Neuraxial Modulation for Refractory Ventricular Arrhythmias

Value of Thoracic Epidural Anesthesia and Surgical Left Cardiac Sympathetic Denervation

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Background—Reducing sympathetic output to the heart from the neuraxis can protect against ventricular arrhythmias. The purpose of this study was to assess the value of thoracic epidural anesthesia (TEA) and left cardiac sympathetic denervation (LCSD) in the management of ventricular arrhythmias in patients with structural heart disease.

Methods and Results—Clinical data of 14 patients (25 to 75 years old, mean ± SD of 54.2 ± 16.6 years; 13 men) who underwent TEA, LCSD, or both to control ventricular tachycardia (VT) refractory to medical therapy and catheter ablation were reviewed. Twelve patients were in VT storm, and 2 experienced recurrent VT despite maximal medical therapy and catheter ablation procedures. The total number of therapies per patient before either procedure ranged from 5 to 202 (median of 24; 25th and 75th percentile, 5 and 56). Eight patients underwent TEA, and 9 underwent LCSD (3 patients had both procedures). No major procedural complications occurred. After initiation of TEA, 6 patients had a large (≥80%) decrease in VT burden. After LCSD, 3 patients had no further VT, 2 had recurrent VT that either resolved within 24 hours or responded to catheter ablation, and 4 continued to have recurrent VT. Nine of 14 patients survived to hospital discharge (2 TEA alone, 3 TEA/LCSD combined, and 4 LCSD alone), 1 of the TEA alone patients underwent an urgent cardiac transplantation.

Conclusions—Initiation of TEA and LCSD in patients with refractory VT was associated with a subsequent decrease in arrhythmia burden in 6 (75%) of 8 patients (68% confidence interval 51% to 91%) and 5 (56%) of 9 patients (68% confidence interval 34% to 75%), respectively. These data suggest that TEA and LCSD may be effective additions to the management of refractory ventricular arrhythmias in structural heart disease when other treatment modalities have failed or may serve as a bridge to more definitive therapy. (Circulation. 2010;121:2255-2262.)

Key Words: tachycardia ■ nervous system, sympathetic ■ nervous system, autonomic ■ ventricles

The autonomic nervous system plays a critical role in the genesis and maintenance of ventricular arrhythmias. Protection from ventricular arrhythmias by use of pharmacological antiadrenergic interventions such as β-blockers is well established.

Clinical Perspective on p 2262

Selective modulation of neuraxial efferents to the heart with thoracic epidural anesthesia (TEA) is a therapeutic option for arrhythmia management in humans. TEA has been used successfully in the management of electrical storm in a patient with ischemic cardiomyopathy. The antiarrhythmic effects of TEA have been demonstrated in animal studies and its effects include lengthening of repolarization and prolongation of refractory periods. The protective effects of left cardiac sympathetic denervation (LCSD) have been demonstrated in patients with long-QT syndrome who continue to experience syncpe or cardiac arrest despite β-blockade and in small numbers of patients with catecholaminergic polymorphic ventricular tachycardia (VT). LCSD has been shown to lengthen ventricular refractoriness and raise the ventricular fibrillation threshold (by ~70%) without impairing cardiac contractility. Although it has been used primarily in the treatment of adrenergically driven arrhythmias in structurally normal hearts, LCSD has also been shown to contribute to a reduction in the incidence of sudden cardiac death among subgroups of post-myocardial infarction patients at high risk.

Ventricular arrhythmias that remain refractory to management present a major clinical challenge and are associated...
with a high mortality. The purpose of the present study was to review the effect of using 2 forms of neuraxial modulation (TEA and LCSD) in the management of malignant ventricular arrhythmias in the presence of structural heart disease (SHD).

Methods

Patient Population
We reviewed data from 14 patients from 3 medical centers between July 2005 and September 2009 who underwent neuraxial modulation with TEA or LCSD for the management of refractory ventricular arrhythmias. These patients were a subset of 154 patients who presented with “refractory” ventricular arrhythmias (over the 51-month period) to the centers involved in the present report. Stepwise arrhythmia management (with ablation in many cases) controlled arrhythmias for the vast majority; the patients who were selected for neuraxial modulation were refractory to all available treatments and were too unstable for any further treatment without arrhythmia control. We included 1 patient in the present series who was included in a previous report from our institution. Review of patient data was approved by the local institutional review boards of each of the medical centers.

Data Collection
The type, cause, and treatment of ventricular arrhythmias, neuraxial modulation used, immediate outcomes, procedural complications, and follow-up were noted in all patients. VT storm was defined as 3 or more sustained episodes of VT within a 24-hour period, each of which required termination by intervention. Incipient VT was defined as continuous sustained VT that recurred promptly despite repeated intervention for termination over several hours. When available, telemetry tracings and implantable cardioverter-defibrillator interrogation details were reviewed for each patient.

Arrhythmia Management
Ventricular arrhythmias were managed aggressively according to the standard clinical practice for management of ventricular arrhythmias at our centers. β-Blockers and antiarrhythmic drugs were given in sequence, devices were reprogrammed to minimize shocks, reversible causes (such as myocardial ischemia and electrolyte disturbances) were treated, deep sedation and intubation with induction of general anesthesia were considered, and catheter ablation was performed where feasible. When arrhythmias remained refractory despite these interventions, and when death was thought to be imminent, use of TEA or LCSD was considered to stabilize the patient before further interventions. The decision for TEA was individualized. If a surgeon who could perform emergent LCSD was not readily available or a patient was awaiting orthotopic heart transplant evaluation or catheter ablation, the patient underwent TEA. Otherwise, the patient underwent LCSD.

Procedural Details

Thoracic Epidural Anesthesia
Under an aseptic technique, with the patient in a left lateral decubitus position, a 17-gauge Tuohy needle (Baxter, Deerfield, Ill, and GPC Medical Ltd, New Delhi, India) was inserted via a paramedian approach into the T1–2 or T2–3 epidural interspace via a standard loss-of-resistance approach. A 19-gauge Flex-Tip Plus epidural catheter (Arrow International, Reading, Pa, and Chennai, India) was advanced 5 cm beyond the needle tip into the epidural space and was secured in a sterile manner. Lack of aspiration of blood and cerebrospinal fluid was determined to exclude intrathecal or intravascular catheter placement; the presence of paresthesia was confirmed, and 1 mL of 0.25% bupivacaine was injected, followed by an infusion at 2 mL/h, which was uptitrated according to the arrhythmic response.

LCSD: Operative Technique
A video-assisted thorascopic surgical approach was used. Under general anesthesia, with the use of a double-lumen endotracheal tube that allowed the ipsilateral lung to be deflated and nonventilated during the procedure, the pleural cavity was entered through three 1.5-cm incisions in the left subaxillary area. The left thoracic sympathetic chain was identified, and the lower half of the stellate ganglion, together with part or all of the T2–4 sympathetic chain, was dissected and resected. Histological confirmation was obtained intraoperatively (Figure 1). The chest drain was removed after confirmation of lung reexpansion.

Response to Neuraxial Modulation and Outcomes

Thoracic Epidural Anesthesia
With TEA, the antiarrhythmic effect is immediately evident; therefore, daily therapy rates before and during TEA were compared to determine the effects of the infusion on arrhythmia burden. An arrhythmia reduction of ≥80% was considered significant. Total therapies included successful antitachycardia pacing and cardioversion for patients with implantable cardioverter-defibrillators and represented the number of external cardioversions for patients without a device.

Left Cardiac Sympathetic Denervation
Response to LCSD was defined as follows: Complete response if no ventricular arrhythmias occurred within 1 week of the procedure, partial response if there was recurrence of ventricular arrhythmias that did not fulfill the definition of VT storm, and no response if VT storm or incessant VT occurred within the first week. Subsequent VT
Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, y/Sex</th>
<th>Cause of VT</th>
<th>Clinical Event</th>
<th>No. of VT Morphologies</th>
<th>Type of VT</th>
<th>EF, %</th>
<th>Medications</th>
<th>Prior VT Ablation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>75/M</td>
<td>Nonischemic CM</td>
<td>VT storm</td>
<td>6</td>
<td>MMVT, ×2 morphologies</td>
<td>20</td>
<td>Metoprolol, amiodarone, mexiletine</td>
<td>Endo</td>
</tr>
<tr>
<td>2</td>
<td>66/M</td>
<td>HOCM</td>
<td>VT storm</td>
<td>21</td>
<td>MMVT, ×3 morphologies</td>
<td>45</td>
<td>Carvedilol, amiodarone, mexiletine</td>
<td>Endo, 1 endo+epi</td>
</tr>
<tr>
<td>3</td>
<td>54/M</td>
<td>Nonischemic CM</td>
<td>VT storm</td>
<td>5</td>
<td>MMVT, ×3 morphologies</td>
<td>20</td>
<td>Carvedilol, amiodarone, digoxin</td>
<td>Endo</td>
</tr>
<tr>
<td>4</td>
<td>75/M</td>
<td>Ischemic CM</td>
<td>Incessant VT</td>
<td>124</td>
<td>PMVT</td>
<td>25</td>
<td>Atenolol</td>
<td>No</td>
</tr>
<tr>
<td>5</td>
<td>66/M</td>
<td>Ischemic CM</td>
<td>VT storm</td>
<td>42</td>
<td>MMVT, ×1 morphology</td>
<td>20</td>
<td>Amiodarone, flecainide, mexiletine</td>
<td>No</td>
</tr>
<tr>
<td>6</td>
<td>26/M</td>
<td>ARVD</td>
<td>VT storm</td>
<td>56</td>
<td>PMVT</td>
<td>45</td>
<td>Amiodarone, sotalol</td>
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</tr>
<tr>
<td>7</td>
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<td>Sarcoid CM</td>
<td>Incessant VT</td>
<td>202</td>
<td>MMVT, ×1 morphology</td>
<td>55</td>
<td>Metoprolol, flecainide, amiodarone, sotalol, quinidine</td>
<td>Endo</td>
</tr>
<tr>
<td>8</td>
<td>38/M</td>
<td>Sarcoid CM</td>
<td>VT storm</td>
<td>110</td>
<td>MMVT, ×3 morphologies</td>
<td>35</td>
<td>Carvedilol</td>
<td>Endo</td>
</tr>
<tr>
<td>9</td>
<td>48/F</td>
<td>Nonischemic CM</td>
<td>Refractory VT after 3rd VT RFA</td>
<td>5</td>
<td>MMVT, ×2 morphologies</td>
<td>30</td>
<td>Carvedilol, mexiletine, digoxin</td>
<td>Endo, 2 endo+epi</td>
</tr>
<tr>
<td>10</td>
<td>57/M</td>
<td>HCM</td>
<td>Incessant VT</td>
<td>24</td>
<td>PMVT</td>
<td>40</td>
<td>Metoprolol</td>
<td>No</td>
</tr>
<tr>
<td>11</td>
<td>69/M</td>
<td>Ischemic CM</td>
<td>Incessant VT</td>
<td>50</td>
<td>PMVT</td>
<td>25</td>
<td>Not on an antarrhythmic drug or β-blocker</td>
<td>No</td>
</tr>
<tr>
<td>12</td>
<td>50/M</td>
<td>Nonischemic CM</td>
<td>Refractory VT after 3rd VT RFA</td>
<td>5</td>
<td>MMVT, ×2 morphologies</td>
<td>40</td>
<td>Amiodarone, metoprolol</td>
<td>Endo, 1 endo+epi</td>
</tr>
<tr>
<td>13</td>
<td>66/M</td>
<td>Ischemic CM</td>
<td>VT storm</td>
<td>20</td>
<td>MMVT, ×4 morphologies</td>
<td>20</td>
<td>Amiodarone, mexiletine</td>
<td>No</td>
</tr>
<tr>
<td>14</td>
<td>44/M</td>
<td>HCM</td>
<td>VT storm</td>
<td>34</td>
<td>MMVT, ×1 morphology</td>
<td>27</td>
<td>Metoprolol, sotalol</td>
<td>Endo</td>
</tr>
</tbody>
</table>

EF indicates ejection fraction; M, male; F, female; CM, cardiomyopathy; MMVT, monomorphic VT; PMVT, polymorphic VT; Endo, endocardial; epi, epicardial; HOCM, hypertrophic obstructive cardiomyopathy; ARVD, arrhythmogenic right ventricular dysplasia; RFA, radiofrequency ablation; and HCM, hypertrophic cardiomyopathy.

Ablation procedures, cardiac transplantation, survival to discharge, and death were documented for all patients.

Follow-Up
Hospitalizations, outpatient visits, and implantable cardioverter-defibrillator interrogation records were used to determine patients’ outcomes after their discharge from hospital.

Statistical Analysis
Continuous variables are summarized with mean±SD or median and quartiles as appropriate. Exact 68% confidence intervals are provided for outcome percentages. Computations were performed with StatXact (Cytel Inc, Cambridge, Mass).

Results

Clinical Characteristics
Clinical parameters of the patients are shown in Table 1. The group consisted of 13 men and 1 woman, with an age range from 25 to 75 years (54.2±16.6 years). Twelve patients were in VT storm (4 were in incessant VT), and 2 experienced recurrent VT on maximal medical therapy despite having had 3 previous VT ablation procedures each. Four patients (29%) had polymorphic VT, and 10 patients (71%) had monomorphic VT. Among the 10 patients with monomorphic VT, 7 (70%) had more than 1 VT morphology; the mean±SD number of morphologies was 2.4±0.9. Nine (64%) of 14 patients had an ejection fraction ≤35%. One patient (patient 4) had active ischemia but had no targets for revascularization. The total number of therapies per patient before either procedure ranged from 5 to 202, with a median of 24 (25th and 75th percentile of 5 and 56). Twelve patients (86%) had an implantable cardioverter-defibrillator. Eleven patients (79%) had a history of VT, 8 (73%) of whom had previously undergone VT ablation.

Treatment of Ventricular Arrhythmias
Treatment of VT and immediate response to neuraxial modulation are summarized in Table 2. β-Blockers were used in 12 of 14 patients but were contraindicated in 2 patients owing to cardiogenic shock and a history of severe bronchospasm. Antiarrhythmic drugs were used in all patients. Three patients were intubated to facilitate arrhythmia management.

VT Catheter Ablation Procedures
Six patients underwent VT ablation before neuraxial modulation, whereas 4 patients were too unstable to undergo a procedure (Table 2). Multiple VT morphologies precluded ablation in 2 patients, and 1 patient had unmappable VT. An ablation procedure was contraindicated in 1 patient because of the presence of severe thrombocytopenia. No patient underwent intra-aortic balloon pump implantation or insertion of a ventricular assist device before neuraxial modulation.

Response to Neuraxial Modulation: Immediate Outcome

TEA Group
Eight patients underwent TEA; a reduction of ≥80% in arrhythmia burden was seen in 6 patients (Table 2; Figure 2). Infusion duration in these 6 patients ranged from 48 to 96 hours (63±19.3 hours). Patient 3 received 1 shock 17 hours after TEA was commenced; no further shocks occurred after uptitration of the bupivacaine infusion to 3 mL/h. After discontinuation of TEA owing to the development of sepsis, patient 2 received 2 shocks
within 24 hours; the patient was reloaded with intravenous amiodarone but continued to receive shocks despite the addition of lidocaine, and he underwent urgent cardiac transplantation.

Patient 4 received a shock within 10 minutes of epidural placement but had no further therapies for the duration of the infusion. Four patients received no shocks during TEA infusion; 1 of these patients received a shock within 4 hours of discontinuation of TEA and continued to receive 4 shocks per day until LCSD was performed 2 days later. A reduction of 17% in daily therapies was seen in 1 patient; catheter displacement occurred, and despite the catheter being repositioned and then replaced, uncertainty remained relative to the duration of medication delivery. An increase of 38% in the daily number of therapies was seen in 1 patient in whom a prior septal myectomy had failed to excise the arrhythmogenic focus. Three patients had LCSD performed after TEA.

**LCSD Group**

Nine patients underwent LCSD. Levels of denervation varied and were as follows: Lower half of left stellate ganglion to T4 (patients 9, 10, 12, and 14), lower half of left stellate ganglion to T2 (patients 6 and 8), and entire left stellate ganglion to T2 (patients 5, 7, and 13). Three patients had a complete response to LCSD, with no VT within 1 week of the procedure. Two patients had a partial response to LCSD, with recurrent VT within 1 week; the VT resolved within 24 hours in 1 patient and required VT ablation in the second. Four patients had no response to LCSD; VT storm persisted in 1 patient; 2 patients had a recurrence within 36 and 48 hours, respectively; and 1 patient with incessant VT unresponsive to drugs, pacing, or external defibrillation had resolution of arrhythmias for 72 hours, although VT storm recurred subsequently.

### Survival to Discharge

**TEA Group**

Five patients had TEA alone; of these, 1 survived to hospital discharge, 1 received an urgent heart transplant, and 3 died.
Table 3. Response to TEA and LCSD According to Type of Arrhythmia*

<table>
<thead>
<tr>
<th>Type</th>
<th>n</th>
<th>Result</th>
<th>Percent (68% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TEA</td>
<td></td>
<td>80% Reduction</td>
<td></td>
</tr>
<tr>
<td>MMVT</td>
<td>5</td>
<td>3</td>
<td>60</td>
</tr>
<tr>
<td>PMVT</td>
<td>3</td>
<td>3</td>
<td>100</td>
</tr>
<tr>
<td>Total</td>
<td>8</td>
<td>6</td>
<td>75 (51.9,11)</td>
</tr>
<tr>
<td>LCSD</td>
<td></td>
<td>Complete/partial</td>
<td>Response</td>
</tr>
<tr>
<td>MMVT</td>
<td>7</td>
<td>4</td>
<td>57</td>
</tr>
<tr>
<td>PMVT</td>
<td>2</td>
<td>1</td>
<td>50</td>
</tr>
<tr>
<td>Total</td>
<td>9</td>
<td>5</td>
<td>56 (34,75)</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; MMVT, monomorphic VT; and PMVT, polymorphic VT.

*Should be interpreted with caution because numbers are small.

(all had a protracted hospital course). The cause of death was pneumonia and asystolic cardiac arrest in patient 1; aspiration pneumonia, and cardiac and renal failure culminating in a pulseless electrical activity arrest in patient 4; and multiorgan failure in patient 11. The 3 patients who had TEA followed by LCSD all survived to hospital discharge.

**LCSD Group**

Of the 9 LCSD patients, 7 survived to hospital discharge. One patient (patient 10) died owing to a recurrence of VT storm 3 days after LCSD; a VT ablation procedure was not performed during this period because of the presence of pulmonary edema and biventricular thrombi. Patient 12 developed refractory VT storm 36 hours after LCSD that responded to intra-aortic balloon pump placement and repeat extensive epicardial ablation after thoracotomy; however, he later developed multiorgan failure, and support was withdrawn.

Response to Intervention (Summary)

Six of 8 patients who underwent TEA had a \( \geq 80\% \) reduction in arrhythmias; this included 3 of 3 patients with polymorphic VT and 3 of 5 with monomorphic VT (Table 3). The causes of the polymorphic VT were ischemic cardiomyopathy in 2 patients and arrhythmogenic right ventricular dysplasia in 1 patient. The causes of the monomorphic VT were ischemic cardiomyopathy in 2 patients and nonischemic cardiomyopathy in 1 patient. Of these 6 patients, 4 survived to discharge, 1 had TEA alone (and underwent urgent cardiac transplantation), and 3 had TEA followed by LCSD. One patient who did not respond to TEA survived to discharge.

Of the 9 patients who underwent LCSD, 5 had either a complete or partial response (Table 3). This included 1 patient with polymorphic VT due to arrhythmogenic right ventricular dysplasia and 4 patients with monomorphic VT due to ischemic cardiomyopathy, nonischemic cardiomyopathy, sarcoïd cardiomyopathy, and arrhythmogenic right ventricular dysplasia (1 patient each). All 5 patients survived to discharge, as did 2 patients in whom no response to LCSD was seen.

Follow-Up

**TEA Group**

Of the 8 patients in this group, 5 survived. Patient 3 was alive and well 37 months after cardiac transplantation. Patient 2 presented to the emergency department with multiple implantable cardioverter-defibrillator firings 8 days after discharge and underwent cardiac transplantation; he was alive and well 31 months postoperatively. Patients 5, 6, and 13 underwent LCSD after TEA, and their follow-up is documented below.

**LCSD Group**

Seven of the 9 LCSD patients survived to discharge, including all 5 patients with complete or partial response. Duration of follow-up ranged from 1.5 to 15 months (6.2 ± 4.6 months). Patient 6 had recurrence of VT storm after 1 month that was managed medically; he has been shock-free for 5 months since that time. Patient 7 had a recurrence of VT storm after 4 months that was treated with rescue ablation; he has been shock-free for 11 months. Patient 8 continued to have intermittent VT after LCSD and catheter ablation; he had another endocardial ablation followed by VT storm 2 months later, which was managed medically. Patient 9 was arrhythmia-free for 4 months before dying of decompensated heart failure. Three patients (5, 13, and 14) had been arrhythmia-free since discharge and had been followed up for 8, 2, and 1.5 months, respectively. All patients were maintained on antiarrhythmic therapy and \( \beta \)-blockade.

Complications

**TEA Group**

Patient 3 developed an elevated temperature and white cell count after 48 hours of TEA. The epidural catheter was removed because the source of infection was unclear; a respiratory cause was later identified. Cultures of the catheter tip were negative.

**LCSD Group**

Patient 7 developed Horner syndrome, which resolved after 6 months of follow-up. Patient 9 developed a small apical pneumothorax after LCSD; this was managed conservatively and resolved within 24 hours. This patient also developed anhydrosis of the left side of her face, which, in combination with a lack of postprocedure VT, served as objective evidence of effective denervation.

Discussion

Major Findings

These observational data suggest that the use of TEA and LCSD can be beneficial for the management of refractory ventricular arrhythmias in patients with SHD. Both procedures were well tolerated, which allowed stabilization of patients before a catheter ablation procedure was performed or acted as a bridge to definitive therapy.

Thoracic Epidural Anesthesia

TEA is a therapeutic option that selectively targets fibers that innervate the myocardium. Its immediate onset of action can interrupt the vicious circle of recurrent shocks that lead to elevation of catecholamine levels that in turn potentiate further arrhythmias, and it may avert the need for intubation. TEA tends to have minimal effects on hemodynamic parameters, including heart rate, mean arterial pressure, cardiac...
index, and central venous pressure. TEA was well tolerated in all the patients in the previous series.

TEA has the potential to provide complete sympathetic blockade, blocking segments C8-T4. Although spinal segments T1–4 give rise to the majority of cardiac accelerator fibers, C8 can form part of the inferior cardiac sympathetic nerve. Therefore, TEA, by inhibiting fibers that are proximal to both the left and right stellate ganglia, could be more effective than LCSD (which is a unilateral intervention). TEA can be instituted at the bedside without specialized equipment. TEA was used as a bridge to more definitive therapy in 5 of 8 patients in this series. Application of local anesthetic to the epidural space results in almost immediate selective sympatholysis, which may be of particular benefit in patients with SHD, in whom the presence of scar may impede effective delivery of β-blockade to the myocardial substrate. However, the dose of TEA is difficult to titrate, because there are no markers that are easy to use, other than an assessment of its efficacy in arrhythmia control.

**Left Cardiac Sympathetic Denervation**

After LCSD, a 90% reduction in cardiac events has been shown in high-risk patients with long-QT syndrome. A reduced number of cardiac events was also seen in a cohort of patients with long-QT syndrome and catecholaminergic polymorphic VT who received LCSD for secondary prevention. LCSD interrupts the major source of norepinephrine release in the heart. The antiarrhythmic effects of LCSD, although present to some extent immediately after denervation, become more complete with chronic denervation. This may be due in part to the massive neuraxial activation at the moment of surgical resection. By our definition of “no response,” we may have excluded some patients in whom transient benefit from LCSD was seen. LCSD involves a preganglionic denervation with removal of synapses, and therefore, neural regeneration does not occur. Furthermore, there is a partial reduction of the catecholamine content of the ventricle, which reduces postdenervation supersensitivity.

LCSD is a more definitive treatment than TEA and has lasting effects. There is objective evidence of denervation after resection of the sympathetic chain, with histological confirmation of the presence of sympathetic chain and ganglia. Surgical LCSD requires general anesthesia and intubation, which alone may help control arrhythmias temporarily; however, hemodynamic instability may preclude this in the clinical setting. The safety and feasibility of a video-assisted thoracoscopic surgical LCSD has been reported previously in several small series. More than half of the LCSD patients in the present series experienced benefit from the procedure; even in the no-response LCSD group, all but 1 patient had temporary arrhythmia resolution, which provided an opportunity to implement other therapeutic options. One patient in whom catheter ablation and TEA were contraindicated because of the presence of severe thrombocytopenia had complete resolution of ventricular arrhythmias after LCSD. Emergent LCSD may not be available in many centers; however, where available, it may be used to stabilize patients, to act as a bridge to ablation or surgical intervention, or potentially to reduce shock frequency when all other therapeutic options have been exhausted. Temporary LCSD block can also be used in this setting; however, repeated dosing and inability to use concurrent anticoagulation are limitations in the clinical setting.

**Potential Mechanisms of Failure**

In SHD, external triggers (including ischemia, reperfusion, autonomic state, and electrolyte disturbance) interact with a fixed substrate (such as prior myocardial infarct in ischemic heart disease or less discrete scarring or myocardial disarray in other forms of SHD) to precipitate and perpetuate an arrhythmia. Sympathetic hyperactivity is an important modulator of ventricular arrhythmias, including electrical storm. The influence and relevance of sympathetic hyperactivity in each patient are variable and are dependent on the type, cause, and mechanism of the underlying arrhythmia and on the clinical scenario. In the present series, despite disparate causes, 80% of polymorphic VT and 58% of monomorphic VT cases responded to neuraxial modulation.

There are several potential reasons for failure of TEA and LCSD in arrhythmia control: (1) A sympathetic trigger may not be responsible for initiation or perpetuation of the arrhythmia, and therefore, its elimination may not affect arrhythmia burden. (2) Sympathetic blockade secondary to TEA may be incomplete. The addition of autonomic nervous system blockade by simultaneous administration of propranolol, atropine, and hexamethonium during TEA has been shown to augment the effects of TEA on repolarization and effective refractory period in an animal model. (3) Denervation secondary to LCSD may also be incomplete; resection of the lower half of the left stellate ganglion to T4 has been suggested, but this level of denervation was not performed in 5 of the patients in the present cohort. (4) The nerve of Kuntz (an inconstant intrathoracic nerve that connects the first and second thoracic nerves, bypassing the sympathetic chain between the T2 ganglion and stellate ganglion) should be sought out and divided if sympathectomy is to be complete. (5) Remaining sympathetic innervation via the right stellate ganglion (which contributes to cardiac sympathetic innervation to varying degrees) may also contribute to the failure of LCSD in controlling arrhythmias in some patients. These limitations of LCSD have also been reported in the long-QT syndrome population; LCSD was shown to reduce but not abolish sudden cardiac death in 2 large studies and in a small series. LCSD proved inadequate for control of symptoms despite addition of β-blockade.

**Potential Clinical Strategy for Management of Ventricular Arrhythmia Storm**

The present data strengthens the available data in the literature on the value of sympathetic blockade for the management of ventricular arrhythmias. The key strategies for management of VT storm include the following: (1) Early pharmacological sympathetic blockade; (2) antiarrhythmic drugs, especially amiodarone and lidocaine; (3) reprogramming of devices to minimize shocks; (4) management of reversible causes that are proarrhythmic, which include electrolyte disturbances, fluid overload, and ischemia; (5) catheter ablation of the clinical arrhythmia if patients can be
transported safely to the laboratory; and (6) deep sedation or intubation with general anesthesia as an adjunct to sympathetic blockade in arrhythmia control, as well as for patient comfort. Of note, TEA can be instituted quickly and has the advantage of providing immediate effect while precipitants are addressed, cardiac transplant evaluation is performed, or surgery or assist device insertion is arranged, or when stabilization of the patient before ablation is required. TEA may also be used as a bridge to LCSD if this is not available emergently. LCSD provides long-lasting effects; it may be indicated if there are no reversible precipitants and no further surgical or ablative options exist, and it may be used as a bridge to nonurgent cardiac transplantation.

Study Limitations
Because of the retrospective observational nature of the present study, some (unavoidable) limitations must be considered. Patients were not randomized; VT storms sometimes do subside spontaneously, and the contribution of such remissions to the study findings cannot be delineated clearly. However, patients were treated unsuccessfully with aggressive medical therapy and catheter ablation (where feasible) before undergoing either procedure. In addition to the small size of the study, the causes of ventricular arrhythmias in the present study population were diverse, and the value of autonomic blockade may vary in cardiomyopathies of different origins.

LCSD procedures were performed by several operators, and levels of denervation differed. The fact that only 4 patients in the present series had complete denervation may have adversely impacted the LCSD outcomes. Of the 8 TEA patients, 3 were already intubated before commencement of TEA infusion, which may have modified the effects of the TEA. Although all 3 patients had arrhythmias despite general anesthesia, the addition of TEA abolished arrhythmias in 2 of 3 patients, which suggests an added beneficial effect.

There is also a referral bias in this study population, because all of the centers involved in the present study are specialized referral centers for catheter ablation of VT. Over the 51-month period of this study, 154 patients presented with refractory ventricular arrhythmias to the centers involved. Medical therapy (with ablation in many cases) controlled arrhythmias for the vast majority of these patients (140; 91%). Of the remaining 14 (9%) very-high-risk patients who underwent neuraxial modulation, 9 (64%) survived to LCSD (91%). Of the remaining 14 (9%) very-high-risk patients who underwent LCSD in patients from Holy Family Hospital, Mumbai, India, CARE Hospital, Hyderabad, India, and UCLA, respectively. We also thank the anesthesiology teams at these hospitals. We would also like to thank Dr Chi Lai (UCLA) for review of the pathology slide, Dr Jeffrey Gornbein (UCLA) for statistical assistance, and Dr Isaac Wiener (UCLA) for thoughtful review of the manuscript and comments.

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Disclosures
None.

References
Our findings are retrospective and will need further evaluation in prospective, randomized studies.

Additional therapeutic strategies such as thoracic epidural anesthesia and left cardiac sympathetic denervation could be considered in this setting. In our study, these procedures were well tolerated, without serious complications. Thoracic epidural anesthesia can be performed at the bedside; it can be used as a bridge to catheter ablation, cardiac transplantation, and left cardiac sympathetic denervation. Left cardiac sympathetic denervation can be performed in an acute setting if it is readily available when no further ablative or surgical options exist or as a bridge to nonurgent cardiac transplantation. Our findings are retrospective and will need further evaluation in prospective, randomized studies.
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