Programmed electrical stimulation in patients with high-grade ventricular ectopy: electrophysiologic findings and prognosis for survival

JOSEPH ANTHONY C. GOMES, M.D., ROBERT I. HARIMAN, M.D., PRITPAL S. KANG, M.D., NABIL EL-SHERIF, M.D., INTIAZ CHOWDHRY, M.D., AND JULIANNE LYONS, R.N.

ABSTRACT The significance and treatment of ventricular premature beats (VPBs) in patients without sustained ventricular tachycardia (VT), sudden death, or syncope remains unclear. We undertook a prospective study of programmed electrical stimulation (up to two extrastimuli and burst pacing) in 73 patients (age 60 ± 10 years) with high-grade VPBs who had no evidence of sustained VT, sudden death, or syncope as determined by 48 hr of monitoring in the cardiac care unit and 48 hr Holter monitoring. Fifty-six patients (76.7%) had atherosclerotic heart disease, 10 (13.7%) had cardiomyopathy or valvular heart disease, and seven (9.6%) had no evident heart disease. Thirty-seven patients (50.7%) had Lown grade IVB VPBs, 30 (41.1%) had Lown grade IVA VPBs, and six (8.2%) had Lown grade III VPBs. Programmed electrical stimulation identified two groups of subjects: group 1 comprised 20 patients (27%) in whom VT or ventricular fibrillation was induced, group 2 comprised 53 patients (73%) in whom no ventricular arrhythmia or only two to four repetitive ventricular responses were induced. There was a significant difference between the presence of atherosclerotic heart disease, old myocardial infarction, and ejection fraction of less than 40% in group 1 compared with group 2. However, there was no significant difference in the grade of VPBs between the two groups. Seventeen of 20 patients from group 1 were placed on antiarrhythmic therapy (defined by programmed electrical stimulation), whereas group 2 patients were randomly assigned to prophylactic antiarrhythmic therapy. A total of 70 patients were followed up for 30 ± 15 months. The incidence of sustained VT and/or sudden death (31.5% vs 2%; p < .001) was significantly higher in group 1 compared with group 2. There was no difference in the occurrence of sudden or nonsudden cardiac death between the treated and untreated patients in group 2. The probability of surviving 1 year (0.75 vs 1.0) and 48 months (0.35 vs 0.67) was significantly lower (p < .0008) in group 1 than in group 2. In conclusion programmed electrical stimulation defines high- and low-risk subsets for sudden death among patients with high-grade VPBs. Patients in whom arrhythmias are not inducible and those with ejection fractions of greater than 40% have a low incidence of sudden death and an excellent 1 to 2 year survival; these patients do not need prophylactic antiarrhythmic therapy.

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SEVERAL STUDIES have demonstrated that patients with recent myocardial infarction1-5 and those with chronic ischemic heart disease and old myocardial infarction6-8 who have high-grade ectopy are at increased risk for sudden or nonsudden cardiac death. Others have found that the presence of high-grade ectopy is a reflection of the severity of underlying heart disease and is not an independent risk factor for sudden cardiac death.9-11 Moreover, there are no studies that have demonstrated that prophylactic antiarrhythmic therapy in patients with high-grade ectopy results in prevention of sudden death.12, 13

In the last few years programmed cardiac stimulation has been used in the diagnosis and management of patients with recurrent sustained ventricular tachycardia (VT) and in survivors of out-of-hospital cardiac arrest.14-19 The results of these studies have demonstrated that programmed cardiac stimulation can induce the clinical ventricular arrhythmia in approximately 75% to 90% of these patients. Furthermore, these studies15-19 have also shown that use of antiarrhythmic agents that prevent the induction of ventricu-
lar tachyarrhythmias in the laboratory results in abolition and/or decrease in frequency of spontaneous VT and reduction in mortality in patients with out-of-hospital ventricular fibrillation (VF).

Ventricular premature beats (VPBs) form the bulk of ventricular arrhythmias seen in clinical practice. The significance and treatment of VPBs in patients without spontaneous VT, out-of-hospital cardiac arrest, and history of syncope remain speculative at best.\textsuperscript{12,13} As yet there are no studies that have assessed the role of programmed electrical stimulation in patients with VPBs. Accordingly, we undertook a prospective study of programmed electrical stimulation in patients with high-grade VPBs who had no evidence of sustained VT, out-of-hospital cardiac arrest, or syncope. The major aim of the study was to estimate the incidence and significance of induced ventricular arrhythmias.

**Materials and methods**

A total of 73 patients (ages 25 to 79 years) with high-grade VPBs were studied. Patients with sustained VT and histories of syncope and sudden death were excluded from the study. None of the patients had an acute or recent myocardial infarction (≤6 months), electrolyte or metabolic disturbance, or drug-induced ventricular ectopy. All were referred for evaluation of high-grade ectopy between February 1979 and February 1983. The presence or absence of heart disease was based on (1) clinical, electrocardiographic, and radiologic findings, (2) echocardiographic results, (3) treadmill exercise testing, and (4) cardiac nuclear scanning. In addition, 35 of 73 patients underwent cardiac catheterization. In all patients the ejection fraction was determined by radionuclide scanning. Patients were monitored in the coronary care unit for 48 hr, and at least two 24 hr ambulatory Holter recordings were obtained from each patient to establish the absence of sustained VT and syncope. The VPBs were graded according to the system devised by Lown et al.\textsuperscript{20,21}

After the experimental nature of the procedure was explained to the patients and written informed consent was obtained, two or three quadrupolar electrode catheters (U.S.C. #6) were introduced percutaneously and advanced under electrocardiographic monitoring and fluoroscopic guidance into the right atrium, across the tricuspid valve for recording His bundle activity, and into the right ventricular apex or outflow tract. The proximal poles of the electrode catheters were used for recording and the distal poles for stimulation. Stimulation was done with a programmable stimulator that delivered impulses of 1.5 msec duration and a mean total current of 1 mA, which corresponded to twice diastolic threshold. Two or more electrocardiographic leads, intracardiac electrograms at filter settings of 30 to 500 Hz, and time lines generated at 40,200 and 1000 msec were displayed on a multichannel oscilloscope (VR 12 multichannel recorder) and recorded on thermal paper at speed of 50 to 100 mm/sec.

The following stimulation protocol was used for all patients:

1. Incremental atrial pacing up to rates of 200 beats/min.
2. Premature atrial stimulation during atrial pacing at a fixed cycle length.
3. Incremental ventricular pacing up to rates of 120 beats/min; then burst pacing up to rates of 240 beats/min. Premature ventricular stimulation consisted of the following:

\textit{S} method. A single premature ventricular stimulus (S) was introduced after every 8 supraventricular beats at progressively decreasing coupling intervals until ventricular muscle refractoriness.

\textit{S} method. A single premature ventricular stimulus (S) was introduced after every 8 ventricular paced beats (S) at decreasing coupling intervals until ventricular muscle refractoriness.

\textit{S} method. Double ventricular stimuli (S, S, S) were introduced during a basic paced ventricular cycle (S) starting at an S, S interval of 60 msec longer than the ventricular effective refractory period and S, S equal to S, S interval. The S, S interval was progressively decreased by 10 msec until S was refractory. S, S was then shortened and S reintroduced until S captured the ventricle or S became refractory. None of the patients had S stimulation or left ventricular stimulation. All patients had premature ventricular stimulation at 2 cycle lengths (600 and 500 msec). If right ventricular apical stimulation did not initiate ventricular arrhythmias then right ventricular outflow stimulation was performed or vice versa.

If sustained or nonsustained VT or VF was induced, sequential drug studies were performed and the patients were discharged on the antiarrhythmic agent that produced a favorable response. If neither of the above was induced then the patients were randomly assigned to oral drug therapy on the day after the electrophysiologic study. Randomization was done on an alternate basis. Placebo was not used for patients who received no antiarrhythmic therapy. Program compliance was assessed by pill count and blood levels of antiarrhythmic agents. The selection of oral drugs was independent of the number of repetitive ventricular responses (RVRs) in these patients. We have previously shown that the induction of RVRs in patients without spontaneous VT is not associated with an increased risk of sudden cardiac death.\textsuperscript{22}

Statistical analysis was performed by \textit{χ}² analysis and Student’s \textit{t} test for unpaired data. Survival curves were determined by the generalized Wilcoxon survivorship analysis.\textsuperscript{23} All values represent the mean ± SD.

**Definition of terms.** Sustained VT was defined as a run of VT in response to any of the stimulation techniques that lasted for 30 sec or longer or required immediate termination due to hemodynamic compromise. Nonsustained VT was defined as a run of 5 or more successive ventricular beats in response to any of the stimulation techniques that terminated spontaneously and did not last for 30 sec or longer.

RVRs were defined as 2 or more but not more than four successive ventricular depolarizations, not bundle branch reentrant in origin, in response to any of the stimulation techniques. The induction of sustained or nonsustained VT and RVRs was considered to be reproducible only if they could be induced on two occasions at the same coupling interval and/or if they could be induced successfully at two different coupling intervals. Induction was not reattempted in those patients whose VT degenerated into VF.

Sudden death was defined as unheralded death occurring within 1 hr of the onset of symptoms. If the patient was found dead in bed, the absence of any change in clinical status before he went to bed was ascertained by questioning family members.

**Results**

**Clinical characteristics.** The important clinical characteristics of the 73 patients are listed in table 1. Fifty-six patients (76.7%) had atherosclerotic heart disease, 10 (13.7%) had congestive cardiomyopathy, valvular heart...
### TABLE 1
Clinical characteristics

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>Frequency^A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>73 (100)</td>
</tr>
<tr>
<td>ASHD</td>
<td>56 (76.7)</td>
</tr>
<tr>
<td>Cardiomyopathy; valvular heart disease</td>
<td>10 (13.7)</td>
</tr>
<tr>
<td>No evident heart disease</td>
<td>7 (9.6)</td>
</tr>
<tr>
<td>Old myocardial infarction (≥6 months)</td>
<td>40 (54.7)</td>
</tr>
<tr>
<td>Ejection fraction &lt;40%</td>
<td>37 (50.6)</td>
</tr>
<tr>
<td>No. of coronary vessels with ≥75% stenosis (n = 30)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>8 (27)</td>
</tr>
<tr>
<td>2</td>
<td>12 (40)</td>
</tr>
<tr>
<td>3</td>
<td>10 (33)</td>
</tr>
<tr>
<td>VPB grading</td>
<td></td>
</tr>
<tr>
<td>Grade IVB</td>
<td>37 (50.7)</td>
</tr>
<tr>
<td>Grade IVA</td>
<td>30 (41.1)</td>
</tr>
<tr>
<td>Grade III</td>
<td>6 (8.2)</td>
</tr>
</tbody>
</table>

ASHD = atherosclerotic heart disease.

^AExpressed as number of patients, with percentage of total in parentheses.

disease, or mitral valve prolapse, and seven (9.6%) had no evident heart disease. A total of 40 patients (54.7%) had old myocardial infarctions. Thirty-six patients (49.4%) had ejection fractions of greater than 40% (range 42% to 76%), whereas 37 patients (50.6%) had ejection fractions of less than 40% (range 12% to 39%). Thirty-three patients (59%) with atherosclerotic heart disease had ejection fractions of less than 40%. Thirty-seven patients (50.7%) had grade IVB VPBs, 30 (41.1%) had grade IVA VPBs, and six (8.2%) had grade III VPBs. None of the patients had sustained VT and/or syncope.

Electrophysiologic findings. On the basis of programmed cardiac stimulation, the patients could be divided into two groups. Group 1 comprised 20 patients (27%) in whom reproducible sustained VT (n = 8) or VT that degenerated into VF (n = 5) and reproducible nonsustained VT (n = 7) was induced. The cycle length of tachycardia ranged from 200 to 280 msec in patients with sustained VT and in those whose VT degenerated into VF. The cycle length of tachycardia was 230 to 340 msec in patients with nonsustained VT. VT was induced in 17 patients (85%) by the S1S2S3 method, in two patients by burst pacing, in one patient by both burst pacing and the S1S2S3 method, and in one patient by the S1S3 method. VT was not induced in any of these patients by the S1 method or by atrial stimulation.

All eight patients with sustained VT had presyncopal symptoms requiring prompt termination of the induced arrhythmia by pacing or external countershock. External countershock was required in all five patients with induced VF.

Group 2 comprised the remaining 53 patients (73%). In 30 patients (57%) no ventricular arrhythmia was induced, whereas in 23 patients (43%) two to four RVRs were induced in response to the S1S2S3, method of stimulation.

Serial pharmacologic and electrophysiologic testing. A total of 26 drug trials were carried out in the 20 group 1 patients. Serial drug testing was done after procainamide in 14 patients and after procainamide and quinidine sulfate in six. Suppression of the inducible arrhythmia (defined as a maximum of two RVRs during programmed stimulation) was achieved in 17 of 20 patients (85%) with one of the above antiarrhythmic agents.

Clinical differences between the two groups. The important clinical characteristics of the patients in the two groups are shown in table 2. The incidence of atherosclerotic heart disease (20/20 patients, 100%), old myocardial infarction (17/20 patients, 85%), and ejection fraction of less than 40% (17/20 patients, 85%) was significantly higher in group 1 than in group 2. However, of the patients in group 2, 36/53 (68%) had atherosclerotic heart disease, 23/53 (43%) had old myocardial infarctions, and 20/53 (38%) had ejection fractions of less than 40%. In addition, 47% of group 2 patients had two of these three clinical features. The mean ejection fraction in group 1 was significantly lower than that in group 2 (33 ± 11% vs 46 ± 19%; p < .0001). There were no significant differences in the AH and HV intervals or in the incidence of bundle branch block between the two groups. Although the incidence of grade IVB VPBs was higher in group 1 and the incidence of grade IVA and III was higher in group 2, these differences were of no statistical significance.

Follow-up studies. Seventeen patients from group 1 were discharged on the antiarrhythmic agent that successfully prevented the induction of VT. Blood levels of procainamide and quinidine on oral therapy were in the therapeutic range and similar to blood levels obtained during the stimulation study. The three patients who did not respond to procainamide and quinidine

### TABLE 2
Differences in clinical features between the two groups

<table>
<thead>
<tr>
<th>Clinical features (%)</th>
<th>VPBs (Low grade)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
</tr>
<tr>
<td>Group 1</td>
<td>20</td>
</tr>
<tr>
<td>Group 2</td>
<td>53</td>
</tr>
<tr>
<td>p value</td>
<td></td>
</tr>
</tbody>
</table>

ASHD = atherosclerotic heart disease; MI = myocardial infarction; EF = ejection fraction.
were placed on oral amiodarone administered as a loading dosage of 1200 to 1800 mg/day for 10 days. The dosage was then decreased to 400 to 800 mg/day if no high-grade VPBs were present on 24 hr ambulatory Holter recording. Group 2 patients were randomly assigned to long-term oral antiarrhythmic therapy consisting of procainamide (n = 13), quinidine sulfate (n = 10), and amiodarone (n = 3). The remaining 27 patients did not receive antiarrhythmic therapy. The patients were followed up in our arrhythmia clinic at 3 month intervals for the first year and at 6 month intervals thereafter. The follow-up protocol consisted of (1) a questionnaire on which the patient recorded history of palpitations, dizzy spells, syncopal episodes, and hospital admission for cardiac-related events, (2) a 12-lead electrocardiogram, and (3) 24-hr ambulatory Holter recording. There was a reduction in the frequency and grade of VPBs (range 65% to 90%) in all group 1 patients and in group 2 patients on antiarrhythmic therapy. There was no appreciable difference in the grade and frequency of VPBs in group 2 patients on no antiarrhythmic therapy.

**Mortality.** A total of 70 patients have been followed for 30 ± 15 months. Three patients, one from group 1 and two from group 2, have been lost to follow up. The overall cardiac mortality was 12.85%. There were six cardiac-related events (31.5%) in group 1 — five sudden deaths and one episode of spontaneous sustained VT (figure 1). In contrast, there were four cardiac-related events (7.8%) in group 2 — one sudden death (2%) and three nonsudden cardiac deaths (figure 1). The incidence of sudden death (p < .001) was significantly higher in group 1 than in group 2. There was no significant difference in the occurrence of sudden death and/or nonsudden cardiac death between the treated and untreated patients in group 2.

Of the six patients in group 1 who developed sudden death and/or spontaneous sustained VT on follow up, two had induced VF, two had induced sustained VT, and two had induced nonsustained VT. The cycle length of induced tachycardia in these patients ranged from 200 to 290 msec and was not significantly different from that of the survivors (245 ± 37 vs 245 ± 33 msec; p = NS). The three patients from group 2 who had nonsudden cardiac death had markedly depressed ejection fractions of 12%, 31%, and 22%, respectively. However, none of these three patients had inducible ventricular arrhythmias (figure 1). All three died in cardiogenic shock.

The relationship between the grade of VPBs, inducibility, and outcome is shown in table 3. Although a higher percentage of patients with grade IVB and IVA VPBs had sudden or nonsudden cardiac death, the differences in outcome for the three grades of VPBs were not statistically significant.

We used generalized Wilcoxon survivorship analysis to compare the cardiac mortality and sudden death mortality of the patients with and without inducible VT and of those with ejection fractions of less than 40% and greater than 40%. Figure 2 shows the survivorship curves for total cardiac death. In the patients with inducible VT the probability of surviving 1 year was 0.75 compared with a probability of 1.0 in the group without inducible VT. The probability of surviving 48 months was 0.35 in the group with inducible VT and 0.67 in the group without inducible VT. These differences in survival were highly significant (p < .0008).

<table>
<thead>
<tr>
<th>Table 3: Relationship between the grade of VPBs, inducibility, and outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>VPBs (Lown grade)</td>
</tr>
<tr>
<td>---------------------</td>
</tr>
<tr>
<td>IVB</td>
</tr>
<tr>
<td>IVA</td>
</tr>
<tr>
<td>III</td>
</tr>
</tbody>
</table>

SD = sudden death.

None of the differences between groups was statistically significant.

![FIGURE 1.](image) Flow diagram of the patients in both groups and their eventual outcomes. ind. = inducible VT; VA = ventricular arrhythmia; SD = sudden death.
In contrast, the probability of surviving 1 year was 0.88 in patients with ejection fractions of less than 40% and 1.0 in patients with ejection fractions of greater than 40%. The probability of surviving 48 months was 0.53 in patients with ejection fractions of less than 40% and 0.97 in patients with ejection fractions of greater than 40%. These differences in survival were statistically significant (p < .008).

The survivorship curves for sudden death in the groups with inducible and noninducible VT and in the groups with ejection fraction of less than 40% and greater than 40% are shown in figure 3. The probability of surviving 1 year was 0.75 in the group with inducible VT and 1.0 in the group without inducible VT. The probability of surviving 48 months was 0.65 in the group with inducible VT and 0.97 in the group without inducible VT. These differences in survival between the two groups were highly significant (p < .0001). In contrast, the probability of surviving 1 year was 0.88 in patients with ejection fractions of less than 40% and 1.0 in patients with ejection fractions of greater than 40%. The probability of surviving 48 months was 0.84 in patients with ejection fractions of less than 40% and 0.97 in patients with ejection fractions of greater than 40%. These differences in survival were significant (p < .03). The relative risk for sudden death as expressed by odds ratio was also significantly greater for inducibility (r = 15.25, p < .001) than for ejection fraction (r = 5.63, p < .08).

Discussion

Several studies have shown that the presence of high-grade VPBs is associated with an increased risk for sudden or nonsudden cardiac death in patients with recent myocardial infarctions1-6 and in those with chronic ischemic heart disease and old myocardial infarctions.7 Despite this contention, there are no studies that have shown efficacy of prophylactic antiarrhythmic agents in the assessment of risk for sudden death. Because of the danger of significant toxic reactions, including possible fatality and the questionable efficacy of prophylactic antiarrhythmic therapy,24 the widespread use of antiarrhythmic agents in patients with high-grade VPBs will require better identification of potential victims of sudden death. Bigger et al.5 found a 37% 1 year mortality despite the use of prophylactic antiarrhythmic therapy in 50 survivors of myocardial infarction, of which 50% had one episode of VT; in
FIGURE 3. Survival curves for sudden death in patients with and without inducible VT and in those with ejection fractions (E.F.) of >40% and <40%. For further explanation see text.

30% of the patients the longest run of VT was three consecutive complexes. Thus they suggested additional studies of arrhythmic potential such as treadmill exercise testing or clinical electrophysiologic studies in these patients.

The role of programmed cardiac stimulation. The results of this study indicate that in patients with high-grade VPBs, programmed electrical stimulation can define high- and low-risk subgroups (with and without inducible VT) irrespective of the grade of VPBs observed on monitoring and ambulatory Holter recordings. Programmed cardiac stimulation initiated ventricular tachyarrhythmia in 27% of 73 patients with high-grade VPBs, whereas in the remaining 73% of patients no ventricular arrhythmia or only two to four RVRRs were induced. The absence of spontaneous sustained VT in these patients was confirmed by extensive monitoring (rest and ambulatory) and by the absence of a history of syncope and sudden death. Furthermore, all these patients were specifically referred for evaluation of high-grade VPBs. It should be noted that an aggressive stimulation protocol (i.e., use of a third extrastimulus [S₃] or left ventricular stimulation) was not used in any of these patients. This was specifically avoided because (1) previous studies with similar stimulation protocols (i.e., up to two extrastimuli and burst pacing) have shown that VT can be induced only in patients with clinical spontaneous VT and in survivors of sudden death, whereas VT and/or VF cannot be induced in patients without spontaneous sustained VT and (2) we could not ethically justify invasion of the left ventricle in the patients without spontaneous sustained VT and/or sudden death. To our knowledge, these observations of programmed electrical stimulation in patients with high-grade ectopy have not been previously reported. It is reasonable to postulate that (1) patients with inducible arrhythmia may be at a higher risk for sudden cardiac death than those without inducible arrhythmia and (2) the inducible ventricular arrhythmia is a laboratory phenomenon of no clinical significance. However, our findings of a significantly higher incidence of sudden death in patients with inducible VT and high-grade ectopy support the former argument. It should be noted that the results of this study are applicable to patients with high-grade ectopy in the presence of ischemic heart disease and old myocardial infarctions (≥6 months) and do not necessarily apply to patients with recent myocardial infarctions.

Factors predictive of inducible VT. Previous studies in patients with ischemic heart disease and recent or old myocardial infarctions have assessed the relationship between the presence of other risk factors and high-grade ectopy and the risk of sudden death. The majority of these studies have found that although there is a significant association between multiple risk factors, including ejection fraction of less than 40%, the presence of high-grade ectopy is an independent risk factor for sudden death. Califf et al., however,
found that the ventricular arrhythmia score does not contribute independent prognostic information when invasive measurements are included. Indeed, they noted that the ejection fraction was more useful than the ventricular arrhythmia score in identifying patients at high risk of sudden death. Ruberman et al. have shown that the enhanced risk of sudden death in patients with high-grade ectopy (grade 3 or higher) can last for up to 5.5 years after myocardial infarction. In this study we assessed the relationship between the presence of other risk factors and inducibility in patients with high-grade VPBs. The results of this study indicate that the patients with inducible VT had a significantly higher incidence of atherosclerotic heart disease, old myocardial infarctions, and ejection fractions of less than 40% when compared with the patients without inducible VT. However, among the patients without inducible VT, 37% to 67% had one of these risk factors and 47% had two of the three risk factors. These observations suggest that although the presence of multiple risk factors is closely associated with induction of VT, induction seems to be dependent on the presence of a requisite electrophysiologic substrate that may or may not be present in all patients with high-grade VPBs.

Of considerable importance is the finding that the grade of VPBs (grade III to IVB) was not significantly different between the patients with and without inducible VT or between survivors and nonsurvivors. In this study we did not include patients with lesser grades of VPBs since it has been shown that patients with grade I to II VPBs do not have a high incidence of sudden death when compared with those with no VPBs.7 Thus, although Holter monitoring is of value in differentiating patients with high-grade ectopy from those with no ectopy or low-grade ectopy, our findings suggest that it provides no information in the selection of a high-risk subset for sudden death in the group with high-grade ventricular ectopy.

Antiarrhythmic therapy. Previous studies have shown that identification of at least one drug that prevents induction of sustained VT over the short term in patients with spontaneous VT is possible in approximately 70% of patients if several drugs are investigated. Recently, however, Spielman et al. and Sverdlow et al. reported on the predictors of the success or failure of medical therapy in patients with chronic recurrent sustained VT by a discriminant analysis. Spielman et al. found a successful medical regimen for only 35% of patients, and Sverdlow et al. found a successful regimen in 30% of patients. In the Spielman study four factors correlated with medical success: age less than 45 years, ejection fraction greater than 50%, hypokinesis as the only contraction abnormality, and the absence of organic heart disease. It is clear that these observations do not apply to patients with high-grade ectopy and absence of spontaneous sustained VT. It is of interest that identification of at least one drug that prevents induction of VT with short-term therapy was possible in 85% of our group 1 patients. Although the reason for this difference between patients with inducible VT and high-grade ectopy and those with spontaneous recurrent VT remains unclear, this observation suggests that patients with inducible VT and high-grade ectopy are more amenable to antiarrhythmic therapy that prevents induction of VT despite the presence of atherosclerotic heart disease, old myocardial infarction, and ejection fraction of less than 40%.

Mortality. We found a substantial and significant difference in sudden death mortality between patients with and without inducible VT. The group with inducible VT had a higher incidence of sudden death and/or spontaneous VT (31.5%) in contrast to the group without inducible arrhythmia. Furthermore, survival curves showed that inducibility and noninducibility of VT were more accurate in distinguishing patients at high and low risk for sudden death at 1 year and 48 months and represented a better risk factor than ejection fraction. In addition, survival curves also showed that inducibility and noninducibility of VT were more accurate in predicting total cardiac death at 1 year, but ejection fraction was a better risk factor at 48 months. Of considerable importance was the finding that in the patients without inducible VT there was no significant difference in the occurrence of sudden death and non-sudden death between treated and untreated patients. These findings suggest that (1) inducibility of VT/VF carries a high risk for future sudden death; (2) patients without inducible VT and those with ejection fractions of greater than 40% have a low incidence of sudden death and an excellent 1 to 2 year prognosis irrespective of antiarrhythmic therapy, and (3) the induction of two to four RVRs in patients with high-grade ectopy is not a predictor for sudden death. This finding is in agreement with our previous observations in patients with and without organic heart disease.

Limitations of the study. In this study a control group was not included among the patients with inducible VT/VF. It was felt ethically unjustifiable to withhold antiarrhythmic therapy in these patients. Thus, because of this limitation it is not possible to determine what role stimulation-guided antiarrhythmic therapy played in progress of these patients. Despite stimulation-guided antiarrhythmic therapy, the sudden death

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mortality was high in this group. However, in the absence of a control group among those patients with inducible VT on no antiarrhythmic therapy, it remains unclear whether the incidence of sudden death would have been higher in the absence of stimulation-guided antiarrhythmic therapy. In addition, it also raises the possibility that the high incidence of sudden death in patients with inducible VT was causally related to the antiarrhythmic therapy itself. This possibility, however, seems unlikely, since none of the patients without inducible VT on prophylactic antiarrhythmic therapy died suddenly.

**Clinical implications.** There are several clinical implications that can be drawn from this study. (1) Programmed cardiac stimulation is of value in the evaluation of patients with high-grade VPBs, since it defines subsets at high risk (with inducible VT) and low risk (without inducible VT) for future sudden death. Nonetheless, the results of this study should be taken as preliminary evidence until more prospective and controlled studies in a larger number of patients are performed to better define the role of programmed cardiac stimulation in identifying patients at risk for sudden cardiac death. (2) The patients without inducible VT and those with an ejection fraction of less than 40% have a low incidence of sudden death and an excellent 1 to 2 year survival irrespective of prophylactic antiarrhythmic therapy. We therefore believe that these patients do not need prophylactic antiarrhythmic therapy. (3) The value of stimulation-guided antiarrhythmic therapy in patients with inducible VT will have to await controlled studies. In addition, since most of these patients have other variables that reflect abnormal left ventricular dysfunction and ischemia, these should also be treated. Until we understand the sequences that lead from asymptomatic high-grade ectopy to the final arrhythmic event, the ability to select the best modality of therapy will be limited. (4) The majority of our patients with inducible VT also had atherosclerotic heart disease, old myocardial infarctions, and ejection fractions of less than 40%. However, among the patients without inducible VT, 47% had two of these three risk factors. Thus we believe that patients with a combination of these well-known risk factors in addition to high-grade ectopy should be selected for programmed cardiac stimulation. In contrast, the results of this study suggest that patients with high-grade ectopy and ejection fractions of greater than 40% do not need electrophysiologic studies. (5) Holter monitoring is of limited value in selecting a high-risk subset for sudden death in patients with high-grade ectopy.

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**References**


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