Relation of Increase in Muscle Mass
to Performance of
Hypertrophied Right Ventricle in the Dog

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ABSTRACT

Right ventricular hypertrophy was produced by chronic constriction (banding) of the pulmonary artery in the dog. Right ventricular muscle mass increased by 40% in 6 to 12 weeks after banding. Maximal work performance of this ventricle also increased; at 12 weeks the mean was 175% more than that of the normal right ventricle.

It was concluded that, per unit of gross myocardial mass, the work performance of the hypertrophied right ventricle of the dog was no less than that of the normal right ventricle.

ADDITIONAL KEY WORDS maximal ventricular work catecholamines pulmonary artery banding myocardium cardiac function tests hypertrophy unanesthetized dogs

Serial studies following long-standing right ventricular outflow obstruction produced by banding the main pulmonary artery of the dog have shown that ventricular hypertrophy is well established within three months of the procedure and approaches its maximum in this period. It has been found also that the infusion of sympathomimetic amines into such an animal induces an increase of right ventricular stroke and minute work exceeding that elicited by severe exercise.

The object of this investigation was to define the relation of the maximal work of the hypertrophied right ventricle of the conscious intact dog to the maximal work of the normal right ventricle and to the absolute change in muscle mass.

Methods

Nineteen trained normal mongrel dogs, restrained in a sling in a comfortable position, were studied while awake and standing at rest, without premedication. Acute right ventricular stress was produced by partial occlusion of the main pulmonary artery with a balloon inflated to the limit of the dog's tolerance, a degree just below that at which the animal would show a reduction in systemic arterial blood pressure. When this level was reached the inotropic agent, noradrenaline (noradrenaline) or isoproterenol (Isuprel, 2.5 μg/min), was infused for six minutes. At each stage of the study, cardiac output was determined by the indicator dye-dilution technique, and right ventricular, pulmonary arterial, and systemic arterial pressures were measured simultaneously by matched strain-gauge manometers. Mean pressures were obtained by planimetry, and an approximate calculation of right ventricular work was derived from the product of effective mean systolic pressure (mean systolic pressure minus end diastolic pressure) and stroke volume. The order of infusion was randomized, and 30 minutes elapsed between infusions.

Following the control study, six animals were killed and their hearts were dissected out and separated into right and left ventricles according to the method of Herrmann, to serve as controls in this experiment. In the remaining 13 dogs the pulmonary artery was banded to provide an average peak right ventricular systolic pressure of 98 mm Hg (range 80 to 113) immediately after banding. These animals were studied three, six, and twelve weeks later. Right ventricular function was then altered by an infusion of sympa-
mimetic amines as used in the control study. Seven of these animals were killed after the six-week study and six after the twelve-week study, and the myocardial mass was determined as outlined above for the control group.

Results

The change in right ventricular muscle mass six weeks after banding is shown in figure 1. The dilatation and hypertrophy are evident in cross sections at the same level through the separated right and left ventricles of the hearts of two dogs of identical body weights (15 kg). In the normal dog (A) the ratio of right ventricular (RV) to left ventricular (LV) weight was 0.61, while in the dog with the pulmonary artery banded for six weeks (B) it was 1.02.

The RV/LV weight ratio in this particular study serves as an expression of right ventricular hypertrophy (fig. 2). Such a ratio reduces the difference between animals when chamber weights are related to various parameters such as body weight and surface area. All our six control dogs had RV/LV ratios that fell within the two standard errors derived from Herrmann's data, averaging 0.68. There was very little difference between the RV/LV ratio at six weeks and that at twelve weeks after banding, the mean values being 0.93 and 0.95 respectively.

Figure 3 shows the average values for right ventricular stroke work and minute work during each state (control, norepinephrine, isopropylarterenol) in the normal animals, and after development of myocardial hypertrophy. The maximal values for stroke work and minute work are reached with administration of iso-
propylarlenol or norepinephrine, or both. Maximal stroke work of the normal right ventricle with balloon occlusion and norepinephrine infusion in the control study averaged 16 gram-meters (g-m), or twice the value for resting stroke work. At three and six weeks after banding, the maximal stroke work with infusion of norepinephrine averaged 27 g-m, and at twelve weeks it averaged 43 g-m, or about 275% of the maximal stroke work of the normal right ventricle. The increase in the average RV/LV weight ratio from 0.68 to 0.95 represents a relative change of +40%. The average stroke work of the right ventricle twelve weeks after banding and without sympathomimetic amine stimulation was 18 g-m, or 50% higher than that of the normal right ventricle subjected to acute occlusion. The maximal minute work, which is often achieved with propylarlenol rather than norepinephrine, parallels the maximal stroke work in general.

The individual value for maximal right ventricular stroke work (whatever the mechanism) recorded for each animal is related to the RV/LV weight ratio in figure 4. It is evident that the maximal stroke work rises with an increasing RV/LV ratio, particularly as this ratio approaches 1.0.

**Discussion**

The behavior of the right ventricle following acute obstruction of the pulmonary artery fits the pattern reported in other studies. The degree of right ventricular hypertrophy observed in this study after a band was placed around the main pulmonary artery and tightened to the limits of tolerance had the same general magnitude as that seen in similar studies in this laboratory in that the right ventricular mass increased by about 40%. This "after-load" hypertrophy due to a pressure overload was selective and was restricted to the right ventricle, as the range of left ventricular mass was the same in all three groups of dogs studied.

Studies comparing performance of the hypertrophied with that of the nonhypertrophied heart are few. Dieckhoff used a heart-lung preparation in testing cat hearts made hypertrophic by avulsion of aortic cusps. Beznak produced hypertrophy in rat hearts by aortic constriction and found cardiac output and work increased at rest and in response to infusions of 3.3% polyvinylpyrrolidone.

Whitehorn and Grimmenga have indicated...
that, for given diastolic lengths, greater tension was developed by strips of columnae carneae from the left ventricle of hypertrophied rat hearts than by strips from littermate controls. Kerr et al.\textsuperscript{10} tested the response of papillary muscle strips from the hypertrophied left ventricle of rats to electrical stimulation, and demonstrated that the maximal tension developed was significantly greater per unit weight than that developed by papillary muscles from normal ventricles.

In contrast, Bretschneider et al.\textsuperscript{11} found in dogs no difference in cardiac work per gram of heart between normal heart-lung preparations and those prepared from hearts enlarged by the combination of aortic stenosis and exercise. Grimm et al.\textsuperscript{12} found that differences were not significant when tension production per unit weight was compared in control and exercised or constricted (or both) rat heart muscle. However, these reports yielded no evidence to support the concept that the performance of the hypertrophied myocardium is necessarily less than that of the normal myocardium.

The studies reported here show that in the conscious intact dog the work performance of the hypertrophied right ventricle per unit weight is certainly no less than that of the normal right ventricle. If the stimulus employed produced a maximal or near maximal response in the control (nonhypertrophied) state, then the increased stroke and minute work performed is proportionally much greater than the increase in gross muscle mass. This implies an increase in ventricular work per unit weight in such hearts, as proposed by others.\textsuperscript{7-10} Other measures of ventricular performance, such as the rate of doing work, show similar directional changes.

The amount of hypertrophy produced in these and other experimental studies is less than that seen in some enlarged human hearts, and would fall below the "critical heart weight" of Linzbach.\textsuperscript{13-14} Such hearts would be designated as having "physiologic hypertrophy." Thus, the performance of hypertrophied hearts noted experimentally need not apply in all clinical instances.

Electron microscopic studies of hypertrophied heart muscle reveal no increase in the number of myocardial fibers but indicate an increase in their size, owing to an increased number of myofilaments within the enlarged fiber.\textsuperscript{15-17} However, the contractile behavior of the individual fiber and of its constituent myofibrils has not been so far quantitated in any way that would permit a comparison between the performance of hypertrophied fibers and that of normal fibers.

References


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