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Determinants of the Outcome of Electrophysiologic Study in Patients With Ventricular Tachyarrhythmias

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To determine those factors predictive of the ability to both initiate and suppress ventricular tachyarrhythmias during electrophysiologic study, the results of programmed cardiac stimulation were evaluated in 261 patients: 66 presenting with nonsustained ventricular tachycardia, 91 with sustained ventricular tachycardia and 104 with ventricular fibrillation. Multivariate logistic regression analysis revealed that the presenting arrhythmia was a potent and independent predictor of the ability to provoke ventricular arrhythmias at electrophysiologic study; a history of myocardial infarction and male sex were also significant independent predictors. Of patients presenting with sustained ventricular tachycardia, 89% (81 of 91) had inducible ventricular arrhythmias compared with 61 (40 of 66) and 66% (69 of 104) of patients with nonsustained ventricular tachycardia and ventricular fibrillation, respectively.

Complete suppression of inducible arrhythmias could be achieved in only 52% (34 of 66) of patients with sustained ventricular tachycardia, compared with 73 (24 of 33) and 75% (46 of 61) of patients presenting with nonsustained ventricular tachycardia and ventricular fibrillation, respectively. Multivariate analysis showed that the major independent determinants of the ability to suppress inducible arrhythmias were the number of drug trials performed before electrophysiologic study (inversely correlated) and the nature of the induced arrhythmia.

The nature of the presenting clinical arrhythmia is, therefore, a highly significant and independent predictor of the ability to induce ventricular arrhythmias during electrophysiologic testing and an important determinant of the ability to suppress induced arrhythmias in patients with spontaneous ventricular tachyarrhythmias.

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Early studies (1–4) of patients with ventricular arrhythmias defined three types of tachyarrhythmias on the basis of configuration and duration: ventricular fibrillation, "persistent" or sustained ventricular tachycardia and "intermittent" or nonsustained ventricular tachycardia. "Intermittent" tachycardia was defined variably as comprising runs of ventricular tachycardia separated by periods of normal sinus rhythm (1), self-terminating within seconds to minutes (2) or four or more beats and lasting less than 30 seconds (3,4); "persistent" ventricular tachycardia was then defined as a run of tachycardia uninterrupted throughout the period of recording (1–4). Programmed electrical stimulation of the heart has been utilized recently to initiate and terminate these arrhythmias under controlled conditions, and it has been demonstrated (5–8) that the suppression of inducible tachyarrhythmias during serial antiarrhythmic drug testing may contribute to a more favorable outcome in patients in whom these arrhythmias have occurred spontaneously.

A number of clinical features, such as the pattern of clinical arrhythmia and the presence of coronary artery disease, have been shown to influence the ability to initiate ventricular tachycardia in the electrophysiology laboratory (9–12). However, it is not known if these clinical features are simply markers of more severe underlying heart disease, and, therefore, not independently related to the outcome of electrophysiologic study. In this study, we have analyzed multiple clinical, hemodynamic and electrophysiologic variables in a large group of patients with spontaneously occurring ventricular arrhythmias to determine which, if any, of these variables independently influenced the outcome of electrophysiologic study.

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Methods

Study patients. Comprehensive clinical and electrophysiologic evaluation was performed in 261 consecutive patients with a history of spontaneously occurring, electrocardiographically documented ventricular tachyarrhythmias not associated with acute myocardial infarction. Of the 261 patients, 197 were male and 64 female, with an age range of 3 to 88 years (mean 57). The underlying cardiac diagnosis was atherosclerotic heart disease in 196 patients, cardiomyopathy in 14 patients, mitral valve prolapse in 11 patients, other valvular heart disease in 11 patients, congenital heart disease (repaired tetralogy of Fallot) in 2 patients, no structural heart disease (defined on the basis of normal physical examination, chest X-ray film, electrocardiogram, echocardiogram and coronary angiography) in 12 patients and not defined in 15 patients. One hundred seven patients were studied because of one or more episodes of cardiac arrest, 29 patients because of a history of unexplained syncope and documented nonsustained ventricular tachycardia (see later) and the other 78 because of recurrent episodes of symptomatic ventricular tachycardia.

Definition of arrhythmias. Ventricular tachycardia was documented in all patients in this series by electrocardiography. A common clinical and laboratory definition of ventricular arrhythmias was used in this study. The arrhythmias with which the patients presented were classified as nonsustained ventricular tachycardia, sustained ventricular tachycardia or ventricular fibrillation. Nonsustained ventricular tachycardia was defined as tachycardia that persisted for at least 5 beats and reverted spontaneously within 100 beats to sinus rhythm. Sustained ventricular tachycardia was defined as tachycardia that persisted for at least 100 beats or that required pacing, drug intervention or external countershock for termination. In a minority of patients who demonstrated more than one type of clinical arrhythmia, the presenting arrhythmia prompting electrophysiologic study was defined as the arrhythmia of greatest severity (ventricular fibrillation > sustained ventricular tachycardia > nonsustained ventricular tachycardia). On the basis of this classification, 66 patients presented with nonsustained tachycardia, 91 with sustained ventricular tachycardia and 104 with ventricular fibrillation.

Electrophysiologic study. All patients gave informed consent to intracardiac electrophysiologic evaluation. Antiarrhythmic drugs were withheld for at least five half-lives before initial electrophysiologic study. Electrode catheters were inserted percutaneously and positioned under fluoroscopic guidance in the high right atrium, across the tricuspid valve in a position that allowed a His bundle deflection to be recorded and in the right ventricular apex. Cardiac stimulation was performed with a programmable constant current stimulator (Medtronic models 5325 or 2346) that delivered rectangular pulses of 2 ms duration at two to five times the diastolic threshold. Stimulation was performed from the right ventricular apex in all patients, with the introduction of up to two premature ventricular depolarizations during normal sinus rhythm and during atrial and ventricular pacing at multiple drive cycle lengths, as well as three to five beat bursts of rapid ventricular pacing at incremental rates until ventricular tachycardia was induced or refractoriness encountered. In the last 43 patients, a third right ventricular extrastimulus (S_4) was introduced if no arrhythmia was initiated by double premature extrastimuli.

The protocol was carried to completion or until the end point of programmed cardiac stimulation was achieved, that is, the initiation of either sustained ventricular tachycardia or the reproducible initiation (≥three times) of nonsustained symptomatic ventricular tachycardia in response to some portion of the stimulation protocol. Asymptomatic nonsustained ventricular tachycardia was not considered an end point in this study. If the initiation of nonsustained ventricular tachycardia resulted in either angina or presyncope, programmed cardiac stimulation was stopped without proceeding to more provocative modes of stimulation. If sustained ventricular tachycardia was induced, extrastimuli or bursts of rapid ventricular pacing were applied in an attempt to interrupt the arrhythmia. Sustained arrhythmias resulting in angina or loss of consciousness were terminated with immediate asynchronous external electrical countershock. The reproducibility of these sustained arrhythmias or induced ventricular fibrillation was not assessed. In those patients in whom both nonsustained and sustained ventricular tachycardias were induced, sustained ventricular tachycardia was defined as the induced arrhythmia.

Serial drug testing. In 133 (70%) of the 190 patients with inducible ventricular arrhythmias, serial drug testing alone was performed in an effort to define a pharmacologic regimen that prevented the initiation of ventricular tachycardia by programmed stimulation. We administered antiarrhythmic drugs according to a previously described protocol, with drug selection on the basis of patient tolerance, ease of administration and drug history (12). Drugs were evaluated after loading and chronic oral therapy for at least 48 hours and only after adequate washout (>five half-lives) of any previously administered antiarrhythmic drugs had occurred. Antiarrhythmic medications were administered in the following daily dose ranges (in mg): quinidine sulfate, 800 to 2,400; procainamide, 3,000 to 8,000; disopyramide, 300 to 800; phenytoin, 200 to 400; propranolol, 40 to 320; mexiletine, 400 to 1,200; tocainide, 1,200 to 2,400; amiodarone, 400 to 1,200; aprindine, 50 to 150; and lorcainide, 200 to 300. When obtainable, plasma concentrations of the drug were determined at the time of testing. The ventricular stimulation protocol employed during serial drug testing was identical to that in the control study. Effective medical therapy was defined by the inability to initiate ventricular tachycardia (≥five beats) by programmed stimulation.

Analysis of data. Univariate statistical methods were used to screen those clinical variables associated with the induction of ventricular arrhythmias by programmed cardiac stimulation at initial electrophysiologic study and the ability to suppress the induced arrhythmia during serial antiarrhythmic testing. The following variables were analyzed: age, sex, underlying cardiac diagnosis, presenting clinical arrhythmia, reasons for electrophysiologic study (cardiac arrest, syncope, recurrent symptomatic arrhythmia, definition of the mechanisms of a wide complex tachycardia), approximate number of symptomatic episodes of tachyarrhythmia before electrophysiologic study, total duration of arrhythmia from first episode, occurrence of one or more myocardial infarctions before study, presence or absence of left ventricular aneurysm as determined by ventriculography or gated blood pool scan, or both, left ventricular ejection fraction defined by ventriculography or gated blood pool scan analysis, number of empiric antiarrhythmic drug trials before electrophysiologic study and number of coronary vessels with significant (>50% narrowing of luminal diameter) stenosis as determined by coronary angiography. The time of entry into the study was also evaluated as a check both on the potential change in the nature of the referred patient group over time and on the refinement of electrophysiologic techniques over the study period. In addition, the subgroup of patients studied with triple premature ventricular extrastimuli was compared with the entire patient group with regard to the incidence of inducible arrhythmia. For the analysis of ability to suppress induced arrhythmia, the following variables also were evaluated: nature of the induced arrhythmia (nonsustained ventricular tachycardia, sustained ventricular tachycardia, ventricular fibrillation), mode of initiation of arrhythmia (number of premature ventricular depolarizations required during sinus rhythm or ventricular pacing or bursts of rapid ventricular pacing) and the rate of induced arrhythmia.

Multivariate methods, logistic regression analysis and the Cox model of proportional hazards with the Breslow modification (13,14) were then applied to those variables determined to have at least marginal ($p < 0.10$) predictive value from the univariate analyses. In this manner, significant ($p < 0.05$) independent predictors of both inducibility and the ability to fully suppress induced arrhythmias were identified. When values for catheterization variables were not available because angiographic studies were not undertaken, patients with missing variables were excluded from univariate analysis. Group mean values for such variables were computed for all patients in whom these variables were not missing and then substituted for the missing values to enable a multivariate analysis of the data (8).

Results

Clinical characteristics of study patients as a function of presenting arrhythmia (Table 1). A significantly greater prevalence of nonatherosclerotic heart disease was found in the group of patients presenting with nonsustained ventricular tachycardia than in the other two groups. A greater prevalence of previous myocardial infarction and left ventricular aneurysm was found in patients with sustained ventricular tachycardia, although this finding was of borderline significance.

Induction of arrhythmia at initial electrophysiologic study. Among 261 patients with previously documented

Table 1. Clinical Characteristics of 261 Patients on the Basis of Presenting Arrhythmia

	Nonsustained VT (n = 66)	Sustained VT (n = 91)	VF (n = 104)
Cardiac diagnosis*			
Atherosclerotic	39 (59%)	76 (83.5%)	81 (80%)
Nonatherosclerotic	27 (50%)	15 (16.5%)	23 (22%)
Sex			
Male	43 (65%)	77 (85%)	77 (74%)
Female	23 (35%)	14 (15%)	27 (26%)
Age (yr)	21 to 28 (mean 58)	17 to 80 (mean 59)	3 to 75 (mean 55)
Myocardial infarction			
None	40 (61%)	34 (37%)	55 (53%)
Anterior	13 (20%)	28 (31%)	24 (23%)
Inferior	9 (14%)	23 (25%)	14 (13.5%)
Both anterior and inferior	4 (6%)	6 (6.5%)	11 (10.5%)
LV aneurysm present	6 (9%)	30 (33%)	15 (14%)
LV ejection fraction (%)	13 to 90 (mean 42)	10 to 79 (mean 37)	8 to 81 (mean 39)
Previous no. of empiric drug trials	0 to 6 (mean 2.2)	0 to 7 (mean 2.9)	0 to 6 (mean 2.6)

*$p < 0.05$. LV = left ventricular; VF = ventricular fibrillation; VT = ventricular tachycardia.

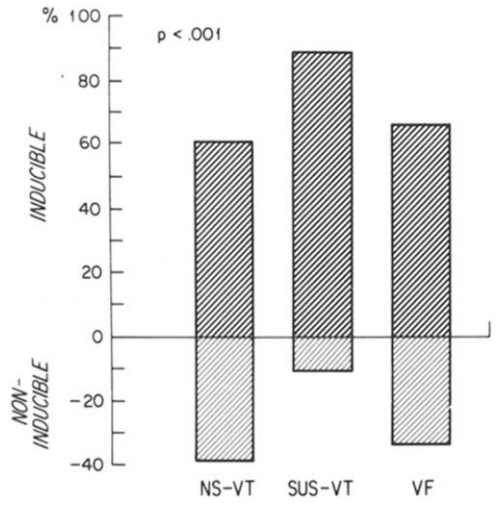

Figure 1. The incidence of inducible ventricular arrhythmias is plotted as a function of the clinical arrhythmia with which the patients presented. NS-VT = nonsustained ventricular tachycardia; SUS-VT = sustained ventricular tachycardia; VF = ventricular fibrillation.

ventricular tachyarrhythmias, ventricular tachycardia or fibrillation was induced at the time of initial electrophysiologic study in 190 patients (73%) in the absence of antiarrhythmic agents. The arrhythmia induced was nonsustained ventricular tachycardia in 83 patients, sustained ventricular tachycardia in 95 patients and ventricular fibrillation in 12 patients. Of the 83 patients in whom nonsustained ventricular tachycardia was induced, 10 patients were symptomatic with associated presyncope, resulting in termination of the study. Induced nonsustained ventricular tachycardia was defined as polymorphic in 27 of the 83 patients, with multiple episodes initiated in each. This subgroup included 9 patients with previously documented nonsustained ventricular tachycardia, 5 with previous sustained ventricular tachycardia and 13 with previous ventricular fibrillation.

Univariate analysis demonstrated that the nature of the presenting clinical arrhythmia was a significant determinant of the ability to induce ventricular arrhythmias during programmed cardiac stimulation (Fig. 1). Of 91 patients presenting with sustained ventricular tachycardia, 81 (89%) had ventricular arrhythmias initiated at initial electrophysiologic study, while only 66 (69 of 104) and 61% (40 of 66) of patients presenting with ventricular fibrillation and nonsustained ventricular tachycardia, respectively, had arrhythmias induced ($p < 0.001$). Of the subgroup of patients studied with triple premature ventricular extrastimuli, similar rates of induction overall were found for the three types of arrhythmias (13 [100%] of 13 patients with sustained ventricular tachycardia, 11 [65%] of 17 patients with ventricular fibrillation and 7 [54%] of 13 patients with nonsustained ventricular tachycardia; $p = 0.016$). The characteristics of the induced arrhythmia as a function of the presenting arrhythmia are depicted in Table 2.

Most patients with induced arrhythmia (157 of 190) required no greater than two ventricular premature depolarizations during sinus rhythm or ventricular pacing to initiate the arrhythmia. The tachyarrhythmia induced was generally nonsustained in patients presenting with nonsustained ventricular tachycardia, and was predominantly sustained in those presenting with sustained ventricular tachycardia; no predominant pattern was evident in patients presenting with ventricular fibrillation. Ventricular fibrillation itself was provoked rarely during these studies.

Multivariate logistic regression analysis was then performed to determine whether the presenting arrhythmia was

Table 2. Characteristics of the Induced Arrhythmia as a Function of the Presenting Arrhythmia

	Presenting Arrhythmia		
	Nonsustained VT (n = 40)	Sustained VT (n = 81)	VF (n = 69)
Induced arrhythmia			
Nonsustained VT	29 (72.5%)	20 (24.7%)	34 (49.3%)
Sustained VT	10 (25.0%)	61 (75.3%)	24 (34.8%)
VF	1 (2.5%)	0 (0%)	11 (15.9%)
Mode of initiation			
1 VPD-NSR/VP	7 (17.5%)	17 (21.0%)	7 (10.2%)
2 VPD-NSR/VP	28 (70.0%)	47 (58.0%)	51 (73.9%)
3 VPD-NSR/VP	1 (2.5%)	4 (4.9%)	2 (2.9%)
RVP	4 (10.0%)	13 (16.1%)	9 (13.0%)
Rate of induced arrhythmia (beats/min) mean (range)	224 (140 to 300)	207 (120 to 300)	245 (140 to 300)

RVP = rapid ventricular pacing; VPD-NSR/VP = ventricular premature depolarizations during normal sinus rhythm or ventricular pacing; VF = ventricular fibrillation; VT = ventricular tachycardia.

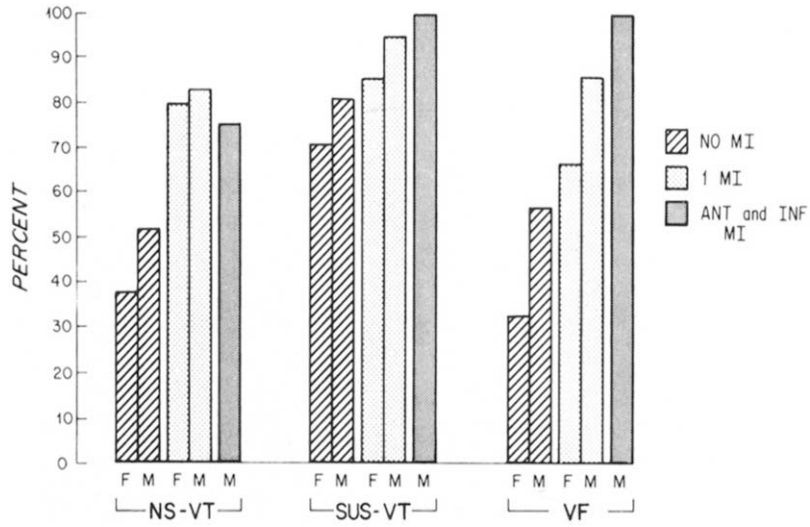

Figure 2. The probability of inducing ventricular arrhythmias in patients with a previously documented tachyarrhythmia is plotted as a function of the presenting clinical arrhythmia, sex of the patient and presence of transmural myocardial infarction (MI) (none [NO], anterior [ANT] or inferior [INF], or both anterior and inferior). F = female; M = male; other abbreviations as in Figure 1.

an independent predictor of the ability to induce arrhythmias during programmed cardiac stimulation. This analysis identified three independent predictors of induction: the nature of the presenting arrhythmia ($p = 0.0015$), a history of one or more transmural myocardial infarctions ($p < 0.001$) and male sex ($p = 0.027$). Probability bar graphs demonstrating the interaction of these three variables and the likelihood of inducing a ventricular tachyarrhythmia during programmed cardiac stimulation are shown in Figure 2.

Suppression of induced arrhythmia. Of 190 patients with an arrhythmia induced at initial electrophysiologic study, 160 patients underwent serial drug testing to determine therapy that would prevent the initiation of ventricular tachyarrhythmias during programmed cardiac stimulation. Of these 160 patients, ventricular arrhythmias could not be provoked on the discharge treatment in 104 patients (65%). This included 24 (73%) of 33 patients presenting with nonsustained ventricular tachycardia and 46 (75%) of 61 patients presenting with ventricular fibrillation, as compared with only 34 (52%) of 66 patients presenting with sustained ventricular tachycardia ($p = 0.016$). Thus, the presenting arrhythmia proved to be a significant univariate determinant of the ability to suppress induced tachyarrhythmias in these patients (Fig. 3). When multivariate logistic regression analysis was performed, however, the presenting arrhythmia did not achieve significance in independently predicting suppression. The two variables identified as independent predictors of suppression were the number of empiric drug trials before electrophysiologic study (inversely correlated) ($p = 0.004$) and the nature of the arrhythmia induced at initial electrophysiologic study. Induced sustained ventricular tachycardia was harder to suppress (40 of 76 patients; 53% suppression rate) than induced nonsustained ventricular tachycardia (56 of 73 patients; 77% suppression rate) or induced ventricular fibrillation (8 of 11 patients; 73% suppression rate) ($p = 0.015$) (Fig. 3).

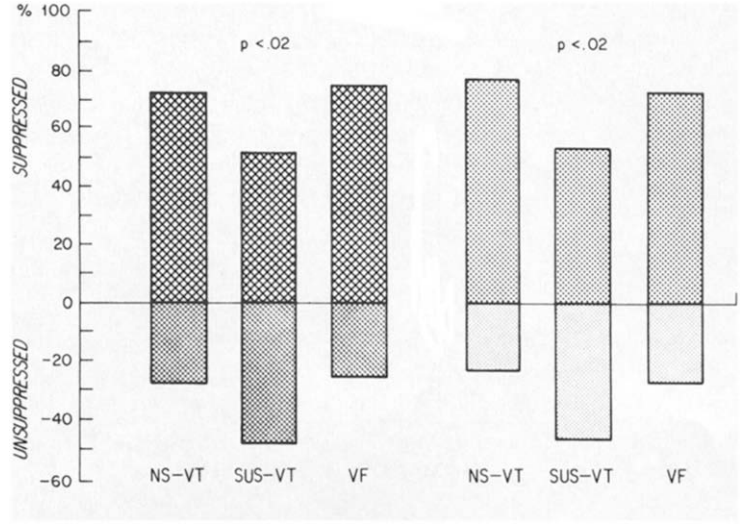

Figure 3. The incidence of full suppression of inducible ventricular arrhythmias is plotted, as a function both of the presenting clinical arrhythmia (**left panel**) and of the ventricular arrhythmia induced at initial electrophysiologic study (**right panel**). Abbreviations as in Figure 1.

Discussion

Programmed cardiac stimulation is widely used to select antiarrhythmic therapy in patients with recurrent sustained ventricular tachycardia. It has been shown that the suppression of induced arrhythmia during serial electrophysiologic testing is predictive of a more favorable long-term outcome in patients with these arrhythmias (5–8,15). The role of electrophysiologic study in patients with either ventricular fibrillation or, in particular, nonsustained ventricular tachycardia, has been less clearly defined (11,12,16–18). We examined a large patient group with these arrhythmias and evaluated the importance of multiple clinical, hemodynamic and electrophysiologic variables in independently defining the likelihood of inducing ventricular arrhythmias during programmed cardiac stimulation and suppressing induced arrhythmias during serial drug study. The identification of such patient characteristics and, therefore, of patients who are optimal candidates for electrophysiologic studies, has become increasingly important, particularly in view of the potential morbidity and cost of these procedures (19–21). Of particular importance in our study is the finding that in patients with previously documented ventricular tachyarrhythmias, the pattern of the presenting clinical arrhythmia is a potent and independent predictor of the ability to electrically induce ventricular arrhythmias and an important determinant, as well, of the ability to suppress induced tachyarrhythmias.

Influence of the presenting arrhythmia on inducibility: comparison of nonsustained and sustained ventricular tachycardia. Recent reports (15,22,23) on the application of electrophysiologic techniques to the management of patients with ventricular tachyarrhythmias have been limited largely to patients with sustained arrhythmias. In two studies (6,7) of relatively few patients with short-lasting, self-terminating episodes of ventricular tachycardia, termed "nonsustained ventricular tachycardia," initiation of arrhythmia by programmed cardiac stimulation was distinctly uncommon. In a larger series of patients, Vandepol et al. (9) compared the induction of arrhythmia during programmed cardiac stimulation in patients with sustained and nonsustained ventricular tachycardia, finding a higher rate of induction in the former group (91 compared with 62%). Naccarelli et al. (24), reporting on a smaller selected group of patients with ventricular tachycardia and no coronary artery disease, found that arrhythmias were induced in 69% of patients with sustained ventricular tachycardia but in only 34% of patients with nonsustained ventricular tachycardia, defined as tachycardia that was self-terminating within 30 seconds. We observed, similarly, a significantly higher incidence of inducible arrhythmias in patients presenting with sustained ventricular tachycardia (89%) than in those with nonsustained ventricular tachycardia (61%). The higher induction rates in our study compared with those observed by Naccarelli et al. (24) presumably reflect the more heterogeneous nature of the underlying cardiac condition in our patient group. Similar rates for induction of arrhythmia in patients with nonsustained ventricular tachycardia were reported recently by Buxton et al. (18).

Comparison of sustained ventricular tachycardia and ventricular fibrillation. Several studies (11,12,16) also have evaluated the role of electrophysiologic study in the management of patients resuscitated from cardiac arrest in whom sustained ventricular tachycardia or ventricular fibrillation was documented at the time of collapse. In the study by Josephson et al. (11), 90% of patients with sustained ventricular tachycardia at the time of cardiac arrest had inducible arrhythmias as compared with only 43% of patients whose initially recorded rhythm was ventricular fibrillation. The higher arrhythmia induction rate noted for patients with sustained ventricular tachycardia compared with that in patients presenting with ventricular fibrillation is in accord with our observations. The higher induction rate in our group with ventricular fibrillation compared with that found by Josephson et al. (11) (61 versus 43%) may reflect differences in the nature of the patient group or the stimulation protocol used. In a preliminary report, Swerdlow et al. (10) found a significant difference in arrhythmia induction rate among patients presenting with sustained ventricular tachycardia (83%), "unsustained ventricular tachycardia" (defined as lasting six beats to 15 seconds) (58%) and ventricular fibrillation (33%), although only a few patients were included in the latter two groups.

Independent influence of the presenting arrhythmia. To date, no study has systematically analyzed the independent determinants of inducibility of arrhythmias during programmed cardiac stimulation. It has been suggested that both sustained ventricular tachycardia (as indicated earlier) and the presence of coronary artery disease are positively correlated with the ability to initiate ventricular tachyarrhythmias (9). In the first large study to examine all three types of spontaneous tachyarrhythmias, we have demonstrated that the presenting ventricular arrhythmia is an important independent predictor of the ability to induce ventricular arrhythmias during programmed cardiac stimulation.

Compared with other groups, the patients presenting with sustained ventricular tachycardia manifested a significantly greater prevalence of atherosclerotic heart disease as well as a greater tendency for both previous myocardial infarction and left ventricular aneurysm. The higher rate of tachycardia induction demonstrated in patients presenting with sustained ventricular tachycardia may, in part, reflect the presence of a stable anatomic substrate for ventricular arrhythmias (25–27). Our study, however, demonstrates that the pattern of ventricular arrhythmia is not simply a marker of the extent of underlying cardiac disease but independently determines the likelihood of inducing ventricular arrhythmias during programmed cardiac stimulation.

Influence of the presenting arrhythmia and other variables on the suppression of induced arrhythmias. Our results demonstrate that, as a group, patients presenting with sustained ventricular tachycardia have inducible arrhythmias that are more difficult to suppress when compared with patients presenting with either nonsustained ventricular tachycardia or ventricular fibrillation. A similar trend, though for a smaller group of patients without coronary artery disease, was observed by Naccarelli et al. (24). When we analyzed multiple variables in a logistic regression model, however, the nature of the presenting arrhythmia itself did not independently predict the likelihood of suppression of induced arrhythmia. Rather, the nature of the induced arrhythmia was of greater importance. The significance of these findings is not entirely clear. We (17) and others (9,24) have observed that the correlation between the presenting and induced arrhythmia is great, although not absolute; the induced arrhythmia may in part reflect the presenting arrhythmia but apparently carries with it additional significance.

Our study found that the number of empiric drug trials before electrophysiologic study was also a significant independent predictor of the ability to achieve full arrhythmia suppression. Swiryn et al. (28) similarly found in a smaller group of patients presenting only with sustained ventricular tachycardia that the number of empiric drug trials before study was the one predictor of suppression. In an analysis of patients with sustained ventricular tachycardia or ventricular fibrillation, Swerdlow et al. (20) identified three variables that were independently predictive of drug response: fewer coronary arteries with 70% or greater stenosis, female sex and fewer episodes of arrhythmias. When a predictor function incorporating these variables was applied prospectively to a small group of patients, the likelihood of benefit from electrophysiologic drug testing was successfully predicted. Spielman et al. (19), using discriminant analysis, similarly constructed a predictor function, utilizing eight variables that included presence of left ventricular aneurysm, left ventricular ejection fraction, age and presence of coronary artery disease.

Study limitations. Recently, the administration of triple ventricular premature depolarizations during sinus rhythm and ventricular pacing has been incorporated into the stimulation protocol of most electrophysiology laboratories. This technique has increased the sensitivity of programmed cardiac stimulation techniques in inducing arrhythmias in patients with previously documented ventricular tachycardia or ventricular fibrillation (29,30). Although this approach was not available to the patients evaluated during the early part of our study, the influence of the presenting arrhythmia on arrhythmia induction was the same for the subgroup of patients studied more recently with triple premature extrastimuli as for the entire patient group; that is, ventricular tachyarrhythmias were most easily induced in patients presenting with sustained ventricular tachycardia. Thus, independent of the stimulation mode used and the time at which patients were entered into the study, the presenting arrhythmia was a significant and independent predictor of the ability to induce ventricular arrhythmias during electrophysiologic testing.

Recently, several studies (31–34) have shown that stimulation from the left ventricular apex and right ventricular outflow tract or during isoproterenol infusion may increase the incidence of inducible ventricular arrhythmias in selected patients. Our findings may not be applicable to the outcome of electrophysiologic studies using these techniques. Similarly, because our study was limited to patients with clinically documented ventricular tachyarrhythmias, the determinants of inducibility and suppression of ventricular tachyarrhythmias in patients undergoing programmed ventricular stimulation for other indications may be different.

The definition of nonsustained ventricular tachycardia used in our analysis is arbitrary. At present, there is no standardization of the definition of electrically induced nonsustained ventricular tachycardia among various electrophysiology laboratories. The observed incidence of nonsustained tachycardia in our series might reflect the end points of our stimulation protocol in that more provocative stimulation was not undertaken once a reproducible but symptomatic nonsustained tachycardia was induced. More persistent stimulation or the use of additional stimulation sites in such cases might have resulted in a sustained tachycardia.

Electrically induced ventricular tachycardia that is nonsustained and polymorphic has been observed increasingly as more provocative stimulation protocols have evolved in various laboratories, and several workers (35–37) have suggested that this response may be a nonspecific finding of uncertain clinical significance. We emphasize that all patients in our study had previously documented spontaneously occurring ventricular tachyarrhythmias and that nonsustained ventricular tachycardia, when elicited, was a highly reproducible end point. In addition, for the subset of patients in whom nonsustained tachycardia was polymorphic, the presenting arrhythmia was primarily either nonsustained ventricular tachycardia or ventricular fibrillation; the question of what constitutes a "specific" stimulation response for such arrhythmias remains uncertain (12,18).

The classification of the presenting arrhythmia may, in some patients, be difficult. This is true for patients with a history of more than one type of ventricular arrhythmia, who were arbitrarily identified with the arrhythmia type of greatest severity, as well as for patients with out-of-hospital cardiac arrest. In this latter group of patients, the definition of the presenting arrhythmia may depend on the time after collapse at which the patient's rhythm was documented. Insofar as it has been recognized that sustained ventricular tachycardia often degenerates to ventricular fibrillation

(5,11,25), some patients with ventricular fibrillation might have been reclassified as having had sustained ventricular tachycardia if monitored earlier. Finally, it is possible that other unknown variables may prove to have independent importance if incorporated into our analysis.

Conclusion. The question of which patient characteristics determine optimal candidacy for serial electrophysiologic investigation is one of major clinical importance in patients with spontaneously occurring ventricular arrhythmias. This study establishes the presenting arrhythmia as a critical and independent determinant of the ability to induce arrhythmias in the electrophysiology laboratory. In particular, patients presenting with sustained ventricular tachycardia are most likely to have inducible ventricular tachyarrhythmias. However, these patients are also the least likely to attain suppression of induced arrhythmia during serial antiarrhythmic testing. Whether early consideration of nonpharmacologic therapeutic techniques may be appropriate in patients with sustained ventricular tachycardia is a question that remains to be explored.

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