Clinical significance of ventricular fibrillation-flutter induced by ventricular programmed stimulation

Two hundred twenty-four patients underwent ventricular programmed stimulation (VPS) without prior documentation of the clinical occurrence of sustained ventricular tachycardia (VT) or ventricular fibrillation-flutter (VF). Indications for VPS were: palpitations or nonsustained VT during ambulatory monitoring (85 patients), syncope or presyncope (137 patients), and a family history of sudden death (two patients). Sustained VF requiring transthoracic defibrillation was initiated by VPS in 18 patients (8.0%). Four patients were treated for inducible VF with antiarrhythmic agents directed by electropharmacologic testing; five patients were treated empirically; nine patients received no therapy. No patient has had a cardiac arrest or sudden death during a follow-up period of 25.2 ± 13.8 months (mean ± standard deviation). VF was initiated by two ventricular extrastimuli in three patients and by three extrastimuli in 15 patients. The incidence of VF was similar in patients with and without previous symptoms (8.8% vs 6.9%) or heart disease (7.1% vs 9.6%). It was significantly higher when VPS at three ventricular sites with a current of 5 mA (pulse width 2 msec) was compared to programmed stimulation at two ventricular sites with a current twice diastolic threshold (pulse width 2 msec) (15.2% vs 3.0%, $p < 0.05$). VF initiated by VPS in patients without prior VT or VF appears to be a nonspecific finding. Antiarrhythmic therapy for VF may not be necessary in these patients. (AM HEART J 109:959, 1985.)

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The clinical significance of ventricular tachycardia (VT) induced by ventricular programmed stimulation (VPS) is well described.[1-5] However, there are little data concerning the prognosis for patients in whom sustained ventricular fibrillation-flutter (VF) is initiated during electrophysiologic testing. A low incidence of VF has been reported by several authors.[6-10] Spielman et al.[6] have reported a 3.3% incidence of VF during VPS in patients with prior documented or suspected VT or VF. They observed a subsequent clinical recurrence of VF in the majority of these patients despite antiarrhythmic therapy directed by electropharmacologic testing, and sug-

gested that VF initiated by VPS occurs primarily in those patients in whom it has previously occurred or in whom it will occur spontaneously.[6] More recent studies have questioned the significance of induced VF, noting that its initiation and incidence may depend on factors such as the number of premature stimuli required and the current strength used during VPS.[7-9] We therefore analyzed the data from 224 consecutive patients within a clinical history of VT or VF who underwent VPS in order to determine the clinical significance of induced VF in this group of patients.
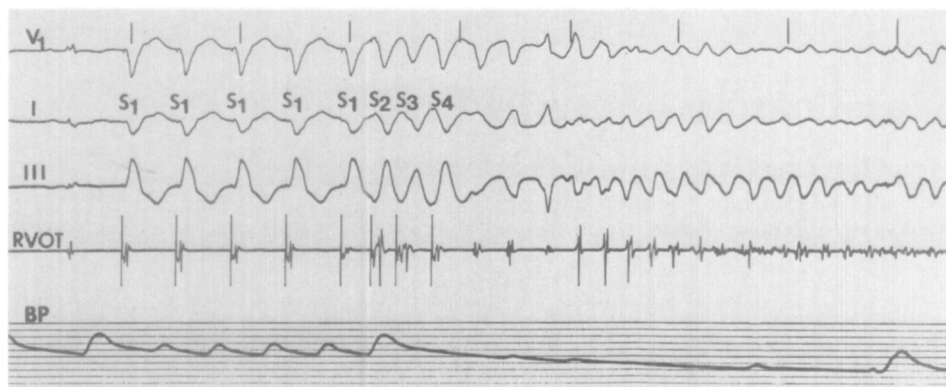
METHODS

Population tested. Two hundred twenty-four patients who underwent electrophysiologic testing were evaluated. Seventy-seven patients had coronary artery disease, with a history of myocardial infarction in 49 patients. Eighteen patients had mitral valve prolapse, 14 patients had mitral regurgitation or aortic insufficiency, 26 patients had dilated cardiomyopathy, four patients had nonobstructive hypertrophic cardiomyopathy, one patient had sarcoid heart disease, and one patient had corrected transposition of the great vessels. Eighty-three patients had no clinical

Fig. 1. Ventricular fibrillation-flutter (VF) initiated with three extrastimuli following ventricular overdrive pacing of the right ventricular outflow tract. From *top* to *bottom* are electrocardiographic leads V_1, I and III, an intracardiac electrogram from the right ventricular outflow tract *(RVOT)*, and arterial blood pressure *(BP)* recorded on a scale of 0 to 200 mm Hg. The VF cycle length is 180 to 200 msec. The QRS complexes and the intraventricular electrograms are polymorphous, and the intraventricular electrograms are fractionated.

evidence of heart disease. Indications for VPS in this group of patients were: palpitations or prior nonsustained VT (85 patients), unexplained syncope (112 patients), presyncope (25 patients), and family history of sudden death (two patients). No patient demonstrated a prolonged QT interval or preexcitation.

For the purpose of this analysis, VF was defined as having a cycle length of ≤200 msec and being polymorphous (Fig. 1). Sustained VF was defined as having a duration of ≥30 seconds or requiring defibrillation due to circulatory collapse and loss of consciousness. Cases in which VF was initiated by ventricular overdrive pacing during sustained VT, or in which unimorphic VT spontaneously degenerated into VF, were not included in this analysis.

Electrophysiologic studies. Electrophysiologic studies were performed in the nonsedated, postabsorptive state after informed consent was obtained. Antiarrhythmic therapy was discontinued for a minimum of 4 half-lives prior to VPS. Two or three quadripolar or bipolar catheters were inserted percutaneously and were positioned in the heart under fluoroscopic guidance. The number of recording sites varied, but usually included the high right atrium, the His bundle electrogram, the right ventricular apex, and/or the left ventricular apex. Ventricular stimulation was performed using a programmable stimulator and an isolated constant current source (Bloom Associates, Ltd., Reading, Pa.).

Our stimulation protocol evolved over the 4.5 years of this study. One hundred eighteen patients underwent stimulation at one right and one left ventricular site with a current twice diastolic threshold (pulse width 2 msec). The next 106 patients underwent stimulation at two right ventricular sites and at one left ventricular site with a fixed current of 5 mA (pulse width 2 msec). Left ventricular stimulation was not performed if sustained VT was induced during right VPS or if there was a contraindication to left ventricular stimulation.

Our protocol for VPS has been described previously.[9] Ventricular overdrive pacing was performed initially at the right ventricular apex at cycle lengths of 600 to 250 msec. Ventricular programmed stimulation was then performed at one or two drive cycle lengths (500 msec, or 500 and 400 msec) using one, two, and three extrastimuli. If VT or VF was not initiated, the next ventricular site was then stimulated in a similar fashion. The protocol was continued until VT or VF with a duration of ≥30 seconds or circulatory collapse was initiated, or until nonsustained, polymorphus VT having a cycle length ≤210 msec and a duration ≥10 seconds was initiated at least twice. During electropharmacologic testing, the same protocol used during baseline study was repeated following acute IV drug administration to determine therapeutic efficacy.

Acute electropharmacologic testing was performed in 15 of 18 cases in which sustained VF was initiated, using procainamide (20 mg/kg), propranolol (0.2 mg/kg), or encainide (0.9 mg/kg). Chronic antiarrhythmic therapy was determined by the individual preferences of each patient and the referring physician. Statistical analysis was performed using the paired *t* test.

RESULTS

Inducible VF. Eighteen of 224 patients (8.0%) had inducible sustained VF. All patients required transthoracic, direct-current defibrillation with 200 to 400 J due to circulatory collapse and loss of consciousness. Four patients received chronic antiarrhythmic treatment based on electropharmacologic testing (three with propranolol, one with procainamide). Five patients were treated empirically (three with amiodarone, one with flecainide, and one with procainamide and quinidine); nine patients received no therapy. Five of 10 patients with heart disease (50%) and four of eight patients without heart disease (50%) were treated. Five of 12 symp-

Table I. Clinical characteristics and results of therapy in 16 patients with ventricular fibrillation-flutter induced by ventricular programmed stimulation

Case no.	Age/gender	Heart disease	Clinical symptoms	Clinical arrhythmia	Chronic therapy
1	60/M	NOAH	Asymptomatic	NSVT	A
2	61/M	None	Asymptomatic	NSVT	A
3	36/F	None	Asymptomatic	None	I
4	58/M	None	Asymptomatic	NSVT	None
5	31/F	None	Asymptomatic	NSVT	Fl
6	28/F	None	Asymptomatic	NSVT	None
7	40/M	MVP	Syncope	VSD	I
8	84/M	None	Syncope	None	P
9	71/M	CAD	Syncope	VPD	I
10	72/M	MVP	Syncope	VPD	None
11	64/M	CAD (IMI)	Syncope	VPD	P, Q
12	62/F	MVP	Syncope	VPD	None
13	63/F	AI	Syncope	VPD	None
14	59/M	None	Syncope	VPD	None
15	89/M	CM	Syncope	None	A
16	31/F	None	Syncope	VPD	None
17	65/M	CM	Syncope	VPD, SVT	None
18	74/M	CAD	Presyncope	VPD	None

Abbreviations: A = amiodarone; AI = aortic insufficiency; CAD = coronary artery disease; CM = cardiomyopathy; F = female; Fl = flecainide; I = propranolol; IMI = remote, inferior myocardial infarction; M = male; MVP = mitral valve prolapse; no. = number; NOAH = nonobstructive, asymmetric hypertrophy; NSVT = nonsustained ventricular tachycardia; P = procainamide; Q = quinidine; SVT = supraventricular tachycardia; VPD = single, premature ventricular depolarizations; VSD = ventricular septal defect.

tomatic patients (42%) with syncope/presyncope and four of six (67%) without syncope/presyncope were treated. No patient has had cardiac arrest or sudden death during a follow-up period of 25.2 ± 13.8 months (mean ± standard deviation).

Patient characteristics. The clinical characteristics of these 18 patients were as follows (Table I). There were 12 men and 6 women with a mean age of 52 ± 18 years (± standard deviation). Ten of these 18 patients had clinical evidence of structural heart disease. Three patients had coronary artery disease with one patient having had a remote myocardial infarction; three patients had mitral valve prolapse; two had an idiopathic congestive cardiomyopathy, one had aortic valvular insufficiency, and one had nonobstructive asymmetric hypertrophy. The remaining eight patients had no clinical evidence of structural heart disease. The indications for VPS in this group were: unexplained syncope (11 patients) or presyncope (one patient), and evaluation of non-sustained VT (five patients). One additional patient (case No. 3), who had no clinical evidence of heart disease and who was asymptomatic, was studied after her monozygotic twin sister died suddenly. Prior to VPS, five patients had had nonsustained VT and 13 patients had had either single premature ventricular depolarizations or no arrhythmia noted during 24 or more hours of continuous ambulatory ECG monitoring.

VPS technique. Ventricular fibrillation-flutter was initiated in the right ventricle in 16 patients and in the left ventricle in two patients. Two extrastimuli were required in three patients and three extrastimuli were required in the remaining 15 patients. The incidence of VF was similar in patients with and without heart disease (7.1% vs 9.6%, N.S.) or previous syncope/presyncope (8.8% vs 6.9%, N.S.). However, it was significantly higher when VPS including three ventricular sites using a current strength of 5 mA (pulse width 2 msec) was compared to programmed stimulation of two ventricular sites using a current twice diastolic threshold (pulse width 2 msec) (15.2% vs 3.0%, $p < 0.05$).

DISCUSSION

Prognostic significance. The results of this study suggest that VF initiated by VPS in patients without a documented history of VT or VF has no clinical or prognostic significance. The incidence of VF was similar in patients with and without structural heart disease or previous symptoms of syncope/presyncope. Regardless of whether or not antiarrhythmic therapy was given, neither cardiac arrest nor sudden death occurred in any patient during the follow-up period.

In contrast to the findings of Spielman et al.,[6] the clinical course subsequent to VPS in our study was not ominous for patients in whom VF was initiated.

This difference in clinical outcome may be due to the differences between the patient groups in the two studies. In the study of Spielman et al.,[6] all patients in whom VF was initiated by VPS had had a previously documented or suspected episode of sustained VT or a cardiac arrest during which VT or VF was documented. Our study was limited only to patients without a documented history of sustained VT or VF.

Nonspecific finding. The results of this study suggest that the initiation of VF by VPS may be a nonspecific finding in patients with a prior history of syncope. The induction of *sustained unimorphic VT* has been reported to have high diagnostic value in patients with unexplained syncope. Treatment aimed at suppression of unimorphic VT results in a high remission rate of syncope.[12] In contrast, the results of this study suggest that *VF* has no clinical significance when it is initiated in patients with unexplained syncope.

In survivors of cardiac arrest, the incidence of inducible sustained, unimorphic VT is quite high (36% to 53%), whereas the incidence of induced VF is low (6.5% to 12%).[8-10] Ambulatory ECG recordings of episodes of sudden death have demonstrated that VF is invariably preceded by unimorphic VT.[13, 14] These findings suggest that VF induction by VPS in survivors of a cardiac arrest may a nonspecific finding as well.

The incidence of VF was increased when a higher current strength was used during VPS. Hamer, et al.,[15] observed a similar finding in normal canine hearts. However, increased current strength alone may not have accounted for the incidence of VF in our study. A greater number of ventricular sites were stimulated when the current strength was increased to 5 mA. Although the VPS protocol in our study did not allow independent analysis of the importance of multiple extrastimuli or ventricular sites, others have found these factors to be significant in increasing the incidence of VF during VPS.[7, 15, 16]

Limitations. There are several limitations in our study. (1) Myocardial biopsy was not performed in the eight patients who did not have clinical evidence of structural heart disease; therefore, the possibility of occult myocardial disease cannot be excluded. (2) Because of contraindications, not all patients underwent left ventricular stimulation; this may have resulted in an underestimation of the incidence of VF during VPS. (3) Ventricular programmed stimulation was terminated when nonsustained, rapid, polymorphous VT or nonsustained VF was reproducibly induced. Continuation of VPS may have

resulted in a high incidence of sustained VF. (4) Nine of 18 patients in whom VF was initiated by VPS were treated with antiarrhythmic agents. We cannot exclude the possibility that their benign course was due to antiarrhythmic therapy.

Conclusion. VF initiated by VPS appears to be a nonspecific finding in patients who have not previously had sustained VT or VF, and does not mandate antiarrhythmic therapy.

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Determinants of simultaneous fast and slow pathway conduction in patients with dual atrioventricular nodal pathways

Double His bundle and ventricular responses to a single atrial impulse caused by a simultaneous fast and slow pathway conduction was observed during electrophysiologic study in three patients with dual-pathway atrioventricular nodal reentrant paroxysmal supraventricular tachycardia. In patient No. 1 this phenomenon occurred during rapid atrial pacing, in patient No. 2 during both rapid atrial pacing and delivery of a single atrial extrastimulus, and in patient No. 3 during delivery of double atrial extrastimuli. Retrograde unidirectional block in the slow pathway was suggested by retrograde induction of tachycardia at a long ventricular paced cycle length and/or long ventricular coupling interval in all three patients. Our findings suggest that major determinants of this phenomenon include: (1) a sufficient conduction delay in the slow pathway so that the distal tissue is able to respond for the second time, and (2) a retrograde unidirectional block in the slow pathway so that the fast pathway impulse will not enter and collide with the oncoming slow pathway impulse. (Am Heart J 109:963, 1985.)

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In 1975, Wu et al.[1,2] described a patient with double His bundle and ventricular responses, as well as a patient with pseudoshortening of atrioventricular (AV) nodal conduction time (AH interval), caused by simultaneous fast and slow AV nodal pathway conduction. Subsequently, Gomes et al.[3] observed simultaneous fast and slow AV nodal pathway conduction after the administration of procainamide in three patients with paroxysmal supraventricular tachycardia (PSVT).[3] In these patients, simultaneous fast and slow pathway conduction was noted only during rapid atrial pacing but not with atrial premature stimulation. Csapo[4] reported one patient and Sutton and Lee[5] reported two patients with a complicated form of nonreentrant supraventricular tachycardia resulting from simultaneous fast and slow AV nodal pathway conduction during sinus rhythm. Because of the rarity of this phenomenon, its electrophysiologic mechanisms have not been completely elucidated. In this study, we describe three additional patients with simultaneous fast and slow AV nodal pathway conduction and further delineate the electrophysiologic determinants of this phenomenon.

METHODS

Electrophysiologic study. Electrophysiologic study was performed in the postabsorptive, nonsedated state after informed written consent was obtained. All cardiac medication was discontinued at least five half-lives before the study. A No. 7 quadripolar electrocatheter (USCI