Distribution of Sympathetic Fibers in the Left Ventricular Epicardial Plexus of the Dog

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ABSTRACT
Myocardial contractile force in five areas of the left ventricle was measured in 14 dogs under chloralose anesthesia prior to and following segmental chemical epicardiectomy. Electrical stimulation of the stellate ganglia was performed before and after each segment of epicardium was destroyed, and records of myocardial contractile response to stimulation were obtained. Epicardiectomy resulted in ablation of contractile response in specific areas of the left ventricle. In a recent publication from our laboratory (Circulation Res. 22: 315, 1968), the predominance of an epicardial distribution of sympathetic fibers was demonstrated. As an extension of that work, this study demonstrates the projection of fibers from both left and right stellate ganglia and the innervation of both anterior and posterior surfaces of the left ventricle. The major projections of sympathetic fibers are oriented along an axis passing from base to apex and can be interrupted by epicardial destruction in the area of the cephalad portion of the anterior descending coronary artery and adjacent to the origin of the left marginal artery.

ADDITIONAL KEY WORDS
epicardiectomy
stellate ganglia stimulation

There is evidence to suggest a specific regional distribution of sympathetic nerves to the heart (1). Stimulation of specific mediastinal sympathetic fibers resulted in a predictable localized inotropic response, and removal of the epicardium from small areas altered the contractile response of ventricular muscle to sympathetic nerve stimulation.

Randall et al. (2) have demonstrated that a major fraction of the efferent sympathetic cardiac nerves to the anterior cardiac surface traverses the epicardial plexus en route to their terminations. Using a technique of chemical epicardiectomy, we have mapped the projections of these nerves through the epicardium enveloping the left ventricle. Analysis of the data obtained now permits us to extend the work of Randall et al. (2) to present a detailed description of the epicardial projections of the cardiomotor nerves to all surfaces of the left ventricle.

Methods
Fourteen healthy mongrel dogs weighing 10 to 16 kg were given phencyclidine (Sernylan), 2 mg/kg intramuscularly, and then anesthetized with alpha chloralose, 60 to 80 mg/kg given intravenously. We opened the thorax through both fifth intercostal spaces andtransected the sternum. Respiration was maintained with a Harvard pump through a tracheotomy tube. We isolated the left and right stellate ganglia and, following an anterior longitudinal pericardiectomy,
constructed a pericardial cradle. We cannulated the right femoral artery and connected this cannula to a Statham P23dB pressure transducer for continuous recording of blood pressure.

Five Walton-Brodie strain gauges were sutured to the surface of the left ventricle, and all tracings were recorded on a Grass Model 5B polygraph with a paper speed of 2.5 mm/sec. Figure 1 shows the placement of the gauges on the left ventricle. In order that placement of these gauges be consistent in all animals, we used the following landmarks:

I. Posterior base of left ventricle parallel to and 1 cm anterior to the posterior descending coronary artery; 1 cm caudal to the circumflex artery;

II. Middle base of the left ventricle parallel to and 1 cm posterior to the left marginal artery; 1 cm caudal to the circumflex artery;

III. Anterior base of the left ventricle parallel to and 1 cm caudal to the circumflex artery;

IV. Anterior surface of the left ventricle immediately caudal to and parallel to the first left ventricular branch of the anterior descending coronary artery; 1 cm lateral to the anterior descending coronary artery;

V. Posterior apical surface of the left ventricle parallel to and 1 cm anteromedial to the posterior descending coronary artery.

Control responses to electrical stimulation of the stellate ganglia were recorded during stimulation with rectangular pulses of 4 to 5 v, 10 cps, and 5-msec duration from a Grass S-5 stimulator. We applied the stimulus for 20 seconds and monitored the voltage throughout the period of stimulation on a cathode-ray oscilloscope.

For the purpose of denervation, the margins of the left ventricle were arbitrarily divided into six areas. A 4-mm wide strip of 85% phenol was applied with a fine camel hair brush to each of these areas parallel to and approximately 4 mm from the major coronary vessels. Following application of the phenol to each area along the left ventricular border, the left and right stellate ganglia were again stimulated and suitable recordings obtained. The phenol was applied to the six areas in the following order:

P—1 apex of left ventricle to second diagonal branch of anterior descending coronary artery;
P—2 from the second diagonal branch to the origin of the anterior descending coronary artery;
P—3 from the origin of the anterior descending coronary artery to the left marginal artery;
P—4 from the left marginal artery to a point one half the distance to the posterior descending coronary artery;
P—5 from the end of the P—4 application to the posterior descending coronary artery;
P—6 from the origin of the posterior descending coronary artery to the apex of the left ventricle.

Figure 1 depicts the steps in the application of phenol to the left ventricular surface. It should be noted that following application of phenol to all six areas, the left ventricular border is entirely encircled.

Results

Figure 2 illustrates the response of the five left ventricular strain-gauge arches and femoral artery blood pressure to stellate ganglia stimulation during a control period and after five epicardial applications of phenol. The position of the gauges and the areas of phenol application are illustrated in Figure 1. Data presented in Figure 2 are characteristic of that obtained from all the animals in this series of experiments. Panel C of Figure 2 illustrates the control myocardial contractile force response and blood pressure response to left and right stellate ganglia stimulation. A significant augmentation of contractile force was noted in all tracings during left stellate ganglion stimulation. Pulse pressure was markedly increased with little change in heart rate. During stimulation of the right stellate ganglion, a marked increase in the force of

Circulation Research, Vol. XXIII, August 1968
contraction was noted in all the gauges except for the middle base gauge (II) which responded with a slow, gradual increase in amplitude. A significant increase in heart rate occurred. Pulse pressure increased in response to right stellate ganglion stimulation, though the magnitude was less than that resulting from stimulation of the left stellate ganglion.

These data indicate that sympathetic efferent motor fibers from both the left and right stellate ganglia innervate both anterior and posterior left ventricular surfaces.

Following application of phenol along the caudal portion of the anterior descending coronary artery (P-1) in this animal, no significant change was observed during either left or right stellate ganglia stimulation.

Panel P-2 of Figure 2 illustrates the contractile responses of the five areas following the second application of phenol. During left stellate ganglion stimulation following this procedure, the response of all base gauges (I, II and III) decreased. The response of the anterior ventricular gauge (IV) was abolished, and the response of the posterior apical gauge (V) decreased. Fibers from the left stellate ganglion traversing the epicardium of the left ventricle to these areas must enter the ventricular surface along the cephalad portion of the anterior descending coronary artery.

During stimulation of the right stellate ganglion (panel P-2, lower tracings) there
was almost no increase in contractile response of regions under gauges IV and V indicating that the pathways of fibers from the right stellate ganglion to both anterior and posterior left ventricular surfaces have been interrupted. There was some decrease in force of contraction in the posterior base gauge indicating a projection of right stellate sympathetic fibers passing from the anterior to the posterior surface near the base of the left ventricle. Heart rate and blood pressure continued to be increased in response to stimulation of the ganglia.

In P-3, the response of the region under gauge I to left stellate ganglion stimulation was abolished. A further attenuation of responses of the regions under gauges II and III occurred during stimulation of the left stellate ganglion.

During right stellate ganglion stimulation, the response of the regions under the posterior and anterior base gauges (I and III) decreased (P-3, lower tracings). A further decrease in the contractile force in these areas occurred following the application of phenol in areas P-4 and P-5. A similar type of progressively decreasing response occurred in the area under gauge III during stimulation of the left stellate ganglion.

No further depression of the contractile response occurred following the sixth application of phenol.

Figure 3 graphically summarizes the results of the experiments in all fourteen animals. The type of response obtained and the abolition of the response to stimulation in all animals was similar to that illustrated in Figure 2. The left stellate motor efferents

![Figure 3](http://circres.ahajournals.org/doi/abs/10.1161/01.RES.23.2.168)

**Figure 3**

Results of denervation in 14 animals. Roman numerals I to V indicate the strain gauges and P-1 to P-6 are steps in denervation as depicted in Figure 1. For each gauge, the number of animals responding to stimulation after each successive denervation is indicated by the vertical bars.

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Schematic representation of lateral views of left ventricle. Blackened areas passing from point of epicardectomy to gauges studied represent pathways of sympathetic epicardial fibers. A, C, E, G, and I represent fibers from left stellate ganglion. B, D, F, H, and J represent fibers from right stellate ganglion.

innervate both posterior (gauges I, II, and V) and anterior (gauges III and IV) surfaces. Fibers from the right stellate ganglion innervate both surfaces of the left ventricle and in particular the posterior base area.

A schematic representation of the proposed pathways of epicardial innervation of the left ventricle is illustrated in Figure 4.

Discussion
There is general agreement that sympathetic cardiomotor efferent fibers traverse the epicardium, but it has been impossible, because of a lack of distinct morphological characteristics, to identify the course of these fibers on the ventricles.

Descriptions of the innervation of the posterior aspect of the left ventricle have emphasized the presence of a dorsal ventricular plexus originating primarily from fibers of the left ventrolateral cervical cardiac nerve (3). A similar pathway for fibers to the posterior aspect of the left ventricle was described by Nonidez (4). Anufriew (5) considered the projection of these fibers onto the ventricle to be the most extensive of all cardiac plexuses.

Although Randall et al. (2) emphasized the importance of the epicardial plexus in cardiac innervation, their studies do not permit a definition of sympathetic pathways to the entire left ventricular surface. The present experiments offer functional evidence to confirm the presence of significant pathways merging into the epicardial plexus of the ventricle in the area of the left marginal artery. Fibers from this area are not restricted to posterior projections but make a significant contribution to the innervation of the anterior left ventricular surface.

Furthermore, our data indicate a significant contribution of cardiomotor nerves from the right stellate ganglion to the posterior surface of the left ventricle. Fibers projected onto this surface are found in the epicardial plexus both at the bifurcation of the left main coronary artery and the left marginal artery.

The innervation of the anterior surface of the left ventricle has been described (4) as arising from fibers originating primarily from the right sympathetic cardiac nerves and traveling beneath the pulmonary artery to be projected onto the ventricular surface from the area of bifurcation of the left main coronary artery. Cooper et al. (6) have described large sympathetic confluences passing to the left of the main pulmonary artery at the heart and innervating the left ventricle. The experiments reported here offer definite physiological evidence that not all innervation of the anterior left ventricle follows this pathway. Fibers from the left stellate ganglion reach the anterior left ventricular surface after entering the epicardial plexus along the A-V groove near the marginal artery. These fibers have their origin in the ventrolateral cervical cardiac nerve.

The data presented demonstrate a dual innervation of all surfaces of the left ventricle from both left and right stellate ganglia. Functional evidence is presented to empha-
size the presence of a posterior ventricular plexus (left posterior longitudinal plexus of Worobiew [7]) originating primarily from fibers of the left ventrolateral cervical cardiac nerve. The projections of these pathways over the left ventricle are in a direction generally oriented along a line from base to apex.

References
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Circ Res. 1968;23:165-170
doi: 10.1161/01.RES.23.2.165

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