

## SHORT COMMUNICATION

# Renal Sympathetic Denervation in Resistant Arterial Hypertension: Long Term and Updated Results

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## Summary

The present paper is an extension to our earlier publication (Šochman *et al.* 2016) documenting a beneficial effect of renal sympathetic denervation on pharmacologically uncontrollable hypertension in a group of seven patients followed up for 1-2 years post-procedure. The same patients remained on ambulatory follow-up for another 5-6 years, with the beneficial effect persisting throughout the follow-up period while on the same medication.

## Key words

Hypertension • Renal sympathetic denervation • Uncontrollable blood pressure

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Renal sympathetic denervation (RSD) as a therapeutic option in conservatively uncontrollable hypertension has experienced a dramatic twist in recent years. While, after the initial results of the SYMPLICITY HTN-1 and -2 trials became available, RSD was looked up to as a revolutionary therapeutic modality, but the procedure was virtually discarded after the publication of the SYMPLICITY HTN-3 trial results. Still, the fact that a small proportion of patients did respond to RSD by a reduction of high blood pressure (BP) has never been

challenged; however, there is no clue to identify RSD responders before the procedure.

The present paper is an extension to our earlier publication (Šochman *et al.* 2016) presenting the outcome of seven patients undergoing RSD, which resulted in long-term BP reduction while on unchanged or decreased medication. The patients were on follow-up for at least 22 months. In this paper, the authors report data obtained during further clinical follow-up of these patients over a period of 24-72 months post-RSD.

Our follow-up group of seven patients included 5 men and 2 women, with a mean age of 64.9 years at the time of RSD. All had ambulatory BP monitoring by the same team as in previous years using the same technique as in the first two years. Table 1 presents more detailed patient characteristics. All other details can be found in our original article (Šochman *et al.* 2016).

Follow-up changes in systolic blood pressure and antihypertensive medication (number of drugs) are shown in Figures 1-2. As clearly seen in the graphs with new data starting one to two years post-RSD, BP levels remained decreased over the next two to four years in all seven patients receiving the same or only slightly changed antihypertensive medication. Importantly, no RSD-related complications were observed throughout the follow-up period.

Catheter-based RSD as a procedure employed for the treatment of pharmacologically uncontrollable hypertension has experienced a dramatic twist in recent years. After the publication of the SYMPLICITY HTN-1

and -2 results, the procedure enjoyed up to uncritical popularity performed as it was in large patient populations worldwide (Esler *et al.* 2010, Krum *et al.* 2009). However, when data of the SYMPLICITY HTN-3 project as a randomized sham-controlled trial became

available in 2014 (Bhatt *et al.* 2014), not confirming a statistically significant beneficial effect on BP reduction, RSD fell into disfavor within a short period of time.

**Table 1.** Characteristics of 7 patients with resistant hypertension undergoing RSD.

	Note
<i>Gender ♂/♀</i>	5/2
<i>Mean age (range 61-68 years)</i>	64.9
<i>Average BMI (kg/m<sup>2</sup>)</i>	$32.3 \pm 4.5$
<i>Medication:</i>	
<i>Beta-blocker</i>	7/7
<i>Angiotensin receptor blocker</i>	7/7
<i>Calcium-channel blocker</i>	6/7
<i>Alpha 1 adrenergic receptor blocker</i>	5/7
<i>α blocker + central 5-HXT receptor agonist</i>	4/7
<i>Diuretic</i>	7/7
<i>Mean creatinine (μmol/l)</i>	$86.7 \pm 15.9$
<i>Mean cholesterol (mmol/l)</i>	$5.25 \pm 0.7$
<i>Mean glycemia (mmol/l)</i>	$5.65 \pm 0.45$
<i>Mean COP (pmol/l)</i>	$7.26 \pm 3.55$
<i>Mean proADM (nmol/l)</i>	$0.67 \pm 0.15$
<i>Mean proANP (pmol/l)</i>	$118.59 \pm 55.14$
	No change in levels at follow-up visits
	No change in levels at follow-up visits
	No change in levels at follow-up visits

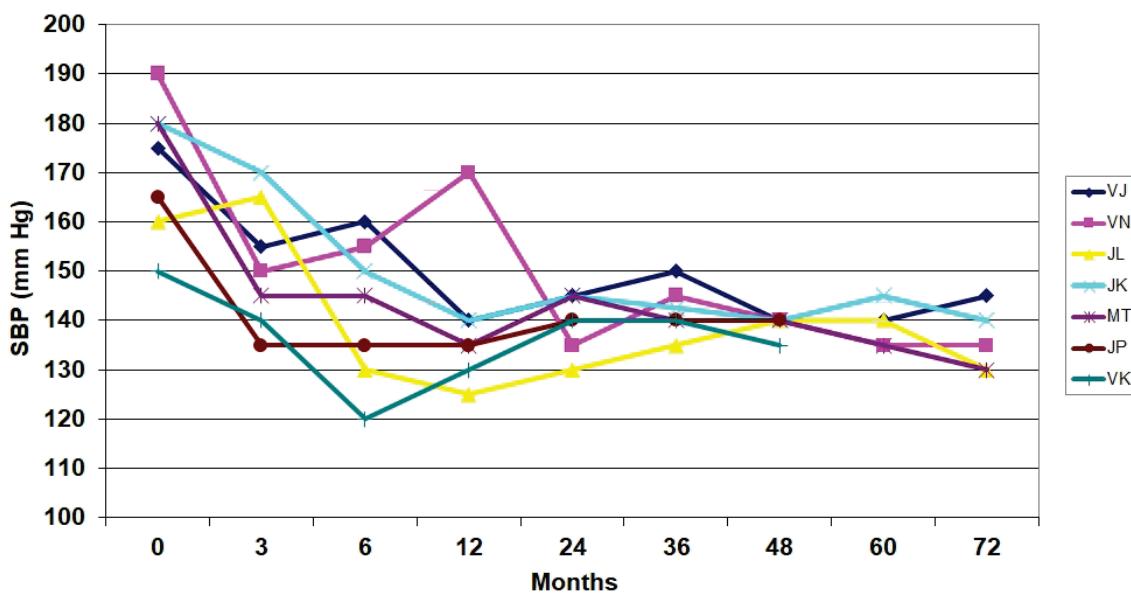
BMI – body mass index; 5-HXT – 5-hydroxytryptamine; COP – copeptin; proADM – proadrenomedullin; proANP – pronatriuretic peptide.

After some time, RSD was re-assessed in seven trials (two of which were sham-controlled ones) (Fadl Elmula *et al.* 2015). Results of these studies copying the SYMPLICITY trial design failed to demonstrate significant improvement in BP control compared with medical therapy. Still, significant improvement in BP control (i.e. an antihypertensive effect) has not been completely challenged in a small proportion of RSD patients; however, this subpopulation has not been clearly defined yet. Several recent studies have shown that RSD is successful in hypertension control in at least some patients; these studies include the French DENERHTN trial published in 2015 (Azizi *et al.* 2015) reporting a reduction in high BP levels post-RSD. A repeat analysis of SYMPLICITY HTN-3 data revealed that, in patients with isolated systolic hypertension, the effect of RSD is smaller to zero compared with individuals with systolic-diastolic hypertension (Mahfoud *et al.* 2016). At the same time, two studies, SPYRAL HTN-OFF MED (Townsend *et al.* 2017) and SPYRAL HTN-ON MED (Kandzarić

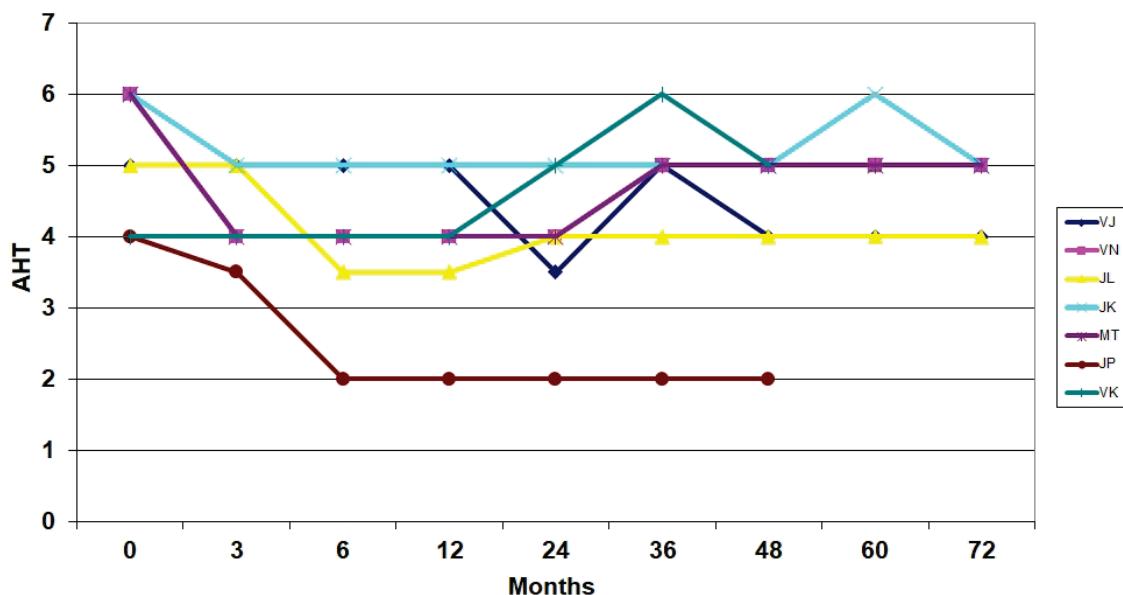
*et al.* 2018), showed BP reduction post-RSD including comparison with a sham-procedure. However, these two studies also used catheters (multi-electrode) other than the original (uni-electrode) Symplicity device.

All in all, RSD seems to be effective – at least in a proportion of hypertensive patients – in decreasing elevated BP levels; unfortunately, researchers have to date been unable to identify those responsive to the procedure.

The question is, whether RSD using the original Symplicity uni-electrode catheter was as complete as anticipated. In an animal study, the uni-electrode catheter was shown to be inferior to the multi-electrode one in destroying sympathetic nerves, although the latter may also fail to achieve complete denervation (Táborský *et al.* 2017, Táborský *et al.* 2018). Other animal studies using chemical agents to accomplish RSD did show a reduction of high BP levels (Consigny *et al.* 2014); however, respective human studies are lacking except for a pilot one with RSD using CT-guided ethanol injection (Ricke *et al.* 2016).



**Fig. 1.** Systolic blood pressure changes.



**Fig. 2.** Number of antihypertensive drug (AHT) changes.

Admittedly, our limited study including a mere seven patients is not as representative as the above multicenter studies. Still, we present data of seven treatment-resistant patients while on maximum medication who all experienced a BP reduction lasting 5 years and longer after RSD (with unchanged or even reduced medication). Over the past two years, we have performed another two RSD procedures using the multi-electrode catheter with both patients showing improved

control of hypertension previously resistant to medical therapy.

Given the above, we are confident that RSD still has a role to play in patients with failed antihypertensive medical therapy.

### Conflict of Interest

There is no conflict of interest.

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