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Efficacy of Stellate Ganglion Blockade in Managing Electrical Storm

A Systematic Review

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ABSTRACT

OBJECTIVES The study sought to characterize the efficacy of stellate ganglion block (SGB) as a treatment for electrical storm (ES).

BACKGROUND The efficacy of percutaneous SGB for managing ES is not well understood.

METHODS The authors conducted published data searches using PubMed/Medline and Google Scholar for mixed combinations of terms including *stellate ganglion block*, **ganglion block(ade)*, *sympathetic block(ade)*, and *arrhythmia*, *ventricular arrhythmia* (VA), or *tachycardia*, *ventricular fibrillation*, *electrical storm*. Inclusion criteria were presentation with guideline-defined ES and treatment with SGB. Exclusion criteria were presentation with any supraventricular arrhythmia, VA without ES, or surgical sympathectomy. Studies lacking basic demographic data, arrhythmia description, and outcomes were excluded.

RESULTS Of 3,374 publications reviewed, 38 patients from 23 studies met study criteria (52.0 ± 19.1 years of age, 11 women, 17 with ischemic cardiomyopathy). Antiarrhythmics were used in all patients. Mean left ventricular ejection fraction was 31 ± 10%. ES was triggered by acute myocardial infarction in 15 patients and QT prolongation in 7 patients. The most common local anesthetic used for SGB was bupivacaine (0.25% to 0.50%). SGB resulted in a significant decrease in VA burden (12.40 ± 8.80 episodes/day vs. 1.04 ± 2.12 episodes/day; $p < 0.001$) and number of external and implantable cardioverter-defibrillator shocks (10.00 ± 9.10 shocks/day vs. 0.05 ± 0.22 shocks/day; $p < 0.01$). Following SGB, 80.6% of patients survived to discharge.

CONCLUSIONS SGB is an effective acute treatment for ES. However, larger prospective randomized studies are needed to better understand the role of SGB in ES and other VAs. (J Am Coll Cardiol EP 2017;3:942–9)

Electrical storm (ES) is commonly defined as the occurrence of 3 or more episodes of sustained ventricular arrhythmia (VA) over 24 h (1,2). Antiarrhythmic medications and catheter ablation remain the standard of care in patients with ES or other refractory VA (3). The role of the autonomic nervous system in ventricular arrhythmogenesis is well recognized (4), and neural modulation via a number of avenues is increasingly gaining traction (5). Cardiac sympathetic denervation (CSD), the surgical resection of the lower half of the stellate (cervicothoracic) ganglion and T2 to T4 sympathetic ganglia, has been shown to be effective in the setting of ES or other refractory VA (6–14). Other forms of neuromodulation include pharmacologic beta-adrenergic receptor blockade, thoracic epidural anesthesia, spinal cord stimulation, and stellate ganglion block (SGB) (5). SGB is performed by injecting local anesthetic agents

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percutaneously to the stellate ganglion, which is less invasive than CSD and can be performed at bedside in emergent setting in patients with hemodynamic instability Currently, besides case reports and small series, limited evidence is available regarding the role of SGB in ES (15-36). To better understand the role of SGB in ES (particularly to address patient characteristics, techniques, and overall efficacy of SGB), we performed dedicated published data searches and performed this systemic review.

METHODS

PUBLISHED DATA SEARCH, AND CRITERIA FOR INCLUSION OR EXCLUSION. Using PubMed/Medline and Google Scholar, we performed varying combinations of searches using the following terms: *left stellate ganglion block*, *ganglion block(ade)*, *sympathetic block(ade)*, *arrhythmia*, *ventricular arrhythmia*, *ventricular tachycardia*, *ventricular fibrillation*, *electrical storm*. ES was defined as 3 or more episodes of sustained ventricular tachycardia (VT) or ventricular fibrillation (VF) within a 24-h period (1). The search was limited to human subjects only. The search strategy was restricted by neither the language nor the date of publication. Inclusion criteria were patients presenting with ES who underwent SGB. Bilateral SGB was also included. Exclusion criteria included patients presenting with any supraventricular tachycardia, VA without ES (e.g., premature ventricular contractions), or patients treated only with surgical sympathectomy. The articles were carefully reviewed for inclusion and exclusion criteria. A lack of basic patient demographics, arrhythmia description, or outcomes, which are critical for this study, was also a reason for exclusion.

All clinical variables were extracted from the selected studies, including number of patients, age, sex, type of VA, episodes of VA and shocks before and immediately after SGB, presence of underlying cardiomyopathy (CMY), left ventricular ejection fraction (LVEF), trigger of ES, antiarrhythmic medications used, other procedures or treatment received before or after SGB, anesthetic administration techniques (i.e., laterality, bolus injection vs. continuous pump infusion, use of imaging guidance), type and volume of local anesthetic agent used, and inpatient survival to discharge. Relative reduction of VA and defibrillator shocks are calculated as the difference in episodes per day pre-SGB versus post-SGB, divided by the number of episodes per day pre-SGB.

STATISTICAL ANALYSIS. Continuous variables were summarized as mean ± SD. Comparison of VA episodes and number of external or implantable cardioverter-defibrillator shocks before and after SGB was performed using Wilcoxon signed rank test, given the non-normal distribution of the data. Change in VA burden or defibrillator shocks was expressed as relative reduction (i.e., post-SGB or pre-SGB). The relationship between arrhythmia reduction and LVEF was examined by linear regression. Comparison of CMY subtypes was performed using analysis of variance, and arrhythmia subtypes were compared using the Kruskal-Wallis test, as these data were non-normally distributed. A p value <0.05 was considered significant.

ABBREVIATIONS AND ACRONYMS

CMY = cardiomyopathy
CSD = cardiac sympathetic denervation
ES = electrical storm
LV = left ventricular
LVEF = left ventricular ejection fraction
SGB = stellate ganglion block
VA = ventricular arrhythmia
VF = ventricular fibrillation
VT = ventricular tachycardia

RESULTS

PATIENT CHARACTERISTICS. A total of 3,374 publications were reviewed and 38 patients from 23 studies published between 1976 and 2016 were included based on inclusion and exclusion criteria. The mean age of the patient population was 52 ± 19.1 years. Twenty-seven (71%) patients were men. CMY was present in 24 (63.2%) patients (ischemic CMY in 17 patients and nonischemic CMY in 7 patients) (Table 1). The mean LVEF was 31 ± 10%. Acute myocardial infarction was the most common trigger of ES (15 patients), followed by prolonged QT interval (7 patients). Interestingly, intracranial hemorrhage was the etiology in 2 patients. In 37% of patients, the

TABLE 1 Patient Characteristics

Age, yrs	52.0 ± 19.1
Male	27 (71)
Presence of cardiomyopathy	35 (92)
Ischemic CMY	17
Nonischemic CMY	7
Unspecified	11
Arrhythmia type	
Mixed VT/VF	15
PMVT	12
MMVT	4
VF	7
Left ventricular ejection fraction, %	31 ± 10
Acute trigger of ES	
Acute MI	15
Prolonged QT interval	7
Intracranial hemorrhage	2
Unspecified	14

Values are mean ± SD, n (%), or n.
CMY = cardiomyopathy; ES = electrical storm; MI = myocardial infarction; MMVT = monomorphic ventricular tachycardia; PMVT = polymorphic ventricular tachycardia; VF = ventricular fibrillation; VT = ventricular tachycardia.

TABLE 2 Medications Used Before Institution of Stellate Ganglion Block

Amiodarone	23 (82)
Beta-blocker	31 (82)
Metoprolol	7 (25)
Propranolol	6 (21)
Esmolol	4 (14)
Carvedilol	1 (4)
Unspecified	14 (50)
Lidocaine	19 (68)
Sotalol	1 (4)
Procainamide	8 (29)
Mexiletine	3 (11)
Quinidine	2 (7)
Ajmaline	1 (4)
Bretylium	1 (4)
Phenytoin	8 (29)
Digitalis	1 (4)
Isoproterenol	1 (4)
Verapamil	1 (4)

Values are n (%).

TABLE 3 Procedures/Interventions Performed Before Stellate Ganglion Block

Intubation and deep sedation	14 (36.8)
Cardiac catheter ablation	6 (15.8)
IABP	6 (15.8)
ECMO	3 (7.9)
TEA	2 (5.3)
Tandem heart	1 (2.6)

Values are n (%).
ECMO = extracorporeal membrane oxygenation; IABP = intra-aortic balloon pump; TEA = thoracic epidural anesthesia.

trigger of ES was unspecified. Of the arrhythmia types, mixed VT-VF was the most common type encountered (n = 15), followed by polymorphic VT (n = 12). Four patients had monomorphic VT and 7 patients had primary VF without VT (Table 1).

Almost all patients were treated with beta-blocker therapy (33 of 38). All patients except 1 received antiarrhythmic medications before SGB (Table 2) and the most common agents were amiodarone (82%) and lidocaine (68%). On average, 1.82 ± 0.82 antiarrhythmic drugs were used, along with beta-blockers or calcium-channel blockers, before SGB. Regarding other interventions before SGB, 36.8% patients were intubated and deeply sedated, whereas 15.8% patients were treated with catheter-based ablation (Table 3).

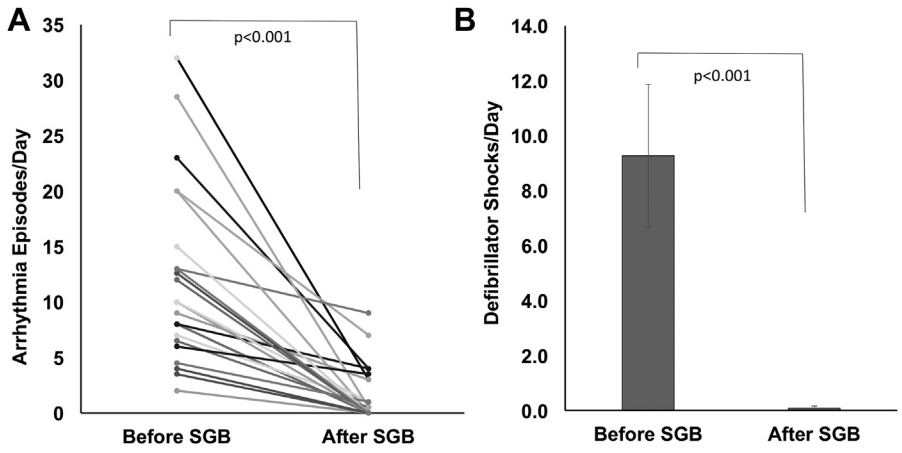
APPROACH TO SGB. SGB was achieved by administering local anesthetic percutaneously to the stellate ganglion. We examined the delivery method, the type and amount of local anesthetic, and the use of imaging guidance with SGB. Thirty-four patients received only left SGB whereas in 4 patients both left and right SGB were performed. As noted in Table 4, local anesthetic agents were administered as bolus injections in 28 (73.7%) patients, whereas continuous infusion with pump system was used in 9 patients (1 patient had both bolus and continuous infusion). Among patients receiving bolus injections, bupivacaine was the most commonly used anesthetic in patients with SGB (n = 16), while ropivacaine was the next most commonly used. The mean volume of bupivacaine used was 9.0 ± 5.6 ml with concentration ranging from 0.25% to 0.50%. We also examined the use of imaging when performing SGB. Ultrasound guidance was used in 21 patients and fluoroscopy was used in 4 patients (Table 4). In the remaining 13 patients, SGB was performed with anatomic landmarks only without imaging guidance.

EFFICACY OF SGB IN IMMEDIATE REDUCTION OF VA BURDEN AND SHOCKS. To determine the efficacy of SGB, we quantified ES burden as the episodes of VA per day and number of external or implantable cardioverter-defibrillator shocks per day. As shown in Figure 1, there was a significant reduction in both the number of episodes of VA and the number of shocks in patients with ES after SGB. SGB decreased VA burden from 12.40 ± 8.80 episodes/day to 1.04 ± 2.12 episodes/day ($p < 0.001$). The number of external or implantable cardioverter-defibrillator shocks was decreased from 10.00 ± 9.10/day to 0.05 ± 0.22/day

TABLE 4 Approaches to Anesthetic Use for Stellate Ganglion Block

Anesthetic Agent	n	Dose Concentration (%)	Volume (ml)
Bupivacaine	16	0.25–0.5	9.0 ± 5.6
Ropivacaine	11	0.2	6.0 ± 5.7
Lidocaine	9	1–4	8.0 ± 3.8
Mepivacaine	2	2	4.0 ± 0.0
Type of administration of anesthetics			
Bolus injections	28		
Continuous infusion	9		
Both bolus injections and continuous infusion	1		
Use of imaging guidance			
Landmark only without imaging	13		
Ultrasound	21		
Fluoroscopy	4		

FIGURE 1 Impact of SGB on Ventricular Arrhythmia Episodes and Defibrillator Shocks

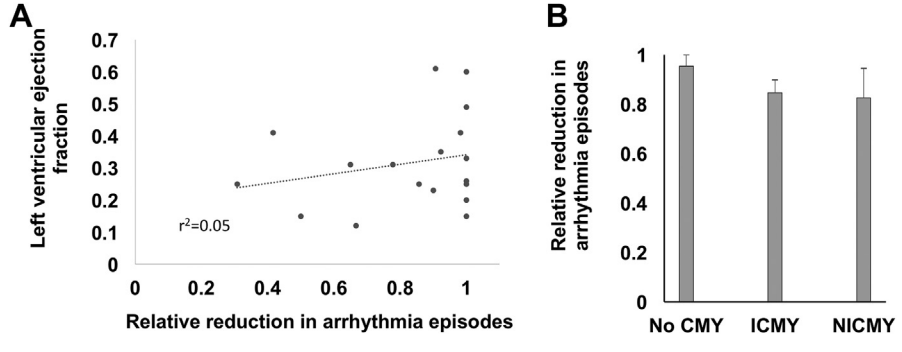


(A) Reduction in the number of ventricular arrhythmia episodes (n = 24) and **(B)** number of internal or external defibrillator shocks (n = 1) before and after stellate ganglion block (SGB) are shown.

($p < 0.01$). In this cohort, 24 of the 38 patients demonstrated complete arrhythmia suppression following SGB during the immediate follow up period, whereas the remaining 14 showed partial success. The impact of SGB did not depend on the subtype of VA causing ES. Relative reduction in VA episodes for the 4 subtypes studied, monomorphic VT, polymorphic VT, mixed VT-VF, and primary VF were 0.94 ± 0.10, 0.76 ± 0.25, 1.00 ± 0.00, and 0.97 ± 0.05, respectively ($p = 0.124$). The duration of clinical suppressive effect after bolus injection was 6 to 24 h for ropivacaine, 8 to 18 h for lidocaine, 6 h to 1 week for bupivacaine, and 11 h to 4 weeks for mepivacaine.

We examined whether the antiarrhythmic benefit of SGB was influenced by the presence and degree of left ventricular (LV) dysfunction. As shown in Figure 2A, there was no correlation between the LVEF and arrhythmia reduction ($r^2 = 0.05$, $p = 0.384$). Patients with normal LV function and mild, moderate, or severe LV dysfunction equally benefitted from SGB. Similarly, the presence and etiology of CMY did not influence the ability of SGB to exert

FIGURE 2 Relationship Between Arrhythmia Burden Reduction and Left Ventricular Dysfunction



(A) The relationship between left ventricular ejection fraction and the relative reduction in ventricular arrhythmia episodes (n = 18), $r^2 = 0.05$, p = 0.384). **(B)** Reduction in arrhythmia episodes was independent of the presence and etiology of cardiomyopathy (CMY) (n = 24, p = 0.78). ICMY = ischemic cardiomyopathy; NICMY = nonischemic cardiomyopathy.

TABLE 5 Comparison of Patients With Poor Response and Good Response to LSGB

	Poor Response	Good Response
Patients	3	35
Age, yrs	61 ± 9	51 ± 20
Male	3 (100)	24 (68.6)
Presence of cardiomyopathy	3 (100)	24 (68.6)
Ischemic CMY	2 (66.7)	15 (42.9)
Nonischemic CMY	1 (33.3)	6 (17.1)
Unspecified CMY	0	3 (8.6)
Arrhythmia type		
Mixed VT/VF	0	12 (34.3)
PMVT	3 (100)	12 (34.3)
MMVT	0	7 (20.0)
VF	0	4 (11.4)
Left ventricular ejection fraction, %	27 ± 13	32 ± 14
Acute trigger of ES		
Acute MI	2 (66.7)	14 (40)
Prolonged QT interval	1 (33.3)	7 (20)
Intracranial events	0	2 (5.7)
Unspecified	0	12 (34.3)
Type of local anesthetic		
Bupivacaine	2 (66.7)	14 (40.0)
Ropivacaine	1 (33.3)	10 (28.6)
Mepivacaine	0	9 (25.7)
Lidocaine	0	2 (5.7)
Method of administration		
Bolus injection	2 (66.7)	27 (77.1)
Continuous infusion	1 (33.3)	7 (20.0)
Both bolus and continuous infusion	0	1 (2.9)
Type of imaging guidance		
Ultrasound	3 (100)	18 (51.4)
Fluoroscopy	0	4 (11.4)
Inpatient survival		
Discharged	1 (33.3)	30 (85.7)
Deceased	2 (66.7)	5 (14.3)

Values are n, mean ± SD, or n (%).
Abbreviations as in Table 1.

antiarrhythmic benefits (Figure 2B). Relative reduction in VA burden was 0.95 ± 0.07, 0.85 ± 0.19, and 0.83 ± 0.29 for no CMY, ischemic CMY, and nonischemic CMY, respectively ($p = 0.78$). Using relative VA reduction <50% as a cutoff for poor response to SGB, 10% of patients were labeled as poor responders to SGB. The rest of the patients were considered to have good response. Characteristics of good and poor responders are summarized in Table 5. All poor responders were men and presented with polymorphic VT. Mean LVEF in this group was 27 ± 13%.

Following SGB, 80.6% of patients survived to discharge (hospital day 6 to 28), and terminal sympathectomy via surgical CSD was performed in 11 patients. One patient underwent orthotopic heart transplantation.

DISCUSSION

The major findings of the present study on the efficacy of SGB for ES are: 1) SGB is effective in reducing the number of episodes and therapies for VA; and 2) this efficacy was independent of the subtype of VA, the presence or absence of CMY, and the degree of LV dysfunction in the patients studied. To our knowledge, this is the first systemic review of the efficacy of SGB in patients with ES, and strongly supports the use of SGB in patients with ES.

There is a strong link between cardiac sympathetic activity and ventricular arrhythmogenesis (5,37). In a rabbit myocardial infarction model, left SGB prolonged the action potential duration (measured as 90% monophasic action potential duration) in all layers of the myocardial wall, reducing transmural repolarization heterogeneity, increasing the effective refractory period, and reducing VF threshold (38). SGB, by mitigating catecholamine release, likely reverses the findings in a canine post-infarct model of shortened effective refractory period in abnormal ventricular myocardium and increases inducibility of arrhythmias in the presence of catecholamines (39). SGB may also be particularly useful for attenuating burst discharge activity in left stellate ganglion, which has been shown to precede most VT and sudden cardiac death in a canine model of ischemic CMY (40,41). Sympathoexcitation increases repolarization heterogeneity (42–44), increases risk of delay after depolarizations (45,46), and increases arrhythmia inducibility (47). It also modulates peri-infarct tissues harboring circuits capable of facilitating monomorphic VT (48). The efficacy of beta-adrenergic receptor antagonism in patients with CMY (49) is related to minimizing the adverse effects of adrenergic activation signaling. However, despite use of beta-adrenergic receptor blockers, antiarrhythmic medications (some of which further antagonize beta-adrenergic receptors), and catheter ablation, some patients continue to have arrhythmias. In this study, we examine the efficacy of SGB in this population.

A number of mechanisms may explain the therapeutic benefits imparted by SGB. The bulk of efferent sympathetic outflow to the heart travels through the stellate ganglion. Pre-ganglionic fibers mediating neurotransmission to the heart synapse on post-ganglionic neurons within the stellate ganglion (and adjacent ganglia within the sympathetic chain) (Figure 3). In addition, post-ganglionic fibers from other ganglia may also travel through the stellate ganglion to middle cervical ganglia and cardiac nerves (50). This represents an effective site to target cardiac

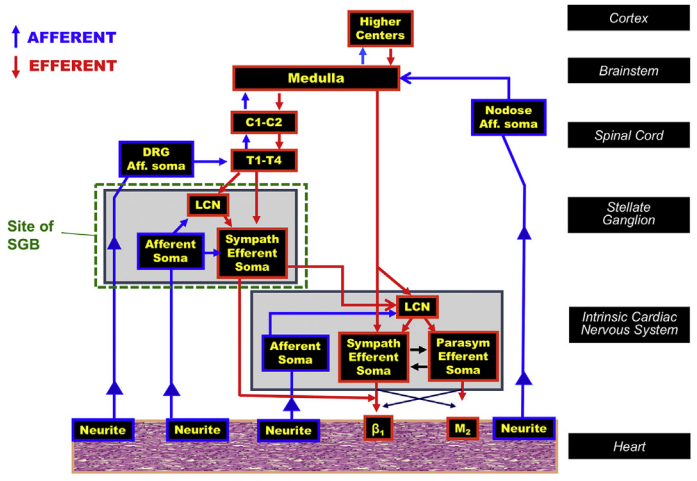
adrenergic activation while limiting systemic effects. Further, post-ganglionic axons release a variety of neurotransmitters, of which noradrenaline, targeted by beta-blockers, is only one. Additional neurotransmitters such as neuropeptide Y and galanin modulate adrenergic signaling at the myocardial level (51,52). However, in some cases, as evidenced by the patients examined in this study, beta-adrenergic blockade, antiarrhythmic drugs, and catheter ablation do not mitigate these other mechanisms. Interventions targeting the stellate ganglion, however, would attenuate not only noradrenaline signaling, but also these additional signaling pathways.

Sensory neurotransmission is also mitigated by SGB. Sympathoexcitatory reflexes are triggered by sensory afferent nerves that relay information intrinsic to the heart, mediastinum, stellate ganglion, spinal cord, and brainstem (5). At these centers, the sensory information is processed and reflex sympathetic activity is generated. The bulk of spinal sensory afferents, which have been implicated in the pathogenesis of heart failure (53,54), and along the same lines arrhythmogenesis pass through the stellate ganglion, en route to the dorsal horn of the spinal cord. Infusion of anesthetic agents to block the stellate ganglion also targets these fibers, and therefore attenuates both afferent and efferent neurotransmission at the stellate ganglion (**Figure 3**). Although SGB does not affect vagal afferents, the reduction of spinal afferents likely debulks overall cardiac afferent neurotransmission.

The burden of VAs and defibrillator shocks was significantly reduced after SGB in patients with ES. This occurred in patients independent of the etiology of the arrhythmia, triggering mechanisms, and LV function. VA suppression varied after bolus of injection of local anesthetics, ranging from hours to weeks. The longer duration of efficacy relative to the anesthetic half-life is most likely related to short- and long-term adaptations in neurotransmission and neural processing. Due to the highly plastic nature of neurons, a short-term intervention can produce long-lasting effects, well beyond what is expected for the drug alone. That said, there is likely to be some variation related to pharmacodynamics of the agents used, proximity of the injection of the ganglion, and thickness of the ganglion sheath.

We present the most commonly used approaches, anesthetic agents, and doses to achieve SGB. The patient characteristics and technical data generated by the present study may be helpful as a reference for the institution of SGB. These data may also be useful in the design and patient selection for randomized prospective studies to improve SGB techniques in clinical practice.

FIGURE 3 Schematic of Cardiac Innervation and Site of SGB



Stellate ganglion block (SGB) directly impacts both efferent and afferent neurotransmission to the heart. The site of action and components are shown. Aff = afferent; β = beta-adrenergic receptor; C = cervical; DRG = dorsal root ganglion; LCN = local circuit neuron; M = muscarinic receptor; Sympath = sympathetic; T = thoracic.

STUDY LIMITATIONS. This study has a number of limitations, which include the number of studies in the published data meeting inclusion or exclusion criteria. As these were predominantly case reports and case series, data reported here are retrospective. Further, the small sample size limits potentially instructive subgroup analyses, as well as the reliability of the analyses made. To improve the accuracy of the present study, reports in the published data lacking basic patient demographics were excluded, reducing the overall number of patients in the study.

CONCLUSIONS

The findings of the present study support the routine use of SGB as an effective adjunct to contemporary therapies in managing ES. SGB is efficacious for a variety of VA subtypes and patient demographics. Prospective randomized studies are needed to better understand the role of the SGB in ES and other VA.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE 1: The role of neuromodulation in managing ES is gaining traction.

COMPETENCY IN MEDICAL KNOWLEDGE 2: Anesthetic blockade of the stellate ganglion achieved percutaneously represents an attractive approach that can be implemented in a variety of settings, including at the patient's bedside.

TRANSLATIONAL OUTLOOK 1: The types of anesthetic agents, doses, and methods of dosing are important in applying SGB. Characteristics of patients, and the arrhythmias controlled by SGB would guide patient care. SGB is effective in controlling ES, and is not limited by the type of VA, or the presence or type of structural heart disease.

TRANSLATIONAL OUTLOOK 2: Additional research is needed to understand the safety and efficacy of SGB in prospective randomized trials to improve is use. It is important to discuss the available options with patients and the medical team.

REFERENCES

1. Aliot EM, Stevenson WG, Almendral-Garrote JM, et al. EHRA/HRS Expert Consensus on Catheter Ablation of Ventricular Arrhythmias: developed in a partnership with the European Heart Rhythm Association (EHRA), a Registered Branch of the European Society of Cardiology (ESC), and the Heart Rhythm Society (HRS); in collaboration with the American College of Cardiology (ACC) and the American Heart Association (AHA). Heart Rhythm 2009;6:886–933.

2. Gao D, Sapp JL. Electrical storm: definitions, clinical importance, and treatment. Curr Opin Cardiol 2013;28:72–9.

3. Zipes DP, Camm AJ, Borggrefe M, et al. ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death–executive summary: a report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death) Developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. J Am Coll Cardiol 2006;48:1064–108.

4. Shen MJ, Zipes DP. Role of the autonomic nervous system in modulating cardiac arrhythmias. Circ Res 2014;114:1004–21.

5. Shivkumar K, Ajijola OA, Anand I, et al. Clinical neurocardiology defining the value of neuroscience-based cardiovascular therapeutics. J Physiol 2016;594:3911–54.

6. Ajijola OA, Lellouche N, Bourke T, et al. Bilateral cardiac sympathetic denervation for the management of electrical storm. J Am Coll Cardiol 2012;59:91–2.

7. Ajijola OA, Vaseghi M, Mahajan A, Shivkumar K. Bilateral cardiac sympathetic denervation: why, who and when? Expert Rev Cardiovasc Ther 2012;10:947–9.

8. Vaseghi M, Gima J, Kanaan C, et al. Cardiac sympathetic denervation in patients with refractory ventricular arrhythmias or electrical storm: intermediate and long-term follow-up. Heart Rhythm 2014;11:360–6.

9. Collura CA, Johnson JN, Moir C, Ackerman MJ. Left cardiac sympathetic denervation for the treatment of long QT syndrome and catecholaminergic polymorphic ventricular tachycardia using video-assisted thoracic surgery. Heart Rhythm 2009;6:752–9.

10. Li J, Liu Y, Yang F, et al. Video-assisted thoracoscopic left cardiac sympathetic denervation: a reliable minimally invasive approach for congenital long-QT syndrome. Ann Thorac Surg 2008;6:1955–8.

11. Moss AJ, McDonald J. Unilateral cervicothoracic sympathetic ganglionectomy for the treatment of long QT interval syndrome. N Engl J Med 1971;16:903–4.

12. Nitter-Hauge S, Storstein O. Surgical treatment of recurrent ventricular tachycardia. Br Heart J 1973;11:1132–5.

13. Schwartz PJ, Priori SG, Cerrone M, et al. Left cardiac sympathetic denervation in the management of high-risk patients affected by the long-QT syndrome. Circulation 2004;15:1826–33.

14. Schwartz PJ, Zaza A, Locati E, Moss AJ. Stress and sudden death. The case of the long QT syndrome. Circulation 1991;83:II71–80.

15. Biagini A, Sabino F, Paladini G, et al. Treatment of perinfarction recurrent ventricular fibrillation by percutaneous pharmacological block of left stellate ganglion. Clin Cardiol 1985;8:111–3.

16. Boe BA, Webster G, Asher Y, Tsao S, Suresh S, Steinhorn DM. Percutaneous, ultrasound-guided stellate ganglion nerve block suppresses recurrent ventricular fibrillation in an infant awaiting heart transplant. Circ Arrhythm Electrophysiol 2012;5:e93–4.

17. Gadhinglajkar S, Sreedhar R, Unnikrishnan M, Namboodiri N. Electrical storm: role of stellate ganglion blockade and anesthetic implications of left cardiac sympathetic denervation. Indian J Anaesth 2013;57:397–400.

18. Garcia-Moran E, Sandin-Fuentes MG, Alvarez Lopez JC, Duro-Aguado I, Uruena-Martinez N, Hernandez-Luis C. Electrical storm secondary to acute myocardial infarction and heart failure treated with left stellate ganglion block. Rev Esp Cardiol 2013;66:595–7.

19. Garcia-Moran E, Sliwinski-Herrera F, Cortes-Villar C, Sandin-Fuentes M, Pastor Baez G, San Roman A. Refractory electrical storm: a role for transient sympathetic blockade. Rev Esp Cardiol 2016;69:76–8.

20. Grossman MA. Cardiac arrhythmias in acute central nervous system disease. Successful management with stellate ganglion block. Arch Intern Med 1976;136:203–7.

21. Hayase J, Patel J, Narayan SM, Krummen DE. Percutaneous stellate ganglion block suppressing VT and VF in a patient refractory to VT ablation. J Cardiovasc Electrophysiol 2013;24:926–8.

22. Hoepp HW, Eggeling T, Hombach V. Pharmacologic blockade of the left stellate ganglion using a drug-reservoir-pump system. Chest 1990;97:250–1.

23. Hulata DF, Le-Wendling L, Boezaart AP, Hurley RW. Stellate ganglion local anesthetic blockade and neurolysis for the treatment of refractory ventricular fibrillation. A A Case Rep 2015;4:49–51.

24. Loyalka P, Hariharan R, Gholkar G, et al. Left stellate ganglion block for continuous ventricular arrhythmias during percutaneous left ventricular assist device support. Tex Heart Inst J 2011;38:409–11.

25. Malik AA, Khan AA, Dingmann K, et al. Percutaneous inferior cervical sympathetic ganglion blockade for the treatment of ventricular tachycardia storm: case report and review of the literature. J Vasc Interv Neurol 2014;7:48–51.

26. Mesa A, Kaplan RF. Dysrhythmias controlled with stellate ganglion block in a child with diabetes and a variant of long QT syndrome. Reg Anesth 1993;18:60–2.

27. Nair L, Tseng PS, Manninen PH, Teo WS. Anaesthetic management of idiopathic long QT syndrome–a case report. Ann Acad Med Singapore 1994;23:582–5.

28. Nielsen H, Badskjaer J. [Blockade of the left stellate ganglion. Treatment of ventricular arrhythmias in secondary QT prolongation]. Ugeskr Laeger 1986;148:3221–3.

29. Parris WC, Reddy BC, White HW, McGrath DM. Stellate ganglion blocks in pediatric patients. Anesth Analg 1991;72:552–6.

30. Patel RA, Priore DL, Szeto WY, Slevin KA. Left stellate ganglion blockade for the management of drug-resistant electrical storm. Pain Med 2011;12:1196–8.

31. Platia EV, Griffith LS, Watkins L, Mirowski M, Mower MM, Reid PR. Management of the prolonged QT syndrome and recurrent ventricular fibrillation with an implantable automatic cardioverter-defibrillator. Clin Cardiol 1985;8:490–3.

32. Prabhu MA, Prasad SB, Abhilash SP, Thajudeen A, R BK, Namboodiri N. Left sympathetic cardiac denervation in managing electrical storm: acute outcome and long term follow up. J Interv Card Electrophysiol 2016;47:285–92.

33. Scanlon MM, Gillespie SM, Schaff HV, Cha YM, Wittwer ED. Urgent ultrasound-guided bilateral stellate ganglion blocks in a patient with medically refractory ventricular arrhythmias. Crit Care Med 2015;43:e316–8.

34. Smith DI, Jones C, Morris GK, Kralovic S, Massey HT, Sifain A. Trial ultrasound-guided continuous left stellate ganglion blockade before surgical gangliolysis in a patient with a left ventricular assist device and intractable ventricular tachycardia: a pain control application to a complex hemodynamic condition. ASAIO J 2015;61:104–6.

35. Tan AY, Abdi S, Buxton AE, Anter E. Percutaneous stellate ganglia block for acute control of refractory ventricular tachycardia. Heart Rhythm 2012;9:2063–7.

36. Fudim M, Boortz-Marx R, Patel CB, Sun AY, Piccini JP. Autonomic Modulation for the Treatment of Ventricular Arrhythmias: Therapeutic Use of Percutaneous Stellate Ganglion Blocks. J Cardiovasc Electrophysiol 2017;28:446–9.

37. Ardell JL, Andresen MC, Armour JA, et al. Translational neurocardiology: preclinical models and cardioneural integrative aspects. J Physiol 2016;594:3877–909.

38. Gu Y, Wang L, Wang X, Tang Y, Cao F, Fang Y. Assessment of ventricular electrophysiological characteristics at periinfarct zone of postmyocardial infarction in rabbits following stellate ganglion block. J Cardiovasc Electrophysiol 2012;23:529–35.

39. Zipes DP, Rubart M. Neural modulation of cardiac arrhythmias and sudden cardiac death. Heart Rhythm 2006;3:108–13.

40. Zhou S, Jung BC, Tan AY, et al. Spontaneous stellate ganglion nerve activity and ventricular arrhythmia in a canine model of sudden death. Heart Rhythm 2008;5:131–9.

41. Doytchinova A, Patel J, Zhou S, et al. Subcutaneous nerve activity and spontaneous ventricular arrhythmias in ambulatory dogs. Heart Rhythm 2015;12:612–20.

42. Ajijola OA, Yagishita D, Patel KJ, et al. Focal myocardial infarction induces global remodeling of cardiac sympathetic innervation: neural remodeling in a spatial context. Am J Physiol Heart Circ Physiol 2013;305:H1031–40.

43. Vaseghi M, Yamakawa K, Sinha A, et al. Modulation of regional dispersion of repolarization and T-peak to T-end interval by the right and left stellate ganglia. Am J Physiol Heart Circ Physiol 2013;305:H1020–30.

44. Yagishita D, Chui RW, Yamakawa K, et al. Sympathetic nerve stimulation, not circulating norepinephrine, modulates T-peak to T-end interval by increasing global dispersion of repolarization. Circ Arrhythm Electrophysiol 2015;8:174–85.

45. Priori SG, Corr PB. Mechanisms underlying early and delayed afterdepolarizations induced by catecholamines. Am J Physiol 1990;258:H1796–805.

46. Priori SG, Mantica M, Schwartz PJ. Delayed afterdepolarizations elicited in vivo by left stellate ganglion stimulation. Circulation 1988;78:178–85.

47. Irie T, Yamakawa K, Hamon D, Nakamura K, Shivkumar K, Vaseghi M. Cardiac sympathetic innervation via the middle cervical and stellate ganglia and anti-arrhythmic mechanism of bilateral stellectomy. Am J Physiol Heart Circ Physiol 2017;312:H392–405.

48. Ajijola OA, Lux RL, Khahera A, et al. Sympathetic modulation of electrical activation in normal and infarcted myocardium: implications for arrhythmogenesis. Am J Physiol Heart Circ Physiol 2017;312:H608–21.

49. Yancy CW, Jessup M, Bozkurt B, et al. 2016 ACC/AHA/HFSA Focused Update on New Pharmacological Therapy for Heart Failure: An Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. J Am Coll Cardiol 2016;68:1476–88.

50. Janes RD, Brandys JC, Hopkins DA, Johnstone DE, Murphy DA, Armour JA. Anatomy of human extrinsic cardiac nerves and ganglia. Am J Cardiol 1986;57:299–309.

51. Herring N, Cranley J, Lokale MN, et al. The cardiac sympathetic co-transmitter galanin reduces acetylcholine release and vagal bradycardia: implications for neural control of cardiac excitability. J Mol Cell Cardiol 2012;52:667–76.

52. Herring N, Lokale MN, Danson EJ, Heaton DA, Paterson DJ. Neuropeptide Y reduces acetylcholine release and vagal bradycardia via a Y2 receptor-mediated, protein kinase C-dependent pathway. J Mol Cell Cardiol 2008;44:477–85.

53. Zucker IH, Patel KP, Schultz HD. Neurohumoral stimulation. Heart Fail Clin 2012;8:87–99.

54. Wang HJ, Wang W, Cornish KG, Rozanski GJ, Zucker IH. Cardiac sympathetic afferent denervation attenuates cardiac remodeling and improves cardiovascular dysfunction in rats with heart failure. Hypertension 2014;64:745–55.

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