Correlates of Myocardial Oxygen Demand Measured By Positron Emission Tomography in the Hypertrophied Left Ventricle

Olakunle O. Akinboboye, Nathaniel Reichek, Steven R. Bergmann, and Ru-Ling Chou

Background: The aim of this study was to identify the best correlate of myocardial oxygen demand (MVO$_2$) in patients with hypertension induced left ventricular hypertrophy (LVH), and to examine whether relationships between these surrogates and MVO$_2$ differed between patients with LVH and control subjects.

Methods: We measured MVO$_2$ by positron emission tomography using carbon-11 acetate in 20 patients and 10 normotensive control subjects, and compared the relationships between commonly used surrogates and MVO$_2$.

Results: With the exception of diastolic blood pressure, the same variables correlated with resting MVO$_2$ in the patients and control subjects.


Key Words: Left ventricular hypertrophy, myocardial oxygen demand, positron emission tomography, hypertension.
recruited from the patient population at New York Presbyterian Medical Center in New York City and the surrounding community. Pre-existing hypertension was validated by blood pressure (BP) measurement on entry.

Exclusion criteria for patients with hypertension and LVH included the following: echocardiographic evidence of significant cardiac abnormality other than hypertrophy, such as valvular heart disease, LV systolic dysfunction, and regional echocardiographic wall motion abnormalities suggestive of coronary artery disease; significant cardiovascular disease other than hypertension with LVH, diabetes mellitus, history of chest pain, and pregnancy. Additional exclusion criteria for normotensive control subjects included hypertension and LVH.

Using these criteria, we recruited 20 patients with hypertension induced LVH and 10 normotensive control subjects.

Measurement of Resting MVO₂ By Positron Emission Tomography Using Carbon-11 Acetate

To measure resting MVO₂ by positron emission tomography (PET) using carbon-11 (¹¹C) acetate, we used a PET scanner (model ECAT EXACT-47 PET, CTI Corp., Knoxville, TN), which provides 47 contiguous transaxial slices and has a postprocessing spatial resolution of 9 to 10 mm in plane and 4 to 5 mm in the axial direction. Subjects were studied after an overnight fast. They were placed supine in the PET scanner, and localization of the heart within the axial field of view of the scanner was confirmed by performing a 2-min “positioning” scan using a rotating ⁶⁸Ge/⁶⁸Ga-rod source. A 20-min transmission scan with the rotating ⁶⁸Ge/⁶⁸Ga-rod source was performed to generate an attenuation correction map for correction of the emission sinogram. Approximately 0.2 mCi/kg of ¹¹C-acetate was injected intravenously as a bolus. A 30-min dynamic data acquisition was performed using multiple frames with progressively increasing scan lengths (10-sec frames × 12, 60-sec frames × 5, 90-sec frames × 10, and 120-sec frames × 4). Emission sinograms were corrected for attenuation and radioactivity decay and reconstructed into transaxial slices. Transaxial slices were reoriented into six short axis slices using standard system software. Each short axis slice was divided into eight equal myocardial sectors, and count data in each sector used to calculate regional variance.

Measurement of LV Mass

An LV mass of >125 g/m² by screening M-mode echocardiography was used as an inclusion criterion for patients and as an exclusion criterion for control subjects. To minimize measurement variability, LV mass and volume were assessed by three-dimensional (3D) echocardiography.

The components, operation, and major features of the 3D echocardiography system developed at Columbia University have been previously described in detail.

Briefly, the 3D echocardiography system (K3 Systems, Darien, CT) comprises an acoustic spatial locater (model GP 8-3D, Science Accessories Corp., Stratford, CT) and personal computer (model 4DX-33V, Gateway 2000, North Sioux City, SD). These components were linked to a conventional two-dimensional echocardiogram. Left ventricular volume was computed from a series of guided, 6 to 8 real-time parasternal short axis images. These images were stored along with their XYZ Cartesian coordinates in the personal computer. End-diastolic video frames from each acquired cine-loop were selected for off-line endocardial and epicardial boundary tracing in diastole. Epicardial and endocardial volumes were determined from their corresponding boundaries using a polyhedral surface reconstruction algorithm. Endocardial volume (EDV) was subtracted from epicardial volume to yield myocardial volume, which was multiplied by myocardial density to yield myocardial mass.

Measurement of LV Wall Stress

Left ventricular peak-systolic stress was calculated using the following formula: 

\[
\text{stress} = \frac{\text{SBP} \times \text{LVDd}}{\text{LVPWT} \times \text{LVDd}^2}
\]

Measurement of Myocardial Contractility

Myocardial contractility in patients was assessed by calculating MFS (%) using the following formula:

\[
\text{MFS} = \frac{\text{LVDd} + \text{LVPWT} + \text{LVAWT}}{\text{LVDd} + \text{LVPWT} + \text{LVAWT}^2}\times100
\]

where LVDd, LVPWT, and LVAWT were all measured in diastole. MFS was calculated for each myocardial sector and for the entire left ventricle. LV mass and volume were assessed by three-dimensional (3D) echocardiography.

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Table 1. Clinical characteristics of patients and control subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>HPTN/LVH</th>
<th>Normotensive Control Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>11 (68%)</td>
<td>4 (40%)</td>
</tr>
<tr>
<td>Age (y)</td>
<td>54 ± 10</td>
<td>53 ± 4</td>
</tr>
<tr>
<td>Body mass index kg/m²</td>
<td>32 ± 8</td>
<td>26 ± 1</td>
</tr>
<tr>
<td>MVO₂ ml/min</td>
<td>23 ± 5†</td>
<td>13 ± 3</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>92 ± 10†</td>
<td>62 ± 9</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>164 ± 17†</td>
<td>109 ± 8</td>
</tr>
<tr>
<td>Mean arterial pressure</td>
<td>115 ± 12†</td>
<td>75 ± 4</td>
</tr>
<tr>
<td>LV ejection fraction (%)</td>
<td>53 ± 5</td>
<td>59 ± 5</td>
</tr>
<tr>
<td>LV mass (g)</td>
<td>199 ± 44†</td>
<td>130 ± 24</td>
</tr>
<tr>
<td>Pulse (beats/min)</td>
<td>68 ± 9</td>
<td>67 ± 7</td>
</tr>
<tr>
<td>Double product (beats/min*mm Hg)</td>
<td>1944 ± 815†</td>
<td>1477 ± 583</td>
</tr>
<tr>
<td>mTTI (mm Hg*beats/min)</td>
<td>945 ± 129†</td>
<td>633 ± 99</td>
</tr>
<tr>
<td>Endocardial fractional shortening (%)</td>
<td>16 ± 4</td>
<td>40 ± 6</td>
</tr>
<tr>
<td>Mid-wall fractional shortening (%)</td>
<td>122 ± 36</td>
<td>118 ± 25</td>
</tr>
<tr>
<td>Relative wall thickness</td>
<td>0.5 ± 0.1</td>
<td>0.3 ± 0.1</td>
</tr>
</tbody>
</table>

HPTN = hypertension; LVH = left ventricular hypertrophy; MVO₂ = myocardial oxygen demand; LV = left ventricular; STR = stress; HR = heart rate; PSS = peak systolic wall stress; mTTI = modified tension-time index; EDV = endocardial volume.

*P < .05.  †P < .001.

Statistical Methods

All values were expressed as mean ± SD. Correlates of MVO₂ on univariate and multivariate analysis were determined by linear regression analyses. A probability value of P < .05 was considered to be statistically significant.

Results

Population Characteristics

There was no significant difference between patients and control subjects in terms of age and sex. The average duration of hypertension in patients was 5 years (Table 1). As expected, patients exhibited significantly higher BP and LV mass measurements (P < .005) (Table 1). Patients also had significantly higher mean values for DP, mTTI, SMH, and total MVO₂. There was no difference in PSS values between patients and control subjects (Table 1).

Correlation With MVO₂

Mean total MVO₂ was significantly higher in patients than in control subjects: 23 ± 5 mL/min v 13 ± 3 mL/min (P = 0.004) (Table 1). However, MVO₂/g was not different between patients and control subjects 0.12 v 0.11 mL/g/min (P = ns). Mean values for tested variables are given in Table 1. By univariate analysis, the variables that correlated with total MVO₂ in the patients were HR (r = 0.65, P = .002, MVO₂ = 0.46 + 0.07 * HR), SMH (r = 0.63, P = .003, MVO₂ = 3.62 + 0.0000008 * SMH), DP (r = 0.63, P = .003, MVO₂ = 2.89 + 0.0002 * DP), mTTI (r = 0.55, P = .01, MVO₂ = 0.48 + 0.0047 * MVO₂), and PSS (r = 0.54, P = .0, MVO₂ = 3.75 + 0.009 * PSS). In the control subjects, the significant correlates of total MVO₂ were HR (r = 0.68, P = .03, MVO₂ = 1.02 + 0.06 * HR), SMH (r = 0.73, P = .02, MVO₂ = 3.82 + 0.000009 * SMH), DP (r = 0.64, P = .04, MVO₂ = 3.00 + 0.0003 * DP), PSS (r = 0.69, P = .03, MVO₂ = 3.81 + 0.007 * PSS) and DBP (r = 0.64, P = .04, MVO₂ = 3.00 + 0.0003 * DBP). In the combined group of patients and control subjects, variables that correlated with total MVO₂ were HR (r = 0.65, P = .0009, MVO₂ = 0.46 + 0.07 * HR), SMH (r = 0.64, P = .0001, MVO₂ = 3.62 + 0.0000008 * SMH), DP (r = 0.56, P = .001, MVO₂ = 2.89 + 0.0002 * DP), PSS (r = 0.46, P = .01, MVO₂ = 3.75 + 0.009 * PSS) and mTTI (r = 0.43, P = .01, MVO₂ = 0.51 + 0.005 * TTI). On multivariate analysis, the single best determinant of total MVO₂ in the patients was SMH (r = 0.67, P = .001, MVO₂ = 3.53 + 0.000019 * SMH).

Discussion

On univariate analyses, the strongest correlates of MVO₂ were SMH in control subjects and SMH, HR, and DP in the patients. In the combined population, SMH and HR had the best correlation with MVO₂. On multivariate analysis, the single best correlate of MVO₂ in the patients was SMH. The moderate correlation between the significant variables and MVO₂ could be attributable to the narrow range of resting MVO₂ values in our study. Although several studies have examined correlates of MVO₂ after pharmacologic stress or atrial pacing, ours is the first study...
to examine correlates of $MVO_2$ in patients with hypertension induced LVH under resting conditions.

With the exception of diastolic BP and peak systolic stress, all of the significant variables are directly related to heart rate, which underscores the impact of the latter on resting $MVO_2$. Several investigators have shown the relationships among heart rate, double product, and $MVO_2$. However, the relationship between stress–mass–heart rate product and $MVO_2$ has not been adequately studied.\textsuperscript{4,13} Because wall stress is directly related to volume/mass ratio and BP, stress–mass–heart rate product essentially incorporates ventricular volume, BP, and heart rate, which explain its relationship to $MVO_2$. Although stress–mass–heart rate product, heart rate, and double product do not account for changes in myocardial contractility (which is a known determinant of $MVO_2$), they did correlate significantly with resting $MVO_2$. This could be attributable to the narrow range of contractility values in the population. Furthermore, heart rate and double product do not account for changes in ventricular volume, a determinant of wall stress, however the range of ventricular volumes in the population is narrow because most of the patients had concentric hypertrophy.

With the exception of DBP, which correlated with $MVO_2$ in the control subjects but not in patients, there was no difference between patients and control subjects in the variables that correlated with $MVO_2$.

The clinical implications of our findings underscore that heart rate is an important determinant of myocardial energy demand under resting conditions, and that SMH is the best correlate of resting $MVO_2$ in patients with hypertension induced LVH. Thus, patients with hypertension induced LVH who have angina would benefit from interventions that lower heart rate.

Some limitations of this study should be recognized. First, we studied all subjects under resting conditions; as a result, our findings may not be applicable to situations in which myocardial energy demands is increased. Second, we did not measure systolic ejection time; consequently, we could not calculate tension–time index or triple product. It is possible that these indices may yield better correlations with $MVO_2$.

In conclusion, heart rate, stress–mass–heart rate product, double product, modified tension time index, and peak systolic stress correlate significantly with $MVO_2$ in patients with hypertension induced LVH. These same variables, along with diastolic BP, correlate significantly with $MVO_2$ in normotensive control subjects. The best correlate of $MVO_2$ in patients with hypertension induced LVH was stress–mass–heart rate product.

References

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