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# Treating Electrical Storm

## Sympathetic Blockade Versus Advanced Cardiac Life Support–Guided Therapy

Koonlawee Nademane, MD; Richard Taylor, MD; William E. Bailey, MD;  
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**Background**—Electrical storm (ES), defined as recurrent multiple ventricular fibrillation (VF) episodes, often occurs in patients with recent myocardial infarction. Because treating ES according to the Advanced Cardiac Life Support (ACLS) guidelines yields a poor outcome, we evaluated the efficacy of sympathetic blockade in treating ES patients and compared their outcome with that of patients treated according to the ACLS guidelines.

**Methods and Results**—Forty-nine patients (36 men, 13 women, mean age  $57 \pm 10$  years) who had ES associated with a recent myocardial infarction were separated into 2 groups. Patients in group 1 ( $n=27$ ) received sympathetic blockade treatment: 6 left stellate ganglionic blockade, 7 esmolol, and 14 propranolol. Patients in group 2 ( $n=22$ ) received antiarrhythmic medication as recommended by the ACLS guidelines. Patient characteristics were similar in the 2 groups. The 1-week mortality rate was higher in group 2: 18 (82%) of the 22 patients died, all of refractory VF; 6 (22%) of the 27 group 1 patients died, 3 of refractory VF ( $P<0.0001$ ). Patients who survived the initial ES event did well over the 1-year follow-up period: Overall survival in group 1 was 67%, compared with 5% in group 2 ( $P<0.0001$ ).

**Conclusions**—Sympathetic blockade is superior to the antiarrhythmic therapy recommended by the ACLS guidelines in treating ES patients. Our study emphasizes the role of increased sympathetic activity in the genesis of ES. Sympathetic blockade—not class 1 antiarrhythmic drugs—should be the treatment of choice for ES. (*Circulation*. 2000;102:742-747.)

**Key Words:** fibrillation ■ antiarrhythmia agents ■ myocardial infarction

Electrical storm (ES) describes the phenomenon of rapidly clustering ventricular fibrillation (VF) that necessitates multiple cardioversions (Figure 1). The conventional antiarrhythmic drug therapy for ES recommended by the American Heart Association Advanced Cardiac Life Support (ACLS) guidelines often fails to maintain sinus rhythm.<sup>1</sup> The unfolding scenario is swift and desperate. Patients repeatedly go into VF, are given antiarrhythmic medication serially, and receive repeated electrical shocks in an attempt to cardiovert the arrhythmia. Despite these efforts, most ES patients die—many within minutes or hours—especially if they have had a recent myocardial infarction (MI) or ongoing myocardial ischemia.<sup>1,2</sup>

Other phenomena probably bear on the development of ischemic VF. Increased sympathetic activity is known to contribute to it<sup>3-6</sup>; sympathetic blockade is known to prevent ventricular arrhythmias in the same animal model.<sup>5-9</sup> These complementary observations in animals support the finding from clinical trials of post-MI patients that sympathetic blockade, either in the form of  $\beta$ -blockade or left stellate ganglionic blockade (LSGB), prevents episodes of VF and sudden death.<sup>10-13</sup> We therefore postulated that sympathetic blockade would be effective for treatment of ES in patients with a recent

MI or ongoing myocardial ischemia. We prospectively evaluated the efficacy of sympathetic blockade in treating patients with ES and compared the outcome with that of patients with ES treated according to ACLS guidelines.

## Methods

### Patients

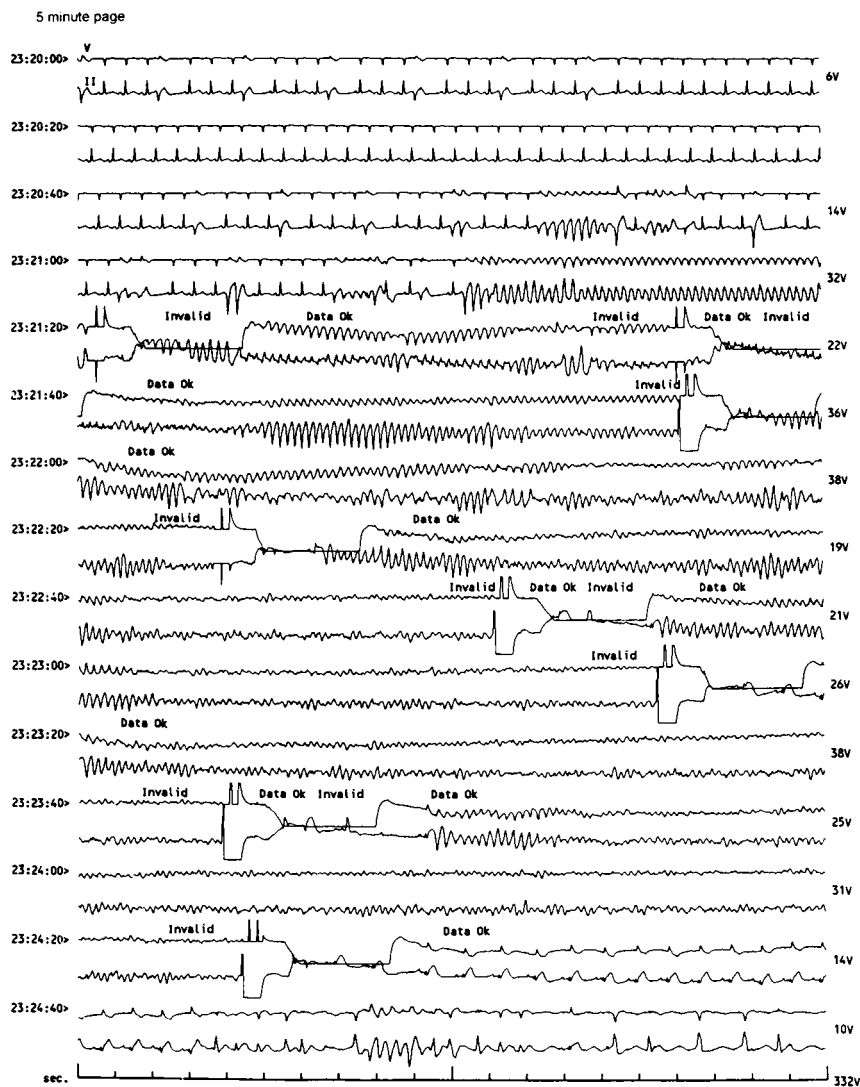
Patients included in this study all had ES with a recent MI. ES was defined as  $\geq 20$  ventricular tachycardia (VT)/VF episodes per day or  $\geq 4$  VT/VF episodes per hour. Recent MI was defined as occurring within 72 hours to 3 months before the onset of ES. We excluded patients in whom the onset of MI was  $< 72$  hours and those with acute pulmonary edema, previous treatment with intravenous amiodarone, acute respiratory failure, acquired or congenital long QT syndrome, or recent coronary revascularization ( $< 1$  week before the onset of ES).

We studied 49 patients with recent MI (36 men, 13 women; mean age  $57 \pm 10$  years) who had ES in the hospital. The ES occurred a mean of  $11 \pm 10$  days after MI (range 4 to 52; median 8 days). The location of the MI was anterior wall in 28 patients, inferior wall in 6, non-Q-wave in 5, and inferior and anterior walls in 10. Nineteen patients received acute thrombolytic therapy at the onset of the MI (Table). Left ventricular dysfunction was detected in all 49 patients either by angiography or 2D echocardiography; mean ejection fraction was  $32 \pm 8\%$  (range 18% to 48%). Twenty-seven patients underwent coronary artery angiography, which revealed 3-vessel

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**Figure 1.** Five-minute, continuous telemetry rhythm strip from 2-channel lead. Note multiple VF and polymorphic VT, necessitating 9 defibrillation shocks within 5 minutes.

disease in 14 patients, 2-vessel disease in 8, and 1-vessel disease in 5. Thirty-two patients had evidence of mild congestive heart failure.

**Treatment Protocol**

ES is, by nature, refractory to antiarrhythmic therapy; the cardiac arrest code is always called. Thus, almost all study patients initially received antiarrhythmic medication according to the ACLS guidelines before the Arrhythmia Service was consulted. Forty-one patients also received general endotracheal anesthesia for 24 to 48 hours after the onset of ES. After initial treatment during the code, 2 treatment approaches were used. Patients in group 1 (n=27) received sympathetic blockade treatment within 1 hour after all of the antiarrhythmic medications initiated during the code were discontinued. Of these patients, 6 were treated with LSGB, 7 with esmolol, and 14 with propranolol. Patients in group 2 (n=22) continued to receive conventional ACLS-guided therapy. Treatment with sympathetic blockade or ACLS-guided therapy was determined by physician preference and predilection for the use of either approach.

**ACLS Protocol**

In accordance with the ACLS guidelines,<sup>14</sup> lidocaine (1 mg/kg IV bolus) was the first antiarrhythmic drug given to treat VF. This was repeated if VF continued and was followed by a continuous infusion of lidocaine (1 to 4 mg/min). If sinus rhythm was not restored, a 100-mg bolus dose of procainamide was given every 5 minutes up to a total dose of 500 to 1000 mg, followed by a continuous infusion of

2 to 4 mg/min. Alternatively, an initial 5-mg/kg IV dose of bretylium tosylate was given and repeated every 5 minutes to the maximum of 25 mg/kg if VF episodes continued.

All 22 patients in group 2 were treated with lidocaine. Sixteen were also treated with procainamide and 18 with bretylium. Twelve patients received all 3 drugs at a given period of the treatment.

**Sympathetic Blockade**

The choices for sympathetic blockade therapy were LSGB or  $\beta$ -blockade. Either intravenous esmolol or propranolol was the  $\beta$ -blocking agent used. Intravenous propranolol was given as a 0.15-mg/kg dose over a period of 10 minutes and then as a 3- to 5-mg dose every 6 hours to maintain sinus rhythm unless the heart rate dropped below 45 bpm. Intravenous esmolol was given as a 300- to 500-mg/kg loading dose for 1 minute followed by a maintenance dose of 25 to 50 mg  $\cdot$  kg<sup>-1</sup>  $\cdot$  min<sup>-1</sup>. The maintenance infusion was titrated upward if necessary at 5- to 10-minute intervals until a maximum dose of 250 mg  $\cdot$  kg<sup>-1</sup>  $\cdot$  min<sup>-1</sup> was reached.

After informed consent was obtained, LSGB was performed by the anterior paratracheal approach. A 21-gauge needle was passed anteriorly between the trachea and the carotid artery to within several millimeters anterior to the lateral process of the spine. Ten to 20 mL of 1% xylocaine (without epinephrine) was injected until Horner's syndrome or partial Horner's syndrome developed. A repeat injection with 10 mL of 0.25% marcaine or xylocaine (without epinephrine) was given as needed.

**Baseline Characteristics of Study Patients**

	Sympathetic Blockade (Group 1) (n=27)	ACLS-Guided Therapy (Group 2) (n=22)
Age, y	58±11	56±9
Men/women	23/4	19/3
Ejection fraction, %	31±9	34±6
Location of MI		
Anterior	16	12
Inferior	2	4
Both anterior and inferior	6	4
Non-Q-wave	3	2
Heart rate, bpm	109±18	103±14
AF and/or atrial flutter (No. of patients)	7 (26%)	10 (45%)
QT <sub>c</sub>	0.41±0.03	0.39±0.05
Medications before ES		
Calcium antagonist	19	17
β-Blockers	6	3
ACE inhibitor	11	15
Onset of VF after MI, d	12±10	11±12
Thrombolytic therapy at MI onset (No. of patients)	11	8
K <sup>+</sup> <3.5 mEq	4	3

There are no statistically significant differences in any variable.

The choice of sympathetic blockade therapy was based on the circumstances. Intravenous propranolol was used most often because of its ease of use and ready availability; LSGB required consultation with an anesthesiologist knowledgeable about the procedure, which was impractical for many of our ES patients.

**Long-Term Care**

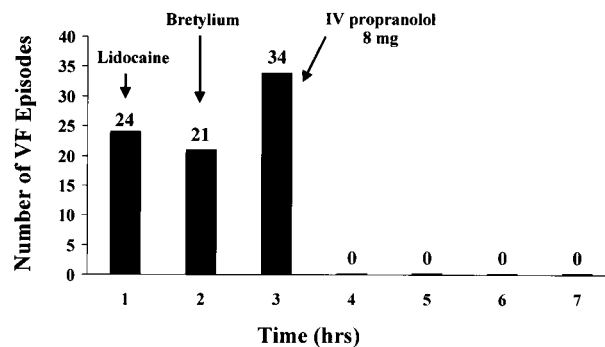
After the initial acute sympathetic blockade treatment, patients who were able to take oral drugs were also given oral amiodarone. A 1200- to 1600-mg/d loading dose was given for 4 to 7 days. This was followed by a 600- to 800-mg/d intermediate dose for 1 week. A 200- to 400-mg/d maintenance dose was continued for the duration of the study. Group 1 patients who survived continued to take oral β-blocking agents (either 40 to 120 mg/d propranolol or 50 to 100 mg/d atenolol). We did not perform permanent sympathectomy in our patients. Implantation of an internal cardioverter-defibrillator or myocardial revascularization after ES subsided was performed at the physician's discretion.

**Data and Statistical Analysis**

Continuous variables are presented as mean±SD. A Student's *t* test and Fisher's exact test were performed when appropriate. The Kaplan-Meier life-table analysis compared the cumulative survival rates of the 2 groups. The start time of the life-table analysis began at 4 hours after the initiation of the cardiac arrest code; this excluded the possibility of treatment bias by avoiding inclusion of patients whose arrhythmias were too severe and irrecoverable. For this reason, 3 group 2 patients who died within that period were excluded from the analysis. A value of *P* <0.05 (2-tailed) was considered significant.

**Results**

Group 1 (patients treated with sympathetic blockade) and group 2 (patients treated according to the ACLS guidelines) were similar with regard to clinical characteristics and the location of MI (Table). Most of our patients were receiving calcium antagonists (73%), but only 18% and were receiving



**Figure 2.** Effects of intravenous propranolol on same patient shown in Figure 1, who had 79 VF episodes despite having been given lidocaine and bretylium. After 8 mg of intravenous propranolol, arrhythmia terminated.

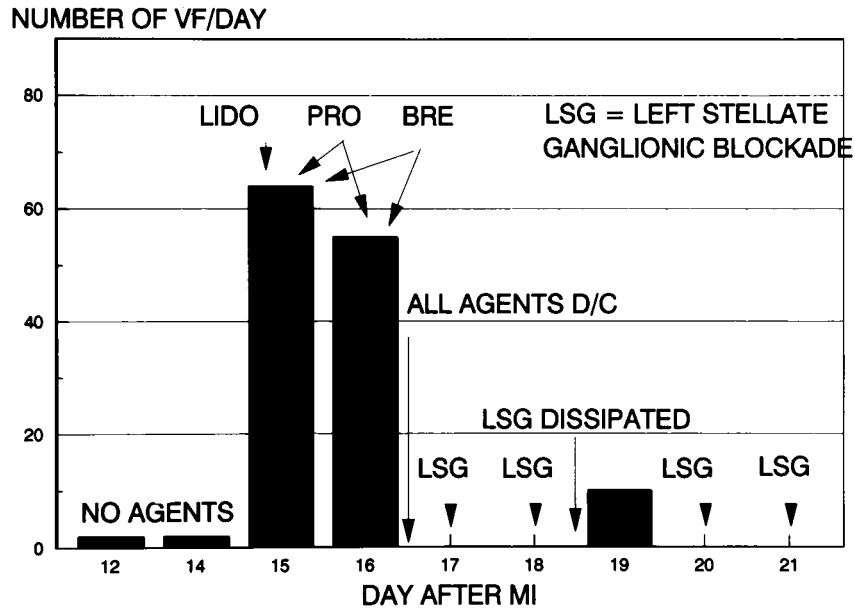
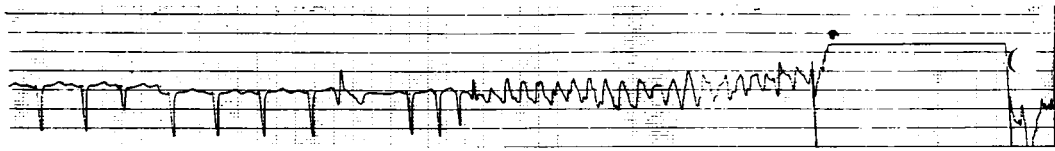
β-blockers and 53% were receiving ACE inhibitors. There were no differences in the relative risk of death among the patients taking calcium antagonists, β-blockers, or ACE inhibitors compared with those who were not. The degree of left ventricular dysfunction based on ejection fraction was comparable between the 2 groups (Table). The QT<sub>c</sub> interval was normal in both groups.

**VF Episodes and Associated Factors**

The first VF episode occurred 12±10 days after the onset of MI in group 1 and 11±12 days after the onset of MI in group 2. All group 1 patients continued to have multiple VF episodes before sympathetic blockade (25±12). The mean period from the onset of VF to administration of sympathetic blockade was 20±21 hours (median 11 hours); for β-blockade it was 17±14 hours (median 10.5 hours) and for LSGB it was 35±32 hours (median 18 hours). After sympathetic blockade therapy was initiated, the mean number of VF episodes was reduced to 2.6±1.7 in group 1 (*P*<0.01). In contrast, 91% of patients in group 2 continued to have VF episodes. The total VF episodes were 28±15 for group 1 and 38±20 for group 2 (*P*<0.01). Both groups had sinus tachycardia; mean baseline heart rate was 109±18 bpm in group 1 and 103±14 bpm in group 2, suggesting the presence of increased sympathetic activity. Atrial tachyarrhythmias occurred in 26% of group 1 patients and 45% of group 2 patients (difference not significant).

Figure 1 is an example of ES in 1 of our patients. This patient had sinus tachycardia and runs of nonsustained polymorphic VT, many degenerating to VF requiring multiple cardioversions over 5 minutes. After intravenous lidocaine and bretylium were given, multiple VF episodes continued until intravenous propranolol abolished the VF episodes (Figure 2).

Figure 3 shows the effects of LSGB on a patient who had VT/VF episodes 12 days after MI. Twenty minutes before the first VF episode, the patient learned that a family member had died; he became agitated and depressed and had VF shortly thereafter. Lidocaine and procainamide increased the number of VT/VF episodes. LSGB was performed and abolished the VT/VF. When the effects of the LSGB dissipated, VT/VF recurred. When the stellate ganglia were blocked, VT/VF again subsided. This patient was subsequently discharged and remained arrhythmia-free during follow-up.



**Figure 3.** Effects of LSGB on VF episodes in 1 patient. Top, VF episodes. Bar graph represents VF episodes occurring after MI. LIDO indicates lidocaine; PRO, procainamide; BRE, bretylium; and D/C, discontinued.

**Clinical Outcomes**

**First Week**

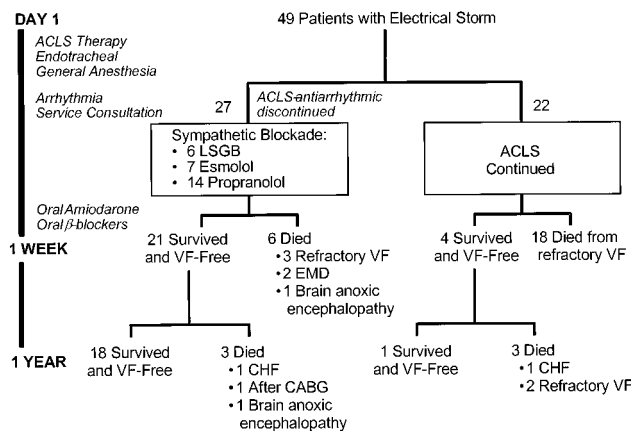
Twenty-four of the 49 patients died within 1 week of the onset of ES (Figure 4). The mortality rate within 1 week of treatment was substantially higher in group 2 than in group 1. Eighteen (82%) group 2 patients died, all of refractory VF. Only 6 (22%) group 1 patients died: 3 of refractory VF, 2 of electromechanical dissociation, and 1 of anoxic encephalopathy and resulting in asystole. The relative risk of dying

within 1 week for the group 2 patients was 3.68 compared with the group 1 patients (range 1.77 to 7.66;  $P < 0.0001$ ). Twenty of the 27 group 1 patients and 5 of the 22 group 2 patients were also treated with oral amiodarone after endotracheal anesthesia was terminated. A larger proportion of group 1 patients was treated with concomitant amiodarone because most group 2 patients died or failed to respond to the antiarrhythmic therapy guided by ACLS, continued to have multiple VF episodes, and continued to be treated with endotracheal anesthesia for the necessity of multiple cardioversions, whereas group 1 patients had a drastic reduction of the number of VF episodes and could be off the ventilators.

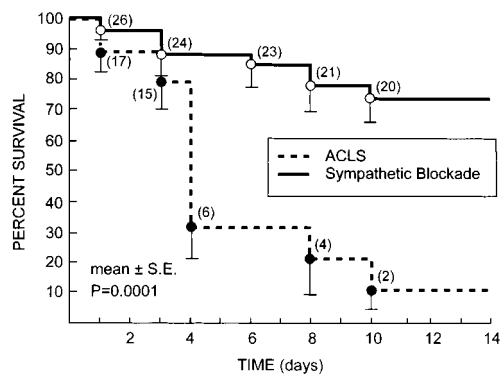
Figure 5 shows the Kaplan-Meier survival curves for the 2 groups. Group 1 patients (sympathetic blockade) had a dramatically better outcome than group 2 patients (ACLS treatment).

**One Year**

Twenty patients from group 1 survived and were discharged from the hospital. Two group 2 patients who survived the first week had recurrent VF and died; thus, only 2 group 2 patients survived to discharge from the hospital. All patients were followed at the Arrhythmia Clinic (follow-up  $17 \pm 8$  months; range 6 to 34 months). Nine patients underwent coronary revascularization (6 coronary artery bypass graft surgery and 3 angioplasty); all procedures were performed within 3 months after discharge from the hospital for documented recurrent ischemia. One group 1 patient died of complications



**Figure 4.** Courses of and outcomes of treatment for patients in group 1 (sympathetic blockade) and group 2 (treatment guided by ACLS recommendations). EMD indicates electromechanical dissociation; CHF, congestive heart failure.



**Figure 5.** Kaplan-Meier survival curves for group 1 (conventional treatment) and group 2 (sympathetic blockade). Numbers in parentheses are number of patients remaining at risk at each interval.

of coronary artery bypass graft surgery. Four patients who underwent the coronary artery bypass graft surgery showed dramatic improvement, and their left ventricular function returned to almost normal (ejection fraction increased from  $29 \pm 5\%$  to  $51 \pm 4\%$ ); this suggests the possibility of “hibernating” myocardium.<sup>15</sup> Two patients (1 from each group) died of congestive heart failure. There was no arrhythmic death during the follow-up period, and the 7 patients who had received an implantable cardioverter-defibrillator did not receive shocks from the device. Eighteen of the 27 group 1 patients continued to fare well during the follow-up period, compared with 1 of the 22 group 2 patients.

### Discussion

Patients with ES have a very high mortality rate, especially when treated according to the ACLS antiarrhythmic medication guidelines. The short-term outcome (1 week) is much better in patients treated with sympathetic blockade; the 1-week survival rate for group 1 (patients treated with sympathetic blockade) was 82%, compared with 22% for the group 2 (patients treated according to the ACLS guidelines). Patients who survived the first week after the onset of ES continued to do well during the 1-year follow-up period (Figure 4). Therefore, the data forcefully argue against using the ACLS guidelines to treat ES. Sympathetic blockade ( $\beta$ -blockade or LSGB), particularly when combined with oral amiodarone, is much more effective than class I antiarrhythmic drugs or bretylium. The finding that sympathetic blockade dramatically improves the mortality rate fits with the evidence that when post-MI patients are treated with  $\beta$ -blockade,<sup>11,13</sup> they live longer and fare better.

Why does sympathetic blockade succeed when ACLS-guided antiarrhythmic treatment fails? Abundant evidence in postinfarct animal studies show that class I drugs can increase the propensity for VF.<sup>16–18</sup> Moreover, class I drugs exert negative inotropic effects and worsen cardiac function, leading to more heart failure, more VF episodes, and, eventually, death in patients who have left ventricular dysfunction and mild congestive heart failure, as did our patients.<sup>19–21</sup> Conversely, sympathetic blockade exerts beneficial effects in post-MI patients. Lombardi et al<sup>6</sup> demonstrated that sympathetic activity reflexively increased during myocardial ischemia; this in turn contributed to a decreased VF threshold during coronary artery occlusion. Sympathetic blockade or vagal stimulation in-

crease the VF threshold in the same model.<sup>6</sup> Schwartz et al<sup>10</sup> showed that oxprenolol (160 mg) or a surgically selective left stellate sympathectomy prevented sudden cardiac death in high-risk post-MI patients compared with placebo. Even though LSGB had an  $\alpha$ -blocking effect in addition to  $\beta$ -blocking effect, our data and those of Schwartz et al demonstrated that LSGB and  $\beta$ -blockade are equally effective in treating post-MI life-threatening ventricular tachyarrhythmias.

These findings indicate that post-MI patients with ES have significantly increased sympathetic activity, which plays a major role in the pathophysiology of ventricular arrhythmogenesis. Zipes<sup>4</sup> reported that MI and myocardial ischemia affected the denervation of sympathetic-parasympathetic fibers, which enhanced sympathetic activity, thereby increasing the propensity for ventricular tachyarrhythmias. Our patients who had left ventricular dysfunction also manifested clinical signs of congestive heart failure and increased sympathetic activity. Sympathetic blockade therapy, while preventing ventricular tachyarrhythmias, did not worsen either cardiac function or heart failure. This finding confirms that of the Beta-Blocker Heart Attack trial that the more severe the left ventricular dysfunction, the more beneficial  $\beta$ -blockade is.<sup>11,13</sup> However, in 2 of our study patients who received  $\beta$ -blocking agents, electromechanical dissociation developed and the patients died. Nevertheless, the data argue strongly that patients who have had a recent MI and profound left ventricular dysfunction should receive  $\beta$ -blockade or sympathetic blockade immediately after the onset of VF rather than some time later.

All study patients who were able to take oral drugs were immediately started on oral amiodarone along with  $\beta$ -blockade medication; amiodarone was continued during the follow-up period. All patients who survived the first week after ES did well over the long term. This observation dovetails with the finding of recent major trials on the beneficial effects of oral amiodarone in post-MI patients.<sup>22</sup> Patients who received a combination of oral amiodarone and  $\beta$ -blockade had the best outcome. There is also evidence supporting the hypothesis that intravenous amiodarone helps these patients.<sup>23,24</sup> The data did not show, however, that intravenous amiodarone yielded a better survival rate than bretylium.<sup>24</sup> Randomized trials comparing intravenous amiodarone and  $\beta$ -blockade therapy are needed to determine whether sympathetic blockade is better than intravenous amiodarone.

Our data also confirm the findings from the studies by Lie et al<sup>25</sup> and Braat et al<sup>26</sup> that the presence of malignant ventricular arrhythmias during the subacute phase of MI in patients with poor ventricular function portends a grave outcome. Despite the initial fury of the VF episodes during ES, if the patient weathers the storm, most stay arrhythmia-free over the long term. It is widely known from animal experiments in the ischemic MI model that after the infarction, the myocardium heals and associated electrophysiological abnormalities develop, serving as a substrate for ventricular tachyarrhythmias.<sup>5,23</sup> This is especially true when modulating factors (eg, increased sympathetic activity and heart failure) are present. After the myocardium is completely healed, many of these electrophysiological abnormalities disappear. This improvement, in tandem with the favorable changes in modulating factors (ie, decreased sympathetic tone or myocardial ischemic episodes), cause the life-threatening ventricular arrhythmias to disappear. One could

speculate that our study patients fit this model. If these patients survive ES, the myocardium heals; when the ischemia is subsequently treated either by revascularization or medication, the arrhythmias then subside.

### Study Limitations

Our study protocol was limited in that patients could not be randomly assigned to a treatment arm because of the emergent nature of ES. Because there are no data showing the relative efficacy of either treatment arm, treatment selection (either sympathetic blockade or ACLS-guided therapy) was determined by physician preference. However, there were no differences in the clinical characteristics between the 2 groups. Also, group 1 patients continued to have multiple VF episodes before sympathetic blockade was initiated. Thus, it is unlikely that patients whose arrhythmias were less recalcitrant had been selected for sympathetic blockade treatment.

### Summary

Although ACLS-guided therapy is most often used to treat patients who have ES, overwhelming data in both animal experiments and clinical trials show that class I antiarrhythmic drugs are harmful rather than helpful.<sup>21</sup> Our study suggests an alternative course: sympathetic blockade. Sympathetic blockade along with oral amiodarone unequivocally improves the survival rate of these patients. If they survive ES, these patients do well over the long term. We propose that patients with ES, even if they have mild congestive heart failure, left ventricular dysfunction, or hemodynamically compromised arrhythmias, should be given  $\beta$ -blockers. Further, patients who have had an MI and left ventricular dysfunction should receive  $\beta$ -blockers whether or not they have ventricular arrhythmias<sup>11,13</sup> Doing so may prevent ES altogether. On the basis of the evidence from our study, this new direction, although in the past the path less traveled, is the better way to save lives.

### Acknowledgments

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