Role of triple extrastimuli during electrophysiologic study of patients with documented sustained ventricular tachyarrhythmias

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ABSTRACT Electrophysiologic studies were performed in 172 consecutive patients for evaluation of documented sustained ventricular tachyarrhythmias. One hundred thirteen patients presented with sustained ventricular tachycardia that was hemodynamically stable, and 59 patients presented with cardiac arrest. Seventy-one patients without previously documented or suspected ventricular arrhythmias were also studied to determine the specificity of our electrophysiologic study protocol. The stimulation protocol included single, double, and triple right ventricular extrastimuli and rapid ventricular pacing at multiple cycle lengths performed at one or more right ventricular sites. Stimulation was performed at one or more left ventricular sites in patients with documented spontaneous arrhythmias when right ventricular programmed stimulation failed to induce sustained ventricular tachycardia. Ventricular tachyarrhythmias were induced in 110 (97%) of the patients who presented with sustained ventricular tachycardia, in 48 (81%) of the patients who presented with cardiac arrest, and in 28 (40%) of the patients without documented spontaneous arrhythmias. Right ventricular triple extrastimuli induced tachycardia in 22% of patients who presented with sustained ventricular tachycardia vs 46% of those who presented with cardiac arrest (p < .001). Left ventricular stimulation was required for tachycardia induction in 3% of patients with stable tachycardia vs 19% of those with cardiac arrest (p < .01). Triple extrastimuli induced 57% of tachycardias in the 28 patients without spontaneous arrhythmias, and virtually all of these tachycardias were polymorphic and nonsustained. The cycle lengths of tachycardias induced in each group by double and triple extrastimuli were similar, but the tachycardias induced in patients with cardiac arrest were significantly faster than those induced in the ventricular tachycardia group (mean cycle length 218 vs 291 msec, p < .001). In spite of the use of triple extrastimuli, the sensitivity of programmed stimulation remains lower in patients with cardiac arrest than in those with stable sustained ventricular tachycardia. The use of triple extrastimuli may decrease the specificity of programmed stimulation, and the clinical significance of induced polymorphic nonsustained tachycardias is uncertain.


PROGRAMMED stimulation is widely used in the evaluation of patients with sustained ventricular tachyarrhythmias. Previous studies that have used up to two ventricular extrastimuli and rapid ventricular pacing have demonstrated inducible tachycardias in 65% to 95% of patients with recurrent sustained ventricular tachycardia (VT) and in 63% to 81% of patients with cardiac arrest.7 The purpose of the present study was to evaluate whether the use of triple extrastimuli in the electrophysiologic study protocol would (1) increase the likelihood of induction of tachycardia in patients presenting with documented sustained VT or cardiac arrest, (2) be more frequently associated with induction of faster and/or polymorphic tachycardias than observed when using two or fewer extrastimuli and rapid pacing, and (3) decrease the specificity of the results of programmed ventricular stimulation.

Methods

Patients. We studied 172 consecutive patients who were referred for evaluation of ventricular tachyarrhythmias. One hundred thirteen had suffered recurrent sustained VT that was...
hemodynamically stable. Fifty-nine were studied after sudden unexpected cardiac arrest. Patients whose arrhythmias occurred only in the setting of acute myocardial ischemia or in whom the arrhythmia appeared to have precipitated by transient metabolic abnormalities, drug toxicity, or the long QT syndrome, were excluded from analysis.

The patients ranged from 13 to 82 years old (mean 57), and the age distribution was similar for patients with cardiac arrest and sustained VT (table 1).

Coronary artery disease was present in a majority of patients who presented with sustained VT (83%) and cardiac arrest (73%) (table 1). Most patients in each group had suffered a prior myocardial infarction. Cardiomyopathy and mitral valve prolapse were found more frequently in patients in the cardiac arrest group than in the sustained VT group. Other associated heart disease found in the group with sustained VT included postoperative congenital heart disease in three patients, sarcoidosis with left ventricular aneurysm in one, and arrhythmogenic right ventricular dysplasia in one. One patient in the cardiac arrest group had rheumatic heart disease. Six patients in the group with sustained VT had no associated structural heart disease.

The initial rhythm recorded at cardiac arrest was ventricular fibrillation in 47 patients and VT in 12 patients. Twenty of 59 patients (34%) in this group were taking antiarrhythmic drugs at the time of their initial arrest. A similar proportion of patients in the group who presented with sustained VT were taking antiarrhythmic drugs at the time of their initial presentation (26 of 102 patients for whom the data were available, 25%, p = NS).

To determine the specificity of our stimulation protocol, we studied a third group of 71 patients who had no previously documented or suspected ventricular arrhythmia. Forty of these patients were undergoing routine diagnostic cardiac catheterization for symptoms of heart disease, primarily angina pectoris and exertional dyspnea. None had a history of symptomatic clinical arrhythmias, and 24 hr Holter monitoring performed for all patients demonstrated no more than isolated single ventricular premature depolarizations with a frequency less than 10 per hr. The remaining 31 patients in this group were undergoing electrophysiologic studies for arrhythmias other than ventricular in origin. The indications for electrophysiologic studies in these patients included paroxysmal supraventricular tachycardia (12 patients), paroxysmal atrial fibrillation or flutter (13 patients), and bradyarrhythmias (three patients). Three patients in this group had no documented arrhythmias and were studied because of protocols. Structural heart disease was present in only 61% of this patient group (table 1), with the most frequent being coronary artery disease.

Definitions. Nonsustained VT was that lasting from 3 beats to 30 sec and terminating spontaneously. Sustained VT was that which lasted greater than 30 sec or which caused hemodynamic compromise requiring termination by pacing or cardioversion in less time.

Tachycardia was considered inducible when programmed electrical stimulation reproducibly initiated (at least twice) ventricular tachyarrhythmias replicating the spontaneous tachycardia.

Electrophysiologic study protocol. Studies were performed with the patients in the nonsedated, postabsorptive state after informed consent had been obtained. The study protocol was approved by the University of Pennsylvania Committee on Human Studies.

Two to four multipolar electrode catheters were introduced percutaneously or by cutdown and were positioned in the heart (under fluoroscopic guidance) at the high right atrium, atrioventricular junction in the His bundle position, and right ventricular apex in all patients. Catheter position was confirmed with multiplane fluoroscopy.

Stimulation was performed with a custom-designed programmable stimulator and an optically isolated constant current source (Bloom Associates Ltd.; Narberth, PA) that produced rectangular impulses 1 msec in duration at twice diastolic threshold. Bipolar intracardiac electrograms were filtered at 30 to 500 Hz and were displayed simultaneously with three surface electrocardiographic leads (I, aVF, and Vf) on a multichannel oscilloscope (Electronics for Medicine, VR16). Data were recorded simultaneously with an ink jet recorder (Siemens Mingograph) and magnetic tape (Honeywell Model 5600).

All antiarrhythmic drugs were discontinued at least five half-lives before the study. The stimulation protocol consisted of incremental atrial pacing beginning at rates just above the sinus rate until atrioventricular block occurred. Progressively premature atrial extrastimuli were then introduced in 10 msec decrements during sinus rhythm and at one or more drive cycle lengths beginning in late diastole, until the atrial refractory period was reached. Ventricular extrastimuli were introduced in sinus rhythm and at one or more paced ventricular cycle lengths (S1-S1 intervals of 400 to 600 msec) beginning in late diastole.

TABLE 1

<table>
<thead>
<tr>
<th>Patients</th>
<th>Associated cardiac diseases</th>
<th>No. of patients on antiarrhythmic drugs (%)a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ageb</td>
<td>CAD (MI)</td>
<td>CM</td>
</tr>
<tr>
<td>Group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sustained ventricular tachycardia (n = 113)</td>
<td>56 (13-82)</td>
<td>94 (91)</td>
</tr>
<tr>
<td>Cardiac arrest (n = 59)</td>
<td>58 (16-81)</td>
<td>43 (38)</td>
</tr>
<tr>
<td>No spontaneous arrhythmia (n = 71)</td>
<td>52 (14-79)</td>
<td>32 (20)</td>
</tr>
</tbody>
</table>

CAD = coronary artery disease; MI = previous myocardial infarction; CM = cardiomyopathy; MVP = mitral valve prolapse; Other = miscellaneous heart disease; NHD = no structural heart disease.

The age given is the mean in years and the numbers in parenthesis are the range.

This category refers to patients taking drugs at the time of initial episode of spontaneous ventricular tachycardia or cardiac arrest.
and were moved earlier in 10 msec decrements until ventricular refractoriness was reached. The initial drive cycle length after sinus rhythm was 600 msec, unless the sinus cycle length was too short to permit ventricular capture at this rate. When a single extrastimulus (S₁) did not induce VT, a second extrastimulus (S₂) was added. Double extrastimuli (S₁-S₂) were introduced, starting with an S₁-S₂ interval 50 to 100 greater than the ventricular effective refractory period and an S₂-S₃ interval equal to the S₁-S₂ interval. S₃ was shortened by 10 msec decrements until it failed to evoke a response. At this point, S₃ was shortened by 10 msec until S₃ evoked a response. This sequence was repeated until both extrastimuli reached refractoriness. Incremental ventricular pacing was then performed at rates of 150 to 250 beats/min for 5 to 30 sec. In patients with documented spontaneous ventricular arrhythmias, this protocol was performed first at the right ventricular apex. When no sustained tachycardia was induced, the protocol was repeated at a second right ventricular site, usually the outflow tract. When sustained VT was not induced, a third extrastimulus (S₃) was added, and programmed stimulation was repeated in a similar fashion. Left ventricular stimulation at one or more sites was performed with the same stimulation protocol when right ventricular stimulation failed to induce sustained VT. The end point for stimulation in all studies in the patients with documented arrhythmias was either induction of sustained VT or ventricular refractoriness. In patients with hemodynamically stable VT having a uniform pattern, the end point for stimulation was induction of the same pattern of VT, even when multiple uniform patterns of VT were induced. We did not attempt to reproduce the spontaneous pattern of VT in patients with induced uniform patterns of VT, which necessitated repeated cardioversions when the induced VT differed from the spontaneous VT. Patients with inducible VT underwent serial electrophysiologic testing of pharmacologic antiarrhythmic therapy according to a previously described protocol.³

Programmed stimulation in the 71 patients without previously documented or suspected spontaneous ventricular arrhythmias was performed 30 min after the last injection of angiographic dye (40 patients) at the right ventricular apex only, at drive cycle lengths of 600 and 400 msec. Stimulation was not performed at a second right ventricular site or in the left ventricle in any patient. In the protocol for programmed stimulation we used the same methods that were used for the patients with documented clinical arrhythmias. However, the end point for stimulation in patients without previously documented or suspected ventricular arrhythmias was induction of 6 or more beats of VT.

**Statistical analysis.** R × C contingency tables were used to compare the differences between proportions. The Mann-Whitney test was used to compare cycle lengths of induced tachycardias. The cycle lengths of rapid polymorphic tachycardias that degenerated into ventricular fibrillation were calculated from the mean of the first 10 beats of the induced arrhythmias for the purposes of this analysis.

**Results**

**Patients with spontaneous ventricular arrhythmias**

**Results of programmed stimulation.** Sustained VT was induced in 108 of 113 patients (96%) with spontaneous VT and in 44 of 59 patients (75%) with cardiac arrest (table 2). Nonsustained VT only (duration 14 to 100 beats) was induced in two patients (2%) in the sustained VT group and in four patients (7%) in the cardiac arrest group. Thus, VT was induced in 98% of the 113 patients who presented with sustained VT and in 81% of the 59 patients presenting with cardiac arrest (p < .001).

VT was induced by right ventricular stimulation in 107 patients and by left ventricular stimulation in three patients (3%) with sustained VT. In contrast, right ventricular stimulation induced ventricular tachycardias in 39 patients in the cardiac arrest group, while left ventricular stimulation was required in nine patients (19%) in this group (p < .01) (table 2). A second site for right ventricular stimulation (right ventricular outflow tract) was required for induction of tachycardia in 12 of 107 (11%) patients in the sustained VT group and in three of 36 (8%) patients in the cardiac arrest group who had tachycardias that could be induced by right ventricular stimulation.

**TABLE 2**

**Results of programmed stimulation**

<table>
<thead>
<tr>
<th></th>
<th>Tachycardia induced</th>
<th>Noninducible</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sustained VT</td>
<td>nonsustained VT</td>
</tr>
<tr>
<td></td>
<td>RV stim</td>
<td>LV stim</td>
</tr>
<tr>
<td>Group</td>
<td>S</td>
<td>D</td>
</tr>
<tr>
<td>Sustained ventricular tachycardia (n = 113)</td>
<td>108 (96%)</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Cardiac arrest (n = 59)</td>
<td>44 (75%)</td>
<td>4 (7%)</td>
</tr>
<tr>
<td>No spontaneous arrhythmia (n = 71)</td>
<td>4 (6%)</td>
<td>24 (34%)</td>
</tr>
</tbody>
</table>

VT = ventricular tachycardia; RV = right ventricle; LV = left ventricle; stim = stimulation; S = single ventricular extrastimuli; D = double extrastimuli; T = triple extrastimuli; SP = straight pacing.

*p < .001. Percent of patients with noninducible arrhythmias in VT group vs those in cardiac arrest group.

**p < .001. No. of patients requiring RV triple extrastimuli for tachycardia induction in VT group vs those in cardiac arrest group.

*Cp < .01. Percent of patients requiring LV stimulation in VT group vs those in cardiac arrest group.
In the patients with sustained VT, single ventricular extrastimuli induced tachycardia in 25 patients, double extrastimuli induced tachycardia in 59 patients, triple ventricular extrastimuli induced tachycardia in 25 patients, and rapid pacing was required for induction of tachycardia in one patient.

Of the patients who presented with cardiac arrest, single ventricular extrastimuli induced tachycardia in two patients, double ventricular extrastimuli induced tachycardia in 15 patients, triple ventricular extrastimuli induced tachycardia in 30 patients, and rapid pacing induced tachycardia in one patient. Triple ventricular extrastimuli were performed in the two patients who required rapid ventricular pacing for induction of tachycardia. In both cases, the triple extrastimuli failed to induce VT. Triple ventricular extrastimuli were required for induction of tachycardia in 23% of the sustained VT group vs 63% of the cardiac arrest group (p < .001). One person each in the sustained VT and cardiac arrest groups had only nonsustained VT induced by triple extrastimuli and were then given quadruple ventricular extrastimuli, inducing sustained tachycardia. VT could be induced by rapid atrial pacing in addition to programmed ventricular stimulation in four patients with sustained VT. However, no patient had tachycardia that could be induced only by atrial pacing, and no patient had tachycardia induced by atrial premature stimulation. Atrial stimulation did not induce tachycardia in any patient with cardiac arrest. Tachycardia was induced in three patients with sustained VT by rapid ventricular pacing in addition to programmed ventricular stimulation, but as noted above, only one patient had tachycardia that could be induced by rapid ventricular pacing alone. Thus, a total of four patients with sustained VT and one patient with cardiac arrest had tachycardias induced by rapid ventricular pacing.

The drive cycle lengths at which programmed stimulation induced ventricular tachyarrhythmias showed a similar distribution in each patient group (table 3). Ventricular tachyarrhythmias were most frequently induced by programmed ventricular stimulation at a drive cycle length of 600 msec. Initial stimulation was performed at a drive cycle length of 500 msec in 12 patients in the VT group and in nine patients in the cardiac arrest group; this was done because their sinus rates were too rapid to permit stimulation at a drive cycle length of 600 msec. Programmed stimulation during sinus rhythm seldom induced tachycardia.

Table 3

<table>
<thead>
<tr>
<th>DCL (msec)</th>
<th>No. of patients with sustained VT (^{a})</th>
<th>No. of patients with cardiac arrest (^{a})</th>
</tr>
</thead>
<tbody>
<tr>
<td>SR</td>
<td>4 (4%)</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>600</td>
<td>53 (48%)</td>
<td>21 (44%)</td>
</tr>
<tr>
<td>500</td>
<td>24 (22%)</td>
<td>13 (27%)</td>
</tr>
<tr>
<td>400</td>
<td>28 (25%)</td>
<td>10 (21%)</td>
</tr>
<tr>
<td>Total</td>
<td>109</td>
<td>47</td>
</tr>
</tbody>
</table>

DCL = drive cycle length; SR = sinus rhythm.

\(^{a}\)VT was induced only by rapid ventricular pacing in one patient in each group.

(mean ± SD) (figure 1). This was significantly longer than the mean cycle length of arrhythmias induced by double ventricular extrastimuli (287 ± 59 msec) and by triple ventricular extrastimuli (291 ± 60 msec, p = .01). All tachycardias induced by single ventricular extrastimuli were of a uniform pattern. The tachycardias induced by double ventricular extrastimuli were of a uniform pattern (96% and 95%, respectively). Four polymorphic tachycardias that were induced (three by double extrastimuli and one by triple extrastimuli) became uniform when induction was repeated after Type I antiarrhythmic drugs had been administered. Ventricular fibrillation was not the initial arrhythmia induced in any patient in this group.

The mean cycle length of tachycardias induced in the cardiac arrest group by single ventricular extrastimuli was 325 msec, and this was significantly longer than those induced by double (213 ± 54 msec) or triple extrastimuli (218 ± 38 msec, p < .01). The mean cycle length of tachycardias induced by double and triple ventricular extrastimuli did not differ significantly (figure 1). Tachycardias induced by single extrastimuli in this group were uniform. In contrast, only 60% of tachycardias induced by double extrastimuli and 50% of those induced by triple ventricular extrastimuli had a uniform pattern. Rapid polymorphic VTs that quickly degenerated spontaneously into ventricular fibrillation were induced in eight patients in the cardiac arrest group.

Multiple uniform patterns of tachycardia were induced in 27 of 107 (25%) patients with uniform induced tachycardia in the sustained VT group and in nine of 29 (31%) patients in the cardiac arrest group (table 4).

Fifteen of the 107 patients (14%) in the sustained VT group and 11 of the 29 patients (38%) in the cardiac groups.
arrest group had polymorphic VT induced in addition to the clinical uniform pattern of tachycardias (table 5). There was no significant difference in the stimulation mode used to induce these polymorphic tachycardias. All polymorphic tachycardias were nonsustained (six complexes up to 30 sec), except in one patient in the cardiac arrest group in whom the induced tachycardia degenerated into ventricular fibrillation requiring cardioversion.

In addition to the increased requirement for triple extrastimuli in the cardiac arrest group, the characteristics of tachycardias induced by triple ventricular extrastimuli in the two patient groups differ significantly. The mean cycle length of tachycardias induced by triple extrastimuli in the sustained VT group was 291 vs 218 msec in the cardiac arrest group (p < .001). The tachycardias induced in patients with cardiac arrest were more frequently polymorphic (50%) than those induced in patients with sustained VT (4%, p < .001).

Right ventricular effective refractory periods were analyzed at a paced cycle length of 600 msec (except in six patients in the VT group and two in the cardiac arrest group).

**TABLE 4**

<table>
<thead>
<tr>
<th>No. of patterns of tachycardia induced</th>
<th>Patient group</th>
<th>No. of patients with sustained VT</th>
<th>No. of patients with cardiac arrest</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td></td>
<td>21</td>
<td>6</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>27</td>
<td>9</td>
</tr>
</tbody>
</table>

**TABLE 5**

<table>
<thead>
<tr>
<th>Patient group</th>
<th>No. of patients by stimulation mode</th>
</tr>
</thead>
<tbody>
<tr>
<td>S D T</td>
<td></td>
</tr>
<tr>
<td>Sustained VT</td>
<td>6 8 1</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>1 8 2^A</td>
</tr>
</tbody>
</table>

S = single ventricular extrastimuli; D = double ventricular extrastimuli; T = triple ventricular extrastimuli.

^Induced tachycardias were nonsustained (six complexes — 30 sec) in all but one patient in this group in whom induced VT degenerated into ventricular fibrillation.
A refractory period was measured at a drive cycle length of 600 msec in 107 patients in the ventricular tachycardia group and in 57 patients in the cardiac arrest group. Refractory periods were measured at drive cycle length 500 msec in six patients in the ventricular tachycardia group and in two patients in the cardiac arrest group.

## Patients without spontaneous ventricular tachyarrhythmias

### Results of programmed stimulation

Sustained ventricular tachyarrhythmias were induced in four patients without previously documented or suspected ventricular tachyarrhythmias, and nonsustained VT was induced in 24 patients in this group (table 2). The nonsustained tachycardias lasted from 6 beats to 30 sec. Nineteen of these induced nonsustained arrhythmias were polymorphic, and five had a uniform pattern. In contrast, two of the sustained VTs were polymorphic, and the remaining two had a uniform pattern. The majority of nonsustained arrhythmias (16) were induced by triple extrastimuli, with only two being induced by single extrastimuli and six by double extrastimuli. In contrast, no sustained arrhythmia was induced by triple extrastimuli. One of the sustained arrhythmias was induced by a single extrastimulus, while the remaining three were induced by double extrastimuli (figure 2). Two of the sustained tachycardias were induced in patients without organic heart disease (one polymorphic and one uniform), while the remaining two sustained VTs were induced in patients with left ventricular aneurysms. When the full stimulation protocol was followed there was no significant difference in the incidence of induction of arrhythmia in patients with myocardial infarction vs that of those without a history of myocardial infarction (figure 2, A). In contrast, when only up to two extrastimuli were used, VT was induced significantly more frequently in patients with a prior infarction (p < .02). Of note, sustained ventricular tachyarrhythmias were induced significantly more frequently in patients with ventricular aneurysms than in those without (two of nine patients with aneurysms vs two of 62 patients without, p < .02, figure 2).

### Discussion

This study has demonstrated that in our patient population programmed stimulation with the described protocol induces ventricular tachyarrhythmias in 98% of patients who present with stable sustained VT and in 81% of patients who present with cardiac arrest. Previous studies that used stimulation protocols with one and two extrastimuli and rapid ventricular pacing have resulted in induction of tachycardia in 63% to 81% of patients presenting with cardiac arrest and in 65% to 95% of patients with sustained VT. When up to two ventricular extrastimuli are used, sustained ventricular tachyarrhythmias have been induced in only 42% to 56% of patients presenting with cardiac arrest and in

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**TABLE 6**

<table>
<thead>
<tr>
<th>Group</th>
<th>S</th>
<th>D</th>
<th>T</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sustained ventricular tachycardia</td>
<td>253 ± 21</td>
<td>242 ± 23</td>
<td>260 ± 26</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>240 ± 107</td>
<td>250 ± 22</td>
<td>254 ± 25</td>
</tr>
</tbody>
</table>

RVERP = right ventricular effective refractory period.

*Values are expressed as msec (mean ± SD). Refractory periods were measured at a drive cycle length of 600 msec in 107 patients in the ventricular tachycardia group and in 57 patients in the cardiac arrest group. Refractory periods were measured at drive cycle length 500 msec in six patients in the ventricular tachycardia group and in two patients in the cardiac arrest group.

FIGURE 2. A, Results of stimulation protocol using up to three ventricular extrastimuli (VES) in 71 patients without previously documented or suspected arrhythmias. There is no significant difference in frequency of arrhythmia induction in patients with or without myocardial infarction, but sustained tachycardia was induced significantly more frequently in patients with aneurysms. B, Results of stimulation protocol using up to two extrastimuli: tachycardia is induced significantly more frequently in patients with prior myocardial infarction. Dotted areas represent induced nonsustained tachycardias. Stippled areas represent induced sustained tachycardias. MI = previous myocardial infarction; An = left ventricular aneurysm.
33% to 91% of patients presenting with sustained VT. To obtain this degree of sensitivity with only double ventricular extrastimuli, left ventricular stimulation has been required in 11% to 12% of patients with sustained VT and in 42% of those presenting with cardiac arrest. In the present study, sustained VT was induced in 96% of patients who presented with sustained VT and in 75% of those presenting with cardiac arrest. Additionally, left ventricular stimulation was required in only 3% of patients who presented with sustained VT and in 19% of patients presenting with cardiac arrest. If triple ventricular extrastimuli were not performed in this patient group, the 24 patients who presented with sustained VT and had tachycardia induced by three right ventricular extrastimuli (21%) and the 22 patients in the cardiac arrest group in whom tachycardias were induced by right ventricular triple extrastimuli (37%) would have undergone left ventricular stimulation, and we would not be able to predict the additional number of inducible arrhythmias. Thus, the ability of electrophysiologic studies to induce ventricular tachyarrhythmias in these patients and, specifically, the ability of right ventricular stimulation to induce tachyarrhythmias, were increased by adding a third ventricular extrastimulus to the protocol.

The requirement for triple ventricular extrastimuli was significantly greater for patients who presented with cardiac arrest than for those presenting with hemodynamically stable sustained VT, but the reason for this difference is not clear. Although the cycle length of tachycardias induced by three ventricular extrastimuli in the cardiac arrest group was significantly shorter than those induced in the patients with sustained VT, within each patient group there was no significant difference in the mean cycle length of tachycardias induced by double vs. triple ventricular extrastimuli; there was also wide scatter in the cycle lengths of tachycardias induced by a given technique of stimulation. Likewise, the morphologic characteristics of tachycardias induced within each patient group did not differ between patients whose tachycardias were induced by double vs. triple ventricular extrastimuli. Thus, the higher frequency of polymorphic tachycardias induced in the patients who presented with cardiac arrest may be related to the shorter cycle length of induced tachycardias in this patient group. These data do suggest that the characteristics of induced arrhythmias appear to depend primarily on the patient population studied rather than on the mode of induction.

Specificity of triple extrastimuli. The induction of polymorphic sustained tachycardias in four patients who presented with sustained VT having a uniform pattern questions the specificity of programmed stimulation in this patient population. However, all four patients were receiving empiric antiarrhythmic therapy at the time they developed the spontaneous arrhythmia, and this uniform tachycardia was reproduced when programmed stimulation was performed in the presence of the same antiarrhythmic drug. The ability of Type I antiarrhythmic drugs to cause polymorphic VT to be uniform has been reported previously.

A second aspect of specificity concerns the induction of multiple uniform patterns of tachycardia in 25% to 31% of patients with documented sustained arrhythmias. Although we have noted that monitoring of repeated episodes of spontaneous sustained VT in these patients with multiple uniform patterns will demonstrate the occurrence of similar patterns occurring spontaneously, there remain some patients with induced patterns that do not resemble those documented to occur spontaneously. The clinical significance of this finding remains to be established, and at this time one can merely hypothesize that multiple uniform patterns of tachycardia may represent multiple potential circuits of tachycardia or varying patterns of ventricular activation, possibly because of varying exit sites from one circuit of tachycardia.

Finally, specificity of the stimulation protocol may be examined by noting the induction of polymorphic tachycardias in patients whose spontaneous tachycardia is uniform and who also have uniform patterns of tachycardias induced by programmed stimulation (Table 5). In the patients with documented sustained ventricular arrhythmias, this occurred with a frequency of 19% (26 of 136 patients). There was no significant difference in the frequency of induction of these apparently ‘‘nonclinical’’ arrhythmias by any mode of stimulation. That is, such tachycardias were not induced more frequently by triple extrastimuli than by single or double ventricular extrastimuli.

The results obtained with this stimulation protocol in the 71 patients without previously documented or suspected ventricular arrhythmias suggest that adding a third extrastimulus reduces the specificity of this protocol in this patient population. Similar observations have been reported previously. In this patient population, the majority of arrhythmias were induced by triple extrastimuli, and these were polymorphic and nonsustained. However, this protocol was specifically designed to attempt to avoid inducing sustained rapid arrhythmias in this patient population and used a different end point for stimulation. Thus, results of this may not be directly applicable to patients having pre-
viously documented arrhythmias. When the results of stimulation with only single and double extrastimuli are examined in this population, there is a marked decrease in the number of arrhythmias induced, especially in those patients without previous myocardial infarction. However, the induction of VT having a uniform pattern in this group, primarily in patients with left ventricular aneurysms, suggests that there is a population of patients who have suffered myocardial infarction with aneurysm formation in whom the substrate for VT exists but remains latent and is presumably “exposed” by programmed ventricular stimulation. How many, if any, of these patients will develop spontaneous ventricular arrhythmias will require long-term follow-up.

A limitation in the evaluation of patients who present with ventricular fibrillation and cardiac arrest is that rapid VTs with uniform patterns are frequently induced in the laboratory, the specificity of which has been questioned. However, these induced tachycardias uniformly are associated with loss of consciousness and/or degeneration into ventricular fibrillation in the laboratory. Likewise, Holter monitoring of patients during cardiac arrest has shown that ventricular fibrillation is usually initiated by VT. This limitation is common to all human studies in which it is frequently impossible to document the onset of arrhythmias in free living subjects. However, the correlation between Holter findings, observations of antiarrhythmic drug effects on induced arrhythmias, and the outcomes of patients whose therapy was guided by the results of electrophysiologic tests, all support the clinical relevance of the induced VT.

Limitations of study. Although we have divided the patients with documented spontaneous tachyarrhythmias into two relatively distinct groups based on clinical presentation, this distinction may be somewhat artifactual. That is, patients who presented with stable VT while taking an antiarrhythmic drug might have developed cardiac arrest had they not been receiving an antiarrhythmic drug that slowed the spontaneous tachycardia. Thus, empiric antiarrhythmic therapy may have influenced the initial clinical presentation of some patients. However, this is not a likely source of major error in the study, as the prevalence of antiarrhythmic therapy at the time of the initial arrhythmia was not significantly different between the two patient groups. In addition, the potential misclassification of some patients would increase the numbers of patients in the VT group rather than in the cardiac arrest group. Some patients classified in the VT group could have rapid polymorphic tachycardias induced in the control state that would be converted into slower and more uniform tachycardias in the presence of antiarrhythmic drugs. Thus, empiric antiarrhythmic therapy taken at the time of the initial event would tend to mask potential differences among the characteristics of induced arrhythmias in the two patient groups, rather than to accentuate them.

Clinical implications. This study has shown that adding a third ventricular extrastimulus to standard ventricular stimulation protocols increases the sensitivity of induction of arrhythmia in patients with documented sustained VT and cardiac arrest. The use of triple extrastimuli virtually eliminates the need for left ventricular stimulation in patients who present with hemodynamically stable sustained VT and may reduce the requirement for left ventricular stimulation in patients presenting with cardiac arrest. Although the likelihood of induction of arrhythmia is increased in both patient groups, the sensitivity of this technique for induction of arrhythmia remains lower in patients presenting with cardiac arrest, regardless of the stimulation mode used. The results of the stimulation protocol, when applied to patients without previously documented or suspected tachyarrhythmias, show that in this patient population the addition of a third extrastimulus decreases specificity. The clinical significance of non-sustained polymorphic tachycardias induced by triple extrastimuli remains uncertain, and these results emphasize the importance of documenting the cause of spontaneous arrhythmias with multiple electrocardiographic leads to ensure the correct interpretation of arrhythmias induced by programmed stimulation.

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