ABSTRACT

The time and sequence of epicardial activation was determined by measuring the onset of activation at 26 to 47 representative epicardial sites on each ventricle. Normal dogs and dogs with right ventricular hypertrophy resulting from various congenital heart lesions were studied. The total right ventricular epicardial activation time was slightly prolonged (10 msec) in some dogs with right ventricular hypertrophy, but it was not directly related to the severity of the lesion. In the dogs with right ventricular hypertrophy and right ventricle-pulmonary artery systolic pressure differences greater than 40 mm Hg, the activation of the right ventricular epicardium was consistently completed after that of the left ventricular epicardium. The delay in right ventricular epicardial activation was best shown by plotting the epicardial data on a simultaneously recorded QRS complex. In the dogs with right ventricular hypertrophy, right ventricular epicardial activation was shifted in time within the QRS complex so that 39% of the sites were activated during the last one-third of the QRS interval; only 1% of the right ventricular epicardial sites were activated during this time in the normal group. The QRS electrocardiographic changes in right ventricular hypertrophy were associated not only with a slight prolongation in epicardial activation time, but also with a shift in timing of this activation within the QRS complex.

ADDITIONAL KEY WORDS
electrophysiology ventricular activation congenital heart disease electrocardiography

Animals with spontaneous heart disease present an opportunity to study the electrical disturbances of cardiac lesions in their natural state without the inherent problems and objections of experimentally produced lesions. In the present study, the time and sequence of ventricular epicardial excitation in dogs with congenital right ventricular hypertrophy have been compared with results obtained in normal dogs. Ventricular epicardial activation was also correlated with the simultaneously recorded lead II QRS complex.

Materials and Methods

Purebred and mongrel dogs were studied. Sixteen were normal and served as controls; they weighed between 5 and 26 kg. Eleven dogs had spontaneous heart disease; they weighed between 8.8 and 24.5 kg. Five dogs had pulmonic stenosis alone; 1 had pulmonic stenosis and interventricular septal defect; 2 had pulmonic stenosis and atrial septal defect (secundum); 2 had double outlet right ventricle, pulmonic stenosis and interventricular septal defect; and 1 had an interventricular septal defect.

The physical examination of each dog included auscultation, a 10-lead electrocardiogram, and vectorcardiograms using both the Wilson equilateral tetrahedron (1) and McFee (2) systems. In addition, in some of the control dogs and all of the abnormal dogs, dorsoventral and lateral radiographs of the heart were taken, right-sided cardiac catheterizations were performed, and right-sided angiograms were taken. The pressure difference across the pulmonic valve was the difference between the peak systolic...
pressures of the right ventricle and main pulmonary artery obtained by withdrawing the catheter from the pulmonary artery into the right ventricle.

For the mapping procedure, the dogs were anesthetized with pentobarbital sodium (30 mg/kg iv) and placed in the supine position. Ventilation was maintained by a positive-negative phase respirator (Bird Corp.). The chest was opened by a midsternal approach and the pericardium incised. An electrode, consisting of 5 silver wires (0.08 inch diam) embedded in an acrylic plaque, was sutured to the epicardial surface of the left ventricle. The wires were 1 mm apart and the bipolar electrogram recorded through any 2 wires of this electrode provided a time reference for ventricular activation. The reference electrode was not influenced by minor changes in the position of the heart which occurred during the mapping procedures. The time of activation of 27 to 47 representative right ventricular epicardial sites was determined by use of a bipolar roving electrode. The roving electrode consisted of silver wires 1 mm apart embedded in an acrylic L-shaped rod. Similar methods have been described previously (3).

![Diagram of electrocardiogram and epicardial mapping](image)

**FIGURE 1**

Normal dog. Total ventricular epicardial activation time was 29 msec. A. Tracing of simultaneously recorded lead II electrocardiogram, left ventricular (LV) reference electrogram, and roving right ventricular (RV) electrogram. Time lines at 0.1 sec. B. Enlarged reproduction of the lead II QRS with time lines at 10 msec. Dots denote the time of activation of specific areas on the RV epicardial surface during the QRS complex, and lined dots denote LV sites. The time of activation at the LV reference electrode is indicated by X. C. Map of the RV epicardium illustrating the time sequence of activation. The site of earliest activity is designated the zero point (area L9) and the other times are adjusted accordingly. D. Map of the LV epicardium. The site of earliest activity is designated the zero point (area H14). The site of the reference electrode is indicated by X. The same conventions are used in Figures 3, 5 and 6.
CONGENITAL RIGHT VENTRICULAR HYPERTROPHY

The lead II electrocardiogram and bipolar electrograms from the reference and roving electrodes were recorded simultaneously on an 8-channel, switched-beam, cathode-ray oscilloscope (Electronics for Medicine) at a paper speed of 200 mm/sec (Fig. 1A). Local activation time was measured at the intrinsic deflection of the electrogram. The difference in activation time of the two electrograms (left ventricular reference minus right or left ventricular roving) was determined by a precision measuring device which enabled differences of 1 msec to be measured reproducibly. These times were plotted on an enlarged reproduction of the lead II electrocardiogram (Fig. 1B).

The site of earliest activation on the right ventricular epicardium was made the zero time reference point (Area L9, Fig. 1C) and the times at the other sites were then adjusted accordingly. These adjusted times were plotted on a map of the right ventricle (Fig. 1C). This map then represents the time sequence of activation of the right ventricular epicardium. The time sequence of the left ventricular epicardium was studied in a similar manner by recording from 26 epicardial sites, and the site of earliest activity was made the zero point for the left ventricle. A zero point was found for each ventricle to visualize the time sequence more easily. The complete right and left ventricular epicardial activation time (Table 1) was determined from the earliest and latest sites recorded from the entire ventricular epicardium.

Following the mapping procedure, euthanasia was performed by an intravenous overdose of pentobarbital sodium, and the hearts were examined to determine the nature and extent of the anatomic lesions. The thickness of the right ventricular wall was measured at two points approximately 5 mm below the basal attachment of the anterior leaflet of the tricuspid valve, carefully avoiding the papillary muscles. The measurements were made with curved calipers and read to the nearest half millimeter by placing the calipers on a standard millimeter ruler. The left ventricular wall was measured at two points approx-

FIGURE 2
Scalar leads and vectorcardiograms recorded by the Wilson equilateral tetrahedron (top) and McFee (bottom) systems from dog 10 in Table 1. Late forces are directed cranially and to the right. The dashes narrow in the direction in which the loop is inscribed. The vectorcardiograms have been retouched. In the Wilson system, the exploring electrode for lead V10 was placed over the dorsal spine of the seventh thoracic vertebra. Calibration lines = 1 mv.
mately 5 mm below the basal attachment of the posterior leaflet of the mitral valve. The mean of the two measurements for each ventricle was used to determine the thickness ratio of the left ventricle to the right ventricle. Twenty hearts from normal dogs were measured for control values by the same individual.

**Results**

**CONTROL PREPARATIONS**

The time of activation at specific sites and their location on the lead II QRS complex varied from individual to individual. The time sequence of activation and the lead II QRS complex may have been slightly altered by the open-chest procedure. The sequence of activity in different gross areas of the right ventricular epicardium has been divided arbitrarily into three regions. In all the control dogs, the region of earliest activity occurred along the ventral interventricular sulcus (anterior in man) of the right ventricular epicardium. The mid-portions of the right ventricular epicardium were activated next. Latest activity occurred along the dorsal interventricular sulcus (posterior in man), the base, and the right ventricular outflow tract (Fig. 1C). Total right ventricular epicardial activation time in the normal dogs varied from 20 to 30 msec. The left ventricular epicardium was studied in only 4 of the control dogs. The left ventricular epicardium was activated in a general direction from apex to base and the total left ventricular epicardial activation time was between 18 and 29 msec. Complete right and left ventricular epicardial activation time varied from

![Diagram](https://example.com/diagram.png)

**FIGURE 3**

From dog 11 in Table 1. The epicardial activation time and sequence are essentially normal (A and C); however, many right ventricular epicardial sites were activated after the last left ventricular epicardial site (B and D).

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24 to 30 msec. These results are in general agreement with those obtained by Lewis and Rothchild (4), Harris (5), Genender et al. (3), and by Moore and co-workers (6).

In each dog, the duration of the QRS complex was divided into three equal parts. Then the percentage of sites activated during each one-third of the QRS complex was computed. In the control dogs, only 1% of the right ventricular epicardial sites were activated during the last one-third of the QRS interval.

**CONGENITAL HEART DISEASE**

In all 11 dogs with congenital heart disease, the QRS interval was within normal limits. In the majority of these dogs, the electrocardiograms and vectorcardiograms had late forces directed cranially and to the right (Fig. 2). These alterations are typical of those seen in right ventricular hypertrophy in the dog (7).

The epicardial mapping data from a 3-year-old male mongrel with pulmonic stenosis are shown in Figure 3. The dog weighed 6.8 kg. The peak systolic pressure difference across the stenotic valve was 150 mm Hg and was the highest of the dogs studied. This untreated dog was not in congestive heart failure and had been kept in our heart disease colony for 2½ years with only limited exercise. The sequence of activation of the left and right ventricular epicardium was essentially normal. The total right ventricular epicardial activation time of 21 msec was the shortest activation time of the abnormal dogs studied and only 1 msec longer than the shortest value found in the control dogs. The shortest control value was found in a 3-year-old normal mongrel weighing 5.0 kg. A cross section of the abnormal dog's heart at the level of the tricuspid valve is shown in Figure 4. Contrast the thickness of the right ventricle of this diseased heart (Fig. 4B) with the heart from a normal dog (Fig. 4A) of the same body weight.

In all 11 dogs with spontaneous congenital heart lesions, the sequence of right ventricular epicardial activation was essentially the same as in the control group. The boundaries of the three major regions of activity and the exact site of the initial point of activation varied from individual to individual as it did in the control group; however, no obvious alterations in the sequence of right ventricular epicardial activation were noted. The total RVE activation time varied from 21 to 40 msec. The delay in right ventricular epicardial activation was best visualized when

**FIGURE 4**

Cross sections of the heart at the level of the tricuspid valve from 2 dogs of the same weight. A, normal dog; B, heart of a dog with congenital pulmonic stenosis (same dog as in Figure 3). Note especially the thickness of the RV free wall around the RV outflow tract.
FIGURE 5

A to D are from dogs 2, 3, 5, and 7 respectively in Table 1. Note the number of right ventricular epicardial sites activated after completion of left ventricular epicardial activation in the more severe lesions. Severity of lesion increases from A to D.

FIGURE 6

Results obtained in 4 dogs having larger pressure differences than the dogs of Figure 5. A to D are from dogs 6, 9, 10 and 11 respectively in Table 1. See Table 1 for meaning of abbreviations.

increased as the severity of the lesion increased. When the right ventricular pulmonary artery systolic pressure difference was 40 mm Hg or more, the right ventricular epicardium consistently completed activation after the left ventricular epicardium with delays ranging from 5 to 22 msec. When the pressure difference was 72 mm Hg or more, the site of earliest ventricular epicardial activity was recorded from the left ventricle. Figures 5 and 6 demonstrate that right ventricular epicardial activation has shifted completely in time so that in the right ventricular
### Epicardial Mapping Studies in Dogs with Congenital Heart Disease

<table>
<thead>
<tr>
<th>No.</th>
<th>Breed</th>
<th>Age</th>
<th>Necropsy diagnosis*</th>
<th>RV—PA systolic pressure (mm Hg)</th>
<th>Total RV epicardial activation time (msec)</th>
<th>Total LV epicardial activation time (msec)</th>
<th>Complete ventricular epicardial activation time (msec)</th>
<th>LV/RV thickness†</th>
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<tr>
<td>1</td>
<td>Wire-haired Fox Terrier</td>
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<td>VSD</td>
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<td>Beagle</td>
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<td>PS, VSD</td>
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<td>21</td>
<td>34</td>
<td>1.04</td>
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<tr>
<td>3</td>
<td>Boxer</td>
<td>8 months</td>
<td>PS, ASD</td>
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<td>23</td>
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*PS = valvular and/or subvalvular stenosis, ASD = atrial septal defect, VSD = ventricular septal defect, RV = right ventricle, LV = left ventricle, and PA = pulmonary artery.

†The mean LV/RV thickness for 20 normal dogs was 2.51; standard deviation ±0.335; standard error of the mean ±0.075; range 2.05 to 3.05.
hypertrophy group, 39% of the right ventricular epicardial sites were activated during the last one-third of the QRS complex as contrasted with only 1% in the control group.

Although more sites were recorded from some dogs than others, the percentages were computed for each dog individually. Removing the extra sites recorded in some dogs does not alter the results, since dots are removed only in those locations on the QRS complex where multiple dots occur.

Table 1 presents the breed, age, necropsy diagnosis, and various measurements obtained in the epicardial mapping studies in the dogs with congenital heart disease.

Discussion

While thickness measurements of the ventricular walls are subject to technical variation, right ventricular hypertrophy was obvious when the pressure difference across the pulmonic valve was 72 mm Hg or more; the ratio of the thickness of the left to right ventricle was unquestionably smaller than the ratio in the control dogs. In general, the ratio of left to right ventricle thickness decreased as the difference between the right ventricle and pulmonary arterial systolic pressure increased. It appears that the total right ventricular epicardial activation time was not directly related to the severity of the lesion. The dog with the highest pressure difference (no. 11) and most severe right ventricular hypertrophy (Fig. 4B) had the shortest epicardial activation time. While this was a small dog (6.8 kg), the right ventricular epicardial activation time does not appear to be directly related to the size of the animal and the severity of the lesion. The largest dog studied (no. 5) weighed 24.5 kg and had a right ventricular epicardial activation time of 28 msec. The pressure difference was 44 mm Hg. A dog of almost comparable size (no. 9; 22.0 kg) with twice the pressure difference (90 mm Hg) also had a total right ventricular epicardial activation time of 28 msec.

After a pressure difference of 40 mm Hg, the total left ventricular epicardial activation time was consistently shorter than the total right ventricular epicardial activation time. The left ventricular epicardial activation times in these dogs with a pressure difference of over 40 mm Hg varied from 16 to 24 msec when body weights ranged between 6.8 to 24.5 kg. The left ventricular epicardial activation times in the 4 normal dogs studied varied from 24 to 30 msec when body weights ranged from 5 to 19.6 kg. Seidenstein and co-workers (8) found total left ventricular epicardial activation times from 30 to 40 msec in normal dogs when body weights were 21 to 23 kg.

Of the 6 dogs with obvious right ventricular hypertrophy (the ratio of left to right ventricular thickness less than 1), the total right ventricular epicardial activation time was definitely prolonged in only 2 dogs and slightly prolonged in 2 dogs. Brusca (9) found that the activation times of the right ventricle in humans was definitely prolonged in the presence of right ventricular hypertrophy. Durrer and co-workers (10) found delays in right ventricular epicardial activation times varying between 10 and 20 msec in humans with it. Boineau and co-workers (11) using intramural techniques found delays of 10 msec in dogs with right ventricular hypertrophy resulting from experimentally produced atrial septal defects. In the present study, the sequence of right ventricular epicardial excitation in dogs with congenital right ventricular hypertrophy was the same as in normal dogs. In Durrer's studies (10) in humans with right ventricular hypertrophy, the sequence of activation resembled the normal pattern with earliest activation of the right ventricular epicardium occurring at the area trabecularis. In extreme cases of it, Brusca (9) found that the trabecular region was no longer the earliest region and that earliest activity occurred along the right paraseptal region.

It appears likely that the forces creating the QRS electrocardiographic changes in right ventricular hypertrophy are associated not only with a slight prolongation in right ventricular epicardial activation time, but also...
with a shift in timing of the activation within the QRS complex. The shift in time is probably caused by the delay in the spread of excitation through the septum and free wall due to increased muscle mass, but could not be measured by the techniques used in this study. The conduction velocity of the intramural myocardium was not altered in dogs with experimental right ventricular hypertrophy (11) or in human patients with it (10); prolonged activation times were attributed to the increased muscle mass. Preliminary results of intramural excitation studies in dogs with spontaneous heart disease have been reported (12) and further cooperative studies are in progress.

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Epicardial Excitation Studies in Dogs with Congenital Right Ventricular Hypertrophy
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