



Neuraxial modulation for treatment of VT storm

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Abstract

In the hyperadrenergic state of VT storm where shocks are psychologically and physiologically traumatizing, suppression of sympathetic outflow from the organ level of the heart up to higher brain centers plays a significant role in reducing the propensity for VT recurrence. The autonomic nervous system continuously receives input from the heart (afferent signaling), integrates them, and sends efferent signals to modify or maintain cardiac function and arrhythmogenesis. Spinal anesthesia with thoracic epidural infusion of bupivacaine and surgical removal of the sympathetic chain including the stellate ganglion has been shown to decrease recurrences of VT. Excess sympathetic outflow with catecholamine release can be modified with catheter-based renal denervation. The insights provided from animal experiments and in patients that are refractory to conventional therapy have significantly improved our working understanding of the heart as an end organ in the autonomic nervous system.

Keywords: neuraxial, ventricular, tachycardia, denervation, autonomic

Introduction

Ventricular tachycardia (VT) storm, defined as > 3 episodes of VT within a 24 hour period, has high morbidity and mortality. VT storm is commonly managed with antiarrhythmic therapy, treatment of reversal causes (ischemia and electrolyte imbalance), and catheter ablation. Additionally, medical optimization of concomitant heart failure is necessary with pharmacologic and/or mechanical support, as refractory arrhythmias may be a symptom of decompensated pump function. In the hyperadrenergic state of VT storm where shocks are psychologically and physiologically traumatizing, suppression of sympathetic outflow from the organ level of the heart up to higher brain centers plays a significant role in reducing the propensity for VT recurrence. For this reason, sedation with general anesthesia is recommended not only for reducing pain and morbidity from

shocks, but also physiologically decreases excessive sympathetic tone.

The autonomic nervous system continuously receives input from the heart (afferent signaling), integrates them, and sends efferent signals to modify or maintain cardiac function and arrhythmogenesis^[1] (**Fig. 1**). In this review, we discuss the rationale and evidence behind neuraxial modulation for the treatment of VT with thoracic epidural anesthesia, sympathectomy, and renal denervation.

Thoracic epidural anesthesia

For patients presenting with VT or ventricular fibrillation storm, β -blockers and other antiarrhythmics not contraindicated are frequently used as primary therapy. Sympathetic tone can be further reduced by intubation and sedation and thoracic epidural anesthesia (TEA). The institution of TEA can be performed at the bedside

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Received 10 November 2014, Accept 18 December 2014, Epub 28 December 2014

The authors reported no conflict of interests.

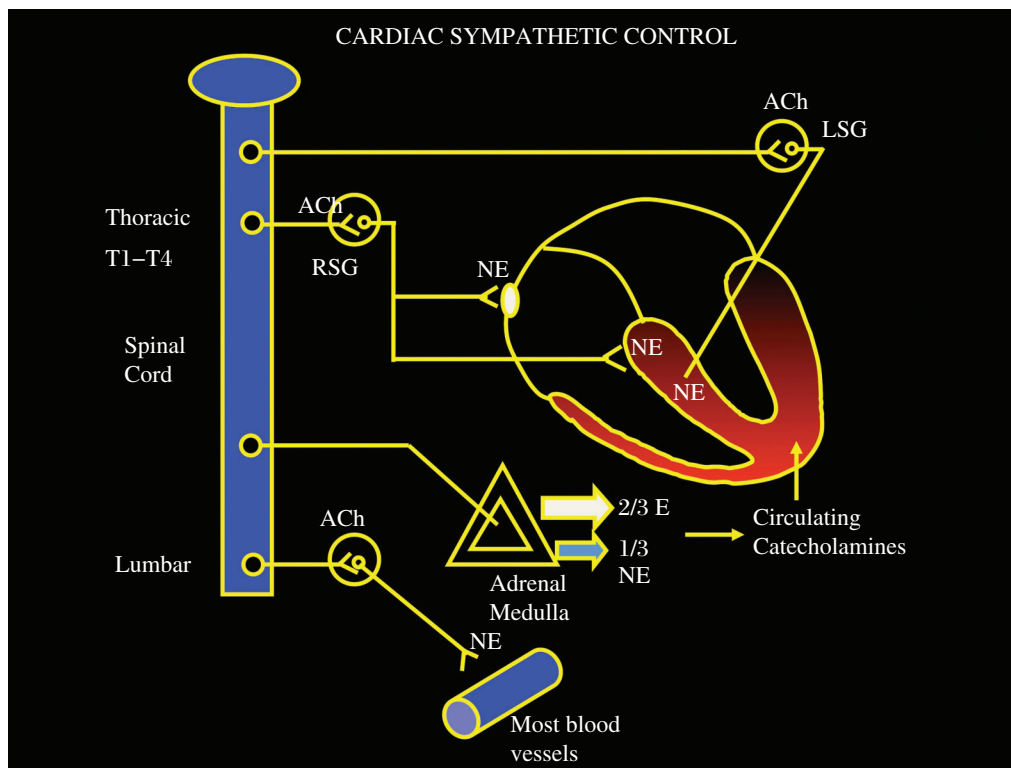


Fig. 1 Cardiac sympathetic regulation via the autonomic nervous system with the heart as an end organ under multiple levels of control. ACh: acetyl choline; LSG: left stellate ganglia; NE: norepinephrine; RSG: right stellate ganglia.

in standard fashion by anesthesiologists. In 2005, intrathecal clonidine was shown to reduce ischemia-induced ventricular arrhythmias in a canine model^[2].

In the same year, our group reported the successful management of electrical storm with use of TEA, using 1 mL bolus 0.25% bupivacaine followed by continuous infusion at 2 mL/hr at the T1-T2 interspace confirmed with fluoroscopy^[3] (**Fig. 2**). TEA is performed via a paramedian approach using a 17 gauge Tuohy epidural needle and a 19 gauge Flex-Tip plus epidural catheter (Arrow International Inc, Reading, PA, USA).

No adverse hemodynamic changes were noted and complete suppression of VT was observed prior to catheter ablation. In our initial series of 8 patients that underwent TEA, >80% burden in VT was observed in 6 patients^[4] (**Fig. 3**).

Sympathetic denervation and stellate ganglionectomy

Efferent sympathetic preganglionic neurons that regulate cardiac function reside within the intermediate

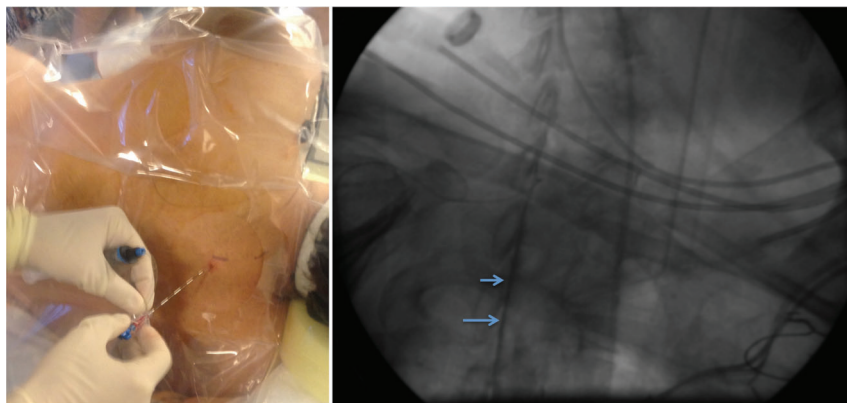


Fig. 2 Placement of thoracic epidural catheter for spinal anesthesia confirmed with contrast injection on fluoroscopy. Blue arrows indicate contrast in epidural space.

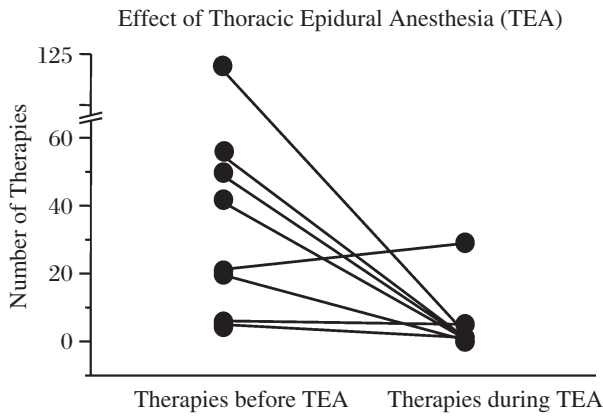


Fig. 3 Reduction in ventricular tachycardia (VT) burden pre and post thoracic epidural anesthesia (TEA).

zone of the thoracic spinal cord at the level of T1-T4. The sympathetic chain lies on either side of the vertebrae and consist of paravertebral ganglia and interconnecting nerves extending from the cervical to the lumbar levels^[5].

Within the sympathetic chain, preganglionic axons synapse on neurons within the stellate ganglion (fusion of inferior cervical and T1 ganglia) and ganglia at spinal levels T2–T4. The left and right stellate ganglia (LSG and RSG) are the predominant ganglia from which postganglionic fibers to the heart arise.

Sympathetic nerve fibers arrive at the base of the heart, and penetrate the myocardium giving off smaller branches that innervate the entire heart with intrinsic cardiac ganglia as they extend to the apex. Denervation with sympathectomy can be safely performed with

single-lung ventilation through a video assisted thoracoscopic approach (**Fig. 4**).

Left cardiac sympathetic denervation (LCSD) interrupts the major source of norepinephrine release in the heart. Schwartz et al. demonstrated that LCSD decreased the propensity for ventricular fibrillation in an animal model of left anterior descending occlusion^[6]. A significant reduction in the number of recurrent arrhythmias has been shown in a cohort of patients with long-QT syndrome and catecholaminergic polymorphic VT who received LCSD for secondary prevention^[7]. In our initial report, amongst 9 patients that underwent LCSD, 5 patients had either complete or partial response^[4].

More recently, our group has been investigating the physiologic and therapeutic differences between left and bilateral sympathectomy^[8]. Clinical reports of bilateral cardiac sympathetic denervation (BCSD) to treat severe ventricular arrhythmias date back to 1961, described by Estes and Izlar^[9]. In prior studies, stimulation or resection of the RSG accelerated or slowed arrhythmias originating from the right border of an anterior infarct^[10], and RSG resection in a canine model of ischemia and ventricular arrhythmias was as potent as LSG resection reducing the incidence of ventricular arrhythmias^[11].

In our early experience, three of the six patients had undergone previous LCSD but developed arrhythmia recurrence. RCSD after prior LCSD was effective in suppressing these arrhythmias. In a series of 6 patients, 4 patients had a complete response with BCSD and 1 patient had a partial response^[12].

With longer follow up, we found that patients that underwent BCSD had significantly improved freedom

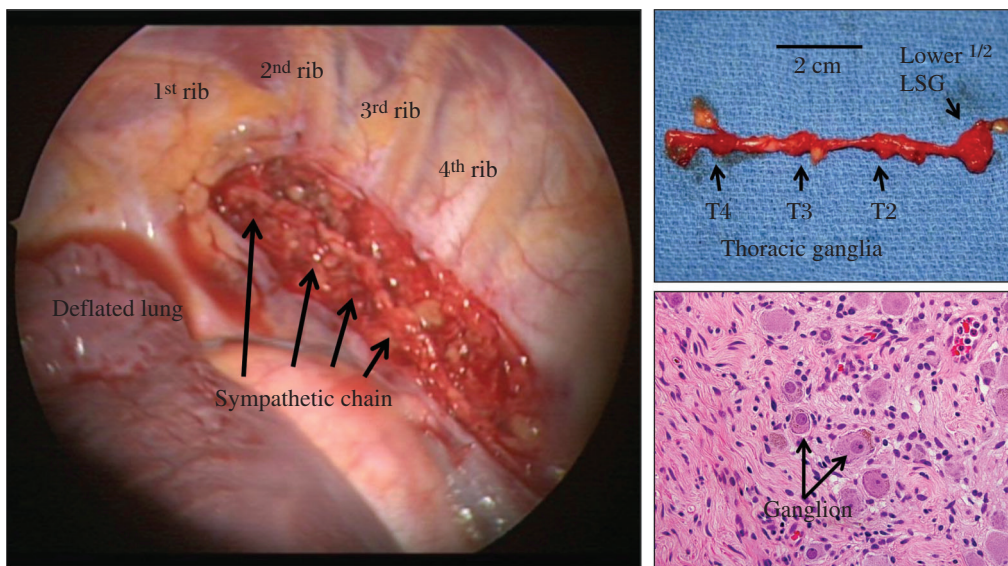


Fig. 4 Thoracoscopic view of sympathetic chain with stellate ganglion and T2-T4 thoracic ganglia. Histopathologic confirmation of neural tissue is performed postsurgically. Arrows in the right lower panel indicates ganglion. Arrow indicates ganglion cell.

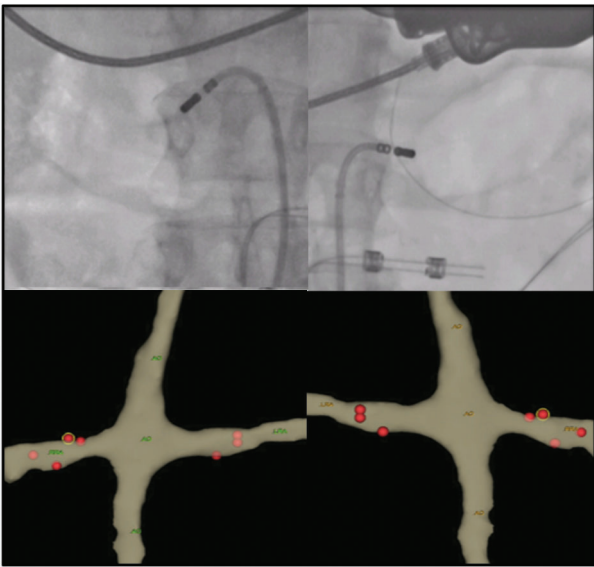


Fig. 5 Fluoroscopic views on bilateral renal denervation using an ablation catheter with lesions guided by electro-anatomic mapping.

from VT recurrence compared to those with unilateral denervation^[13]. Amongst 41 patients that underwent CSD (14 LCSD, 27 BCSD), the number of ICD shocks was reduced from a mean of 19.6 ± 19 preprocedure to 2.3 ± 2.9 postprocedure ($P < 0.001$), with 90% of patients experiencing a reduction in ICD shocks. At mean follow-up of 367 ± 251 days postprocedure, survival free of ICD shock was 30% in the LCSD group and 48% in the BCSD group. Shock-free survival was greater in the bilateral group than in the LCSD group ($P = 0.04$).

Renal denervation

Catheter-based renal denervation (RDN) is currently being studied as a treatment option for drug-refractory hypertension. Although the results from Symplicity-HTN3 trial did not meet the prespecified endpoint^[14], post hoc analysis demonstrated that patients with more extensive ablation, with higher BP preprocedurally, non-African American, and non-use of vasodilators may represent a subgroup more likely to derive clinical benefit^[15]. Ablation within the renal arteries, by altering efferent and afferent signaling, has the potential to improve blood pressure, as well as heart failure, atrial, and ventricular tachyarrhythmias. By decreasing norepinephrine spillover, the propensity for VT may be decreased.

Ablation is performed within the renal arteries from proximal to the first bifurcation in a spiral fashion sparing the ostium (**Fig. 5**). The renal nerves run on the adventitia in a complex interlaced network, necessitating transmural lesions, although the precise location

and number of ablation lesions required is currently not known. Contrary to electrophysiologic ablation, a standardized endpoint has not reached consensus for renal denervation, although blunting of a hypertensive response with high frequency stimulation has been used.

Multiple case reports have highlighted the potential role of renal denervation for the treatment of refractory VT^[16,17]. Ventricular fibrillation thresholds were decreased in an animal model when surgical renal denervation was performed^[18]. In a multi-center case series of 4 patients^[19], 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). 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.

Neuraxial modulation has emerged as a promising therapeutic strategy for patients with refractory ventricular arrhythmias. Arrhythmogenesis requires a substrate and a trigger and autonomics may largely account for the timing of clinical presentation. The uniting pathophysiologic basis for these interventions is suppression of excessive sympathetic activation. In current practice, TEA can be instituted by anesthesiologists and thoracic sympathectomy via a minimally-invasive thoracoscopic approach can be performed by thoracic surgeons. The role of renal denervation warrants further study but holds promise. The insights provided from animal experiments and in patients that are refractory to conventional therapy have significantly improved our working understanding of the heart as an end organ in the autonomic nervous system.

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