Left Ventricular Volume in Aortic Stenosis Measured by an Angiocardiographic and a Thermodilution Method

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The action of the left ventricle is impaired in aortic stenosis to a variable degree, and since the extent of myocardial damage will influence the management and prognosis in the individual patient, some way of determining myocardial function is required. For a full assessment of left ventricular performance it is necessary to measure the changes in both volume and pressure throughout the cardiac cycle. Pressure measurements are easily obtained by left heart catheterization, but provide an incomplete picture if the left ventricular volume is not known. The heart size on the chest radiograph is often used in the estimation of left ventricular volume in aortic stenosis, but a more precise measurement is desirable. The two presently available methods of volume determination involve measurement of the angiocardiogram taken in two planes, or the injection of cold saline into the left ventricle and the recording of the beat by beat temperature change in the ascending aorta. These methods are subject to different technical difficulties, and, as neither has received wide acceptance as providing an accurate estimate of left ventricular volume, we have included both in our routine pre-operative assessment of patients with aortic stenosis. In this report we give the results of volume measurements in aortic stenosis, compare the angiocardiographic with the thermodilution technique, and show the poor relation between these measurements and the size of the heart in the conventional radiograph.

PATIENTS AND METHODS

Left ventricular volume measurements were made during the course of pre-operative left heart catheteriza-

tion in 23 patients with aortic stenosis, aged from 9 to 62 years, the obstruction being at valve level in all but one, where the stenosis was a subvalvar fibrous ring (Table I). All patients were in sinus rhythm and, despite the frequent finding of an early diastolic murmur, none of the patients was judged on clinical or haemodynamic grounds to have significant aortic regurgitation. Volume measurements were not made when there was any mitral valve regurgitation.

A postero-anterior chest radiograph was available, taken at a tube to film distance of six feet for each patient, and from this the heart size was expressed as the cardiothoracic ratio.

In early studies promethazine (phenergan) 50 mg. was given intramuscularly before the procedure, but later investigations were carried out without premedication. Catheterization of the right heart from the right long saphenous vein using local skin anaesthesia was followed in each case by transseptal puncture, placing a Brockenbrough catheter in the left ventricle. A No. 6 Gensini catheter was placed in the femoral artery by the percutaneous method and advanced to the ascending aorta. The cardiac output was measured by the injection of indocyanine green into the left ventricle and the withdrawal of blood from the aorta through a Gilford cuvette, calibration being carried out by the dynamic method (Emanuel *et al.*, 1966; Shinebourne, Fleming, and Hamer, 1967). Simultaneous left ventricular and aortic pressures were recorded photographically, with the baseline at the sternal angle, using Statham P23Gb strain gauge transducers, and left ventricular volume was then measured by a thermodilution and an angiocardiographic method.

Thermodilution Method (20 patients). A fine chromel-constantin thermocouple in an 0.020 in. diameter sheath 8 ft. in length, specially adapted for the detection of intravascular temperature (B. Watson and J. Fleming, in preparation), was threaded up the aortic catheter until the tip just protruded immediately above the aortic valve. Between 5 and 8 ml. of cold saline were injected by hand into the left ventricle and the resulting step-

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TABLE I
CLINICAL DETAILS OF PATIENTS

Patient	Age (yr.)	Body surface area (m. ²)	Symptoms			Electrocardiogram left ventricular hypertrophy	Chest x-ray cardiothoracic ratio
			Dyspnoea	Angina	Syncope		
H.B.	61	1.78	—	+	+	Severe	0.42
M.B.	28	1.85	+	—	—	Moderate	0.58
A.B.	60	1.42	+	+	+	Severe	0.70
D.G.	46	1.44	+	—	—	Severe	0.72
F.H.	48	1.58	+	+	—	Moderate	0.47
W.H.	56	1.79	+	+	—	Severe	0.49
E.H.	44	1.50	+	+	—	Severe	0.59
E.L.	51	1.97	+	+	—	Moderate	0.54
C.L.	15	1.55	—	—	—	Moderate	0.41
U.M.	62	1.70	+	+	+	Severe	0.54
E.O.	52	2.02	+	+	+	Severe	0.55
H.O.	61	1.86	—	+	—	Severe	0.53
D.O.	59	1.74	+	—	—	Severe	0.49
R.P.	50	1.85	—	+	+	Moderate	0.48
C.P.	50	1.81	+	—	—	Severe	0.64
*S.R.	9	0.98	+	—	—	Normal	0.54
H.R.	61	1.78	+	—	—	Severe	0.49
H.Ru.	49	1.80	+	—	—	Slight	0.60
V.S.	31	1.74	+	+	+	Severe	0.50
R.T.	55	1.68	+	—	+	Slight	0.56
D.W.	55	1.81	+	+	+	Normal	0.56
N.W.	39	1.78	—	—	—	Moderate	0.45
J.W.	57	1.85	+	+	—	Severe	0.55

* Subvalvar fibrous ring.

wise change in temperature in the ascending aorta recorded photographically. At least five thermodilution curves were obtained from each patient and the ratios of the temperature at successive beats were measured, beginning with the fourth beat after injection and continuing as long as clear steps were visible. The average of all measured ratios (r), and the stroke volume (SV), calculated from the indicator dilution curves, were used for the calculation of the left ventricular end-diastolic volume (EDV) from the formula $EDV = SV/1-r$ (Holt, 1956; Hamer and Fleming, 1967).

Angiocardiographic Method (19 patients). Angiocardiography was performed without general anaesthesia, 40–80 ml. 85 per cent Hypaque being injected in two seconds through the Brockenbrough catheter into either the left atrium or the left ventricle. Left atrial injection was preferred, as this provided good visualization of the left ventricle without causing many extrasystoles. Simultaneous biplane films were obtained using an Elema Schonander roll-film changer at an exposure rate of 4 or 8 per second, and the exact timing of each exposure was marked on the patient's electrocardiogram, using a small silicone solar cell placed on the chest in the path of the x-rays (Fleming and Watson, 1967). The average magnification factors for the apparatus, determined by direct measurement of Starr-Edwards valve rings in a number of patients, are 1.2 for the antero-posterior view and 1.3 for the lateral, and these average factors were used for every patient. The left ventricular volume was calculated according to the method of Arvidsson (1961), assuming the chamber to be an ellipsoid and measuring the long and short axes in both planes. The left ventricular end-diastolic volume was measured from the film exposed during the inscription of the R wave and the

end-systolic volume at the end of the T wave of the electrocardiogram. No beat was used for volume measurements unless separated from a premature contraction by a normal beat.

In 14 patients, angiocardiography was performed within 10 minutes of completing the thermodilution studies, without any evident change in the physiological state. In these patients the end-diastolic volumes obtained by the two methods were compared.

RESULTS

The average end-diastolic volume for the 20 patients studied by thermodilution was 142 ml./m.², SD 34 ml./m.², and for the 19 patients in whom angiocardiographic measurements were made, the average was 141 ml./m.², SD 36 ml./m.² (Table II). The frequency distribution of the thermodilution and angiocardiographic volume measurements is illustrated in Fig. 1 and 2.

The end-diastolic volume of the left ventricle measured within a ten-minute period by both the angiocardiographic and the thermodilution method in 14 patients during the course of one catheter study are compared in a scatter diagram (Fig. 3). The mean value is similar by both methods, and for the individual patients there is reasonable agreement ($r = 0.66$, $p < 0.01$).

The cardiothoracic ratio was measured from the postero-anterior chest radiograph and compared with the measured end-diastolic volume for each patient (Fig. 4). There was no significant correlation between the heart size on the chest x-ray, and

TABLE II
HAEMODYNAMIC MEASUREMENTS AND LEFT VENTRICULAR VOLUME STUDIES

Patient	LV systolic pressure (mm. Hg)	LV end-diastolic pressure (mm. Hg)	Cardiac output (l./m. ²)	Aortic valve area (cm. ² /m. ²)	LV end-diastolic volume (ml./m. ²)	
					Angio-cardiogram	Thermo-dilution
H.B.	205	12	2.52	0.33	97	116
M.B.*	220	30	2.05	0.16	177	119
A.B.	300	22	2.52	0.17		98
D.G.	215	10	2.00	2.00		135
F.H.	200	41	2.80	0.22	145	141
W.H.	220	28	2.30	0.21	99	115
E.H.*	215	25	3.20	0.24	110	146
E.L.	210	10	2.84	0.26	159	178
C.L.	105	9	3.86	> 2.00	132	155
U.M.	225	6	2.18	0.26		135
E.O.	190	40	2.52	0.43	207	188
H.O.	185	8	2.50	0.32	129	154
D.O.	210	-5	3.16	0.43	150	195
R.P.	195	0	2.27	0.27	157	124
C.P.	200	5	1.93	0.29	206	157
S.R.	170	10	4.30	0.44	123	
H.R.	225	12	2.36	0.22	106	80
H.Ru.	110	5	2.44	0.63	172	169
V.S.	250	20	3.28	0.24	97	
R.T.	170	-3	1.60	0.30	105	
D.W.	165	7	2.66	0.22	131	128
N.W.	160	1	3.90	0.93	178	144
J.W.	235	18	3.02	0.25		169
					Average 141	142
					SD 36	34

* Not used in comparison between angiocardigraphic and thermodilution method. (M.B., no suitable end-diastolic film; E.H., ventricular aneurysm.)

left ventricular volume as determined by thermodilution (Fig. 5) or by angiocardigraphy (Fig. 6).

In Fig. 7 the left ventricular end-diastolic volume is compared with the end-diastolic pressure measured through the transeptal catheter. No relation is apparent between left ventricular volume and end-diastolic pressure.

DISCUSSION

None of the presently available techniques for the measurement of left ventricular volume during life can be accepted unreservedly. Both the thermodilution method and the angiocardigraphic method are open to criticism.

FIG. 1.—Left ventricular end-diastolic volume determined by thermodilution in 20 patients.

FIG. 2.—Left ventricular end-diastolic volume determined by angiocardigraphy in 19 patients.

FIG. 3.—Comparison of two methods for measuring end-diastolic volume. $r = 0.66$ $p < 0.01$.

FIG. 5.—Scatter diagram comparing end-diastolic volume measured by thermodilution with cardiothoracic ratio.

Thermodilution Method. The possible errors in our technique for the measurement of left ventricular volume by thermodilution and details of the reproducibility of the measurement are given elsewhere (Hamer and Fleming, 1967). The thermo-

dilution method for measuring left ventricular volume is only applicable if adequate mixing of the cold saline takes place within the ventricle. Rapaport (1966) found that two matched thermistor probes placed randomly in different parts of the

FIG. 4.—Cardiothoracic ratio as an index of left ventricular volume. (A) Cardiothoracic ratio 0.49; end-diastolic volume 195 ml./m². (B) Cardiothoracic ratio 0.70; end-diastolic volume 98 ml./m².

FIG. 6.—Scatter diagram comparing end-diastolic volume measured by angiocardigraphy with cardiothoracic ratio.

FIG. 7.—No correlation is apparent between end-diastolic pressure and end-diastolic volume.

left ventricle of dogs showed equilibration of temperature by the second beat after injection in 75 per cent of cases. Swan and Beck (1960), however, have shown by cine-angiocardigraphy in animals that atrial blood appears in the ventricular outflow tract at the onset of systole, and Bartle and Sanmarco (1966) found that this also applied in man. While there is little doubt that left ventricular mixing is not always complete, indirect evidence that mixing is adequate is provided by Folse and Braunwald (1962), who used a praecordial counting technique after the injection of radio-active ¹³¹I albumin. This method is less influenced by variations in mixing and gives close agreement with thermodilution estimates of ventricular volume. An examination of successive thermodilution ratios in our studies shows no systematic trend, indicating that no further mixing takes place after the third beat. There is no significant mixing of blood in the aorta with the blood of the previous beat, as laminar flow with a flat velocity profile is established just above the aortic valve.

Loss of thermal indicator to the left ventricular wall is a further source of error and an overestimation of left ventricular volume seems likely on this basis, but Rolett, Sherman and Gorlin (1964) estimate the error from this source to be less than 5 per cent. The accuracy of thermodilution is, of course, less at larger left ventricular volumes where the ratio of the steps in the indicator dilution curve is closer to unity. Accurate measurement of the

thermodilution curve needs a sensor with a high frequency response to allow satisfactory equilibration between each beat: our thermocouple fulfils these requirements. Any errors of measurement are compounded, as a separate estimate of stroke volume must be made in addition to the thermodilution curve. Although many factors tend to interfere with the estimation of left ventricular volume by the thermodilution method, analysis of the possible errors does not show any single factor which might invalidate the results.

Radiographic Method. Measurement of the left ventricle opacified by contrast medium might seem a simple approach to estimating left ventricular volume, but the geometrical complications are formidable. The assumption that the left ventricle is ellipsoidal in shape is obviously a gross approximation, but may not give rise to great error as regions of increased curvature are compensated for by other less curved areas of the left ventricular wall. The papillary muscles are included and the sub-aortic region excluded from the volume which is measured, and the irregular trabeculae make it difficult to define the limits of the ventricular cavity, particularly in systole. Estimation of the three diameters of the ellipsoid from angiocardigrams in two planes requires correction of the measurements made on the radiograph to allow for the oblique position of the heart in the chest. Arvidsson (1961) proposed to make this correction for the long dia-

meter only, and we have followed his technique. Various proposals have been made to make the method easier, but any simplification must necessarily increase the error (Dodge *et al.*, 1960). Planimetry of the left ventricular shadow on the angiocardiograms has not, in our hands, led to any significant alteration in the values determined for the short ventricular diameters.

It is difficult to ensure accurate correction for the distortion produced by the x-ray tube being close to the patient when the angiocardiograms are taken. We have estimated the correction factors by observing the magnification of Starr-Edwards valve rings in patients of similar build, and have assumed that these factors are the same for each patient. Clearly some error is produced by variations in the size of the patients, and the distortion is greater for some parts of the ventricle than others, but Dodge *et al.* (1966) estimate these errors at approximately 5 per cent.

We have had particular difficulty in making satisfactory measurements of left ventricular volume in systole in our patients with aortic stenosis, as the left ventricular cavity is often distorted under these circumstances. This problem may be less troublesome in the larger, thinner-walled ventricles of aortic and mitral regurgitation. Such estimates as we have made of left ventricular stroke volume have given unduly large values which we attribute to errors in the measurement of systolic volume. Other workers (Dodge, Hay, and Sandler, 1962; Miller and Swan, 1964) have reported that angiocardigraphic measurements tend to overestimate the stroke volume, and have proposed various arbitrary correcting factors to produce more realistic results. These corrections will have a disproportionate effect on the end-diastolic volume. We have not applied any such correction to our measurements of diastolic left ventricular volume, as no satisfactory justification for their use has been put forward.

The injection of hypertonic contrast medium may in itself alter left ventricular volume and invalidate comparison with measurements made under other circumstances. Although the blood volume and cardiac output are increased after the injection (Hallerman, Rastelli, and Swan, 1963), the immediate effect may be compensated by a transient decrease in venous return, particularly in the presence of left ventricular failure. The action of the contrast medium on the coronary vascular bed may also lead to dilatation of the left ventricle. However, the extent of these changes at the time the angiocardigram is taken is still in doubt, and Dodge *et al.* (1966) have shown that no significant change in left ventricular volume took place during

the five consecutive beats in which the films were taken.

Comparison of Methods. Most comparisons of these two techniques have been indirect. There is a consistent tendency for angiocardigraphic measurements to show a greater degree of emptying of the left ventricle than is found with the thermodilution technique. Good agreement has been demonstrated between left ventricular casts and angiocardigraphic measurements when an arbitrary correction is applied (Dodge *et al.*, 1960). The need to apply correcting factors suggests that the angiocardigraphic measurements overestimate left ventricular volume, but the relevance of these measurements to the situation *in vivo* is doubtful.

The lesser degree of emptying of the left ventricle found with the thermodilution technique is confirmed by other indicator methods (Wilcken, 1965) and by radioisotope methods (Folse and Braunwald, 1962), suggesting that loss of the thermal indicator through the ventricular wall is not a major source of error. The changes in myocardial fibre length needed for this degree of emptying are consistent with microscopical evidence of the behaviour of the sarcomere (Sonnenblick, Spiro, and Spotnitz, 1964), and it is difficult to explain the greater degree of emptying predicted from angiocardiology on this basis.

Few direct comparisons of the two techniques have been reported. Hallerman *et al.* (1963) found poor agreement in dogs using cine-angiocardiology in one plane only, with much larger values by the thermodilution method. The technical errors with fast heart rates in small animals are formidable. Bartle and Sanmarco (1966) compared biplane angiocardiology with simultaneous thermodilution measurements in both men and dogs, and also found significantly larger values by thermodilution.

The good agreement between thermodilution and angiocardigraphic estimates of left ventricular volume in the present study suggests that both methods are valid. The results of thermodilution measurements have been amply confirmed during the techniques of dye dilution and radioisotope injection, and we suggest that the discrepancy between thermodilution and angiocardigraphic estimates of left ventricular volume found by others is due in part to the application of an arbitrary correction factor when using the angiocardigraphic method. Our difficulties with the angiocardigraphic measurement of end-systolic volume lead us to suspect that it is an error in this measurement that has given rise to unacceptable values for the

stroke volume and the adoption of this correction factor.

It is, of course, possible that both methods overestimate the end-diastolic volume to a similar extent. Mixing errors are suspected as a cause of such an effect in the thermodilution technique and the injection of a large volume of contrast medium into the left ventricle may increase the volume of this chamber. Despite these objections, it seems reasonable to conclude from the data presented that our measurements provide a satisfactory indication of the left ventricular volume in our patients with aortic stenosis.

It is unlikely that the cardiothoracic ratio measured from the straight chest x-ray could provide a good measure of left ventricular volume and this has been our finding. Linear measurements on the plain x-ray do not conform to any specific anatomical planes, and include a variable and unknown contribution from right ventricle, right atrium, and occasionally even left atrium.

Left Ventricular Volume in Aortic Stenosis. The mean values for the end-diastolic volumes of the groups of patients with aortic stenosis studied here are significantly in excess of the figures quoted for normal subjects: 70 ml./m.² (SD 20 ml./m.²) for angiographic measurement (Kennedy *et al.*, 1966), 96 ml./m.² (SD 30 ml./m.²) for thermodilution measurement (Gorlin *et al.*, 1964). However, 6 of our patients studied by thermodilution had end-diastolic volumes within the normal range. These results are in close agreement with the findings of other workers who also report abnormally large end-diastolic volumes in some patients when measured by indicator dilution (Gorlin *et al.*, 1964; Bristow *et al.*, 1964; Folse and Braunwald, 1962) and by angiography (Jones *et al.*, 1964).

Linden and Mitchell (1960) have shown that in dogs the end-diastolic length of a ventricular muscle segment is related to end-diastolic pressure, and Braunwald *et al.* (1960) have demonstrated that this also applies in man. End-diastolic pressure measured in the left ventricle has been used by some workers, in the absence of volume studies, to assess the probable size of the left ventricular cavity. When the end-diastolic pressure in the left ventricle measured at left heart catheterization is compared with the end-diastolic volume calculated from the angiogram (Fig. 7), a wide variation in end-diastolic pressures is found, at both normal and large end-diastolic volumes. Of particular interest are the patients having high end-diastolic pressures, but volumes within the normal range, agreeing with the findings in aortic stenosis of Gorlin *et al.* (1964), Braunwald and Ross (1963), and Dodge *et al.* (1962).

Braunwald *et al.* (1960) and Lewis *et al.* (1965) have concluded that the physical properties of the ventricle are altered by left ventricular hypertrophy, the outstanding example being hypertrophic obstructive cardiomyopathy, in which the left ventricular cavity is small and the left ventricular end-diastolic pressure often considerably raised. This concept of an altered compliance of the left ventricular wall during diastole as a result of left ventricular hypertrophy may explain the frequent finding of high end-diastolic pressure with normal end-diastolic volume in patients with aortic valve stenosis, and will also account for the lack of correlation between pressure and volume in the patients studied here. It seems clear from the lack of correlation between pressure and volume measurements in this and other studies that in aortic stenosis the left ventricular volume cannot be predicted from a measurement of the left ventricular end-diastolic pressure.

SUMMARY

Left ventricular end-diastolic volumes have been measured in 23 patients with aortic stenosis, and the agreement between the values obtained by the angiographic method and the thermodilution method when both were used in the same patient suggests that both methods give valid estimates of ventricular volume in this condition. The transverse diameter of the heart, measured as the cardiothoracic ratio on the straight postero-anterior chest radiograph, correlates poorly with the direct measurement of left ventricular volume. Left ventricular volume is well above the accepted limit of the normal in many patients with aortic stenosis.

The left ventricular end-diastolic pressure gives no indication of the volume of the left ventricle in aortic stenosis, and it appears that the distensibility of the left ventricle varies widely from one patient to another.

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