Myosin Adenosine Triphosphatase Activity in the Volume-Overloaded Hypertrophied Feline Right Ventricle

RITA A. CAREY, GANGAIAH NATARAJAN, ALFRED A. BOVE, RICHARD L. COULSON, AND JAMES F. SPANN

SUMMARY Chronic pressure overload leads to hypertrophy, depressed mechanical function, and reduced myosin ATPase activity. However, it is not known whether the lowered myosin ATPase activity results from the hypertrophic process per se or whether the elevated afterload is required for the depressed myosin ATPase activity. Further, a causal relationship between lowered myosin ATPase and weakened mechanical function in pressure overload has not been established. Chronic volume overload on the myocardium, leading to hypertrophy equivalent to that in pressure overload, allows the effects of pressure overload to be separated from the effects of hypertrophy and provides insight into the association between myosin ATPase and mechanical function. We produced large atrial septal defects (ASD) with a transvenous biopsy catheter in six adult cats. This resulted in 63% right ventricular hypertrophy, normal (P > 0.05) papillary muscle mechanical function (velocity at 0.5 g/mm² load: control = 1.01 ± 0.05 muscle lengths per second; ASD = 1.02 ± 0.26 muscle lengths per second), and normal (P > 0.05) myosin ATPase activity in three activating mediums (actin: C = 0.20 ± 0.02, ASD = 0.21 ± 0.03; Ca²⁺: C = 0.41 ± 0.03, ASD = 0.38 ± 0.02; K-EDTA: C = 1.67 ± 0.05, ASD = 1.69 ± 0.07 μmol Pi/min • mg). We concluded that pressure overload is required for depression of myosin ATPase activity. Our study supports the concept that depression of myosin ATPase is causally related to depressed mechanical function in chronic pressure overload.

CHRONIC pressure overload on the myocardium leads to cardiac hypertrophy and severely impaired mechanical function (Spann et al., 1967; Spann et al., 1972; Carey et al., 1978a, 1978b). It also has been shown that depressed myosin ATPase activity accompanies the contractile deficit characteristic of severe afterload hypertrophy (Aras and Haas, 1962; Shiverick et al., 1976; Swynghedauw et al., 1973; Wikman-Coffelt et al., 1975b). Recently we demonstrated that myosin ATPase activity returns to normal in parallel with contractile function upon relief of the hemodynamic stress and reversal of hypertrophy (Carey et al., 1978a, 1978b). Since mechanical function and myosin ATPase activities decline and recover together, one could hypothesize that decreased myosin ATPase activity and the decreased contractile function in hypertrophy and congestive heart failure are causally related. Conversely, normal contractile function is associated with volume overload-induced hypertrophy of a magnitude equal to that observed in pressure overload (Cooper et al., 1973). Thus pressure overload rather than cardiac hypertrophy per se is required for weakened mechanical function. However, it is not known whether elevated afterload is required for a decline in myosin ATPase activity or whether hypertrophy alone is sufficient to cause a defect in myosin ATPase. Investigation of volume overload (VO) hypertrophy equal in magnitude to that observed in pressure overload allows the biochemical phenomenon associated with hypertrophy to be separated from the combined effects of hypertrophy and mechanical impairment. The purpose of this study, therefore, was to examine myosin ATPase activity in VO hypertrophy. If hypertrophy per se did not result in lowered myosin ATPase activity (and since hypertrophy alone does not cause reduced mechanical function), then additional support would be given to the hypothesis that the decline in myosin ATPase and mechanical function are causally related in pressure overload and heart failure.

Methods

Definition of Experimental Groups and Production of Volume Overload

Two groups of normal adult cats were studied. Six cats served as controls (C), and six were sub-
jected to a 6-week period of chronic VO secondary to atrial septotomy.

Production of VO by atrial septotomy has been developed in this laboratory (Natarajan et al., unpublished observation). The cats were anesthetized with sodium pentobarbital (30 mg/kg, ip) and allowed to breathe spontaneously. The ascending aorta and right ventricle were catheterized via the carotid artery and jugular vein, respectively. After measurement of cardiac output by a dye dilution technique, a flexible bronchoscopy biopsy forceps was advanced via the femoral vein into the right atrium. When the limits of the right atrium were defined, using small amounts of a radio-opaque contrast material, the mouth of the biopsy forceps was placed adjacent to the atrial septum, opened, and closed on the septum. The catheter then was pulled down, forcibly pinching off the septum. The magnitude of the atrial septal defect (ASD) thus created was assessed by repeating the dye dilution procedure and calculating the pulmonary blood flow to systemic blood flow ratio (QP/QS) by the method of Carter et al. (1960). The cats were maintained for 50 ± 5.46 days (mean ± se) prior to final study.

Measurement of Hemodynamic Parameters

Immediately prior to excision of the heart, the cats were anesthetized with sodium pentobarbital (30 mg/kg, ip) and allowed to breathe spontaneously. A cannula (PE-190) was placed in the ascending aorta, and a no. 4 French catheter was placed in the right ventricle. Right ventricular pressure was recorded, and heart rate was measured from the pressure record. The magnitude of the ASD at the time of final study was determined from the QP/QS ratio determined as described above.

Myosin and Actin Isolation

Following hemodynamic study, a thoracotomy was performed and the heart excised. Within 90 seconds after excision of the heart, the right ventricular free wall was dissected from the remaining tissue, frozen, and stored in liquid nitrogen for 1-10 days. Myosin was isolated as described by Shiverick et al. (1975).

Tissue weights were 1.5-2.3 g. All subsequent steps were carried out at 4°C. The right ventricle was homogenized by a motor-driven homogenizer (Tekmar SDT) in a solution (10 ml/g) of 0.3 M KCl, 0.15 M K2HPO4, 0.01 M Na2P2O7, and 1 mM MgCl2 (pH 6.8). The homogenate was extracted by stirring for 90 minutes, followed by centrifugation for 10 minutes at 12,000 g. The supernatant fluid was diluted with 20 volumes of water, and the myosin precipitate was allowed to settle overnight. Myosin was collected by centrifugation at 12,000 g for 10 minutes and redissolved in 0.3 M KCl, 0.01 M imidazole, 5 mM MgCl2, and 5 mM Na2 ATP, pH 6.8 (10 ml/g). The solution was centrifuged at 43,000 g for 30 minutes. Myosin was precipitated from the supernatant fluid by the addition of 8 volumes of water, allowed to stand for 3 hours, and collected by centrifugation at 12,000 g for 10 minutes. The pellet was redissolved in 0.3 M KCl, 0.01 M imidazole, pH 6.8 (6 ml/g), followed by centrifugation at 43,000 g for 30 minutes. The supernatant fluid was diluted with 6.5 volumes of water and allowed to stand for 1 hour, and the myosin precipitate was collected by centrifugation at 12,000 g for 10 minutes. The final pellet was redissolved in 0.5 M KCl, 0.01 M imidazole, pH 6.8 (2.5 ml/g). All solutions used in the isolation contained 2 mM dithiothreitol to prevent oxidation of sulphydryl groups thought to be associated with the active site of the enzyme.

G-actin was isolated according to the method of Pemrick (Pemrick and Weber, 1976). Immediately prior to the study of actomyosin ATPase, a sample of G-actin was used for preparation of F-actin. F-actin was then combined with myosin, and magnesium-stimulated actomyosin ATPase activity was determined.

Actin Acetone Powder

Actin acetone powder was used for the preparation of G-actin. All steps and solutions were at 4°C unless stated otherwise. The tissue residue remaining after the initial step in the extraction of myosin from muscle was washed twice with 10 volumes of water. The volume of residue remaining after the water wash was measured and 4 volumes of room temperature 0.4% NaHCO3 added. After the mixture had been stirred at room temperature for 45 minutes, the fluid was removed. The residue was washed twice with 4 volumes of 1 mM Tris-Cl, pH 8.5, at 4°C. The residue from this wash was extracted four times, for 10 minutes each time, with 2 volumes of cold acetone. The resulting powder was allowed to air-dry overnight, and then was ground with mortar and pestle before being stored over desiccant at -20°C. The yield was approximately 50 mg/g ground muscle.

Preparation of Pure G-Actin

Depolymerizing solution (250 ml/10 g acetone powder) was prepared: 0.5 mM ATP, pH 8.0; 0.5 mM CaCl2, 2 mM Tris-Cl, pH 8.5 (4°C). Ten grams of acetone powder were suspended in 140 ml of depolymerizing solution and stirred gently for 30 minutes followed by centrifugation (16,000 g for 10 minutes). Subsequently, collection of supernatant fluid, resuspension of the pellet in 60 ml depolymerizing solution, and stirring as above for 10 minutes were carried out. The centrifugation was repeated and the supernatant extracts were recombined. The pellet was discarded, and suspension was filtered through a Millipore 0.8- or 0.45-μm filter. The solution was brought to 2.0 mM in MgCl2, then 100 mM in KCl, and the new total volume was recorded. The mixture was covered and placed in warm water.
(27-30°C) for 30 minutes, then transferred to the cold room to stand overnight. The following day, KCl was added to achieve an 0.8 M solution; i.e., 0.7 M was added with stirring and on ice until KCl dissolved. The solution was chilled until the temperature was approximately 10°C and the pH adjusted to 8.5 with 1 M KOH. Additional ATP (0.5-1 mM final concentration) was added. Subsequently, the mixture was centrifuged 100,000 g for 3 hours, the supernatant fluid was discarded, and the pellets were drained. Depolymerizing solution (1-2 ml was layered on top of the pellet. The next day the pellets were suspended gently and homogenized. Dialysis was carried out for 2-3 days against 2 liters of depolymerizing solution plus 1 mM sodium azide. As depolymerization proceeded, the protein in the sac became clearer. Following dialysis, the G-actin was clarified by centrifugation at 100,000 g for 1 hour.

**Preparation of Pure F-actin**

A sample of G-actin solution was adjusted to 2 mM MgCl₂ and 100 mM KCl, and the mixture was allowed to stand at room temperature for 10 minutes. The F-actin was collected by spinning at 240,000 g for 2 hours. The supernatant was poured off and the appropriate buffer (50 mM Tris-Cl, pH 7.6) was layered on top of the pellet. The pellet was allowed to stand overnight in the cold room. The next day, the pellet was taken up in the above buffer and homogenized as described above.

To evaluate the purity of the myosin and actin, polyacrylamide (7.5%) sodium dodecyl sulfate (0.6%) disc electrophoresis was carried out by a modified Weber-Osborn technique (Weber and Osborn, 1969). Minimal contamination was observed by visual inspection as well as by densitometric evaluation.

**ATPase Kinetics**

Three different enzyme "activation" systems were used. Specifically, actin, K-EDTA and Ca²⁺ stimulating mediums were employed.

**Actin-Stimulated Hydrolysis of ATP**

Actin was combined with myosin in ratios of from 0.5:1 to 4:1 (w/w), and the actomyosin ATPase was activity determined. The incubation medium (2 ml) contained a constant amount of myosin, 1 mM MgCl₂, 5 mM MgATP, 10 mM imidazole (pH 7.0), and 1 mM EDTA. The ATPase reaction was started by the addition of ATP. Following incubation at 30°C for 5 minutes, the reaction was stopped with cold 20% trichloroacetic acid, and the protein-free filtrate was assayed for inorganic phosphate.

**K-EDTA Activation of Myosin**

Purified myosin (0.1 mg/ml) ATPase activity was determined in a medium (2 ml) containing 0.1 M Tris-HCl (pH 7.5), 1 mM EDTA, 0.65 mM KCl, 0.5 mM phosphoenolpyruvate, and 10 units of pyruvate kinase. After temperature equilibrium was established, the hydrolytic reaction was initiated by the addition of 0.2 mg of enzyme protein, and the reaction was incubated at 30°C for 5 minutes. The reaction was stopped by the addition of cold 20% trichloroacetic acid, and the protein-free filtrate was assayed for inorganic phosphate.

**Ca²⁺ Activation of Myosin**

Purified myosin (0.1 mg/ml) ATPase activity was determined in a medium (2 ml) containing 0.2 M Tris-maleate (pH 6.5), 0.1 M CaCl₂, and 5 mM ATP. Following incubation at 30°C for 5 minutes, the reaction was stopped with cold 20% trichloroacetic acid, and the protein-free filtrate was assayed for inorganic phosphate.

**Phosphate and Protein Assay**

One-milliliter samples of the mixture from the ATPase procedures described above were assayed for phosphate spectrophotometrically by the method of Fiske and Subbarow (1925). A Lowry procedure was used to determine protein concentration (Lowry, 1951). All glassware was acid-rinsed, and disposable test tubes were used for the phosphate assay.

**Data Analysis for ATPase Assay**

The yield of inorganic phosphate was plotted as a function of substrate concentration for the K-EDTA-stimulated ATPase and as a function of the ratio of actin to myosin (w/w) for the actin-stimulated myosin. The maximal velocity of ATP hydrolysis in K-EDTA, Ca²⁺, and actin-activating media was also determined. The values for the control group were compared to the values for the VO group by Student's t-test for unpaired data.

**Papillary Muscle Mechanics**

Within 15-30 seconds after excision of the heart, a papillary muscle was removed from the right ventricle. As previously described (Spann et al., 1967; Carey et al., 1978a, 1978b), the papillary muscle was immediately transferred to a myograph containing oxygenated Krebs-Henseleit solutions at 30°C modified to contain 2.5 mM CaCl₂. After placement in the myograph apparatus, the muscle was allowed to achieve stable function for approximately 1 hour, and, subsequently, the length-tension and force-velocity relationships as well as the time derivative of force development were determined. The preparation remained stable for a period sufficient to complete all studies (at least 3 hours). Force development, length changes, the first derivatives with respect to time of these parameters, and the stimulus artifact were recorded. All results were expressed as the mean ± SE values of each group. Student's t-test for unpaired data was employed to compare the two groups.
Results

Heart Weights and Criteria for Heart Failure

Body weights of the control and VO groups were 2.53 ± 0.15 and 2.70 ± 0.14 kg, respectively (Table 1). The experimental group was not significantly different from control. The right ventricle-to-body weight (RV/BW) ratios were significantly greater ($P < 0.01$) in VO than in controls, as was the right ventricular-to-left ventricular weight (RV/LV) ratio ($P < 0.001$).

Although we appreciate that there is no absolute criterion for documenting heart failure, one or more of the following characteristics were used to define the presence of heart failure in this study: (1) pleural effusion, (2) ascites, (3) abnormally elevated right ventricular end-diastolic pressure (>7 mm Hg), and (4) depressed cardiac index (<100 ml/min · kg). None of the cats in the present study displayed any signs of heart failure.

Hemodynamic Findings

As shown in Table 1, the ratio of pulmonary blood flow to systemic blood flow was significantly elevated ($P < 0.05$) in the VO group. The right ventricular peak systolic pressure and end-diastolic pressure in each group were not significantly different ($P > 0.05$) and were within the normal range. At the time of final study, the arterial pressures of each group were within the normal range and not significantly different ($P > 0.05$) from each other. The heart rate of both groups was within the normal range, and no significant difference ($P > 0.05$) between the two groups was observed.

Myosin ATPase Kinetics

Actin-Stimulated ATPase Activity

Myosin ATPase activity isolated from control and VO hearts was determined as a function of actin concentrations. The myosin concentration was 0.1 mg/ml for all assays, and the purified actin concentrations ranged from 0.05 to 0.4 mg/ml. No significant differences in enzyme activity ($P > 0.05$) were observed between the two groups at any concentration of actin (Fig. 1). The actin-stimulated ATPase activity values are similar to those observed by other investigators (Thomas and Alpert, 1977).

K-EDTA and Ca$^{2+}$-Stimulated ATPase Activity

When myosin from control and VO hearts was activated by 0.65 M KCl, 1 mM EDTA, 0.1 M Tris-HCl, and concentrations of ATP ranging from 0.45 to 11.25 mM, enzyme activity rose with increasing substrate concentrations (Fig. 2). All ATPase activity values in VO were nearly identical to control, with no significant differences observed at any ATP concentrations. Myosin ATPase activity of control and VO cardiac tissues was determined in a medium containing 0.1 M CaCl$_2$, 0.2 M Tris-maleate, and a saturating concentration of ATP. No significant difference ($P > 0.05$) was observed between the enzyme activities of the two groups (Fig. 3).

Maximum Velocity of ATP Hydrolysis ($V_{max}$)

Actin-stimulated myosin ATPase $V_{max}$ values averaged 0.21 ± 0.03 μmol P$_i$/min · mg in C (Fig. 3). The actin-stimulated $V_{max}$ values were normal in VO.

When myosin was activated in a medium containing K-EDTA and an optimal concentration of ATP, the average maximal velocity of ATP hydrolysis ($V_{max}$) in VO was 1.69 ± 0.07 μmol P$_i$/min · mg, which was not significantly different from the con-

Table 1  Right Ventricular Weights and Hemodynamic Data

<table>
<thead>
<tr>
<th>Group</th>
<th>No of cats</th>
<th>Body wt (kg)</th>
<th>RV/BW (g/kg)</th>
<th>RV/LV (g/g)</th>
<th>Heart rate (beats/min)</th>
<th>QP/QS</th>
<th>RV pressure (mm Hg)</th>
<th>Arterial pressure (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Systole</td>
<td>Diastole</td>
</tr>
<tr>
<td>Control</td>
<td>6</td>
<td>2.53 ± 0.15</td>
<td>0.67 ± 0.04</td>
<td>0.28 ± 0.01</td>
<td>223.20 ± 13.94</td>
<td>1.12</td>
<td>26.33 ± 2.00</td>
<td>157.67 ± 10.74</td>
</tr>
<tr>
<td>VO</td>
<td>6</td>
<td>2.70 ± 0.14</td>
<td>1.09* ± 0.11</td>
<td>0.47† ± 0.02</td>
<td>211.20 ± 3.82</td>
<td>3.82</td>
<td>24.27 ± 2.27</td>
<td>157.67 ± 10.74</td>
</tr>
</tbody>
</table>

Values are expressed as means ± SE. Symbols show VO significantly greater than control: * $P < 0.01$; † $P < 0.001$; ‡ $P < 0.05$. 

![Figure 1](http://circres.ahajournals.org/figure1.png) RV actin-activated myosin ATPase activity for the control and VO groups. The mean value for six cats in each group is shown. ATPase activity is expressed as the yield of inorganic phosphate per minute per milligram of enzyme protein. The concentration of actin is expressed as the ratio of actin to myosin (w/w).
FIGURE 2  Right ventricular K-EDTA-stimulated myosin ATPase activity substrate saturation curve. The mean values for six cats in each group is shown. Myosin ATPase activity is expressed as in Figure 1, and millimolar ATP concentrations were used.

Papillary Muscle Mechanics

As shown in Table 2, the velocity of papillary muscle shortening at the lightest load employed was 1.01 ± 0.05 and 1.02 ± 0.16 muscle lengths per second for control and VO, respectively. No significant difference (P > 0.05) was observed. In a similar manner, the peak isometric force development in VO was not different from control. Also, the first derivative of peak force with respect to time in VO was unchanged from control.

Discussion

The physiological significance of altered cardiac muscle myosin ATPase activity relative to changes in contractile function is yet to be fully explained. This information is essential to an understanding of myocardial diseases as well as normal cardiac function. The data reported in this study show that myosin isolated from the chronic volume-overloaded myocardium and stimulated by actin, K-EDTA, or Ca²⁺ exhibits normal ATPase activity. Further, the normal enzymatic characteristics of myosin parallel the normal mechanical function of the volume-overloaded myocardium.

Severity of VO and Magnitude of Hypertrophy

The atrial septotomy produced a VO on the right ventricle, which resulted in a pulmonary systemic blood flow ratio of 3.82 ± 0.87. This value is 3.4 times the control value and is similar to that observed by Cooper et al. (1973) for surgically created atrial septal defects in the cat. This VO was associated with a RV/LV ratio of 0.47 ± 0.02. Both values are significantly above normal and similar to the magnitude of hypertrophy previously found in cats with atrial septal defects (Cooper et al., 1973). The degree of hypertrophy in this study was similar to that determined when VO was created by chronic aortic insufficiency in the rabbit (Swynghedauw et al., 1973) and by pulmonic insufficiency (Wikman-Coffelt et al., 1975) and mitral insufficiency in the dog (Luchi et al., 1969). It is of interest that there was no indication of heart failure in any of the cats in the present study. Thus, the animal model employed in this study produces hypertrophy comparable to that studied by other investigators, and there was no evidence of myocardial failure.

Previous work from this laboratory (Carey et al., 1978a, 1978b) demonstrated that pressure overload results in the same degree of cardiac hypertrophy.

Normal Myosin ATPase in VO

An important finding in this study is that the myosin ATPase activity is normal in the myocardium subjected to chronic VO. Others (Swynghedauw et al., 1973) have found that aortic insufficiency in the rabbit leads to reduced calcium-stimulated myosin ATPase activity. Mitral insufficiency (Luchi et al., 1969) and pulmonic insufficiency (Wikman-Coffelt et al., 1975) in the dog also have been shown to lower calcium-activated myosin ATPase activity. There were no evaluations of myocardial contractile function in these earlier studies; thus it is not possible to determine accurately whether the animals were in heart failure. Some
Clinical signs of failure were evident, however, in the subjects of the previous investigators. Also, some of the previous animal models, such as the aortic insufficiency model, provide a combination of pressure and VO. Thus it is not possible to separate clearly the effects of the two types of overload. It is possible that VO leading to heart failure is associated with depressed enzyme activity, whereas VO in the absence of heart failure is accompanied by normal myosin ATPase activity. In the previous study mechanical function of the myocardium was normal. Normal myosin ATPase activity was associated with normal mechanical performance. A further procedure not carried out in previous studies was the use of purified actin to stimulate myosin. Actin activation is considered to reflect the true physiological condition more accurately than any other stimulating medium (Katz, 1977). In the present study, actomyosin was reconstituted from purified actin and myosin and stimulated with magnesium. Purified myosin was also studied with potassium-EDTA and with calcium as the activator ion. In all instances there was no difference between the control and the experimental groups. It seems reasonable to conclude that the chronic VO produced by atrial septotomy leads to cardiac hypertrophy with normal myosin ATPase activity, which in turn parallels normal contractile function. In contrast, pressure overload resulted in reduced myosin ATPase activity (Carey et al., 1978b; Thomas and Alpert, 1977).

### Normal Mechanical Function

Normal velocity of muscle shortening, peak isometric force development, and maximal $dF/dt$ were observed in the present study of chronic VO. This observation supports the previous work of Cooper et al. (1973). The values for these parameters are similar to those reported by this laboratory (Carey et al., 1978a, 1978b) and others (Spann et al., 1967) in several studies of normal cats.

As shown previously by this laboratory (Spann et al., 1967, Carey et al., 1978a, 1978b), mechanical function is impaired in pressure overload-induced hypertrophy.

### Theoretical Implications Concerning the Role of Myosin in Contractile Function

From the data of this study and previously reported work from this and other laboratories, chronic pressure overload and chronic VO on the myocardium appear to be distinctly different stresses. In this laboratory, chronic pressure overload produced $65\%$ hypertrophy and a $76\%$ decline in velocity of papillary muscle shortening, peak isometric tension development, and papillary muscle maximal $dF/dt$. The mechanical defect was accompanied by depressed myosin ATPase activity (Carey et al., 1978a, 1978b).

Others (Thomas and Alpert, 1977; Hamrell and Alpert, 1977) have shown that pressure overload-induced hypertrophy, even in the absence of failure, results in depressed myosin ATPase activity, functionally deficient myosin SH class of sulphydryl groups, and a length- and time-independent depression of contractile element shortening. These authors postulated that an isozyme of myosin was formed in hypertrophy.

It is not known whether the altered enzyme activity in pressure overload is a consequence of the increased afterload or whether the hypertrophic process alone is sufficient to lower myosin ATPase activity. In the present study, a chronic VO was established that produced cardiac enlargement equal in magnitude to that caused by pressure overload. Since this study showed that myosin ATPase activity was normal in the presence of VO-induced hypertrophy, it is reasonable to conclude that the depressed enzyme activity in pressure overload results from the hemodynamic stress rather than the hypertrophic process per se.

It is of interest that the VO reported here did not lead to heart failure and that myosin ATPase activity was normal. Myosin ATPase activity may parallel contractile performance. It has been suggested that myosin ATPase activity is closely related to the velocity of muscle contraction (Bárány, 1967). Investigations in this laboratory (Carey et al., 1978a, 1978b) have demonstrated that, when velocity is depressed in failure, myosin ATPase activity is also depressed. Further, it was shown in this laboratory that both the depressed mechanical function and lowered enzyme activity recover to normal on relief of the hemodynamic stress. The present study demonstrates that enzyme activity again parallels mechanical function in VO. Thus, further support is given to the concept that myosin ATPase activity and mechanical function are causally related and that the myosin ATPase depression observed in the pressure overloaded heart may be a cause of the reduced contractile function.

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### Table 2 Right Ventricular Papillary Muscle Mechanics

<table>
<thead>
<tr>
<th>Group</th>
<th>Velocity at load - 0.5 g/mm² (1/s)</th>
<th>Peak force (g/mm²)</th>
<th>Peak $dF/dt$ (g/s mm⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>±0.06</td>
<td>6.55</td>
<td>±0.51</td>
</tr>
<tr>
<td>VO</td>
<td>±0.16</td>
<td>6.57</td>
<td>±2.78</td>
</tr>
</tbody>
</table>

Values are expressed as means ± SE; 1/s = muscle lengths per second.
Acknowledgments

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