Ultrafast Computed Tomography Analysis of Regional Radius–to–Wall Thickness Ratios in Normal and Volume-Overloaded Human Left Ventricle

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Background. This study tested two hypotheses: 1) regional left ventricular radius–to–wall thickness ratios (R/T) are uniform in normal subjects, and 2) patients with left ventricular hypertrophy secondary to compensated volume overload normalize global and regional R/T.

Methods and Results. Ultrafast computed tomography was used to measure regional short-axis ventricular R/T in 11 normal subjects and 13 patients with compensated aortic insufficiency (AI) of moderate severity (regurgitant fraction, ≥25%). Radius and wall thickness dimensions were calculated by two different methods. In method 1, the average radius and wall thickness were determined for each planimetric transaxial tomographic image. In method 2, the left ventricle was three-dimensionally reconstructed; then, new radii and wall thickness were recalculated as if all the images were acquired orthogonal to the endocardial surface at each tomographic level. In normals, the mean R/T ratio was 1.75±0.11 (SEM) with method 1 and 1.80±0.07 with method 2. The R/T ratios varied as a function of the relative apex-to-base position. R/T ratios at the basal four levels were relatively uniform, whereas R/T at the lower three tomographic levels were significantly less than those at the base (p<0.01). Patients with AI had a mean regurgitant fraction of 44±3.8% (range, 25–63%). The mean R/T ratio was 2.18±0.16 with method 1 and 2.55±0.18 with method 2. Similar to the pattern observed in normals, the regional R/T ratios at the lower three or four levels were significantly less than the basal R/T ratios (p<0.01). Regional comparison of the normal to the volume-overloaded ventricles demonstrated that R/T ratios in the AI patients were significantly greater at the upper five levels with method 1 and at all eight levels with method 2 (p<0.01–0.001, AI versus normal).

Conclusions. These findings demonstrate that regional R/T ratios are heterogeneous in both normals and patients with left ventricular hypertrophy secondary to compensated aortic insufficiency. Furthermore, these findings challenge the accepted hypothesis that global and regional R/T ratios normalize in patients with compensated volume-overload hypertrophy. (Circulation 1992;85:1423–1432)

Key Words: aortic insufficiency • tomography, ultrafast computed • wall stress

The radius–to–wall thickness ratio (R/T) and volume-to-mass relation are indexes that reflect left ventricular geometry and myocardial loading condition. It has been postulated that the teleologic significance of the normal base-to-apex pattern of myocardial wall thinning in the normal ventricle is the maintenance of a constant regional R/T ratio.1–4 In accordance with an idealized Laplacian relation, if cavity pressure is uniform, then the R/T ratio should be the primary determinant of average ventricular wall stress. Therefore, if regional R/T measurements were observed to be homogeneous, this finding would support the hypothesis that the regional distribution of left ventricular wall stress is relatively uniform.1–3 However, despite general acceptance, these principles have never been examined or confirmed in a clinically relevant setting.

In a related issue, it has been widely accepted that patients with compensated chronic left ventricular volume overload hypertrophy respond to the initial increase in end-diastolic wall stress by subsequently normalizing the global and regional R/T ratios.5–13 Earlier studies have asserted that the hallmark of physiological compensation in patients with volume overload hypertrophy is restoration of the normal R/T ratio. This pattern has been termed "eccentric hypertrophy,"5,7,9,10,13 and is defined as the "enlargement of the ventricle without change in shape or relative wall thickness." Based on this theory, the relation between the ventricular R/T ratio has provided a conceptual framework for explaining the differential genesis of pressure and volume overload hypertrophy states (concentric versus eccentric hypertrophy).5–13 In previous studies, the regional R/T measurements were obtained by contrast ventriculography5–7 or echocardiography.4–14 How-
ever, the well-known technical limitations of these methods do not permit precise regional measurements of radii and wall thickness as a function of relative three-dimensional apex to base position.

Pursuant to these issues it was the intent of this study to examine the following hypotheses: 1) Regional left ventricular R/T ratios are uniform in normal subjects and in patients with volume overload hypertrophy secondary to hemodynamically compensated aortic insufficiency, and 2) hemodynamically compensated volume overload hypertrophy secondary to aortic insufficiency is characterized by normalization of global and regional R/T ratios.

Ultrafast computed tomography (CT) was used to measure regional left ventricular end-diastolic dimensions and volumes. Ultrafast CT permits polytomographic image acquisition at 17 frames per second, with known and consistent three-dimensional orientation and registration of the images. The spatial resolution is nominally 0.94 mm²/pixel with an effective slice thickness of 10 mm. Additionally, unlike other cardiac imaging formats, the ultrafast CT edge detection algorithm is precise having undergone extensive validation. Using these unique capabilities, we have previously demonstrated that ultrafast CT is a highly accurate means of measuring ventricular volumes and masses independent of geometric assumptions.

**Methods**

**Data Acquisition**

The technical details of the ultrafast CT scanner have been previously described. Studies were performed in 13 healthy male volunteers ages 21–36 years (mean age, 23±4 years) who were free of cardiac disease as assessed by history, physical examination, and ECG. Additionally, 18 patients with moderate-to-severe aortic insufficiency were imaged. Informed consent was obtained from all subjects in compliance with protocols approved by investigational review boards at the University of Iowa and Mayo Clinic. Portions of the data from the normal subject group have been previously reported. Two studies were excluded from analysis, one secondary to contrast-induced nausea and another because of failure to adequately opacify both ventricular chambers. Thus, 11 normal subjects were analyzed. Eighteen patients with hemodynamically compensated moderate-to-severe aortic insufficiency were evaluated. Isolated aortic valvular insufficiency was confirmed in all subjects by two-dimensional/Doppler echocardiography. Only patients who were functional class II or less, with normal regional wall motion, ultrafast CT–determined global ejection fraction ≥50%, and a regurgitant fraction of ≥25% (i.e., moderate or greater severity), were analyzed. Thirteen patients met these criteria. Subjects fasted for 4 hours before study. ECG monitoring provided a physiological trigger for the ultrafast CT. Heart rate and rhythm were monitored continuously. Contrast agent was delivered via an 18-gauge intravenous catheter placed in a right antecubital vein. As previously described, the subjects were positioned in the scanner to obtain short-axis tomographic images. The first tomographic image was obtained one level below the cardiac apex. Thus, the tomographic images from all groups and within each group could be indexed and compared to a similar anatomical (apical) position. In the normal subjects images were acquired into a 256×256 matrix resulting in an effective resolution of 1.37 mm²/pixel. Patients with aortic insufficiency were imaged using a 360×360 matrix yielding a nominal resolution of 0.94 mm²/pixel.

To ensure adequate opacification for the right and left ventricular cavities, the circulation time was estimated as previously detailed. Contrast was administered by power injector over a duration equal to the circulation time. Normals received 0.35 ml/kg meglumine diatrizoate (370 mg I₂/ml). Potential hemodynamic perturbations secondary to ionic contrast were obviated by injecting contrast at rates less than 2–3 ml/sec. Patients with aortic insufficiency received only nonionic media (iopamidol, 370 mg I₂/ml). Cine tomograms of the entire cardiac cycle were obtained at each tomographic level. In normal subjects two cine runs (six to eight levels per run) were sufficient to image the entire left ventricle. To calculate the regurgitant fraction in patients with aortic insufficiency, it was often necessary to acquire an additional cine run to completely image the entire right ventricle and outflow tract. Arterial pressure was measured by cuff before and after each contrast injection.

**Data Analysis—Mass, Volume, Radius, and Wall Thickness Calculations**

Global myocardial mass and left ventricular cavity volume were calculated as the product of their respective planimetered areas, tomographic slice thickness (0.8 cm), and the specific gravity of muscle (1.05 g/cm³) or blood (1.03 g/cm³). To avoid dimensional confusion, the volume/mass relation was expressed as a dimensionless ratio (cm³/cm²) rather than as milliliters per gram. Failure to convert myocardial wall volume to myocardial mass by multiplying by the appropriate specific gravities introduces an error of 0.02%.

The geometric configuration of the ultrafast CT target rings results in a 4-mm gap of unscanned myocardium between every third slice. Since only a small portion of myocardial mass and ventricular volume was not directly imaged, mass and volume were accounted for by linear interpolation between the tomographic slices above and below the gap. Global left ventricular mass and volume relations were calculated by summing across the individual scans and employing a modified Simpsons’ approximation, as previously described. At each ventricular level, the cine tomograms were reviewed, and the end-diastolic frames were chosen for specific analysis. According to previously established criteria, the end-diastolic frame was identified as the image with the greatest cavity volume that occurred within ±58 msec of the beginning of the R wave. From these images, the average radii and wall thicknesses at a given tomographic level were determined by two methods.

**Method 1: “Axial” technique.** At each tomographic level, the average endocardial radius of curvature and wall thickness were determined without any attempt to realign the images perpendicular to the long axis of the ventricle. Acquiring transverse cardiac images (i.e., “short axis”) in this fashion invariably results in some tomographic images that are more oblique than others.
Each study was set up so that the tomographic images obtained at the mid left ventricle were as close as possible to a true short-axis scan, analogous to two-dimensional echocardiographic images. However, unlike echocardiography, ultrafast CT acquires sequential and parallel tomograms. Thus, although the imaging plane at times transectts the ventricle at oblique angles, because the images are acquired with consistent and sequential three-dimensional registration, the left ventricle can be three-dimensionally reconstructed.

By this method, the average wall thickness and cavity radius for each tomogram was determined from the planimetric cross-sectional area of the endocardial and epicardial tomographic contours. The planimetric endocardial areas were assumed to be circular, thus the mean radius (R) for a given tomographic level was solved: 

\[ R = \sqrt{\frac{A}{\pi}}. \]

The average myocardial wall thickness (T) was determined as \( T = (\sqrt{A1/\pi}) - (\sqrt{A2/\pi}) \), where A1 and A2 are the respective epicardial and endocardial boundaries.

Method 2: "Orthogonal" technique. Method 2 attempted to obviate the confounding influence on radius and wall thickness measurements that may arise secondary to using fixed-image plane acquisition to an object that takes an oblique path through the imaging plane. This method calculated the average radius of curvature (R) and wall thickness (T) at end diastole for a given tomographic level as if the images were acquired perpendicular to the left ventricular endocardial surface (Figure 1). The epicardial and endocardial contours of each tomographic slice were assumed to be circular, and the average radius and wall thickness were determined as in method 1. Next, these epicardial and endocardial radii were fit to second-order polynomial curves. Previously, we have demonstrated that the left ventricular surfaces in the "long axis" can be approximated by a quadratic equation. At each tomographic level, the line tangent to the endocardial surface was solved. Then, the unique equation for the line perpendicular to the endocardial tangent line was solved. Finally, the coordinates along this perpendicular line intersecting the endocardial and epicardial curves were solved. From these coordinates, the orthogonally corrected endocardial radius and wall thickness were determined for all tomographic levels.

The mean left ventricular volume/mass and R/T ratios for all eight apex-to-base tomographic images were calculated as the sum of the volumes (or radii) divided by the sum of the masses (or wall thickness). The regurgitant fraction was calculated as the difference between the left and right ventricular stroke volumes divided by the left ventricular stroke volume.

**Statistical Analysis**

Data are presented as mean±SEM unless otherwise indicated. The end-diastolic tomographic volumes and R/T ratios were plotted as a function of ventricular tomographic level (base defined as level 1 and apex as level 8). When indicated, Friedman's two-way ANOVA was applied to the data. Significant ANOVA results (p<0.05) were analyzed by the Newman-Keuls multiple comparison test with α=0.05 to identify significant differences.

**Results**

**Hemodynamic and Global Left Ventricular Function**

The global left ventricular hemodynamic and volumetric data are presented in Table 1. During image acquisition, changes in arterial blood pressure were small and varied less than 10% of baseline values in both study groups. Portions of the data from these normal subjects have been previously reported and are comparable to the accepted normal values.

![Figure 1](http://circ.ahajournals.org/)

**Figure 1.** This example compares the differences between method 1 and method 2. The epicardial and endocardial lines are composite contours derived from all subjects with aortic insufficiency. At level 3, method 1's voxel of acquisition is depicted by a dark vertical rectangle, and method 2's voxel is demarcated by the less dense parallelogram. The line extending from the abscissa to the endocardial surface is the isocenter of the orthogonal voxel. Method 2 results in over-scanning the ventricular cavity (darkly shaded cavity triangle), which results in overestimation of true volume. The diagonal hatched area between epicardial and endocardial lines corresponds to the myocardium that is underscanned with method 2.

**Table 1.** Global Left Ventricular Hemodynamic and Volumetric Data

<table>
<thead>
<tr>
<th></th>
<th>Normals</th>
<th>Aortic insufficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (bpm)</td>
<td>76±10</td>
<td>80±12</td>
</tr>
<tr>
<td>Mean ABP (mm Hg)</td>
<td>92±5</td>
<td>95±10</td>
</tr>
<tr>
<td>Global ejection fraction</td>
<td>70±6.5</td>
<td>64±10</td>
</tr>
<tr>
<td>LV end-diastolic mass</td>
<td>187±31</td>
<td>234±20 (25%)*</td>
</tr>
<tr>
<td>LV end-diastolic mass/ index</td>
<td>98±17</td>
<td>123±8.3</td>
</tr>
<tr>
<td>LV end-diastolic volume</td>
<td>145±38 ml</td>
<td>225±20 ml (55%)*</td>
</tr>
<tr>
<td>LV end-diastolic volume/index</td>
<td>76±20</td>
<td>125±11</td>
</tr>
<tr>
<td>LV end-systolic volume</td>
<td>46±19 ml</td>
<td>81±20 ml (76%)*</td>
</tr>
<tr>
<td>LV end-systolic volume/index</td>
<td>24±10</td>
<td>43±10</td>
</tr>
<tr>
<td>Global volume/mass</td>
<td>0.78±0.12</td>
<td>0.97±0.15 (25%)*</td>
</tr>
<tr>
<td>Regurgitant fraction</td>
<td>44±3.8%</td>
<td></td>
</tr>
<tr>
<td>Method 1</td>
<td>1.11±0.04</td>
<td>1.36±0.06*†</td>
</tr>
<tr>
<td>Method 2</td>
<td>1.07±0.06</td>
<td>1.18±0.07††</td>
</tr>
</tbody>
</table>

*p<0.05 normals versus aortic insufficiency.

†p<0.05 method 1 versus method 2.

(‡), Percent change, normals versus aortic insufficiency.
mean global volume/mass ratio (all ventricular slices) was 0.78±0.12 for normal subjects and 0.97±0.16 for patients with aortic insufficiency (p<0.01 normal versus aortic insufficiency). The calculated regurgitant fraction for patients with aortic insufficiency was 44±3.3%.

**Ventricular Dimensions as a Function of Tomographic Level in Normals**

In normal subjects, the average wall thickness for the axial (method 1) and orthogonally corrected data (method 2) were 1.11±0.05 cm and 1.07±0.09 cm, respectively (p=NS) (Table 1). However, for both methods, wall thickness was appreciably less at the apical two tomographic levels compared with the basal four levels (p<0.01). Compared with method 2, there was a trend for method 1 to overestimate wall thickness, although this difference did not reach statistical significance.

The average global R/T ratios for methods 1 and 2 were 1.73±0.12 and 1.8±0.10, respectively. Regional ventricular R/T ratios measured by methods 1 and 2 are presented in Table 2. Regardless of the method, significant differences were observed between regional R/T ratios at the most apical levels 6, 7, and 8 compared with those at the basal three tomographic levels (p<0.01). In normal patients, the three lowest tomographic levels corresponded to 24% of the total myocardial mass imaged. When method 1 was used, the apical and penultimate R/T ratios were 60% and 40% smaller than the R/T observed at the cardiac base. With method 2, these same two levels were 48% and 26% smaller than the R/T observed at the cardiac base.

Figure 2A illustrates the contours of a composite left ventricle derived from all 11 normal subjects employing both methods 1 and 2. Note that the epicardial and endocardial contours are similar regardless of the method employed. The second-order regression equations and correlation coefficients for the epicardial and endocardial curves are seen in Table 3.

**Ventricular Dimensions in Patients With Volume-Overload Hypertrophy**

The mean wall thicknesses in patients with aortic insufficiency were 1.36±0.06 and 1.18±0.07 (p<0.01) for methods 1 and 2, respectively. Method 1 did not demonstrate any significant differences between apical and basal wall thicknesses. However, method 2 demonstrated the expected apical thinning of levels 7 and 8 compared with the upper tomographic levels (p<0.05). At all levels, regardless of the method used, the regional endocardial radii were significantly greater in the volume-overload patients than in normal subjects (p<0.001).

Similar to the pattern in normal subjects, the endocardial radius of curvature at the upper four tomographic levels were relatively uniform whereas these radii varied significantly at levels 5–8 when compared to the base (p<0.01). At the four lowest levels the endocardial radius of curvature, measured by method 2, was significantly larger than that calculated by method 1 (p<0.01).

Regional left ventricular end-diastolic R/T ratios in patients with compensated volume overload are tabu-

![Figure 2](image-url)

**Figure 2.** Panel A: Depicts the composite epicardial (upper curve) and endocardial (lower curve) contours for the normal left ventricle as determined by both methods. The range of orthogonal correction needed to convert the axial to orthogonal data was −2° at the base and +28° at the apex. Panel B: Depicts the composite contours in patients with aortic insufficiency by both methods. The range of orthogonal correction needed to correct the axial to orthogonal data was −6° at the base and +44° at the apex.

<table>
<thead>
<tr>
<th>Table 2. Regional Left Ventricular End-Diastolic R/T Ratios</th>
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</thead>
<tbody>
<tr>
<td>R/T ratio</td>
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<tr>
<td>--------------------</td>
</tr>
<tr>
<td>Normal</td>
</tr>
<tr>
<td>Method 1</td>
</tr>
<tr>
<td>Method 2</td>
</tr>
<tr>
<td>Aortic insufficiency</td>
</tr>
<tr>
<td>Method 1</td>
</tr>
<tr>
<td>Method 2</td>
</tr>
</tbody>
</table>

* indicates p<0.05 versus levels 1, 2, and 3.
† indicates p<0.05 between methods 1 and 2.
lated in Table 2. The mean global R/T ratios for methods 1 and 2 were 2.18±0.16 and 2.55±0.18, respectively (p<0.001). With method 1, the apical and penultimate R/T were 72% and 61% smaller than the R/T at cardiac base. With method 2 these same levels were 50% and 37% smaller than the basal R/T. Both methods demonstrated significant differences between the R/T at levels 8, 7, 6, and 5 versus those of levels 1–3 (p<0.01). The images at these four lower levels corresponded to 33% and 35% of myocardial and 25% and 30% of the ventricular volume imaged by methods 1 and 2, respectively. In contradistinction to the pattern seen in normal subjects, significant intermethod variation was observed at the four lowest levels where method 2 resulted in a significantly greater R/T ratio than method 1 (Table 2).

Figure 2B compares the ventricular epicardial and endocardial contours for methods 1 and 2 in all patients with aortic insufficiency. The regression equations and correlation coefficients for curve fitting these data are seen in Table 3.

FIGURE 2B. Comparison of the ventricular epicardial and endocardial contours for methods 1 and 2 in all patients with aortic insufficiency. The regression equations and correlation coefficients for curve fitting these data are seen in Table 3.

| Table 3. Second-Order Regression Equations and Correlation Coefficients for Epicardial and Endocardial Curves |
|-------------------------------------------------|-------------------------------------------------|-----|-------------------------------------------------|-------------------------------------------------|
| Patients                                      | Epicardial                                      | r  | Endocardial                                      | r  |
| Normals                                       | y=-0.45x²+0.11x+3.78                           | 0.98| y=-0.41x²+0.12x+2.51                            | 0.99|
| Method 1                                      | y=-0.49x²+0.14x+3.72                           | 0.99| y=-0.43x²+0.16x+2.44                            | 0.99|
| Aortic insufficiency                          | y=-0.05x²+0.10x+4.95                           | 0.98| y=-0.05x²+0.07x+3.75                            | 0.99|
| Method 1                                      | y=-0.09x²+0.33x+4.77                           | 0.99| y=-0.07x²+0.25x+3.59                            | 0.98|

Although tomographic ventricular mass always exceeded its corresponding ventricular volume, the magnitude of this difference was small and relatively constant irrespective of ventricular level. The mean difference between myocardial mass and the corresponding tomographic ventricular volume was 4.05±0.71 cm³ and 3.7±0.46 cm³ by methods 1 and 2, respectively.

**Regional Left Ventricular Volume and Mass in Aortic Insufficiency**

The base-apex relation between regional left ventricular mass and volume for patients with volume overload secondary to aortic insufficiency is shown in Table 5. The mean global volume/mass ratio for all eight tomographic levels was 0.97±0.06 and 1.19±0.04 by methods 1 and 2, respectively (p<0.01 between methods). As anticipated, the global volume/mass ratio determined by

**Regional Left Ventricular Mass and Volume in Normal Subjects**

The mean global volume/mass ratios for methods 1 and 2 were 0.69±0.08 and 0.74±0.06, respectively. Estimates of regional left ventricular wall mass and cavity volumes in normal subjects measured by methods 1 and 2 are provided in Table 4. In normals, the regional myocardial mass and volume were found to be nearly constant for the basal four tomographic levels. However, with increasing radius of curvature as the apex is approached, greater variations between ventricular mass and volume are observed. Both methods 1 and 2 demonstrated that tomographic volume and mass at the upper five levels were significantly different from the apical levels 6–8 (p<0.01).
method 2 was greater than that measured by method 1. Method 2 tended to overestimate ventricular volume and underestimate mass when compared to method 1.

In contradistinction to the normal regional pattern where mass exceeds volume at all levels, patients with volume-overload hypertrophy demonstrated that ventricular tomographic volume was significantly greater than corresponding mass at the upper three levels (p<0.01). With method 2, ventricular volume was significantly greater than corresponding mass at the upper three levels and demonstrated a nonsignificant trend (p=0.06) for volume to exceed mass down to the sixth tomographic level (Table 5). With method 2, the average regional myocardial volume exceeded the corresponding mass by 4.98±0.06 cm³, whereas with method 1 myocardial volume was not significantly different than the corresponding mass (0.32±0.08 cm³).

Discussion

This study underscores four major findings.

In normal subjects, regional left ventricular end-diastolic R/T ratios vary as a function of the relative base-to-apex tomographic position. Therefore, the hypothesis stating that regional R/T ratios are homogeneous cannot be substantiated.

The hypothesis stating that global and regional R/T ratios normalize in patients with volume overload hypertrophy cannot be supported. Both global and regional R/T ratios were significantly greater in patients with compensated aortic insufficiency than those found in normal subjects. However, the pattern of regional R/T ratios in both normals and the aortic insufficiency patients was similar, suggesting a degree of chamber homology.

In normal subjects, regardless of the method of analysis, regional left ventricular short-axis tomographic mass always exceeds its corresponding ventricular volume.

In contradistinction to the normal pattern, regional left ventricular volume exceeded corresponding mass at the upper ventricular levels in subjects with compensated volume overload hypertrophy. The magnitude of this difference was greatest at the basal portions of the left ventricle where volume exceeded mass by as much as 44%.

Regional R/T in Normals and Patients With Aortic Insufficiency

There is little prior information regarding the normal pattern of in vivo regional R/T ratios in normal subjects and those with volume-overload hypertrophy. It has been postulated that normal base-to-apex thinning of the myocardium is related to maintenance of a constant regional R/T ratio that in turn might aid in maintaining normalized regional wall stress.1-4 However, the findings of this study fail to support this hypothesis. It was observed in normal and hypertrophied volume-overloaded ventricles that regional left ventricular R/T ratios progressively increase from apex to the mid ventricular level. From mid level to the base, R/T remains relatively constant. For example, with method 1, R/T at the apex and penultimate levels were 2.54 and 1.64 times greater than those found at the base. Using

**Table 4. Estimates of Regional Left Ventricular Wall Mass and Cavitary Volumes**

<table>
<thead>
<tr>
<th>Volume/mass (normals) (cm³)</th>
<th>Tomographic level</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(Base)</td>
</tr>
<tr>
<td>Method 1</td>
<td></td>
</tr>
<tr>
<td>Volume</td>
<td>20.9±1.5</td>
</tr>
<tr>
<td>Mass</td>
<td>24.4±2.4</td>
</tr>
<tr>
<td>Method 2</td>
<td></td>
</tr>
<tr>
<td>Volume</td>
<td>20.9±0.4</td>
</tr>
<tr>
<td>Mass</td>
<td>24.8±1.2</td>
</tr>
</tbody>
</table>

*p<0.05-0.005, volume versus mass.

**Table 5. Base–Apex Relation Between Regional Left Ventricular Mass and Volume**

<table>
<thead>
<tr>
<th>Volume/mass (aortic insufficiency) (cm³)</th>
<th>Tomographic level</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(Base)</td>
</tr>
<tr>
<td>Method 1</td>
<td></td>
</tr>
<tr>
<td>Volume</td>
<td>43.1±2.6</td>
</tr>
<tr>
<td>Mass</td>
<td>33.5±1.5</td>
</tr>
<tr>
<td>Method 2</td>
<td></td>
</tr>
<tr>
<td>Volume</td>
<td>48.6±3.9</td>
</tr>
<tr>
<td>Mass</td>
<td>35.5±2.5</td>
</tr>
</tbody>
</table>

*p<0.05-0.005, volume > mass.

†p<0.05-0.005, mass > volume.
method 2, these values are 1.92 and 1.36 times greater. These data lend credence to reports suggesting that left ventricular wall stress is greater at the base than at the apical levels.24–27

In a pattern similar to that in normal subjects, the R/T ratios in patients with compensated aortic insufficiency were relatively uniform at the upper three or four tomographic levels and progressively decreased toward the apex (Table 2). However, the R/T ratios at the lowest four levels were significantly smaller than those of the base. With method 1, the R/T ratio at the base was 3.52 and 2.57 times greater than that observed at the apex and penultimate levels, respectively. With method 2, the basal values were 1.98 and 1.59 times greater than the apical and penultimate levels. It is hazardous to infer patterns of wall stress from these data without the corresponding instantaneous cavitary pressure. Nevertheless, the regional variability of R/T ratios suggests that wall stress may be regionally heterogeneous in both normals and patients with compensated volume overload hypertrophy. However, in addition to chamber pressure, radius, and wall thickness, longitudinal and shear deformations may be important in determining the overall regional stress. Recent studies have demonstrated regional differences in cardiac twist, suggesting that shear forces may also be heterogeneous. Whether these additional variables might compensate for regional differences in the R/T ratio, thus resulting in a more homogeneous distribution of stress, is unknown.28–30

Global and Regional R/T Ratios Measured by Ultrafast CT

The ultrafast CT measurements of regional R/T ratios at the base are significantly different from the results of earlier studies. In the seminal study by Grossman et al.,7 the mean end-diastolic R/T ratios in normals and aortic insufficiency patients were both 2.9 ± 0.02 (reported as T/R ratio of 0.34). Since the R/T ratios in normal and the volume overload patients were identical, the authors concluded that the hallmark of compensated volume overload was the normalization of the R/T ratio. However, the validity of their data and subsequent conclusions must be doubted because the geometric conversion of this R/T ratio translates into a left ventricular volume exceeding the mass by a ratio of 1.24:1. Similarly, Gaasch et al9–10 observed an R/T ratio in normals of 2.98, which translates into left ventricular volume exceeding mass by a ratio of 1.28:1. However, because normal left ventricular mass always exceeds its corresponding volume, these ratios and attendant conclusions are likely to be in error. The R/T ratios reported in these older studies were obtained from single M-mode echocardiographic measurements. Thus, it is likely that the normal R/T ratios were overestimated as a consequence of lack of standardization of echocardiographic measurement criteria and M-mode orientational ambiguity. In contrast to these earlier studies we observed the R/T ratio at the base of the normal heart to be 2.05 ± 0.1, which is similar to the reported postmortem R/T value of 1.9.31 Consequently, the hypothesis that the R/T ratio normalizes in patients with compensated volume overload should no longer be accepted.

In patients with aortic insufficiency and varying degrees of ventricular function prior studies measured equatorial R/T ratios between 3.3 and 3.4.7,9 In the present study, the mean R/T ratios at the cardiac base were 3.1 and 3.2 by methods 1 and 2, respectively. As a consequence of the normal base-to-apex variability, the global R/T ratios were much smaller, 2.18 and 2.55, with methods 1 and 2, respectively. Thus, because the R/T ratio varies relative to cardiac position, a single radius and wall thickness measurement at the cardiac base will overestimate the average R/T ratio and cannot be used to characterize global R/T values.

Regional Variability of R/T Ratios

Previous studies have suggested that R/T and volume-to-mass ratios are regionally constant throughout the left ventricle.1–4,32,33 However, in vivo measurements of these indexes have not been made in either the normal or volume-overloaded ventricles. Janiki et al32,33 analyzed the left ventricular volume/mass relation in extirpated dog hearts. From their observations, they concluded that the average R/T ratio (and consequently wall stress) was homogeneous over the basal one half of the heart and was more variable at the lower ventricular levels. They attributed this variability to inadvertent inclusion of extraneous papillary muscle mass, thus increasing the apparent wall thickness. However, the degree to which this additional mass actually altered the volume/mass ratio was not addressed or quantified. In contrast, we excluded all visible papillary muscle before analysis and still found R/T to be variable. Furthermore, the greatest variability in R/T ratios was found at the three lowest tomographic levels, whereas in humans we observed little papillary muscle mass. Finally, the reliability of data obtained from examining a limited number of formaldehyde-fixed canine hearts that undergo unpredictable postmortem morphometric changes must be approached with great caution.

Volume-to-Mass Relation

The values for the normal global volume/mass relation reported in this study are in concert with previous investigations,1,4,21–23 although comparative studies analyzing regional volume/mass variability are lacking. The volume/mass relation conveys additional information that is not readily apparent from its related R/T ratio. For example, although the volume/mass ratio is regionally variable in normals, the absolute difference between regional mass and volume was relatively constant (Table 4). In normals at each level, myocardial mass always exceeded corresponding ventricular volume, although the absolute magnitude of this difference was small, averaging only 3.7 ± 0.4 g per level. The significance of this observation is unclear. However, one may speculate that when myocardial mass exceeds its corresponding volume, the mechanical efficiency of the contracting segment is enhanced since less work would be needed to displace a given load. This relation should hold true so long as the energy savings realized by the reduction in work were greater than the energy lost in maintaining the extra myocardial mass.

In contrast to normals, the patients with compensated aortic insufficiency demonstrated a unique regional volume/mass pattern. In these patients, left ventricular
volume was significantly greater than corresponding left ventricular mass at the three highest tomographic levels regardless of the method used. With method 2, there was a trend for regional ventricular volume to exceed ventricular mass at three additional, contiguous levels. This relation, which has not been previously reported, suggests that chronic volume overload may induce a regionally heterogeneous pattern of left ventricular hypertrophy.

The geometric relation between R/T and volume/mass ratios are such that when the cavity radius is greater than 58.5% of corresponding wall thickness (radius/thickness, 2.41/1), ventricular volume will always exceed myocardial mass. The nature of the geometric relation between a variable ventricular volume and mass and constant wall thickness is explained by Figure 4. Previously, postmortem and ventriculographic studies of the normal ventricle have established that left ventricular mass always exceeds its volume.21-23 Consequently, studies that report normal R/T ratios of 2.5–3.3 are of questionable validity since this ratio would indicate that ventricular volume exceeded ventricular mass by a ratio of 1–1.3:1.7-13

Axial Versus Orthogonal Method

No attempts were made to determine a "true central axis" for reconstruction of the left ventricle since there is little consensus regarding the preferred axis.33 Imaging the heart from base to apex with multiple fixed-plane detectors results in acquisition of lower-level tomographic scans that become progressively more oblique with respect to the basal short-axis view. In normal subjects, "planar" (method 1) imaging resulted in a mild overestimation of wall thickness and underestimation of radius at the lower ventricular levels. The mean out-of-plane angles ranged from -2° at the base to +28° at the apex (Figure 2A). Since the meridional radius of curvature is gentle in normals, methods 1 and 2 yielded nearly identical results. Patients with aortic insufficiency demonstrated a steeper base-to-apex radius of curvature. In these patients, the mean out-of-plane angles ranged from -6° at the base to +44° at the apex (Figure 2B). The more severe meridional radius of curvature ultimately results in a greater tomographic obliquity at the lower ventricular levels. This obliquity of tomographic images results in an underestimation of the expected cavitary radius and an overestimation of the wall thickness at the lower tomographic levels.

An explanation for these findings may be found in Figure 1. Imaging the heart with ultrafast CT is analogous to sectioning an egg, placed obliquely, in a hard-boiled egg slicer. Since each slice (tomogram) cannot be acquired exactly perpendicular to the endocardium, the orthogonally reconstructed slices will at times (and to varying degrees) overestimate ventricular radius (and volume) and underestimate wall thickness (and mass) when compared to the uncorrected axial tomogram. This occurs as a consequence of imaging the myocardium at rigid intervals, with relatively thick voxels. The meridional radius of curvature, progressively increases from the upper mid ventricle to the apex that corresponds to levels 3–5, which is the greatest slope of transition in both normals and aortic insufficiency patients. Thus, as illustrated in Figure 1 at level 3, the myocardium will be underscanned and the ventricular cavity oversampled when orthogonally correcting axial data. Likewise, the greatest disparity between axial and orthogonal data will be found when measuring the wall thickness and radius at the apical levels. Similar findings were recently observed by Beyar et al,34 who demonstrated in normal dog hearts that planar acquisition introduced a bias which tended to overestimate wall thickness as compared to methods that measure it perpendicular to the endocardium.

It is unclear which, if any, of the two methods employed is most applicable for measuring regional radius, wall thickness, or R/T ratios or calculating wall stress. If a modified Laplacian theorem is to be applied, then these indexes must be calculated perpendicular to the endocardial surface. Thus, the greater volume defined by the orthogonal method may represent the "effective" volume (load) exerted and distributed over the "effective" wall thickness (myocardial mass).

Advantages and Limitations of Ultrafast CT for Measuring the Volume/Mass and R/T Ratios

Imaging the heart with ultrafast CT permits acquisition of multiple, serial, real-time tomographic images that are parallel, spatially oriented, and registered to each other. The favorable spatial resolution and known tomographic slice thickness facilitate accurate edge detection, permitting faithful measurement of ventricular mass and volume independent of geometric assumptions.15-17 Additionally, this technique is relatively non-invasive and can be performed on an outpatient basis. The need for ionizing radiation and iodinated contrast agents are a minor limitation of the technique. The risk-benefit ratio of studying patents with moderate renal insufficiency, contrast allergy, or irregular cardiac rhythm should be carefully weighed.

In this study, radius and wall thickness measurements were derived from the appropriate planimetric surface areas. Converting cross-sectional area to mean radii and wall thickness is preferable to discrete linear sampling of radius and wall thickness. As previously demonstrated,35 a 3-mm error in wall thickness results in a 29% error in calculated ventricular volume and a 21% error in myocardial mass. In this study, the normal subjects were imaged employing a spatial resolution of 1.4 mm²/pixel. Thus, if absolute linear measurements had
been employed, a random error of one pixel would translate into a 10% and 15% error in volume and mass, respectively. To minimize random errors in edge placement, radius and wall thickness were measured from the planimetric myocardial area.

Two different contrast agents were used in this study. When the normal subjects were scanned, only ionic contrast agent was commercially available. With the availability of nonionic agents, all further ultrafast CT studies were performed with these agents. Although it is unfortunate that two different contrast agents were used, it is unlikely that the ionic agent would significantly alter the results and conclusions of this study for the following reasons: 1) Measurement of myocardial mass and wall thickness is not affected by the type of contrast agent used. The initial validation studies demonstrating the precision and accuracy of ultrafast CT measurements of myocardial mass were performed with the ionic contrast agents Renografin 76, 10 and 2) unlike traditional contrast ventriculography where large volumes of contrast are rapidly injected into the central circulation, in this study contrast was injected into a peripheral vein, at much reduced rate (over 15–20 seconds) and at a much lower dose (0.35 ml/kg). Administering ionic contrast at a rate of 2–3 ml/sec is devoid of significant hemodynamic effect in normal subjects. Thus, although it is best to avoid high-osmolality ionic agents, it is unlikely that these agents, in normal subjects and in the doses used, would have significant impact on the measurement of ventricular volumes and masses in normal subjects.

When calculating average dimensions for a given tomographic level, it is difficult to perfectly align comparable tomographic slices from other ventricles because each heart is a different length. To circumvent this, we acquired the first tomographic image immediately above the apex, which is the most consistent anatomic landmark. Thereafter, the next eight images could be sequentially registered. Since interslice registration between patients is not perfect, this mode of analysis introduces a slight degree of misregistration. Thus, averaging dimensions from each level across many patients introduces a variance in the data. Since this variance would tend to obscure an even more pronounced variability in regional R/T ratios, it is not detrimental to the study, but rather strengthens the confidence in the results.

Finally, the method used to reconstruct the ventricle is only an approximation. There is significant room for improvement in the methods used for three-dimensionally reconstructing the ventricle and obtaining measurements orthogonal to the endocardium.

Conclusions

Contrary to postulates that presuppose the uniformity of the left ventricular R/T ratio, direct measurements of regional volume/mass and radius—wall thickness ratios indicate that ventricular loading conditions vary significantly from apex to base in the normal and hemodynamically compensated volume-overloaded left ventricle. Furthermore, the findings of this study seriously question the accepted hypothesis that the left ventricle compensates for chronic volume overload by normalizing the R/T ratio. Finally, because left ventricular volume loading conditions are regionally variable, methods that calculate ventricular wall stress based on a limited number of “representative” radii and wall thickness measurements are likely to be incorrect, especially when idealized assumptions of ventricular architecture and wall motion are altered by pathologic states.

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