Quantitative Angiocardio-angiography

III. Relationships of Left Ventricular Pressure, Volume, and Mass in Aortic Valve Disease

By J. Ward Kennedy, M.D., R. D. Twiss, M.D., J. R. Blackmon, M.D., and H. T. Dodge, M.D.

SUMMARY

Quantitative angiographic techniques have been used to determine left ventricular volume and mass in 100 patients with isolated aortic valve disease. The patients were divided into three groups: aortic stenosis (AS), 22 patients; aortic regurgitation (AR), 38 patients; and combined stenosis and regurgitation (AS+AR), 40 patients. The distribution of left ventricular volume and mass and their relationship to standard intracardiac pressure and flow determinations are presented for each group in order to define the hemodynamic and functional characteristics of the left ventricle in these patients. Mean values for end-diastolic volumes (EDV) in the three groups were AS = 85 ml/m², AS+AR = 143 ml/m², and AR = 197 ml/m². Mean values for ejection fraction (EF = SV/EDV) were similar in the three groups, AS = 61%, AR = 55%, AS+AR = 58%. Left ventricular mass (LVM) was smaller in AS, mean = 167 g/m², and similar in AR, mean = 232 g/m², and AS+AR, mean = 235 g/m².

Left ventricular filling pressure (LVEDP) was correlated with EDV in AS, r = 0.45, P < 0.05, and AS+AR, r = 0.51, P < 0.001, but not in AR. A similar relationship was seen between LVEDP and EF. The arteriovenous oxygen difference correlated well with EF in AS, r = −0.76, P < 0.001. This relationship was weaker in AS+AR, r = −0.45, P < 0.01, and AR, r = −0.45, P < 0.01. Correlations were also present between increased LVM and elevated LVEDP and increased LVM and decreased EF in patients with AS and AS+AR.

Additional Indexing Words:
Rheumatic heart disease Left ventricular hypertrophy Left ventricular function Ejection fraction

This paper presents the quantitative angiographic findings in 100 cases of aortic valve disease. Patients have been divided into three groups; those with pure aortic regurgitation, those with pure aortic stenosis, and those with combined aortic stenosis and regurgitation. Patients associated with mitral valve disease were excluded. This spectrum of disease provides an opportunity to study the effects of pressure and volume overload, and the combination of these stresses on the functional characteristics of the left ventricle.

Methods

Patients with isolated aortic valve disease were selected from the cardiac catheterization files of the University of Washington, and the VA Hospital, Seattle. One hundred patients with reliable hemodynamic data, biplane angiograms with adequate visualization of the left ventricle, and without significant arrhythmia during ventricular opacification were included in this study. Patients were classified into three groups: (1) 22 patients with aortic stenosis (AS), (2) 38 with aortic regurgitation (AR), and (3) 40 with combined aortic stenosis and regurgitation (AS...
Patients in group 1 had an aortic valve gradient of more than 15 mm Hg and less than 25% of the left ventricular minute flow (LVMF) regurgitating through the aortic valve. Patients in group 2 had no more than a 5-mm gradient across the aortic valve (usually none) and greater than 25% regurgitation. Those in group 3 had aortic valve gradients greater than 5 mm Hg and greater than 25% regurgitation.

All patients had right and left heart catheterization with left ventricular and aortic or peripheral arterial pressures recorded. Significant

### Table 1

Quantitative Angiocardiographic and Hemodynamic Data

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*N = 16.
†AS N = 22; AS+AR N = 40; AR N = 38.
‡N = 22.
§N = 26.
**From Barratt-Boyes and Wood.8
††From Samet and associates.9

Abbreviations: AR = aortic regurgitation; AS = aortic stenosis; AS+AR = combined aortic stenosis and regurgitation; EDV = end-diastolic volume; SV = stroke volume; ESV = end-systolic volume; EF = ejection fraction (ratio of stroke volume to end-diastolic volume); LVM = left ventricular mass; LVMF = left ventricular minute flow; CI = cardiac index; RF = regurgitant flow; LVEDP = left ventricular end-diastolic pressure.
mitral stenosis was ruled out by the absence of a pressure gradient across the mitral valve. Mitral regurgitation was absent in all but a few patients who had marked dilatation of the left ventricular chamber resulting from severe aortic insufficiency. As mitral regurgitation in these patients was thought to have developed as a result of severe aortic insufficiency, they were included in the study. The mean pressure gradient across the aortic valve during systole was measured by planimetry of the area between the left ventricular and central aortic or peripheral arterial tracing. The aortic valve area was calculated by the Gorlin formula utilizing the LVMF determined from the angiocardiograms (the actual flow across the aortic valve, not the forward cardiac output, as is generally used in this formula). Angiocardiography was carried out with a pressure injection of 40 to 80 cc of contrast material into the left atrium, left ventricle, or aortic root. Films were exposed at 6/sec with a biplane Elema-Schonander film changer. Simultaneous electrocardiogram and film exposures were recorded. Left ventricular volumes were calculated by the length-area method of Dodge and associates, and left ventricular mass (LVM), by the method of Rackley and co-workers. In about half of the cases studied, complete time-volume curves were constructed, and in the remaining cases the volumes were calculated at end-diastole and end-systole for two or three consecutive beats. Angiographic stroke volume (SV) was determined by subtracting end-systolic volume (ESV) from the end-diastolic volume (EDV). The left ventricular minute flow (LVMF) was determined by multiplying the SV by the heart rate during angiocardiography. Forward flow was measured prior to angiocardiography by the direct Fick method. Regurgitant flow (RF) was determined by subtracting the forward from the LVMF. The ejection fraction (EF) was determined by dividing SV by the EDV to express the SV as a percentage of the EDV. The three groups were analyzed with routine computer programs to yield means, standard deviations, correlation coefficients and P values. A computer program for the estimates of population cumulatives recently reported by Kronmal and Tartar was utilized to derive the cumulative percentage curves which were written out on an x-y plotter and photographed for publication.

Results

Quantitative data for the three groups of patients and normal individuals are presented in table 1. In AS the EDV/m² ranged from 51 ml to 190 ml with a mean of 85 ml. In AR, EDV/m² ranged from 98 ml to 393 ml with a mean of 197 ml. Figure 1 shows the distribution of this variable in terms of the cumulative percentage curve for all patients in each group. Normal values of EDV/m² for this laboratory for 16 patients without heart disease ranged from 53 ml to 120 ml with a mean of 70 ml. As indicated by the graph, approximately 86% of those with AS demonstrated an EDV/m² within this range. In comparison, fewer than 10% with AR had a normal EDV/m². Forty per cent of the AS + AR group had an EDV/m² within the normal range.

Cumulative percentage plots of LV stroke volume/m² (LVSV/m²) are given in figure 2. The relationship between the distribution of values in the three groups was similar to that seen for EDV/m² (fig. 1). LVSV/m² was within the range of normal for this laboratory (31 ml to 75 ml; mean, 45 ml/m²) in 85% of patients with AS, whereas 15% of the cases had diminished stroke volumes. Eighty percent of patients with AR and 50% with AS + AR had an LVSV/m² greater than normal.

There was only a 6% spread in the means for EF in the three groups, AS = 61%, AS + AR = 58%, and AR = 55%, and the cumulative distribution of values was similar in the three groups. The EF was within the

![Figure 1](http://circ.ahajournals.org/lookup/fig/XXXVIII.1168)

_Cumulative distribution plot for end-diastolic volume in patients with aortic stenosis, aortic regurgitation, and combined aortic stenosis and regurgitation. The normal range is indicated by the vertical lines._

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Figure 2
Cumulative distribution plot for left ventricular stroke volume in patients with aortic stenosis, aortic regurgitation, and combined aortic stenosis and regurgitation. The normal range is indicated by the vertical lines.

normal range (56% to 78%) in approximately one half of the patients; a few supernormal values occurred in each group.

LVM/m² was nearly identical in both magnitude and distribution in AR and in AS + AR, whereas LVM/m² was distinctly smaller in patients with pure AS (fig. 3). Body surface area averaged 0.15 m² less in patients with AS than in those with AR or AS + AR, but this minor difference does not account for the smaller LVM in this group.

The cumulative distribution of LVMF/m² for each group was similar to the distribution of EDV in these groups (fig. 4). Flows greater than 10 L/min/m² were observed in 15% of patients with AR.

Data for forward cardiac output/m² by the Fick principle were similar in the three groups and lower than normal values for this and other laboratories. The cumulative distribution of values for regurgitant flow (RF) in liters per minute in the three groups of patients is shown in figure 5.

Left ventricular end-diastolic pressure (LVEDP) was highest in AS + AR with a mean of 20.8 mm Hg, and lowest in the group with AS with a mean of 13.7 mm Hg. The high value of 60 mm Hg was present in

Figure 3
Cumulative distribution plot for left ventricular mass in patients with aortic stenosis, aortic regurgitation, and combined aortic stenosis and regurgitation. The normal range is indicated by the vertical lines.

Figure 5
Cumulative distribution plot for regurgitant flow in L/min in patients with aortic stenosis, aortic regurgitation, and combined aortic stenosis and regurgitation.
A patient with severe AR and profound heart failure.

Although EDV and regurgitant SV are statistically dependent variables, their relationship was variable between the AR and AS + AR groups. Figure 6 presents the close relationship in AR (r = 0.91). In AS + AR this correlation is not as close (r = 0.46). This difference probably results from the additional pressure load in patients with AS + AR with resultant myocardial dysfunction. Because of this observed difference, EDV alone is not a valid indicator of the magnitude of regurgitation in AS + AR. In patients with AR and myocardial dysfunction, excessive LV dilatation is indicated by a low EF. Several such patients are included in figure 6 and are represented by points which are considerably above and to the left of the regression line.

Figure 7 presents the relationship between EDV (ml/m²) and LVEDP in 39 patients with AS + AR. In these 39 patients the correlation coefficient (r = 0.51, P < 0.001) was significant, but the relationship is not close enough to predict EDV from LVEDP. A less significant correlation was seen in 22 patients with AS (r = 0.45, P < 0.05). In 33 patients with AR, the relationship between EDV and LVEDP (r = 0.31, P < 0.1) was not significant.

Since EF has been used as an index of LV function,⁠¹⁰ its comparison with other parameters of cardiac function is of interest. The EF was compared with LVEDP in the three groups (AS: r = −0.45, P < 0.05; AS + AR: r = −0.46, P < 0.01 and AR: r = −0.19, not significant). Although the correlation coefficients were statistically significant in patients with AS and AS + AR, the relationship was not close.
The relationship between EF and arteriovenous oxygen difference (A-V O₂) in patients with AS is presented in figure 8 (AS: r = -0.76, P < 0.001). Significant correlations are also present in the other two groups (AS + AR: r = -0.45, P < 0.01; AR: r = -0.38, P < 0.001). These data indicate that EF and A-V O₂ differences are closely correlated in patients with aortic valve disease, although this relationship is less valid in those with valvular regurgitation.

Although the EF and EDV are statistically dependent variables, the EF is independent physiologically. This is clear from the variable relationship between EDV and EF in these groups of patients. A good correlation was seen in AS (r = -0.71, P < 0.001) and in AS + AR (r = -0.64, P < 0.001), and no correlation was present in AR (r = -0.02). These differences emphasize the fact that the EDV increases normally and in proportion to the magnitude of regurgitation in patients with AR, whereas an increase in EDV in patients with pure AS is indicative of decreased myocardial function.

In chronic heart disease, increase in LVM might be expected to be relative to the magnitude of work imposed on the LV. For this reason, the relationship between LVM and the severity of aortic stenosis as judged by the aortic valve area and the severity of aortic regurgitation as indicated by RF have been studied. In patients with AS, LVM was found to have no correlation with aortic valve area which ranged from 0.45 to 1.90 cm², mean, 0.88 cm², or aortic valve gradient which ranged from 16 to 90 mm Hg (mean, 49 mm Hg). In AR a correlation was found between LVM and RF (r = 0.48, P < 0.01).

An increase in LVM might be expected to change LV compliance and result in an elevation in LV filling pressure. For this reason, LVM has been compared with LVEDP in each group. A significant relationship was seen between an increase in LVM and an increase in LVEDP in AS (r = 0.38, P < 0.05), and in patients with AS + AR (r = 0.734, P < 0.001). No correlation was present between these variables in patients with AR (r = 0.001).

It is also pertinent to study the relationship between an increase in LVM and the function of the LV as judged by the EF. As noted above, significant correlations are seen in AS and AS + AR (in AS, r = -0.58, P < 0.01; in AS + AR, r = -0.40, P < 0.01), but no relationship was apparent in patients with AR (r = 0.02).

Discussion

The addition of quantitative angiographic data to standard intracardiac pressure and flow observations permits a more precise description of changes in ventricular anatomy and function due to disease. Since the filling pressure of the left ventricle has been used traditionally as an indicator of left ventricular function, it is of interest to examine the relationship of the LVEDP and EDV. Previous reports have pointed out the weak relationship between these variables in a variety of cardiac patients. Those studies related EDV and LVEDP in patients with mixed hemodynamic lesions. This study has examined the relationship between EDV and filling pressure in three large, relatively homogeneous groups of patients. With this separation of hemodynamic lesions, it is clear that EDV and LVEDP are related in patients with AS but not in those with AR. Patients with combined lesions tend to be similar to those with AS in this respect. This relationship, however, is not close enough to predict EDV from LVEDP in any of the groups. These studies have also shown that, as an isolated variable, an elevated LVEDP is not a reliable indicator of LV dysfunction in any given individual, since some patients without other evidence of myocardial failure (normal EF and A-V O₂ difference) have high filling pressure. Nevertheless, changes in LVEDP observed during exercise or drug administration may be helpful in defining the functional characteristics of the left ventricle.

Left ventricular volume is normal in most patients with AS. The patient with ventricular dilatation usually has both an elevated...
LVEDP and A-V O₂ difference. Since the patient with AS has a normal or decreased stroke volume, ventricular dilatation must result in a low EF. The EF and the A-V O₂ difference have a high correlation in this group, indicating that the measurement of A-V O₂ difference is a valid index of the ventricular function in these patients. When significant regurgitation is present, however, the A-V O₂ difference becomes less reliable in this respect. Advanced myocardial failure in patients with AS is characterized by an EF less than 40% and an A-V O₂ difference greater than 60 ml/L. The severity of AS as judged by the aortic valve area or the aortic valve gradient does not correlate with these parameters of ventricular function. This is probably because of the important role played by time, as well as by the severity of the outflow obstruction in the development of ventricular failure. The magnitude of myocardial hypertrophy in AS also fails to correlate with the severity of the valvular lesion. Here again, the duration of disease may be the determining factor.

Measurements of left ventricular volume in patients with aortic regurgitation have shown, as previously reported,¹⁰⁻¹³ that the increase in EDV is proportional to the amount of regurgitation present. Because of this constant relationship between EDV and the magnitude of regurgitation, in the absence of myocardial dysfunction, appropriate LV dilatation can be assessed for each patient. Inappropriate or excessive dilatation is characteristic of myocardial failure and is indicated by a low EF. Since ventricular volumes are normally large in patients with AR, further dilatation resulting from myocardial failure is not readily appreciated. Quantitation of ventricular volume and RF has been most helpful in making clinical decisions in this group of patients.

Since the EF is derived from the ratio of the LV stroke volume and the EDV, it is statistically dependent upon EDV. Physiologically, however, the EF appears to be independent of EDV. This is seen in the close relationship between the EF and the EDV in patients with AS, and the absence of such a relationship in those with AR. Further evidence for the physiological independence of EDV and EF is seen in patients following aortic valve replacement.¹⁴ The EF was normal preoperatively in all but one of these patients, despite a wide range in the EDV. Following surgery, a marked reduction in EDV occurred in several, while the EF changed substantially in only one.

Considerable efforts are currently being made to define the functional characteristics of the left ventricle in terms of force-velocity relationships.¹⁵ These studies have added to the understanding and definition of myocardial contractility, but at present are too complex for application in the clinical laboratory. The determination of left ventricular volume during diastole and systole is now a relatively simple technique and allows the calculation of the ejection fraction. This ratio of stroke volume to end-diastolic volume appears to us to be the best single expression of the functional status of the left ventricle in patients with chronic heart disease. Wide application of this method of hemodynamic evaluation will help to evaluate the role of myocardial failure in patients with valvular heart disease. This method will also make it possible to evaluate better myocardial function as a determinant of operative risk and of the likelihood for benefit from surgical correction of valvular defects.

These studies have shown that patients with AS have less LVM (hypertrophy) than patients with AR or AS+AR. This finding may indicate only that patients with AS come to medical attention earlier in the course of their disease. An alternative explanation is that work imposed on the left ventricle by a pressure load is less than that resulting from a volume load or the combination of these stresses. Badeer,¹⁶ in his excellent review of myocardial hypertrophy, was of the opinion that in most instances increased stroke work was the stimulus to hypertrophy. The observations by Dodge and Baxley¹⁷ that LV systolic stroke work and LVM are well correlated in various types of heart disease are consistent with this view. Our postoperative
observations indicate that the reverse is also true; that is, that with a reduction in stroke work following surgical repair of the aortic valve, a parallel reduction in LVM occurs. These studies have shown a correlation between increased LVM and elevated LVEDP and between increased LVM and decreased EF in patients with AS and AS + AR. These relationships were not present in those with AR. These findings may indicate that a greater degree of myocardial fibrosis occurs in such patients. Studies are currently underway to quantitate fibrosis in postmortem hearts in an attempt to evaluate the relationship between these parameters of myocardial function and alterations in myocardial structure.18

References
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