evidence of the efficacy of bevacizumab in patients with HHT. Both cases also show that symptoms and transfusion requirements improve with this therapy, without an appreciable change in arteriovenous malformations. Like Oosting et al., we found no difference in the size of our patient's pulmonary arteriovenous malformations on CT before and after bevacizumab. Their experience demonstrates the long-term safety and tolerability of bevacizumab in such patients. Our patient continues to report symptomatic benefit more than a year after completing therapy, and he has required only one intravenous infusion of iron during this time. His hemoglobin levels have remained stable at 14 to 15 g per deciliter. The cost of our patient's regimen (a total of 30 mg per kilogram over four cycles) would be approximately $12,000 today. The costs of continuing the drug in the long term, especially without a Food and Drug Administration–approved indication, would be prohibitive. Our case shows that intermittent dosing allows for long-term, symptomatic improvement and stability of pulmonary arteriovenous malformations.

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Renal Sympathetic-Nerve Ablation for Uncontrolled Hypertension

TO THE EDITOR: The renal sympathetic nerves have been identified as a major contributor to the complex pathophysiology of hypertension in both experimental models and in humans.[1] Patients with essential hypertension generally have increased efferent sympathetic drive to the kidneys, as evidenced by elevated rates of renal norepinephrine spillover, defined as the amount of transmitter that escapes neuronal uptake and local metabolism and thus "spills over" into the circulation. Hypertension is also characterized by an increased rate of sympathetic-nerve firing, possibly modulated by afferent signaling from renal sensory nerves.[2-4]

A 59-year-old male patient with long-standing essential hypertension that was resistant to pharmacologic treatment with seven different antihypertensive drugs underwent catheter-based radiofrequency ablation to excise renal nerves that carry both efferent sympathetic and afferent sensory fibers. The patient had a history of two transient ischemic attacks and sleep apnea that was untreated because of an inability to tolerate therapy with continuous positive airway pressure. Secondary forms of hypertension and heart failure were excluded. The mean office blood pressure was 161/107 mm Hg, with a heart rate of 76 beats per minute at baseline.

Radiofrequency ablation was applied to both renal arteries without apparent procedural complications. There were no vascular or subsequent biochemical complications, and renal function was unaltered. Renal norepinephrine spillover, as assessed by the radiotracer dilution method[2,4] from both the left and right kidneys, was approximately three times the normal level at baseline (72 and 79 ng per minute, respectively). Bilateral renal-nerve ablation resulted in a marked reduction in renal norepinephrine spillover from both kidneys, with a reduction of 48% from the left kidney and 75% from the right kidney, which demonstrated the effectiveness of the intervention (Fig. 1A). This effect was accompanied by halving of renin activity (from 0.30 to 0.15 μg per liter per hour), an increase in renal plasma flow from 719 to 1126 ml per minute, and a progressive and sustained reduction in systemic blood pressure from 161/107 mm Hg at baseline to 141/90 mm Hg at 30 days to 127/81 mm Hg at 12 months. Whole-body norepinephrine spillover was reduced by 42% (Fig. 1B).

Microneurography at baseline and at 30 days and 12 months showed a gradual reduction in muscle sympathetic-nerve activity to normal levels (56, 41, and 19 bursts per minute, respectively) (Fig. 1C). We also observed an improvement in cardiac baroreflex sensitivity after renal denervation (from 7.8 to 11.7 msec per millimeter of mercury). Cardiovascular magnetic resonance

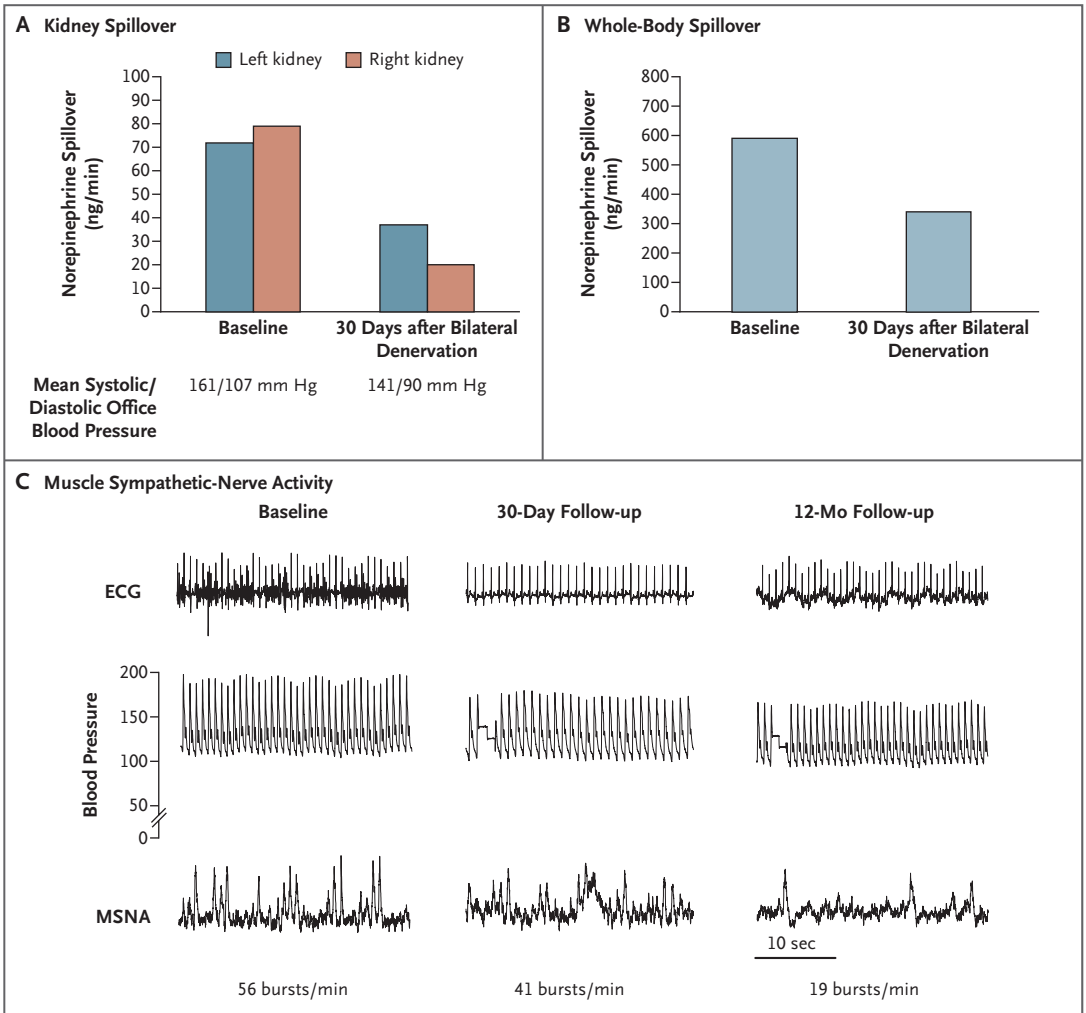

Figure 1. Norepinephrine Renal and Whole-Body Spillover and Results of Microneurography before and after Renal-Nerve Ablation.

Panel A shows the results of bilateral renal denervation, as assessed by the radiotracer dilution method, at baseline and 30 days after the procedure. After ablation, decreases in renal norepinephrine spillover were observed in both kidneys (48% in the left kidney and 75% in the right kidney), indicating substantial modulation of renal sympathetic efferent-nerve activity after the procedure. Simultaneously, a marked reduction in whole-body sympathetic-nerve activity was apparent, with a decrease in whole-body norepinephrine spillover of 42% (Panel B). Panel C shows a reduction in muscle sympathetic-nerve activity (MSNA), as assessed in the peroneal nerve on microneurography, after bilateral renal-nerve ablation, which highlights the possibility that inhibition of afferent renal-nerve activity may contribute to a reduction in central sympathetic drive.

imaging at baseline and at 12 months showed a reduction in the left ventricular mass from 184 to 169 g (78.8 to 73.1 g per square meter of body-surface area).

This procedure, which aimed to modulate renal sympathetic-nerve activity through catheter-based radiofrequency ablation, resulted in a 42% reduction in whole-body norepinephrine spillover and a substantial and sustained reduction in blood pressure, findings that were compatible with the results of a recent safety and proof-of-concept trial.[5] Furthermore, at 1-year follow-up, there was evidence of normalization of sympathetic-nerve firing rates, accompanied by a reduced left ventricular mass and a decreased requirement for antihypertensive medication. (Two antihypertensive drugs were withdrawn.) These findings suggest that continued research into

therapeutic renal-nerve ablation for the treatment of hypertension is of interest.

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Supported by Ardian and the National Health and Medical Research Council of Australia.

Dr. Schlaich reports receiving consulting fees from Ardian, lecture fees from Solvay, Servier, and AstraZeneca, and research support from Ardian; Dr. Sobotka, being an employee of Ardian and having an equity interest in the company and in CHF Solutions; Dr. Krum, receiving grant support from Ardian; and Dr. Esler, receiving consulting fees and research support from Ardian. No other potential conflict of interest relevant to this letter was reported.

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