Myocardial Oxygen Consumption and the Left Ventricular Pressure–Volume Area in Normal and Hypertrophic Canine Hearts

Gerald Iazzi, MD; Michael R. Zile, MD; and William H. Gaasch, MD

Background. To assess and compare the energy demands of normal and hypertrophic hearts, we defined the relation between myocardial oxygen consumption (MVO₂, an index of the energy consumed by contraction) and the left ventricular pressure–volume area (PVA, an index of the total mechanical energy generated by contraction) in eight normal and eight hypertrophic (aortic band model) dog hearts; MVO₂ was also measured in the nonworking (empty beating) and basal (potassium arrest) states.

Methods and Results. The hearts were studied in an isolated, blood-perfused heart apparatus. The slope of the MVO₂–PVA relation (the inverse of which reflects myofibrillar efficiency) was similar in normal and hypertrophic hearts (3.89±1.91 and 4.19±1.25 ml O₂/mm Hg·ml·10⁵, p=NS). The MVO₂ in empty beating (0.038±0.006 and 0.041±0.015 ml/beat/100 g, p=NS) and potassium-arrested (1.95±0.06 and 1.98±0.20 ml/min/100 g, p=NS) hearts was likewise similar in the two groups.

Conclusions. Basal and nonworking energy demands and working efficiencies of hypertrophic hearts are equivalent to those of normal hearts. (Circulation 1991;84:1384–1392)

Concentric hypertrophy of the left ventricle is generally considered an appropriate and beneficial physiological adaptation to high intracavitary pressures.¹² This compensatory change, however, carries certain clinical risks that include a greater cardiovascular morbidity and mortality caused by myocardial infarction, heart failure, and arrhythmias.³⁻⁷ In addition, some clinical and experimental data indicate a tendency for hypertrophic hearts to exhibit a decreased tolerance to ischemia.⁸ In an attempt to define the mechanisms underlying such changes, we considered the possibility that abnormal energy demands or inefficient energy metabolism could be responsible. This notion was based on studies that indicate increased nonwork-related myocardial oxygen requirements in hyperthyroidism and under the condition of inotropic stimulation.⁹,¹⁰ Not only does the hyperthyroid rabbit heart exhibit a decreased working efficiency and increased energy costs of excitation–contraction coupling, but there is also a tendency for basal oxygen consumption to be higher than normal in hyperthyroid hearts.⁹ Since nonwork-related energy demands can also be increased during inotropic interventions,¹⁰ it would seem that such changes, if present in hypertrophy, might contribute to an altered tolerance to ischemia. Accordingly, we compared the relative energy demands and efficiencies of normal and hypertrophic dog hearts by measuring oxygen consumption under working, nonworking (empty beating), and basal conditions.

The heart derives essentially all of its energy from aerobic metabolism; thus its oxygen consumption provides a measure of its total energy utilization.¹⁰⁻¹² These energy requirements are influenced by a complex interplay among a variety of factors, all of which were recognized by Suga and associates¹³,¹⁴ when they developed what appears to be a reliable yet relatively simple method to assess cardiac energetics. This method is based on their demonstration of a direct relation between the total mechanical energy (or work) generated by the ventricle and the total energy utilization of the ventricle. This unique relation, formulated in terms of a time-varying elastance model, used the left ventricular (LV) pressure–volume area (PVA) as an index of the mechanical energy generated by the ventricle and the myocardial oxygen consumption (MVO₂) as an index of energy utilization. Although this approach does not address underlying mechanisms, the MVO₂–PVA relation, like the relation between oxygen...
consumption and the force–length area,15 provides a method to predict energy demands and allows a description of efficiency. Suga et al16–18 and others have used this method in normal hearts during a variety of pharmacological and other interventions, but there is little such information available in hypertrophic hearts.10,19 Thus, within the framework of the MV-o2–PVA relation, we compared working, nonworking, and basal energy demands as well as efficiencies among normal and hypertrophic hearts.

Methods

Left ventricular hypertrophy (LVH) was produced by banding the aorta of puppies at 8 weeks of age. One year later, when substantial hypertrophy was present, the functional state of the ventricle was described (combined echocardiographic and catheterization techniques). The hearts were then excised, placed in an isolated blood-perfused heart apparatus, and myocardial energetics were studied. Eight hyper trophyed hearts and eight normal control hearts were evaluated.

All animals received humane care in compliance with the principles of laboratory animal care formulated by the National Society for Medical Research and the Guide for the Care and Use of Laboratory Animals prepared by the National Academy of Sciences and published by National Institutes of Health (NIH Publication No. 85-23, reviewed 1985).

Left Ventricular Hypertrophy Model

At 8 weeks of age, puppies were anesthetized with sodium pentobarbital (25 mg/kg i.v.) and ventilated with a mechanical respirator. A right thoracotomy was performed through the third right intercostal space, the pericardium was opened, and the aorta was dissected free from the periaortic fat and connective tissue. A 5-mm-wide nonconstricting band was placed around the aorta approximately 2 cm above the aortic valve. After the banding procedure, the pericardium was loosely approximated and the thoracotomy was closed. The animals recovered and were then allowed to “grow into” supravalvular aortic stenosis.

At 12 months, when substantial LVH was present, the banded animals underwent cardiac catheterization and echocardiography to define the functional state of the left ventricle. The normal control dogs did not undergo catheterization. The details of these methods and techniques were published previously.

Isolated Heart Preparation and Measurements

Our methods and a description of the isolated blood-perfused dog heart preparation have previously been described in detail.21,22 Briefly, in each experiment a support dog was anesthetized with pentobarbital (15–20 mg/kg), anticoagulated with intravenous heparin, and mechanically ventilated. The heart from the experimental dog was placed on cardiopulmonary bypass (perfused with blood from the femoral artery of the support dog); the heart was then excised, placed in the isolated heart chamber, and perfused at a constant pressure of 100 mm Hg. The coronary venous blood from the isolated heart was drained from the right atrium and right ventricle (by a large-bore catheter with multiple side holes) and returned to the femoral vein of the support dog. This system provided empty right-heart chambers throughout the experiment.

Ventricular fibrillation was induced and the left atrium was opened. A balloon on a silastic mount was placed in the left ventricle through the mitral annulus and the heart was submerged in a blood bath maintained at 37°C. A heat exchanger system was used to maintain the coronary perfusion temperature at 37°C. The heart was defibrillated and the preparation was allowed to stabilize for 30 minutes before starting the experiment. All studies were performed at constant heart rate (atrial pacing at approximately 120 beats/min).

LV pressure was measured with a Statham P23Db pressure transducer. Systolic and diastolic pressures were measured during incremental additions of saline to the ventricular balloon until systolic pressure exceeded 100 mm Hg. The volume associated with this peak systolic pressure was assigned a value of 100% (V100) and all other volumes were related to the 100% volume. Thus, LV pressures were assessed over a range of five volumes (i.e., V20, V40, V60, V80, V100).

Coronary blood flow was measured with an in-line flowmeter. Blood was sampled from the arterial (perfusion) and coronary venous catheters and pH, PO2 and PCO2 were determined using a blood gas analyzer (Instrumentation Laboratory, Watertown, Mass.). Arterial and venous oxygen contents were calculated from the blood oxygen saturation and the measured hemoglobin concentration using the nomogram of Rossing and Cane.

Pressure–Volume Area

In each heart, five coordinates of systolic pressure and volume were obtained by incrementally filling the LV balloon over a range of volumes from V20 to V100. A volume equal to that of the plastic balloon mount (4 ml) was added to each of the five saline volume values so the pressure–volume plots reflected total LV volume. The five pressure–volume coordinates were fit by a linear equation and the slope of the systolic pressure–volume relation that represents maximum systolic elastance (Emax) was determined by least-squares analysis. This systolic pressure–volume line represents the upper border of the PVA. In a similar fashion, the diastolic pressure–volume coordinates were fit by a linear equation; this line defined the lower border of the PVA. Thus, at any volume, the PVA is the area encompassed by the systolic and diastolic pressure–volume lines and the vertical isovolumic pressure trajectory at that volume. The PVA is expressed in millimeters of mercury times milliliters per beat per 100 g of myocardium; alternatively,
it may be expressed as joules per beat per 100 g (1 mm Hg · ml=0.000133 J).

Myocardial Oxygen Consumption

At each of the five volume states, total coronary blood flow and arteriovenous oxygen difference were measured. MVO₂ of the entire heart was calculated as the product of coronary blood flow (milliliters per minute) and the arteriovenous oxygen difference (milliliters of O₂ per 100 ml of blood). The MVO₂ of the total heart was determined with the right and left ventricles empty. The MVO₂ of the right ventricle was calculated as the product of the total heart MVO₂ and the ratio of the right ventricular weight to the combined weight of both ventricles; this ratio averaged 0.25±0.02 in the normal hearts and 0.19±0.02 in the hypertrophic hearts. Since the right ventricle was empty throughout the experiments, we assumed that the right ventricular contribution to total MVO₂ remained constant throughout each experiment. Thus, the LV MVO₂ at any volume is equal to the total heart MVO₂ minus the (empty) right ventricular MVO₂. Oxygen consumption is expressed in milliliters of O₂ per beat per 100 g and in joules per beat per 100 g of myocardium (1 ml of oxygen is equivalent to 20 J).

Potassium Arrest

After baseline measurements of coronary blood flow and arteriovenous oxygen difference in the empty beating heart, potassium chloride (50 meq/l) was infused into the arterial perfusion line at a rate sufficient to produce asystole. After an initial bolus, an infusion rate of approximately 35 ml/min was sufficient to maintain an asystole state. Asystole was confirmed by the absence of pressure development and a flat EKG signal; manual palpation of the LV confirmed a flaccid asystolic heart in all experiments. Coronary blood flow and arteriovenous oxygen difference were measured at 1-minute intervals for 7 minutes and the MVO₂ of the total heart was calculated from these data; as before, the LV MVO₂ was determined by subtracting the right ventricular contribution to total heart MVO₂.

MVO₂—PVA Relation

Each of the five PVAs was plotted against the corresponding values for oxygen consumption, and the slope of the MVO₂—PVA relation was determined by fitting the five coordinates by a linear equation. The extrapolated y intercept is an index of the MVO₂ of the empty beating heart. The MVO₂ of the empty beating heart (Vₐ0) was also measured directly. This analysis is illustrated in Figures 1 and 2.

Myofibrillar efficiency was calculated as the ratio of PVA to excess MVO₂ (the excess MVO₂ equals total oxygen consumption minus that required for basal metabolism plus activation). This ratio is equivalent to the inverse slope of the MVO₂—PVA relation. To calculate efficiency, both PVA and MVO₂ are expressed in joules per beat per 100 g (see above). Thus, the ratio of PVA (in joules) to excess MVO₂ (in joules) is a dimensionless parameter that reflects the chemomechanical energy transduction efficiency of the contractile machinery; we refer to this as myofibrillar efficiency.

Data Analysis

Data in the table and text are presented as mean±SD; mean±SEM is used in the figures. Differences in the slopes (Emax and MVO₂—PVA relation) and intercepts between normal and hypertrophic groups were analyzed by using an analysis of variance of regression and an analysis of covariance with a
repeated-measures design. Differences in other parameters were assessed with an unpaired t test. Differences were considered significant if \( p < 0.05 \).

**Results**

As in our previous studies,\(^{20}\) the group of aortic-banded animals developed a substantial increase in LV mass; the LV/body weight ratio was 9.2±1.6 g/kg. The functional state of the LV assessed by echocardiography and cardiac catheterization remained normal; fractional shortening was 40±9% and LV end-diastolic pressure was 9±3 mm Hg. Thus, the eight banded dogs in the current study are comparable with those reported in our previous studies of LV function, myocardial blood flow, and the tolerance to ischemia in LVH.\(^{8,20}\) The LV/body weight ratio of the normal control hearts was 5.2±1.2; these dogs did not undergo cardiac catheterization.

Representative examples of the \( \text{MV} \text{O}_{2} \text{-PVA} \) relations in normal and hypertrophic hearts are shown in Figures 1 and 2. The data are presented in Tables 1 and 2, and a summary of the results is shown in Figure 4.

**\( \text{MV} \text{O}_{2} \text{-PVA} \) Relations**

At \( V_{100} \) (i.e., the volume required to produce a systolic pressure of approximately 100 mm Hg) there were no significant differences in LV systolic pressure, diastolic pressure, volume, or \( E_{\text{max}} \) between the two groups (Table 1). The average values for the PVA in the normal and LVH groups (1,230±300 and 1,130±200 mm Hg times milliliters per beat) were not significantly different. When expressed per 100 g of LV, the PVA in the group with LVH was significantly less than normal (928±321 versus 565±202 mm Hg times milliliters per beat per 100 g). The \( \text{MV} \text{O}_{2} \) (expressed per 100 g of LV) was likewise lower than normal in the LVH group, but this difference did not achieve statistical significance.

There was no significant difference in the slope of the \( \text{MV} \text{O}_{2} \text{-PVA} \) relation between normal and hypertrophic groups (3.89±1.91 versus 4.19±1.25 ml \( \text{O}_{2} \) per millimeter of mercury times milliliters times 10\(^{5} \)). Thus, the relation between energy used (i.e., \( \text{MV} \text{O}_{2} \)) and energy generated (i.e., PVA) is essentially equal in normal and hypertrophic hearts; myofibrillar efficiency is similar in normal and hypertrophic hearts (21±9 versus 19±11, \( p = \text{NS} \)).

**Nonworking and Basal \( \text{MV} \text{O}_{2} \)**

At zero PVA, the \( \text{MV} \text{O}_{2} \) was almost equal in the two groups (0.040±0.006 versus 0.043±0.012 ml/beat/100 g); these extrapolated values are similar to those obtained by direct measurement (0.038±0.006 versus 0.041±0.015 ml/beat/100 g). During potassium arrest (Figure 3), \( \text{MV} \text{O}_{2} \) was essentially equal in the normal and hypertrophic groups (1.95±0.06 and 1.98±0.20 ml/min/100 g); thus, basal oxygen requirements in this model of LVH is not significantly different from normal. Our interpretation of these data is that the nonwork-related energy demands (basal plus activation) are normal in concentric LVH. These results are summarized graphically in Figure 4.

**Discussion**

The uniquely aerobic character of myocardial metabolism underlies the use of \( \text{MV} \text{O}_{2} \) as an index of the heart’s total energy utilization. The factors that influence conversion of chemical energy into mechanical work (i.e., the factors governing \( \text{MV} \text{O}_{2} \)) are well described, and several indexes have been proposed as major and minor determinants of \( \text{MV} \text{O}_{2} \).\(^{12}\) Prominent among the major factors are those related to the development of systolic force; changes in force development or the time integral of force exhibit strong positive correlations with \( \text{MV} \text{O}_{2} \).\(^{24–27}\) An essential limitation of these indexes is that the \( \text{MV} \text{O}_{2} \) is related
to factors other than force development and external work. Recognizing that myocardial energy requirements are determined by the sum of external and internal work, Britman and Levine\(^{28}\) used a model of the myocardium consisting of a contractile element in series with an elastic element. With knowledge of the elastic element stiffness, it was possible to calculate contractile element work (CEW) and to relate this variable to \(\text{MV}_{\text{O}2}\) over a wide range of altered hemodynamics in anesthetized dogs. They found a high correlation between CEW and \(\text{MV}_{\text{O}2}\), and they demonstrated that this relation was significantly better than that found between oxygen consumption and pressure–time per minute, force–time per minute, or fiber shortening. This model of a contractile element in series with an elastic element has significant shortcomings\(^{28}\) and partly for this reason, CEW is not widely used as an index of energy utilization. However, the principle that \(\text{MV}_{\text{O}2}\) is influenced by mechanical factors other than external work is of major physiological importance.

Using a time-varying elastance model of the left ventricle, Suga et al\(^{13,14}\) recognized a positive linear relation between the \(\text{MV}_{\text{O}2}\) and the total PVA of the working left ventricle. Thus, the energy used by the left ventricle was found to be closely related to the size of the area defined by the end-diastolic and end-systolic pressure–volume lines (and the systolic trajectory of pressure–volume between end diastole and end systole). In the ejecting heart, this area consists of the systolic pressure–volume loop (external work) plus the triangular area to the left of this loop (potential energy); in the non-ejecting (isovolumic) condition, there is no external work and the total mechanical energy is represented by the triangular area to the left of a vertical line defined by the systolic pressure development. Importantly, \(\text{MV}_{\text{O}2}\) is linearly related to the PVA regardless of whether the

<table>
<thead>
<tr>
<th>Left ventricular pressure at (V_{100})</th>
<th>Normal ((n=8))</th>
<th>Hypertrophy ((n=8))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak systolic (mm Hg)</td>
<td>110±9</td>
<td>112±6</td>
</tr>
<tr>
<td>End diastolic (mm Hg)</td>
<td>5.6±2.5</td>
<td>8.8±3.1</td>
</tr>
<tr>
<td>Left ventricular volume ((V_{100}) in ml)</td>
<td>24.9±4.2</td>
<td>22.6±9.0</td>
</tr>
<tr>
<td>Left ventricular mass (g)</td>
<td>132.7±20.4</td>
<td>205.0±44.5*</td>
</tr>
<tr>
<td>(E_{\text{max}}) (mm Hg/ml)</td>
<td>5.36±1.17</td>
<td>5.97±2.96</td>
</tr>
<tr>
<td>Total mechanical energy at (V_{100})</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PVA (mm Hg · ml/beat)</td>
<td>1,230±296</td>
<td>1,130±200</td>
</tr>
<tr>
<td>(mm Hg · ml/beat/100 g)</td>
<td>928±321</td>
<td>565±202*</td>
</tr>
<tr>
<td>Myocardial oxygen consumption</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Working LV (ml (\text{O}<em>2)/beat/100 g at (V</em>{100}))</td>
<td>0.073±0.015</td>
<td>0.067±0.019</td>
</tr>
<tr>
<td>Empty beating LV (ml (\text{O}_2)/beat/100 g)</td>
<td>0.038±0.006</td>
<td>0.041±0.015</td>
</tr>
<tr>
<td>Potassium arrest (ml (\text{O}_2)/min/100 g)</td>
<td>1.95±0.06</td>
<td>1.98±0.20</td>
</tr>
<tr>
<td>(\text{MV}_{\text{O}2})–PVA relation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slope (ml (\text{O}_2)/mm Hg · ml · 10(^{3})) (dimensionless)</td>
<td>3.89±1.91</td>
<td>4.19±1.25</td>
</tr>
<tr>
<td>Intercept (ml (\text{O}_2)/beat/100 g)</td>
<td>5.83±3.03</td>
<td>6.25±2.01</td>
</tr>
<tr>
<td>(joules/beat/100 g)</td>
<td>0.040±0.006</td>
<td>0.043±0.012</td>
</tr>
<tr>
<td>Myofibrillar efficiency (%)</td>
<td>21±9</td>
<td>19±11</td>
</tr>
</tbody>
</table>

LV, left ventricle; PVA, pressure–volume area.

\(^{*}p<0.05\)

**Table 2. Regression Equations for the \(\text{MV}_{\text{O}2}\)–Pressure–Volume Area Relations in Normal and Hypertrophied Hearts**

<table>
<thead>
<tr>
<th>Regression equation</th>
<th>(r)</th>
</tr>
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<tbody>
<tr>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>(\text{MV}_{\text{O}2}=5.23\ PVA+0.82)</td>
<td>0.97</td>
</tr>
<tr>
<td>(\text{MV}_{\text{O}2}=4.99\ PVA+0.58)</td>
<td>0.97</td>
</tr>
<tr>
<td>(\text{MV}_{\text{O}2}=5.44\ PVA+0.97)</td>
<td>0.95</td>
</tr>
<tr>
<td>(\text{MV}_{\text{O}2}=12.06\ PVA+0.82)</td>
<td>0.95</td>
</tr>
<tr>
<td>(\text{MV}_{\text{O}2}=2.96\ PVA+0.69)</td>
<td>0.99</td>
</tr>
<tr>
<td>(\text{MV}_{\text{O}2}=4.54\ PVA+0.77)</td>
<td>0.99</td>
</tr>
<tr>
<td>(\text{MV}_{\text{O}2}=8.39\ PVA+0.93)</td>
<td>0.99</td>
</tr>
<tr>
<td>(\text{MV}_{\text{O}2}=3.01\ PVA+0.84)</td>
<td>0.83</td>
</tr>
<tr>
<td>Hypertrophy</td>
<td></td>
</tr>
<tr>
<td>(\text{MV}_{\text{O}2}=6.11\ PVA+0.73)</td>
<td>0.99</td>
</tr>
<tr>
<td>(\text{MV}_{\text{O}2}=9.36\ PVA+0.85)</td>
<td>0.97</td>
</tr>
<tr>
<td>(\text{MV}_{\text{O}2}=5.42\ PVA+1.51)</td>
<td>0.99</td>
</tr>
<tr>
<td>(\text{MV}_{\text{O}2}=2.17\ PVA+0.74)</td>
<td>0.86</td>
</tr>
<tr>
<td>(\text{MV}_{\text{O}2}=6.72\ PVA+0.60)</td>
<td>0.97</td>
</tr>
<tr>
<td>(\text{MV}_{\text{O}2}=7.06\ PVA+0.92)</td>
<td>0.89</td>
</tr>
<tr>
<td>(\text{MV}_{\text{O}2}=6.72\ PVA+0.92)</td>
<td>0.87</td>
</tr>
<tr>
<td>(\text{MV}_{\text{O}2}=6.44\ PVA+0.91)</td>
<td>0.96</td>
</tr>
</tbody>
</table>

Linear regression analysis was used to determine the correlation coefficient \((r)\). The \(\text{MV}_{\text{O}2}\) and pressure–volume area (PVA) are expressed in joules per beat per 100 g; thus, the slope of the \(\text{MV}_{\text{O}2}\)–PVA relation is dimensionless and the intercept is given in joules per beat per 100 g.
heart is freely ejecting, auxotonic, or isovolumic; it is not determined by the time course of the isovolumic pressure–volume coordinates.30

**MV02–PVA Relation and Efficiency**

It is generally accepted that, when systolic wall stress and inotropic state are considered, MV02 is normal in human hypertrophic hearts.26,27,31 Such studies, however, do not disentangle the relative contributions of basal and activation energy requirements, nor do they provide information on myofilament efficiency. Other more basic studies are important in terms of underlying mechanisms,32–34 but we reasoned that an assessment of myocardial energetics within the MV02–PVA framework would be more relevant to the clinical problem of altered tolerance to ischemia in hypertrophic hearts.8 Therefore, we determined the slope of the MV02–PVA relation and used the inverse of this relation as an index of efficiency. To date, only hyperthyroidism (in rabbits) has been shown to affect the slope; this is thought to be mediated through a change in the V1/V3 isomyosin ratio; such changes are apparently not seen in dogs.35 Although basal and nonwork-related oxygen requirements are affected by the inotropic state, the slope of the MV02–PVA relation is remarkably in-

**FIGURE 3.** Plot showing left ventricular oxygen consumption during potassium arrest in normal hearts and hearts with left ventricular hypertrophy (LVH). Baseline data were obtained in the empty beating (nonworking) state. The oxygen consumption fell from baseline values of 4.7 and 5.1 in normal and LVH to approximately 2 ml O2/min/100 g during arrest. There was no significant difference in oxygen consumption between the two groups.

**FIGURE 4.** Plot showing summary of the relations between myocardial oxygen consumption and the left ventricular pressure–volume area (PVA) in normal hearts and hearts with left ventricular hypertrophy (LVH). Oxygen consumption is expressed in milliliters of O2 per beat per 100 g and in joules per beat per 100 g (1 ml of oxygen is equivalent to 20 J). The PVA is expressed in millimeters of mercury times milliliters per beat per 100 g and in joules per beat per 100 g (1 mm Hg ml is equivalent to 0.000133 J). Symbols indicate oxygen consumption at a working volume of V100; see text for details. Basal and nonworking (zero PVA) energy requirements and myofilament efficiencies of normal and hypertrophic hearts are essentially equal.
sensitive to pharmacological and other acute interventions that affect contractility. The inverse slope of the $MVo_2$–PVA relation can be taken to represent the efficiency of chemomechanical energy conversion. This is not merely the efficiency of performing external work; rather, it reflects a total efficiency of performing external work plus a residual "potential energy" that remains after end systole. With each cardiac cycle some of this potential energy is converted to internal work, but most of it is dissipated as heat. Sugawreported several differences between the potential energy in his PVA analysis and the internal work in Britman and Levine's CEW analysis; recognizing and comparing the differing energy costs of potential energy and internal work may provide a better understanding of ventricular energetics.

Myofibrillar efficiencies calculated from the inverse slope of the $MVo_2$–PVA relation were essentially the same in our normal and hypertrophic hearts (21% and 19%, respectively). These data are consonant with those of Starling et al., who studied normal in situ dog hearts and reported $MVo_2$–PVA slopes of 3.15 and 3.48 ml O$_2$ per millimeter of mercury times milliliters times 10$^2$; thus, the dimensionless slope was approximately 5 and myofibrillar efficiency was approximately 20%. Nozawa et al. reported a similar efficiency in normal in-situ hearts. There is no obvious reason why these efficiency values are lower than those reported by Suga et al., but a common feature of our methods and those of Starling et al. is the use of calculated oxygen contents of coronary arterial and venous blood. Suga measured oxygen content directly, and it is possible that the differences in the $MVo_2$–PVA slope (and efficiency) is somehow related to the oximetry method. These considerations, however, have little bearing on our comparisons between normal and hypertrophic hearts; our data indicate that myofibrillar efficiency in pressure-overload hypertrophy is not significantly different from normal.

$MVo_2$ in Empty Beating Hearts

The energy demands of a nonworking heart can be estimated by extrapolation of the $MVo_2$–PVA relation to zero PVA or by directly measuring $MVo_2$ in the empty beating condition. The extrapolated values for $MVo_2$ in our normal (0.040 ml/beat/100 g) and hypertrophic hearts (0.043 ml/beat/100 g) were essentially equal; these extrapolated values were not significantly different from those measured directly (Table 1). In an extensive review of this topic, Suga reported values ranging from 0.017 to 0.047 ml/beat/100 g; the average value from his five most recent studies was 0.028 ml/beat/100 g in empty beating hearts; this is equivalent to approximately 3–4.5 ml/min/100 g. Due in part to the wide range of heart rates in published experiments, the $MVo_2$ of nonworking hearts reportedly ranges from 2.5 to 5.5 ml/min/100 g. In our experiments, the normal and hypertrophic hearts (nonworking) consumed approximately 5 ml O$_2$/min/100 g.

Direct measurements of the energy demands of empty beating hearts theoretically overestimate those of a pure nonworking state (i.e., activation plus basal requirements) for at least two reasons. First, our experimental preparation precludes measurement in a truly empty condition (the LV contains a plastic balloon mount); thus, some isometric force is developed in the area of the mitral annulus. Second, low levels of crossbridge cycling (even in a totally empty heart) require energy; ideally, such an unmeasured contribution to the energy demands should be considered. Thus, to assess accurately the energy demands of a true nonworking state (i.e., basal plus activation) it would be necessary to inhibit all crossbridge cycling; this could be accomplished with 2,3-butanedione (BDM), a cardioplegic agent that (at low doses) selectively inhibits crossbridge cycling in a reversible manner. Such studies would be necessary to avoid an overestimation of the nonworking (i.e., basal plus activation) requirements. However, our observation that the extrapolated value for $MVo_2$ is similar to the measured value suggests that any such error is probably small.

Basal Oxygen Consumption

The resting or basal metabolic rate of the intact LV is difficult to assess because the heart does not normally exhibit sufficiently long diastolic intervals to permit measurements of oxygen consumption in the absence of contraction. In our experiments, we rendered the heart inactive by infusing potassium into the coronary arterial perfusion line and thus we were able to measure an asystolic $MVo_2$ during a continuous, stable coronary perfusion. Within 2 minutes of asystole, the $MVo_2$ fell to approximately 2 ml/min/100 g and remained constant for the duration of the potassium infusion; the results were essentially equal in the normal and hypertrophic hearts (Figure 3). Our average values are similar to the basal $MVo_2$ (1.9 ml/min/100 g) that Britman and Levine derived from their calculations of contractile element work in the intact working heart. The results are also similar to the normal basal requirements (1.5–2.0 ml/min/100 g during potassium arrest) reported by Suga et al. and others. Sink et al. found a slightly lower value in hypertrophied hearts (1.3 ml/min/100 g), and they also concluded that this was the same as that seen in normal hearts.

Within the range of data reported here, basal requirements are approximately 40% of that required by empty beating hearts and 20% of that required by working hearts (Figure 4). Since basal $MVo_2$ may increase as a function of myocardial fiber length, it is possible that the relative contribution of basal to total $MVo_2$ might increase as the chamber is filled. If this were the case, the myofibrillar efficiencies might be greater than we calculated.
Implications

During cardiac surgery, the left ventricle is subjected to ischemic arrest, potassium arrest, and on occasion the empty beating state is maintained for variable periods of time. During these periods, any increased oxygen requirement (basal or activation) might lead to increased ischemic injury. The current results indicate that oxygen requirements are normal in our model of concentric LVH. Therefore, any reduced tolerance to such surgical procedures is not likely to be due to increased oxygen demands per se. It is possible, however, that heightened sympathetic tone or the administration of positive inotropic agents might augment basal or activation-related oxygen demands and in this manner contribute to an impaired tolerance to ischemia, independent of work-related demands. In the absence of such increased “basal plus activation” oxygen demands, abnormal myocardial perfusion or depressed baseline energy stores are likely responsible for the increased sensitivity to ischemic injury seen in some hypertrophic hearts.8

The MVo2-PVA relation that we applied in these studies of isolated dog hearts might have potential in clinical studies of myocardial energetics. The echocardiogram is ideally suited to measure LV cavity size or volume and wall mass. Coupled with measurements of intracavitary pressure, a PVA is relatively easy to obtain. Methods to measure coronary blood flow and MVo2 in humans are likewise available. Thus, LV energetic and efficiency in patients with and without heart disease can be described; such methodology might be particularly useful in the evaluation of new pharmacological therapies for patients with heart disease.

References

2. Swynghedauw B, Schwartz K, Apstein CS: Decreased contractility after myocardial hypertrophy: Cardiac failure or successful adaptation? Am J Cardiol 1984;54:437–440

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G Izzi, M R Zile and W H Gaasch

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