Left Ventricular Mechanical Efficiency in Man with Heart Disease

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HAROLD Sandler, M.D., and DAVID PUGH, M.D.

SUMMARY Thirty-eight adults with valvular and/or myocardial disease had heart catheterization with coronary blood flow and myocardial O₂ consumption (MVO₂) per 100 g measured by the nitrous oxide washout technique. Quantitative biplane angiography was performed to assess left ventricular volume, mass, ejection fraction and work. Left ventricular efficiency was calculated from work, MVO₂/100 g and mass. Efficiency ranged from 4 to 40% and was normal in some patients with severe ventricular pressure-volume work overloads. Total left ventricular MVO₂ ranged up to 461 ml/min. Neither total MVO₂ nor MVO₂/100 g was significantly related to ventricular work, ejection fraction, or tension-time index. These data suggest 1) a relationship between left ventricular efficiency and myocardial function in chronic valvular or myocardial disease, 2) that efficiency may be normal in hypertrophied ventricles, and 3) that chronic increases in resting ventricular metabolic requirements are met by hypertrophy rather than by increased MVO₂/100 g.

MECHANICAL EFFICIENCY is a performance parameter of energy-transfer systems, most commonly used in an engineering context. Expressed as a percent, it is the dimensionless ratio of mechanical work performed to energy utilized over a given time period. In terms of human left ventricular dynamics, energy utilized has been shown to result relatively exclusively from aerobic metabolism in the absence of ischemic coronary disease.1,4 Thus left ventricular efficiency can be calculated from its rate of performing work and the rate of energy consumption (oxygen consumption or MVO₂) over the same time interval.2 In this way ventricular efficiency has been calculated in animals.3 In man, methods utilized for coronary blood flow determination have included the nitrous oxide washout,3,4,5 helium washout6 and other techniques.6 MVO₂ is then computed as the product of coronary blood flow and coronary arterial venous oxygen difference. The values of MVO₂ obtained by these methods are expressed in MVO₂/min/100 g of myocardium. Thus, knowledge of the left ventricular weight or mass is also necessary to calculate total left ventricular MVO₂ and hence left ventricular efficiency. Left ventricular mass in normal humans has been estimated for this purpose, and ventricular efficiency calculated.3 However, the variable degrees of ventricular hypertrophy associated with chronic left ventricular hemodynamic abnormalities make ventricular mass measurements necessary for determination of efficiency in patients with long-standing disease. Previous reports of left ventricular efficiency calculated with ventricular mass measurements in resting patients with chronic valvular or myocardial disease have not been reported. In the present investigation, 38 adults with such diseases were studied by quantitative angiographic techniques with coronary blood flow/100 g measured by the nitrous-oxide washout technique. Calculation of left ventricular mass and chamber volumes in combination with left ventricular pressure measurements and MVO₂ values permitted determination of total left ventricular MVO₂, coronary blood flow, work, and efficiency values together with ejection fraction as a measure of myocardial function. These data provide further information on the functional characteristics of the left ventricle in man with chronic valvular and myocardial disease.

Materials and Methods

The subjects of this investigation were 38 adult male patients, age range 25-65 years, studied by right and left heart catheterization and biplane angiography at the University of Alabama Hospital, the University of Washington Hospital or the Seattle Veterans Administration Hospital. The patients all had valvular or myocardial disease with symptoms of heart failure, at least NYHA class III. None had evidence of coronary artery disease by history or electrocardiogram. All were studied as part of a diagnostic evaluation. Initially coronary sinus and systemic arterial catheterization were performed. Coronary blood flow per 100 g of left ventricular myocardium was measured by the N₂O desaturation curves following a 15 minute period of 15% N₂O inhalation.7 The desaturation curves were constructed from N₂O analysis data from multiple arterial and coronary sinus blood samples drawn simultaneously over a 10 minute period immediately following cessation of the N₂O inhalation. The O₂ content of the coronary sinus and systemic arterial blood was determined by the Van Syke method, and coronary arteriovenous O₂ difference calculated. MVO₂/100 g myocardium was then computed as the product of coronary flow/100 g and coronary arteriovenous O₂ difference. Following completion of the coronary sinus portion of the study, pulmonary artery catheterization was performed, and left heart catheterization was done by the retrograde arterial or transseptal approach. The catheters utilized were #8 French fluid-filled, and pressures were measured with Statham P23d transducers recorded on an Electronics for Medicine recorder. Cardiac output was measured by the Fick technique. Finally biplane left heart angiography was performed during quiet respiration at filming rates of 6 or 12 per second with power injection of 50-75 ml of contrast material. Coronary angiography was not performed in these patients, since there was no clinical evidence of coronary disease. Left ventricular volumes, mass, forward and regurgitant flows, and ejection fraction were calculated.

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Table 1. Hemodynamic Data in 38 Patients

<table>
<thead>
<tr>
<th>Left ventricular variable</th>
<th>Mean ± standard deviation</th>
<th>Ranges of values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All patients</td>
<td>PMD* group</td>
</tr>
<tr>
<td>Stroke volume (ml)</td>
<td>118 ± 54</td>
<td>38-323</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>0.53 ± 0.18</td>
<td>0.10-0.86</td>
</tr>
<tr>
<td>Total output/minute (L/min)</td>
<td>8.21 ± 3.35</td>
<td>3.40-20.00</td>
</tr>
<tr>
<td>Forward cardiac output (L/min)</td>
<td>4.38 ± 1.15</td>
<td>2.58-7.28</td>
</tr>
<tr>
<td>Regurgitant flow (L/min)</td>
<td>3.76 ± 2.90</td>
<td>0.00-15.10</td>
</tr>
<tr>
<td>Mass (g)</td>
<td>321 ± 126</td>
<td>106-609</td>
</tr>
<tr>
<td>End-diastolic pressure (mm Hg)</td>
<td>14 ± 9</td>
<td>12-25</td>
</tr>
<tr>
<td>Peak systolic pressure (mm Hg)</td>
<td>121 ± 29</td>
<td>68-196</td>
</tr>
<tr>
<td>Tension-time index (mm Hg/sec/min)</td>
<td>2840 ± 818</td>
<td>1724-5537</td>
</tr>
<tr>
<td>Stroke work (g-m)</td>
<td>198 ± 104</td>
<td>49-510</td>
</tr>
<tr>
<td>Work/minute (kg-m/min)</td>
<td>13.3 ± 5.90</td>
<td>4.03-31.10</td>
</tr>
<tr>
<td>Coronary blood flow/100 g (ml/min/100 g)</td>
<td>78.5 ± 25.2</td>
<td>46.1-157.4</td>
</tr>
<tr>
<td>Total coronary blood flow (ml/min)</td>
<td>219 ± 105</td>
<td>36-461</td>
</tr>
<tr>
<td>O₂ consumption/100 g (ml/min/100 g)</td>
<td>10.7 ± 3.3</td>
<td>5.9-19.4</td>
</tr>
<tr>
<td>Total O₂ consumption (ml/min)</td>
<td>33.3 ± 13.4</td>
<td>7.9-60.6</td>
</tr>
<tr>
<td>Efficiency (%)</td>
<td>21 ± 9</td>
<td>4-40</td>
</tr>
</tbody>
</table>

*PMD - primary myocardial disease.
**Mixed group contains one patient with isolated mitral stenosis.

by quantitative biplane angiographic techniques described previously.11-13 It would have been of interest to calculate left ventricular wall stress in these patients. However, filtering rates of 6/second were not considered adequate for construction of accurate stress curves. Left ventricular stroke work and work per minute were calculated utilizing the product of angiographic stroke volume (end-diastolic volume minus end-systolic volume) and mean ventricular systolic ejection pressure. Mean pressure was obtained by planimetry of the area under the left ventricular pressure curve from the time of mitral valve opening to aortic valve closure. Total left ventricular MVO₂ was computed as ventricular mass/100 g × MVO₂/100 g. Left ventricular efficiency was calculated by relating left ventricular work to total left ventricular MVO₂ as described by Bing.8 The assumed energy equivalent for oxygen was 2.059 kg-m of energy liberated per ml of O₂ metabolized; left ventricular efficiency in percent was determined as:

\[
\text{Left ventricular work in kg-m/min} = \frac{\text{Total MVO₂ in ml/min} \times 2.059 \times 100}{\text{Total MVO₂}}
\]

These calculations involve the following assumptions: 1) Coronary blood flow as measured by the N₂O method, with coronary sinus sampling, provides a measure of left ventricular blood flow.5-7 Although the N₂O washout method may give falsely elevated values of coronary blood flow in patients with coronary disease,15-18 none of the patients in this series had evidence of coronary disease. 2) Venous blood sampled from the coronary sinus reflects the O₂ content of the left ventricular myocardial venous drainage. 3) The value of the energy equivalent of O₂ assumes a respiratory quotient of 0.82.4 4) The physiologic condition of the patient remains relatively unchanged between the time of coronary blood flow determination and the time of quantitative angiography. 5) Anaerobic myocardial metabolism is negligible in the absence of evidence of coronary artery disease.1,4 6) The mass value computed by the angiographic method represents perfused tissue for which N₂O determined blood flow measurements is applicable. 7) Left ventricular work as determined from total stroke volume and mean systolic ejection pressure provides a reasonable measure of the external work of the ventricle.

The data acquired by these studies were tabulated according to major disease categories and analyzed statistically.

Results

Of the 38 patients, four were found to have primary myocardial disease; they had ejection fractions < 0.25 without evidence of significant valvular abnormality. Six had predominant left ventricular pressure overload due to aortic valve stenosis, and 12 patients had predominant aortic and/or mitral regurgitation causing left ventricular volume overload. The 16 remaining patients had either pure mitral stenosis (one patient) or mixed lesions with combinations of mitral and aortic involvement. Table 1 shows the hemodynamic data for the 38 patients both collectively and subdivided into the four diagnostic categories. A wide spectrum of values is seen, with end-diastolic volumes ranging up to 490 ml, ejection fractions as low as 0.10, mass values as high as 609 g, and ventricular work up to 31.1 kg-m/min. Total left ventricular coronary blood flow was as high as 461 ml/min, and MVO₂ to 60.6 ml/min. Left ventricular efficiency extended from 4 to 40% within the patient group.

Figure 1 shows graphically the coronary blood flow and MVO₂ values per 100 g of myocardium, grouped according to major cardiac diagnosis. No significant differences among the various disease categories were present. It is noteworthy that a three to four-fold range of these values contrasts with a ten-fold range of values for stroke work, total left ventricular coronary flow, and efficiency; and a seven-fold range of values for total MVO₂.

Left ventricular mass did not correlate significantly with either coronary blood flow or with MVO₂ where these values were expressed per 100 g myocardium. Significant correlations between mass and total coronary flow or MVO₂ would be expected if the mass itself is utilized in the calculation of these total values.* It is noteworthy that the amount of

* \( r = 0.82 \) and 0.70, respectively.
hypertrophy compared to the left ventricular work is generally similar for the different types of workloads in the valve patients. Thus, mass/work ratio was 22.68 ± 8.81 g/min/kg-m for the pressure-load patients, 23.03 ± 9.00 for the volume-load group, and 25.76 ± 9.76 for the mixed-valve group. There was no significant difference between these groups.

Figure 2 shows the relationship of left ventricular work and total MVO₂ for the 38 patients, with symbols depicting the different diagnoses. The mathematically computed isograms reveal the relationship between these two variables expressed as efficiency. A graphic expression of this type helps clarify the relationship between the three variables of ventricular work, MVO₂ and mechanical efficiency. No significant grouping according to disease type is noted, other than the self-evident relatively low ventricular work values for the primary myocardial disease patients. Likewise, the tension time index was not significantly correlated with either total MVO₂ (r = 0.03) or MVO₂ per 100 g (r = 0.08).

Figure 3 shows ejection fraction, as a measure of myocardial function, plotted against left ventricular efficiency. The relationship between these two parameters was not close (r = 0.58). No particular grouping of patient diagnoses is evident other than the low values exhibited by the myocardial disease patients. Ejection fraction did not correlate significantly with coronary blood flow nor with MVO₂, expressed either in total terms or per 100 g of myocardium. Also, there was no correlation whatsoever in comparing coronary arterial venous O₂ difference with efficiency or with ejection fraction.

A comparison of left ventricular ejection fraction with ventricular work per 100 g of myocardium is shown in figure 4. The patients with primary myocardial disease, in addition to having low ejection fraction, have the lowest work performed per 100 g of myocardium, indicating excessive ventricular hypertrophy relative to mechanical workload. None of the 38 patients had low ejection fraction with average or high work values per 100 g.

Discussion

This report describes quantitatively the mechanical efficiency of the left ventricle, in terms of external work performed compared to energy utilized, in a series of resting adult patients with valvular and/or myocardial disease. The range of efficiency values was 4 to 40%, with the lowest values found in those patients with primary myocardial disease. A weak association (r = 0.58) existed between efficiency and ejection fraction. It is of interest that left ventricular efficiency may be normal in the setting of severe chronic ventricular work overload if myocardial function is good. Indeed, as shown in figure 2, the six patients with the highest ventricular workloads all had efficiency values greater than 24%. These findings reflect the relationships among efficiency, hypertrophy, and myocardial function in the resting, chronically diseased human heart. These relationships are complex and, as noted by others, the factors influencing efficiency are difficult to analyze and discuss. Starling and Visscher commented in 1926 that as the "heart tires," mechanical efficiency decreases. In 1949, Bing et al. calculated efficiency values utilizing estimates of ventricular weights derived from separate autopsy data rather than from in vivo ventricular mass measurements of the subjects.
studied. Similar to the present findings, they described values from 19.2–24.5% in normal humans; those with heart failure had efficiencies down to 12.9%. In 1973, Malik et al. induced chronic left ventricular pressure overloads in dogs and later studied multiple parameters of ventricular function, including efficiency, in the intact heart. Compared to controls, the hypertrophied ventricles exhibited normal or above normal values of efficiency and ventricular function. Also, Cooper et al. induced chronic right ventricular volume overload in cats by surgical creation of atrial septal defects. Myocardial function, including MVO₂ per unit tension development at maximum muscle length, was found to be normal, in spite of the ventricular hypertrophy present.

The two variables which determine efficiency are ventricular work and MVO₂. It is noteworthy that the ranges of both the MVO₂ and coronary blood flow values per 100 g of myocardium were generally unrelated to the type of left ventricular hemodynamic abnormality (fig. 1). Also, as shown in table 1, these values per 100 g did not extend over as wide a range in this series as did other parameters of total left ventricular dynamics, such as stroke work, total MVO₂ and coronary flow, and efficiency. Indeed, as shown in the table, total MVO₂ extended up to 60.6 ml/min and coronary flow to 461 ml/min, in patients with severely hypertrophied left ventricles. These figures indicate that left ventricular VO₂ and coronary flow may represent a significant portion of total body VO₂ and cardiac output in these disease states. Furthermore, these data support in quantitative terms the principle suggested by Bing that chronically increased resting left ventricular workloads and hence chronically increased ventricular metabolic requirements are fulfilled by hypertrophy more than by increased coronary flow and MVO₂ per unit of myocardium. He reported a range of values for MVO₂/100 g myocardium of 3.5 to 18.8 ml in different diseases; the values for patients in heart failure were only slightly higher than the normal controls. Also, Badeer noted that MVO₂ per unit myocardium is relatively constant in different size dog hearts. Thus, the extent of hypertrophy, rather than the left ventricular workload, is a major determinant of total resting MVO₂ in chronic disease states. It is of interest that the amount of hypertrophy compared to the workload appears generally the same in valvular heart disease whether the workload is from pressure or volume or mixed. Thus there was no significant difference between the three work-overload groups when mass/work ratio values were compared.

Previously published findings concerning MVO₂ changes in response to acute intervention in animals are difficult to interrelate with data obtained in the chronically diseased, resting state in humans. Thus, numerous animal studies, primarily of in vitro muscle preparations or intact isolated hearts, have described the factors influencing MVO₂. In these studies, acute hemodynamic or pharmacologic interventions have been instituted and the resultant alterations in MVO₂ measured. Classically the findings have been that MVO₂ is primarily related to myocardial tension or stress, contractile state, and heart rate with less important relationships to myocardial work or contractile element work, basal metabolism, and the energy of activation for contraction and relaxation. The tension-time index calculated as the area under the systolic portion of the aortic pressure curve and the product of blood pressure times heart rate have been regarded as major determinants of MVO₂. Multiple reports have shown that acute pressure loads on the left ventricle increase MVO₂ more than do volume loads. In one such study, Urschel et al. produced acute mitral incompetence in dogs, and noted that MVO₂ increased only slightly although work was significantly increased. Ventricular efficiency has also been measured after acute intervention. Rodbard and co-workers measured MVO₂ and efficiency in dogs with different acute ventricular hemodynamic alterations and found efficiency values from 3.9 to 32.7%. These values varied proportionally but nonlinearly with stroke volume. Studies of humans by Gorlin revealed that the left ventricular efficiency index, calculated without use of ventricular weight, increased with exercise in normals. Levine et al. reported that this efficiency index was low in a series of patients with heart failure and failed to rise normally with exercise. Rowe et al. reported that MVO₂/100 g and coronary flow/100 g rose with exercise both in normal patients and those with aortic valve disease. The reason that efficiency may increase with exercise in normals is unclear, since the augmented contractility with exercise should increase the O₂ cost per unit work. Decreasing ventricular size with exercise in normals, but not in disease states, has been implicated, since this should reduce wall tension.

In contrast to left ventricular responses to acute hemodynamic changes, the left ventricle cavity size and mass change significantly in response to chronic alteration in workload and myocardial function. In comparison to the findings in acute hemodynamic alterations in individual hearts, the data of this study were obtained from a series of resting patients with chronic disease. Thus, as expected, there is no significant relationship between the tension-time index and either total MVO₂ or MVO₂/100 g. In long-standing volume overload conditions such as mitral or aortic valvular incompetence, the left ventricular end-diastolic volume usually increases to allow a greater stroke volume without increase in ejection fraction. In chronic left ventricular pressure overloads such as aortic valve stenosis the chamber volumes may remain normal. In conditions with diffusely decreased myocardial function, with or without co-existent valvular disease, the end-diastolic volume usually increases out of proportion to the stroke volume, with resul-

\[ \text{Primary Myocardial Disease, LV Pressure Overload, LV Volume Overload, Mixed} \]

**Figure 4.** Left ventricular ejection fraction compared to left ventricular work/mass, or work per gram of myocardium.
tant decrease in ejection fraction.\textsuperscript{12, 20-27} The MVO\textsubscript{2} should decrease with decreased ventricular function.\textsuperscript{28} In this regard, Henry and co-workers reported a significant correlation between circumferential fiber shortening velocity and MVO\textsubscript{2}/100 g measured by helium washout techniques in 14 patients.\textsuperscript{9} Left ventricular transmural wall tension, on the other hand, is related to both intracavitary pressure and chamber dimensions by the La Place relationship.\textsuperscript{30} Thus, elevated ventricular end-diastolic volume or high systolic pressure loads will increase wall tension. In these situations, the left ventricular mass tends to increase to the extent that wall stress per cm\textsuperscript{2} cross-sectional area regresses toward normal.\textsuperscript{44} With this increase in left ventricular mass comes increased total MVO\textsubscript{2}. Consideration of all these factors leads to the theoretical possibility that decreased ventricular function could, by virtue of decreased MVO\textsubscript{2}, increase efficiency. However, as indicated by the data of this study and others,\textsuperscript{4, 19, 20} apparently the hypertrophy and ventricular shape changes assume primary significance, such that efficiency is usually decreased with chronic myocardial failure. Although this study reveals the range of these efficiency values in this group of patients, the basic etiology of low efficiency remains unknown. It is suspected that low efficiency results from a primary abnormality in conversion of energy to contractile work. Other possibilities, however, such as internal cellular alignment abnormalities with ineffective coordination of contraction must also be considered.

In this group of 38 patients with various combinations of pressure overload, volume overload and decreased ventricular function, there is evident reason for the observed wide spectrum of values for ventricular mass, workload, and efficiency.

References

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