Letters

RESEARCH LETTER

Case Series of Transcutaneous Magnetic Stimulation for Ventricular Tachycardia Storm

Numerous studies suggest the therapeutic benefit of autonomic neuromodulation to reduce cardiac sympathetic input in patients with ventricular tachycardia storm.[1] Neuromodulation includes local blockade of the left stellate ganglion, a significant source of cardiac sympathetic innervation.[2] Transcutaneous magnetic stimulation (TCMS) has a role in noninvasive and nondestructive modulation of nervous system activity.[3,4] Animal studies have demonstrated the ability of magnetic stimulation to modify arrhythmias by targeting cardiac sympathetic innervation.[5,6] In this study, the first of its type involving human participants to our knowledge, we investigated the feasibility and adverse events of TCMS for left stellate ganglion inhibition in ventricular tachycardia storm.

Supplemental content

Methods | The institutional review board of the University of Pennsylvania approved this study, and all patients or their surrogate decision makers provided written informed consent prior to enrollment. Between March 2019 and June 2019, 5 consecutive adult patients with at least 3 episodes of sustained ventricular tachycardia (>30 seconds) in the preceding 24 hours were enrolled. Patients were excluded if they had an implantable cardiac device. A figure 8 TCMS coil attached to a magnetic stimulation system was positioned lateral to the C7 spinous process in approximation of the left stellate ganglion (eFigure in the Supplement). Repetitive TCMS was delivered at 80% of the left trapezius motor threshold at 0.9 Hz frequency for 60 minutes. We compared the number of ventricular tachycardia episodes in the 72 hours after TCMS with the baseline 24-hour period. Patients were monitored during and immediately following stimulation for adverse events including hemodynamic compromise, local discomfort, or skin irritation.

Results | All patients were men aged 40 to 68 years with 3 to 53 episodes of sustained ventricular tachycardia in the baseline 24 hours **(Table 1)**. The treatment protocol was completed without any clinically important change in vital signs or electrocardiogram intervals during or following the procedure **(Table 2)**. After 17 minutes, TCMS for patient 4 was automatically shut off due to coil overheating, which could not be resolved to complete the protocol. In the 3 patients who were not under sedation, each reported no discomfort (a 10-point scale, 0 [no pain] to 10 [worst possible pain]) from TCMS.

Compared with the baseline 24 hours, there was a lower burden of sustained ventricular tachycardia in the 48 hours following TCMS (99 vs 5 episodes). Over this period, the incidence of nonsustained ventricular tachycardia was also lower (150 vs 58 episodes). In aggregate, 41 external shocks were performed prior to treatment and none were required in the following 48 hours.

Prior to TCMS treatment, ventricular tachycardia had been refractory to a mean (SD) of 2.4 (2.1) antiarrhythmic drugs per patient. In the following 48 hours, patients received a mean of 1.2 (0.7) antiarrhythmic drugs and no additional antiarrhythmic drug was added. In the 72-hour follow-up period, only patient 4 underwent ablation 36 hours after enrollment.

Table 1. Characteristics of the 5 Patients at Time of Enrollment

	Polymorphic resulting in cardiac arrest			Monomorphic	
Qualifying arrhythmia	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
No. of episodes of sustained ventricular tachycardia 24 hours before TCMS	5	7	31	53	3
No. of episodes of sustained ventricular tachycardia 6 hours before TCMS	5	2	7	50	3
No. of episodes of nonsustained ventricular tachycardia 24 hours before TCMS	22	10	26	88	4
No. of external shocks 24 hours before TCMS	0	4	31	3	3
Antiarrhythmic drugs prior to TCMS	Amiodarone	Amiodarone, lidocaine, mexiletine	Amiodarone, general anesthesia	Amiodarone, lidocaine, verapamil	Amiodarone, lidocaine, general anesthesia
Hemodynamic support at the time of TCMS	None	Milrinone	Extracorporeal membrane oxygenation, phenylephrine	None	Epinephrine, norepinephrine
Left ventricular ejection fraction, %	35	25	5-10	5	10

Abbreviation: TCMS, transcutaneous magnetic stimulation.

Table 2. Adverse Events and Efficacy Outcomes After Transcutaneous Magnetic Stimulation of the Left Stellate Ganglion

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Hemodynamic changes before and immediately following treatment					
Pretreatment heart rate, bpm	103	98	76	55	128
Posttreatment heart rate, bpm	101	98	74	50	118
Pretreatment MAP, mm Hg	109	75	86	100	114
Posttreatment MAP, mm Hg	104	77	83	97	120
Electrocardiographic changes before and immediately following treatment					
Pretreatment PR interval, ms	Atrial fibrillation	162	138	208	Atrial fibrillation
Posttreatment PR interval, ms	Atrial fibrillation	130	140	210	Atrial fibrillation
Pretreatment QRS interval, ms	86	106	88	102	168
Posttreatment QRS interval, ms	88	108	80	100	160
Pretreatment QTc interval, ms	644	482	477	419	586
Posttreatment QTc interval, ms	656	492	489	411	533
Adverse events					
Self-reported pain[a]	0	0		0	
Local skin irritation	None	None	None	None	None
Arrhythmia burden after treatment					
Sustained VT episodes, h					
0-24	0	0	0	5	0
25-48	0	0	0	0	0
49-72	0	15	0	0	0
Nonsustained VT episodes, h					
0-24	4	0	0	37	0
25-48	6	0	0	9	2
49-72	0	56	28	0	0
External shocks, h					
0-24	0	0	0	0	0
25-48	0	0	0	0	0
49-72	0	4	0	0	0

Abbreviations: MAP, mean arterial pressure; VT, ventricular tachycardia.

[a] Self-reported pain was indicated on a 10-point scale (0, no pain to 10, worst possible pain) for the 3 patients who were not under sedation.

Discussion | In this case series involving 5 patients with ventricular tachycardia storm refractory to antiarrhythmic drug therapy, a lower burden of ventricular tachycardia was observed after noninvasive TCMS targeting the left stellate ganglion with no adverse events. The observed ventricular tachycardia reduction suggests that TCMS may serve as a bridge in this population, sparing patients from ventricular tachycardia, antiarrhythmic drug therapies, and associated risks until more definitive management. Limitations of the study include the small number of cases, the absence of controls, and the exclusion of implantable cardiac device recipients. Given the multifaceted treatment of ventricular tachycardia storm, which includes the potential for delayed effect of antiarrhythmic therapy, the ventricular tachycardia reduction cannot be completely attributed to TCMS. A randomized, sham-controlled trial to evaluate the safety and efficacy of TCMS in patients with ventricular tachycardia storm, including implantable cardiac defibrillator recipients, is under way (ClinicalTrials.gov identifier: NCT04043312).

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Concept and design: Markman, Hamilton, Marchlinski.
Acquisition, analysis, or interpretation of data: Markman, Nazarian.
Drafting of the manuscript: Markman.
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1. Al-Khatib SM, Stevenson WG, Ackerman MJ, et al. AHA/ACC/HRS guideline 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 on Clinical Practice Guidelines and the Heart Rhythm Society. *Heart Rhythm*. 2018;15(10):e190-e252. doi:10.1016/j.hrthm.2017.10.035

2. Tung R, Shivkumar K. Neuraxial modulation for treatment of VT storm. *J Biomed Res*. 2015;29(1):56-60.

3. Gaynes BN, Lloyd SW, Lux L, et al. Repetitive transcranial magnetic stimulation for treatment-resistant depression: a systematic review and meta-analysis. *J Clin Psychiatry*. 2014;75(5):477-489. doi:10.4088/JCP.13r08815

4. McClintock SM, Reti IM, Carpenter LL, et al; National Network of Depression Centers rTMS Task Group; American Psychiatric Association Council on Research Task Force on Novel Biomarkers and Treatments. Consensus recommendations for the clinical application of repetitive transcranial magnetic stimulation (rTMS) in the treatment of depression. *J Clin Psychiatry*. 2018;79(1):1-32. doi:10.4088/JCP.16cs10905

5. Wang S, Zhou X, Huang B, et al. Noninvasive low-frequency electromagnetic stimulation of the left stellate ganglion reduces myocardial infarction-induced ventricular arrhythmia. *Sci Rep*. 2016;6:30783. doi:10.1038/srep30783

6. Yu L, Dyer JW, Scherlag BJ, et al. The use of low-level electromagnetic fields to suppress atrial fibrillation. *Heart Rhythm*. 2015;12(4):809-817. doi:10.1016/j.hrthm.2014.12.022