Correlation of Angiographic and Autopsy Left Ventricular Dimensions in Children

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SUMMARY To evaluate controlled pressure coronary artery perfusion fixation of hearts as a means of obtaining meaningful cardiac measurements at autopsy, left ventricular (LV) autopsy measurements were correlated with in vivo end-diastolic (D) and end-systolic (S) angiographic (angio) values from biplane cineangiograms in the same patients. Mitral (MV) and aortic valve (AV) circumferences, LV equatorial circumference (Circ), spatial inflow and outflow lengths, wall thickness (W) and LV volume (Vol) were measured in 34 children with congenital heart disease. All dimensions showed significant correlation of angiographic and autopsy data from which linear regression equations were derived. The r values obtained were: MV 0.74; AV 0.85; D Circ 0.83; S Circ 0.82; D inflow 0.92; S inflow 0.90; D and S outflow 0.96; W 0.78; D Vol 0.92; S Vol 0.86. Mean angio and autopsy values were not significantly different for AV, S inflow, and S Vol. Autopsy values were lower than all D angio values and MV (P < 0.001 for all), and higher than angio W and S outflow (P < 0.001 for both). The data show that changes of LV morphology with this fixation method are predictable, making estimation of in vivo values from autopsy measurements possible using the derived linear regression equations.

ANGIOGRAPHIC TECHNIQUES for determining in vivo cardiac chamber volumes and dimensions have contributed greatly to the understanding of the pathophysiology of heart disease. Recognizing the limitations and variability of cardiac measurements made at autopsy, Glagov et al.1 developed a method of controlled pressure fixation which provided a standardized autopsy preparation. A modification of this method was shown to yield reproducible measurements with little variation in hearts from similar-sized pigs.2 We have compared measurements of the left ventricle from human hearts fixed by this method with in vivo angiographic measurements in the same patients in an attempt to further validate this fixation technique in a clinical setting.

Methods

Study Group

Thirty-four children, primarily with congenital heart disease, who underwent diagnostic cardiac catheterization and cineangiography and subsequently came to autopsy at the University of Illinois Hospital, Chicago, Illinois, comprised the study group. The types of heart defects included are shown in table 1. Age of patients was 900 ± 222 days or 2.5 ± 0.61 years (mean ± SEM), range 0-4,289 days (11.8 years) at angiography and 960 ± 225 days or 2.6 ± 0.62 years at autopsy. The interval between angiography and autopsy ranged from 0-300 days (mean ± SD, 60 ± 87 days). Body surface area (BSA), averaged 0.40 ± 0.04 m² (mean ± SEM) at angiography and 0.41 ± 0.04 at autopsy. Table 2 shows the average intervals and changes in body surface areas in various age ranges. Twenty-nine patients underwent cardiac surgical procedures, 16 open and 13 closed, in that interval. Twenty-five died in the immediate postoperative period.

Angiographic Methods

Biplane antero-posterior (AP) and lateral (L) cineangiograms were filmed using a Philips biplane cineangiography system. Cines were recorded at 64 or 80 frames/sec after high speed injection of 1-2 ml/kg of contrast medium (Conray 400P) into the inferior vena cava or right atrium. In a few patients it was necessary to use selective left ventricular injections in order to visualize ventricular outlines adequately. Cardiac cycles with arrhythmias were excluded. The earliest cycle with sufficient contrast to allow accurate drawing of left ventricular outlines was used. Correction of all measurements for linear x-ray magnification was made utilizing a grid system. Plastic grids etched with 1 x 1 cm lines filled with lead powder in a glue base were radiographed at midchest level in AP and L planes. The radiographic area of a known number of squares roughly overlying the cardiac image was determined by planimetry and divided by the actual area as determined by the known number of squares to yield a separate magnification factor (MF) for each plane. Projected ventricular areas were corrected by dividing by this factor. Projected linear measurements were divided by the square root of the appropriate MF.

Various left ventricular dimensions corresponding to dimensions at autopsy were measured from the drawings. Two angiographic (angio) measurements — end-diastolic (D) and end-systolic (S) — were compared with a single autopsy measurement of each dimension, with the exceptions of valve circumferences and wall thickness, where only D angiographic measurements were made. All

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Received January 23, 1978; revision accepted June 5, 1978.
Circulation 58, No. 4, 1978.

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TABLE 1. Patient Population

<table>
<thead>
<tr>
<th>Lesion</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrioventricular canal</td>
<td>8</td>
</tr>
<tr>
<td>Tetralogy of Fallot</td>
<td>4</td>
</tr>
<tr>
<td>Pulmonary atresia</td>
<td>4</td>
</tr>
<tr>
<td>Transposition of the great arteries</td>
<td>3</td>
</tr>
<tr>
<td>Coarctation of aorta</td>
<td>3</td>
</tr>
<tr>
<td>Aortic stenosis</td>
<td>3</td>
</tr>
<tr>
<td>Ventricular septal defect</td>
<td>3</td>
</tr>
<tr>
<td>Myocardial defect</td>
<td>3</td>
</tr>
<tr>
<td>Other</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>34</td>
</tr>
</tbody>
</table>

Abbreviation: N = Number of patients.

Measurements could not be made in all patients due to poor visualization at angiography or valve replacement before autopsy. The following angiographic measurements were made:

1) Mitral valve circumference (MV) — calculated from the maximum mitral valve diameter measured from the superior to inferior aspects of the valve in L view at D as π × diameter.

2) Aortic valve circumference (AV) — calculated from aortic valve diameter measured from the lateral borders of the valve just below the sinuses of Valsalva in AP view at D as π × diameter.

3) Left ventricular equatorial circumference (Circ) — circumference approximated from the diameter (d) measured in AP and L views at the midpoint of and perpendicular to aorta (or pulmonary artery in patients with transposition of great arteries) to apex axis (AA) (dAAAP, dAAAL) at D and S, assuming the crosssection of the ventricle to be an ellipse, as

\[
\text{Circ} = 2\pi \sqrt{\frac{(dAAAP)^2 + (dAAAL)^2}{2}}
\]

4) Spatial left ventricular inflow tract length (MAS) — calculated from the maximum measured long axis of the left ventricle (LV) in the MV area to the apex (MAL) in the L view and from the right-sided, inferior portion of the mitral annulus to the apex in the AP view (MAAP) at D and S. If the axes of the measured lengths are expressed as:

\[
\text{MAAP} = \sqrt{X^2 + Y^2}
\]

\[
\text{MAL} = \sqrt{Y^2 + Z^2}
\]

Two calculated spatial lengths — D inflow and S inflow — were compared with the corresponding autopsy measurement.

5) Spatial left ventricular outflow tract length (AAS) — similarly calculated from the measured lengths from the center of the aortic valve to the apex (AA) in AP and L views at D and S, as

\[
\text{AAS} = \sqrt{X^2 + Y^2 + Z^2}
\]

Two spatial lengths — D outflow and S outflow — were calculated for each patient.

6) Left ventricular wall thickness (W) — measured in AP view at D along left lateral heart border midway between the LV apex and the semilunar valve, where wall thickness appears uniform. An average of four values was used.

7) Left ventricular volume (Vol) — measured at D and S by the standard area length method. Calculated volumes were corrected using a regression equation determined from ventricular cast studies in our laboratory and previously reported, where \( V' = 0.85V \), where \( V' \) = corrected volume and \( V \) = calculated volume. Average error (mean ± 1 sd) for the cast studies was 13 ± 10%. Two calculated volumes — D Vol and S Vol — were compared with the autopsy volume in each patient.

In the course of this study, Circ, inflow and outflow tract lengths were measured in several ways. Diameter was measured at the midpoint of and perpendicular to both inflow and outflow axes in both views and the calculated Circs each compared with autopsy measurement, eight measurements in addition to the measurements as described in #3 above. Direct measurements of inflow and outflow tract lengths in AP and L views were compared to the autopsy values, four measurements of each in addition to the spatial measurements described under #4 and #5 above. The data presented here represent the measurements which correlated best with autopsy measurements.

TABLE 2. Intervals and BSA Changes Between Angiography and Autopsy

<table>
<thead>
<tr>
<th>N</th>
<th>Age at angio</th>
<th>Interval days, mean ± 1sd</th>
<th>BSA Change m², mean ± 1sd</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>0-7 d</td>
<td>1 ± 1</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>7-14 d</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>15-21 d</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>22-28 d</td>
<td>8 ± 10</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>1-2 mo</td>
<td>6 ± 7</td>
<td>0.01 ± 0.02</td>
</tr>
<tr>
<td>2</td>
<td>2-6 mo</td>
<td>18 ± 2</td>
<td>0.01 ± 0.01</td>
</tr>
<tr>
<td>3</td>
<td>6 mo-1 yr</td>
<td>31 ± 22</td>
<td>0.01 ± 0.01</td>
</tr>
<tr>
<td>5</td>
<td>1-2 yr</td>
<td>157 ± 134</td>
<td>0.03 ± 0.03</td>
</tr>
<tr>
<td>2</td>
<td>2-3 yr</td>
<td>124 ± 43</td>
<td>0.06 ± 0.04</td>
</tr>
<tr>
<td>1</td>
<td>3-4 yr</td>
<td>23</td>
<td>0.06</td>
</tr>
<tr>
<td>1</td>
<td>4-5 yr</td>
<td>165</td>
<td>0.06</td>
</tr>
<tr>
<td>3</td>
<td>5-6 yr</td>
<td>184 ± 51</td>
<td>0.03 ± 0.03</td>
</tr>
<tr>
<td>1</td>
<td>7-8 yr</td>
<td>12</td>
<td>0.06</td>
</tr>
<tr>
<td>3</td>
<td>11-12 yr</td>
<td>25 ± 30</td>
<td>0.01 ± 0.01</td>
</tr>
<tr>
<td>Total 34</td>
<td>60 ± 87</td>
<td>0.02 ± 0.02</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: N = number of patients; Angio = angiography; sd = standard deviation; BSA = body surface area; m² = meters squared; d = days; mo = months; yr = years.
Cineangiographic frames with measurements are shown in figure 1 for patients with pulmonary stenosis, ventricular septal defect and common atrioventricular canal.

Autopsy Methods

After death, routine hospital procedures were followed. No attempt was made to control the time from death to autopsy, and there was no special handling of the body or heart before removal of the specimen for fixation. After routine autopsy, the heart and lungs were removed together. Fixation was carried out at room temperature with 10% buffered formaldehyde solution infused via a cannula into the aortic arch at pressure just above aortic diastolic pressure as recorded at cardiac catheterization, with the resultant continuous flow of fixative through the coronary arteries causing rapid and complete myocardial fixation. Another cannula was used to distend the pulmonary artery with formaldehyde at pressure just above pulmonary artery diastolic pressure observed at cardiac catheterization. The myocardium is distended by perfusion of the coronary arteries and veins, and the cardiac chambers passively fill with formaldehyde during fixation. The heart was suspended in formaldehyde solution during fixation, which was complete in 2 hours. More detailed descriptions of the fixation method and apparatus have been previously reported. Standard autopsy measurements of left ventricular dimensions corresponding to the above described angiographic measurements were made as previously described. Left ventricular volume index was computed according to the formula of Lev et al. as \( LV = \left( \frac{MA + AA}{2} \right) \times (P - LV)^2 \); where \( LV \) = left ventricular volume index, \( MA \) = mitral valve ring to apex length, \( AA \) = aortic (or pulmonary) valve ring to apex length, and \( P - LV \) = greatest circumference of the left ventricle midway between the mitral orifice and apex. Actual volume was calculated from this volume index utilizing a regression equation based on chamber cast studies, \( LV = 0.151 + 0.038 \left( \frac{MA + AA}{2} \right) \times (P - LV)^2 \). All linear measurements and circumferences were expressed in cm and all volumes in ml.

![Figure 1. End-diastolic angiographic frames from patients with (left to right; antero-posterior on top, lateral on bottom) pulmonary stenosis (PS), ventricular septal defect (VSD), and atrioventricular canal (AVC). Injection of contrast medium via catheter (c) in right atrium or left ventricle. Sites of measurement of aortic and mitral valve diameters, inflow tract length, outflow tract length, and wall thickness are indicated by short dashes, solid lines, long dashes and open arrows, respectively.](http://circ.ahajournals.org/doi/abs/10.1161/01.CIR.741.5.1044?journalCode=circ)
Analysis of Data

Autopsy measurements were plotted against corresponding angiographic measurements; and mean, SEM, SEE and linear regression equations were determined for each comparison. Using the t test for paired data, age and BSA at angiography and autopsy were compared.

Regression analysis yielded r values indicating the correlation of measurements made at autopsy and angiography. Measurements were also compared using the t test for paired data, and the resultant P values in the text, table, and figures refer not to the validity of the correlation, but to the probability of whether or not the measurements are different. Thus, sets of measurements may be highly correlated (high r value), and either the same (P = NS) or different (P ≤ 0.05).

Results

Age and BSA at angiography were lower than at autopsy, (P < 0.001 and < 0.025, respectively), although differences in the younger patients were of lesser magnitude than those observed in the older patients (table 2).
**Valve Circumferences (figs. 2A and B)**

AV could be measured in all 34 patients. Angio values correlated well with autopsy values \(r = 0.85\) and, in addition, were not significantly different. MV could not be measured in 13 patients due to poor visualization at angio in 10 and valve replacement in three. The correlation of values was not as good as for AV \(r = 0.74\); and measurements were significantly smaller at autopsy \(P < 0.001\).

**LV Circumference (figs. 3A and B)**

Autopsy Circ correlated well with both D and S angio values \(r = 0.83\) and \(0.82\), respectively and was smaller than both \(P < 0.001\) for both.

**Spatial Lengths (figs. 4A and B; 5A and B)**

Autopsy inflow length correlated highly with D and S angio measurements \(r = 0.92\) and \(0.90\), respectively, was smaller than D values \(P < 0.001\), but not significantly different from S values. For outflow length, correlation was very high \(r = 0.96\) for D and S, and the mean autopsy value fell between D and S angio values and was significantly different from both \(P < 0.001\) for both.

**Wall Thickness (fig. 6)**

Angiographic measurement could not be made in nine patients due to poor visualization or right ventricular dilatation. Correlation was relatively low.
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OCTOBER
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2

Diff.: P < 0.001

I 0
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56

I

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(higher than any value P < Y (Cm).

FGR6. Correlation of values with autopsy calculations. The solid and dashed lines represent the mean ± 2 SEE, respectively.

(r = 0.78) and autopsy values averaged over two times higher than angio values (P < 0.001).

Ventricular Volume (figs. 7A and B)

Correlation of autopsy values with D and S angio values was good (r = 0.92 and 0.86, respectively). Autopsy values were considerably smaller than D values (P < 0.001) but not significantly different from S values.

In fitting curves to the plots of angio vs autopsy data, the best fits were obtained using straight lines. The derived linear regression equations (table 3) can be used to estimate in vivo measurements from autopsy measurements when the heart is fixed as described.

Discussion

Postmortem measurements of the left ventricle, reflecting the geometric alterations caused by the hemodynamics of the lesion and not fixation artifacts, were the goal of this study.

Although physiology cannot be separated from geometry, the most commonly used autopsy and fixation methods have long been recognized as destroying the functional geometry of the heart. Measurements from such specimens are of very limited value, and may even be misleading. Several autopsy studies of normal human cardiac dimensions have been published with widely varying "normal" values and even some obvious conflicts. One group reported atrophy of the right ventricular wall after birth, while another showed an increase in right ventricular wall thickness. Both studies were done in fresh hearts. A third study in formaldehyde-fixed specimens, dissected before fixation, showed no change in right ventricular wall thickness with age. Normal mean aortic valve circumference for a patient 190 cm in height ranges from 5.4 cm²-7.4 cm² depending on the reference. For mitral valve, means range from 7.7 cm²-10.1 cm² for the same-sized patient. Similar wide variations in measurements can be found for other LV dimensions. Widely varying dimensions were found in normal

![Figure 7](http://circ.ahajournals.org/)

Correlation of angiographic left ventricular volumes, end-diastole (A) and end-systole (B) with autopsy calculations. The solid and dashed lines represent the mean ± 2 SEE, respectively.

Figure 6. Correlation of angiographic left ventricular wall thickness, end-diastole, with autopsy measurements. The solid and dashed lines represent the mean ± 2 SEE, respectively.
animal hearts of comparable size when the specimens were handled by the various "standard" autopsy methods.\(^2\) Standardization of autopsy procedures and fixation methods designed to preserve the functional geometry of the heart are vital to the acquisition of meaningful, reproducible, quantitative postmortem cardiac measurements. Toward this end, investigators have described standard methods for dissecting hearts, and suggested packing the specimen with cotton before fixation.\(^3\) Fixation under controlled pressure, described in 1963,\(^1\) yielded specimens fixed in a distended state.

A systematic study of a modification of this method, utilizing controlled pressure coronary artery perfusion and distention of the pulmonary artery trunk, showed specimens fixed in this manner had the least variation in dimensions compared with other fixation methods and fresh specimens.\(^2\) This method presumably preserved the shape and geometry of the intact heart. Using this method, Eckner et al.\(^5\) reported normal cardiac dimensions in humans and showed these dimensions to follow the law of allometric growth, which governs the relationship between size of parts of the body and the whole body, providing further evidence for the validity of the preparation. Correlating autopsy measurements from such preparations with in vivo cardiac dimensions in humans was the next logical step.

To become a viable, acceptable, routine part of autopsy procedure, there must be virtually no interference with routine hospital and autopsy procedures. Therefore, no attempt was made to control handling of the body or timing of the autopsy. There was no special handling of the specimen before fixation. Also, certain other unavoidable and variable sources of error must be accepted in such a clinical study in humans. The time interval between angiography and autopsy is perhaps the largest potential problem. In this study, however, this period was quite short in the younger patients and there was no significant change in BSA.

Medical and surgical interventions may also contribute to differences in measurements. Direct alteration of left ventricular size or morphology by surgery is less likely than for the right ventricle, where common procedures such as ventriculotomy and resection of outflow obstruction with or without an outflow patch may cause marked changes. Mitral valve replacement and resection of subvalvular aortic obstruction seem to carry the greatest potential for altering LV morphology. Additional possible sources of error are the assumption of circular valve orifices in vivo and variations in sites of measurement. Under these circumstances, the results of this study were encouraging.

Shrinkage of the heart does occur with this fixation method. Left ventricular wall thickness at autopsy averaged more than twice that at angiography, reflecting thickening of the wall as the chamber shrinks in size. As expected, end-systolic angiographic values were closer to those at autopsy than end-diastolic values. For two dimensions, inflow length and ventricular volume, average end-systolic angiographic and autopsy values were not significantly different. Shrinkage of the aortic valve annulus was insignificant, since the average end-diastolic angiographic circumference was not significantly different from that at autopsy. The lack of shrinkage of the AV is at-
tributable to distention of the aorta during fixation. Autopsy values for mitral valve circumference of the pressure-fixed, rigor mortis contracted heart were considerably smaller than angiographic end-diastolic values.

The excellent linear correlation obtained for most dimensions studied is evidence for the predictable morphologic alteration of cardiac structure by pressure fixation. Simple estimation of in vivo values from autopsy values is therefore possible. Large numbers of comparable, meaningful quantitative measurements can and should be accumulated in various cardiac defects, providing data for understanding the hemodynamics and for evaluating cardiac surgical procedures.

References
Correlation of angiographic and autopsy left ventricular dimensions in children.
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Circulation. 1978;58:739-746
doi: 10.1161/01.CIR.58.4.739

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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