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CLINICAL STUDIES

The Role of Silent Ischemia, the Arrhythmic Substrate and the Short-Long Sequence in the Genesis of Sudden Cardiac Death

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To study the role of silent ischemia and the arrhythmic substrate in the genesis of sudden cardiac death, 67 patients were studied (mean age 62 ± 12 years). Of these, 14 patients (Group I) had an in-hospital episode of ventricular tachycardia or fibrillation while wearing a 24 h Holter ambulatory electrocardiographic (ECG) monitor, 33 (Group II) had a documented episode of sustained ventricular tachycardia or fibrillation, or both, and 20 (Group III) had angina pectoris but no ventricular tachycardia or fibrillation. Eight Group I survivors underwent programmed electrical stimulation or ECG signal averaging, or both. All Group II patients underwent 24 h Holter monitoring and ECG signal averaging to detect late potentials before programmed electrical stimulation. Group III patients underwent both 24 h Holter recording and coronary angiography. The 24 h ECG tapes were analyzed for ST segment changes, prematurity index and characteristics of ventricular premature depolarizations. Any ST depression ≥1 mm for >30 s was considered to be a reflection of silent ischemia, and the induction of ventricular tachycardia or fibrillation by programmed electrical stimulation or the presence of late potentials, or both, was considered to be a reflection of the arrhythmia substrate.

Silent ischemia preceded ventricular tachycardia in only 2 (14%) of the 14 Group I patients. The prematurity index was <1 in only 18% of ventricular tachycardia episodes. However, 14 (64%) of 22 episodes of ventricular tachycardia in 9 (64%) of the 14 patients were initiated by a ventricular premature depolarization preceded by a short-long sequence (sinus beat-ventricular premature depolarization-sinus beat) with a ratio of 0.5 ± 0.1. Six (75%) of eight in-hospital survivors of ventricular tachycardia or fibrillation (Group I) had an arrhythmic substrate. A significantly ($p < 0.0001$) higher percent of the 33 Group II patients had an arrhythmic substrate (93%) than had silent ischemic episodes (45%). Silent ischemia resulted in ventricular tachycardia in only 1 (7%) of 15 Group II patients. There was no significant difference between the incidence of silent ischemia (45% versus 35%) and the extent of coronary artery disease between Groups II and III.

It is concluded that: 1) Silent ischemia was not a major determinant of ventricular tachycardia. 2) Although silent ischemia was common in survivors of ventricular tachycardia or fibrillation, its incidence was not significantly different from that in patients with angina pectoris and no sustained ventricular arrhythmias. 3) A high percent of patients (75% to 93%) with ventricular tachycardia and fibrillation have an arrhythmic substrate. 4) In the absence of acute myocardial infarction, sudden cardiac death is frequently triggered by a ventricular premature depolarization, with a preceding short-long cycle that likely produces dispersion of refractoriness in the arrhythmic substrate.

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Sudden cardiac death is a major health problem in the United States, claiming approximately 450,000 lives each year. Out-of-hospital resuscitation studies (1–4) have shown that the rhythm disturbance resulting in sudden cardiac death is usually ventricular tachycardia that degenerates into ventricular fibrillation. Although most patients with sudden cardiac death have coronary artery disease, the majority do not have a history of chest pain before collapse (5). Thus, circumstantial evidence points to silent myocardial ischemia as a

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potentially important causative factor in the genesis of sudden cardiac death. It has also been demonstrated (6–9) that the majority of patients with sudden cardiac death have inducible ventricular tachyarrhythmias, pointing to the arrhythmic substrate as an important determinant of ventricular tachycardia and fibrillation. However, the specific roles of silent ischemia and the arrhythmic substrate and their interaction have not been appropriately defined. The purpose of this study was to address this issue.

Methods

Study patients. A total of 67 patients (mean age 62 ± 12 years) were studied. The patients had a history and electrocardiographic (ECG) or angiographic evidence, or both, of coronary artery disease. To satisfy the objectives of the study, the following three groups of patients with different clinical presentations were selected. Group I comprised 14 patients who had in-hospital ventricular tachycardia and fibrillation while wearing a 24 h ambulatory ECG (Holter) monitor. Five of these patients were receiving an antiarrhythmic agent (procainamide in three and quinidine in two); however, none had QT prolongation (≥0.44 s) or evidence of drug toxicity or hypokalemia within 24 h of the episode. Group II comprised 33 patients who had a documented episode of sustained ventricular tachycardia (17 patients) and ventricular fibrillation (16 patients) and were referred for electrophysiologic studies. Group III comprised 20 patients with angina pectoris (13 unstable and 7 stable). None of these patients had a history of ventricular tachycardia or fibrillation and all were referred for cardiac catheterization. The exclusion criteria for all three groups included: 1) ≥1 mm baseline ST depression on Holter monitoring; hypokalemia, and 3) antiarrhythmic drug toxicity (Group I) as well as antiarrhythmic drug therapy (Groups II and III).

All 67 patients had 24 h Holter monitoring utilizing the Marquette 8500 two channel recorder and an 8000 playback analysis system with a frequency response of 0.05 to 60 Hz. Only 5 of the 14 Group I patients and none of the Group II and III patients were receiving antiarrhythmic drug therapy during the 24 h Holter monitoring. In Group I, the Holter tapes were analyzed for ST segment depression preceding ventricular tachyarrhythmias, as well as heart rate changes and characteristics of ventricular premature depolarization preceding ventricular tachycardia and fibrillation. Eight and seven patients from Group I underwent programmed ventricular stimulation and ECG signal averaging, respectively.

Group II patients additionally underwent ECG signal averaging of the surface QRS complex performed with commercially available systems (Arrhythmia Research Technology and Corazonix Corporation), coronary angiography and programmed electrical stimulation. The latter was performed according to a standard protocol that consisted of up to three extrastimuli at two basic pacing drives (600 and 450 ms) and burst ventricular pacing at the apex and outflow tract of the right ventricle. Isoproterenol and left ventricular stimulation were not used in any of Group II patients. All Group III patients had coronary angiography in addition to 24 h Holter monitoring.

Validation of the Holter system for ST segment changes. To validate the Holter monitoring system for determining ST segment changes, an additional 20 patients had an exercise test and simultaneous Holter ECG monitoring. The exercise test was done using the Marquette Case 12 treadmill with automatic 12 lead ECG recording. The stress ECG and Holter ECG were considered positive if ≥1 mm horizontal or downsloping ST depression, or both, was present 80 ms after the J point. There were 10 episodes of significant ST depression by either method; 8 of the 10 episodes were detected on the Holter ECG and 9 of the 10 on the 12 lead ECG. Concordant results between the Holter and stress ECG monitoring were obtained in 17 (85%) of the 20 patients. An excellent correlation (r = 0.95) was also noted between the computer readouts for the magnitude of ST changes and manual readouts.

Definition of terms. *Silent ischemia.* This was defined as painless ST segment depression ≥1 mm 80 ms after the J point and lasting for ≥30 s. The ST segment changes were determined by computer, and the ischemic episodes by two of the senior investigators who read the real time printouts without knowledge of each other's findings.

Arrhythmic substrate. An arrhythmic substrate was considered present on the basis of 1) inducibility of ventricular tachycardia or ventricular fibrillation, or 2) an abnormal signal-averaged ECG, or both 1 and 2. An abnormal signal-averaged ECG was defined if the root mean square voltage of the terminal 40 ms was <20 μV, the duration of low amplitude signals of <40 μV was >38 ms, the duration of the signal-averaged QRS complex was >114 ms at 40 Hz high pass filtering in the absence of bundle branch block or combinations of these variables (10).

Prematurity index. This index was the coupling interval of the ventricular premature depolarization initiating ventricular tachycardia divided by the QT interval.

Statistics. All data represent mean values ± SD. Statistical analysis was performed with the Student's *t* test and chi-square analysis where appropriate.

Results

Group I

Ventricular tachycardia or fibrillation. There were 22 episodes of ventricular tachycardia, of which 12 were sustained and 10 were nonsustained. The 10 episodes of nonsustained ventricular tachycardia lasted for 37 ± 23 beats (range 15 to 90) and terminated spontaneously. Nine of the 22 episodes were monomorphic and 13 episodes were polymorphic or of the "torsade de pointes" type. Ventricular

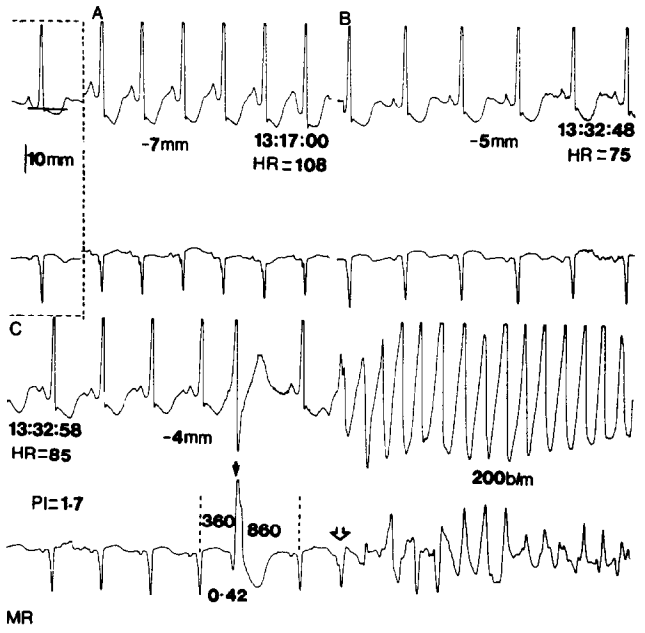

Figure 1. Holter monitor electrocardiographic (ECG) recordings showing the initiation of polymorphic ventricular tachycardia (C) during a silent ischemic episode (ST depression 4 to 7 mm). For further explanation, see test. HR = heart rate; MR = mitral regurgitation; PI = prematurity index.

tachycardia degenerated into ventricular fibrillation in 7 of the 14 patients. Only 2 (14%) of the 14 patients manifested silent ischemia before ventricular tachycardia, for a total of 6 (27%) of the 22 episodes. In one of the two patients (Fig. 1C), significant horizontal and downsloping ST segment depression of −7 to −4 mm occurred before ventricular tachycardia. The ventricular tachycardia that was polymorphic in configuration was initiated by a late-coupled ventricular premature depolarization with a prematurity index of 1.7 and was preceded by a sinus beat-ventricular premature depolarization-sinus beat sequence and a short-long interval with a ratio of 0.42.

Heart rate preceding ventricular tachycardia. The heart rate just preceding ventricular tachycardia was significantly faster than the minimal heart rate (79 ± 15 versus 56 ± 16 beats/min, $p < 0.001$) for the duration of Holter monitoring; however, it was not significantly different from the average heart rate (79 ± 15 versus 81 ± 8 beats/min). The maximal heart rate for the monitoring period was significantly faster than the heart rate just preceding ventricular tachycardia (120 ± 20 versus 79 ± 15 beats/min). The prematurity index of the ventricular premature depolarization initiating ventricular tachycardia was <1 in only 18% of the 22 episodes of ventricular tachycardia.

Short-long cycle preceding ventricular tachycardia. In 9 (64%) of the 14 Group I patients for a total of 14 (64%) of the 22 episodes of ventricular tachycardia, ventricular tachycardia was preceded by a short-long cycle that consisted of a sinus beat followed by a ventricular premature depolarization (short cycle) and a pause followed by another sinus beat (long cycle). The short-long sequence had a mean ratio of 0.5 ± 0.1. Of the 14 ventricular tachycardia episodes that were preceded by a short-long cycle, 9 (64%) were polymorphic. An example of this phenomenon is illustrated in Figure 2 from a patient who had ventricular tachycardia that degenerated into ventricular fibrillation 10 days after inferior wall myocardial infarction. The patient was not taking antiarrhythmic or beta-adrenergic blocker therapy before the episodes of in-hospital ventricular tachycardia and fibrillation. At 8:57:07, a ventricular premature depolarization with a premature index of 0.9 initiated a run of nonsustained ventricular tachycardia. At 9:53:07, a ventricular premature

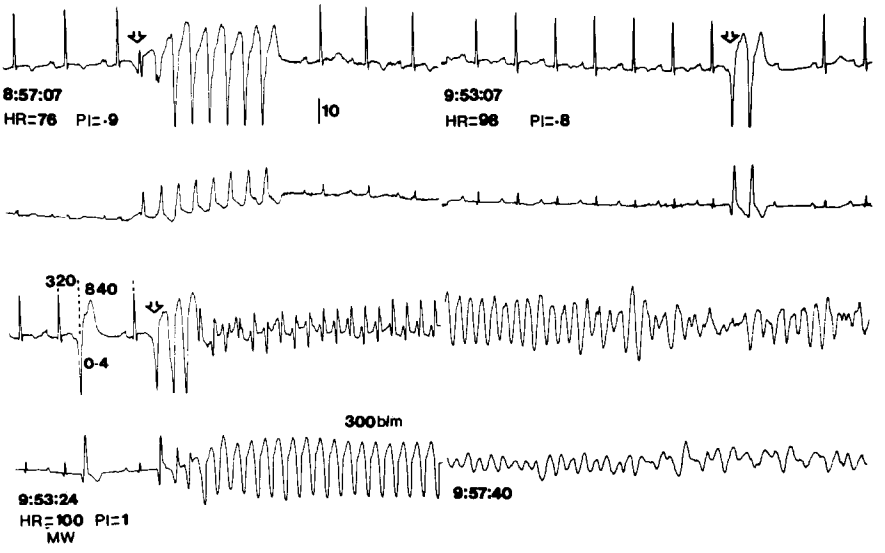

Figure 2. Holter monitor ECG recordings showing the initiation of ventricular tachycardia that degenerates into ventricular fibrillation after a short-long sequence. For further explanation, see text. Abbreviations as in Figure 1.

Table 1. Holter Electrocardiographic Findings in Groups II and III

	Group II	Group III	p Value
SI	15 of 33 (45%)	7 of 20 (35%)	NS
Arrhythmic substrate	31 of 33 (93%)	—	
SI before VT	1 of 15 (7%)	0 (0%)	NS
Max ST depression (mm)	2.93 ± 1.58	2.7 ± 2	NS
No. of episodes of SI	3.86 ± 2.66	4.2 ± 3	NS

Group II = patients with ventricular tachycardia or ventricular fibrillation; Group III = patients without ventricular tachycardia or fibrillation; Max = maximal; SI = silent ischemia; VT = ventricular tachycardia.

depolarization with a premature index of 0.8 resulted in a couplet. At 9:53:24, a ventricular premature depolarization with a premature index of 1 and a configuration similar to that noted previously resulted in a rapid ventricular tachycardia (300 beats/min) that degenerated into ventricular fibrillation in approximately 4 min. Note that the onset of ventricular tachycardia is preceded by a short-long cycle (sinus beat-ventricular premature depolarization-sinus beat) with a ratio of 0.4. Also note that, when nonsustained ventricular tachycardia and couplets occurred, these were not preceded by a short-long cycle.

Eight of 14 patients who survived underwent follow-up programmed electrical stimulation, and 7 had ECG signal averaging of the surface QRS complex. An arrhythmic substrate was present in six (75%) of the eight patients.

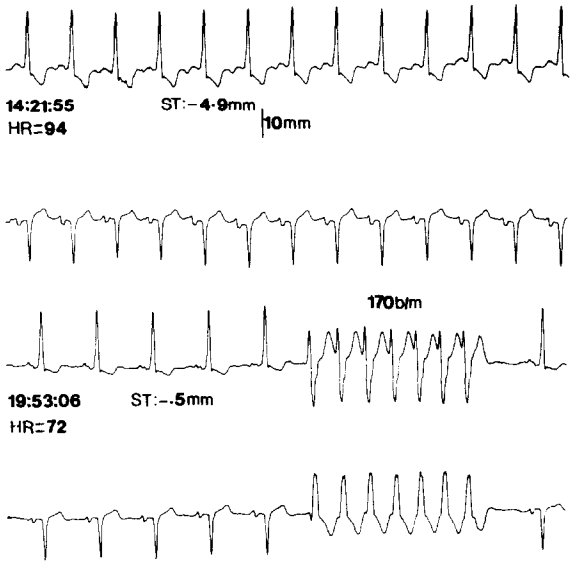

Figure 3. Holter monitor ECG recordings showing silent ischemia and nonsustained ventricular tachycardia in the absence of silent ischemia in a patient in Group II. At 14:21:55 (**top**), the patient has a sinus rate of 94 beats/min and ST depression of 4.9 mm. During the next episode of silent ischemia, there were no ventricular arrhythmias. At 19:53:06 (**bottom**), the heart rate is 72 beats/min and there is no significant ST depression. A run of nonsustained (seven beat) ventricular tachycardia at a rate of 170 beats/min is initiated by a late coupled ventricular premature depolarization. The patient had an arrhythmic substrate with the induction of a similar ventricular tachycardia by programmed electrical stimulation. HR = heart rate.

Groups II and III

Silent ischemia (Table 1). Silent ischemic episodes occurred in 15 (45%) of the 33 Group II patients and in 7 (35%) of the 20 Group III patients (p = NS). There was no significant difference between the two groups in the number of episodes of silent ischemia or the maximal ST depression during silent ischemia. Of the 15 Group II patients with silent ischemic episodes, sustained ventricular tachycardia was noted on the Holter monitor in only 1 patient (7%) and was preceded by ST segment depression of 1 to 1.5 mm. None of the remaining 14 patients had sustained or nonsustained ventricular tachycardia during or after the episodes of silent ischemia (Fig. 3).

Arrhythmic substrate (Table 1). Thirty-one (93%) of 33 patients in Group II had an arrhythmic substrate. Thus, a significantly higher number of patients in this group had an arrhythmic substrate than had silent ischemic episodes (93% versus 45%, respectively, $p < 0.0001$). Figure 4 is an example from the single patient who had a silent ischemic episode before a spontaneous episode of ventricular tachycardia on the Holter monitor. The patient had severe triple vessel coronary artery disease and an old inferolateral myocardial infarction. The signal-averaged ECG revealed the presence of late potentials. The patient also had inducible rapid monomorphic ventricular tachycardia with the use of double extrastimuli during programmed ventricular stimulation.

Coronary angiography and left ventriculography (Table 2). There was no significant difference in the incidence of triple, double or single vessel disease between Groups II and III; however, a significantly higher number of patients in Group II had a left ventricular aneurysm.

Discussion

Analysis of silent ischemia and arrhythmic substrate in the genesis of sudden cardiac death. In this study, we assessed the role of silent myocardial ischemia and the arrhythmic substrate in the genesis of sudden cardiac death due to ventricular tachycardia and fibrillation. Silent ischemic episodes were assessed on a Holter ECG monitor utilizing appropriate frequency response (11–13) and validation studies for ST segment analysis. Although some controversy exists regarding the significance of ST changes on Holter monitoring several previous studies (14–23) have amply documented the validity of Holter ST segment analysis for the assessment of silent ischemia. To test whether silent

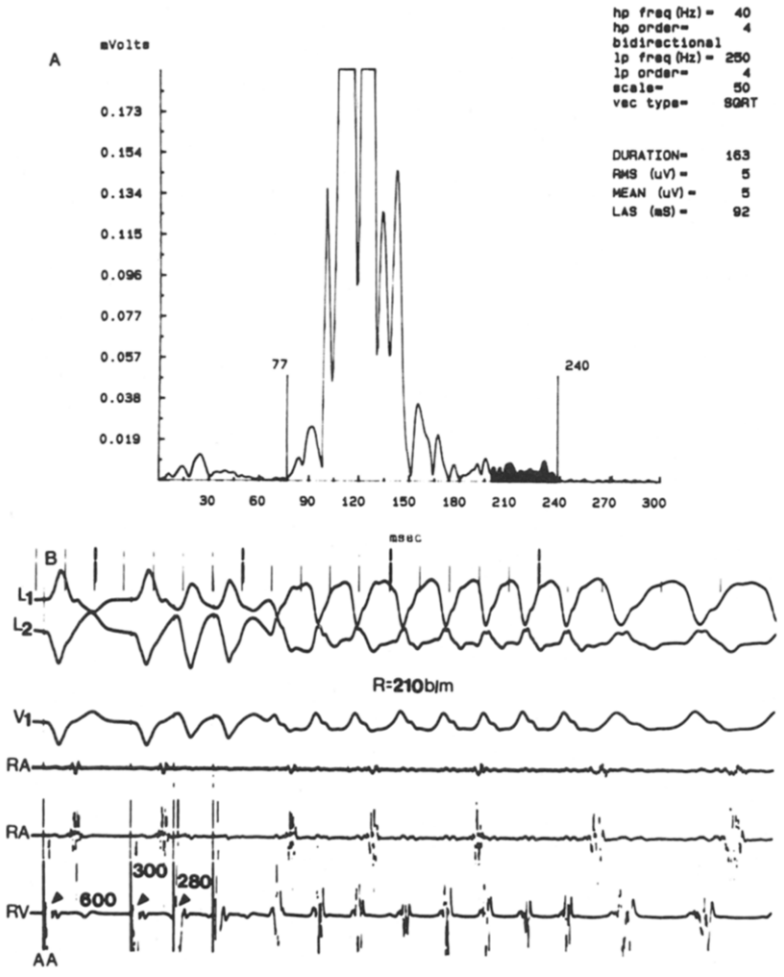

Figure 4. Signal-averaged ECG (**panel A**) and programmed electrical stimulation (**panel B**) in the only patient from Group II who also had silent ischemia before spontaneous ventricular tachycardia on 24 h Holter recording. In **panel A**, the vector magnitude of the signal-averaged ECG shows late potentials. Note that all quantitative variables, namely, the duration of the vector magnitude (163 ms), root mean square (RMS) voltage (5 μV) and duration of low amplitude signals (LAS) of 92 ms, are abnormal. In **panel B,** programmed electrical stimulation with the use of two extrastimuli (300 and 280 ms) at a basic cycle length of 600 ms induced sustained rapid monomorphic ventricular tachycardia similar in configuration to the spontaneous tachycardia. For further explanation, see text. R = rate.

ischemia or the arrhythmic substrate, or both, was the major determinant of sudden cardiac death, we studied three groups of patients.

From Group I, information was obtained regarding the electrical and ischemic behavior of the ventricular myocardium before ventricular tachycardia and fibrillation; from Group II, information was derived regarding the incidence of silent ischemia, its relation to the development of spontaneous ventricular tachycardia or fibrillation and the presence of an arrhythmic substrate. The presence of an arrhythmic substrate was defined on the basis of inducible ventricular tachycardia or fibrillation by using standard stimulation protocols in the laboratory, as well as ECG signal processing techniques to assess the presence of late potentials. An abnormal signal-averaged ECG has been amply shown (24–26) to reflect delayed and inhomogeneous propagation of electrical activity in scarred myocardium. Information obtained from Group III served as control information for Group II patients regarding the incidence of silent ischemic episodes, as well as coronary anatomy and left ventricular geometry. It was hypothesized that this analysis in the three groups of patients would provide a clearer understanding of

Table 2. Coronary Anatomy on Angiography in Groups II and III

	Three Vessel Disease	Two Vessel Disease	One Vessel Disease	LV Aneurysm
Group II	12 of 33 (36%)	11 of 33 (33%)	10 of 33 (30%)	14 of 33 (42%)
Group III	10 of 20 (50%)	7 of 20 (35%)	3 of 20 (15%)	1 of 20 (5%)
p value	NS	NS	NS	0.01

Group II = patients with ventricular tachycardia or ventricular fibrillation; Group III = patients without ventricular tachycardia or fibrillation. LV = left ventricular.

the role of silent ischemia and the arrhythmic substrate in the genesis of sudden cardiac death.

Role of silent ischemia in the genesis of ventricular tachycardia and fibrillation. Our results suggest that silent ischemia was not a major determinant of ventricular tachycardia and fibrillation. Indeed, silent ischemic episodes preceded ventricular tachycardia in only 2 of 14 patients who had ventricular tachycardia or fibrillation, or both, on a Holter monitor recording (Group I). Although silent ischemic episodes were common (45%) in patients with documented ventricular tachycardia or fibrillation (Group II), in only one patient (7%) did silent ischemia precede ventricular tachycardia. However, this patient also had an arrhythmic substrate as suggested by inducibility of sustained ventricular tachycardia and late potentials on the signal-averaged ECG. Furthermore, the incidence of triple, double and single vessel coronary artery disease was not significantly different in patients with ventricular tachycardia or fibrillation, or both (Group II) from that in patients with symptomatic coronary artery disease and no history of sustained ventricular arrhythmias. Thus, observations in Group II and III patients suggest that the high incidence of silent ischemia seen in patients with sustained ventricular arrhythmias is a reflection of its prevalence in patients with coronary artery disease in general and is not specific to patients with sustained ventricular arrhythmias. Several previous studies (18,21,22) noted a high prevalence of silent ischemic episodes in patients with stable and unstable angina pectoris.

A few isolated reports (27–30) clearly noted an association between painless myocardial ischemia during exercise testing or Holter ECG monitoring and the initiation of ventricular tachycardia and fibrillation. Sharma et al. (27) demonstrated silent myocardial ischemia and wall motion abnormalities by means of exercise testing in 12 of 15 patients who had survived an out-of-hospital cardiac arrest. Six of their patients demonstrated episodes of ventricular tachycardia on 24 h Holter monitoring and 11 had frequent ventricular premature depolarizations (>30/h). However, in their study, Sharma et al. did not analyze ST segment depression preceding episodes of ventricular tachycardia on Holter recording or determinants of the presence of an arrhythmic substrate. Thus, it is highly likely that the demonstration of silent ischemic episodes on exercise testing in their patients merely reflected the prevalence of such episodes in patients with coronary artery disease, as demonstrated in our study. Although acute myocardial infarction and significant painful and painless myocardial ischemia may result in sustained ventricular tachyarrhythmias, the transient and painless ischemic episodes generally described by the term "silent ischemia" are not specific triggers for sustained ventricular arrhythmias. In fact, most patients with these malignant arrhythmias do not show silent ischemic episodes before the occurrence of ventricular tachycardia or fibrillation.

Role of the arrhythmic substrate in the genesis of sudden cardiac death. Our results suggest that the majority of patients with sustained ventricular tachyarrhythmias (Group II) have an arrhythmic substrate, as evidenced by the presence of late potentials on the signal-averaged ECG or inducible ventricular tachycardia and fibrillation on programmed ventricular stimulation, or both. These findings are in agreement with previous studies (5–8) in survivors of out-of-hospital sudden cardiac death and point to the arrhythmic substrate as an important determinant of ventricular tachyarrhythmias. Furthermore, the arrhythmic hypothesis is favored over the ischemic hypothesis in our patients by the observations of a significantly higher incidence of left ventricular aneurysm and lack of appreciable differences in the extent and degree of coronary artery disease in patients in our Group II (sustained ventricular tachyarrhythmias) when compared with patients in our Group III (no sustained ventricular tachyarrhythmias).

The trigger for ventricular tachycardia and fibrillation: the short-long sequence. Our results suggest that ventricular tachycardia is often triggered by a ventricular premature depolarization with a preceding short-long cycle. The short cycle comprises a sinus beat followed by a ventricular premature depolarization, and the long cycle comprises the ventricular premature depolarization followed by a sinus beat. The long cycle is approximately twice that of the short cycle. Kay et al. (31) noted that a "long-short" initiating sequence triggered torsade de pointes in 41 of 44 episodes associated with antiarrhythmic drug toxicity and baseline prolongation of the QT interval and hypokalemia or hypomagnesemia alone or in combination. However, a review of their published ECG examples demonstrates that their "long-short sequence" is indeed a "short-long cycle" preceding the ventricular premature depolarization that triggered the torsade de pointes. Thus, our findings suggest that a short-long cycle often but not always, serves as a trigger for ventricular tachycardia even in the absence of antiarrhythmic drug toxicity alone or in association with electrolyte abnormalities. It is of additional interest that nearly twice as many episodes of ventricular tachycardia that were initiated by a ventricular premature depolarization with a short-long sequence were polymorphic or torsade de pointes type, whereas monomorphic ventricular tachycardia was less often initiated by a short-long sequence. The underlying mechanism for this phenomenon is unclear; however, the following hypotheses are offered.

1) It is possible that the short-long sequence preceding the ventricular premature depolarization initiating ventricular tachycardia produces dispersion of refractoriness in the arrhythmic substrate. Additionally, it is possible that a larger mass of Purkinje muscle fibers achieves critical conduction delays and blocks favoring a sustained reentrant tachycardia. A similar mechanism could likewise activate multiple circuits, resulting in polymorphic ventricular tachycardia

and fibrillation. Divergence between refractoriness of the His-Purkinje system and ventricular myocardium was demonstrated after programmed ventricular stimulation by Denker et al. (32), using a short-long pacing protocol. These investigators (33) also demonstrated induction of ventricular tachycardia in the electrophysiology laboratory by utilizing a pacing protocol that incorporated a short-long sequence in the absence of antiarrhythmic drugs.

2) An alternative mechanism for the initiation of ventricular tachycardia after the short-long cycle is early afterdepolarizations (34–36). Because of the compensatory pause after the ventricular premature depolarization, the next sinus impulse could result in repolarization abnormalities that trigger repetitive activity. The lack of QTu prolongation in the postextrasystolic sinus beat may be related to early afterdepolarizations arising in a small arrhythmic focus, as suggested by Cranefield and Aronson (36).

3) It is possible that both of the mechanisms just mentioned play a role in the genesis of ventricular tachycardia initiated by a preceding short-long cycle. Shortening of muscle refractoriness (32) in the arrhythmic substrate after the short-long cycle could enable penetration of the arrhythmic substrate by ventricular depolarizations due to early afterdepolarization after the long cycle, triggering a reentrant ventricular tachycardia, as previously discussed.

Our study showed that prematurity of ventricular premature depolarizations was not a trigger for ventricular tachycardia in the majority of patients because a ventricular premature depolarization with a prematurity index <1 induced only 18% of the ventricular tachycardia episodes. The lack of a significant increase in heart rate before ventricular tachycardia or fibrillation over that of the mean heart rate suggests a lack of significant increase in sympathetic tone as one of the trigger factors for ventricular tachycardia. These observations are in accordance with previous findings (37,38) from Holter recordings during ventricular tachycardia and fibrillation. However, recent studies (39–41) have shown that decreased heart rate variability appears to characterize the risk for sudden cardiac death in the canine infarct model and in human patients.

Limitations of the study. 1) In this study, the presence of an arrhythmic substrate was not tested in all Group I and Group III patients. However, this was not possible in those patients from Group I who did not survive the episode of ventricular fibrillation. Group III patients had no history of ventricular tachyarrhythmia and were primarily used as control subjects for Group II patients to assess the relative incidence of silent ischemia in the two groups. 2) The occurrence of monomorphic and polymorphic ventricular tachycardia was based on the configuration of the QRS complex on the two channel Holter recorder. It is possible that if multiple leads had been obtained, some monomorphic ventricular tachycardias might have been classified as polymorphic. However, this limitation cannot be overcome in a Holter ECG study.

Implications. The following implications may be drawn from this study. 1) Silent myocardial ischemia was not a major determinant of ventricular tachycardia or fibrillation in this group of patients. Nevertheless, the observation of frequent silent ischemic episodes in patients with ventricular tachycardia and fibrillation lends credence to the use of anti-ischemic agents in these patients. Therapy, however, should be focused on the arrhythmic substrate in those patients with sustained ventricular tachyarrhythmias who reveal electrophysiologic characteristics of the latter. 2) Because this is a select group of patients, the majority of whom survived the episode of ventricular tachycardia and fibrillation and were referred to electrophysiologic study, our observations should not be applied to the entire spectrum of patients with sudden cardiac death. 3) Pacing algorithms to prevent the short-long sequence by aborting the long sequence after a ventricular premature depolarization may indeed be a preventive measure that can be incorporated in pacemakers as well as in the automatic cardioverter-defibrillator.

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