An Angiocardiographic Method for Directly Determining Left Ventricular Stroke Volume in Man

By Harold T. Dodge, M.D., Robert E. Hay, M.D., and Harold Sandier, M.D.

In previous studies from this and other laboratories, rapid biplane angiocardiography has been utilized to quantify left ventricular chamber volume and volume changes in man and experimental animals. Arvidsson measured left ventricular stroke volume in several subjects with valvular heart disease in the course of extensive studies on left atrial volume changes, and Chapman and coworkers determined left ventricular volume curves and stroke volume in canines and a normal man using a biplane cineangiocardiographic technique. Others have utilized a single-plane technique to determine left ventricular volume in experimental animals. The validity of corrections for x-ray distortion and of calculations of volume from biplane x-rays has been demonstrated using models and contrast-filled postmortem hearts. Recently, Arvidsson compared left ventricular minute volumes determined by an angiocardiographic method with minute volumes determined by the Fick method and found close agreement in the majority of subjects. In his studies, angiocardiography was performed under conditions of general anesthesia and positive intrathoracic pressure. In the present study, stroke volumes determined from biplane angiocardiograms were compared with stroke volumes determined by Fick and indicator-dilution techniques. The physiological state of the patient just prior to angiocardiography was similar to that present at the time of the Fick and indicator-dilution cardiac output determinations. These studies were reported earlier in preliminary form.

Methods

Fourteen adult male subjects with pulmonary or cardiac disease, as indicated in table 1, were selected for study after clinical examination revealed no evidence of congenital cardiac defects, valvular insufficiency, or arrhythmia. All were studied in the resting, recumbent, fasting state. Sodium pentobarbital, 100 mg., was given orally or intramuscularly 30 to 60 minutes before the start of the procedure. An indwelling needle was placed in a brachial artery, a no. 9 angiocardiographic catheter was passed via an antecubital vein to the pulmonary artery, and duplicate cardiac outputs were determined by the direct Fick technique. The heart rate was recorded during each of the collection periods. Duplicate cardiac outputs were then determined by the indicator-dilution technique with a cuvette densitometer and direct-writing recorder, using Evans blue dye with pulmonary arterial injection and brachial arterial sampling. Details of the Fick and indicator-dilution techniques as used in this laboratory have been previously described.

The catheter was withdrawn so that its tip was near the junction of the superior vena cava and the right atrium. Contrast medium, 40 to 50 cc. (0.65 to 1.15 cc./Kg. of 70 per cent sodium acetrizoate*), was injected through the catheter by a Glundt power syringe at a pressure of 4 Kg. per cm. Two and one-half to three seconds were required for the injection. Subjects were instructed to continue quiet breathing during filming. By means of a Schonander biplane x-ray unit, films were exposed in the anteroposterior and left lateral projections at the rate of four to six films per second for a period of from five to seven seconds. The duration of each exposure was

*Urokon, Mallinckrodt Chemical Works, New York City.
was 0.03 to 0.04 second at 300 to 400 ma. and 100 to 120 kv. The time to activate the film changer, in order to obtain a maximum number of x-ray exposures during left ventricular opacification, was ascertained from the previously recorded indicator-dilution curves. A photo-cell recorded on a direct-writing multichannel recorder the time of exposure of each pair of films with respect to the electrocardiogram and brachial arterial pressure (fig. 1). In one subject, the angiocardiographic examination was repeated approximately 30 minutes after the initial examination because of malfunction of the film changer.

CALCULATIONS

For purposes of volume calculation, it was assumed that the left ventricular chamber could be represented as an ellipsoid figure and volume calculated by using the formula for the volume of an ellipsoid:

\[ V = \frac{4}{3} \pi \frac{lm}{2} \cdot \frac{d'}{2} \cdot \frac{d''}{2} \]  

(1)

where \( V \) = volume, \( lm \) = length of the major axis, and \( d', d'' \) = the lengths of the two minor axes.

The above axes were determined as follows: The margins of the opacified left ventricular chamber were drawn on each set of films and transferred to tracing paper. In each projection, the area of the left ventricular chamber was determined by planimetry and the maximum length of the chamber measured directly. The transverse chamber diameters in the anteroposterior and lateral projections were calculated from the following ellipse formula:

\[ d = \frac{4A}{\pi} \]  

(2)

where \( d \) = transverse chamber diameter in a given projection, \( A \) = area of the chamber in the projection, and \( l \) = maximum length of the chamber in the projection. Each of the above diameters was corrected for x-ray distortion from knowledge of x-ray tube-to-film distances, which were measured, and left ventricle-to-film distances, which were calculated from the relationship of the left ventricle to the central x-ray beam of each tube, which was recorded on each film. In calculating chamber volume, the two transverse diameters and the longest directly measured length, following correction for x-ray distortion, were used. These methods have been described in greater detail elsewhere and tested on human postmortem hearts, with establishment of a regression equation relating known to calculated volumes together with the standard error of estimate of the method. In the present study, the volumes were all corrected, using the regression equation determined in the previous study:

\[ V' = 0.928V - 3.5 \]  

(3)

where \( V' \) = corrected volume in cc, and \( V \) = volume calculated by applying equation 1.

Each volume determination was plotted at the point corresponding to its time of exposure on the recording strip, as shown in figure 1. Each determination was then timed with respect to the onset of the QRS complex of its particular heart cycle, and finally, all determinations were combined on the basis of time from the onset of the QRS to form a single composite volume curve (fig. 2). These composite curves were made up of from eight to 26 observations (mean 17) obtained during the two to eight heart cycles selected on the basis of adequate opacification of the left ventricular chamber and freedom from evident physiological effects of the injection or the contrast material. The points of maximum and minimum volume on the composite curve represented the end-diastolic and end-systolic vol-
STROKE VOLUME BY ANGIOCARDIOGRAPHY

TABLE 1
Comparison of Stroke Volumes Determined by Angiocardiographic, Fick, and Dye-Dilution Methods

<table>
<thead>
<tr>
<th>Patient</th>
<th>Diagnosis</th>
<th>Fick</th>
<th>Dye</th>
<th>Fick and dye</th>
<th>Angiocardiography</th>
</tr>
</thead>
<tbody>
<tr>
<td>I.W.</td>
<td>Idiopathic cardiomyopathy</td>
<td>4.53</td>
<td>4.53</td>
<td>4.53</td>
<td>225</td>
</tr>
<tr>
<td>C.S.</td>
<td>Idiopathic cardiomyopathy</td>
<td>78</td>
<td>78</td>
<td>78</td>
<td>175</td>
</tr>
<tr>
<td>A.N.</td>
<td>Bronchiogenic carcinoma</td>
<td>4.60</td>
<td>4.60</td>
<td>4.60</td>
<td>50</td>
</tr>
<tr>
<td>H.B.</td>
<td>Bronchiogenic carcinoma</td>
<td>3.55</td>
<td>3.55</td>
<td>3.55</td>
<td>54</td>
</tr>
<tr>
<td>J.T.</td>
<td>Bronchiogenic carcinoma</td>
<td>4.17</td>
<td>4.17</td>
<td>4.17</td>
<td>1.1</td>
</tr>
<tr>
<td>L.M.</td>
<td>Bronchiogenic carcinoma</td>
<td>4.13</td>
<td>4.13</td>
<td>4.13</td>
<td>4.35</td>
</tr>
<tr>
<td>W.H.</td>
<td>Bullous emphysema</td>
<td>3.57</td>
<td>3.57</td>
<td>3.57</td>
<td>8.1</td>
</tr>
<tr>
<td>D.W.</td>
<td>Pulmonary infiltrate, etiology</td>
<td>4.91</td>
<td>4.91</td>
<td>4.91</td>
<td>5.2</td>
</tr>
<tr>
<td>H.H.</td>
<td>Idiopathic cardiomyopathy</td>
<td>5.85</td>
<td>5.85</td>
<td>5.85</td>
<td>3.46</td>
</tr>
<tr>
<td>H.S.</td>
<td>Bronchiogenic carcinoma</td>
<td>4.53</td>
<td>4.53</td>
<td>4.53</td>
<td>3.36</td>
</tr>
<tr>
<td>M.H.</td>
<td>Pulmonary emboli</td>
<td>3.32</td>
<td>3.32</td>
<td>3.32</td>
<td>3.15</td>
</tr>
<tr>
<td>F.P.</td>
<td>Hypertension</td>
<td>3.08</td>
<td>3.08</td>
<td>3.08</td>
<td>3.0</td>
</tr>
<tr>
<td>J.E.</td>
<td>Mitral stenosis</td>
<td>5.62</td>
<td>5.62</td>
<td>5.62</td>
<td>4.66</td>
</tr>
<tr>
<td>B.N.</td>
<td>Aortic stenosis</td>
<td>4.35</td>
<td>4.35</td>
<td>4.35</td>
<td>4.35</td>
</tr>
</tbody>
</table>

Mean differences of paired samples ± SD:

Dye: 2.3 ± 8.1 cc. > Fick, or 7.3 ± 16% of Fick
Angio: 3.5 ± 7.8 cc. > Fick, or 8.0 ± 16% of Fick
Angio: 11 ± 5.0 cc. > dye, or 11 ± 8.2% of dye
Angio: 23 ± 5.2 cc. > average of dye, or 3.8 ± 9.5% of dye

*Per cent difference relates dye-Fick, angio-dye, angio-Fick.

Results

The measurements of stroke volume obtained by the various methods are listed in Table 1 and compared graphically in Figure 3. The mean stroke volumes of the different subjects ranged from 32 to 110 cc. and end-diastolic volumes from 49 cc. in subject H.S. to 345 cc. in subject C.S. An attempt was made to include subjects who demonstrated differing levels of both stroke volume and end-diastolic volume. Two of the subjects (I.W. and C.S.) had moderate and marked...
left ventricular dilatation, respectively, and two others had end-diastolic volumes that were larger than normal. Although there were few stroke volume determinations at any given diastolic volume, the agreement between the methods seemed similar at the various volumes represented.

In eight of 11 subjects, the stroke volumes determined by the Fick method were smaller than those determined angiographically. The mean algebraic difference between the two methods, however, was only + 3.5 ± 7.6 cc. This difference was not statistically significant in the number of cases studied. A similar, although smaller, difference was obtained between stroke volumes determined by the Fick and the indicator-dilution methods and the indicator-dilution and the angiocardiographic techniques. In table 1 and figure 3, the mean of the Fick and indicator-dilution determined stroke volumes has also been compared with the angiographically determined stroke volumes in an attempt to avoid the extremes of variation in the Fick and dye-dilution methods.

Observations of heart rate, rhythm, and arterial pressure from the time of injection of contrast material through the period of filming demonstrated changes in some subjects. A premature beat during the injection, which was usually several seconds prior to filming of the left heart, was occasionally observed. In 10 of the subjects, varying degrees of hypotension and bradycardia developed after most or all of the filming was completed. Of the remaining four subjects, one (A.N.) experienced a 20-mm. Hg fall in systolic blood pressure during filming. In another (B.N.), bradycardia was noted, the heart rate decreasing from 100 to 80 per minute. Two others (J.E. and I.M.) had mild bradycardia and a 10-mm. Hg fall in blood pressure. In spite of these physiological changes, in each instance the angiocardiographically determined stroke volume was similar to that determined earlier by the Fick and indicator-dilution techniques.

Discussion

Angiocardiography has been used extensively in physiological and diagnostic studies in experimental animals and man, but the observations, with a few exceptions, have been qualitative or semiquantitative. Previous studies have been performed on models and postmortem hearts to develop and test methods for quantifying left ventricular chamber volume from biplane films of the opacified left ventricular chamber. Gribbe demonstrated a close correlation between left ventricular stroke volumes calculated from single-plane angiograms and stroke volumes determined by the Fick method in experimental animals. In a recent study, Arvidsson found close agreement between left ventricular minute outputs determined from biplane angiograms and cardiac outputs determined by the Fick method. This agreement in results prevailed in spite of the fact that the angiocardiographic observations were made during general anesthesia and induced

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positive intrathoracic pressure, a different physiological state from that existing at the time of the Fick cardiac output determinations.

In studies where angiocardiography has been used as a quantitative method, there has been uncertainty about the effects of the sudden injection of a volume of contrast material, the contrast material itself, the varying degrees of left ventricular opacification, and the varying configurations of the left ventricular chamber on calculated ventricular volume and volume changes. Accordingly, it has been uncertain to what extent data obtained by angiocardiographic techniques are comparable with data obtained by other methods. The comparison of stroke volume, as determined by three independent methods in these subjects without clinical evidence of valvular insufficiency, has provided an in vivo test of the angiocardiographic method for determining left ventricular volume changes. Testing of the in vivo determination of absolute left ventricular chamber volume must await development of a suitable alternative method for determining this volume.

In the group as a whole, stroke volume as determined by the Fick, indicator-dilution, and angiocardiographic methods agreed closely. However, in an occasional subject, such as W.H. (table 1), stroke volumes determined by these independent methods were considerably different. Whether these differences were due to changes in the physiological state of the patient or to problems inherent in the methods for determining stroke volume was not defined. Table 2 contains a summary of published work by others relating stroke volumes determined by Fick and indicator-dilution methods. It is of interest that the mean differences and standard deviations of stroke volumes determined by these two methods in earlier studies were similar to those observed in the present study. In each of these earlier studies, fairly large differences in stroke volumes as determined by these two methods were occasionally observed, in spite of the fact that the determinations were performed more or less simultaneously. These differences have been ascribed, in part, to a summation of the technical difficulties inherent in the two methods. In the present study, left ventricular stroke volume determined by the angiocardiographic method correlated with the stroke volume determined by the Fick and dye-dilution methods as well as or better than the Fick and dye-dilution determined stroke volumes correlated with one another.

It is of note that this angiocardiographic method provides a method for directly determining left ventricular stroke volume in man. The Fick and indicator-dilution techniques, as usually applied, provide a measure of mean pulmonary, or systemic, blood flow per stroke. Although under normal conditions these flow values and left ventricular output are equal, left ventricular output may differ from these flow values in subjects with valvular insufficiency or certain cardiac shunts. The difference between left ventricular stroke volume determined by the angiocardiographic method and the stroke volume determined by the Fick or indicator-dilution methods has
TABLE 2
Comparison of Stroke Volumes Determined by the Fick and Indicator-Dilution Methods from Data Published by Others

<table>
<thead>
<tr>
<th>Series</th>
<th>Number of observations</th>
<th>Mean differences of paired samples ± SD</th>
<th>Maximum difference*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hamilton et al.17</td>
<td>39</td>
<td>Dye 1.7 ± 12.5 cc. &gt; Fick or 2.6 ± 18.1% of Fick*</td>
<td>46%</td>
</tr>
<tr>
<td>Werko et al.15</td>
<td>66</td>
<td>Dye 3.7 ± 12.7 cc. &gt; Fick or 7.8 ± 18.2% of Fick 52%</td>
<td></td>
</tr>
<tr>
<td>Kopelman and Lee2</td>
<td>28</td>
<td>Dye 0.2 ± 6.2 cc. &gt; Fick or 0.9 ± 10.4% of Fick 37%</td>
<td></td>
</tr>
</tbody>
</table>

*Per cent difference relates dye-Fick.

been used to quantify aortic and mitral valvular insufficiency.18

One of the most important problems in quantitative angiocardiography is concerned with obtaining satisfactory left ventricular opacification with a minimum of untoward cardiovascular reactions. Unfortunately, both the degree of opacification and the severity of reactions seem directly related to the volume and concentration of contrast material. To apply this quantitative angiocardiographic method requires films that demonstrate an opacified left ventricle with margins that can be defined and traced. Experience in this laboratory indicates that in subjects with marked heart enlargement or marked valvular insufficiency, it is often not possible to obtain this degree of left ventricular opacification with right heart injections of the amounts of contrast material used in this study. The chief cardiovascular reactions seen in this study were premature contractions, extrasystoles, bradycardia, and hypotension, which are common during angiocardiography and are described in some detail by others.19-23 With respect to the quantitative aspects of angiocardiography, the time sequence of these phenomena is of some importance. When right-sided injections are used, the arrhythmias occur during the actual moment of injection, several seconds prior to filming of the left heart. Bradycardia and hypotension, when present, are usually noted as the contrast material leaves the left ventricle and follow left ventricular opacification.4,12 Others have found that left ventricular stroke volume remains relatively constant prior to the appearance of bradycardia and hypotension.4,12 This observation was also made in the present studies when sufficient films were available and the timing of film exposure made possible stroke volume determinations of individual beats.

Summary

A method has been described for directly determining left ventricular stroke volume in man through the use of biplane angiocardiography. Left ventricular stroke volume determined by this method has been compared with stroke volumes determined by the Fick and/or indicator-dilution methods in 14 subjects without arrhythmias or clinical evidence of valvular insufficiency. Stroke volumes determined by these various methods showed close agreement.

Acknowledgment

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References

STROKE VOLUME BY ANGIOCARDIOGRAPHY


Book Review


In the preface, the author rightfully calls the reader's attention to the fact that the only authoritative treatise on the blood capillaries is still the monograph by August Krogh, first published in 1926. The present monograph adequately fills the need for a brief monograph covering the functional behavior of the capillaries. The structural basis, vascular reactivity, capillary permeability, tissue injury, and experimental shock are discussed in individual chapters.

The regional considerations of the capillaries are limited to the skeletal muscle, skin, mesentery, and kidney. The lung has been omitted entirely, except to mention its role in gaseous equilibrium (page 135), its few discrete arteriovenous thoroughfares (page 22), and endothelial phagocytes (page 48). This shortcoming can be overlooked in favor of a clear exposition of the systemic capillaries.
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