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## CLINICAL VIGNETTE

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# Renal Artery Denervation: A Safe and Effective Approach for Management of Refractory Ventricular Tachycardia Storm

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### *Case Presentation*

A 69-year-old male with cardiac sarcoidosis complicated by ventricular tachycardia (VT). Who presented with recurrent ICD shocks for 1 day. He had previously undergone endocardial ablation and stellate ganglionectomy as well as placement of an implanted cardiac defibrillator (ICD). Additional history included paroxysmal atrial fibrillation and prior pulmonary emboli. ICD interrogation revealed 4 episodes of monomorphic VT requiring shock delivery. Upon admission electrocardiogram (EKG) showed atrial pacing. Subsequently, the patient had multiple recurrent episodes of polymorphic VT at rate 175-180 with a right bundle branch pattern and inferior axis. The VT storm continued despite the initiation of amiodarone and lidocaine drips. Given frequent ICD shocks, the patient was intubated and sedated. He required vasopressors for maintaining blood pressure. Transthoracic echocardiogram showed an ejection fraction (EF) of 35%, reduced from 55% previously. The patient was extubated on day 3 of hospitalization, but he continued to have frequent runs of non-sustained VT and sustained VT despite continuation of Amiodarone, Esmolol, and Lidocaine drips. PET scan showed no active sarcoidosis, therefore corticosteroids were not initiated. The patient was not a candidate for epicardial ablation of ventricular tachycardia due to risk of damage to the Obtuse Marginal coronary artery given proximity to the VT focus. The patient underwent a successful renal artery denervation (RAD) through a right common femoral artery access using an 8-French SideArm sheath. The patient received transcatheter renal artery denervation at 6 separate sites within the right renal artery and 5 sites within the left renal artery for 60 seconds each at 10 watts. There were no complications associated with the procedure. Post-op, he had a significantly decreased VT burden with only short runs of non-sustained VT lasting less than 25 beats. On discharge his arrhythmia was controlled on oral Amiodarone, Mexiletine, and Metoprolol with no recurrence of sustained VT.

### *What is a VT Storm*

An electrical storm (ES) is a life-threatening state of electrical instability characterized by multiple episodes of ventricular tachycardia (VT) or ventricular fibrillation (VF) in a short period of time. In patients without implantable cardiac defibrillators (ICD), an ES is defined as 3 distinct episodes of sustained VT or VF within 24 hours or the occurrence of incessant VT for 12 hours. In patients with an ICD, an ES is defined by  $\geq 3$  appropriate

device interventions in the last 24 hours that are separated by at least 5 minutes.<sup>1</sup>

Effective management of VT storm in a timely manner is essential for reducing morbidity and preventing unnecessary shocks by ICD. In addition to the physical discomfort, ICD shocks have been associated with an increased mortality when adjusted for other prognostic factors.<sup>2</sup> Unfortunately, treating ES is often difficult as reversible causes account for less than 15% of cases. Heart failure and electrolyte imbalances are the most common culprits. However, in majority of cases no reversible cause for ES is identified.<sup>3</sup>

### *Risk Factors*

Myocardial infarction (MI) is a major risk factor for development of VT. Ischemic damage to the myocardium has been associated with a sequence of histological changes that involve denervation of the cardiac tissue followed by subsequent nerve regeneration. This process can lead to regional or global increase in sympathetic nerve density causing electrical instability and leading to ventricular tachyarrhythmias.<sup>4</sup> Other risk factors associated with ES are low EF and chronic renal failure. These processes can increase strain on the cardiac tissue through volume overload as well as electrolyte imbalances.<sup>5</sup>

### *Management of VT Storm*

**Beta Blockers:** Beta blockers have been associated with decreased occurrence of ventricular tachyarrhythmias, and are the mainstay of treatment for recurrent VT and VF episodes.<sup>6</sup> Ventricular remodeling in heart failure patients leads to down-regulation of  $\beta_1$ -receptors, which in turn leads to an increase in sympathetic activity.<sup>7</sup> Early initiation of beta blockers has been shown to reduce the occurrence of ventricular tachyarrhythmias in post MI patients by directly targeting the nerve fibers that innervate the myocardium.<sup>8,9</sup> In addition the lipophilic nature of some unselective  $\beta$ -blockers like propranolol, enables them to penetrate the central nervous system and block presynaptic adrenergic receptors.<sup>7</sup> In a non-randomized trial of patients with VF and symptomatic VT who were not treated with Amiodarone or ICD, beta-blocker use was associated with an independent mortality reduction.<sup>10</sup>

**Anti-Arrhythmics:** A variety of anti-arrhythmic medications have been used for treatment of electrical storms. Amiodarone, a class III anti-arrhythmic, is widely used for treatment of VT episodes. Amiodarone has been shown to control ventricular arrhythmias in up to 40% of patients within 24 hours of intravenous administration. Amiodarone can also reduce recurrent VT episodes in the follow-up period.<sup>7</sup> The combined use of both amiodarone plus  $\beta$ -blockers significantly reduces the risk of recurrent ICD-shocks compared to beta-blockers alone.<sup>11</sup> Although it has not been shown to improve mortality, Amiodarone has been shown to significantly reduce the risk of VT recurrence in patients with heart failure.<sup>12</sup>

Procainamide is a less commonly used, class IC, antiarrhythmic. The PROCMAIO trial recently demonstrated that Procainamide is associated with less major cardiac adverse events and higher proportion of tachycardia termination within 40 minutes of administration than Amiodarone in treatment of monomorphic VT.<sup>13</sup> The use of Procainamide is limited by the concerns for QRS prolongation.

Lidocaine and its oral form mexiletine, are class IB antiarrhythmic medications. They have anti arrhythmic effects by prolonging repolarization and QT interval.<sup>14</sup> The prolonged use of lidocaine is limited by the concerns for CNS and other systemic toxicity.

**Ablation of Arrhythmia Focus:** Cardiac catheter ablation of VT has been shown to be safe and effective in multiple randomized controlled trials. Most recently, the VANISH trial showed a reduction in the composite rate of cardiac death, VT storm, and appropriate ICD shocks when compared to escalation of medical therapy. A recent meta-analysis showed ablation using different methods results in elimination of all inducible Ventricular arrhythmias in 72% and clinically effectively suppression in 91% of patients. The procedure was associated with a complication rate of 2% with a procedure-related death rate of less than 1%. After 1.2 years, 94% of the patients were free from ES and 72% were free from any VT.<sup>15</sup>

**Stellate Gangliectomy:** Stellate gangliectomy involves the removal of the lower third of the stellate ganglion and T2-T4 thoracic ganglia. The procedure is usually performed through a video-assisted thorascopic approach.<sup>7</sup> In a recent series of 41 patients with refractory VT undergoing either left or bilateral stellate gangliectomy, a significant reduction of ICD-shocks during a mean follow-up of 12 months was observed in 90% of the patients. The study also showed a significantly higher ICD-shock free survival of 48% in the bilateral gangliectomy group compared to 30% in the isolated left-sided gangliectomy group.<sup>16</sup>

Stellate ganglion blockade by percutaneous injections of agents such as Bupivacaine or Ropivacaine is also effective in the setting of hemodynamic instability. This method has significantly reduced the number of episodes of VA and shocks from ICD. The suppression of arrhythmia by stellate ganglion blockade can last from hours to weeks.<sup>17</sup>

**General Anesthesia:** General anesthesia with mechanical ventilation is a particularly useful strategy for treatment of VT storms in hemodynamically unstable patients. However, in hemodynamically stable patients the risk of depressing the cardiac function may supersede the benefits. Benzodiazepines are usually the agent of choice for anesthesia due to minimal effects on cardiac activity. The addition of Remifentanyl, can decrease the benzodiazepine requirements.<sup>18</sup> The selection of other agents, such as Propofol and Dexmedetomidine should be carefully weighed against their risk of causing hypotension and bradycardia.

### **Renal Artery Denervation**

**History:** The effects of stimulating dorsal and splanchnic nerves on blood pressure were first demonstrated in 1889. However, the first surgical sympathectomy for treatment of malignant hypertension was performed several decades later in 1925. Unsatisfactory results with blood pressure control in unilateral renal artery denervation lead to the first bilateral sympathetic denervation of the kidney in 1934. Despite these efforts, RAD was not shown to have a permanent effect on blood pressure (BP) control in the early 20<sup>th</sup> century. The major breakthrough came with the removal of splanchnic nerves, which showed dramatic results in patients with malignant hypertension. This was the treatment of choice for malignant hypertension until the development of antihypertensive medications in 1950s.

Subsequently RAD fell out of favor as a means of controlling blood pressure. However, later studies continued to demonstrate the role of the sympathetic nervous system in release of dopamine in humans and animals.<sup>19</sup> This idea was further reinforced by animal studies showing protective effect of RAD on ventricular arrhythmias during ischemic events. These new findings led to the use of RAD as a treatment approach for ventricular arrhythmias.<sup>20</sup>

**Approach to Renal Artery Denervation:** There are a variety of instruments and techniques used for RAD. However, the main goal is to disrupt the conduction of the renal nerve fibers leading to release of catecholamines. Sympathetic fibers course in the adventitia of the renal arteries are mostly situated within 2 to 3 mm from the inner layer of the renal artery. Thermal energy is often used to place discrete lesions in a circumferential pattern. It is essential not to create a lesion at the same cross-section of the vessel in order to minimize the risk of renal artery stenosis.<sup>19</sup>

**Efficacy:** The efficacy of RAD relies on reducing the effects of stress hormones on the myocardium. Myocardial infarction leads to profound changes in the myocardium. Tissue hypoxia leads to generation of a denervated scar tissue with reduced contractility. Other observed effects include nerve sprouting along the border zones of infarcts, increase in B1 adrenergic receptors, and super-sensitivity of the myocardium to circulating stress hormones. The viable myocardium distal from the infarct also undergoes global changes. This heterogeneity in the

myocardium can lead to an increase in dispersion of repolarization as well as cardiomyopathy allowing for VT storms to persist.<sup>21</sup> By reducing the supersensitivity to catecholamines, RAD reduces the electrical heterogeneity that usually precedes VT storms.

Several small studies have shown the efficacy of RAD in preventing cardiac arrhythmias. An animal study subjecting 13 pigs to RAD vs. a SHAM procedure before undergoing LAD occlusion showed reduced occurrence of ventricular arrhythmias and atrial fibrillation in the treatment group. The treatment group was also noted to have a decreased elevation in left ventricular end-diastolic pressure. However no changes in infarct size, blood pressure, ventricular contractility, or reperfusion arrhythmias were observed compared to the control group.<sup>20</sup> A study of rats undergoing RAD before or after LAD occlusion showed the procedure can prevent and lessen the deterioration of LV function including reduction in EF and LV dilation.<sup>22</sup>

In humans, small case studies have shown a reduction in premature ventricular contractions and complex ventricular arrhythmias on holter monitor in patients undergoing RAD.<sup>23</sup> Pokushalov et al compared RAD vs. pulmonary vein isolation in 27 patients with refractory atrial fibrillation and drug resistant hypertension. The study showed a significant reduction in blood pressure and AF recurrence when RAD is combined with pulmonary vein isolation compared to pulmonary vein isolation alone.<sup>24</sup> In addition, RAD has been shown to significantly reduce heart rate, with more prominent effects in patients with HR greater than 71 compared to patients with a lower heart rate.<sup>25</sup>

**Safety and Risk:** Multiple small studies have been performed on the safety and efficacy of RAD for the treatment of arrhythmias. In the majority of these studies, the procedure was associated with a significant decrease in arrhythmias without major complications. Risks of RAD include femoral artery pseudoaneurysm and dissection, renal artery dissection, and post-procedure stenosis which can lead to renal failure. However, these events have been extremely rare in previous studies. In the simplicity HTN-3 trial, 1 out of 352 patients had vascular complication requiring intervention, and 1 patient had renal artery stenosis after ablation, which did not lead to permanent renal dysfunction.<sup>26</sup> Other theoretical concerns include worsening of hemodynamic instability during periods of ischemia due to the reduced effectiveness of catecholamines. However, RAD has not been associated with hemodynamic instability during episodes of ischemia in animal studies.<sup>20</sup>

### Conclusion

This case report adds to the existing evidence for the safety and efficacy of RAD for treatment of VT storms. The procedure is generally very safe, and previous small human and animal studies have shown significant positive short-term outcomes. More studies need to be performed to investigate the mechanism behind the efficacy of RAD—especially in situations

where stellate gangliectomy and other approaches to decreasing the sympathetic drive are not successful. Larger studies need to be done to determine the long-term outcomes of RAD on improving morbidity and quality of life with patients who are at risk for frequent VT storms.

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