Editorial Comment

Infarct Age and Reproducibility of Ventricular Tachycardia Induction*

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Experimental versus clinical ventricular tachycardia. Several animal models of ventricular tachycardia associated with myocardial infarction have been utilized to define the mechanism of ventricular tachycardia and develop improved therapy for this arrhythmia (1-3). Although these models have increased our understanding of the mechanism of ventricular tachycardia in humans, they all differ in some ways from the clinical situation. For example, early models of subacute ischemia localized the area of slow conduction and reentry to the epicardium (1). It has been demonstrated in other animal studies (4) and quite convincingly in human studies (5) that the area of slow conduction and reentry in humans more often arises in the subendocardial region. Other models utilizing coronary occlusion and reperfusion (2) followed by programmed electrical stimulation have produced arrhythmias similar to those seen in the electrophysiology laboratory during programmed electrical stimulation in patients. Although this artificial type of infarction produced in the canine model has histopathologic features resembling those seen in humans, spontaneous sustained ventricular arrhythmias similar to those observed clinically have not been reported with this model. Furthermore, although the mottled appearance of this infarction is similar to that seen in the border zone in human infarction, the overall architecture is less similar.

Present study. In the current issue of the Journal, Hunt and Ross (6) report an important study utilizing a simple canine model of coronary occlusion produced by single stage occlusion of the left anterior descending artery and two diagonal branches. No detailed pathologic studies were performed; nevertheless, this model of myocardial infarction probably produces an infarction more homogeneous than that observed with the occlusion-reperfusion model and less homogeneous than that of other models attempting to exclude collateral flow. Pathologically, it may be more similar than other models to the human condition. In their study, Hunt and Ross (6) demonstrate reproducible induction of sustained ventricular arrhythmias from 2 weeks until 4 months after infarction. During the 1st week after infarction, the reproducibility was considerably lower. Most importantly, the authors observed sustained ventricular tachycardia in eight dogs and sudden death in four (22% of those with inducible ventricular tachycardia at a cycle length >140 ms). This finding of spontaneous ventricular tachycardia and sudden death in an animal model is extremely important because it significantly strengthens the similarity of this canine model to the human situation.

Potential limitations of study. The study has a number of methodologic problems. First, Hunt and Ross (6) studied some dogs in the conscious state and some in the unconscious state and, in addition, used several different types of anesthesia. Obviously, their work was part of another study to determine the effects of consciousness and the effect of different anesthetic agents on the inducibility of ventricular arrhythmias. Fortunately, it does not appear that these differences significantly affected the outcome of the present study. Second, Hunt and Ross chose to select 10 s as the definition of sustained ventricular tachycardia. More often, 30 s or an arrhythmia requiring cardioversion or pacing for termination because of hemodynamic compromise is chosen as the end point in human studies.

The most important shortcoming of the study is that the same set of dogs was not used throughout the experiment. The authors used various cohorts of dogs at different times and discarded dogs with no inducible ventricular tachycardia. This procedure was most likely followed because this study combines multiple other studies to generate the data presented, but it makes interpretation of the data more difficult and less reliable. The authors did not monitor a large number of dogs with no inducible arrhythmias to determine whether the animals later exhibited inducible tachyarhythmia or had spontaneous arrhythmia of a type that was previously nondetectable. It was thus assumed that dogs with no inducible ventricular tachycardia would be unlikely to have spontaneous arrhythmias. This is certainly not true in humans: a significant number of patients who have had spontaneous sustained ventricular tachycardia or cardiac arrest and have no inducible arrhythmias in the electrophysiology laboratory later have a recurrent clinical event (7). Thus, the sensitivity and specificity of arrhythmia induction cannot be evaluated in this animal study. Nevertheless, the authors (6) have demonstrated reproducible induction of...
ventricular tachycardia as well as spontaneous sustained ventricular arrhythmias in this animal model. For this reason, the model certainly warrants further study.

The authors employed a very aggressive stimulation protocol, using up to seven extrastimuli to assure reproducibility of ventricular tachycardia induction from study to study. This type of stimulation protocol in humans has been shown to produce a high incidence of false positive studies most often manifested as polymorphic ventricular tachycardia or ventricular fibrillation (8,9). Although not specifically addressed in their report, the authors describe relatively little polymorphic ventricular tachycardia and I assume that most of the ventricular tachycardia patterns they observed were monomorphic. In addition, they report only a relatively small number of dogs having ventricular fibrillation induced with this very aggressive stimulation protocol. It is difficult to correlate the standard stimulation protocol used in humans with those employed in animal studies because of the differences in heart rate, ventricular refractoriness and ventricular tachycardia cycle length. Nevertheless, it is clear that the stimulation protocol used in the present study was quite aggressive.

Comparison with clinical studies. Studies in humans (10) have demonstrated a very high mortality rate from sustained ventricular arrhythmias in the first several weeks to months after acute myocardial infarction. Both medical and surgical therapy have failed to produce a good outcome in these patients. It has been hypothesized that the changing milieu during this early phase after myocardial infarction makes selection of definitive therapy difficult. The results in the present study support changes in inducibility of ventricular tachycardia in the early postmyocardial infarction period that might make selection of therapy difficult, as found in human studies. Once again, this suggests a similarity between this animal model and the human situation.

Several studies have attempted to use programmed electrical stimulation to select patients at high risk for sudden cardiac death or sustained ventricular arrhythmias after acute myocardial infarction. Although the initial reports (11,12) were optimistic, subsequent studies (13,14) failed to validate the early findings. Nevertheless, all of these studies used different stimulation protocols and studied the patients relatively early after myocardial infarction. The failure to reproduce ventricular tachycardia induction in the present animal study, suggesting a changing milieu during this period, may explain some of the lack of predictive value noted during early postmyocardial infarction electrophysiologic testing in humans. The present study would suggest that programmed stimulation performed 2 to 4 weeks after infarction might be more predictive than that performed within the 1st to 2 weeks after myocardial infarction. In addition, this study would suggest that quite an aggressive stimulation protocol may be needed although it may reduce specificity. In addition, even in this study, only 22% of dogs with inducible "slow ventricular tachycardia" were observed to have spontaneous arrhythmias. Thus, even if a similar condition were found in humans, it would require treating a great number of patients with inducible sustained ventricular tachycardia who would not later experience spontaneous arrhythmias. Additional studies to evaluate the sensitivity and specificity of stimulation protocols and timing of programmed stimulation to evaluate the predictive value of programmed stimulation in the postmyocardial infarction period are probably warranted.

Role of signal-averaged electrocardiogram. The present study did not address the role of the signal-averaged electrocardiogram (ECG). Previous work (15) has shown that results of this study are more often abnormal in patients with than in those without spontaneous ventricular tachycardia and that is is a useful technique for selecting patients at risk for inducible sustained ventricular tachycardia (16). This study, coupled with the electrophysiologic study, might be a useful method of selecting those patients after myocardial infarction who are most appropriate for programmed electrical stimulation and ultimately antiarrhythmic therapy.

References


