Safety and efficacy of renal denervation as a novel treatment of ventricular tachycardia storm in patients with cardiomyopathy

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BACKGROUND Modulation of the autonomic nervous system has been used to treat refractory ventricular tachycardia (VT). Renal artery denervation (RDN) is under investigation for the treatment of sympathetic-driven cardiovascular diseases.

OBJECTIVE The purpose of this study was to report the largest case series to date using RDN as adjunctive therapy for refractory VT in patients with underlying cardiomyopathy.

METHODS Four patients with cardiomyopathy (2 nonischemic, 2 ischemic) with recurrent VT despite maximized antiarrhythmic therapy and prior endocardial (n = 2) or endocardial/epicardial (n = 2) ablation underwent RDN ± repeat VT ablation. RDN was performed spirally along each main renal artery with either a nonirrigated (6 W at 50°C for 60 seconds) or an open irrigated ablation catheter (10–12 W for 30–60 seconds). Renal arteriography was performed before and after RDN.

RESULTS RDN was well tolerated acutely and demonstrated no clinically significant complications during follow-up of 8.8 ± 2.6 months (range 5.0–11.0 months). No hemodynamic deterioration or worsening of renal function was observed. The number of VT episodes was decreased from 11.0 ± 4.2 (5.0–14.0) during the month before ablation to 0.3 ± 0.1 (0.2–0.4) per month after ablation. All VT episodes occurred in the first 4 months after ablation (2.6 ± 1.5 months). The responses to RDN were similar for ischemic and nonischemic patients.

CONCLUSION This case series provides promising preliminary data on the safety and effectiveness of RDN as an adjunctive therapy in the treatment of patients with cardiomyopathy and VT resistant to standard interventions.

KEYWORDS Renal denervation; Ventricular tachycardia; Cardiomyopathy; Ventricular tachycardia storm

ABBREVIATIONS **AF** = atrial fibrillation; **ATP** = antitachycardia pacing; **BP** = blood pressure; **CL** = cycle length; **EGM** = electrogram; **FDA** = Food and Drug Administration; **HR** = heart rate; **ICD** = implantable cardioverter-defibrillator; **LAD** = left anterior descending; **LB** = left bundle; **LI** = left inferior; **LS** = left superior; **LV** = left ventricle; **LVAD** = left ventricular assist device; **LVEF** = left ventricular ejection fraction; **MRI** = magnetic resonance imaging; **PVI** = pulmonary vein isolation; **RB** = right bundle; **RDN** = renal artery denervation; **RF** = radiofrequency; **RS** = right superior; **RV** = right ventricle; **VT** = ventricular tachycardia

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Introduction

The demonstrated effectiveness of implantable cardioverter-defibrillators (ICDs) for primary and secondary preventions of sudden cardiac death has resulted in an increasing number of patients presenting with recurrent, appropriate ICD shocks for ventricular tachycardia (VT).[1–3] Because of the frequently insufficient success of pharmacologic therapy, catheter-based VT ablation is commonly used in these patients but is associated with limited long-term efficacy and significant complications.[4] The multicenter ThermoCool VT Ablation Trial reported recurrence of VT in 47% of patients at 6 months and a periprocedural complication rate of 7.3%. Therefore, adjunctive treatment approaches are desirable in this patient population.[5]

Given the established interaction of ventricular arrhythmias and the autonomic nervous system,[6] cardiac sympathetic

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denervation using left stellate gangliectomy has been tested successfully in patients with long QT syndrome,[7] catecholaminergic polymorphic VT,[8] and cardiomyopathy and refractory ventricular arrhythmias.[9]

Renal artery sympathetic denervation (RDN) recently has emerged as a less invasive means for modulating the autonomic nervous system. Endovascular catheter-based ablation of the renal arteries is emerging as a possibly more direct, organ-specific therapeutic strategy. Preclinical swine studies[10] and subsequent human studies[11,12] have demonstrated catheter-based RDN to be an effective treatment in patients with resistant hypertension, with an excellent safety profile. Consequently, catheter-based RDN is currently being evaluated as a potential adjunctive therapy in a spectrum of sympathetically modulated cardiovascular diseases, including impaired glucose metabolism,[13] left ventricular (LV) hypertrophy and diastolic dysfunction,[14] congestive heart failure,[15] obstructive sleep apnea,[16] and atrial fibrillation (AF).[17] Importantly, catheter-based RDN recently has been described as a possible treatment strategy in patients with chronic heart failure and recurrent ventricular arrhythmias.[18]

Here we report the largest case series to date of catheter-based RDN as an adjunctive therapy in patients with refractory VT in the setting of underlying cardiomyopathy.

Methods and Results

Four patients with cardiomyopathy (2 nonischemic, 2 ischemic) and VT refractory to therapy were recruited from 3 contributing centers. All patients had not responded to antiarrhythmic therapy and had undergone either endocardial catheter ablation (n = 2) or both endocardial/epicardial catheter ablation (n = 2). Given that no U.S. Food and Drug Administration (FDA) approval for RDN was available outside of clinical trials, detailed informed consent was obtained from all patients. In preparation for RDN, extensive discussions were conducted with all patients and/or the patients' family regarding compassionate off-label use of an FDA-approved product/institutional review board (IRB) consultation/emergency hospital credentialing and/or inclusion of operators with previous experience in RDN. RDN was performed with the patient under general anesthesia, with an end-point of delivery of circumferential lesions from first bifurcation to the os of the renal artery as determined by the operator.

Patient 1

The patient was a 68-year-old obese man with a history of hypertension and AF who presented after an episode of slow VT (left bundle [LB] pattern, left superior [LS] axis with a cycle length [CL] of 495 ms) during anesthesia induction for elective prostate surgery. Transthoracic echocardiography demonstrated mild global hypokinesis with a left ventricular ejection fraction (LVEF) of 45% to 50%. Cardiac catheterization revealed nonobstructive coronary artery disease. Cardiac magnetic resonance imaging (MRI) was significant for an inferobasal septal and focal inferior midseptal scar. Despite maximal medical therapy with amiodarone, lidocaine, procainamide, and esmolol, the patient continued to have frequent recurrences of clinical VT requiring multiple cardioversions for hemodynamic instability.

Two distinct VT morphologies were inducible during a first VT ablation, originating from either the inferior mid-right ventricular (RV) septum (LBLS axis, CL 457 ms, correlating with the clinical VT), or the distal RV apex (LBLS axis, CL 255 ms), correlating with scar seen on MRI. After endocardial ablation targeting best pace-mapping sites, VT was noninducible with up to 3 ventricular extrastimuli.

Two days postablation, 3 previously unobserved VTs occurred spontaneously despite medical therapy with procainamide and amiodarone (LBLS axis, CL 510 ms; LB VT with alternating left superior/inferior axis, CL 460 ms; LB, right superior [RS] axis, CL 290 ms; right bundle [RB] pattern, left inferior [LI] axis, CL 280 ms). Six days after the original procedure, repeat VT ablation only induced 3 previously unobserved VT morphologies (all LBLI axis, CL 330/325/280 ms) originating from midseptal MRI scar. Despite extensive LV and RV endocardial ablation of the septal substrate, VT remained inducible. Given the residual inducibility of VT, bilateral RDN was performed during the same procedure as previously discussed with the patient.

Bilateral renal arteriography was performed through an 8Fr sheath. A 7Fr, 4–mm nonirrigated ablation catheter (Blazer II, Boston Scientific, Natick, MA) was advanced into each renal artery, and delivery of radiofrequency (RF) energy was performed at sequential sites at 6 W and 50°C for 60 seconds. No acute or delayed hemodynamic sequelae were seen (pre-RDN blood pressure [BP] 102–106/52–54 mm Hg, heart rate [HR] 60–70 bpm; acute post-RDN BP 103–120/50–56 mm Hg, HR 60–70 bpm; 2–hour post-RDN BP 109–120/52–59 mm Hg, HR 60–70 bpm, 24–hour post-RDN 110/58 mm Hg, HR 92 bpm). Three days post-RDN, MR angiography of the renal arteries showed no vascular stenosis or dissection. Three days post-RDN, the patient developed slow VT at 110 bpm, which was treated with metoprolol. An ICD was placed for secondary prevention. Sixteen days post-RDN, the patient received antitachycardia pacing (ATP) for VT (CL 285 ms). Additional ATP was programmed, but given the prevalent pacing requirement, he was upgraded to a Bi-V ICD system using the new ICD settings. Medical therapy with beta-blockade and amiodarone was continued. After these cumulative interventions, the patient has received no other device therapies at 10 months post-RDN (Figure 1 and Table 1). Renal function has remained stable over 10–month follow-up (glomerular filtration rate >60, creatinine 0.8–1.0).

Patient 2

The patient was an 83-year-old man with a history of paroxysmal AF, nonischemic cardiomyopathy (LVEF 30%–35%), and previous ICD placement. Seven years