Letter to the Editor

Action Potential Duration, Activation-Recovery Interval and Effective Refractoriness: A Well Known but Unresolved Trinity

To the Editor:

The clinical investigation published in the Japanese Circulation Journal was an excellent study of the correlation between the effective refractory period (ERP) and activation–recovery interval (ARI) using the intracardiac unipolar electrogram recorded at multiple sites in the human right ventricle. This electrophysiologic study (EPS) clarified the close correlation between ARI and ERP and hence addressed the utility of ARI as a parameter of local ERP, the distribution of which is difficult to evaluate simultaneously in the clinical EPS. The ARI is also obtained during the basic EPS, using a microelectrode that is usually applied to record intracellular action potential. Action potential duration (APD) has also been reported to reflect the ARI derived from an extracellular unipolar electrogram under microelectrode recording in an in vivo animal study.

The authors investigated the relationship between the ARI and ERP in control and dl-sotalol groups and found an identical linear regression in both groups, which contained various heart diseases. These findings indicate ARI is a reasonable parameter of local ERP under the pharmacologic intervention for a variety of organic heart diseases. However, as the authors noted in their study limitations, the unipolar electrogram is distorted and obtained by pacing with a relatively higher end diastolic threshold intensity in the arrhythmogenic substrate, such as the ischemic or degenerated area. Dispersion of the ERP is of paramount importance in clarifying the arrhythmogenic mechanisms in such an area. Therefore, in order to extrapolate the correlation between ARI and ERP to the arrhythmogenic substrate, measurement of the ARI should be conducted under exact exclusion criteria.

Moreover, postrepolarization refractoriness (PRR), which obscures the perfect correlation between ARI and ERP, is evident in such a diseased area. PRR is dependent on the heart rate and external potassium concentration and these 2 determinants of PRR also influence the effectiveness of dl-sotalol by modulating the magnitude of IkA one of the major repolarizing currents and the target of dl-sotalol. In this light, investigation of the close correlation between ARI and ERP should be conducted over a wide range of steady-state pacing rates and is doubtful in the subjects with electrolyte abnormalities. Current sophisticated EPS devices are expected to lead to better understanding of the trinity of ARI, APD and ERP, which is dependent on the site of EP recording, heart rate, autonomic nervous tone, electrolytes and antiarrhythmic agents individually and in concert.

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References


Author’s Reply

Correlation Between the Effective Refractory Period and Activation-Recovery Interval Calculated From the Intracardiac Unipolar Electrogram of Humans With and Without dl-Sotalol Treatment

We would like to thank Drs Maruyama and Kubota for their thoughtful comments and appreciate their interest in our study. Recent basic studies have shown that repolarization abnormalities can partly lead to construction of the arrhythmogenic substrate of ventricular tachyarrhythmia but in the clinical electrophysiologic study, either the effective refractory period (ERP) measured by premature stimulation or the monophasic action potential recording has limitations in analysis of the beat-to-beat change of distribution of ventricular repolarization. We reported the clinical usefulness of the activation–recovery interval (ARI) as another parameter to assess ventricular repolarization both in the control state and when the patient is treated with dl-sotalol. However, as with other techniques, measurement of ARI has several limitations, which Drs Maruyama and Kubota have highlighted.

The unipolar electrogram can be recorded even from an arrhythmogenic area with an abnormal local electrogram, and ARI can be analyzed on the basis of the previous definition. However, it would be technically difficult to confirm whether ARI obtained from the unipolar electrogram in the arrhythmogenic area reasonably approximates the local refractoriness. In the normal myocardium, the T
waves of the unipolar electrogram usually show a monophasic configuration and the local ERP can be estimated using an extrastimulation technique. On the other hand, the high pacing threshold at the arrhythmogenic area may excite a large area of the myocardium surrounding the site and induce an error of spatial difference. Further, complex configurations of the unipolar T wave may create difficulties in identifying the reasonable terminal point of repolarization.

Postrepolarization refractoriness (PRR) is an important factor in modulating the activation and repolarization in the heart, especially in the arrhythmogenesis, and can modulate the close correlation between ARI and ERP. As we reported in our clinical studies of reentrant ventricular tachycardia, class I antiarrhythmic drugs (procainamide, mexiletine, etc) could induce PRR in the slow conduction area of the reentry circuit and this is related to the therapeutic effects of the drugs. Although the effect of PRR was minimal in our study, electrolyte abnormalities, myocardial ischemia and/or alteration of the autonomic tone may accentuate the PRR associated with class III antiarrhythmic drugs.

With regard to the measurement of ARI, we need to pay attention to its limitations. We intend to focus on the correlation between ARI and ERP in patients with long QT syndrome and Brugada syndrome because the ventricular tachyarrhythmia in those diseases originates from the ventricle that has the repolarization abnormality.

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References