Correlation Between In Vivo Transmembrane Action Potential Durations and Activation-Recovery Intervals From Electrograms
Effects of Interventions That Alter Repolarization Time

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Classic cable theory was used to analyze the relation between the activation-recovery interval measured from unipolar electrograms and transmembrane action potential duration. Theoretic analysis demonstrated that the temporal derivative of the extracellular potential is proportional to a spatial weighting of the third temporal derivative of the transmembrane action potentials along a cable with uniform propagation in a homogeneous medium. Thus, the activation-recovery interval, measured as the interval between times of minimum derivative ($V_{min}$) of the QRS and maximum derivative ($V_{max}$) of the T wave, should be related to action potential duration, measured as the interval between times of $V_{max}$ of the upstroke and $V_{min}$ of the downstroke of the transmembrane action potential. This relation was examined experimentally in 12 anesthetized dogs. Unipolar electrograms and transmembrane action potentials were recorded simultaneously from sites within 2 mm of each other during control states, cardiac sympathetic nerve stimulation, localized epicardial warming, and graded reductions in myocardial perfusion. The heart was paced from several sites. There was close correlation between activation-recovery interval and action potential duration measurements taken during cardiac sympathetic nerve stimulation and local epicardial warming ($r=0.96$ and 0.99 for cardiac sympathetic nerve stimulation and warming, respectively). In five animals in which coronary perfusion pressure was gradually lowered, the variables correlated closely over a range of values from 62 to 212 msec ($r=0.98$). However, although the overall correlation was good and mean differences between activation-recovery interval and action potential duration were small, in individual cases there were differences up to 24 msec. This study provides new data that are consistent with the theoretic prediction that time of $V_{max}$ of the T wave is related to time of $V_{min}$ of the local action potential and that activation-recovery interval is directly related to action potential duration. In addition, the results provide evidence that the activation-recovery interval is a good estimate of the action potential duration independent of T waveform, drive site, or the presence of localized steep gradients of repolarization. (Circulation 1990;81:281–288)

The activation-recovery interval (ARI), defined as the interval between times of minimum derivative ($V_{min}$) of the QRS and maximum derivative ($V_{max}$) of the T wave in unipolar electrograms, has been proposed as a useful measure of local repolarization duration. Such a measurement is desirable because, in contrast to ventricular refractory periods, ARIs can be determined from multiple, simultaneously recorded electrograms to provide both beat-to-beat changes and spatial characteristics of repolarization. The potential usefulness of the measurement underscores the importance of establishing its theoretic basis and experimentally defining its validity and limitations. The validity of the measurement has been demonstrated mainly with respect to refractory period. Millar et al showed that ARIs from unipolar electrograms correlated closely with ventricular refractory periods under conditions of varying cycle length and adrenergic stimulation. Blanchard et al concluded that the ARI measures local events since the measurement was not significantly altered by changing the timing of distant electrical events. Wyatt examined the relation between ARIs and action potential durations (APDs) during changes...
in cycle length and coronary occlusion. However, that work was limited by the small numbers of animals studied and interventions performed. An analytic derivation for the theoretical basis of the ARI measurement has not been reported, nor has the correlation between ARIs and APDs been systematically studied. The purposes of the present study were 1) to provide an analytic derivation of a theoretic basis for the correlation between times of $V_{\text{min}}$ of the QRS and $V_{\text{max}}$ of the action potential upstroke and times of $V_{\text{max}}$ of the T wave and $V_{\text{min}}$ of the action potential downstroke and 2) to determine the correlation between ARIs and in vivo transmembrane APDs under a variety of conditions.

Methods

Animal Experiments

Experiments were done on 12 mongrel dogs anesthetized with sodium pentobarbital (30 mg/kg i.v.). Additional small doses were given as needed to maintain deep anesthesia. The animals were ventilated with room air supplemented with oxygen using a fixed volume respirator. Arterial pressure, blood gases, and pH were monitored continuously and kept within the normal range. The heart was exposed with either a midline or left lateral thoracotomy and cradled in the open pericardium. In different animals the heart was paced at cycle lengths from 380 to 400 msec at twice-diastolic threshold voltage through bipolar hook electrodes placed in the left or right atrial appendage, anterior right ventricle, and posterior left ventricle. Silver wire unipolar electrodes (0.005-in. diameter) were mounted on a nylon sock that was stretched over the heart and anchored to the pericardium. Transmembrane action potentials and unipolar electrograms were recorded simultaneously within 1–2 mm of each other. Action potentials were recorded with floating microelectrodes made from borosilicate capillary tubing and filled with 3 M KCl to give resistances of less than 20 MΩ. The microelectrode was placed intracellularly within 1–2 mm of and referenced to the unipolar recording lead. Acceptable impalements lasted up to 2 minutes, at which time waveforms deteriorated. Criteria for an acceptable impalement included qualitative assessment of waveform stability, upstroke sharpness, and observance of transmembrane action potential morphology. Transmembrane action potentials and unipolar electrograms were recorded simultaneously during an impalement. If the transmembrane action potential recording became unstable, another cell as close as possible to the same site was impaled. Recordings were taken under control conditions and during sympathetic nerve stimulation, warming, or ischemia while pacing the atrium or the atrium and the anterior right ventricle or posterior left ventricle.

The amplification and recording system used in this study permitted signals from 10 channels to be simultaneously amplified, digitized, and stored on magnetic tape. This custom-built system allowed for selection of amplification, low and high frequency cutoffs, sampling rate, and sampling duration. Electrograms were recorded using a 0.03–500 Hz band width and sampled at 1,000 Hz. Action potentials were recorded using a 0–500 Hz band width and a 1,000 Hz sample rate, and recordings were taken simultaneously with the electrograms. Although these recording procedures were not adequate for assessing $V_{\text{max}}$, they were appropriate for measuring time of $V_{\text{max}}$ to within the ±1 msec experimental error acceptable in this study.

In seven dogs the chest was opened with a midline incision, and the ventromedial and recurrent cardiac nerves were isolated 1–2 cm below the caudocervical ganglia. They were stimulated simultaneously for approximately 30 seconds with 10 V, 2 msec square wave pulses at 20 Hz. Unipolar electrograms and action potentials were recorded from the anterior cardiac surface in the control state and during nerve stimulation during atrial, right ventricular, and left ventricular pacing. Following nerve stimulation there was a 20-minute recovery period before the next control recording.

In five of the seven dogs, local changes of repolarization were produced by warming a 1 cm diameter area surrounding one anterior unipolar electrode. A light beam from a tungsten-halogen lamp was directed through a condenser lens assembly to warm the epicardium, as described previously. Action potentials were recorded alternately from a site within the warmed region and an unwarmed site 1 cm away from the warmed area during atrial, right ventricular, and left ventricular pacing. Electrograms from both sites were recorded simultaneously with the action potential. The time between recordings taken at the unwarmed and warmed sites was less than 1 minute.

In five additional dogs the chest was opened via a left lateral thoracotomy. The proximal left anterior descending coronary artery was dissected free over a 1 cm length beyond the first diagonal branch. After injection of heparin (5,000 units i.v.), the left anterior descending coronary artery was cannulated and perfused with femoral arterial blood, which was first run through a peristaltic pump, reservoir, and warming coil. Use of graded perfusion permitted better control and reproducibility of the ischemic state than could be obtained with complete coronary occlusion. Perfusion pressure was monitored continuously at the cannula tip. The perfusion pump was controlled by a servo mechanism that kept coronary perfusion pressure constant at preset levels. Coronary blood flow was continuously monitored by an electromagnetic flow probe in the perfusion system. Coronary perfusion pressure was lowered in increments of 10–20 mm Hg, beginning at a mean pressure of 80–100 mm Hg. At each level of perfusion, coronary flow was allowed to stabilize for 5 minutes before recording electrograms and action potentials from a site within the perfusion field. In four dogs radio-labeled microspheres were injected into the perfusion line for determination of myocardial perfusion.
Recordings were taken, and microsphere injections were made at each level of perfusion pressure until blood flow, as measured by the electromagnetic flow probe, was zero. The entire procedure took less than 30 minutes. Perfusion pressure was then increased to 80–100 mm Hg and blood flow allowed to normalize for 30 minutes. Additional recordings were then taken at different sites within the perfusion field.

Data Analysis

A two-pass, semiautomated computer program was used to identify activation and recovery times from the derivatives of electrograms and action potentials. Activation times were defined as times of \( V_{\text{min}} \) in electrogram QRS downstrokes (intrinsic deflection) and \( V_{\text{max}} \) in action potential upstrokes. Recovery times were defined as times of \( V_{\text{max}} \) near the peak of electrogram T waves and \( V_{\text{min}} \) in action potential downstrokes. Rationale for using the latter measurement in these studies was based on inability to measure action potential baselines, a requirement for traditional duration measures such as APD_{90}. During the first pass the appropriate times were measured from the digitally smoothed derivative of the signals. Electrograms and action potentials and the selected activation and recovery times from the first pass analysis were graphically recorded on an electrostatic printer plotter. During the second, editing pass data with questionable times were displayed along with derivatives and measured times on a computer terminal and new times selected if necessary. Such editing was usually necessary only when stimulus artifacts were mistaken for activation times or interventions caused ST-T waveforms to have ambiguities as to recovery times.

Figure 1 shows several ST-T waves and their first derivatives (V) from electrograms recorded in these experiments. A vertical marker indicates time of recovery. In Panels A and B, electrograms with negative and positive T waves are shown. For negative T waves \( V_{\text{max}} \) occurred after the nadir of the T wave while for positive T waves \( V_{\text{max}} \) occurred before the peak of the T. When T waves were biphasic, as in Panel C, the positive phase always occurred after the negative phase, and \( V_{\text{max}} \) was taken on the upstroke of the positive peak. In cases such as those shown in Panels A, B, and C, editing of activation and recovery times was generally unnecessary. Panels D, E, and F show the ST-T segments from electrograms recorded during ischemia. In some ischemic electrograms there was an “inflection point” just beyond the peak T (Panel D), which corresponded to the time of recovery and was consistent with a “local recovery wave” (see the theoretic justification which follows). When there was no clear “inflection point,” time of \( V_{\text{max}} \) was taken on the upstroke of the T wave (Panel E). When ST segment elevation obscured the onset of a positive T wave, the time of \( V_{\text{max}} \) was taken as the point beyond which the T wave slope became negative (Panel F). Transmembrane APD was defined as the interval between times of maximum and minimum derivative of the action potential upstroke and downstroke, respectively.

Linear regression plots of ARI versus APD during the control state and interventions of sympathetic nerve stimulation, warming, and ischemia were constructed using paired data. Mean differences between ARI and APD and their SDs (mean ARI−APD±SD) were determined for control and intervention groups independent of drive site and for three different drive sites independent of control or intervention. A two-way analysis of variance (ANOVA), with intervention and drive as the two factors, was used to test for differences among the mean ARI-APD groups. The range of differences between ARI and APD for each group was also determined.

Results

Analytic Derivation

Classic cable theory was used to derive a theoretic basis for the relation between activation and recovery times from electrograms and times of cellular depolarization and repolarization. If one assumes idealized conditions of an infinitely long one-dimensional cable in a homogeneous, isotropic volume conductor and an action potential propagating at a constant
velocity, it may be shown that the extracellular potential at an arbitrary location \((r)\) and time \((t)\) is given by

\[
\phi(r,t) = \frac{1}{\sqrt{V}} \int \frac{\partial^2}{\partial x^2} V(x,t) f(r,x) dx
\]  

where \(V(x,t)\) is the action potential at \(x\) and \(t\), \(f(r,x)\) is a spatial weighting function dependent on observation site, and the integration is over the length of the cable. Assuming plane wave propagation at uniform velocity, \(V\), along the cable, Equation 1 becomes

\[
\phi(r,t) = \frac{1}{\sqrt{V}} \int \frac{\partial^2}{\partial x^2} V(x,t) f(r,x) dx
\]

Differentiating Equation 2 with respect to time yields

\[
\phi'(r,t) = \frac{\partial}{\partial t} \phi(r,t) = \frac{1}{\sqrt{V}} \int \frac{\partial^3}{\partial t^3} V(x,t) f(r,x) dx
\]  

Equation 3 documents that the temporal derivative of the extracellular potential is proportional to a spatial weighting of the third temporal derivative of the transmembrane action potentials along the cable.

Figure 2 shows an epicardial transmembrane action potential and its first three temporal derivatives \((V, \dot{V}, \ddot{V})\). Times of activation and recovery are indicated by \(t_a\) and \(t_r\), respectively.

![Figure 2](image_url)

**Figure 2.** Epicardial transmembrane action potential (TMAP) recorded in normal myocardium and its first three temporal derivatives \((V, \dot{V}, \ddot{V})\). Times of activation and recovery are indicated by \(t_a\) and \(t_r\), respectively.

The time of steepest downstroke velocity. Correspondence of times would be exact in the case of symmetric waveshapes of action potential upstroke and downstroke. Since peaks of \(V\) and \(\dot{V}\) for both depolarization and repolarization corresponded closely and estimation of \(\ddot{V}\) required additional smoothing, we felt that \(V\)-based times would provide an acceptable estimate.

Equation 3 suggests that \(\phi'(r,t)\) is a spatial average of the distribution of \(\partial^3 V/\partial t^3\) with \(f(r,x)\) operating as the weighting function. As the observation site, \(r\), becomes arbitrarily close to the active cable, \(f(r,x)\) approaches an impulse function effectively filtering out effects of electrical activity from distant parts of the cable. The derivative of this “direct” unipolar recording would then be dominated by a minimum at the time of depolarization and a maximum at the time of repolarization, corresponding to the upstroke and downstroke, respectively, of the action potential of the cells closest to the recording site. Clearly, the actual relation between ARI and APD will depart from the ideal, in part because of tissue inhomogeneity and anisotropy as well as nonuniform propagation. The magnitude of these effects has not yet been reported.

**Experimental Studies**

Cardiac sympathetic nerve stimulation. Representative electrogram and transmembrane action potential recordings taken during control and cardiac sympathetic nerve stimulation are shown in Figure 3. Recordings were taken during pacing from three sites. As expected, the QRS and T waveforms of the electrograms varied depending on the drive site. For example, the QRS polarity was positive and T wave polarity biphasic during left ventricular drive while the QRS polarity was biphasic and T wave polarity positive during right ventricular drive. Sympathetic
nerve stimulation resulted in decreased APD, altered electrogram T waveform, and decreased ARI during all drives. Average decreases in ARI and APD were 21 and 22 msec. In this example, the range of ARIs over all drives was 3 msec during control and 9 msec during nerve stimulation. The range of APD over all drives was 2 msec during control and 4 msec during nerve stimulation. Paired ARI and APD measurements were within 4 msec of each other during control and within 3 msec of each other during nerve stimulation. Figure 4 shows the linear regression curve comparing ARIs and APDs ($n=138$, 11 sites, seven animals). The measurements were closely correlated ($r=0.96$, SEE=4.8 msec) regardless of T wave configuration. Mean differences between ARI and APD (mean ARI–APD±SD) were 1.2±4.2 and 2.5±6.0 msec during control and sympathetic nerve stimulation, respectively. Similar values were obtained when the data were grouped according to drive site. There were no significant differences between mean ARI-APD groups (control, sympathetic nerve stimulation, three drives) when the data were analyzed using ANOVA. The greatest difference between ARI and APD was 24 msec. Thus, although the mean differences between ARI and APD were small, for some paired determinations the differences were large.

**Myocardial warming.** Electrograms from two right ventricular sites within 1 cm of each other and the simultaneously recorded transmembrane action potential (TMAP) from one of those sites are shown in Figure 5. TMAPs were recorded within 1–2 mm of the electrogram recording sites. Site 1 was outside the area that was warmed, and site 2 was inside the area that was warmed. Panel A shows the electrogram and TMAP from the site to be warmed (site 2) before warming as well as an electrogram from site 1. ARI and APD, measured from recordings from site 2, were 196 and 194 msec, respectively. The ARI measured from a recording from site 1 was 194 msec. The T waves were negative in both electrograms. Panel B shows the electrogram and TMAP recorded from the warmed site (site 2) as well as an electrogram from site 1. During warming, ARI and APD, measured from recordings from site 2, shortened to 161 and 165 msec, respectively. T wave polarity changed from negative to positive. At site 1 the ARI was 189 msec, and T wave polarity was negative. Panel C shows the electrogram and TMAP recorded from site 1 during warming of site 2 as well as the electrogram recorded from site 2. The ARI and APD from site 1, outside the warmed area, were 191 and 190 msec, respectively. The ARI from site 2 was 161 msec. The T wave was positive at the warmed site and negative at the adjacent unwarmed site 1 cm away. Thus, under conditions of localized ventricular warming, ARI and APD decreased only in the recordings from within the warmed region. Measurements of ARI and APD from within the warmed region corresponded to each other regardless of the longer values of repolarization at surrounding unwarmed sites. Measurements at unwarmed sites corresponded to each other regardless of the shorter values at nearby warmed sites. This finding suggests that the ARI is a measure of local duration of repolarization within a diameter as small as 1 cm.

Figure 6 shows the linear regression curve for data from this group of studies comparing ARI and APD during control periods and warming during drive from three sites ($n=75$, seven sites, five animals). There was close correlation between ARI and APD ($r=0.99$, SEE=4.2 msec). Mean ARI–APD±SD were $-1.8±4.1$ and $1.5±3.5$ msec for control and warming groups, respectively. Similar values were obtained.
when the data were grouped according to drive site. No significant differences between mean ARI-APD groups (control, warming, three drive sites) were identified using ANOVA. The greatest difference between ARI and APD was 13 msec.

**Myocardial ischemia.** In five animals ARI, APD, and coronary flow (microspheres and electromagnetic flow probe) were determined while coronary perfusion pressure was gradually lowered to produce ischemia. Figure 7 shows simultaneous electrograms and action potentials recorded during one experiment during supraventricular drive at perfusion pressures of 60, 40, 30, and 20 mm Hg. Coronary flow was 62 ml/min/100 g at a perfusion pressure of 60 mm Hg and decreased to 11 and 5 ml/min/100 g at pressures of 40 and 30 mm Hg, respectively. Coronary flow, as determined by the flow probe, was zero at a pressure of 20 mm Hg. In this example, at a perfusion pressure of 60 mm Hg, ARI and APD were 206 and 205 msec, respectively. At a perfusion pressure of 40 mm Hg, the action potential shortened and became triangular. At this pressure the T wave of the electrogram became upright and notched, and there was ST segment elevation. ARI and APD were 151 and 159 msec, respectively. At pressures of 30 and 20 mm Hg, action potential amplitude and duration decreased further, ST segment elevation increased, and the T waves became taller. As ischemia became more severe and the action potential waveform changed further, \( V_{\text{min}} \) was in the midportion of phase 3 rather than near the end of the action potential. ARI and APD corresponded less closely under these conditions. At a pressure of 20 mm Hg, ARI and APD were 63 and 71 msec, respectively.

Figure 8 shows the linear regression curve comparing ARI to APD during normal myocardial perfusion and ischemia. Values of ARI and APD were between 62 and 212 msec. There was close correlation between ARI and APD (\( r=0.98, \text{ SEE}=6.7 \)). Mean ARI-APD±SD was 1.8±4.5 and 1.6±7.3 msec for control and ischemia groups, respectively. Similar values were obtained when the data were grouped according to drive site. No differences were identified between mean ARI-APD groups (control, ischemia, three drives) when analyzed by ANOVA. SDs of mean ARI-APD were greater in the ischemia group than the sympathetic nerve stimulation or warming groups (7.3 msec compared with 6.0 and 3.5 msec, respectively). The greatest difference between ARI and APD was 23 msec, which was comparable to the 24 msec ARI-APD difference for the sympathetic nerve stimulation group but greater than the 13 msec ARI-APD difference in the warming group.

**Discussion**

This study provides an analytic derivation using a simple model to justify use of ARI as measures of recovery properties. Justification of the ARI as a local measure of repolarization is based on the assumption that both activation and recovery occur
as propagated wavefronts. In normal cardiac tissue, transmembrane currents propagate actively in a wavefront originating at the stimulus site. During excitation, an electrode records a positive deflection as the wavefront approaches. As the excitation wave passes and recedes, the deflection rapidly becomes negative and then returns to baseline. Thus, the time of $V_{min}$ of the QRS corresponds to time of activation. Spach et al.\(^6\) reported a theoretic basis for this relation and computer simulations which showed that $V_{max}$ of the action potential occurred at the same time as $V_{min}$ of the extracellular potential recorded along a cable. Recovery can also be thought of as a propagating wavefront in the sense that it occurs in a systematic sequence. It differs from propagated activation wavefronts in that it is largely passive, has a slow velocity, and is of opposite polarity. Because the polarity of recovery is opposite to that of activation, the deflection of the T wave corresponding to time of recovery should be the time of maximum positive derivative. The justification for the relation between the maximum derivative of the T wave and the minimum derivative of the action potential we have presented is similar to the justification for the relation between the minimum derivative of the QRS and the maximum derivative of the action potential in idealized circumstances reported by Spach et al.\(^6\)

This experimental study provides evidence supporting the relation between the ARI and transmembrane APD. We studied the effects of pacing site on the relation between ARI and APD because drive site affects T wave configuration. Local epicardial warming and sympathetic nerve stimulation were used to examine the effects of local and more diffuse gradients in repolarization on the relation between the two measurements. Our data are consistent with the previous study by Millar et al., who found that ARIs from unipolar electrograms were closely correlated to refractory periods over a range of cycle lengths during infusion of norepinephrine and during cardiac sympathetic nerve stimulation. The finding that in individual cases the differences between ARI and APD are large, although mean differences are small, is also consistent with the study of Millar et al.\(^1\)

We chose ischemia as a worst case in which to apply the measurement of ARI because ischemia results in ST segment elevation, which can obscure the T wave, and decreased amplitude, shortening, and triangulation of the TMAP. These changes cause the maximum derivative of the T wave and the minimum derivative of the action potential downstroke to become less distinct, introducing the possibility of error into both measurements. The relation between ARI and APD during coronary occlusion was examined in an earlier limited study by Wyatt.\(^3\) In that study $r$ and SEE's for individual experiments were quite variable. This variability is not surprising because in coronary occlusion, the electrophysiologic state is rapidly changing, and altered membrane potential and local conduction block progressing to inexcitability could influence recorded action potentials and ARI measurements. To create a less rapidly changing ischemic environment, we used a method of stepwise decreases in coronary perfusion pressure to produce ischemia. It is possible that the correlation between ARI and APD would not be as good in the case of sudden, complete coronary occlusion. Under the described conditions of graded ischemia, the correlation between ARI and APD remained good, and $r$ values were not different from those calculated for the other interventions. However, there was greater variability about the regression curve as evidenced by a larger SEE in the ischemia group compared with other interventions. In addition, there was greater variability in the difference between ARI and APD manifested by the larger standard deviation of the mean ARI-APD in the ischemia group as compared with the sympathetic nerve stimulation and warming groups. The maximum difference for individual paired measurements in the ischemia group was similar to that for sympathetic nerve stimulation but larger than that for the warming group. The increased variability in the measurement of ARI with respect to APD in the ischemia group is probably the result of difficulties in determining $V_{max}$ of the T wave as a result of ambiguities in the STT wave caused by ischemia. It was in the ischemia group that the second editing pass for data analysis and the constraints on the measurement of ARI were most used. The use of the inflection point near the peak of the T wave as $V_{max}$ is somewhat empiric but is consistent with a local recovery wave.

In addition to demonstrating that ARIs correlate well with APDs, this study provides some additional evidence as to the local nature of the ARI measurement. In the warming studies, APD was greatly shortened in a localized area, and ARI still correlated very closely with APD. At adjacent sites no more than 1 cm distant, ARI and APD were also closely correlated and had durations much greater than at the warmed site. Thus, under these conditions the ARI was an accurate measure of local repolarization. The extent to which the ARI is a local measurement is dictated by the observed standard errors, which were less than 7 msec. These errors make it unlikely that nonuniform dispersion of refractoriness can be measured by the technique within small regions. The findings are consistent with those of Blanchard et al.\(^2\) who found that ARIs were not altered by changing the timing of distant electrical events.

A potential application of the measurement of ARIs is the experimental and clinical study of the temporal and spatial characteristics of repolarization. Refractory period determinations are time consuming and cannot be made simultaneously from multiple leads. TMAPs can be recorded from only a few sites simultaneously and only from an exposed cardiac surface. In contrast, ARIs can be determined from many electrograms recorded simultaneously on a beat-to-beat basis. There are potential limitations of the method. In ischemia alterations in the ST
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segment and T wave may make determination of the maximum derivative of the T wave difficult or impossible. In addition, although the measurement correlates well with APD, it may not always correlate with the refractory period. In ischemia prolongation of the refractory period beyond the duration of repolarization, a phenomenon known as post repolarization refractoriness, is frequent.7,8 In this setting the refractory period, more than the duration of repolarization, is a determinant of excitability. When postrepolarization refractoriness occurs, there is greater disparity of ARIs than disparity of refractoriness.9 Thus, in the setting of ischemia, the refractory period may be of greater clinical significance than duration of repolarization as measured by either APD or ARI. This circumstance is a potential limitation of the usefulness of the measurement of ARIs in ischemia.

Findings in this study do not conflict with those of a recently reported simulation study, even though that study demonstrated that substantial errors in estimation of activation and recovery times from electrograms can occur.10 Factors responsible for those errors included nonuniform coupling resistance, nonuniform membrane properties, and alterations in recording site relative to activation sequence. Results of the present study suggest that these factors were not sufficiently important in the conditions investigated to prevent practical estimation of activation and recovery times from electrograms. Moreover, the error analyses presented provide guidelines for using the technique in a variety of settings.

In summary, we have reported an analytic derivation for the theoretic basis of the relation between ARI and APD. In addition, we have demonstrated that ARI and APD correlate under a variety of conditions including changes in T wave polarity, drive site, steep gradients of repolarization, and myocardial ischemia. The study provides evidence for the local nature of the measurement and the usefulness of the measurement in worst cases such as ischemia, steep gradients of repolarization, and ectopic activity. Measurements of ARI from many simultaneously recorded sites will permit reasonable estimates of temporal and spatial changes in repolarization in experimental and clinical studies.

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References


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