The Prognostic Significance of Nonsustained Ventricular Tachycardia in Hypertrophic Cardiomyopathy

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SPIRITO et al report on the prognostic significance of nonsustained ventricular tachycardia (VT) during Holter monitoring in a highly selected cohort of 151 asymptomatic patients with hypertrophic cardiomyopathy (HCM). Patient selection excluded patients with moderate to severe symptoms (New York Heart Association functional classes III and IV), those with previous syncopal episodes, and those receiving antiarrhythmic or symptomatic pharmacological treatment. The finding of nonsustained VT in this low-risk cohort was associated with a relative risk of sudden death of 2.4 compared with those without nonsustained VT on Holter. In the 106 patients who were excluded, the cardiac disease-related annual mortality was 2.4%, similar to the overall annual mortality in adults in most published series. The major conclusion of the study was that the finding of nonsustained VT should not necessarily lead to initiation of antiarrhythmic therapy. This study focuses attention on an area of interest and importance in the practical management of patients with HCM.

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Historical Background

Sudden death is a well-recognized complication in patients with HCM. Retrospective reviews do not suggest that symptomatic therapy (β-blockers, calcium antagonists, myectomy) prevent sudden death. Indeed, symptoms and morphological as well as hemodynamic features of severity are not useful predictors of risk of sudden death. Clinical management, then, requires independent evaluation in relation to symptoms and prognosis. In every patient with HCM, the question should be asked, “Is this individual at risk of sudden death?” regardless of markers of symptomatic severity (for example, symptoms, left ventricular hypertrophy, left ventricular outflow tract gradient).

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Nonsustained Ventricular Tachycardia as a Marker of Sudden Death Risk

In 1981, two independent studies reported in the same month the association of nonsustained VT on Holter and subsequent sudden death. When the data in those patients who were treated medically were subsequently combined, the finding of nonsustained VT was found to be sensitive and specific, with high negative (97%) and low positive (22%) predictive accuracy for sudden death within 3 years. In practical terms, the adult (25 years of age) without nonsustained VT on Holter is at very low risk and can be reassured. Those patients with nonsustained VT had an 8% annual mortality and formed a high-risk cohort; the majority, however, did not die suddenly, suggesting that risk was variable and indicating the need for further risk stratification. The article from Spirito et al. by selecting the low-risk cohort, reinforces the fact that patients with nonsustained VT are not a homogenous group, and the lower annual sudden death mortality (1.4%) provides apparent justification for the conclusion “that the finding of nonsustained VT on Holter should not be considered, per se, an indication for antiarrhythmic treatment.”

This conclusion begs the question, “Can we identify the high-risk cohort, and should they receive antiarrhythmic therapy?” Nonsustained VT is presumably a marker of arrhythmic potential. The fact that the incidence of arrhythmia is low in the young and that there is a strong positive correlation of ventricular arrhythmias with age suggests that their presence is not simply a function of myocyte disarray, which is unlikely to be developmental into adult life, but that ventricular arrhythmias relate to myocyte replacement fibrosis as well as to interstitial fibrosis. Electrophysiological studies have been promoted to further refine the identification of those with the “electrophysiological substrate” for sudden death. Programmed electrical stimulation has been advocated. The predictive accuracy of inducible arrhythmias for subsequent sudden death has not been rigorously assessed, although an association between inducibility and adverse outcomes has been established. The fact, however, that with the recommended protocol, 40% to 50% of patients have an inducible ventricular arrhythmia and that only a minority of these will die suddenly indicates that the positive predictive accuracy is low. Recently, a novel electro-
physiological technique that assesses the inhomogeneity of intramyocardial conduction has shown that the early onset of electrogram fractionation after decremental ventricular extrastimuli is associated with sudden death. The principle that electrophysiological studies should further define the electrophysiological substrate in those identified by nonsustained VT on Holter is undoubtedly correct. In practice, the ideal electrophysiological study remains to be determined, although the results thus far favor approaches that make measurements that reflect the substrate rather than provoke nonspecific arrhythmia. The mechanisms of sudden death in HCM are complex and involve more than the electrophysiological substrate or predisposition to sustained ventricular fibrillation. Numerous triggers have been documented, although the relative importance and the true incidence of these are unknown. The triggering mechanisms include paroxysmal atrial fibrillation, clinical VT, conduction disease that may be occult, supraventricular arrhythmias associated with rapid atrioventricular (AV) conduction, and ischemia. The response to an arrhythmia or physiological tachycardia may be modulated by vascular responses that are abnormal in 30% to 40% of young patients. Assessment in relation to these potential triggers may require prolonged Holter monitoring, the use of patient-activated ECG monitoring devices, careful assessment of the exercise blood pressure response, and evaluation for evidence of ischemia, even in the young. Detailed characterization of patients who are known to be in a higher risk cohort because of previous syncopal episodes, sudden deaths in first-degree relatives, or the presence of nonsustained VT on Holter reveals that a minority (perhaps 20% to 30%) will have a probable documented initiating mechanism of sudden death that is amenable to specific therapy. These include paroxysmal atrial fibrillation (amiodarone), conduction disease (pacemaker), rapid AV conduction (ablation), clinical VT (drugs or implantable cardioverter-defibrillator [ICD]), and ischemia (high-dose verapamil). In the remaining patients who are recognized to be at increased risk, either multiple or no potential triggers will be identified. The choice of treatment in these patients will reflect the local expertise, bias, and resources. For the past 15 years, we have used low-dose amiodarone (plasma concentration <1.0 mg/L) successfully in the cohort with nonsustained VT. The initial practice of starting all patients with nonsustained VT on amiodarone has been modified with the ability to identify the high-risk cohort and the finding of intracardiac conduction that patients with nonsustained VT, not unexpectedly, span the gamut of responses from those seen in normal patients to those seen in patients who have or will experience ventricular fibrillation (Figure). The utility of these electrophysiological studies now needs to be tested prospectively. If they can select the highest-risk cohort with nonsustained VT with sufficient predictive accuracy, this may provide the basis for ICD implantation rather than pharmacological therapy. The role of myectomy in modifying risk also requires evaluation; again, patients undergoing surgery need to be characterized in relation not just to markers of symptomatic severity but also in relation to potential triggers and risk of ventricular fibrillation.

Two features of paced electrograms in hypertrophic cardiomyopathy (HCM) are associated with ventricular fibrillation (VF). Early increase in electrogram delay with long extrastimulus coupling intervals and a large increase in electrogram duration with premature stimulation. The electrophysiological characteristics of HCM patients with nonsustained ventricular tachycardia range from those seen in VF patients to those seen in controls. It is possible that those patients with a major substrate, ie, similar characteristics to VF patients, are vulnerable to relatively minor triggers, while those with characteristics similar to controls are relatively invulnerable.

The finding of nonsustained VT on Holter monitoring in the patient with HCM can then be seen as analogous to an 18-year-old with a sports car. Insurance companies make no attempt to define further the difference between those who will drink, drive, and crash their car versus those who will remain safe drivers; all such young individuals have their insurance premiums weighted. More detailed characterization should permit identification of that cohort at particular risk. Like the insurance weighting of all 18-year-olds, treatment of all patients with nonsustained VT may provide a measure of security in this case to the physician and perhaps the patient, but it will involve treatment of a significant cohort with a negligible benefit-to-risk ratio. The identification of nonsustained VT on Holter as stated in the conclusions of Spirito et al should not trigger reflex antiarrhythmic therapy, but it should lead to more detailed characterization to identify those individuals who are most likely to benefit from ideally targeted therapy to initiating mechanisms of sudden death, and, failing that, to the most appropriate therapy in the individual, be it amiodarone, ICD, or perhaps myectomy.

References


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