Characterization of fibrillatory rhythms by ensemble vector directional analysis

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RECENT STUDIES HAVE DEMONSTRATED that atrial and ventricular fibrillation are not random phenomena but have definable patterns (1, 2, 5–7, 9, 10, 12, 21). Of particular potential clinical importance is the observation that there may be a localized region critical to the maintenance of atrial fibrillation (13, 19, 24). Organized reentry in such a region could appear fibrillatory in the remainder of the atria due to irregular activation of the remaining atrial myocardium (26). Ventricular fibrillation has also been demonstrated to have organization of its activation (1, 5, 6). One potential problem in defining activation during fibrillation is the difficulty in assigning “activation times” to complex electrograms noted during fibrillation. Isopotential mapping, which eliminates the need for defining activation times, has its own limitations. Techniques such as coherence (31), eigenvector analysis, nonlinear dynamic modeling (8, 9), and fast Fourier transform have been used to model activation during fibrillation but cannot provide a rapid determination of activation direction or organization (16, 34). Optical mapping is a powerful technique that uses voltage-sensitive dyes to estimate cardiac activation at a large number of sites (17, 18, 21, 28). However, optical mapping has some limitations. To obtain an adequate signal-to-noise ratio, most investigators require the use of agents that reduce contractility and can potentially alter calcium currents. We and others (5, 6, 10) have previously described the use of vector mapping and linking analysis to define the organization of activation during fibrillation, but this technique has quantitative and practical limitations.

We (32) have previously applied a new technique called ensemble vector analysis to the study of ventricular fibrillation in normal dogs. The purpose of the present study was to validate and apply this technique for the analysis of fibrillatory rhythms. The results demonstrate that the technique can rapidly identify whether a particular myocardial region displays repetitive activation and that a subset of sites during experimental fibrillation shows consistent repetitive activation directions.

Although simultaneous mapping of multiple sites was performed in the present study, analysis of the ensemble vector index (EVI) requires recording from only four simultaneously unipolar electrodes.
METHODS

Experimental Model

The protocol was approved by the Animal Care and Use Committee of Northwestern University and was conducted in accordance with the principles of the American Physiological Society.

Studies were performed in 29 normal mongrel dogs. The dogs were anesthetized with pentobarbital (30 mg/kg iv initial dose and 4 mg·kg⁻¹·h⁻¹ subsequently), intubated, and mechanically ventilated (20). Blood pressure was monitored by means of a carotid arterial line, and the standard ECG limb leads were continuously monitored. A median sternotomy was performed, and the heart was suspended in a pericardial cradle. A rectangular 8 × 14 electrode array (Bard; Billerica, MA) was sutured to the epicardial surface of the left ventricle or right atrium. The plaque array has an edge-to-edge interelectrode distance of 2.5–2.75 mm and an electrode diameter of 0.25 mm. The ventricular plaque was placed with its long axis parallel to the left anterior descending artery. Pacing electrodes were sutured to the epicardial surface of the right ventricle, basal left ventricle, and right atrium. A separate bipolar pacing electrode was also embedded in the center of the multielectrode plaque. Recordings from the 112 unipolar leads of the anterior plaque electrode, and the surface ECG limb leads were acquired and stored in a digitized form on videotape using a cardiac mapping system (Map Tech; Maastricht, The Netherlands). A brief description of the methodology has been previously published (32). Different experiments were described in that publication.

Protocols

Protocol 1. In 10 experiments performed on normal mongrel dogs, 5 repeated inductions of ventricular fibrillation each separated by a 25-min waiting period were performed. Ventricular fibrillation was induced using burst pacing and allowed to persist for 10 s before termination by defibrillation using a 10-J shock via internal paddles.

Protocol 2. In six experiments, activation was evaluated during the induction of one to two episodes of fibrillation and during fixed-rate ventricular pacing.

Protocol 3. In three experiments, multisite pacing was performed from several sites around the plaque at pacing cycle lengths (PCLs) of 200–300 ms. A 10- to 50-ms time delay was introduced between the application of pacing impulses at each of the sites. This protocol is described in more detail in RESULTS.

Protocol 4. Episodes of atrial fibrillation were induced in 10 normal mongrel dogs. The chest was opened via a median sternotomy, and, in contrast to protocols 1–3, a 112-electrode plaque was placed on the epicardial surface of the right atrium. The plaque covered the anterior and lateral surfaces of the right atrium. Atrial fibrillation was induced by the application of 0.25 g aconitine, which was placed in the center of the myocardium located under the right atrial epicardial plaque (29).

Vector Mapping

The methods for creating vector loops have been previously described in detail (5, 20). Briefly, a vector is created by summing two bipolar electrograms at each time to create a vector loop. The bipolar electrograms (representing the x- and y-axes) are recorded from two pairs of electrodes with orthogonal axes. The direction of the maximum vector of a given vector represents the direction of local activation in cardiac tissue. Bipolar electrograms were created by summing the opposite “corners” of each group of four electrodes. Repeating this process for all 112 unipolar electrograms in the recording plaque resulted in the generation of 91 separate pairs of orthogonal bipolar electrograms for each cycle of ventricular fibrillation. These electrogram pairs were summed, and an array containing the vector loops was created (Fig. 1).

Ensemble Vector Analysis

To determine the consistency of the myocardial activation direction over a given time period, an index referred to as the...
Fig. 2. Activation during ventricular pacing at a cycle length of 300 ms. Recordings from a single cycle of pacing are shown. Missing data points contained pacing artifacts. Vector loops (A) showed activation directions consistent with the isochronal map (B). The EVM shown in C had directions that also corresponded to the isochronal map but had variable magnitude due to variations in electrogram amplitude. D: shows raw and time-corrected EVM (EVM_t) results for 1-, 2-, and 4-s windows at a pacing cycle length of 300 ms.
EVI was derived and validated. The EVI was designed to have a larger magnitude at recording regions that showed a consistent activation direction and lower values where activation was random. Although the EVI was calculated based on multiple simultaneous recordings, only four bipolar electrograms are needed to create the EVI.

Determination of the EVI involved the following steps.

**Scaling of parameters.** The vector at each time \( t \) was scaled using a nonlinear scaling function that accentuated vectors with large magnitude and attenuated vectors of small amplitude so that the activation amplitude was emphasized and the effects of repolarization on the ensemble vector were minimized. Standard high-pass filtering was not employed because we have previously demonstrated that it distorts vector directions (20). The scaling function \( f(x) \) was a tangent function with a range of 0 to 0.8\( \pi/2 \). The maximum gain value of 0.8\( \pi/2 \) was chosen arbitrarily to limit the maximum distortion and avoid the asymptote at \( \pi/2 \). We scaled all values relative to the maximum magnitude vector across all sites. The maximum vector gain was set equal to 0.8\( \pi/2 \), and the minimum vector gain was equal to 0. Thus values that map at \( >\pi/4 \) are amplified, and values that map at \( <\pi/4 \) are attenuated. Thus the phase relationship within the vector is maintained and the magnitude is scaled equally across the plaque, making comparisons across sites valid.

**Summation to create ensemble vectors.** An ensemble vector magnitude (EVM) over the entire recording period (Fig. 1) was derived using the following equation

\[
EVM = \sum_{0}^{n} T
\]

where \( n \) represents the number of time points in the data set.

The angle of the ensemble vector was calculated as \( \text{Arg} (\sum_{n}^{T}) \), where the \( \text{Arg} \) function is the arc tangent (\( y/x \)) but takes the sign of its arguments in consideration to assign the angle to the appropriate quadrant.

**Creation of the EVI.** The EVM was then corrected for variability in the local electrogram (and thus vector loop) magnitude to create an index of consistency of activation direction that is amplitude independent. Three different normalization techniques were evaluated to create an index using the following equations.

The variance in each direction \((x,y)\) was calculated as \( D_{x} = \frac{(x - \bar{x})^2}{n} \) and \( D_{y} = \frac{(y - \bar{y})^2}{n} \), where \( \bar{x} \) and \( \bar{y} \) are the mean \( x \) and \( y \) values, respectively; \( D_{x} \) represents the \( x \)-coordinate of the vector \( \vec{E}_{n} \) at time \( n \); and \( D_{y} \) represents the \( y \)-coordinate of the vector \( \vec{E}_{n} \) at each time period within the signal.

\[
M_{1} = \frac{\vec{E}_{n}}{\sqrt{D_{x} + D_{y}}}
\]

\[
M_{2} = \left( \frac{\vec{E}_{x}^{2}}{D_{x}} + \frac{\vec{E}_{y}^{2}}{D_{y}} \right)^{1/2}
\]

\[
M_{3} = \frac{\vec{E}_{xy}}{\sqrt{V_{xy}}}
\]

where \( M_{1} - M_{3} \) refer to methods 1–3 of correction of the EVI; \( \vec{E}_{x} \) and \( \vec{E}_{y} \) represent the magnitude of the vector in the \( x \) and \( y \) direction at each time \( n \), respectively; \( D_{x} \) and \( D_{y} \) represent the variance of the \( x \) and \( y \) magnitudes at each time \( n \), respectively; and \( \vec{E}_{n} \) represents the magnitude of the vector \( \vec{E} \) at the \( x \) and \( y \) directions.

The resulting EVI was expected to be high when activation was consistent from beat to beat and low when activation directions were different on different beats within the recording period.

The EVI was expected to be time (duration of recording) and frequency dependent. To adjust for this, two different correction methods were utilized: time correction and frequency correction. To perform time correction, the EVI was divided by the time of recording and expressed as millivolts per second. To justify this procedure, recordings of different durations (1, 2, and 4 s) during sinus rhythm and ventricular pacing were compared with ensure that the time-corrected
EVI (EVI$_1$) was truly time independent. Frequency correction was performed by dividing the EVI by the number of activations within a given window to produce the frequency-corrected EVI (EVI$_f$). This procedure was trivial for sinus rhythm and paced rhythms. During fibrillation, this required assigning the number of activation times for each window based on inspection of unipolar and bipolar electrograms as previously described (6). Unipolar atrial electrograms occasionally displayed ventricular activation. The data were manually overread to exclude the time window of ventricular activation and then processed in an automated fashion as described above.

A time period of 4.096 s was selected for most of the analyses in the present study for the following reasons. Ventricular fibrillation was induced in the intact dog heart without cardiopulmonary bypass or other support. To allow for repeated interventions, fibrillation was terminated after 8–10 s. Ventricular fibrillation was preceded by a 0.5- to 3-s period of polymorphic tachycardia. The period of polymorphic ventricular tachycardia was not included in the analysis. Thus the maximum time period that was available for analysis in all animals was $\sim$4 s. Although atrial fibrillation was allowed to persist for longer periods of time, a 4.096-s window was also used for atrial fibrillation analysis to allow comparisons with ventricular fibrillation.

**Isochronal Activation Mapping**

To compare vector results with standard mapping techniques, isochronal activation maps were constructed as previously described (20). Activation was determined at the time of peak negative change in voltage over time of the unipolar electrogram or baseline crossing in the bipolar electrogram. Fibrillation was divided into “cycles” based on visual inspection of activation times.

**Statistical Analysis**

Comparisons of the EVM and EVI during repeated inductions of fibrillation, during different time segments of recording, and among different experimental conditions (pacing, sinus rhythm, or fibrillation) were performed using repeated-measures, factorial, or mixed-model ANOVA when appropriate. Data are expressed as means ± SD. A P value of $<0.05$ was taken as significant.

**RESULTS**

**Ventricular Pacing**

An example of an isochronal activation map and multiple superimposed loops obtained during 4 s of ventricular pacing from the anterolateral left ventricle...
are shown in Fig. 2. The pacing site is near the plaque center. As expected, during ventricular pacing, vector loops were highly reproducible, demonstrating a constant activation direction during ventricular pacing (Fig. 2A). These directions accurately mirror activation directions expected from the isochronal activation map (Fig. 2B). The EVM over the same 4-s window at each site is shown in Fig. 2C. To examine the dependence of the EVM on the length of the data-acquisition period, the EVM during windows of 1, 2, and 4 s was calculated. Summary data from all experiments are shown in Fig. 2D. The EVM during ventricular pacing was linearly related to the recording duration. Thus when the EVM per second was calculated, the magnitude was similar for each of the recording time periods. Note that a wide range of magnitudes is present in Fig. 2C due to variability in electrogram amplitudes across the recording region. Thus EVMs were normalized for local electrogram or vector loop magnitudes to create the EVI (Fig. 3). M1 produced the most consistent EVI and was utilized in the calculations. To validate that the EVI was high when activation was consistent and low when activation was changing, variability of the activation direction was artificially created using protocol 3. In the experiment shown in Fig. 4, the basic PCL was 300 ms. Pacing was performed from both the lateral and septal margins of the multielectrode array at the sites shown in Fig. 4A. However, pacing from the septal margin was performed only on alternate cycles. The lateral margin of the plaque was thus activated consistently on all cycles, whereas the septal margin of the plaque was not. Figure 4A shows vector loops recorded over a 4-s period. Note that, although the vector direction is consistent on the lateral margin of the plaque (bottom portion of Fig. 4A), it alternates along the septal margin. Figure 4, B and C, shows vector loops on alternate cycles. The EVI (Fig. 4D) was high on the lateral margin of the recording plaque where activation was consistent and low along the septal margin.

Summary data from protocol 2 showing the calculated EVI at all plaque sites during sinus rhythm, ventricular pacing at a cycle length of 300 ms, and ventricular pacing at a cycle length of 220 ms are shown in Fig. 5 and Table 1. Note that during repetitively consistent activation, a normal distribution of the EVI is obtained. The mean raw EVI and EVI at a PCL of 220 ms were higher than those at a PCL of 300 ms (Fig. 5). However, EVI was 36.2 ± 9.8 mV/activation at a PCL of 220 ms versus 41.0 ± 11.0 mV/activation at a PCL of 300 ms (P < 0.05) because occasional sites that demonstrate functional conduction block at a PCL of 220 ms were noted that decreased the EVI.

**Ventricular Fibrillation**

Figure 6 shows an example of superimposed vector loops and a plot of the EVI during an episode of induced ventricular fibrillation. Note that the vector loops ap-

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<th>Atrium (n = 10)</th>
<th>Ventricle (n = 6)</th>
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<tbody>
<tr>
<td>NSR</td>
<td>90.2 ± 20.1*</td>
<td>85.3 ± 25.1*</td>
</tr>
<tr>
<td>300-ms PCL</td>
<td>115.4 ± 27.1</td>
<td>137.1 ± 35.6</td>
</tr>
<tr>
<td>Fibrillation</td>
<td>60.2 ± 54.3*</td>
<td>39.1 ± 23.5*</td>
</tr>
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Values (in mV/s) are means ± SD. EVI, ensemble vector index; NSR, normal sinus rhythm; PCL, pacing cycle length. *P < 0.05 vs. 300-ms PCL.
pear variable in most of the recording region where the EVI is low. When data from all experiments were analyzed, the mean EVIt during ventricular fibrillation was $39.1 \pm 23.5$ mV/s, which was significantly lower than during pacing or sinus rhythm (Figs. 5 and 6C and Table 2). Unlike the normally distributed EVI during sinus rhythm or pacing, the EVI histogram during ventricular fibrillation demonstrates a skewed distribution, with a subset of sites showing consistent activation (such as the top left portion of Fig. 6B). The EVIf provided a cleaner separation between ventricular fibrillation and regular rhythms. The mean EVIf during ventricular fibrillation (VF). Several data points were missing and are blank due to noise at these sites. In most of the sites, the vector loops are distributed equally around the center of the axis. However, in a subset of sites, a preferential activation direction is noted. The subset of sites is most easily seen in B, which shows the EVIs of the 4-s window. Sites such as in the top middle portion of the plaque with a large-magnitude EVI have reproducible activation directions during fibrillation. C: histogram showing the EVI during VF. Corresponding data during ventricular pacing and sinus rhythm are shown in Fig. 5.
was 5.6 ± 3.6 mV/activation during ventricular fibrillation and >30 mV/activation during sinus rhythm or pacing (Table 2). In all experiments, the EVIf was <10 mV/activation, and thus there was a clean separation between fibrillation and sinus rhythm.

Repeated induction of ventricular fibrillation in the same animal resulted in arrhythmia episodes that were superficially reproducible, as described in a previous report (5). However, when ensemble vector anal-

Table 2. Frequency-corrected EVI

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<th>Atrium (n = 10)</th>
<th>Ventricle (n = 6)</th>
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<tbody>
<tr>
<td>NSR</td>
<td>45.4 ± 17.3</td>
<td>32.1 ± 8.9</td>
</tr>
<tr>
<td>300-ms PCL</td>
<td>35.2 ± 19.1</td>
<td>41.0 ± 11.0</td>
</tr>
<tr>
<td>Fibrillation</td>
<td>8.1 ± 6.8°</td>
<td>5.6 ± 3.6**†</td>
</tr>
</tbody>
</table>

Values (in mV/cycle) are means ± SD. *P < 0.05 vs. 300-ms PCL; P < 0.05 vs. the atrium value.

Fig. 7. Reproducibility of EVI during repeated inductions of VF in the same animals (protocol 2). Note that during inductions 2–5, the EVIf is similar. In contrast, the EVIf was different during the first VF induction, suggesting that subtle changes in characteristics of VF occur after the first VF induction even when the animal appears to have returned to a stable baseline state. In particular, as repeated VF inductions occur, the more reproducible sites (EVIf > 100) disappear.
ysis was performed, there was a progressive decline in the EVI after two episodes of fibrillation (Fig. 7, A and B) with a dropout of the subset of sites with a high EVI.

**Atrial Pacing and Fibrillation**

Both EVI$_t$ and EVI$_f$ during atrial fibrillation were lower than those during atrial pacing ($P < 0.005$). After aconitine was applied, focal atrial tachycardia developed and lasted from 1 to 8 min. This tachycardia accelerated and then degenerated to atrial fibrillation. The spontaneous transition from atrial tachycardia to atrial fibrillation in aconitine-treated animals provided an opportunity to examine the results of isochronal and ensemble vector mapping 1) during a focal tachycardia with consistent activation patterns beat to beat, 2) in a transitional rhythm where an apparently focal tachycardia was present but where the surface QRS suggested irregular atrial activation but that had some characteristics of fibrillation, and 3) during sustained atrial fibrillation. Figure 8 shows examples of surface ECGs, and Figs. 9–11 show an isochronal activation map for each of these three arrhythmias. Note that during atrial tachycardia, the right atrial isochronal activation maps show consistent impulse spread from a single site and the surface ECG shows organized atrial activity. The EVI is consistent and high (mean EVI$_f$ 31 ± 42 mV/activation). During the transitional rhythm, the EVI was intermediate (mean EVI$_f$ 22 ± 30 mV/activation), the surface ECG is similar to clinical type I atrial fibrillation, and the isochronal activation map shows more rapid and variable beat-to-beat activation at the site of aconitine application. Finally, during atrial fibrillation, the surface ECG and right atrial activation maps show irregular activation and the EVI is lowest (mean EVI$_f$ 5 ± 6 mV/activation). Figure 12 shows a plot of vector loops from a sample experiment. Note that the EVI$_t$ (Fig. 9C) is higher than that during ventricular fibrillation. Figure 13 shows average EVI$_f$ from all experiments. The differences are similar to the example shown in Figs. 9–11.

The right atrial EVI during sinus rhythm was slightly higher than that obtained in the left ventricle (Table 1 and 2). In contrast, values for the EVI during atrial pacing at a cycle length of 300 ms were slightly lower than those obtained in the left ventricle during ventricular pacing (Tables 1 and 2). However, the EVI during atrial fibrillation was higher than that seen in the ventricle during ventricular fibrillation (Tables 1 and 2).

**DISCUSSION**

There are two major findings of the present study: 1) the EVI can calculate the consistency of activation during a variety of cardiac rhythms, and 2) there are major differences in the temporal organization between atrial and ventricular fibrillation. Although
Fig. 9. Isochronal activation maps of an episode of atrial tachycardia. A–C: three consecutive cycles recorded from a single experiment. The right atrial appendage is at the right portion. The middle of the plaque was overlying the pectinate muscle region, and the left portion of the strip was over the smooth-walled right atrium. Isochronics were drawn 10-ms intervals. The solid areas indicate that no activation was observed during that particular cycle. During the atrial tachycardia, beat-to-beat activation pattern is consistent and surface ECG suggests atrial tachycardia. The EVI was high during this rhythm.

Fig. 10. Isochronal activation maps of a transitional rhythm in which focal atrial tachycardia began to generate into fibrillation. A–C: three consecutive cycles recorded from a single experiment. The figure is organized in a fashion similar to Fig. 9. Activation on the right atrial epicardium is more variable, and the EVI is intermediate. See text for details.
most sites during both atrial and ventricular fibrillation showed variable beat-to-beat activation directions, the degree of variability was greater during ventricular fibrillation than during atrial fibrillation.

**Ensemble Vector Mapping**

Vector mapping has been used to analyze activation directions during sinus rhythm, ventricular pacing, ventricular tachycardia, supraventricular tachycardia, and fibrillatory rhythms (4, 5, 10). Although assigning activation times can create vectors of activation directions, the creation of vector loops by summing orthogonal bipolar electrograms has the advantage of not requiring assignment of activation times. Defining activation time may be particularly difficult during fibrillatory rhythms, in which multicomponent electrograms and electrograms with low slew rates may be common. We and others (6, 10) have previously utilized vector loops on a single cycle to define activation during fibrillation.

The present study represents an extension of the vector mapping and averaging techniques. Although multiple sites are more analyzed, simultaneously using plaque recordings in the present study, only four unipolar recordings are required to construct the EVI. Because the EVI is dependent on the number of cycles of activation within a given analysis window, it was normalized using both time and frequency correction methods. Both methods produced a separation between rhythms in which activation was stable from those in which it was changing, but the frequency-corrected method produced a cleaner discrimination among rhythms, although it had the disadvantage of requiring the assignment of activation intervals. When ensemble vector analysis is performed at different sites within a single rhythm, the time-corrected method may be preferable because of its relative simplicity. In contrast, when different rhythms with vastly different cycle lengths are compared, the frequency-corrected technique is preferable. However, the basic findings comparing different rhythms were similar regardless of whether time or frequency correction was utilized.

Although the relevance of any experimental model to clinical situations needs validation, the present study examined an experimental model of atrial fibrillation that may correspond to some clinical reports of “focal” fibrillation. In this model, aconitine application resulted in the gradual transition from regular atrial tachycardia to a transitional rhythm in which the surface ECG was consistent with fibrillation but focal activation was present on isochronal mapping and finally to atrial fibrillation. The EVI was capable of distinguishing among these arrhythmias in that it was highest during atrial tachycardia, intermediate during the transitional rhythm, and lowest during irregular atrial fibrillation. Thus ensemble vector mapping has the ability to distinguish among these different possibilities and potentially identify “focal fibrillation” in clinical situations. In the present study, we examined

Fig. 11. Isochronal activation maps from an episode of atrial fibrillation. A–C: three consecutive cycles recorded from a single experiment. The figure is organized in a fashion similar to Fig. 9. During sustained atrial fibrillation, beat-to-beat activation is variable when the ensemble vector is lowest. See text for details.
activation at multiple sites to obtain an evaluation of simultaneous activation at multiple sites. However, the EVI at each individual site (4 unipolar or 2 bipolar electrode recording) was capable of providing data on the consistency of activation at each site. Other techniques such as linking analysis and coherence analysis have also been utilized to examine the extent to which activation on a single cycle during fibrillation is similar...
regarding sensitive dyes has also provided important information of optical mapping data obtained using voltage-sensitive dyes to provide complimentary information. Quantitative analysis of activation patterns and subsequently quantitative indexes. They

Other investigators have used numerical techniques to identify the reproducibility of activation patterns during ventricular fibrillation. Huang et al. (15) described the quantitative application of a series of eight techniques to analyze ventricular fibrillation. Two of these techniques, multiplicity and repeatability of the rhythm, provide information that is qualitatively similar to the EVI. To analyze multiplicity, activation patterns of an entire wavefront are examined and analyzed into clusters. When activation directions fell into clusters that accounted for 90% for wavefronts, the pattern was said to represent high multiplicity. Repeatability of the rhythm was derived in a similar fashion to multiplicity. Both of these techniques rely on isochronal activation times to derive wavefront patterns and subsequently quantitative indexes. They thus differ from the ensemble vector technique, which does not require a predefined characterization of an activation wavefront to create the EVI. Another technique that can define quantitative activation patterns during fibrillation is the calculation of entropy. Kim et al. (22) described the use of Kolmogorov entropy to examine the decrease in the number of activation wavefronts that occur during fibrillation. This technique does not require the assignment of activation times but does require the simultaneous examination of multiple recording sites to create an “embedding dimension.” We and others (27, 33, 34) have used fast Fourier transform to describe the frequency of activation during fibrillation. A narrow frequency distribution suggests but does not provide information that is equivalent to activation directions being identical. For example, several sources with similar frequencies could produce divergent activation directions while producing a narrow bandwidth on fast Fourier transform. In such a case, the EVI would be low, indicating varying activation directions. A limitation of the present study is that we did not quantitatively fast Fourier transform compare entropy, multiplicity, repeatability, and ensemble vector mapping.

Activation During Fibrillation

Fibrillation is superficially a random process; however, a large number of studies in recent years have demonstrated that fibrillation has structure and that consistency of activation can be demonstrated (1, 9). Although the precise mechanism has not been determined with certainty, multiple reentrant wavefronts that proceed in patterns that vary from beat to beat appear to be responsible for clinical fibrillatory rhythms (12, 23, 25, 28). Such activation is not random, and consistent patterns of beat-to-beat activation and large moving wavefronts are present during fibrillation. In some patients, single-site mapping techniques have been able to demonstrate a focal origin for some arrhythmias that superficially appear to resemble atrial fibrillation (13, 19). Experimental studies have suggested that fibrillation may be modeled by meandering rotors or “scroll waves” that are a property of all excitable media and maintain fibrillation (28). Regardless of whether one utilizes a model of leading circle reentry, rotors of reentry, or other qualitative or quantitative descriptions of activation during fibrillation, the consistency of activation at certain regions of the atrium or ventricle may indicate a reentrant circuit or a focus consistently spreading activation to the remainder of the heart, as seen in our experimental model of acetylcholine-induced atrial fibrillation. Differences in the consistency of activation thus may have pathophysiological and clinical significance.

At most recording sites, the EVI during atrial and ventricular fibrillation was clearly different from that during pacing, indicating a less consistent activation direction. However, in a small subset of sites that were not normally distributed, the EVI during ventricular fibrillation was in a range similar to that seen during consistent activation. This suggests that there are a subset of epicardial sites in which consistent beat-to-beat activation is present during ventricular fibrillation. Interestingly, the proportion of sites with high “organization” during ventricular fibrillation decreased during repeated inductions of fibrillation despite the fact that other measures of fibrillation organization determined from isochronal mapping, linking analysis, and single-loop vector mapping showed no change. Thus repeated inductions of fibrillation such as might be performed during defibrillator implantation or experimental fibril-

![Graph](image-url)

Fig. 13. Mean frequency-corrected EVI during atrial tachycardia, transitional rhythm, and atrial fibrillation. See text for details.
lation models produce subtle changes in the physiology of fibrillation.

Comparison among different kinds of fibrillation demonstrated that the degree of consistency of activation varies in different models of fibrillation. Epicardial left ventricular activation during ventricular fibrillation was more variable than activation during atrial fibrillation. This may in part be contributed to by the complex three-dimensional structure of ventricular fibrillation in the intact dog. However, an alternative possibility is that intrinsic differences in the nature of activation during fibrillation are responsible for some of these findings.

Limitations

One limitation of the present study is that left ventricular activation was evaluated only on the epicardium, and thus the consistency of three-dimensional activation during ventricular fibrillation could not be evaluated. Other models of atrial and ventricular fibrillation could have produced different results, but the most appropriate model for clinical fibrillation is still a matter of controversy. No attempt was made to address the mechanism of fibrillation in the present study or to determine whether the organization of fibrillation was consistent with various models of fibrillation such as the description by nonlinear methods or modeling by rotors (3, 11, 27). In addition, reentrant circuits were not characterized directly. An additional limitation is that only one acute model of atrial fibrillation was studied. Nonetheless, the results of the present study demonstrate that ensemble vector mapping has the ability to identify the consistency of activation during fibrillation.

Clinical Implications

Several clinical studies have suggested that there may be different patterns of atrial fibrillation in different patients and that in some patients a focal source may be responsible for an arrhythmia that appears to be fibrillation (26). However, distinguishing among these possibilities in experimental models or in the clinical electrophysiology laboratory using standard mapping techniques may be difficult. The results of the present study suggest that ensemble vector mapping may help clarify the pathophysiology of fibrillation by separating tachycardias with relatively uniform involvement throughout the myocardium from those in which a focal source is present. In addition, the technique can be adapted to make this determination in clinical situations (4).

REFERENCES


