Interrelationship of architecture and function of the right ventricle

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MATERIALS AND METHODS

Sixteen open-chest dogs, weighing 15–20 kg, were studied under phencyclidine hydrochloride (2 mg/kg im) and α-chloralose (60–80 mg/kg iv) anesthesia and positive-pressure respiration. Four modified Walton-Brodie strain-gauge arches, with essentially linear recording characteristics up to 100 g weight deflection, were sutured to the anterior epicardial surfaces of the right ventricle. The limbs of the gauges were compressed so that the underlying myocardium was stretched significantly. The axis of gauge placement coincided with the major direction of the underlying myocardial fibers. The gauges were positioned as follows: 1) the conus, the major axis being circumcaval, with the sutures located 4 to 5 mm proximal to the pulmonic valve ring; 2) the midposition, just below the left border of the tricuspid ring and parallel to the major orientation of superficial fibers, the paracordal sinus fibers being directed approximately 30° from the vertical (base to apex), 3) the lateral border of the right ventricle (the main sinus region) at approximately 20° from the vertical, parallel to the superficial fibers; 4) sometimes a fourth gauge was placed parallel to and between the second and third gauges. The sutures were superficially placed so that the underlying tissue was held taut and the direction of fibers under the gauge was uniform. In five experiments the gauges were switched from one position to another in order to insure that the contractile force changes were not gauge dependent, but represented a true function of the underlying myocardium. Walton-Brodie gauges are considered to record essentially isometric force from underlying myocardial segments (8). The maximal force and rate of development of force were measured during different interventions and compared as percent change from control values; maximal rate of force development was measured as the steepest slope of the contraction curve. The gauge outputs were recorded on either a Grass polygraph or a four-channel Tektronix cathode-ray oscilloscope. Right ventricular sinus and conus pressures were recorded using a Statham transducers connected to special cannulas inserted through the wall (15). The natural frequency of the special cannulas with a 3.5-cm length of PE-50 polyethylene was tested using the step pressure ("pop") technique and was consistently found to be above 100 cycles/sec. Arterial pressures were recorded through an 8-cm length of PE-100 polyethylene. In each animal both vago sympathetic trunks and both stellate ganglia were exposed and stimulated via a Grass square-wave stimulator.
RIGHT VENTRICULAR STRUCTURE AND FUNCTION

FIG. 2. Tracing from an oscilloscope demonstrates forces recorded from Walton-Brodie gauges on same three regions as in Fig. 1. First trace is from bulk of sinus musculature, followed by force gauge on the sinus adjacent to conus region. Tracing on right is recorded from conus. Onset of sinus contraction preceded that in conus by 50 msec. Vertical lines are 50 msec apart.

(model S5) at parameters of 2-5 v, 4 msec, and 4 cycles/sec, before and after atropine. Augmented contraction of the right ventricle was also elicited by the intravenous administration of 1.0 μg/kg of norepinephrine diluted in 2 ml of normal saline.

RESULTS

Figure 1 illustrates the simultaneous responses in contractile force from the three regions of the right ventricle. Fast traces during control and stimulation (right stellate) periods permit comparison of the rate of development in contractile force (dF/dt) as well as the maximal force. The contractile force of the conus increased 100%, whereas that of the paraconal (mid) and sinus regions increased 70 and 60%, respectively; dF/dt increased 177% on the conus segment and 138% on the sinus segment. It is of interest that mechanical alternans appeared during the period of stimulation on the midventricular segment but was absent from each of the other regions of the right ventricle. The onset of sinus contraction preceded that in conus by 6-12 msec.

Oscilloscopic traces from gauges recording contractile force from identical positions of the right ventricle from another animal illustrates the precedence of sinus contraction (Fig. 2). The earliest onset of contraction occurred in the main sinus region, followed in 20 msec by the paraconal segment with conal contraction 30 msec later. Time intervals required for attainment of maximum force followed a similar sequence. Thus, a major fraction of sinus musculature was recruited considerably in advance of that of the conus.

Figure 3 illustrates changes in both contractile force and in intraventricular pressures accompanying electrical excitation of the left stellate ganglion. In confirmation of earlier reports, augmentation in both contractile force and pressure was more prominent than during right stellate stimulation. The percent increase in contractile force on the conus region markedly exceeded that on the midventricular and lateral (sinus) portions of the right ventricle. Simultaneous measurement of intraventricular pressures, on the other hand, revealed much greater development of intrasinus pressure as compared with that in the intracavitary portion of the ventricle. In the control period the sinus and conus region developed similar pressures, during stellate stimulation the differential pressure developed between the sinus and conus is dramatically illustrated. The minimal pressure increase in the conus is faithfully represented in the pulmonary artery pressure.

Figure 4 reveals simultaneous changes in contractile force as well as in dF/dt on all three portions of the right ventricle during electrical excitation of the right cervical vagosympathetic trunks in the atropinized preparation. Again, augmentation was more prominent in the conus segment. Differences in magnitude of change in contractile force as induced by excitation of right and left vagosympathetics were not significant.

In the absence of atropine, vagal stimulation significantly elongated the interval of time between excitation (as indicated by the Q wave of the ECG) of the ventricle and mechanical contraction of each of the three test regions (P value < 0.001). In addition, the time interval between initial contraction of the sinus and conus musculature was distinctly exaggerated. Alterations in contraction sequence are illustrated in Fig. 5. In order to achieve minimal alterations in contractile force and heart rate, relatively low stimulation intensities (2 v, 4 cycles/sec, 2 msec) were employed. In Fig. 5, heart rate was decreased from 198 to 170 beats/min with little or no change in contractile force or dF/dt. The initial defection in the conus gauge record was downward during stimulation, suggesting a preliminary distension of the conus segment.

Figure 6 illustrates the simultaneous changes in force and dF/dt resulting from intravenous injection of norepinephrine.
Again, the most prominent increase in force and \(\text{d}F/\text{d}t\) was observed on the conus region, superimposed upon a slight but consistent elevation in base line. Under these experimental conditions, the onset of contraction occurred almost simultaneously in the three regions of the ventricle. Figure 7 is a cathode-ray oscilloscope trace from similar experiment in which the sinus region (solid line) contracted before the conus (broken line) during the control period (upper trace). During the positive inotropic response to norepinephrine (lower trace), the onset of contraction in the conus preceded that in the sinus region by approximately 50 msec. This directional shift in contractile sequence was observed in all animals in which this procedure was carried out.

Table 1 summarizes the comparative responses of the three regions of the right ventricle to electrical stimulation of the right and left vagosympathetic trunks in the atropinized animal. In all experiments, regional responses to stimulation represented statistically significant changes from control force and \(\text{d}F/\text{d}t\). Comparisons between response of the conus and sinus to vagosympathetic stimulation reveal equally significant changes, the conus showing markedly increased.

Fig. 3. Upper three traces are from strain gauges placed on right ventricle, as in Fig. 1. Lower three traces show sinus and conus intraventricular pressures with the pulmonary artery pressure (PAP). Note that force of contraction from all areas of right ventricle were augmented during left stellate stimulation, with conus force showing greatest augmentation. In contrast, peak intracaval pressure was minimally elevated. Peak intr sinus pressure was markedly increased.

Fig. 4. Effects of right vagosympathetic trunk stimulation after atropine. Force gauges were placed as in previous figures and maximal augmentation occurred in conal region.

Fig. 5. Minimal right vagal stimulation elicited a slight bradycardia. Contractile force from various regions was not depressed, but sequence of contraction from sinus to conus was delayed. Conus force gauge recorded a downward deflection when sinus fibers are first contracting.
Infusion of norepinephrine increased force of contraction in all three regions of right ventricle. Conal fibers are augmented almost twice that of rest of right ventricle. Diastolic force base line is elevated in conus and depressed in sinus regions.

FIG. 6. Oscilloscopic tracings of a control period (upper trace) of sinus (solid line) and conus (broken line) force patterns. Lower trace illustrates change in contraction sequence between sinus and conus after infusion of norepinephrine. Onset of conus contraction preceded sinus contraction by 50 msec.

greater increases in both contractile force and in rate of change in force.

Similarly, electrical excitation of the right and left stellate ganglia elicited expected augmentation in force and rate of change in force on all three segments of the right ventricle. Again, differences in response on the conus and sinus were significant, although changes induced by the left stellate were more convincing than those from the right stellate.

Finally, norepinephrine injection resulted in consistent augmentation in all three zones of the ventricle. Although the conus region again responded with the greater changes in contractile force when compared with the sinus region, it is of great interest that the paraconal zone showed equally marked augmentation, whereas this region did not respond as forcefully during nervous stimulation. Statistical significance of the differences in responses of conus and sinus regions is shown for each of the procedures.

Table 2 summarizes the sequential order of contraction on the same three anatomical zones of the right ventricle during control, vagosympathetic (in absence of atropine), stellate stimulation, and norepinephrine injection. Measuring from the initial deflection in Q wave of the ECG to the beginning of mechanical contraction, the time intervals are compared. Control measurements were performed early in the experiment, at which time the sequence of contraction was regularly from sinus to conus. Following repeated sympathetic stimulation, or as the preparation progressively deteriorated, these intervals were shortened and contraction frequently became more nearly synchronous.

Vagal bradycardia induced by stimulating voltages sufficiently low to maintain sinus rhythm, invariably prolonged the time interval in each of the test regions. The interval from onset of Q wave to contraction of the conus was most strikingly extended.

Both right stellate stimulation and norepinephrine injection induced an opposite change in which the interval was markedly shortened until the three regions contracted more nearly simultaneously. Indeed, norepinephrine consistently reversed the sequence so that conus contraction preceded that of the sinus. All of these alterations were found to be statistically significant (P = .001).

DISCUSSION

The right ventricle is considered a low-pressure volume pump (20) and its function has been minimized to the point of questioning whether it is required to move blood (9). Strain gauges are frequently applied to the conus to record changes in contraction thought to be characteristic of the right ventricle and often treated as typical of the entire heart. Interest in its function may be focused upon certain
peak force and maximum dF/dt in cunus, Faraconal sinus, and sinus force is invariably higher on the conus region, intracavity sinus, and cunus tabulated as interval between Q wave and onset of force from various regions.

Norepinephrine 14
Left stellate 12
Atropinized left vagus 11

Inasmuch as the radius of curvature of the conus is a fifth or sixth that of the sinus chamber (5, 6), the circumconal fibers act in a similar fashion in the mammalian right ventricle. The circumarterial muscle fibers of the right ventricle can act as a functional stricture directing flow into the systemic circulation (22, 25). The conus normally dilates with blood expelled from the sinus. March et al. (14) noted that the conus normally dilates with blood expelled from the sinus.

The effect of sympathetic stimulation is opposite to that observed during vagal stimulation. Thus, sympathetic innervation elicits regional functional alterations in the right heart comparable to those reported for the left heart (17). Sympathetic fibers in the vago-sympathetic trunk have similar augmentor actions, with predominant influences also on the conal fibers. It is apparent that sympathetic fibers carried in the vago-sympathetic trunk primarily serve the conus region, whereas those from the stellate ganglia provide important innervation to both regions.

When the right ventricle contracts vigorously under stellate stimulation or noradrenaline influence, a visible groove becomes apparent in the region of muscular fiber transition between the sinus and conus, thus accentuating the functional compartmentalization of the right ventricle.

Conus contraction following 15 msec after the right lateral border.

Weak vagal stimulation causing bradycardia prolonged the normal sequence of contraction. The sequence of contraction is frequently so delayed that the conus gauge recorded a downward deflection before the usual upward deflection, indicating a separation of the gauge legs by distension of the conus. March et al. (14) noted that the conus normally dilates with blood expelled from the sinus.

The circumarterial muscle fibers of the right ventricle act as a functional stricture directing flow into the systemic circulation (22, 25). The circumarterial muscle fibers of the right ventricle can act as a functional stricture directing flow into the systemic circulation (22, 25). The circumarterial muscle fibers of the right ventricle can act as a functional stricture directing flow into the systemic circulation (22, 25).

Values are means ± sem. * 1 μg/kg.

### Table 1. Influence of nerve stimulations and injection of norepinephrine* on heart rate, and percent change from control in peak force and maximum dF/dt in conus, paraconal sinus, and sinus

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of Animals</th>
<th>Heart Rate, beats/min</th>
<th>Maximum Force</th>
<th>Maximum dF/dt</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Conus</td>
<td>Paraconal sinus</td>
<td>Sinus</td>
</tr>
<tr>
<td>Control</td>
<td>16</td>
<td>138 ± 7</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Atropinized right vagus</td>
<td>11</td>
<td>144 ± 13</td>
<td>180 ± 22</td>
<td>126 ± 33</td>
</tr>
<tr>
<td>Atropinized left vagus</td>
<td>11</td>
<td>131 ± 9</td>
<td>159 ± 20</td>
<td>126 ± 5</td>
</tr>
<tr>
<td>Right stellate</td>
<td>12</td>
<td>169 ± 5</td>
<td>293 ± 50</td>
<td>189 ± 22</td>
</tr>
<tr>
<td>Left stellate</td>
<td>12</td>
<td>150 ± 7</td>
<td>253 ± 44</td>
<td>178 ± 21</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>14</td>
<td>193 ± 33</td>
<td>306 ± 84</td>
<td>302 ± 86</td>
</tr>
</tbody>
</table>

Values are means ± sem. * μg/kg.

### Table 2. Time sequence of onsets of contraction as recorded with Walton-Brodie strain gauges on sinus, paraconal sinus, and conus tabulated as interval between Q wave and onset of force from various regions

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of Animals</th>
<th>Heart Rate, beats/min</th>
<th>Maximum Force</th>
<th>Maximum dF/dt</th>
</tr>
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<tr>
<td></td>
<td></td>
<td>Conus</td>
<td>Paraconal sinus</td>
<td>Sinus</td>
</tr>
<tr>
<td>Control</td>
<td>16</td>
<td>138 ± 7</td>
<td>52 ± 2</td>
<td>67 ± 3</td>
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<td>88 ± 14</td>
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<tr>
<td>Right stellate</td>
<td>12</td>
<td>169 ± 5</td>
<td>44 ± 3</td>
<td>48 ± 3</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>14</td>
<td>193 ± 33</td>
<td>43 ± 3</td>
<td>36 ± 2</td>
</tr>
</tbody>
</table>

Values are means ± sem.
in these two regions. Figure 3 demonstrates the greater augmentation of contractile force in the conal fibers compared to the sinus fibers. Thus, the conal fibers appear to create a functional resistive element preventing the high sinus pressure from reaching the pulmonary artery. Norepinephrine causes the conus to contract as much as 40 msec before the sinus regions. This early onset of contraction creates a functional resistive element preventing the high ventricular pressures developed are highly dependent on mural force (19), anatomic structure, and autonomic innervation.

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REFERENCES

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