Electrophysiologic Abnormalities in Patients With Hypertrophic Cardiomyopathy
A Consecutive Analysis in 155 Patients

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Electrophysiologic studies (EPS) were performed in 155 patients with hypertrophic cardiomyopathy (HCM). Indications for EPS were cardiac arrest in 22 patients, syncope in 55 patients, presyncope in 37 patients, asymptomatic ventricular tachycardia (VT) in 24 patients, palpitations in 10 patients, and a strong family history of sudden cardiac death in seven patients. Thirty-five (23%) patients had significant resting left ventricular outflow tract obstruction. Electrophysiologic abnormalities were present in 126 (81%) patients. A high prevalence of abnormal sinus-node function (66%) and His-Purkinje (HV) conduction (30%) was noted. The most commonly induced supraventricular arrhythmias were atrial reentrant tachycardia and atrial fibrillation (10% and 11% of patients, respectively). Accessory atrioventricular pathways were present in seven (5%) patients. Programmed ventricular stimulation (PVS) induced nonsustained ventricular tachycardia in 22 (14%) patients and sustained ventricular arrhythmia in 66 (43%) patients. Sustained ventricular arrhythmia was polymorphic VT in 48 (73%) patients, monomorphic VT in 16 (24%) patients, and ventricular fibrillation in two (3%) patients. Induction was with two premature stimuli in 19 (29%) patients and three premature stimuli in 47 (71%) patients. Of 17 cardiac arrest survivors with sustained ventricular arrhythmia, 16 (94%) patients required three premature stimuli for arrhythmia induction. Sustained ventricular arrhythmia was induced at a right ventricular site in 51 (77%) patients and at a left ventricular site in 15 (23%) patients. Univariate analysis showed a significant (p < 0.05) association between inducibility of sustained ventricular arrhythmia and VT on Holter in patients with a history of cardiac arrest or syncope but not in patients with presyncope or asymptomatic patients. Multivariate logistic regression analysis revealed that the following were significantly associated with inducibility of sustained ventricular arrhythmia: clinical presentation (cardiac arrest more than syncope more than presyncope more than asymptomatic patients, p = 0.0002; chronic or inducible atrial fibrillation, p = 0.002; and male gender, p = 0.04). In contrast, there was no clinical correlate of induced nonsustained VT. We conclude that: 1) EPS commonly identify abnormalities in selected HCM patients, 2) induction of VT occurs more commonly in patients with severe clinical manifestations of HCM, 3) VT on Holter is associated with increased ventricular electrical instability in patients with sudden cardiac arrest or syncope but not in less symptomatic patients, 4) PVS using less than three premature stimuli induces VT in only a small percentage of HCM patients with serious clinical manifestations, and 5) induction of sustained ventricular arrhythmia with three or less premature stimuli (polymorphic VT in most patients) is an abnormal finding in HCM that may provide a useful guide to therapy. (Circulation 1989;80:1259–1268)

Cardiac death and syncope occur frequently in patients with hypertrophic cardiomyopathy.1–10 Death is usually sudden, unheralded by symptoms.14,19 and in all probability, arrhythmic in origin.1–5,16–18,20–26 Despite numerous studies, there is no single clinical variable capable of reliably
predicting which individual patient is at risk. Thus, although sudden death often occurs in young patients with hypertrophic cardiomyopathy, this observation provides little help in identifying specific patients as being at risk of sudden cardiac death. Similarly, although a family history of sudden premature cardiac death may identify a group of patients at high risk, such a family history is rare among all patients who die suddenly. The best predictor of sudden cardiac death at present is the demonstration of ventricular tachycardia on 24-48-hour Holter monitoring. About 25% of such patients die within 3 years. Although this finding identifies most adult patients with hypertrophic cardiomyopathy who are at risk of sudden cardiac death, it is sufficiently nonspecific (75% of patients with ventricular tachycardia do not die during 3 years of follow-up) to make clinical decisions difficult.

Electrophysiologic studies have an established role in the diagnosis and management of sudden cardiac arrest, syncope, and arrhythmias in patients with cardiac disease states other than hypertrophic cardiomyopathy. Several authors have reported on a variety of electrophysiologic findings in patients with hypertrophic cardiomyopathy, including induction of supraventricular and ventricular arrhythmias and conduction abnormalities. Because these studies have involved small selected groups of patients, however, the clinical relevance of these findings and the role of electrophysiologic studies in patients with hypertrophic cardiomyopathy remain to be established.

The purpose of the present study was therefore twofold: First, to determine the prevalence of electrophysiologic abnormalities in a large group of hypertrophic cardiomyopathy patients at risk of sudden cardiac death or with symptoms of syncope, presyncope, and only mild palpitations; and second, to examine the relation of the electrophysiologic findings and, in particular, inducibility of ventricular arrhythmias to the patient’s symptomatic presentation and to the presence of ventricular tachycardia during Holter monitoring.

**Methods**

**Study Population**

Patient population consisted of 155 consecutive patients with hypertrophic cardiomyopathy who underwent electrophysiologic evaluation of out-of-hospital cardiac arrest, syncope, presyncope, palpitations, ventricular tachycardia, or family history of sudden cardiac death at the National Institutes of Health (Table 1). All patients had full hemodynamic assessment before the electrophysiologic study.

![See p 1489](http://circ.ahajournals.org/)

Hypertrophic cardiomyopathy was defined as the presence of a hypertrophied, nondilated left ventricle demonstrated by echocardiography in the absence of another cardiac or systemic disease that might produce left ventricular hypertrophy. A malignant family history of hypertrophic cardiomyopathy was defined as patients with two or more first-degree relatives suffering sudden premature (less than 55 years old) cardiac death. Obstructive hypertrophic cardiomyopathy was defined as the presence of a basal left ventricular outflow tract gradient of 30 mm Hg or more, a left ventricular outflow tract gradient of 50 mm Hg or less with provocative maneuvers (e.g., isoproterenol infusion, amyl nitrite inhalation, or Valsalva maneuver), or both.

**Electrophysiologic Study**

All cardioactive drugs were discontinued five half-lives or more before study. Electrophysiologic study was performed with the patient fasting and sedated with 10 mg oral diazepam. Informed consent was obtained in accordance with a study protocol approved by the Institute Review Board of the National Heart, Lung, and Blood Institute. Three multiple electrode catheters (5F or 6F, Bard or Mansfield) were introduced percutaneously into a femoral vein and positioned under fluoroscopic guidance in the high right atrium, across the tricuspid valve in the region of the His bundle, and at the

**TABLE 1. Clinical Findings in 155 Patients With Hypertrophic Cardiomyopathy Who Underwent Electrophysiologic Studies**

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>Patients (n) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>96 (62)</td>
</tr>
<tr>
<td>Female</td>
<td>59 (38)</td>
</tr>
<tr>
<td>Age (yr)</td>
<td></td>
</tr>
<tr>
<td>Mean±1 SD</td>
<td>40±16</td>
</tr>
<tr>
<td>Range</td>
<td>7–72</td>
</tr>
<tr>
<td>LVOT gradient</td>
<td></td>
</tr>
<tr>
<td>Basal</td>
<td></td>
</tr>
<tr>
<td>≤29 mm Hg</td>
<td>120 (77)</td>
</tr>
<tr>
<td>≥30 mm Hg</td>
<td>35 (23)</td>
</tr>
<tr>
<td>Provocable</td>
<td></td>
</tr>
<tr>
<td>≤49 mm Hg</td>
<td>82 (53)</td>
</tr>
<tr>
<td>≥50 mm Hg</td>
<td>73 (47)</td>
</tr>
<tr>
<td>Family history of sudden cardiac death</td>
<td></td>
</tr>
<tr>
<td>One member</td>
<td>28 (18)</td>
</tr>
<tr>
<td>≥Two members</td>
<td>13 (8)</td>
</tr>
<tr>
<td>Previous operation for LVOT obstruction</td>
<td>33 (21)</td>
</tr>
<tr>
<td>Indication for electrophysiologic study</td>
<td></td>
</tr>
<tr>
<td>Sudden cardiac arrest</td>
<td>22 (14)</td>
</tr>
<tr>
<td>Syncope</td>
<td>55 (36)</td>
</tr>
<tr>
<td>Presyncope</td>
<td>37 (24)</td>
</tr>
<tr>
<td>Asymptomatic VT</td>
<td>24 (16)</td>
</tr>
<tr>
<td>Palpitations (no VT)</td>
<td>10 (6)</td>
</tr>
<tr>
<td>Malignant family history (no VT)</td>
<td>7 (5)</td>
</tr>
<tr>
<td>24–48-Hour Holter</td>
<td></td>
</tr>
<tr>
<td>VT</td>
<td>89 (58)</td>
</tr>
<tr>
<td>Atrial flutter/fibrillation</td>
<td>17 (11)</td>
</tr>
<tr>
<td>Supraventricular tachycardia</td>
<td>14 (9)</td>
</tr>
</tbody>
</table>

LVOT, left ventricular outflow tract; VT, ventricular tachycardia.
right ventricular apex. In patients with supraventricular tachycardia, a quadripolar catheter was also placed in the coronary sinus through a subclavian vein. A femoral artery was cannulated (8F Cordis sheath) for continuous recording of the systemic arterial pressure and, in some patients, for left ventricular stimulation. After programmed atrial stimulation, the high right atrial catheter was repositioned in the right ventricular outflow tract for programmed ventricular stimulation. Intracardiac electrograms were filtered at 30–500 Hz and standard electrocardiographic leads I, II, and V1, or V6, were filtered at 0.1–20 Hz, displayed on a multichannel oscilloscope (Electronic for Medicine, VR16), and recorded on light sensitive paper at 100 mm/sec. Twelve lead electrocardiograms were recorded, when possible, during induced arrhythmia. Programmed stimulation was performed using a digital programmable stimulator (Bloom Associates) using a 2.0-msec rectangular pulse at twice late diastolic thresholds.

**Stimulation Protocol**

The following pacing protocol was used: 1) introduction of single atrial premature stimuli during sinus rhythm, 2) atrial overdrive pacing at several cycle lengths for 30 seconds and with more than 30 seconds of rest in between each pacing drive, 3) introduction of atrial premature stimuli (S2) after eight driven (S1) atrial beats at pacing cycle length of 600 msec, the premature interval (S1-S2) was decreased in 10–20 msec intervals, 4) atrial pacing at progressively higher rates until atrioventricular block occurred or until limited by symptoms or hypotension, and 5) programmed ventricular stimulation. In patients with preexcitation syndrome, the site and characteristics of the accessory pathway were determined by standard methods.\(^{31,42}\)

Programmed ventricular stimulation protocol involved a stepwise increase in “aggressiveness” as follows: 1) insertion of one, two, and three premature stimuli during sinus rhythm at the right ventricular apex; 2) introduction of one and two premature stimuli after three paced ventricular drive-cycle lengths of 600, 500, and 400 msec (450 msec if 400 msec was not tolerated), first, at the right ventricular apex and, second, at the right ventricular outflow tract; 3) introduction of three premature stimuli after the three paced ventricular drive-cycle lengths at the right ventricular apex and right ventricular outflow tract; and 4) introduction of one, two, and three premature stimuli after the three paced ventricular drive-cycle lengths at a left ventricular site. The end point of the stimulation protocol was refractoriness or induction of a sustained ventricular arrhythmia.

The following were determined: basic intervals (i.e., AH, HV, QRS, QT, QTC), sinus-node recovery time,\(^{43}\) sinoatrial conduction time,\(^{44,45}\) atrial effective and functional refractory periods, atrioventricular nodal effective and functional refractory period, Wenckebach cycle length, maximum atrial rate with 1:1 atrioventricular conduction, and ventricular refractory periods at the three ventricular PCLs, determined at the three ventricular sites.

**Definitions**

Nonsustained ventricular tachycardia is defined as three to 30 consecutive ventricular beats, at 120 or more beats/min and terminating spontaneously. Sustained ventricular tachycardia is ventricular tachycardia of more than 30 beats’ duration or requiring termination because of hemodynamic compromise. Ventricular tachycardia with continuous changing QRS morphology was termed polymorphic and one with uniform QRS complexes was termed monomorphic. Ventricular fibrillation is ventricular arrhythmia with no discernible discrete ventricular beats identifiable on the surface 12-lead electrocardiogram and with continuous intracardiac ventricular electrical activity. Sudden cardiac arrest is a history of a resuscitation attempt requiring direct current cardioversion within 2 hours of collapse.

**Statistics**

Data are expressed as mean±1 SD. Continuous variables were analyzed using Student’s t test for unequal data. Contingency tables were evaluated by Fisher’s exact test. Univariate and multiple stepwise logistic regression analysis were used to determine the clinical, hemodynamic, Holter, and electrophysiologic predictors of inducibility of ventricular arrhythmias (dependent variable). The independent variables were: age, gender, clinical presentation, presence or absence of atrial fibrillation and ventricular tachycardia from 24–48-hour Holter, previous operation for relief of left ventricular outflow obstruction, resting or provokable left ventricular outflow tract obstruction, atrial refractoriness, sinus node, atrioventricular node and His-Purkinje conduction disease, induction of atrial reentrant tachycardia or atrial flutter or fibrillation, ventricular refractoriness, and aggressiveness of programmed ventricular stimulation. Nine levels of increasing aggressiveness of programmed ventricular stimulation were recognized based on the number of ventricular sites tested, drive pacing cycle length, and number of premature stimuli. A probability value of p less than 0.05 was considered significant.

**Results**

**Sinus Node Function**

Although only six of 82 (7%) patients had abnormal sinus-node recovery times (>1,500 msec), prolonged sinoatrial conduction times (>120 msec) were noted in 61 of 93 (66%) patients.

**Atrioventricular Node Function**

Chronic atrial fibrillation was present in nine (6%) patients. The AH interval was delayed (>120 msec) in nine of the remaining 146 (6%) patients.
premature stimulation was performed in 136 patients and, of these, only six (4%) patients had prolonged atrioventricular nodal refractory periods (>450 msec). Right atrial incremental pacing was performed in 101 patients; six (6%) patients had long Wenckebach cycle length (>500 msec), and seven (7%) patients had enhanced atrioventricular nodal conduction (1:1 atrioventricular conduction at paced cycle length of ≤300 msec).

**His Bundle–Purkinje Conduction**

The HV interval was prolonged (>55 msec) in 44 of 148 (30%) patients. In six of these patients, the HV interval increased or infra-Hisian block developed during atrial premature stimulation, atrial incremental pacing, or both.

The prevalence of sinus-node, atrioventricular node, or His-Purkinje conduction was not significantly higher in patients with cardiac arrest, syncope, or presyncope compared with asymptomatic patients.

**Supraventricular Arrhythmias**

Sustained (>30 seconds) atrial flutter or fibrillation was induced in 15 of 136 (11%) patients who underwent atrial premature stimulation, atrial incremental pacing, or both; atrial fibrillation was induced in six of 11 (55%) patients with paroxysmal atrial fibrillation but only in nine of 125 (7%) patients without paroxysmal atrial fibrillation (p<0.002).

Atrial reentrant tachycardia was induced in 14 of 136 (10%) patients; the cycle length of the tachycardia was 275±35 msec (range, 230–385 msec). In four of the 14 patients, a similar arrhythmia was recorded during Holter monitoring.

Accessory atrioventricular pathways were present in seven of 155 (5%) patients. Three patients presented with palpitations, one patient with syncope, one with presyncope, and one patient had a malignant familial history of sudden cardiac death. Four years after initially presenting with palpitations, one patient developed frequent episodes of orthodromic reciprocating tachycardia that, on several occasions, degenerated after about 10 beats into atrial fibrillation complicated by hypotension. The accessory pathway was single in all seven patients and situated in the posteroseptal region in four patients, left posterior region in one patient, and left lateral region in two patients. The accessory pathway was capable of anterograde and retrograde conduction in five patients and was concealed in two patients. The shortest preexcited RR’ interval during induced atrial fibrillation was more than 260 msec in the five patients with anterograde conduction over the accessory pathway.

Dual atrioventricular nodal pathways were present in three patients; in two patients, this was of the common (slow-fast) variety, and in the remaining patient, it was of the uncommon (fast-slow) variety. None of the three patients had spontaneous episodes of atrioventricular nodal tachycardia.

**Induction, Characterization, Hemodynamic Consequences, and Termination of Ventricular Arrhythmias Induced by Programmed Ventricular Stimulation**

Programmed ventricular stimulation induced nonsustained ventricular tachycardia in 22 (14%) patients. Nonsustained ventricular tachycardia was polymorphic ventricular tachycardia in 12 patients and monomorphic ventricular tachycardia in 10 patients. Inducibility of nonsustained ventricular tachycardia was unrelated to clinical, Holter, or electrophysiologic findings.

Sustained ventricular arrhythmias were induced in 66 of 155 (43%) patients. Sustained ventricular arrhythmia was induced with two premature stimuli in 19 (29%) patients. The S1, S2, and S3 intervals in these patients were as follows: S1, 468±82 msec; S2, 252±13 msec; and S3, 209±35 msec. Forty-seven (71%) patients required three premature stimuli for induction of sustained ventricular arrhythmia: S1, 450±75 msec; S2, 255±20 msec; S3, 212±26 msec; and S4, 203±27 msec.

In 89 of 155 (57%), a significantly (p<0.007) more aggressive programmed ventricular stimulation protocol failed to induce sustained ventricular arrhythmias: S1, 412±40 msec; S2, 261±18 msec; S3, 221±19 msec; and S4, 201±20 msec.

Programmed stimulation with two or less premature stimuli failed to distinguish between patients with severe clinical manifestations and “asymptomatic” patients. Only one of 22 (5%) cardiac arrest patients, 11 of 55 (20%) syncope patients, and three of 37 (8%) patients with presyncope had an inducible sustained ventricular arrhythmia, compared with one of 24 (4%) asymptomatic patients with ventricular tachycardia on Holter and none of 10 asymptomatic patients without ventricular tachycardia on Holter recordings. The sensitivity of programmed stimulation was significantly improved with the use of three or less premature stimuli; 17 of 22 (77%) cardiac arrest patients, and 27 of 55 (49%) syncope had an inducible sustained ventricular arrhythmia. The specificity of the programmed stimulation was reasonable; only five of 24 (21%) asymptomatic patients with ventricular tachycardia on Holter recordings, and only one of 10 (10%) asymptomatic patients with normal Holter recordings had an inducible sustained ventricular arrhythmia (Table 2).

Induction of sustained ventricular arrhythmia was at the right ventricular apex in 26 (39%) patients, right ventricular outflow tract in 25 (38%), and at a left ventricular site in 15 (23%) patients. Induced sustained ventricular arrhythmia was polymorphic ventricular tachycardia in 48 of 66 (73%) patients, monomorphic ventricular tachycardia in 16 (24%) patients, and ventricular fibrillation in two (3%) patients. Morphology of monomorphic ventricular tachycardia was right bundle branch block in six (38%) and left bundle branch block configuration in 10 (62%) patients.
There were no significant differences in the aggressiveness of programmed ventricular stimulation protocol used to induce sustained polymorphic ventricular tachycardia compared with monomorphic ventricular tachycardia. The cycle lengths of sustained polymorphic ventricular tachycardia (221±26 msec) were significantly shorter (p<0.025) than those of sustained monomorphic ventricular tachycardia (266±59 msec). The rapid rates of both morphologies of ventricular tachycardia resulted in marked and prompt systemic arterial hypotension and loss of consciousness in 64 of 66 (97%) patients. In 31 (47%) patients, ventricular tachycardia degenerated into ventricular fibrillation within 11±4 seconds of induction. Overdrive ventricular pacing successfully terminated ventricular tachycardia in only two (3%) patients. Direct current cardioversion was successful using a single direct current (DC) shock of 200 J in 61 (92%) patients but required a second DC shock of 300 J in the remaining five (8%) patients.

**Induction of Ventricular Arrhythmias Unrelated to Programmed Ventricular Stimulation**

In two patients, sustained ventricular arrhythmias were induced by mechanisms other than programmed ventricular stimulation.

**Case 1.** An 18-year-old man with obstructive hypertrophic cardiomyopathy presented with presyncope and was noted to be in a rapid (220 beats/min) regular narrow-complex tachycardia. The clinical arrhythmia was induced by rapid atrial pacing only, and was shown to be monomorphic ventricular tachycardia.

**Case 2.** A 7-year-old girl with nonobstructive hypertrophic cardiomyopathy presented with recurrent sudden cardiac arrest and syncope. Holter monitoring during an episode of sudden cardiac arrest showed a rapid narrow-complex regular tachycardia that altered its morphology abruptly to a wide-complex tachycardia and then degenerated into ventricular fibrillation. At the electrophysiologic study, atrial pacing at rates in excess of 120 beats/min resulted in marked hypotension and ST-segment depression, associated with a similar alteration of the QRS morphology and HV interval prolongation. We concluded that rapid supraventricular rhythms resulted in aberrant conduction, with ventricular fibrillation occurring secondary to hypotension and myocardial ischemia.

**Factors Associated With an Increased Inducibility of Sustained Ventricular Arrhythmia**

Univariate regression analysis showed that the following were significantly associated with increased inducibility of sustained ventricular arrhythmia: 1) type of clinical presentation, p=0.0008, (Table 2); and 2) chronic or inducible atrial fibrillation, p=0.01.

Thus, 16 of 24 (67%) patients with chronic or inducible atrial fibrillation had an inducible sustained ventricular arrhythmia compared with 50 of 131 (38%) patients without atrial fibrillation. Multivariate logistic regression analysis showed that the following were significant independent predictors of increased inducibility of sustained ventricular arrhythmia: 1) type of clinical presentation, p=0.0002, (Table 2); 2) chronic or inducible atrial fibrillation, p=0.002; and 3) male gender p=0.044. (Forty-eight of 96 [50%] men had an inducible sustained ventricular arrhythmia compared with 18 of 59 [31%] female patients.)

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**Table 2. Relation of Inducibility of Sustained Ventricular Arrhythmia by Programmed Stimulation (Maximum of Three Premature Stimuli) to Clinical Presentation and Presence of Ventricular Tachycardia on Holter Monitoring**

<table>
<thead>
<tr>
<th>Clinical presentation</th>
<th>N</th>
<th>Holter ±VT (%)</th>
<th>Induced-VA ±VT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sudden cardiac arrest</td>
<td>22</td>
<td>{10 (48)}</td>
<td>9 (90)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>{12 (52)}</td>
<td>8 (67)</td>
</tr>
<tr>
<td>Syncope</td>
<td>55</td>
<td>{28 (51)}</td>
<td>20 (71)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>{27 (49)}</td>
<td>7 (26)</td>
</tr>
<tr>
<td>Presyncope</td>
<td>37</td>
<td>{25 (64)}</td>
<td>10 (40)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>{12 (36)}</td>
<td>2 (17)</td>
</tr>
<tr>
<td>Asymptomatic/palpitations</td>
<td>34</td>
<td>{24 (79)}</td>
<td>5 (21)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>{10 (21)}</td>
<td>1 (10)</td>
</tr>
<tr>
<td>Malignant family history</td>
<td>7</td>
<td>{2 (29)}</td>
<td>2 (100)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>{5 (71)}</td>
<td>2 (40)</td>
</tr>
<tr>
<td>Total</td>
<td>155</td>
<td>{89 (58)}</td>
<td>46 (52)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>{66 (42)}</td>
<td>20 (29)</td>
</tr>
</tbody>
</table>

VA, sustained ventricular arrhythmia; VT, ventricular tachycardia on 24–48-hour Holter.
Patients With and Without Inducible Sustained Ventricular Arrhythmias

Effective refractory periods were determined at all three ventricular sites (right ventricular apex, right ventricular outflow tract, and a left ventricular site) and at all three paced ventricular drive-cycle lengths (600, 500, and 400 msec) in 35 patients without inducible sustained ventricular arrhythmia, and in 12 patients with sustained ventricular tachycardia (induced at the left ventricular site). In patients without an inducible sustained ventricular arrhythmia, for each paced ventricular drive-cycle length, the effective refractory periods determined at the three ventricular sites were not significantly different. In contrast, in patients with inducible sustained ventricular tachycardia, although the effective refractory periods determined at the right ventricular apex and right ventricular outflow tracts were similar, the left ventricular effective periods were significantly ($p<0.02$) shorter than those determined at the right ventricular apical and outflow tract sites (Figure 1).

Relation of Spontaneous Ventricular Tachycardia on Holter Monitoring and Inducibility of Sustained Ventricular Arrhythmia

In all clinical subgroups, patients with ventricular tachycardia on Holter monitoring had a higher prevalence of inducible sustained ventricular tachycardia compared with patients without ventricular tachycardia (Table 2). This association, however, was significant (univariate regression analysis; $p=0.05$) only in patients with cardiac arrest or syncope, and not in patients with presyncope or asymptomatic patients (Table 2). Thus, 29 of 38 (76%) patients with cardiac arrest or syncope and ventricular tachycardia on Holter monitoring had an inducible sustained ventricular arrhythmia compared with only 14 of 38 (37%) patients with cardiac arrest or syncope without ventricular tachycardia on Holter monitoring. It is noteworthy, however, that ventricular tachycardia recorded during Holter monitoring had a low sensitivity in identifying patients at risk of sudden cardiac arrest; only 10 of the 22 (45%) sudden cardiac arrest survivors had ventricular tachycardia during 24–48-hour Holter monitoring (Table 2). In contrast, 77% of these patients had ventricular tachycardia induced by programmed ventricular stimulation.

The prevalence of induced sustained ventricular arrhythmias was unaffected by age, previous cardiac surgery for left ventricular outflow obstruction, or resting or provokable left ventricular outflow tract obstruction.

Prevalence of Abnormal Electrophysiologic Findings in Hypertrophic Cardiomyopathy Patients

A significant abnormality of the sinus node, atrioventricular node, His-Purkinje conduction, inducible supraventricular arrhythmia, or sustained ventricular arrhythmia was recorded in 126 of the 155 (81%) patients. Sinus node disease was as prevalent in patients with severe manifestations of the disease (cardiac arrest or syncope, 70%) as in asymptomatic patients with normal Holter recordings (60%). However, although 26 of 77 (34%) cardiac arrest or syncope patients had His-Purkinje conduction abnormalities and 40 of 77 (52%) patients had an inducible sustained ventricular arrhythmia, none of the 10 asymptomatic patients without ventricular tachycardia on Holter monitoring had abnormalities of His-Purkinje conduction and only one (10%) patient had an inducible sustained ventricular arrhythmia (Table 2).
Interestingly, electrophysiologic abnormalities were recorded in all seven asymptomatic patients with a malignant family history of sudden cardiac death (no arrhythmia on Holter monitoring); three patients had sinus node disease, four patients had abnormal His-Purkinje conduction, one patient had an accessory pathway, one patient had an inducible reentrant atrial tachycardia, and four patients had an inducible sustained polymorphic ventricular tachycardia.

Discussion

A minority of patients with hypertrophic cardiomyopathy die from progressive cardiac failure or systemic embolization;19,20 death in most cases is sudden and probably related to an arrhythmia.1-5,16,17,21-27 The evidence for this conclusion rests partly on two findings: First, no hemodynamic parameter, such as severity of left ventricular outflow tract obstruction or left ventricular filling pressures, predicts sudden cardiac death;19,20 and second, adult patients with hypertrophic cardiomyopathy who have three- or fourfold episodes of ventricular tachycardia during 24-48-hour Holter monitoring have a 25% 3-year mortality compared with a less than 5% mortality during the same follow-up period in patients without ventricular tachycardia.16,17

Although the demonstration of the presence or absence of ventricular tachycardia on 24-48-hour Holter monitoring does identify subgroups of patients at high or at low risk of sudden cardiac death, this information, alone, is inadequate for clinical decision making. Thus, although the detection of ventricular tachycardia has a reasonable sensitivity for identifying adult patients at risk of sudden cardiac death, the specificity of this finding is poor. Noninducible ventricular tachycardia is common in patients with hypertrophic cardiomyopathy, occurring in nearly 20% of patients during 24-hour Holter monitoring,29 and about three fourths of these patients have an uneventful 3-year follow-up period.17 Thus, therapy based on the presence of noninducible ventricular tachycardia during Holter monitoring would result in overtreatment with antiarrhythmic medications that have potentially serious side effects. Absence, however, does not confer immunity from sudden cardiac death, particularly in the young.26

Electrophysiologic studies are an integral part of the diagnosis and management of arrhythmias, syncope, and sudden cardiac arrest in patients with other cardiac disease states.31,32 Electrophysiologic studies have also been performed in patients with hypertrophic cardiomyopathy, to provide a more specific guide to therapy.33–40 The value of these previous studies, however, is seriously diminished by the fact that only small numbers of highly selected patients were investigated. Hypertrophic cardiomyopathy has a very heterogenous presentation, and thus, relatively large numbers of patients must be studied to evaluate the relation of abnormal electrophysiologic findings to various clinical presentations. Our study, in which 155 patients with hypertrophic cardiomyopathy with various clinical presentations were studied, provides information that may have important clinical implications.

First, our study indicates that although normal sinus-node recovery times are the rule in patients with hypertrophic cardiomyopathy, a high percentage of patients have abnormal sinoatrial conduction times. Atrial fibrillation and atrial reentrant tachycardia were induced in 11% and 10% of patients, respectively. There was an association between inducibility of atrial tachycardia and atrial fibrillation and the spontaneous occurrence of these arrhythmias. Accessory atrioventricular pathways were present in seven (5%) patients and accounted for a minority of symptoms and supraventricular arrhythmias.

Second, although atrioventricular nodal function was normal in most patients, about one third of the patients had delayed His-Purkinje conduction. This finding reflects the marked involvement of the ventricular septum in the disease process in patients with hypertrophic cardiomyopathy and is consistent with the report that patients with hypertrophic cardiomyopathy who die suddenly have a variety of cystic and vascular abnormalities affecting the His bundle.1

Third, a finding with potentially important clinical implications was the association between inducibil-
ity of sustained ventricular arrhythmia and clinical presentation. A very high percentage of patients selected for study due to earlier cardiac arrest or syncope had inducible ventricular arrhythmia at electrophysiologic study; 77% of patients with cardiac arrest had sustained ventricular arrhythmia during programmed ventricular stimulation, as did 49% of patients with syncope. This prevalence of sustained ventricular arrhythmia compared with a prevalence of only about 20% in asymptomatic patients with ventricular tachycardia on Holter, and only 10% of patients with mild palpitations and no arrhythmias on Holter. In all clinical subgroups, patients with ventricular tachycardia detected on 24–48-hour Holter monitoring had a higher prevalence of inducible sustained ventricular tachycardia. This relation between spontaneous episodes of nonsustained ventricular tachycardia recorded on Holter monitoring and inducibility of sustained ventricular tachycardia was only significant in patients with cardiac arrest or syncope. Furthermore, sustained ventricular arrhythmia was more frequently induced in patients who had chronic or inducible atrial fibrillation. This attests to the widespread nature of the electrical disease in these patients. It is noteworthy that although patients without an inducible sustained ventricular arrhythmia had similar effective refractory periods determined at the three ventricular sites, patients with an inducible sustained ventricular arrhythmia had left ventricular effective refractory periods that were significantly (20–30 msec) shorter than the effective refractory periods measured at the two right ventricular sites. These differences may reflect increased ventricular dispersion of refractoriness and may determine, in part, arrhythmia induction at a given site in preference to other sites. In contrast, induction of nonsustained ventricular tachycardia was unrelated to any clinical finding.

It has been noted that programmed electrical stimulation in hypertrophic cardiomyopathy patients often results in the induction of polymorphic ventricular tachycardia. Because this is usually considered a nonspecific finding in other cardiac disease states, it has been suggested that to avoid the induction of polymorphic ventricular tachycardia in patients with hypertrophic cardiomyopathy, a more conservative programmed ventricular stimulation protocol involving no more than two premature stimuli should be adopted.

Our results, however, provide important information about 1) the optimal stimulation protocol necessary to elicit information appearing to be clinically relevant in hypertrophic cardiomyopathy, and 2) the clinical significance of induced polymorphic ventricular tachycardia.

In our study, the sensitivity of two premature stimuli for induction of sustained ventricular tachycardia was low; only 16% of patients with cardiac arrest or syncope had inducible sustained ventricular tachycardia using two premature stimuli. The cumulative yield of the programmed ventricular stimulation, however, was significantly improved with three premature stimuli; 67% of patients with cardiac death or syncope had inducible sustained ventricular tachycardia with this number of premature stimuli. The specificity of using three versus two premature stimuli also seems reasonable, because, of patients with mild palpitations and normal Holter recordings, only 10% had an inducible sustained ventricular tachycardia with three premature stimuli.

The following points pertain to the relevance of inducible sustained polymorphic ventricular tachycardia in hypertrophic cardiomyopathy patients. We found 1) a standard programmed ventricular that was not more aggressive than that used for investigating other cardiac disease states resulted in the induction of sustained polymorphic ventricular tachycardia in a high number (32%) of our patients. (Polymorphic ventricular tachycardia accounted for 73% of sustained ventricular arrhythmias.); 2) sustained polymorphic ventricular tachycardia was induced by a programmed stimulation protocol that was not more aggressive than that resulting in the induction of sustained monomorphic ventricular tachycardia; and 3) the inducibility of sustained ventricular arrhythmia, including polymorphic ventricular tachycardia, was highly significantly associated with a clinical presentation of sudden cardiac arrest and with syncope. In addition, previous studies have shown that although programmed ventricular stimulation protocols that involve the use of two to four premature stimuli may induce nonsustained ventricular arrhythmias in up to 40% of patients without structural heart disease, sustained ventricular arrhythmias, including sustained polymorphic ventricular tachycardia, are rarely induced. These findings lead us to conclude that the induction of sustained polymorphic or monomorphic ventricular tachycardia by our programmed ventricular stimulation protocol is clinically relevant in hypertrophic cardiomyopathy patients.

Occasionally patients with hypertrophic cardiomyopathy have large fibrotic areas separating myocardial muscle bundles, conditions that favor large reentrant circuits and relatively slow monomorphic ventricular tachycardia. In most patients, however, the ventricles are often diffusely diseased with dispersed regions of fibrosis and myocardial fiber disarray. These substrates may support smaller reentrant circuits and permit the arrhythmia to frequently change direction, resulting in a rapid polymorphic ventricular tachycardia.

In experienced hands, programmed electrical stimulation studies can be performed safely in hypertrophic cardiomyopathy patients. Most important, they frequently reveal electrophysiologic abnormalities that appear causally related to sudden cardiac arrest and syncope. Whether detection of these abnormalities will facilitate the development of treat-
ment strategies that prevent sudden cardiac death remains to be determined.

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KEY WORDS • electrophysiology studies • hypertrophic cardiomyopathy
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