The Role of the Pericardium in Conditioning the Effects of Physical Training*

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More work needs to be done on the extent to which the pericardium can modulate the cardiovascular response to exercise and the mechanisms whereby this modulation is brought about. Studies are needed to differentiate the effects of the pericardium on the cardiovascular exercise response, comparing trained with untrained subjects. Evidence is accumulating that exercise training in patients with heart failure improves not only the performance of exercising muscles, but also has some beneficial effects on central hemodynamics. The extent to which these beneficial effects can be attributed to conditioning the pericardium remains speculative.

Numerous studies have shown that the pericardium exerts a restraining effect on cardiac size. Furthermore, it has been demonstrated convincingly that pericardial restraint of left ventricular volume is small or negligible when left ventricular end-diastolic pressure and volume are low and that this restraint becomes significant when these volumes are increased.1

Data concerning the effects of upright exercise on left ventricular end-diastolic volume measured in humans and animals have shown somewhat variable results.4 Some of the variability may be explained by the type of exercise performed, the baseline central blood volume, and species differences. However, the consensus is that left ventricular end-diastolic volume and pressure fall when the erect posture is adopted and that with the onset of mild exercise, left ventricular end-diastolic volume rapidly returns to the value that pertained when the subject was in a supine position. With further exercise and increase in work load, left ventricular end-diastolic volume increases above the level found with the subject supine, but thereafter attains a plateau, perhaps accounted for by the greatly abbreviated duration of diastole. Commensurate with this observation, stroke volume measured during upright exercise increases, although to a much lesser extent than heart rate, but plateaus during the later stages of exercise.

Regrettably, there are very few available data on the effects of upright exercise on the volume of the left atrium, right atrium, and right ventricle. These chambers are considerably more compliant than the left ventricle; therefore, it is entirely conceivable that their exercise-induced increment in volume considerably exceeds that found for the left ventricle.

Although it has been shown in recent studies that pericardial contact pressure is not uniform and that furthermore, it increases regionally in response to dilatation of specific cardiac chambers,5 it is nevertheless apparent that pericardial constraint on total cardiac volume should be considered as a function of the volume of the entire pericardial contents, not just that of the left ventricle.1 When considering the effect of increased cardiac volume on the extent of pericardial restraint, it is critically important to take into consideration the time course of the change in cardiac volume. Rapidly performed stress strain curves of normal pericardial tissue and of the complete pericardial sac are similar, having a J shape. Thus, acutely, the pericardium can stretch to accommodate a small change in cardiac volume. Thereafter, at the bend of the curve, the pericardium becomes increasingly stiff and along the vertical portion of the vertical limb of the J curve, the pericardium is essentially rigid.4 On the other hand, when the pericardium is stretched slowly, it adapts by undergoing hypertrophy and developing decreased stiffness (Fig 1).

Long-term exercise training generates an increase in cardiac size. It seems reasonable to hypothesize that in response to the resulting chronic stretch, the pericardium should adapt, much as it does in response to normal growth and to chronic cardiac enlargement induced in animals by creating an aortocaval shunt.6 Unfortunately, definitive data regarding the effects of long-term exercise training on pericardial restraint during maximal and submaximal exercise are not yet available. However, tantalizing data are available concerning the effects of pericardiectomy in untrained animals.

In untrained dogs and pigs, pericardiectomy produces a significant increase in cardiac output, oxygen consumption, and stroke volume. Data from our laboratory7 indicate that left ventricular end-systolic volume during exercise is not smaller after pericardiectomy, indicating that the procedure does not enhance contractility. On the other hand, serial studies of left ventricular end-diastolic volume and its pressure-volume relationship indicate that following pericardiectomy in pigs, a progressive increase in left ventricular end-diastolic volume and a shift to the right of its pressure volume relation occur. These data are highly compatible with the thesis that the increase in cardiac performance consequent on pericardiectomy should be ascribed to increased utilization of the Frank-Starling mechanism, not increased contractility. In our laboratory, we are presently performing studies on the effects of pericardiectomy in trained as opposed to the previously mentioned untrained pigs. Unfortunately, as of this writing, even preliminary results are not yet available.

A precedent for the effects of the pericardium on regulating the cardiovascular response to exercise can be found in comparative physiology. We have studied...
fishes because many of their anatomic and physiologic characteristics favor their use as a model for the effects of the pericardium on cardiovascular performance. In this class, sympathetic innervation of the heart is absent (although the heart is supplied by the vagus nerve). The heart rate response to exercise is therefore much more sluggish and far less impressive than in mammals. In addition, the fluid-filled pericardial space is much larger in relation to cardiac volume when elasmobranch fishes are compared with mammals. Finally, a valved canal connects the pericardial and peritoneal spaces, allowing flow only from pericardium to peritoneum. Flow occurs whenever pericardial pressure rises from its normally ambient or slightly subambient level to a critical value usually several cm H₂O above ambient. When elasmobranch fish swim, this critical level of pericardial pressure may be exceeded when the cardiac volume increases as a result of increased venous return. Fluid may also be displaced through the canal whenever sharp turns or body movements exert external pressure on the pericardium. When fluid is ejected from the pericardial to the peritoneal space, pericardial pressure falls substantially. By this means, elasmobranch fish can regulate stroke volume by exploiting the large pericardial reserve volume and their ability to alter cardiac transmural pressure by abruptly changing pericardial volume and therefore pericardial pressure.

In mammals, the pericardium fits the heart quite snugly. While pericardial spaces can be demonstrated along the grooves, the space between the pericardium and the surfaces of the ventricles may be to a large extent potential rather than real, the pericardial fluid representing little more than a lubricating monolayer. This close apposition of pericardium to heart has raised the serious question of whether it is legitimate to measure pericardial pressure as fluid pressure using conventional catheters and transducers or catheter-tipped micromanometers. It has been suggested that true pericardial contact pressure, often referred to as contact force, should be assessed by means of a flat unstressed

**Figure 1A** (left). Pericardial pressure/volume curve from the pericardium of a dog. Cardiac volume was 200 ml. **B** (right). Pericardial pressure/volume relation of a more compliant, prestretched pericardium. The data were obtained during pericardiocentesis for relief of cardiac tamponade.

**Figure 2.** Left ventricular diastolic pressure-segment length relation before and after removal of the pericardium. With pericardium intact, fluid infusion shifts the curve up and nitroprusside infusion shifts it back down. After pericardiectomy, these interventions shift the points along a single curve (reproduced with permission).
balloon placed between the cardiac surface and the pericardium. In the absence of pericardial effusion, contact pressure measured in this way is several millimeters of mercury higher than pericardial pressure measured through a catheter and in fact, is usually close to right atrial and right ventricular diastolic pressures. Thus far, a means of measuring pericardial pressure without altering it in any way has yet to be developed. It is for this reason that pericardial restraint is best assessed by the effects of pericardial removal on left ventricular pressure and volume and their interrelationship, rather than by attempting to measure intrapericardial pressure directly by any means. Because of these technical and conceptual limitations, experiments in which the effects of exercise on transmural cardiac pressure in mammals without pericardial effusion need to be interpreted with caution. However, it has been demonstrated that in dogs, after the pericardium has been separated from the heart by adding a small quantity of fluid, pericardial contact pressure and pericardial liquid pressure are identical and close to atmospheric. Adding 30 ml of fluid to the pericardial space of dogs causes only slight hemodynamic abnormalities but may provide an acceptable compromise for those wishing to study transmural cardiac pressure during exercise. The fundamental difference between contact and fluid pressure is illustrated by the observation that adding 30 ml of fluid to the pericardial space slightly increases or does not affect fluid pressure, but causes contact pressure to drop.

PERICARDIAL EFFECTS IN CONGESTIVE HEART Failure

Acute volume overload induced experimentally or as a result of either acute mitral regurgitation, or acute heart failure and acute exacerbations of chronic heart failure, cause the entire left ventricular pressure-volume relationship to be displaced upwards (Fig 2). When a venodilator such as nitroglycerin or nitroprusside is infused in any of these situations, left ventricular diastolic pressure drops, not as a result of a fall of pressure along the diastolic pressure volume relationship, but by a drop in the entire curve, such that for any ventricular diastolic volume, the diastolic pressure is lower. These results are consistent with the hypothesis that the major effect of short-term administration of a venodilator under these circumstances is to decrease cardiac volume, thereby shrinking the heart from the pericardium and increasing transmural cardiac pressure. Thus, in acute heart failure or acute volume overload, disengagement of the heart from the pericardium may be the principal explanation for the beneficial effects of intravenous vasodilator treatment. On the other hand, a purely arteriolar vasodilator, like amyl nitrite, lowers ventricular diastolic pressure by movement down and to the left along the original pressure volume curve, because these agents do not reduce the size of the heart (Fig 3).

These observations together with the knowledge that cardiac size is likely to be considerably larger during exercise than at rest, lead to consideration of the idea that when patients with chronic heart failure exercise and cardiac size thereby increases, a point may be reached when the heart engages the pericardium which then limits subsequent increase in cardiac performance. This possibility was investigated by Janicki who measured right atrial pressure, pulmonary wedge pressure, and stroke volume in patients with heart failure performing upright exercise. He proposed that if the heart and pericardium were not engaged, incremental exercise would cause a progressive sharp increase in pulmonary wedge pressure, little or no increase in right atrial pressure, and a progressive increase in stroke volume. He further posited that when the heart engaged the pericardium, the slope of increase of pulmonary wedge and right atrial pressure would be identical and furthermore, stroke volume would become fixed. When he set out to test this hypothesis by means of a retrospective analysis of a large number of patients with congestive heart failure in whom he had carried out measurements of hemodynamics and oxygen uptake during exercise, he found that the patients fell into 3 groups: those in whom the heart engaged the pericardium at some point during an exercise study, those in whom the heart and pericardium appeared to be engaged from the very onset of exercise, and those in whom pericardial engagement could never be demonstrated. Somewhat unexpectedly, he could not show any relationship between the type of response obtained and the severity of heart failure.

We have prospectively carried out bicycle exercise in patients with heart failure measuring oxygen uptake, arte-
riovenous oxygen difference, and pulmonary arterial, pulmonary wedge, and systemic arterial pressures. We have found no instance in which right atrial pressure rose appreciably at any stage of exercise, even though this pressure was often abnormally elevated at rest. Furthermore, stroke volume continued to increase, albeit inadequately, up until the time of exhaustion. Thus, we have not been able to confirm that the pericardium plays an important role in the hemodynamic response to exercise of patients with congestive heart failure. We attribute this finding to chronic and repeated stretching of the pericardium, enabling it to adapt by hypertrophy and increased compliance to the maximum cardiac size achieved during exercise. For clinical and ethical reasons, we exercised these patients after we had compensated their heart failure to the best of our ability and therefore we have no data on the effects of the pericardium on the hemodynamic response to exercise of patients with acute or decompensated heart failure. This policy may explain why we could not demonstrate pericardial restraint developing during exercise, while we and others, by measuring the left ventricular diastolic pressure-volume relation and its response to short-term venodilation treatment were able to demonstrate pericardial restraint in acute experimental volume overload and in acute heart failure.

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