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Renal Artery Stenosis After Renal Sympathetic Denervation

To the Editor: Renal sympathetic denervation (RDN) has been adopted in a number of countries as an additional treatment option to supplement antihypertensive therapy in patients with resistant hypertension. Concerns have been raised with regard to the possible occurrence of renal artery stenosis (RAS). In the following, we present a case of RAS as the consequence of RDN.

Baseline angiography demonstrated a right main and upper pole accessory renal artery (Fig. 1) and a single left renal artery without significant stenoses. Six ablations were performed in each main renal artery, and 2 ablations were performed in the smaller right upper pole accessory renal artery. There were no procedural complications. After 5 months, due to recurrent hypertension, renal angiography was performed demonstrating an 80% ostial and 70% mid-segment right main renal artery stenosis and a mid 50% stenosis in the right upper pole accessory renal artery (Fig. 1). There was no significant stenosis in the left renal artery. The 2 (ostial and mid) right main renal artery stenoses were successfully stented.

The merit of RDN to treat hypertension has been demonstrated in 2 trials using one type of radiofrequency catheter, the same used in the case described (1). The basis of this technology is an intended tissue injury caused by heat generated by radiofrequency energy. Injury is predominantly limited to the renal sympathetic nerve fibers that are more sensitive to heat than the remainder of the surrounding tissue. Nevertheless, unintended tissue injury to surrounding vascular structures causing edema and, perhaps, inflammation and fibrosis is conceivable. This might result in vessel stenosis. Therefore, it is not surprising that pulmonary vein stenoses have been described after pulmonary vein isolation with radiofrequency energy (2). Human data characterizing the early histological changes are not available, but radiofrequency application to pulmonary veins in an animal model causes endothelial denudation, organizing thrombus within a thickened intima, disruption and thickening of the internal elastic lamina, and necrotic myocytes (3). Importantly, the energy used to achieve pulmonary vein isolation is typically several magnitudes higher than that used for RDN. Moreover, despite the use of higher energy levels, pulmonary vein stenosis after pulmonary vein isolation is rare (<1.5%) (2). Similar to changes observed after pulmonary vein isolation, apart from the intended sympathetic nerve fibrosis, mild changes in other parts of the vessel wall after radiofrequency denervation of the renal sympathetic nerves were seen in all treated arteries of an animal model at 6-month follow-up, including fibrosis of the deep media and underlying adventitia as well as disruption of the external elastic lamina and intimal thickening (4). These changes were not accompanied by any significant angiographic changes. In all human studies thus far performed, focal luminal irregularities have been observed immediately after the procedure and were attributed to vasospasm and/or edema. In a combination of patients from the proof-of-principle Symplicity HTN-1 (Catheter-based Renal Sympathetic

Denervation for Resistant Hypertension) study and registry patients as well as patients from the Symplicity HTN-2 (Renal Sympathetic Denervation in Patients with Treatment-Resistant Hypertension) study, 202 underwent RDN. Twenty patients were studied with surveillance angiography at 14 to 30 days, and 124 patients with magnetic resonance angiography, computed tomography angiography, or duplex evaluation at 6-month follow-up without evidence of renal artery stenosis with the exception of 2 cases of a stenosis reportedly remote from the ablation site in a segment with pre-existent mild renal artery stenosis (5,6). Moreover, despite the widespread performance of this procedure, a RAS directly related to the procedure has not yet been reported. This might be due to the rare occurrence of this event or less-stringent follow-up outside of trials or registries and frequent absence of clinical symptoms related to it. A definitive statement cannot be made. However, the most likely etiology of the RAS in our patient was injury related to radiofrequency energy, perhaps the consequence of tissue fibrosis in a more extensive manner than previously described in animal models. Other possibilities include ablation catheter-induced mechanical injury and a de novo atherosclerotic lesion. However, both of these possibilities are less likely, given the absence of dissection by angiography immediately after ablation and mid location of one of the stenoses—a rather uncommon finding with atherosclerotic RAS, because they are located predominantly at the ostium. Renal sympathetic denervation remains a very promising tool for the treatment of resistant hypertension. The incidence of RAS seems to be low. Nevertheless, given the small number of individuals with surveillance imaging follow-up after RDN reported thus far and the frequently clinically silent nature of RAS, it is conceivable that we have not yet learned the true incidence and magnitude of this complication. Taking into account the large number of patients with resistant hypertension worldwide and, hence, expected number of patients referred for and treated with RDN, it is very important to continue close follow-up of patients treated with RDN. Therefore, participation in registries with reliable imaging follow-up allowing consistent reporting of this complication should be encouraged. Further, device technology minimizing either mechanical or heat-related vascular tissue injury needs to be explored, because—only if the complications remain at an absolute minimum—will this technology will prevail as an important adjunct to conventional antihypertensive therapy.

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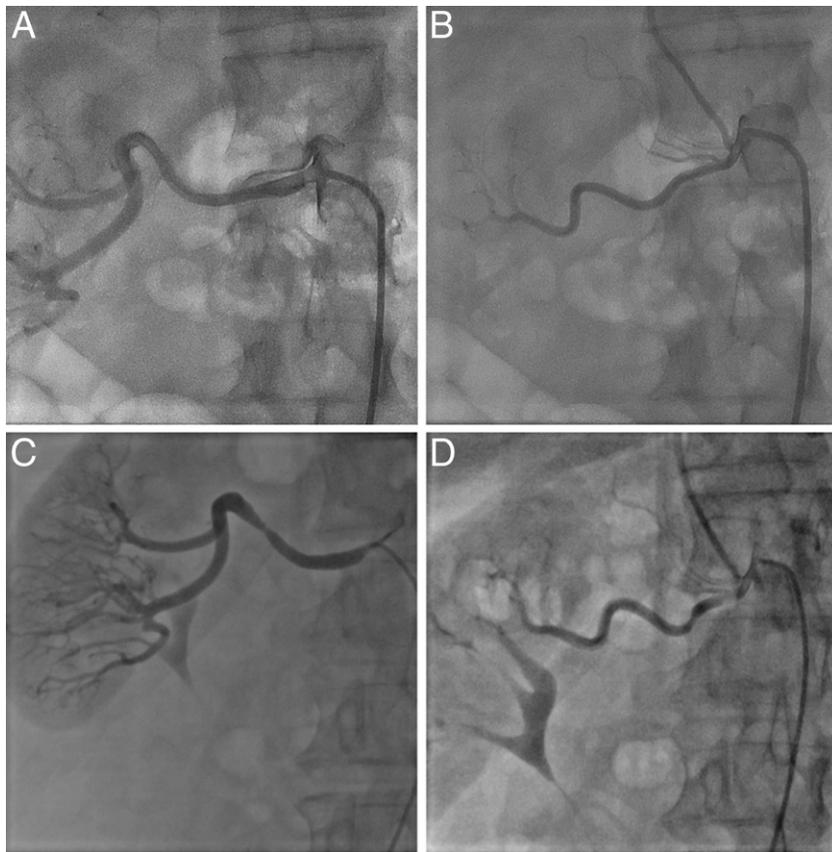


Figure 1 Angiographic Images

The right main renal artery and right upper pole accessory renal artery are illustrated at baseline (**A and B**, respectively) and once again 5 months after renal sympathetic denervation (**C and D**, respectively).

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