP at 6 months between groups in the intention to treat population. Secondary end points included the change in diastolic and mean BP at 6 months and the change in 24-hour mean systolic BP between the per-protocol population. In addition, safety events, such as procedural vascular complications and all-cause death, were analyzed.

Sample Size
Sample size was calculated for the between-group comparison with regard to the primary end point.

At the time of trial planning, previous data to guide calculation were scarce. The only available randomized trial of RSD in resistant hypertension (Symplicity HTN-2) compared RSD against no-sham control in patients with resistant hypertension and severely elevated BP. ABPM recordings were available for a subgroup of patients: the mean reduction in 24-hour systolic BP at 6 months was 1±15 mm Hg in patients assigned to RSD and 3±19 mm Hg in control patients (for a net difference of 8 mm Hg between groups).

For the current trial, we assumed a less pronounced effect of RSD on BP in light of inclusion of patients with only mildly elevated BP. We speculated that RSD would lead to a difference of at least 6 mm Hg between groups with regard to the primary end point (75% of the treatment effect observed in Symplicity HTN-2). We assumed a lower SD of systolic BP values based on a more homogeneous population compared with Symplicity HTN-2. Based on data from a previous trial in mildly hypertensive patients, the presumed SD was set at 8 mm Hg for both groups. Thus, 29 patients per treatment arm needed to be analyzed to reject the null hypothesis of equal means between the 2 groups to provide a statistical power of 80% (2-sided test, α=0.05). To account for potential dropouts or nonanalyzable ABPM recordings, an additional 20% of patients were randomized in each arm. Sample size was calculated using nQuery Advisor 7.0 (Statistical Solutions, Saugus, MA).

Statistical Analysis
BP changes between baseline and follow-up were calculated for both treatment groups and compared using a 2-tailed independent samples t test. Baseline characteristics were compared using Fisher exact test for categorical variables and independent samples t tests for continuous data. Categorical variables are expressed as number and percentage of patients. Continuous data are reported as means and SD, as well as 95% confidence interval (CI), when appropriate. Data were analyzed for both the intention to treat (cohort for primary end point analysis) and the per-protocol population. The per-protocol analysis included all patients who completed the entire trial according to the rules outlined in the study protocol. The intention to treat cohort comprised all patients who underwent randomization irrespective of treatment actually received or protocol adherence. Because age was found to be not perfectly balanced between groups at baseline, an additional analysis of covariance was performed to compare the change in 24-hour systolic BP from baseline to 6 months between groups with age as covariate. The primary end point was also analyzed in the
prespecified subgroups of diabetes mellitus, baseline dipper status, and age according to median. A 2-tailed \( P \) value of <0.05 was considered statistically significant. Statistical analyses were performed with SPSS 17.0 (SPSS Inc, Chicago, IL).

**Results**

**Patients**

A total of 106 potentially eligible patients underwent ABPM of whom 71 patients with resistant hypertension and mildly elevated BP underwent randomization (Figure 1). Baseline characteristics were well balanced between the 2 treatment groups except for age (64.5\( \pm \)7.6 years in RSD group versus 57.4\( \pm \)8.6 in sham group; \( P<0.001; \) Table 1). Day-time systolic BP was 144.4\( \pm \)4.8 mm Hg in patients assigned to RSD and 143.0\( \pm \)4.7 mm Hg in patients randomized to the sham procedure (\( P=0.22 \)). Patients received an average of 4.3 antihypertensive agents including in the vast majority diuretics (96%) and renin angiotensin aldosterone system inhibitors (97%).

According to the intention to treat principle, the primary end point could be analyzed in 67 of the 71 patients who were randomly assigned to RSD or sham procedure (Figure 1). The per-protocol cohort comprised 63 patients (Figure 1).

The mean number of complete ablations of 2 minutes each in patients undergoing RSD was 11.1\( \pm \)1.7 (5.7 for the right and 5.5 for the left renal artery). The rate of patients with a change in medication during the study course was 21% and was not significantly different between treatment groups (\( P=0.23 \)).

**ABPM Results**

The mean change for the primary end point of 24-hour systolic BP at 6 months in the intention to treat cohort was \(-7.0 \text{ mm Hg (95\% CI, } -10.8 \text{ to } -3.2) \) for patients undergoing RSD and \(-3.5 \text{ mm Hg (95\% CI, } -6.7 \text{ to } -0.2) \) in the sham group (\( P=0.15 \); Table 2 and Figure 2A). In the per-protocol population, the change in 24-hour systolic BP at 6 months was \(-8.3 \text{ mm Hg (95\% CI, } -11.7 \text{ to } -5.0) \) for patients undergoing RSD and \(-3.5 \text{ mm Hg (95\% CI, } -6.8 \text{ to } -0.2) \) in the sham group (\( P=0.042 \); Table 3 and Figure 2B). These results did not change materially when adjusted for baseline age by analysis of covariance (\( P=0.15 \) for intention to treat cohort; \( P=0.05 \) for per-protocol cohort). There was also a significant reduction in the secondary end point of day-time systolic BP in RSD patients in the per-protocol analysis (\(-9.9 \text{ [95\% CI, } -13.4 \text{ to } -6.5) \) versus \(-3.7 \text{ mm Hg [95\% CI, } -7.1 \text{ to } -0.2) \); \( P=0.012 \); Table 3). No statistically significant changes in 24-hour diastolic or mean BP or any measures of night-time BP were recorded in either intention to treat or per-protocol analysis.

![Flowchart](http://hyper.ahajournals.org/)

Figure 1. Study profile. Shown is the study flow (CONSORT [Consolidated Standards of Reporting Trials] diagram). ABPM indicates ambulatory blood pressure monitoring; and RSD, renal sympathetic denervation.
Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>RSD (n=35)</th>
<th>Sham (n=36)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>64.5±7.6</td>
<td>57.4±8.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Men</td>
<td>27 (77)</td>
<td>25 (69)</td>
<td>0.59</td>
</tr>
<tr>
<td>Current smoking</td>
<td>6 (17)</td>
<td>4 (11)</td>
<td>0.51</td>
</tr>
<tr>
<td>History of stroke/transient ischemic attack</td>
<td>2 (6)</td>
<td>3 (8)</td>
<td>1.0</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>21 (60)</td>
<td>17 (47)</td>
<td>0.34</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>4 (11)</td>
<td>2 (6)</td>
<td>0.43</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>19 (54)</td>
<td>13 (36)</td>
<td>0.16</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>31.9±4.4</td>
<td>31.2±4.6</td>
<td>0.57</td>
</tr>
<tr>
<td>Glomerular filtration rate, mL/min per 1.73 m²*</td>
<td>79±20</td>
<td>84±20</td>
<td>0.27</td>
</tr>
<tr>
<td>24-h heart rate, bpm</td>
<td>67±11</td>
<td>68±12</td>
<td>0.53</td>
</tr>
<tr>
<td>Isolated systolic hypertension</td>
<td>23 (66)</td>
<td>20 (56)</td>
<td>0.47</td>
</tr>
<tr>
<td>Ambulatory blood pressure, mm Hg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24-h systolic</td>
<td>140.2±4.6</td>
<td>140.4±5.6</td>
<td>0.51</td>
</tr>
<tr>
<td>24-h diastolic</td>
<td>78.2±7.4</td>
<td>80.6±7.1</td>
<td>0.16</td>
</tr>
<tr>
<td>24-h mean</td>
<td>100.1±4.9</td>
<td>100.9±5.5</td>
<td>0.55</td>
</tr>
<tr>
<td>Day-time systolic</td>
<td>144.4±4.8</td>
<td>143.0±4.7</td>
<td>0.22</td>
</tr>
<tr>
<td>Day-time diastolic</td>
<td>80.6±7.8</td>
<td>82.9±7.3</td>
<td>0.21</td>
</tr>
<tr>
<td>Day-time mean</td>
<td>102.6±4.9</td>
<td>103.2±5.8</td>
<td>0.63</td>
</tr>
<tr>
<td>Night-time systolic</td>
<td>130.5±9.7</td>
<td>132.3±11.7</td>
<td>0.50</td>
</tr>
<tr>
<td>Night-time diastolic</td>
<td>69.7±8.0</td>
<td>73.2±8.4</td>
<td>0.07</td>
</tr>
<tr>
<td>Night-time mean</td>
<td>91.4±7.4</td>
<td>93.4±8.1</td>
<td>0.29</td>
</tr>
<tr>
<td>Dipper</td>
<td>16 (48)</td>
<td>14 (39)</td>
<td>0.63</td>
</tr>
</tbody>
</table>

Antihypertensive medication

| 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±1.3    | 4.3±1.3     | 0.84    |
| ≥3 antihypertensive agents               | 14 (40)    | 14 (39)     | 1.0     |

*Estimated according to MDRD (modification of diet in renal disease) formula.

(Tables 2 and 3). In the per-protocol population, 22 patients in the RSD group and 29 patients in the sham group completed the study without any change in medication. When analyzing only these patients, RSD was followed by a significant reduction in 24-hour systolic BP compared with the sham group (RSD: −9.5 mm Hg [95% CI, −13.1 to −5.9]; sham: −3.2 mm Hg [95% CI, −6.1 to −0.3]; P=0.007).

There was a slight increase in the heart rate in both groups from baseline to 6 months (RSD, +2.4 bpm; sham, +2.0) with no significant between-group difference (P=0.83). The percentage of patients who converted from a nondipper to a dipper status at 6 months was similar (4 [13%] in the RSD group versus 6 [17%] in the sham group; P=0.74). There was no significant difference between groups with regard to the primary end point in any of the prespecified subgroups.

Safety

There were no deaths, other serious adverse events, or vascular complications. Kidney function as estimated by the glomerular filtration rate remained unchanged at 6 months (−2.8 mL/min per 1.73 m² in the RSD group and −0.01 in the sham group; P=0.30 for between-group comparison).

Discussion

This is the first randomized sham-controlled study to examine a possible antihypertensive effect of RSD in patients with resistant hypertension yet only mildly elevated BP. There was no significant reduction in the primary end point of 24-hour systolic BP at 6 months between groups after RSD in the intention to treat cohort. However, we found a significant decline in 24-hour systolic BP after RSD in the per-protocol cohort, which is likely a better indicator of biological effectiveness of the procedure.

Previous randomized trials to study the effects of RSD in resistant hypertension have yielded conflicting results. The first small randomized controlled trial (Symplicity HTN-2) showed marked reductions in both systolic and diastolic BP in severely hypertensive patients. The trial ignited euphoric reactions about the therapeutic potential of RSD in the treatment of hypertension and other diseases associated with sympathetic overactivity (eg, heart failure and atrial fibrillation). However, the study was also criticized mainly because there was no-sham control group, and therefore, blinding was inadequate. A larger successor trial (Symplicity HTN-3) in a similar patient population was recently published, which tried to correct some of the shortcomings of Symplicity HTN-2, including a sham control group. To the surprise of many, the study did not show a significant reduction in BP 6 months after RSD when compared with the sham control group.

Discussed causes for these disappointing results are ineffective procedures, inappropriate patient selection, confounding effects of a presumed Hawthorne effect, and thereby improved medication adherence during the study period, and the possibility that sympathetic nerve activity might by only a minor contributor to severe hypertension.

The present trial differs from the aforementioned studies in that it exclusively enrolled patients with resistant hypertension yet only mildly elevated BP (corresponding to stage 1 hypertension), whereas both Symplicity HTN-2 and -3 randomized patients with resistant hypertension and markedly elevated systolic office BP values of at least 160 mm Hg (≥150 mm Hg for patients with diabetes mellitus in Symplicity HTN-2). For comparison, systolic day-time BP was 144 mm Hg (RSD group) and 143 mm Hg (sham group) in this study, whereas corresponding values in the Symplicity HTN-3 study were 163 mm Hg (RSD) and 164 mm Hg (sham).
small nonrandomized patient series reported on the outcome of RSD in patients with resistant hypertension yet only mildly elevated BP. Both found a reduction in BP in patients treated by RSD. However, results must be interpreted with caution because these trials were purely observational.

It has been argued that RSD might be most effective in patients with severe treatment-resistant hypertension. However, this chain of thought must undergo critical reappraisal. Results from the Symplicity HTN-3 trial show that although the absolute fall in BP after RSD is indeed the greatest with higher pretreatment values, this is also true for the sham group. There was no significant difference in the change of 24-hour ambulatory systolic BP between RSD and sham in any of the tertiles of baseline BP. Thus, the relative efficacy—if there is any—might be similar in severe and mild resistant hypertension.

Over half of the patients with so-called treatment-resistant hypertension show nonadherence to medication when examined by objective urine analysis of antihypertensive drugs. Patients with poor adherence display significantly higher BP levels when compared with their truly treatment-resistant adherent counterparts. It is therefore likely that the percentage of noncompliant patients is substantially higher in patients with severely elevated when compared with only moderately elevated BP. Because in noncompliant patients, sympathetic overdrive is likely not the leading mechanism in the pathogenesis of treatment resistance, the response to RSD will be blunted. This might explain the partly discrepant results of RSD on BP seen in the present trial of moderately hypertensive patients when compared with the Symplicity HTN-3 study in severe resistant hypertension. In line with this hypothesis is the observation that in patients from the per-protocol population in the present trial who completed the study without any change in medication, RSD was followed by a significant reduction in 24-hour systolic BP compared with the sham group.

Furthermore, patients with only mild forms of resistant hypertension may display less advanced structural changes in the renal arteries (eg, vessel calcification) such that energy delivery is more stable. This might lead to a more favorable BP response after RSD.

When compared with Symplicity HTN-3, all RSD procedures in this study were performed by only 3 interventionalists experienced in RSD procedures. This might have led to more...
consistent BP results. However, we think this to be of only minor importance because RSD is not a complex procedure from an interventional standpoint.

In Symplicity HTN-3, RSD was followed by a significant office BP reduction compared with sham in the prespecified subgroup of nonblack patients. It is therefore important to note that in this study, all enrolled patients were of white origin, which might partly explain the overall positive trend of RSD on BP.

This trial is the first to use BP values derived from 24-hour recordings as entry criteria, as well as for the primary end point. ABPM is superior to office BP in predicting the risk of cardiovascular outcome. Consistent with previous trials, RSD was safe and well tolerated.

Limitations
The main limitation is the sample size, which might be too small to detect an unquestionable treatment effect of RSD reflecting the possibility of type II error (the error of failing to observe a difference between the study groups when in truth there is one). Suboptimal power is also reflected by the discrepant results between intention to treat and per-protocol population. Thus, our results should be considered exploratory and be interpreted with caution.

We recorded only complete ablation runs of 2 minutes, however not interrupted ablations where the generator or the operator stopped the run early. Recent data suggest that the combined number of complete and incomplete ablation runs (ie, overall number of ablation attempts) is associated with greater BP reductions. However, the number of complete runs in our trial (11.1) compares favorably with the Symplicity HTN-3 trial where the number of complete runs was 9.2. In fact, the number of complete ablations in the present trial is similar to the total number of ablation attempts of 11.2 in Symplicity HTN-3. We therefore think that the present trial is not at the lower end of the spectrum of overall ablation attempts. Medication adherence was assessed by patient interrogation at the follow-up visits, however not by an objective measure, such as urine analysis. Because medication compliance seems to be a major confounder in all randomized trials to date, this might have influenced the overall results. We did not assess the success of the blinding procedure, for example, by a dedicated questionnaire. The rate of patients taking mineralocorticoid receptor antagonists was low which might have influenced results. Recent data from the Symplicity HTN-3 trial suggest that BP decline after RSD is more pronounced in patients taking aldosterone antagonists. Reasons discussed with regard to the Symplicity HTN-3 cohort are higher baseline BP for patients on aldosterone antagonists, differences in baseline characteristics, additive effects of RSD to pre-existing neurohormonal blockade, or chance findings. The Simplicity Flex catheter used in this study has, to date, been the standard of care in RSD. However, newer generation devices with multiple electrodes, a more consistent circumferential ablation or alternative sources of energy delivery, might improve the BP response. A significant shortcoming of RSD as performed currently is that there is no immediate feedback if renal nerve ablation was technically effective.

Perspectives
In patients with mild resistant hypertension, RSD failed to show a significant reduction in the primary end point of 24-hour systolic BP at 6 months between groups in the intention to treat analysis. However, in the per-protocol population of patients who actually received the treatment as planned RSD was followed by a significant reduction in systolic BP compared with a sham procedure.

In light of the conflicting evidence with regards to the effectiveness of RSD in resistant hypertension, additional research is needed. Mainly 2 aspects warrant further study. First, more emphasis must be placed to identify groups of patients who might benefit from RSD; second, technical aspects of RSD must be further developed, especially with regard to consistent renal nerve disruption.

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Disclosures
Dr Lurz has received speaker honoraria from Medtronic.
References


What Is New?

• First randomized sham-controlled study to examine a possible antihypertensive effect of renal sympathetic denervation in patients with resistant hypertension yet only mildly elevated blood pressure.

What Is Relevant?

• In patients with mild resistant hypertension, renal sympathetic denervation failed to show a significant reduction in the primary end point of 24-hour systolic blood pressure at 6 months between groups in the intention to treat analysis. However, in the per-protocol population of patients who actually received the treatment as planned, renal sympathetic denervation was followed by a significant reduction in systolic blood pressure compared with a sham procedure.

Summary

Renal sympathetic denervation holds promise in the treatment of mild resistant hypertension; however, further study is needed.
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临床试验 - ACS1研究（摘要）

血管紧张素受体拮抗剂和钙通道拮抗剂在亚裔高血压患者中降低睡眠血压作用的年龄相关性差异——ACS1研究

Age-Related Difference in the Sleep Pressure-Lowering Effect Between an Angiotensin II Receptor Blocker and a Calcium Channel Blocker in Asian Hypertensives-The ACS1 Study

Kazuomi Kario, Satoshi Hoshide

李勇 译

睡眠血压水平部分取决于盐敏感性及盐摄人，是高血压患者的一个重要心血管风险。然而，目前尚无研究考察血管紧张素受体拮抗剂（angiotensin II receptor blockers, ARB）和钙通道拮抗剂（calcium channel blockers, CCB）对亚裔人群睡眠血压降低作用的年龄相关差异。阿齐沙坦昼夜节律和睡眠血压（Azilsartan Circadian and Sleep Pressure）第一项研究（ACS1）是一个多中心、随机、开放标签2个平行组对照研究，比较口服ARB（阿齐沙坦20 mg）或CCB（氨氯地平5 mg）治疗对动态血压监测评估的睡眠血压的疗效。总体上，与阿齐沙坦相比，氨氯地平治疗降低睡眠血压、清醒血压及24小时平均血压的幅度更大。对>60岁的老年高血压患者，氨氯地平降压作用更加显著。在>60岁患者中，氨氯地平治疗后睡眠血压达标率趋向高于阿齐沙坦，但未达到统计学差异。在清醒血压及24小时平均血压的达标率上亦呈相似结果。这些结果提示，氨氯地平降压效果及血压控制能力优于阿齐沙坦，对老年高血压人群，氨氯地平的降压及血压控制作用均优于阿齐沙坦。正美国高血压学会（American Society of Hypertension）/国际高血压学会（The international Society of Hypertension），以及英国国立健康和临床优化研究所（National Institute for Health and Clinical Excellence）等指南推荐，根据年龄选择降压治疗药物时，氨氯地平应作为老年人起始治疗的选择之一。

（Hypertension. 2015;65:729-735.）

高血压的介入治疗（摘要）

一项随机假手术对照试验评估去肾交感神经术对轻度顽固性高血压患者的降压疗效

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

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目前关于去肾交感神经术治疗轻度顽固性高血压患者的研究数据较少。轻度顽固性高血压（24小时动态血压监测日间收缩压；135~149，舒张压；90~94 mmHg）患者，按1:1比例随机分为去肾交感神经术组（Symplicity Flex导管，美敦力公司）或假手术组。主要疗效终点为在意向性治疗（intention to treat, ITT）人群中比较两组患者术后6个月时24小时收缩压的变化。共有71例患者参与随机分组。去肾交感神经术组的基线日间收缩压为144.4 ± 4.8 mmHg，假手术对照组为143.0 ± 4.7 mmHg。6个月后ITT分析显示，去肾交感神经术组24小时平均收缩压下降7.0 mmHg（95% CI：-10.8~3.2），假手术组下降3.5 mmHg（95% CI：-6.8~-0.2）（P=0.15），完成治疗方案（per protocol）人群分析显示，去肾交感神经术组24小时平均收缩压下降8.3 mmHg（95%CI：-11.7~5.0），假手术组下降3.5 mmHg（95% CI：-6.8~0.2）（P=0.042）。对于轻度顽固性高血压患者，ITT分析显示去肾交感神经术与假手术组6个月后的24小时收缩压没有显著差异。

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