Hypertrophy has been thought to be one of the important compensating mechanisms for excessive load on the hearts, especially in chronically loaded hearts, and a hearts with an increased cardiac mass has been believed to be able to perform an increased work. Linzbach suggested that cardiac hypertrophy increased until the force generated per unit cross section of ventricular wall returned to normal value.

Although hypertrophy might be an adaptation to an increased load, it does not necessarily mean that cardiac functions are restored completely to normal levels by hypertrophy. It might even be considered that the abnormal ventricular function of the hypertrophied heart, per se, leads the heart into the final decompensation.

In this study, we selected patients with regurgitation and with cardiomyopathy, and compared their hemodynamics to those of normal left ventricle. Alterations in left ventricular stress and pump functions were particularly emphasized.

Subjects and Methods

Thirty-one adult patients were studied during diagnostic right and left heart catheterization. They were categorized according to their major cardiac involvement. Four patients, who were considered as having normal left ventricles after the examination, were categorized as normals. Five patients had mitral stenosis (MS) without significant regurgitation. Nine patients had significant mitral or aortic regurgitation (MI, AI), and they were regarded as the left ventricular volume-overloaded group. Nine patients were diagnosed as having cardiomyopathy (CM), one of which was secondary to progressive muscle dystrophy, and the others were idiopathic. Four patients, categorized as "others", included 2 with ASD, 1 with healed carditis and another with prolapse of mitral valve of slight degree, and their left ventricle were considered to be almost normal.

Left ventricular catheterization was performed in all patients through retrograde or transseptal route, and pressure was recorded by fluid-filled catheter connected to a TMI transducer. After measurement of cardiac output by Fick or dye-dilution method, left ventriculography were performed using either 16 mm cine at 48 frames/sec, 35 mm cine at 60 frames/sec or large roll film at 6 frames/sec. Left ventricular volumes were calculated by the single plane area-length method described by Sandler and Dodge. Various values were introduced from these data of left ventricular pressures, volumes and dimensions, as were described in the following section.

Calculations

1) Left ventricular wall mass was determined using left ventriculogram at the end-diastole.

\[
LV \text{ Mass} = \frac{4}{3} \pi \left( L/2 + h \right) \left( D/2 + h \right)^2 - \frac{L/2 \cdot D^2}{4} \times 1.05 \text{ (Gm)} \ldots (1)
\]

where \( L \) : long axis of left ventricular cavity at end-diastole in cm,

\( D \) : short axis of left ventricular cavity derived by the area-length method in cm,

\( h \) : wall thickness of the midportion of left ventricle measured by planimetry in cm,

1.05 : specific gravity of cardiac muscle

2) Left ventricular total stroke work: Total stroke volume \times\text{ mean systolic pressure} \times 1.36

(Gm. cm)

The second Department of Internal Medicine, University of Tokyo, Tokyo, Japan

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3) Left ventricular wall stress

The force generated in a unit cross section area of the left ventricular wall is defined as left ventricular wall stress, and expressed in Gm/cm² or dyne/cm². Although stress in the ventricular wall is not distributed evenly from epicardium to endocardium, and from equator to apex, several investigators calculated an averaged stress between epicardium and endocardium. In this study, the left ventricle was assumed to be a thick-walled prolated spheroid, and average stresses were calculated at the equator according to the method of Falsetti et al., which was thought to be suitable for application to thick walled model (Fig. 1).

The averaged stress in the equatorial direction at the equator ($\sigma_e$) was given by

$$\sigma_e = \frac{P \cdot D (2L^2 - D^2)}{4h (L^2 + D \cdot L)} \times 1.36 \text{ (Gm/cm}^2\text{)}$$

where $P$ : left ventricular pressure in mmHg.

Averaged stress in the meridional (longitudinal) direction ($\sigma_m$) was given by

$$\sigma_m = \frac{P \cdot D^2}{4h (D + h)} \times 1.36 \text{ (Gm/cm}^2\text{)}$$

The time-course of stresses were calculated through one cardiac cycle in several patients, and examples were shown in Fig. 5. Since frame-to-frame calculation was not feasible in all the ventricles, a peak systolic stress of model was also calculated. Here, the equatorial peak systolic stress ($\sigma_{c-s}$) was calculated for the sphere, which had a volume equal to the average of observed end-diastolic and end-systolic volumes, a pressure equal to the peak systolic pressure and a wall thickness pertinent to the observed left ventricular mass. The simplification seems to be justified, because peak systolic $\sigma_e$ and $\sigma_m$ occur usually in early systole when ventricle has ejected about half of its stroke volume, and when the pressure has reached near the peak systolic level (Fig. 5). The modification was supported further by a significant linear correlation between $\sigma_{c-s}$ and $\sigma_e$ or $\sigma_m$ (unpublished observation).

Thus, peak systolic stress ($\sigma_{c-s}$) was expressed by

$$\sigma_{c-s} = \frac{Ps \cdot r_s^2}{h_s (2r_s + h_s)} \times 1.36 \text{ (Gm/cm}^2\text{)}$$

where $Ps$ : left ventricular peak systolic pressure in mmHg.

$$r_s : \left\{ \frac{3}{4h} \cdot \frac{LVEDV + LVESV}{2} \right\} ^{1/2} \text{ in cm}$$

$$h_s : | (r_{ED} + h_{ED})^3 - r_{ED}^3 + r_s^3 | ^{1/2} - r_s \text{ in cm}$$

$r_{ED}$ : radius of the sphere compatible to the observed left ventricular end-diastolic volume

$h_{ED}$ : wall thickness of the sphere recalculated from $r_{ED}$ and the obesrbed left ventricular mass.

4) Intrastate left ventricular mid-wall tension (T) was calculated assuming the left ventricle to be a sphere, and was given by

$$T = \frac{P(r + h/2)}{2} \times 1.36 \text{ (Gm/cm)}$$
where $P_s$ : left ventricular pressure in mmHg,  
$r$ : radius of sphere in cm, compatible to the observed left ventricular volume.  
h : wall thickness observed instantaneously in cm.

Since frame-to-frame calculation of instantaneous tension was impracticable to perform in all patients, a systolic tension ($T_s$) was also calculated as:

$$T_s = \frac{P_s \cdot (r_s + h_s/2)}{2} \times 1.36 \text{ (Gm/cm)}$$  \(\ldots (7)\)

where $P_s$, $r_s$ and $h_s$ were same as described for equation (5).

5) Mean circumferential fiber shortening velocity (mean $V_{cf}$) was given by

$$\text{mean } V_{cf} = \frac{(r_{ED} + h_{ED}/2) - (r_{ES} + h_{ES}/2)}{\text{circ/sec}}$$

where $SEP$ : systolic ejection period, in sec.

**Results**

1) Left ventricular volume and mass

Left ventricular end-diastolic volume index (LVEDV/BSA) ranged from 65 to 100 ml/M$^2$ (mean 78, SD ± 13.9) in the normal group, between 82 and 112 (98.5 ± 11.2) ml/M$^2$ in MS group, and between 70 and 109 (84.3 ± 15.2) ml/M$^2$ in the group of “others”. The average values in these 3 groups were not different significantly from each other as shown in Fig. 2a. LVEDV/BSA in the group of volume load (MI, AI) was 227.2 ± 76.5 (98 ~ 367) ml/M$^2$, and that in the group of cardiomyopathy (CM) was 134.3 ± 48.6 (77 ~ 246) ml/M$^2$. The average values in the latter 2 groups were higher significantly than in the normal group ($p < 0.01$).

Left ventricular wall mass was much larger in the groups of volume load and cardiomyopathy than in the groups of normal, MS and “others” as shown in Fig. 2b. Average value in Gm/M$^2$ was 216.1 ± 82.9 in volume load, 293 ± 150.2 in
cardiomyopathy, 75.9 ± 24.4 in normal, 59.5 ± 5.1 in MS and 74.8 ± 16.7 in “others”. The relation between LVEDV/BSA and LV mass/BSA was shown in Fig. 3. The increase in LV mass tended to be proportional to the increase in LVEDV in the group of volume load, while in the group of cardiomyopathy such a tendency was not found and the increase in mass seemed to be improporionately larger than increase in LVEDV in 5 out of 8 ventricles.

When LV mass was related to the midwall peak systolic tension (Tₚ) as was shown in Fig. 4, larger mass tended to be accompanied by higher systolic tension in both volume loaded and cardiomyopathic ventricles. This suggested a possibility that the increase in mass might be compensatory to the increase in systolic tension resulting from ventricular dilatation. The relation was, however, obscured by the wide scatter of individual value. To clarify this possibility, left ventricular wall stress was calculated, and was described in the next section.

2) Left ventricular wall stress

Fig. 5 shows time-courses of left ventricular tension and stresses through one cardiac cycle (upper panel), as well as left ventricular pressure, volume and wall thickness (lower panel) in 3 patinetts. A case with ASD who was thought to have normal left ventricle was shown in the left column. The equatoritorial stress at equator (σₑ) had much higher values than meridional stress (σₑ) throughout systole, and had its peak in early systole, then decreased rapidly. A case with aortic...
regurgitation in the central column had an increased left ventricular end-diastolic volume and its systolic tension was higher than that of the case with ASD. Peak equatorial stress was, however, not different from, or even lower than in ASD. A case of hypertrophic cardiomyopathy in the right column had a lower equatorial stress than in either ASD or aortic regurgitation.

Peak systolic stress ($\sigma_{c-s}$) was calculated in all cases using equation (5), and was shown in Fig. 6. Averaged systolic stress was 189 ± 32.7 (SD) Gm/cm² in the normal group, 160.9 ± 45.8 in MS and 157.0 ± 14.8 in "others". These 3 values were not different significantly. In the group of volume load, 2 cases had abnormally high systolic stress, and the remaining 6 had stress values in the normal range. In the group of cardiomyopathy, one case had abnormally high systolic stress, another one had normal stress and remaining 6 had subnormal stress. The 2 cases with volume load and the one with cardiomyopathy who had increased systolic stress had severe symptoms of congestive failure clinically.

3) Pump function of the left ventricle

A kind of myocardial efficiency was expressed in terms of left ventricular stroke work per unit weight of left ventricular wall mass, and was plotted against total ejection fraction in Fig. 7. The area surrounded by the broken lines was the normal range of distribution. Stroke work per unit weight of myocardium was within normal range in most of the cases of both groups of MS and "others", although ejection fraction was decreased slightly in these groups. In the group of volume load, 3 out of 9 cases had subnormal efficiency and 7 out of 9 had decreased ejection fraction, indicating slight or moderate impairment of their left ventricular pump function. In the group of cardiomyopathy, all, except one, had decreased myocardial efficiency and 5 out of 8 had decreased ejection fraction. This indicated severe deterioration of pump function in most cases with cardiomyopathy.

In Fig. 8, the relation between the peak systolic stress ($\sigma_{c-s}$) and the mean circumferential fiber shortening velocity (mean Vcf) was demonstrated. The square circumscribed by the broken lines shows the range of normal distribution. The plots for the volume loaded ventricles.
distributed along the arbitrary hyperbolic line, the higher the systolic stress, the lower being the mean Vcf. In group of cardiomyopathy, mean Vcf were much lower than cases with volume overload, despite of low peak systolic stress, and this also suggested that deterioration of pump function was more apparent for ventricle with cardiomyopathy.

**DISCUSSION**

Ventricular dilatation is expected to be accompanied by an increase in wall tension according to Laplace's law. In clinical setting, however, a chronically dilated heart usually has a thickened wall, suggesting a form of adaptation to increased tension. The aim of present study were 1) to test the extent of stress normalization with ventricular hypertrophy, and 2) to clarify if the normalization of stress is accompanied by normal pump function in the hypertrophied ventricle. Therefore, hypertrophied left ventricles of 2 different natures, one with volume load and another with primary myocardial involvement were studied. Three groups with normal or near-normal left ventricles served as controls.

Normal values of left ventricular volume and mass obtained by us were compatible with values reported by other investigators. Increased volume and mass were frequently seen in both the volume loaded and cardiomyopathic left ventricles, but mass-volume ratio was not similar in both groups. The increase in mass was proportional to the increase in volume in the former

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Fig. 7. Total ejection fraction derived from left ventriculogram and stroke work per unit left ventricular wall mass (LV total work/LVmass).

Fig. 8. Left ventricular peak systolic stress and mean circumferential fiber shortening velocity (mean Vcf).

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group, while it was disproportionately large in the latter group (Fig. 3).

The difference between the 2 groups with hypertrophy was even more obvious when the systolic stress was compared. In volume loaded ventricles, peak systolic stress was within normal range, except in 2 cases with coagestive heart failure (Fig. 5). This suggested that the degree of cardiac hypertrophy was adjusted just to maintain the systolic stress at the normal level. The 2 cases with elevated systolic stress had either chronic or acute left ventricular overload. The cause of the high systolic stress and clinical heart failure was likely to be development of myocardial failure leading to further ventricular dilatation in the former, and unfinished process of hypertrophy supplying insufficient muscle mass relative to the degree of overload in the latter. Similar findings were observed also by other investigators. Hoed et al. calculated peak systolic stress in pressure-overloaded ventricle (aortic stenosis), and found that compensated ventricle had normal stress, but decompensated ventricle had elevated stress value.

The systolic stress of patients with cardiomyopathy without severe congestive failure was normal or below normal in our study. This finding suggests that the degree of cardiac hypertrophy in cardiomyopathy is not adjusted to maintain systolic stress at normal level; in other words, cardiac hypertrophy of cardiomyopathy may not be an adaptational mechanism to high wall tension. However, one possibility must be considered in this connection: the fraction of efficiently contracting myofibrillar unit in the total left ventricular mass is unknown in our study, and may be reduced in cardiomyopathy. If this is the case, the actual stress per unit of contractile element may be normal or even elevated in cardiomyopathy. Although definite conclusion cannot be obtained at the present time, the low calculated systolic stress seemed to be a sign of cardiac hypertrophy which is different from that in volume-loaded hearts.

Mason et al. have shown a depression in myocardial contractility in hypertrophied hearts even in absence of clinical failure, and stated that the conclusion applied both to hypertrophy from primary myocardial disease and to that from pressure overload. In our study, ventricular pump function, in terms of stroke work per unit wall mass, total ejection fraction or mean Vcf was depressed frequently in hypertrophied left ventricles in both groups of volume load and of cardio-

myopathy in clinically compensated states. The deterioration of the left ventricular pump function was more severe in cardiomyopathy than in volume load, despite the lower systolic stress in the former.

SUMMARY

A total of 31 patients were studied during cardiac catheterization. Hemodynamics in 9 cases with cardiac hypertrophy secondary to chronic volume load (MI, AI) and in 9 cases with cardiomyopathy were compared to those in 5 normal cases, 5 cases with MS and 5 cases with near-normal left ventricle. A hypertrophied left ventricle had an enlarged cavity, an increased wall mass and an elevated systolic midwall tension. Peak systolic stress in left ventricular wall was normal in compensated patients with volume load, but below normal in compensated patients with cardiomyopathy. Peak systolic stress was elevated in decompensated patients either with regurgitation or with cardiomyopathy. The significance of this stress difference between volume over load and cardiomyopathy was discussed. Depressed pump function was observed in hypertrophied left ventricle especially in cardiomyopathy.

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