Quantitative Contrast Angiography for Assessment of Ventricular Performance in Heart Disease

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Contrast angiography provides much information about ventricular and valvular size and function. This review describes the calculation of left ventricular chamber volume and wall thickness and the derivation of ejection fraction, cardiac output, mass and wall tension and stress. In patients with valvular regurgitation, valve orifice area can be calculated by using the angiographic output and regurgitant flow determined by comparing the angiographic output with the cardiac output measured using Fick or indicator-dilution techniques. By analyzing ventricular volume in conjunction with pressure, it is possible to assess pressure-volume work, compliance and contractility. Regional wall motion can be measured from the change in ventricular contour with time. When applied clinically, these methods and measurements have been used to determine the hemodynamic characteristics of the compensated and decompensated left ventricle in valvular and coronary heart disease. The information derived from quantifying information in angiographic images contributes to patient diagnosis, assessment of prognosis and evaluation of therapy, and has added to our knowledge concerning the pathophysiology of heart disease.

The development of improved X-ray technology, image intensifiers and filming techniques over the past 30 years has made imaging of the left ventricle by angiographic methods a valuable clinical technique. From images of the left ventricle, methods have been developed for determining dimensions, volume, stroke volume, wall thickness, mass and wall motion of the left ventricular chamber.

The first reports of measurements of left ventricular chamber volumes in human beings using angiography were made more than 25 years ago (1). These data were followed by studies in both experimental animals and human beings to develop and validate methods (2–5), establish normal values for left ventricular volume (6,7) and determine the changes that occur in ventricular volumes with various types of heart disease (as described in a previous review [8]). The various methods for quantifying volume determinations have been adapted to improved high speed filming techniques using cineangiography with differing projections (9–12).

Methods developed for determining left ventricular dimensions and mass (2,3,9–11,13), when combined with cardiac catheterization and measurement of left ventricular pressure, have made it possible to determine wall forces in terms of tension and stress (14) and to estimate elastic properties of the ventricular myocardium in disease (15,16).

This review will discuss the methods and their accuracy for determining left ventricular chamber dimensions, volume and mass from ventriculograms. The hemodynamic characteristics of various heart diseases as determined by applications of these techniques are described. With further development of X-ray technology by such techniques as digital subtraction angiography, improved imaging and further automation of various measurements, quantitation of information in cardiac images will very likely have an increasingly important role in clinical cardiology and cardiovascular research.

Methods of Measurement

Ventricular Volume

Problems. There are three major problems when determining left ventricular chamber volumes from contrast ventriculograms: 1) image distortion from nonparallel X-ray beams, from pincushion distortion in image intensifier systems and from cine projection; 2) differing left ventricular image projections on the X-ray films resulting from the left ventricular spatial position and projections used for filming; and 3) selection of a suitable reference figure for volume calculation from two projections or a single projection (3).
Methods of measurement. In early studies to develop and evaluate methods for computing left ventricular chamber volumes, the left ventricles of human hearts were dis tended with known volumes of barium sulfate paste and imaged with biplane orthogonal filming in differing projections (3). The projected dimensions and areas were determined from the images and corrected for X-ray distortion, and chamber volumes were calculated by several methods and compared with the known volumes (3). These studies demonstrated that chamber volumes that were computed from the projected area of the left ventricular chamber and the longest projected length (so-called area-length method) and by assuming an ellipsoid reference figure were closely correlated with known chamber volumes (r = 0.995) and had a standard error of estimate of ± 8.2 cc.

With this method, volumes (V) were computed as

\[
V = \frac{4}{3}\pi L (Da)(Db),
\]

where L is the longest measured chamber length on either of the biplane films and Da and Db equal the transverse diameters in the orthogonal projections computed from the respective projected chamber areas and lengths. Comparisons of known chamber volumes with computed volumes using the calculated spatial length of the chamber and also by Simpson’s rule were similar to those obtained by using the area-length method but required more complex calculations (3).

An analysis of biplane ventriculograms from subjects with heart disease of various origins demonstrated that the minor diameters of the left ventricular chamber in the two projections were similar and that the direction of the long axis of the left ventricle usually changed only a few degrees during systole (9). Therefore, the projection of the long axis is thought to be relatively constant during systole and diastole. Furthermore, the maximal projected length of the chamber agreed closely with the calculated spatial length (midaortic valve to apex), and chamber volumes were calculated by several projection methods (3). This method compared with the known volumes (r = 0.995) had a standard error of estimate of ± 8.2 cc.

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Kennedy et al. (10) demonstrated that left ventricular chamber volumes computed from films taken in the single right anterior oblique as well as the single anteroposterior projection could be closely correlated with volumes computed from biplane films, but with a systematic overestimation of volume. Because of the known systematic overestimation of volume obtained with all of these methods, the computed volumes in our laboratory are adjusted by regression equations that were determined in these earlier studies (9,10). Both Wynne et al. (11) and Rogers et al. (12) demonstrated that similar equations can also be applied to adjust volumes computed from biplane films taken in both the right and left anterior oblique projections.

Interobserver and intraobserver variability. Accuracy and reliability of volume measurement are also affected by interobserver and intraobserver variability in tracing the endocardial contour. Interobserver variability ranged from 6.6 to 20 ml for end-diastolic volume, from 5.9 to 10 ml for end-systolic volume, and from 0.04 to 0.05% for the ejection fraction (12,17,18). Intraobserver variability was 3.3 ml in measuring end-diastolic volume, 3.2 ml for end-systolic volume, and 0.02% for ejection fraction (18). The greater variability between observers as opposed to within observers suggests that repeated studies on the same patient should be analyzed by the same observer.

Stroke volume. The difference between the end-diastolic volume and the end-systolic volume provides a measure of left ventricular stroke volume. Several studies (4,19) have shown that stroke volumes computed from the ventriculograms agree closely with stroke volumes computed by the independent Fick or indicator-dilution methods. A study (20) in which cardiac dimensions in human subjects were monitored by measurements from epicardial radiopaque markers failed to demonstrate a systematic change in diastolic volume or stroke volume due to contrast medium until at least the seventh beat after injection.

Normal values. Normal values for left ventricular chamber volume as determined by these methods have been established (Table 1). In the average adult, the normal end-diastolic volume ranges from 120 to 130 ml (6). The normal ejection fraction or fraction of the end-diastolic volume that is ejected is 0.67 ± 0.08 (mean ± standard deviation) (6). These values representing the normal adult are similar to those found by other investigators (11,21). Normal values have also been determined for children and infants (7,22).

Values in ventricular dysfunction. In patients with depressed left ventricular myocardial function, the stroke volume is small relative to the end-diastolic volume, the left ventricle is usually dilated and the ejection fraction is reduced (23). An ejection fraction of less than 0.5 is usually considered abnormal. In patients with severe cardiomyopathy or myocardial damage from ischemic heart disease, the end-diastolic volume may be increased to 400 to 500 ml and the ejection fraction depressed to less than 0.10. Even in the presence of compensated valvular heart disease, when there is ventricular dilation and hypertrophy in response to pressure and volume overloads, values for ejection fraction are similar to those found in normal subjects (23).

<table>
<thead>
<tr>
<th>Table 1. Normal Values for Left Ventricular Mass and Volume in Adults</th>
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<td>End-diastolic volume</td>
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<td>End-systolic volume</td>
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<td>Ejection fraction</td>
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<td>Mass</td>
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<td>Wall thickness</td>
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Regurgitant Flow and Valve Areas

The demonstration that, in subjects without arrhythmias, shunts or valvular regurgitation, the angiographic stroke volume agrees closely with stroke volume determined by Fick or indicator-dilution methods (4,19) has aided in the development of a method to quantify mitral or aortic valve regurgitant flow, or both (24). The regurgitant volume per stroke is calculated by subtracting the forward or effective stroke volume determined by the Fick or indicator-dilution methods from the stroke volume measured by angiography (Fig. 1). The accuracy of this method was confirmed by comparing the valve orifice areas determined from the calculated regurgitant flow with orifice areas measured at surgery or postmortem examination (24).

Left Ventricular Mass

In films having proper contrast, the thickness of the ventricular wall usually can be measured and used to estimate the mass of the left ventricle (13). This method of measuring mass was validated by comparing calculated mass with left ventricular weight recorded at postmortem examination (25,26). Errors are found to arise when hypertrophy is eccentric or when pericardial thickening or fluid is present.

In chronic heart disease ventricular hypertrophy occurs in response to 1) increased work from pressure and volume overload, and 2) chronic left ventricular dilation, even when stroke work values are low. The type of hypertrophy differs with pressure and volume overload. With volume overload, ventricular mass increases proportionately to the increase in volume with little increase in wall thickness, so that the end-diastolic volume to mass ratio is approximately 1.0. With pressure overload, there is little or no increase in volume, but wall thickness and mass are increased and mass to end-diastolic volume ratio exceeds 1.0 (27). The hypertrophy and increased wall thickness in compensated pressure and volume overload states are such that peak systolic wall stress values remain within the normal range (28).

Tension and Stress

From knowledge of ventricular dimensions, wall thickness and pressure, it is possible to estimate the forces within the ventricular wall. Tension is the force that tends to pull apart the edges of a slit in a thin-walled structure (for example, a balloon), expressed in terms of force per unit length of slit by the Laplace equation. Stress is the wall force in a thick-walled chamber, expressed in units of force per unit area of the cut surface of a slit; it is equal to tension divided by wall thickness. In an ellipsoid, tension (T_1 and T_2) and stress (S_1 and S_2) in the equatorial and meridional directions, respectively, are proportional to the principal radii of curvature (R_1 and R_2) (14).

Initially, stress was calculated assuming a thin-walled model (14). Stress was also assumed to be constant from the endocardium to the epicardium. This model has provided information about the relation between stress and ventricular dilation and the effect of hypertrophy on stress (28–30). More detailed thick-walled and finite element mathematical models have also been developed (31).

Volume Curves and Pressure-Volume Relations

Volume curve for the cardiac cycle. If ventricular chamber volume is calculated from each frame taken at rapid filming rates such as 60 or 30 frames/s, volume measurements can be plotted with respect to time to construct a volume curve for the cardiac cycle. From analysis of the slopes of the ejection and filling values on these curves, the rates of ventricular volume change during ejection and filling can be determined (27). The maximal rates of ejection and filling are usually similar and typically in the range of 500 mL/s. In patients with severe aortic or mitral valve insufficiency, peak values of over three times the normal are observed. Values for peak systolic volume change as low as 200 mL/s are observed in patients with mitral and aortic stenosis and heart failure from severe myocardial disease.

Pressure-volume curves. Construction of ventricular pressure-volume curves using the relation of chamber pressure and volume with respect to time provides information concerning the mechanical performance of the ventricle (Fig. 2) (4,5,8,15). The work performed in systole to eject blood and the work performed in diastole to distend and fill...
the ventricle are determined from the area under the systolic and diastolic portions of the curve, respectively. The rate at which work is performed is ventricular power (27).

Left ventricular work and peak ejection rates and power normalized for end-diastolic volume have been used to assess myocardial performance (27). However, these values are difficult to determine and interpret, and at present seem to have no advantage over the simple measurement of ejection fraction.

Ventricular compliance can be assessed from the diastolic portion of the pressure-volume curve. Reduced compliance may be caused by an increase in wall thickness or in muscle stiffness, and results in elevation of end-diastolic pressure (16).

Contractility has been evaluated using the pressure-volume relations at end-systole to determine the slope, E\textsubscript{ES}, of the line connecting end-systolic pressure and volume measurements recorded under different loading conditions. E\textsubscript{ES} is nearly independent of preload and afterload. In patients, the method requires repeated ventriculograms and there is disagreement about the value of E\textsubscript{ES} curves for comparing subjects, because the pressure-volume curves of patients with volume or pressure overload differ from those of normal patients regardless of contractile state (32).

**Regional Left Ventricular Wall Motion**

Many laboratories have developed quantitative methods to measure the extent of wall motion (33–36). These methods differ primarily in the motion vector assigned to the points or regions around the left ventricular contour (Fig. 3). Normal motion differs in different regions of the ventricle (34,36). To make comparisons, the motion of each region can be expressed in units of standard deviations from the mean of a normal reference group (34). Frame by frame analysis of regional wall motion yields information on both the timing and the extent of motion in normal and diseased segments of the ventricle during systole and diastole (33,35).

**Valvular Heart Disease**

The application of quantitative angiographic measurements is particularly helpful in evaluating patients with valvular heart disease.

**Aortic Insufficiency**

**Ventricular volume and mass.** In patients with aortic insufficiency, the left ventricle dilates in response to the volume overload. As in patients with mitral valve insuffi-
Figure 3. Methods of measuring regional left ventricular wall motion. The chord and radial coordinate methods assume, respectively, that motion proceeds toward a long axis or central point. The area method measures change in area of the regions of the ventricle.

Figure 4. Pressure-volume curves from patients with different types of heart disease. The curve from the patient with mitral stenosis (1) shows well defined isovolumic contraction and relaxation periods, a normal stroke volume and relatively normal stroke work. The other patients have larger stroke work values as estimated by the areas under the systolic limbs of the curves. The patients with aortic (4) or mitral (2) regurgitation and aortic stenosis and regurgitation (5) have elevated stroke work values with large stroke volumes, as is shown by the excursion of the curves along the horizontal or volume axis. Patients with valvular insufficiency have a shortening or absence of isovolumic contraction and relaxation periods. Patients with aortic valve stenosis (3) have elevated systolic pressures. Patients with large stroke volumes have elevated end-diastolic volumes. (Reprinted, with permission, from Sodeman WA Jr and Sodeman WA. Pathologic Physiology. Philadelphia: WB Saunders, 1973:286.)

Efficiency, this volume overload may be very large, with stroke volumes approaching (but rarely exceeding) 300 ml and outputs of 25 to 30 liters/min. Left ventricular stroke work may be elevated to three or four times the normal amount. The increase in end-diastolic volume is proportional to the volume of regurgitant flow. The end-systolic volume is also increased so that in compensated aortic insufficiency the ejection fraction remains relatively normal (8,23,27,37–40).

An increase in muscle mass, or hypertrophy, accompanies the ventricular dilation (29,30,38), of the hypertrophy, peak systolic wall stress usually remains normal, although the left ventricular chamber is dilated and the ventricle becomes more spherical. This distributes stress more evenly than is the case in normally eccentric hearts where stress is much greater in the equatorial than in the meridional direction (29).

As seen in pressure-volume curves (Fig. 4), isovolumic relaxation and isovolumic contraction are shortened or eliminated (5,23,40). Diastolic pressure is often normal, even in patients with considerable ventricular enlargement. This indicates that the elastic properties of the ventricle are altered in chronic disease, resulting in increased compliance (38,40).

Effect of heart rate. Heart rate influences the hemodynamics of aortic insufficiency. Judge et al. (41) showed that increasing the heart rate, particularly when there is bradycardia, causes a reduced regurgitant flow per stroke and reduced end-diastolic volume and pressure, although regurgitant flow per minute is essentially unchanged. This hemodynamic effect of heart rate may account for the observation that some patients with aortic insufficiency may experience dyspnea and angina at rest, but tolerate exercise well.

Ejection fraction. A reduced ejection fraction in patients with chronic aortic insufficiency indicates decreased myocardial performance rather than inadequate hypertrophy for the work overload, as is evidenced by normal or depressed peak systolic stress values (42). With a decrease in
the dilation and increased compliance in the left atrium regurgitation flows into a low pressure left atrium in early compliance to accept the volume of regurgitant flow. Because (15,23). The left atrium is also dilated with increased compliance may have normal left ventricular diastolic pressure. Nevertheless, left ventricular hypertrophy is less severe for comparable regurgitant volumes. probably because much of the regurgitation flows into a low pressure left atrium in early systole during what is normally isovolumic systole (37). Isovolumic contraction is shortened or eliminated (Fig. 4) (15,23). The left atrium is also dilated with increased compliance to accept the volume of regurgitant flow. Because of the dilation and increased compliance in the left atrium and ventricle, patients with chronic mitral valve insufficiency may have normal left ventricular diastolic pressure, left atrial pressure and pulmonary vascular pressure despite large volumes of regurgitant flow. Thus, patients are often able to tolerate considerable volumes of mitral regurgitation for extended periods without having symptoms (46).

Chronic mitral insufficiency. In this condition, as in chronic aortic insufficiency, the left ventricle is dilated in proportion to the regurgitant flow and stroke volume. However, left ventricular hypertrophy is less severe for comparable regurgitant volumes, probably because much of the regurgitation flows into a low pressure left atrium in early systole during what is normally isovolumic systole (37). Isovolumic contraction is shortened or eliminated (Fig. 4) (15,23). The left atrium is also dilated with increased compliance to accept the volume of regurgitant flow. Because of the dilation and increased compliance in the left atrium and ventricle, patients with chronic mitral valve insufficiency may have normal left ventricular diastolic pressure, left atrial pressure and pulmonary vascular pressure despite large volumes of regurgitant flow. Thus, patients are often able to tolerate considerable volumes of mitral regurgitation for extended periods without having symptoms (46).

The ejection fraction is usually normal in primary mitral valve insufficiency, but is reduced when the insufficiency is secondary to ischemic heart disease or cardiomyopathy. As in patients with aortic regurgitation, dilation is accompanied by decreased eccentricity as the ventricle assumes a more spherical shape (29,47).

Acute mitral insufficiency. The development of compensatory left ventricular and left atrial dilation and of increased compliance are functions of chronicity of the disease (45). In patients with acute mitral valve insufficiency, as occurs in patients with ruptured chordae tendineae, there is little ventricular dilation and hypertrophy and the compliance of the left ventricle, left atrium and pulmonary venous system is low. Accordingly, there may be significant increases in left ventricular end-diastolic pressure, left atrial pressure and pulmonary vascular pressure, even with only moderate volumes of mitral regurgitant flow (48).

Aortic Stenosis

In response to chronic pressure overload in patients with aortic valve stenosis, the left ventricle is hypertrophied with an increased wall thickness but with little or no increased volume (39). Despite ventricular systolic hypertension, peak systolic wall stress is normal in patients with compensated aortic stenosis because the wall forces are distributed over a greater cross-sectional area (8,14,39). However, the increased wall thickness may result in a stiff diastolic ventricle with reduced compliance and an elevated diastolic pressure, which does not necessarily indicate failure (38–40).

Symptoms and signs of decompensation may occur because of the severity of the stenosis or because of depressed myocardial performance. The degree of stenosis becomes critical and limits cardiac output when the orifice area is less than 1.0 cm². Depressed myocardial performance is indicated by a reduced ejection fraction and increased diastolic volume (28,40). The increased afterload may cause a greater depression of the ejection fraction than is observed in other types of heart disease having depressed myocardial performance.

Mitral Stenosis

In patients with mitral stenosis, stroke volume and cardiac output are reduced because of obstruction of the mitral valve. Although the left ventricular ejection fraction is reduced to less than 0.40 in approximately one-third of patients with mitral stenosis, the left ventricle is usually not dilated (49). The mechanism for the reduced ejection fraction is unknown, but it may be a result of previous rheumatic carditis.

Evaluation of Valve Surgery

Aortic regurgitation. Quantitative angiography has been useful for evaluating the functional response to surgery in valvular heart disease. Valve replacement for aortic regurgitation results in reductions of end-diastolic and end-systolic volumes, mass, wall stress and stroke work to normal or near normal levels. The end-diastolic pressure, aortic pressure, eccentricity and cardiac output also return toward normal (50,51). The ejection fraction changes little if it was normal preoperatively: it may improve from a depressed
preoperative level, but this is not always the case (50,51). Studies have shown that depressed preoperative ventricular function, as indicated by the ejection fraction, is associated with a poorer prognosis and recovery of function after surgery. Accordingly, it has been recommended (52) that patients undergo aortic valve replacement before depressed myocardial performance develops.

**Aortic stenosis.** In patients with aortic stenosis or combined aortic stenosis and regurgitation, valve replacement results in reductions in left ventricular mass, end-diastolic and peak systolic pressures, stress and stroke work, and increases in aortic systolic and diastolic pressure (50). Ejection fraction improves in most cases, even if it was low preoperatively (50).

**Mitral regurgitation.** In patients with mitral regurgitation, the ejection fraction does not increase after surgery and may even decrease (53). Although there are reductions in end-diastolic volume, end-diastolic pressure and stroke volume, hypertrophy does not regress and stroke work decreases only slightly (53). Nevertheless, long-term survival in patients with mitral regurgitation is significantly improved by surgery (54). Patients with a severely abnormal left ventricle, with a greatly reduced ejection fraction and marked dilatation, have a poorer long-term prognosis even with surgery than do patients with mitral insufficiency and more normal ventricular performance (53,54).

**Coronary Artery Disease**

**Regional wall motion abnormalities.** Coronary artery disease causes regional wall motion abnormalities, which in early studies (55) were found in the distribution of stenosed or occluded arteries. More recent studies (56) using techniques for quantifying the extent of coronary artery stenosis and for more accurately determining the extent and timing of regional wall motion abnormalities have demonstrated a significantly increased frequency of regional hypokinesia and delayed regional contraction or relaxation, or both, when stenoses in the major coronary arteries cause more than 60 to 70% reduction of diameter or a minimal luminal area of less than 1.0 mm². This occurs in patients without a history of myocardial infarction (34,35,57). When more than 20 to 30% of the endocardial contour becomes akinetic, end-diastolic volume is increased and ejection fraction reduced (58). However, the extent of regional hypokinesia or akinesia may not be reflected by the global ejection fraction because of compensatory hyperkinesia of uninvolved regions of the myocardium (Fig. 5) (35).

**Delayed regional wall contraction or relaxation** (Fig. 5) is common and contributes to the decreased systolic function and increased diastolic stiffness of the left ventricle in patients with coronary heart disease (33,35,57). The mechanisms for the regional asynchrony are not completely understood.

**Ventricular dilation in patients with coronary heart disease,** as in patients with other forms of heart disease, is associated with hypertrophy, but to a lesser extent than is seen in those patients having other types of heart disease. Ventricular aneurysms may cause substantial increases in ventricular dimensions and volume, resulting in increased wall stress. The volume of the aneurysm usually changes little during systole; therefore systolic expansion does not contribute significantly to the mechanical defect.

**Ejection fraction and revascularization surgery.** Ventricular performance as expressed by the global ejection fraction has been shown to be an important predictor of survival in patients with coronary heart disease (59). Indeed, it is a more important predictor than is the number of stenosed coronary arteries. Studies to date (59) have indicated that survival is improved after coronary revascularization surgery, particularly in patients with two or three vessel...
disease and moderate depression (0.30 to 0.50) of ejection fraction.

Although survival improves after surgery, global left ventricular function as measured by the ejection fraction does not improve as a result of surgery in the majority of patients (60). However, some studies (61) have demonstrated lessening of regional hypokinesia after successful revascularization surgery. These results indicate that regional wall motion analysis is more sensitive than the global ejection fraction (60). However, some studies (61) have demonstrated lessening of regional hypokinesia after successful revascularization surgery. These results indicate that regional wall motion analysis is more sensitive than the global ejection fraction not only for detecting ventricular dysfunction but also for evaluating therapy.

References
18. Dodge HT, Sheehan FH, Stewart DK. Estimation of ventricular vol-