Editorial:
Antiarrhythmic Therapy, Ventricular Premature Depolarizations and Sudden Cardiac Death: The Tip of the Iceberg

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In acute myocardial infarction it is generally accepted that ventricular premature depolarizations (VPDs) lead to ventricular tachycardia and ventricular fibrillation (VF). Therefore, suppression of VPDs should result in a lower incidence of fatal ventricular dysrhythmias. Randomized controlled trials in patients with acute myocardial infarction have demonstrated fewer episodes of VF and ventricular tachycardia with the routine prophylactic administration of lidocaine or procainamide. However, it is not clear whether this salutary response is effected by suppression of VPDs per se, modification of underlying myocardial vulnerability to VF, or perhaps by affecting a critical interaction between the two.

Several workers have demonstrated that frequent, complex VPDs are associated with sudden cardiac death, presumably resulting from VF. This association has been observed in post-myocardial infarction patients and in patients who have survived previous episodes of out-of-hospital VF. While high-density ventricular ectopic activity is a predictor for future sudden death in patients with underlying cardiac disease, it has not been shown to be definitely independent of associated manifestations of heart disease, such as depressed ventricular function or the extent of coronary artery obstruction. An additional confounding factor in assessing the prognostic significance of ventricular ectopic activity is the spontaneous variability of VPD frequency in a patient.

In this issue of Circulation, Myerburg and co-workers report the results of a long-term follow-up of 16 survivors of out-of-hospital VF treated with procainamide or quinidine. The authors observed that patients whose plasma levels of these drugs were in the therapeutic range had fewer episodes of recurrent sudden death than patients in whom lower plasma levels were obtained. This apparent effect on recurrent sudden death was not consistently related to suppression of VPDs. In addition, the presence of therapeutic levels of antidysrhythmic agents was not correlated with control of ventricular ectopic activity.

However, these findings should be interpreted cautiously, particularly as they relate to the large groups of patients who are at risk for sudden cardiac death. The group studied by Myerburg was small, and there was no satisfactory control group or pretreatment assessment of VPD frequency. Additionally, the incidence of recurrent sudden death (eight of 16) reported in the present study is high compared with the incidence (one of 16) reported earlier by this same group of investigators.

Nonetheless, the findings in this study are provocative. The suggestion that recurrent VF might be prevented by relatively high (therapeutic) plasma levels of antidysrhythmic agents in spite of uncontrolled VPD frequency and complexity has important implications. First, if this suggestion is correct, the role of ambulatory ECG monitoring in the regulation of antidysrhythmic therapy should be reexamined. Perhaps there has been excessive dependence on the readily available technology for quantitation of VPDs and related dysrhythmias. Second, the well-entrenched concept that VPDs are initiators of sudden cardiac death has been investigated extensively; the underlying mechanisms of electrical instability, such as the role of mechanical events, disordered higher nervous activity or the cellular events whose final clinical expression may be ventricular ectopic activity, have not been emphasized. Perhaps investigative efforts should be refocused.

A majority of cardiac deaths are sudden and almost certainly due to the emergence of a "primary" dysrhythmic event in otherwise apparently stable cardiac patients, and several investigators have provided evidence that VF may be prevented. Therefore, future endeavors aimed at decreasing excess cardiac mortality are clearly needed. These should include:

1) Well-controlled clinical trials in patients at high risk for sudden cardiac death. The Beta-blocker Heart Attack Trial, a multicenter study of propranolol in post-myocardial infarction patients, is an example of this.

2) Studies designed to recognize and develop other predictors for sudden cardiac death. For example, the concept that latent electrical instability may be unmasked and used to identify individuals at high risk for subsequent VF should be studied.

3) Approaches for uncovering the pathophysiologic processes that render the myocardium vulnerable to VF. Additional studies on the role of neural activity in modulating this dysrhythmia will undoubtedly be fruitful.

4) Translation of such data into clinically useful tools with which appropriate patients can be identified for effective intervention.

As discussed by Julian, we are entering an era in which we may finally have the opportunity to reduce the enormous mortality from sudden cardiac death. While the importance of this task is compelling, a sim-
ple, singular approach to the prevention of VF is probably not attainable. Sudden cardiac death probably results from the interplay of many mechanisms. An organized approach to the recognition of each contributing influence and the subsequent application of therapeutic techniques to appropriate patient groups will be most successful.

References


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