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# Long-term benefit of renal denervation on blood pressure control in a patient with hemorrhagic stroke

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**Abstract**

A 49-year-old man with malignant hypertension had been admitted with hemorrhagic stroke. Refractory hypertension had been observed during hospitalization and the decision had been made to perform renal denervation. A significant blood pressure reduction was obtained immediately after renal denervation and persists at 2-year follow-up. This case demonstrates the long-term sustained efficacy of renal denervation performed in the acute phase of hemorrhagic stroke. In addition, it supports the notion that renal denervation–induced normalization of blood pressure may contribute to better outcomes in a challenging setting such as intracranial bleeding.

**Keywords**

Hypertension, renal denervation, renal artery disease, resistant hypertension, hemorrhagic stroke

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## Introduction

Arterial hypertension is the most important risk factor for ischemic and hemorrhagic stroke; in turn, an acute increase in blood pressure (BP) can be often observed in patients presenting with intracranial hemorrhage (ICH).[1] Indeed, a large proportion (>70%) of patients with acute ICH have a systolic blood pressure (SBP) above 140 mm Hg at the time of evaluation in the ED and up to 20% have SBP values above 180 mm Hg. Severe BP elevation in the presence of ICH represents a hypertensive emergency, frequently leading to worsening clinical conditions in the first hours after admission[2]; an aggressive early management is therefore required for these patients. Nonetheless, appropriate management of BP in acute ICH is still controversial, due to pathophysiological complexity and heterogeneous results obtained in clinical trials.

Bilateral renal denervation (RDN) is a promising option of anti-hypertensive therapy in some hypertensive patients, such as those with resistant hypertension.[3–6] Apart from the effects on BP, RDN is suggested to exert beneficial cardiovascular and cerebral effects.[7,8] We describe a case of sustained long-term reduction of BP in a patient having received RDN because of resistant hypertension leading to hemorrhagic stroke.

## Case report

Full details of the clinical case, the RDN procedure, and the acute effects have been described before elsewhere.[9] Briefly, we treated with RDN a 49-year-old man with malignant hypertension leading to acute renal failure and hemorrhagic stroke. Besides the neurologic consequences of the left thalamo-capsular hematoma, we had observed refractoriness to anti-hypertensive therapy consisting of six full-dose drugs including loop and thiazide-like diuretics (ramipril, bisoprolol, amlodipine, furosemide, metolazone, and urapidil). Interestingly, a significant and sustained reduction in both

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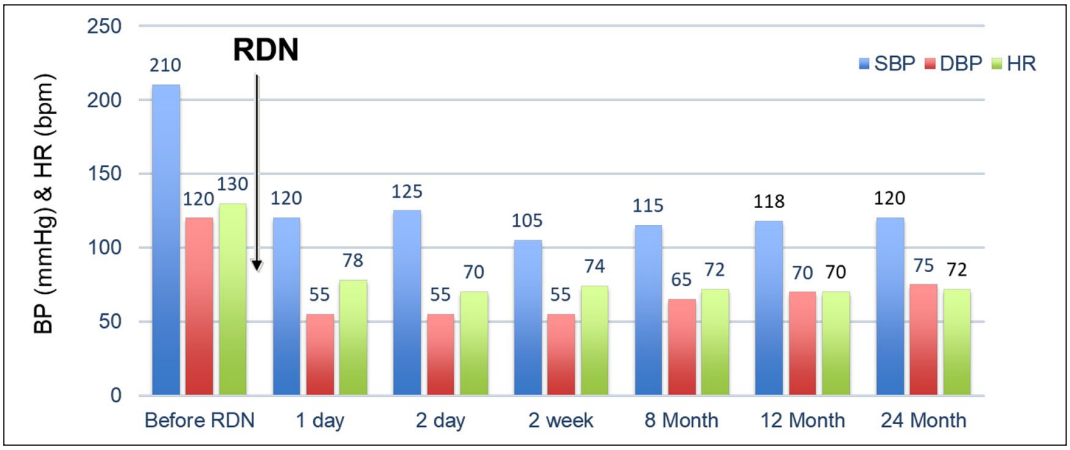


**Figure 1.** A significant and sustained BP and heart rate (HR) reduction was obtained immediately after the RDN procedure and persisted during the follow-up.

BP and heart rate (HR) was obtained immediately after the procedure at cath lab discharge and persisted during the follow-up (Figure 1). We now report on the long-term benefits of the procedure. At 2-year follow-up, after a proper rehabilitation program, the patient is in good health with only slight right-sided hyposthenia of the lower limb. BP is well controlled with an association of Angiotensin Receptor Blocker and Calcium Antagonist and only mild-to-moderate renal impairment persisted: creatinine is 1.5 mg/dL and estimated glomerular filtration rate (eGFR) is 53 mL/min/1.73 $m^2$.

## Discussion

We had reported this case, to the best of our knowledge, as the first case of RDN performed in the acute phase of hemorrhagic stroke because of resistant hypertension.[9] Soon after the procedure, we had obtained a significant BP reduction, much larger than in previous trials.[1,2] Specifically, BP reduction had been of the same magnitude than in cases where high sympathetic activity is likely, such as specific subgroups of Simplicity HTN-3[6] or in patients with subarachnoid hemorrhage.[10]

Resistant hypertension associated with ICH represents a medical emergency requiring an aggressive early management because of the risk of cardiovascular and general complications.[11,12] An admission systolic BP of more than 180 mm Hg is associated with hematoma expansion and a higher risk of death.[3,6–8,10] Despite the well-known relationship between elevated BP and worse outcomes in acute ICH, standard management of BP in ICH is often conservative[11] and consists only in cautious reduction in BP, due to concerns about the possible harm related to peri-hematoma ischemia. In fact, some data[13] suggest a "U" shaped relationship between BP and adverse outcomes, as for ischemic stroke, with an increase in mortality in patients with low BP at admission.

Current European Stroke Organisation (ESO) guidelines for the management of spontaneous ICH[14] recommend BP reduction to below 140 mm Hg in patients with acute ICH within 6 h of onset. In addition, the 2015 American Heart Association/American Stroke Association (AHA/ASA) Guidelines for the Management of Spontaneous ICH[15] underline that acute lowering of SBP to 140 mm Hg is safe and can be effective for improving functional outcome. The 2017 AHA High Blood Pressure Clinical Practice Guideline[16] recommend that in adults with ICH "who present with SBP greater than 220 mm Hg, it is reasonable to use continuous intravenous drug infusion and close BP monitoring to lower SBP," although they do not indicate a specific BP target for the initial hours of treatment. Furthermore, they recommend that

> immediate lowering of SBP to less than 140 mm Hg in adults with spontaneous ICH who present within 6 h of the acute event and have a SBP between 150 and 220 mm Hg is not of benefit to reduce death or severe disability and can be potentially harmful [basing this last recommendation on the results of Antihypertensive Treatment of Acute Cerebral Hemorrhage 2 (ATACH-2) trial[17]].

In an experimental model of hypertensive rats, Hasegawa and colleagues[18] demonstrated that RDN post-treatment in the acute phase of ischemic stroke can improve outcome as demonstrated by the amelioration of neurological deficit and cerebral infarction. Chronic hypertension causes cerebral vascular remodeling and dysfunction, leading to loss of the cerebral blood flow (CBF) auto-regulation system.[19,20] Under the lost CBF auto-regulation system, further increase of high BP in acute ischemic stroke can promote cerebrovascular over-perfusion and therefore exacerbate ischemic injury by aggravating cerebral edema.[19,20] This reversal of BP elevation by RDN was associated with a significant reduction of CBF in the reperfusion period.[18] As recently demonstrated, cerebral superoxide levels were significantly reduced by RDN post-treatment, and associated with the decrease in cerebral gp91phox, a major subunit of nicotinamide adenine dinucleotide phosphate oxidase.[18] Taken together, these findings support the notion that normalization of elevated BP

obtained with RDN contributes to better outcomes in acute ischemic stroke, by attenuating high BP–induced cerebrovascular over-perfusion and brain oxidative stress.

In conclusion, we had obtained the first clinical evidence, to our knowledge, that RDN can improve patients' outcome in the acute phase of hemorrhagic stroke associated with malignant hypertension. Follow-up demonstrates the long-term sustained efficacy of RDN and supports the notion that RDN-induced normalization of BP may contribute to better outcomes in a challenging setting such as intracranial bleeding. However, a larger amount of studied cases is necessary to confirm the efficacy of RDN in similar acute settings with critically ill patients.

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This work represents the follow-up of a previously published case report; therefore, some overlap in data reporting with the previous publication is possible; all authors have read and approved the final manuscript.

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The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

## Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

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## Informed consent

Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

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