Determinants of Left Ventricular Hypertrophy and Oxygen Supply in Chronic Aortic Valve Disease

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SUMMARY Ventricular mass and O2 supply of the myocardium were evaluated in patients with left ventricular hypertrophy due to stenosis or insufficiency of the aortic valve and in control patients without cardiac disease. Calculation of left ventricular mass from the angiogram was verified by autopsy data in seven patients. Total mass, O2 consumption, and coronary blood flow, each was related quantitatively to left ventricular total load (force) in all patients. Left ventricular equatorial tension, however, was greater in proportion to mass in aortic stenosis than in aortic insufficiency patients. This discrepancy could be explained by the more eccentric shape of the left ventricle in aortic stenosis. Oxygen consumption and coronary blood flow per gram of myocardium were normal at rest in patients with hypertrophy. Tachycardia induced by atrial pacing provoked myocardial lactate production in half of the patients with aortic stenosis but in none of the patients with aortic insufficiency. Surgical mortality was related to myocardial mass and lactate production.

HYPERTROPHY OF THE LEFT VENTRICLE, which involves both contractile and mitochondrial elements, presumably is a result of the increase in ventricular wall force (total load) and metabolic rate. The degree of the hypertrophy as assessed by left ventricular wall thickness has been found to be related quantitatively to the increase in left ventricular systolic blood pressure. Left ventricular wall force per unit cross-sectional area (i.e., stress) and O2 consumption per gram* have been reported to be nearly normal in chronically hypertrophied hearts. These observations suggest that the extent of hypertrophy may be regulated to keep wall force and O2 consumption per unit of myocardium within normal limits, a finding consistent with the theory that myocardial growth is regulated by the steady-state level of adenosine nucleotide phosphorylation.

The objectives of the present investigation were to delineate more precisely the mechanical determinants of left ventricular hypertrophy and to evaluate the adequacy of the compensatory increase in coronary blood flow in meeting the augmented myocardial O2 requirements of the hypertrophied heart. We calculated equatorial tension and total force4 (load) of the left ventricular wall and determined the quantitative relationship between these mechanical expressions and left ventricular mass, O2 consumption, and coronary blood flow. The studies were performed in patients whose left ventricular hypertrophy was in response to one of two different types of chronic hemodynamic burden: isolated aortic stenosis or insufficiency.

Methods

Subjects

We studied 24 patients with aortic valve disease: 15 had nearly pure aortic stenosis (AS) and nine nearly pure aortic insufficiency (AI) (patients with mixed stenosis and insufficiency were not studied). Their clinical characteristics are presented in table 1. Absence of significant coronary disease was established in each patient by selective coronary angiography. No patient had evidence of right ventricular hypertrophy, which might have influenced measurement of left ventricular wall thickness. Control data for left ventricular mechanics and mass were obtained from 11 patients investigated for atypical chest pain but found to have normal stress electrocardiography, left ventriculography and selective coronary angiography, and no other objective evidence of cardiac disease. Control data for myocardial O2 and lactate extraction were obtained from 16 other similar patients previously reported.

Procedures

Observations were made during diagnostic cardiac catheterization in the aortic valve disease patients and during coronary and left ventricular angiography in the control patients. The patients did not eat breakfast and received 5-10 mg diazepam or 100 mg secobarbital intramuscularly as premedication. Catheters were positioned in the brachial artery percutaneously, in the coronary sinus via basilic vein cutdown, and in the left ventricle either retrograde via femoral artery puncture or transseptally via femoral vein puncture. To evaluate myocardial O2 supply, heart rate was increased to 120-140 beats/min by atrial pacing from the coronary sinus catheter.

Pressures were recorded on a photographic Electronics for Medicine Recorder (Electronics for Medicine, Inc., White Plains, N.Y.) with P23Gb Statham transducers (Statham Instruments, Inc., Oxnard, CA). Single plane 35 mm cineangiography of the left ventricle was filmed at 60 frames/second in the 30° RAO projection, after injecting 36-45 ml meglumine diatrizoate 76% (Renografin-76) in 3 sec. Paired arterial and coronary venous blood samples were obtained for Pco2 and pH (Radiometer Co., Copenhagen), hemoglobin (spectrophotometric), and lactate determinations. Blood O2 concentration was calculated, assuming normal blood O2 affinity adjusted for pH. Coronary blood flow was determined in 17 patients (11 AS and 6 AI) by the N2O desaturation method and in seven patients (4...
AS and 3 AI) by the 133Xenon clearance method. In 19 patients, all observations were made during the same catheterization procedure, whereas in five patients coronary blood flow and metabolic data were obtained on a separate day (heart rate and blood pressure were comparable on the two days).

Calculations

The left ventricular end-diastolic volume (EDV) and end-systolic volume (ESV) were calculated by the area-length method using the largest and the smallest angiographic silhouettes corrected for magnification. The major (longest) axis (2a) was measured, and the minor axis (2b) was calculated.

Rackley et al. have determined the left ventricular mass (V_m) by the following equation:

V_m = (V_C+W - V') 1.05

1
V_C+W = 4  π (b + h)^2 (a + h)

where V_C+W = volume (V) of left ventricular chamber (C) plus wall (W); V' = EDV (chamber only); h = left ventricular wall thickness at end diastole; and 1.05 = density of myocardium.

This equation assumes that the left ventricular wall is of uniform thickness throughout. The left ventricular wall is, however, thinner at the apex and interrupted at the base. We arbitrarily assumed that the thickness of the wall at the apex and at the base was one-half that of the free wall where it is measured on the angiogram and modified the formula as follows:

V_C+W = 4  π (b + h)^2 (a + h/2)

The tracing of a left ventricle and its idealized representation according to equations 1 and 2 are illustrated in figure 1. Calculation of left ventricular mass by equation 2 was verified in seven patients (including three in this study) who died within three months after obtaining a technically satisfactory left ventricular angiogram. The left ventricular mass calculated from the angiogram is compared in table 2 with the mass measured at autopsy using a chamber partition technique. The mean calculated mass (434 g) was close to the mean autopsy mass (429 g), and the correlation coefficient was 0.97. On the other hand, left ventricular mass calculated by equation 1 (mean 526 g) was consistently larger than the autopsy value (P < 0.01).

We calculated left ventricular wall tension at the equator of the minor axis exerted in the direction of that equator (TE) by using Gault's modification of the stress equation of Sandler and Dodge.

Table 1: Clinical Data

<table>
<thead>
<tr>
<th></th>
<th>AS N = 15</th>
<th></th>
<th>AI N = 9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (mean ± sd)</td>
<td>58 ± 8</td>
<td>50 ± 13</td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>10 (67%)</td>
<td>5 (36%)</td>
<td></td>
</tr>
<tr>
<td>Angina</td>
<td>13 (87%)</td>
<td>3 (33%)</td>
<td></td>
</tr>
<tr>
<td>Syncope</td>
<td>7 (46%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>ECG—LVH</td>
<td>14 (93%)</td>
<td>8 (57%)</td>
<td></td>
</tr>
<tr>
<td>Chest X-ray—LVH</td>
<td>6 (40%)</td>
<td>5 (36%)</td>
<td></td>
</tr>
</tbody>
</table>

Vc+w = ventricular wall

Stress = \( \frac{P \cdot b}{h} \left( 1 - \frac{b}{2a^2} \right) \) (3)

where P = blood pressure in dynes/cm²; a = major semi-axis; b = minor semi-axis; and h = wall thickness.

Since tension (TE) = stress • wall thickness,

TE = \( \frac{P \cdot b}{h} \left( 1 - \frac{b}{2a^2} \right) \) (4)

we used Hood's method for determining the total force, or load (TL), on the left ventricle:

TL = \( P \cdot 2\pi \left[ \frac{b}{a} - a \cdot b \cdot \frac{\arcsin \sqrt{1 - (b/a)^2}}{\sqrt{1 - (b/a)^2}} \right] \) (5)

The maximum left ventricular wall tension has been shown to occur at approximately the same time as maximum left ventricular pressure. We assumed, as others have, that approximately one-third of the stroke volume has been ejected at the time when the maximum pressure is reached. Therefore, the volume at maximum left ventricular tension (V_{mt}) was calculated as follows:

V_{mt} = \frac{2 EDV + ESV}{3} (6)

Figure 1. To the left is the left ventricular silhouette as traced from the cineangiogram in a patient with AI whose ventricular wall was exceptionally well visualized. Solid lines represent visualized endocardial and epicardial surface outlines, and dashed lines extended to the base of the heart are hypothetical. The lightly shaded area, thus, represents a longitudinal section of the left ventricular muscle. Wall thickness (h) was measured as the mean thickness within the darker shaded region. The major axis (2a) is indicated by the length of the arrow. The idealized model, shown to the right, was constructed from Equations 1 and 2, assuming an ellipsoid shape with wall thickness at the apex and base equal to one half the thickness measured at the mid-wall. The calculated minor axis (2b) is indicated. The shaded areas of the cine tracing and ideal model are approximately equal, which supports the validity of the model as a means of calculating left ventricular mass.
V_m can also be expressed as:

$$V_m = \frac{4}{3} \pi a_m \cdot b_m^2$$  \hspace{1cm} (7)

Where $a_m$ = major semiaxis at maximum tension; $b_m$ = minor semiaxis at maximum tension.

To estimate the major and minor axes at maximum tension, we assumed that during the transition from end diastole (ed) to end systole (es) the change in eccentricity $(a/b)$ with respect to the change in volume was linear. Therefore:

$$\frac{(a/b)_{ed}}{(a/b)_{es}} = \frac{2(a/b)_{ed} + (a/b)_{es}}{3}$$  \hspace{1cm} (8)

We solved equation 7 for $b_m$ in terms of $(a/b)_{es}$ and substituted the calculated values of $(a/b)_{es}$ and $V_m$ into the following equation:

$$b_m = 0.62 \sqrt[3]{\frac{V_m}{(a/b)_{es}}}$$  \hspace{1cm} (9)

Thus:

$$a_m = b_m \cdot (a/b)_{es}$$  \hspace{1cm} (10)

Knowing the left ventricular pressure and semiaxes at the time of maximum tension, the maximum equatorial tension $(T_{E_{\text{max}}})$ and the maximum total load $(T_{L_{\text{max}}})$ can be calculated by equations 4 and 5, respectively.

Myocardial $O_2$ consumption/100 g - min was calculated from the product of coronary blood flow/100 g - min (xenon or $N_2O$ method) and coronary $(a-v)O_2$ difference. Total coronary blood flow and total myocardial $O_2$ consumption for the left ventricle were calculated from the product of the values per 100 g multiplied by the angiographically determined left ventricular mass. Myocardial lactate production or lactate extraction (L $(a-cv/a)$) values less than 0.09 were interpreted as evidence of myocardial hypoxia.

Results

LV Mechanics and Mass

Data pertaining to left ventricular dimensions and mechanics are presented in Table 3. Left ventricular end-diastolic and end-systolic volumes were larger than normal in aortic insufficiency (AI) patients ($P < 0.01$) but not in aortic stenosis (AS) patients, as shown previously in other studies. The left ventricle was more spherical in AI patients as reflected in the proportionately greater increase in their minor semiaxis (b) as compared to the increase in their major semiaxis (a), resulting in a smaller a/b ratio ($P < 0.05$). Left ventricular wall thickness was greater than normal in AS patients ($P < 0.01$), whereas the slight increase in wall thickness in AI patients was not significant. Left ventricular mass was increased in both AS and AI patients ($P < 0.01$). Our values for left ventricular mass for normal patients and patients with aortic valve disease were comparable to those reported by other investigators using similar angiographic techniques.\cite{18, 20}

Left ventricular peak systolic and end-diastolic pressures were higher than normal in both AS and AI patients ($P < 0.01$), and the peak systolic pressure was highest in the AS patients. The maximum left ventricular wall tension at the equator $(T_{E_{\text{max}}})$ and the maximum total force or load of the left ventricular wall $(T_{L_{\text{max}}})$ were greater than normal in AS and AI patients ($P < 0.01$). In contrast to the quantitative difference in left ventricular systolic pressure, $T_{E_{\text{max}}}$ and $T_{L_{\text{max}}}$ were approximately as great in AI as in AS patients due to the larger left ventricular volumes in AI patients.

Wall thickness of the left ventricle as measured near the

### Table 3. Left Ventricular Dimensions and Mechanics

<table>
<thead>
<tr>
<th></th>
<th>Normals ($N = 11$)</th>
<th>AS ($N = 15$)</th>
<th>AI ($N = 9$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BSA (m$^2$)</td>
<td>$1.9 \pm 0.20$</td>
<td>$1.9 \pm 0.12$</td>
<td>$1.9 \pm 0.16$</td>
</tr>
<tr>
<td>EDV (ml)</td>
<td>$152 \pm 23$</td>
<td>$168 \pm 43$</td>
<td>$253 \pm 80\dagger$</td>
</tr>
<tr>
<td>ESV (ml)</td>
<td>$35 \pm 13$</td>
<td>$60 \pm 24$</td>
<td>$94 \pm 44\ddagger$</td>
</tr>
<tr>
<td>C.O. (l/min)</td>
<td>$-5.7 \pm 1.8$</td>
<td>$5.5 \pm 0.96$</td>
<td>$-0.05$</td>
</tr>
<tr>
<td>LV thickness (cm)</td>
<td>$1.1 \pm 0.21$</td>
<td>$1.4 \pm 0.26\dagger$</td>
<td>$1.3 \pm 0.23$</td>
</tr>
<tr>
<td>$2a_{ed}$ (cm)</td>
<td>$9.1 \pm 0.81$</td>
<td>$9.5 \pm 0.94$</td>
<td>$10.1 \pm 0.94$</td>
</tr>
<tr>
<td>$2b_{ed}$ (cm)</td>
<td>$5.4 \pm 0.85$</td>
<td>$5.8 \pm 0.53$</td>
<td>$6.8 \pm 0.92\ddagger$</td>
</tr>
<tr>
<td>$2a_{es}$ (cm)</td>
<td>$7.2 \pm 0.60$</td>
<td>$7.6 \pm 1.3$</td>
<td>$8.3 \pm 1.1\dagger$</td>
</tr>
<tr>
<td>$2b_{es}$ (cm)</td>
<td>$3.8 \pm 0.42$</td>
<td>$3.8 \pm 0.63$</td>
<td>$4.3 \pm 0.96\ast$</td>
</tr>
<tr>
<td>$(a/b)_{es}$ (a-cv/a)</td>
<td>$1.62 \pm 0.18$</td>
<td>$1.66 \pm 0.16$</td>
<td>$1.49 \pm 0.22\dagger$</td>
</tr>
<tr>
<td>$(a/b)_{ed}$</td>
<td>$1.91 \pm 0.23$</td>
<td>$2.04 \pm 0.41$</td>
<td>$1.89 \pm 0.37$</td>
</tr>
<tr>
<td>LV mass (g)</td>
<td>$171 \pm 31$</td>
<td>$265 \pm 80\dagger$</td>
<td>$307 \pm 92\dagger$</td>
</tr>
<tr>
<td>LVSP (mm Hg)</td>
<td>$123 \pm 14$</td>
<td>$201 \pm 27\dagger$</td>
<td>$163 \pm 16\ddagger$</td>
</tr>
<tr>
<td>LVEDP (mm Hg)</td>
<td>$9 \pm 3$</td>
<td>$16 \pm 5\dagger$</td>
<td>$18 \pm 13\ast$</td>
</tr>
<tr>
<td>$T_{E_{\text{max}}}$ (dynes/cm)</td>
<td>$338 \pm 39$</td>
<td>$581 \pm 94\dagger$</td>
<td>$533 \pm 64\dagger$</td>
</tr>
<tr>
<td>$T_{L_{\text{max}}}$ (dynes $\times 10^3$)</td>
<td>$77 \pm 10$</td>
<td>$138 \pm 33\ddagger$</td>
<td>$143 \pm 32\dagger$</td>
</tr>
</tbody>
</table>

*Values are given as mean $\pm$ standard deviation.

$\ast P < 0.05$, $\ast\ast P < 0.01$; AS or AI vs Normals, by unpaired $t$-test.

$\dagger P < 0.05$, $\dagger\dagger P < 0.01$; AI vs AI, unpaired $t$-test.

Abbreviations: AS = aortic stenosis; AI = aortic insufficiency; BSA = body surface area; EDV = end-diastolic volume; ESV = end-systolic volume; C.O. = cardiac output; LV = left ventricle; $2a$ = major axis; $2b$ = minor axis; es = ed = end-diastolic; eg = end-systolic; LVSP = left ventricular systolic peak pressure; LVEDP = left ventricular end-diastolic pressure; $T_{E_{\text{max}}}$ = maximum equatorial tension; $T_{L_{\text{max}}}$ = maximum total load.

### Figure 2. Wall thickness and maximum equatorial tension ($T_{E_{\text{max}}}$) of the left ventricular wall ($r = 0.61$). Both parameters pertain to the ventricular wall near the equator. $\bullet = AS$, $\square = AI$. 

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equator from the left ventricular angiogram was associated with $T_{E_{\text{max}}}$ ($r = 0.61$) as illustrated in figure 2.

The relationship between muscle mass and peak systolic pressure of the left ventricle is presented in figure 3 ($r = 0.52$). Aortic insufficiency patients (open squares) had larger masses in proportion to their pressures than AS patients (closed circles). Left ventricular mass was more closely correlated with $T_{E_{\text{max}}}$ ($r = 0.73$) than with peak systolic pressure since $T_{E_{\text{max}}}$ takes into account both ventricular volume and pressure. However, mass relative to $T_{E_{\text{max}}}$ still was systematically larger in AI than in AS patients. The relationship between left ventricular mass and $T_{L_{\text{max}}}$ is presented in figure 5. In this case, AS and AI patients are not separated, and the correlation coefficient is higher ($r = 0.79$). There was no significant correlation between left ventricular mass and pressure-volume work.

**Myocardial Metabolism**

Mean data for AS and AI patients and 16 normal patients previously published$^8$ are presented in table 4. Coronary (a-v)$O_2$ and coronary venous blood $P_{O_2}$ were not significantly different between normals, AS or AI patients. Coronary blood flow and myocardial $O_2$ consumption per 100 g of left ventricular myocardium for the AS and AI patients were within the normal range, as previously demonstrated,$^4$,$^21$ whereas coronary blood flow and myocardial $O_2$ consumption of the total left ventricle in AS and AI were above normal due to the larger ventricular mass. The relationships between total left ventricular coronary blood flow and $T_{L_{\text{max}}}$ ($r = 0.67$) and total left ventricular $O_2$ consumption and $T_{L_{\text{max}}}$ ($r = 0.68$) are shown in figures 6 and 7.

Lactate extraction by the myocardium in the resting state was essentially the same for normals, AS, and AI patients (table 4). During atrial pacing, however, lactate extraction

**TABLE 4.** Coronary Blood Flow and Myocardial Metabolism

<table>
<thead>
<tr>
<th></th>
<th>Normals ($N = 16$)</th>
<th>AS ($N = 10$)†</th>
<th>AI ($N = 9$)‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>$CaO_2$ (ml/100 ml)</td>
<td>$17.5 \pm 1.8$</td>
<td>$18.1 \pm 2.0$</td>
<td>$17.5 \pm 2.2$</td>
</tr>
<tr>
<td>$C$ (a-cv) $O_2$ (ml/100 ml)</td>
<td>$11.8 \pm 1.4$</td>
<td>$11.9 \pm 1.6$</td>
<td>$12.2 \pm 2.0$</td>
</tr>
<tr>
<td>$P_{cvo_2}$ (mm Hg) rest</td>
<td>$20.6 \pm 1.4$</td>
<td>$20.5 \pm 3.1$</td>
<td>$19.6 \pm 2.0$</td>
</tr>
<tr>
<td>$La$ (mM) rest</td>
<td>$.56 \pm .20$</td>
<td>$.50 \pm .13$</td>
<td>$.52 \pm .29$</td>
</tr>
<tr>
<td>$La_{cv/a}$ rest</td>
<td>$.29 \pm .14$</td>
<td>$.31 \pm .14$</td>
<td>$.30 \pm .16$</td>
</tr>
<tr>
<td>CBF (ml/100 g · min)</td>
<td>—</td>
<td>$.94 \pm .24$</td>
<td>$.92 \pm .18$</td>
</tr>
<tr>
<td>CBF (ml/min)</td>
<td>—</td>
<td>$250 \pm 97$</td>
<td>$285 \pm 114$</td>
</tr>
<tr>
<td>$MVO_2$ (ml/100 g · min)</td>
<td>—</td>
<td>$11.2 \pm 3.6$</td>
<td>$11.2 \pm 3.0$</td>
</tr>
<tr>
<td>$MVO_2$ (ml/min)</td>
<td>—</td>
<td>$29 \pm 11$</td>
<td>$35 \pm 15$</td>
</tr>
<tr>
<td>$P_{cvo_2}$ (mm Hg) pace</td>
<td>$20.8 \pm 1.5$</td>
<td>$21.2 \pm .40$</td>
<td>$19.4 \pm 1.8$</td>
</tr>
<tr>
<td>$La$ (mM) pace</td>
<td>$.53 \pm .18$</td>
<td>$.50 \pm .15$</td>
<td>$.55 \pm .37$</td>
</tr>
<tr>
<td>$La_{cv/a}$ pace</td>
<td>$.29 \pm .10$</td>
<td>$.004 \pm .44^*$</td>
<td>$.29 \pm .13$</td>
</tr>
</tbody>
</table>

All values expressed as mean ± SD.

$^a$Prepared $N = 12$ for data during atrial pacing.

$^b$Abbreviations: $C =$ concentration; $a =$ arterial; $cv =$ coronary venous; $P =$ partial pressure; $L =$ lactate; $CBF =$ coronary blood flow; $MVO_2 =$ myocardial $O_2$ consumption.
reversed to lactate production in six of 12 AS patients (fig. 8), and the mean value for lactate extraction in all AS patients decreased during pacing (P < 0.05). No normal subject or AI patient exhibited lactate production during pacing. There were no significant corresponding changes in coronary venous blood Po2 during pacing.

Surgical Mortality

All AS patients underwent surgery for insertion of a Starr-Edwards aortic valve prosthesis, and there were four cardiac deaths during surgery or within three months postoperatively. Mortality was higher in patients with left ventricular mass greater than 300 g (table 5) and the mean left ventricular mass of patients who died (363 ± 55 g) was greater (P < 0.01) than of patients who survived (229 ± 52 g). Mortality also was higher in patients with myocardial lactate production during atrial pacing (table 5). Mean lactate extraction during pacing was less in nonsurvivors (−0.31 ± 0.64) than in survivors (0.15 ± 0.22) although the difference was not statistically significant. The five AI patients who received aortic valve prostheses survived surgery.

Discussion

Validity of Mass and Tension

We measured left ventricular wall thickness at a point on the cineangiogram which corresponds to the equator of the idealized model (fig. 1). The model attempts to take into account the thinning of the wall toward the apex and the absence of muscle at the other end of the chamber where valves form a portion of the left ventricular wall. Although the model does not accurately reproduce the complex shape of the left ventricle that actually exists, it is a better approximation than assuming a uniform wall thickness; and mass calculated on the basis of this model agreed well with the mass as determined at autopsy.

Calculation of wall tension depends upon left ventricular chamber dimensions, which were calculated from a single plane cineangiogram, assuming that the left ventricle was an ellipsoid of revolution. Since dimensions at the subendocardial surface were the only ones available from the angiograms, we considered the left ventricle as if it were a thinwalled shell located at the endocardium. Our data do not deal with the question of the distribution of forces across the left ventricular wall. To determine the maximum tension, we did not calculate tensions throughout systole, but assumed

![Figure 6](http://circ.ahajournals.org/)

**Figure 6.** Coronary blood flow to the entire left ventricle related to maximum total load (r = 0.67). • = AS, □ = AI.

![Figure 7](http://circ.ahajournals.org/)

**Figure 7.** Myocardial O2 consumption of the entire left ventricle compared with maximum total load (r = 0.68). • = AS, □ = AI.

![Figure 8](http://circ.ahajournals.org/)

**Figure 8.** Myocardial lactate extraction (a - cv/a) during atrial pacing (heart rate: 120–140 min⁻¹). Positive values indicate lactate uptake and negative values indicate lactate production by the myocardium. • = patients with history of angina pectoris, O = no angina pectoris.
that the time of maximum tension in each patient occurred at the time of peak left ventricular pressure, an assumption others have demonstrated to be approximately true.\textsuperscript{3, 16} To calculate dimensions of the left ventricle at maximum tension, we assumed that one-third of the stroke volume had been ejected at the time of peak pressure.\textsuperscript{17} We have presented only maximum tension data, realizing that hypertrophy might be related to some other expression of tension such as its mean value throughout systole. Furthermore, left ventricular load and tension fluctuate throughout the day, whereas left ventricular mass remains essentially constant. To calculate tension we used pressures recorded immediately before the angiogram. Other investigators have found satisfactory agreement between pressures measured before and during the angiography.\textsuperscript{18}

Basis of Hypertrophy

Left ventricular hypertrophy in chronic aortic valvular disease presumably is related in some manner to the extra hemodynamic burden imposed during systole. Our data demonstrate that the mass was related quantitatively to the left ventricular peak systolic pressure (fig. 3) and not to the aortic valve area in AS patients nor to the arterial pulse pressure or the left ventricular end-diastolic pressure in AI patients, as expressions of the severity of the aortic valve disease itself. When AS and AI patients were compared, the AI patients had a greater mass with respect to left ventricular peak systolic pressure (fig. 3). This difference probably was related to their greater left ventricular volumes since intracavitary pressure affects the myocardium through its influence on left ventricular wall tension, which is proportional to both pressure and volume. Thus, the total load during systole, TL\textsubscript{max}, was as great in AI patients, who had a combination of increased pressure and volume, as it was in AS patients, who had markedly increased pressure with near normal volume. Therefore, as pointed out by others, it is inappropriate to consider AI as a pure volume load.

TL\textsubscript{max} was the expression of left ventricular wall force which was best related quantitatively to the degree of hypertrophy in terms of myocardial mass. The relationship was not influenced by whether stenosis or insufficiency of the aortic valve was responsible for the increased force (fig. 4), and was independent of the volume of blood ejected by the left ventricle during systole, as illustrated by the lack of correlation between left ventricular mass and left ventricular pressure-volume work. The correlation between mass and TL\textsubscript{max} seems logical since TL\textsubscript{max} expresses force operating throughout the entire left ventricle.

We also evaluated the relationship between hypertrophy and tension at the level of the equator (TE\textsubscript{max}). TE\textsubscript{max} represents the force at a specific location acting in a specified direction. If the left ventricle were a sphere, TE\textsubscript{max} and all other tensions in the wall would be equal. In the ellipsoid model of the left ventricle, however, TE\textsubscript{max} is the greatest tension, and the degree to which TE\textsubscript{max} exceeds tensions elsewhere is proportional to the degree of eccentricity. Since the ellipsoid representation of the left ventricle was more eccentric in AS than in AI patients (larger a/b), one would expect that TE\textsubscript{max} would overestimate the overall wall force more in AS than in AI patients. Thus, the difference in left ventricular shape could explain the separation of AS and AI patients when mass was plotted against TE\textsubscript{max} as in figure 4. In our view, it would seem more appropriate to relate TE\textsubscript{max} to wall thickness at the equator (fig. 2) rather than to overall mass.

Myocardial O\textsubscript{2} Supply with Hypertrophy

Total O\textsubscript{2} consumption and coronary blood flow of the left ventricle also were correlated with TL\textsubscript{max}, showing an interrelationship between muscle mass, O\textsubscript{2} consumption, and O\textsubscript{2} delivery to the muscle. This association suggests that the determinants of hypertrophy, metabolic rate, and O\textsubscript{2} delivery are based on a common mechanism, as proposed by others,\textsuperscript{7} keeping O\textsubscript{2} consumption per unit mass of myocardium constant and coronary blood flow appropriate to the myocardial metabolic needs.

Although the coronary blood flow and oxygen consumption per unit mass of myocardium were normal in these patients in the resting state, half of the patients with AS developed lactate production during atrial pacing. Similar findings have been reported by Fallen et al.\textsuperscript{21} Lactate production indicates that oxygen supply to myocardial tissue was inadequate in proportion to oxygen needs during moderate stress. This chemical evidence of myocardial hypoxia occurred in AS patients and not in AI patients, which is consistent with the greater frequency of exertional angina pectoris found in AS patients.

Either stenosis or insufficiency of the aortic valve lead to high extravascular compression within the myocardium and low diastolic coronary perfusion pressure, an unfavorable combination for subendocardial perfusion. The myocardial lactate production in these patients was not accompanied by a fall in coronary venous blood PO\textsubscript{2}, which is similar to the results in experimental coronary stenosis in dogs\textsuperscript{22} and in human patients with ischemic coronary heart disease.\textsuperscript{8} Coronary stenosis\textsuperscript{23, 24} or acute aortic stenosis\textsuperscript{25} have been shown to cause a transmural redistribution of blood flow from subendoocardium to subepicardium. The fact that coronary venous PO\textsubscript{2} remains constant despite the presence of subendocardial hypoxia which occurs in both ischemic coronary disease and aortic stenosis can be explained by a transmural shift in blood flow so that a larger percentage of the coronary sinus blood drains the subepicardial region where the PO\textsubscript{2} is greater.\textsuperscript{26, 27}

Left ventricular mass greater than 300 g in AS patients was associated with a high surgical mortality. A similar correlation has been shown between mortality and cardiothoracic ratio as measured on the chest X-ray.\textsuperscript{28} The myocardial lactate extraction data suggest that the high risk was related to myocardial hypoxia (table 5). These observations emphasize the desirability of performing valve surgery before hypertrophy progresses to this degree. Furthermore, if valve replacement is carried out in a patient with a very large left ventricle, special attention should be given to maintain myocardial O\textsubscript{2} supply by coronary perfusion during surgery.

References

7. Meerson FZ, Pomoinitsky VD: The role of high-energy phosphate compounds in the development of cardiac hypertrophy. J Molec Cell Cardiol 4: 571, 1972
27. Gamble WJ, LaFarge CG, Fyler DC, Weisul J, Monroe RG: Regional coronary venous oxygen saturation and myocardial oxygen tension following abrupt changes in ventricular pressure in the isolated dog heart. Circ Res 34: 672, 1974
Determinants of left ventricular hypertrophy and oxygen supply in chronic aortic valve disease.

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