Ventricular fibrillation threshold

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VANTYN, Robert A., and Lloyd D. Maclean. Factors of importance in determining ventricular fibrillation threshold. Am. J. Physiol. 201(3): 457-461. 1961.—The use of single rectangular stimuli, applied directly to the heart surface, has been confirmed as a reliable method for measurement of the ventricular fibrillation threshold (VFT). The following factors which influence reproducibility were investigated: 1) spatial separation of bipolar electrodes, 2) interval between stimuli, and 3) anatomical position of electrodes on the heart. With bipolar electrodes placed 10-30 mm apart and an interval of 10-15 cycles between stimuli the VFT was remarkably constant for any single dog. An interelectrode separation of 2-4 mm or the placement of electrodes in a coagulated area of epicardium produced high, widely variable, and at times unobtainable thresholds believed due to short circuiting of the current delivered. Thresholds determined with stimuli 3-4 beats apart were significantly lower than when stimuli were delivered 10-15 beats apart. The VFT was significantly higher at the base than at the apex of the left ventricle. Investigations which measure the effect of a given influence on the VFT should control the factors studied here.

Methods

All experiments were performed on healthy adult mongrel dogs, ranging in weight from 6.8 to 25 kg, anesthetized with intravenous sodium pentobarbital (33 mg/kg). The temperature of all dogs was measured with an electronic thermometer placed in the distal esophagus and was maintained constant by the intermittent use of an electrical heating pad or by covering the animal with 3-4 layers of surgical drapes. Blood pressure was monitored with a mercury manometer connected to a catheter in the femoral artery. A left thoracotomy was performed in the 5th intercostal space, the pericardium was incised longitudinally, and the left ventricle exposed. Ventilation was maintained with a positive pressure respirator using room air.

The stimulating electrodes were two stainless steel 3/8 inch circle eye suture needles 0.3 mm in diameter (Davis & Geck, product 243) shaped into small hooks and soldered to insulated braided phosphor bronze wire leads (0.012 inch, 7 strand). This type of electrode was chosen because of ready availability, ease of placement with a minimum of trauma, and freedom to vary interelectrode distance. The electrodes were hooked in the epicardium, care being taken not to injure the myocardium.

INSTRUMENTATION

The electronic equipment used was similar to that described by Shumway, Johnson, and Stish (3). Amplified electrocardiogram potentials were fed into a triggering circuit, the output of which was coupled to the synchronizing input of a Grass stimulator (model S-4-C). The output of the stimulator was connected to the above described electrodes. The anodal lead to the electrode contained a 2.500-ohm resistor to minimize the effects of changing resistances between the electrodes and cardiac surface. The cathode lead was grounded, and no other ground was employed on the animal. The magnitude of the current delivered to the electrodes was obtained by observing with a cathode-ray oscilloscope (DuMont 304-A), the voltage drop produced across a precision 10-ohm resistor placed in the cathode lead of the electrode system. The electrocardiogram was displayed on a second cathode-ray oscilloscope (DuMont 401). The stimulator output was applied to the Z axis of this oscilloscope so that a brightening of the trace at the moment of stimulation provided a direct method of determining precisely the location of the stimulus in the cardiac cycle.
FIG. 1. Multiple determinations of VFT in 7 dogs with mean value and SE for each animal. Greatest SE was .4 ma.

FIG. 2. Effect of interelectrode distance on VFT. Each point represents coordinated thresholds with closely and widely spaced bipolar electrodes in a single dog. All points are above the line of no difference indicating a higher threshold with stimuli using electrodes closely spaced (2-4 mm), compared to 10-15 mm. In 2 animals it was not possible to produce fibrillation with electrodes 2-4 mm apart.

FIG. 3. Effect of time interval between stimuli on VFT. Each point represents coordinated thresholds with 3-4 and 10-15 cardiac cycles between stimuli in a single dog. If time between stimuli made no difference all points would lie on the line. Most points are below the line of no difference indicating a lower threshold when stimuli are repeated at intervals of 3-4 cycles as compared to 10-15 cycles.

FIG. 4. Effect of anatomical location of electrodes on VFT of dogs. Each point represents coordinated thresholds with electrodes at base and at apex of heart in a single dog. All points are above the line of no difference indicating a higher threshold at base than at apex of left ventricle.
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The trigger circuit provided a single synchronizing pulse for the stimulator upon the occurrence of the first R wave after a reset button was released. A wide range of stimulus strength and delay following the R wave was provided by the stimulator. This instrumentation permitted the accurate placement of a stimulus of known strength and duration in any desired part of the cardiac cycle. The maximum stimulus strength available was approximately 45 ma. In all groups tested the duration of stimulus was maintained at 10 msec and each stimulus was delivered during the expiratory phase of the respiratory cycle. A single stimulus of subthreshold strength was delivered to the heart shortly after the QRS complex and repeated in subsequent cardiac cycles throughout and beyond the vulnerable period (terminal 30-90 msec of systole) while increasing the delay period after the R wave by 5 msec following each stimulus. After sweeping the entire vulnerable period at one subthreshold strength, the procedure was repeated after increasing the current strength by from 1.0 to 2.0 ma. This was repeated until ventricular fibrillation was produced. The heart was allowed to fibrillate for 2 sec. after which defibrillation was effected with standard equipment. A minimum period of 15 min was allowed for the heart to recover in which time the electrocardiogram returned to normal. The following groups were studied:

**Group 1.** Forty-four determinations of the ventricular fibrillation threshold were made in seven dogs, and the variability of this determination in each dog was established. All thresholds were determined with the interelectrode distance between 25 mm and 30 mm. The position of the electrodes was not changed between determinations of the fibrillation threshold.

**Group 2.** The effect of interelectrode distance on the ventricular fibrillation threshold was determined. Fifty-eight determinations were made in seven dogs. The interelectrode distance varied between 2 mm and 35 mm. The choice of distance for each determination was randomized.

**Group 3.** The effect on the ventricular fibrillation threshold of coagulation of the myocardium in addition to electrode separation was studied in six dogs. After initial thresholds were determined, the surface of the left ventricle was cauterized with an electrocautery in two small areas 25 mm apart and in one larger area 15 mm in diameter. Ventricular fibrillation thresholds were then determined with each electrode in a small coagulated area separated by normal tissue and with both electrodes placed at least 10 mm apart in a large coagulated area.

**Group 4.** The effect on the ventricular fibrillation threshold of the time interval between stimuli was studied in 11 dogs. Thresholds were alternately determined with an interval between stimuli of either 3-4 or 10-15 heart beats. Interelectrode distance in this group was between 25 and 30 mm.

**Group 5.** The effect on the ventricular fibrillation threshold of the anatomical position of the electrodes was studied in eight dogs. Three locations on the anterior surface of the left ventricle were tested: the base, midventricle, and apex. In this group the distance between electrodes was maintained at between 25 and 30 mm.

### Table 1. Effect of interelectrode distance on ventricular fibrillation threshold

<table>
<thead>
<tr>
<th>Dog No.</th>
<th>Wt., kg</th>
<th>Temp., C</th>
<th>Ventricular Fibrillation Thresholds, ma</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Electrodes 2-4 mm apart</td>
</tr>
<tr>
<td>12</td>
<td>7-3</td>
<td>37-38</td>
<td>35, 38, 26, 34, 29, 42, 39</td>
</tr>
<tr>
<td>13</td>
<td>16</td>
<td>36.5-37.5</td>
<td>38, 39, 38, 28</td>
</tr>
<tr>
<td>14</td>
<td>24.5</td>
<td>37-38</td>
<td>17, 18, 24, 21, 32, 26, 28, 22, 28, 32, 31, 39</td>
</tr>
<tr>
<td>15</td>
<td>23.2</td>
<td>37-37.5</td>
<td>39, 42</td>
</tr>
<tr>
<td>16</td>
<td>23.2</td>
<td>38-38.5</td>
<td>38, 26, 38</td>
</tr>
<tr>
<td>18</td>
<td>16</td>
<td>38-39</td>
<td>38</td>
</tr>
<tr>
<td>19</td>
<td>11.4</td>
<td>38-39</td>
<td>38</td>
</tr>
</tbody>
</table>

RESULTS

Reproducibility of determination of ventricular fibrillation threshold (group 1). As illustrated in Fig. 1, with electrodes placed 25-30 mm apart and an interval between stimuli of 10-15 heart beats, the ventricular fibrillation threshold was remarkably constant for any single dog. The largest standard error of the mean of multiple determinations of the ventricular fibrillation threshold in any single dog was less than 1 ma. There was considerably more variation among dogs. These results compare to those obtained in previous experiments from this laboratory using larger surface electrodes with a fixed interelectrode distance. In previous work care was taken to move the electrodes, which were hand held, after each two or three stimuli so as to avoid surface charring. This was not necessary in the present study using small electrodes. As many as ten determinations of the ventricular fibrillation threshold (400-700 stimuli) were made without changing electrode position. The threshold remained constant under these circumstances.

Effect of interelectrode distance (group 2, 3). As illustrated in Table 1 and Fig. 2, when the interelectrode distance was very small (2-4 mm) the thresholds were higher and varied greatly when compared to the results obtained in the same dogs with an interelectrode distance of 10-35 mm.

It was thought likely that local tissue damage with short circuiting of the current delivered was responsible for the high and occasionally unobtainable thresholds found when the interelectrode distance was small (2 to 4 mm). The results of the experiment, group 3, as illustrated in Table 2 substantiates this theory in that place-
TABLE 2. Effect of coagulation of epicardium on ventricular fibrillation threshold

<table>
<thead>
<tr>
<th>Dog No.</th>
<th>Wt., kg</th>
<th>Temp., °C</th>
<th>Mean Threshold, ma</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Control</td>
</tr>
<tr>
<td>9</td>
<td>8.6</td>
<td>36.5-37</td>
<td>22.6</td>
</tr>
<tr>
<td>10</td>
<td>18</td>
<td>36-38.5</td>
<td>22.4</td>
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<tr>
<td>11</td>
<td>8.6</td>
<td>37/37.5</td>
<td>18</td>
</tr>
<tr>
<td>36</td>
<td>16.8</td>
<td>36.5-37</td>
<td>26</td>
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<tr>
<td>37</td>
<td>18.3</td>
<td>37.5-38</td>
<td>25</td>
</tr>
<tr>
<td>38</td>
<td>25</td>
<td>38-39</td>
<td>23.5</td>
</tr>
</tbody>
</table>

Discussion of both electrodes in one continuously cauterized area of epicardium yielded significantly higher thresholds than those obtained with electrodes in separate coagulated areas. The latter coagulated areas were separated by normal tissue and the results were comparable to the control values. The electrode separation was 10 mm or greater for all determinations in group 3.

Effect of stimulus interval (group 4). The results are illustrated in Fig. 3. The ventricular fibrillation thresholds were significantly higher when stimuli were applied 10-15 beats apart as compared to the thresholds obtained when the stimuli were 3-4 beats apart (P = < 0.02).

There was little variation in threshold in a given dog if the interval between stimuli was kept constant at either 3-4 beats or 10-15 beats.

Effect of anatomic location of stimulus (group 5). The results are illustrated in Fig. 4. The ventricular fibrillation threshold was significantly higher at the base than at the apex (P = < 0.001). The threshold values remained constant in each dog at each anatomic location whether base, midventricle, or apex.

Comment

The basic requirements for determining the ventricular fibrillation threshold as outlined by Brooks et al. (7) and Wiggers and Wegria (8) are: 1) adequate and accurately measurable stimulus strength, 2) known and constant duration of the stimulus, and 3) accurate placement of the stimulus in the vulnerable period of the cardiac cycle. In addition to these requirements, if one wishes to compare results at different times in the same dog or among different dogs, it appears to be of importance from the present investigation to control the following variables:

Spatial separation of electrodes. In experiment 2 electrodes placed 3 mm apart gave variable, high, or unobtainable thresholds. Shumway et al. (3) noted that applying frequent stimuli with surface electrodes in one place causes charring of the epicardium and results in fictitiously high thresholds. In the present study, it was observed that a small area of coagulated tissue developed around each electrode after a number of shocks had been applied. This does not affect the ventricular fibrillation threshold when the electrodes are separated by at least 10 mm. As the interelectrode distance becomes smaller, however, two such areas can form a bridge of coagulated tissue between the electrodes and thus provide a short circuit for the stimulus current. The current density in the adjacent normal myocardium will be considerably decreased and may never reach the value necessary to produce ventricular fibrillation.

The results of group 3 show that such a bridge can be formed by cauterized tissue and will provide a short circuit yielding high thresholds.

With the stimulating method used in the present study the results indicate that coagulation will not affect ventricular fibrillation thresholds if the electrodes are placed at least 10 mm apart.

Interval between stimuli. Close spacing of testing shocks is commonly assumed to be undesirable when determining cardiac excitability or ventricular fibrillation thresholds. Brooks et al. (7) applied stimuli 6-12 beats apart and state that a strong shock has a long-lasting effect on the refractory period and that the same is true for an extrasytole produced by the stimulus. In some instances when we applied one stimulus every two beats, including the extrasytole produced by the stimulus and the following normal beat, the thresholds were unreliable. The present investigation shows that thresholds tend to be higher when stimuli are spaced farther apart although they remain consistent for each rate. Keeping the stimulus rate constant therefore is more important than the rate itself, provided stimuli are at least 3-4 beats apart. There are other reasons that make a ratio of one stimulus every 10-15 beats more desirable. The accuracy of placement of the stimulus in the cardiac cycle can be affected by the intermittent occurrence, during the respiratory cycle, of a notched R wave or a slight change in heart rate, which has an effect on the refractory period period (7, 9). Stimuli were applied in the phase of the respiratory cycle in which the R wave had the maximum amplitude and a single peak which resulted in a rate of one shock every 10-15 cardiac cycles.

Anatomical position of electrodes. Shumway et al. (3) found a significant difference in ventricular fibrillation thresholds between the right and the left ventricle and between the posterior and anterior surface of the left ventricle. The results of the present study indicate that there exists a narrower anatomical difference in vulnerability for the left ventricle. There is a significantly lower threshold at the apex than at the base. This indicates the need to place electrodes in the same anatomical position if thresholds are to be compared at other times in the same dog or among dogs.

The ventricular fibrillation threshold is considerably lower in hypothermia (2). Wiggers and Wegria (10) found no significant change in threshold if the temperature did not vary by more than 4 °C from the normal value. However, previous experiments in our laboratory (2) indicate that changes in temperature of 2 °C can alter the fibrillation threshold. Maintenance of constant body temperature therefore is advisable. In the present...
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investigation body temperatures in any given dog did not vary by more than 1.5°C.

Failure to produce ventricular fibrillation with single rectangular stimuli in the normothermic dog as reported by Covino and Beavers (1) can probably be explained by the fact that the limit of stimulus strength available was only 15 ma in this investigation. Eighty percent of thresholds in the present study were higher than 15 ma.

The small interelectrode distance (3 mm) of the bipolar electrode used by Maaske and Bromberger-Barnea (5, 6) is probably responsible for the reported inability to produce ventricular fibrillation with single rectangular wave stimuli. The absence of myocardial injury or the use of long intervals between stimuli (20-30 beats) appear from the present investigation less likely to be responsible for the inability to produce ventricular fibrillation. The upper limit of stimulus strength used by these workers was 25 ma. With electrodes placed 2-4 mm apart only 5 out of 30 fibrillation thresholds were 25 ma or less in the present investigation. Additionally, Maaske et al. (5) attempted to produce ventricular fibrillation only after many stimuli had been used to construct strength-interval curves. The close approximation of electrodes and repeated application of stimuli both favor a short circuit. This coupled with relatively low maximal current strength makes the inability to produce ventricular fibrillation understandable in their investigation.

In experiment 3 considerable myocardial injury was produced deliberately by cauterizing the cardiac surface and the thresholds were equal to control thresholds determined when myocardial injury was minimal provided normal tissue intervened between the electrodes. Even under control conditions, tissues around the electrodes were damaged and stimulation probably occurred at some distant site in more normal myocardium. In the absence of local injury, the requirement for an electrode separation of greater than 2-4 mm might not hold. However, the multiple stimuli necessary to determine the ventricular fibrillation threshold result in unavoidable local injury. The threshold remained constant for any single dog in the presence of this injury unless there was obvious opportunity for short circuiting or when both electrodes were in a deliberately cauterized area.

The reason for placing electrodes close together (3 mm) has been to sample the vulnerability to fibrillation in a small area of myocardium which would presumably have a synchronous and smooth recovery of excitability. In the present study no difference was noted when interelectrode distance varied from 10 to 35 mm. It would be likely if asynchrony of repolarization as brought about by wide separation of electrodes played a role that a lower threshold would be found with the greater interelectrode distance. This was not the case. The determination of the ventricular fibrillation threshold is readily measured in the normal heart, is reproducible, and is recommended to evaluate quantitatively the effect of factors—physiological, physical, or chemical—believed to have an antifibrillary action.

Previous work has suggested that ventricular fibrillation can be produced only when the stimulus is delivered immediately prior to diastole or within the terminal 30-90 msec of systole. This corresponds to the period of hyperexcitability immediately prior to diastole observed by Covino and Beavers (1), the major dip of Hoffman et al. (11) and the vulnerable period of Wiggers and Wegria (8). It has been shown clearly by Covino and Beavers (1) that the evaluation of various antifibrillary procedures by determination of the diastolic ventricular threshold alone is misleading. The determination of ventricular fibrillation threshold is necessary and appears to be a valuable quantitative measurement of the susceptibility of the myocardium to ventricular fibrillation.

REFERENCES