Estimation of Left Ventricular Mass in Normal and Infarcted Canine Hearts Using Thallium-201 SPECT

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A new automated edge detection program has been developed to estimate left ventricular mass from single photon emission computed tomographic (SPECT) ²⁰¹TI images and 14 dogs were studied. Six of the 14 dogs underwent imaging before and 5 hr after coronary artery occlusion with a closed-chest technique. True left ventricular mass was determined at time of killing within 1 hr of the last ²⁰¹TI study. Left ventricular mass determined by tomography correlated well with autopsy left ventricular mass (r = 0.94; p < 0.001, s.e.e. = 5.9 g) over a range of 62–156 g. The intraobserver variation between repeated measurements of the same SPECT study yielded an r = 0.99; p < 0.0001; s.e.e. = 2.3 g. The reproducibility of the mass determination was assessed in four animals with two studies performed 10–14 days apart. The estimate of left ventricular mass from the two studies were highly correlated (r = 0.98; p < 0.001) with a mean absolute difference of 4 g (3.3%). In the six dogs with a control and postinfarct study the mean total left ventricular mass by ²⁰¹TI tomography varied by <3.8% (r = 0.89; p < 0.001). In conclusion, tomographic imaging with ²⁰¹TI can define left ventricular mass accurately and reproducibly in the dog model. The ability of this ²⁰¹TI tomographic left ventricular mass program to measure both normal and infarcted tissue accurately suggests the possibility of (a) documenting interventions designed to alter left ventricular mass and (b) of sizing acute infarcts and assessing interventions that may alter acute infarct size.


The ability to measure left ventricular (LV) mass could provide prognostic information regarding the clinical course of patients with ischemic (1) and hypertrophic heart disease (2).

Thallium-201 (²⁰¹TI) single photon emission computed tomography (SPECT) has shown the potential for estimating LV mass. Reliable estimates of left ventricular mass have been calculated from ²⁰¹TI tomographic images of both normal (3) and infarcted canine tissue (4,5). The purpose of our investigation was to estimate the mass of both normal and infarcted myocardial tissue in a canine model, and to assess the accuracy and reproducibility of such measurements.

MATERIALS AND METHODS

Animal Studies

Fourteen mongrel dogs weighing 15–43 kg were studied. After a 24-hr fast, each dog was anesthetized with i.v. pentobarbital sodium. Two to four millicuries of ²⁰¹TI was injected through a peripheral vein and tomographic imaging was performed 15–20 min thereafter. Four animals had a single ²⁰¹TI tomographic study without any intervention. In four of 14 dogs, a second thallium tomographic study was performed 10–14 days after the first study to assess the reproducibility of the mass determination. An additional six of 14 dogs underwent coronary artery occlusion with a balloon occluder 10–14 days after their initial ²⁰¹TI tomographic study to assess our ability to measure both normal and infarcted tissue with the tomographic technique. The coronary occlusion was created using a catheter guided-detachable balloon ordinarily used to occlude cerebral arteriovenous malformations. Occlusion of the vessel was verified by repeat coronary arteriography and by subsequent biochemical staining. Imaging after the creation of an infarct was begun 5 hr after the occlusion of a coronary artery. All study procedures were approved by the

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Harbor-UCLA Animal Research Committee and conformed to the position of the American Heart Association on research animal use.

Studies were obtained on a large field-of-view rotating gamma camera equipped with a parallel hole, low-energy high resolution collimator. The full width half maximum resolution of the imaging system is ~19 mm at 20 cm using water as the scatter medium. No electrocardiographic gating was employed and the animals were allowed to breathe spontaneously. Studies were obtained with the spectrometer adjusted for the simultaneous acquisition of the 69-83 keV x-ray emissions of $^{201}$TI with a 25% window and for the 167 keV gamma-ray emissions with a 12.5% window. Thirty-two $64 \times 64$ matrices were obtained during a 180° rotation. Each $64 \times 64$ matrix was collected for 40 sec during each of the 32 steps and contained 150,000–200,000 counts. Data processing was performed on a dedicated computer using a backprojection algorithm with pure ramp filtering and no attenuation correction.

The series of planar views acquired are reconstructed using the manufacturer's software, to obtain one pixel thick transaxial (transverse) slices. These transaxial slices are then smoothed with a 1-2-1 three-point weighted smooth applied in each dimension. The smoothed slices are then realigned to produce 1 pixel (~0.6 cm) thick slices parallel to the long axis of the left ventricle (long axis slices). Using these long axis slices as a guide, the operator defines the apex and base of the myocardium. Next, 2 pixel thick slices perpendicular to the long axis of the left ventricle (short axis slices) are created between the operator defined apex and base and are expanded by a ratio of 1:2. All measurements of myocardial mass are made from geometrical calculations on these expanded short axis slices. No background subtraction was utilized.

**Estimation of LV Myocardial Volume and Mass from $^{201}$TI SPECT**

A new method was developed in our laboratory for approximating the epicardial and endocardial borders of the left ventricle using $^{201}$TI single photon tomographic imaging. The program developed by one of us (CJT) is an automated technique to reduce inter- and intraobserver variability. The technique does not depend on threshold measurements as has been described by others (3–5).

**Initial determination of the epicardium.** A composite image representing the sum of all short axis slices was created and displayed on a television monitor. The operator defines the approximate center of the left ventricle with a cursor displayed over the composite image. The $(x,y)$ coordinates of the operator defined center are then stored. Next, two 64-point profiles are created from the composite image. The first profile represents the sum of counts occurring in each row and the second profile represents the sum of counts in each column. A schematic representation of one of the resulting profiles is shown in Figure 1.

The maximum upslope and the maximum downslope (point a and point b, respectively) are determined for each profile. The average of $\frac{1}{2}$ the distance between point a and point b determined from the two profiles defines a radius $(r)$. This radius and the operator defined LV center describe a circular region for each short axis slice which represents a first approximation of epicardium’s location.

**Profile creation.** For each short axis slice, a set of 60 radial profiles $6°$ apart is created. Each profile originates at the operator defined LV center and proceeds outward radially for a distance equal to the radius $r$ previously defined.

**Edge detection.** A schematic example of a profile created from normal myocardium is depicted in Figure 2A (radius #x) and an example of a profile created through myocardium with a perfusion defect is shown in Figure 2B (radius #z).

The maximum downslope (i.e., the minimum of the first derivative of the profile) was used as the next step in defining the epicardial boundaries of a profile created from any short axis slice. The maximum downslope is point $d$ in both figures. The only constraint placed on the location of the maximum downslope was that it must fall in the outermost two-thirds of the profile. This step is taken because the origin of a profile (which was defined manually in previous steps) may not coincide with the true center of an individual LV slice and could lie at point a rather than point b in both figures. Such a profile could begin with a decline of activity representing the transition from the opposite endocardial cardiac wall (on which point a lies) to the LV center. However, since the maximum downslope must fall in the outer two-thirds of the profile, erroneous detection of points with a minimum first derivative between point a and b was prevented. The maximum downslope of each of the 60 radial profiles in a short

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**FIGURE 1**
Initial definition of LV epicardium. See text for detail.
axis slice (origin to point d in Figures 2A and 2B) represent the second approximation of the LV epicardial edge.

The endocardial boundary along a profile is then approximated by defining the maximum upslope (i.e., maximum of the first derivative) within the profile interval from the origin to point d. This procedure is repeated for each profile of each short axis slice and results in one set of 60 radii for the endocardial boundary of that slice (origin to point c in Figures 2A and 2B).

Each endocardial and epicardial boundary is then redefined. The center of each boundary was redefined as the center of mass of all 60 (x,y) locations that were described in the preceding two paragraphs. The radius of each endocardial and epicardial boundary was redefined as the average of all 60 radii as described above. These new radii calculated for the endocardial and epicardial edges are connected and smoothed. These boundaries define the final computed regions of interest (ROIs) which define the myocardium in each short axis slice.

Although this edge detection algorithm makes certain assumptions regarding the shape and structure of the left ventricle, it provides accurate and reproducible estimates of LV mass. Since it is possible for an epicardial or endocardial border to be calculated erroneously, each LV slice with its computer defined boundary ROIs are displayed and stored. Visual inspection of all LV slices in this study (and in 40 routine patient studies) failed to show any obvious misplacement of epicardial or endocardial ROIs.

**Quantification of total myocardial mass.** The ROIs for the endocardial and epicardial borders as described above are used to calculate myocardial volumes for each short axis slice. The estimated myocardial volume was based on the total number of volume elements (voxels) in all sections multiplied by the volume of each voxel which was in turn multiplied by a mass of myocardium (1.05 g/cm³). This automated technique required ~4 min to process all myocardial sections. The intraobserver variability in processing the same 201TI tomographic 2 wk apart was minimal with a correlation of 0.99 and a standard error of the estimate of 2.3 g.

Infarct size was estimated by superimposing a 40% threshold (40% of maximal counts) within the epicardial and endocardial borders defined above. Infarct mass was then calculated from the voxels contained within the 40% isocount line. The choice of a 40% threshold was based on our previously published observations (6) and an analysis of the “best fit” of the tomographic estimates of infarct mass to the observed LV infarct mass.

**Postmortem Determination of LV Mass in Normal and Infarcted Tissue**

Twelve dogs were killed immediately after imaging by an overdose of i.v. pentobarbital sodium. The remaining two animals received an overdose of concentrated potassium chloride. The heart was removed, and the great vessels, atra, right ventricular free wall and papillary muscles, epicardial fat and A-V valves were excised. The left ventricle was then weighed, cut into 1-cm-thick slices, and stained with triphenyltetrazolium chloride. Infarct area was determined by planimetry of enlarged photographs of both sides of each of the stained myocardial slices and expressed as a percentage of the total slice weight. Infarct mass was determined by summing the infarct mass of each of the stained heart sections. A typical short axis section through an infarcted heart is depicted with its corresponding 201TI tomographic short axis image in Figure 3.

The two animals killed with potassium chloride underwent a repeat 201TI tomographic study immediately after killing to assess the role of wall motion and wall thickening on estimates of myocardial volume and mass.

**Statistical Methods**

The actual and estimated total LV mass and infarct mass were compared using linear regression analysis (least squares method). Correlation coefficients for paired data were obtained using standard methods.

**RESULTS**

The estimated LV mass from tomographic imaging was highly correlated with the postmortem LV mass. Despite a relatively narrow range of heart weights (62–156 g at autopsy), the estimated tomographic mass correlated with postmortem LV mass with an r value of 0.94; p < 0.001; s.e.e. = 5.9 g (Fig. 4).

The reproducibility of mass determinations by thallium-201 201TI SPECT is illustrated in Table 1 where comparison of the initial and second 201TI tomographic study yielded a correlation coefficient of 0.98; p < 0.001. The mean absolute difference was 4 g (3.3%) with a s.d. of the absolute difference of 1.8 g.

Six animals underwent myocardial infarction (five left anterior descending, one circumflex occlusion). The estimated LV mass after the myocardial infarction differed from the control value by an average of 4.2 g (+3.8%) with an r = 0.89; p < 0.001. In general, the postinfarction estimate of total LV mass was the same or slightly greater than the control value (Table 2).

An attempt to use thresholds to determine LV mass resulted in a 15–26% underestimation of mass in the infarcted SPECT studies when compared with control values. To demonstrate the reproducibility of the edge.
FIGURE 3
A triphenyltetrazolium chloride stained short axis section from the heart from one of the animals studied is depicted on the right. The small arrow indicates the location of the occluded left anterior descending coronary artery. The corresponding short axis $^{201}$TI tomographic image is depicted in the left hand portion of the panel, with a color scale on the far left indicating the amount of $^{201}$TI activity present in the left ventricular (LV) slice (white—indicating the highest degree of activity, blue—the lowest degree of activity). The estimated endocardial and epicardial borders are projected over the LV section in blue.

detection program, the initial LV mass determination of all ten animals with sequential studies were averaged (mean = 114.2 ± 16.3 g) (mean ± s.d.). These studies were then compared with the second control study (four animals) and the postinfarct studies (six animals). The mean estimated LV mass of the second study was 115.3 ± 15.0 g. The mean difference between the two studies was 1.1 g with a mean absolute difference of 4.1 ± 2.4 g (3.6%). This represents a “worst case” analysis of the reproducibility data since control estimates of mass were compared with both infarcted and noninfarcted hearts in the second study.

Infarct mass at autopsy (mean = 12.2 g; range 4–25 g) also correlated highly with tomographically determined infarct mass with $r = 0.94$; p < 0.001; and a s.e.e. of 2.9 g. A small 4-g apical myocardial infarct was not identified by the tomographic infarct detection routine (Fig. 5). The use of a 40% isocount threshold to define infarcted tissue was chosen prospectively and was based on our previous observations (6). Analysis of other threshold values after the completion of this study yielded poorer correlation coefficients, thus validating our initial choice of isocounts for infarct definitions.

The effect of cardiac and respiratory motion on the LV mass determination was assessed in two animals. They were imaged with $^{201}$TI tomography while in sinus rhythm and immediately after an overdose of potassium chloride. One had undergone a myocardial infarct, the other had not. The $^{201}$TI SPECT estimates of LV mass varied by +2 and +3 g in the respective animals despite a subjectively more crisp definition of the endocardial and epicardial borders in the arrested heart.

DISCUSSION

Quantitation of LV mass may have importance in establishing the prognosis of patients with ischemic heart disease or cardiac diseases associated with hypertrophy. The relative size of a planar $^{201}$TI defect after an acute myocardial infarction has been proposed as one of the best methods for defining a patient group at high risk for subsequent cardiac events (7). In patients with hypertrophic cardiac disorders the amount of myocardial mass or degree of hypertrophy may be an important determinant of long term survival and prognosis. Finally, a reproducible method for defining LV
FIGURE 4
SPECT estimates of LV mass are compared with LV weight measured at the time of autopsy (r = 0.94). The closed circles indicate SPECT estimates of mass in animals which did not undergo a myocardial infarction. The open circles represent SPECT mass determined from images of the infarcted heart compared with the LV weight measured after killing the animal. The solid line is the linear regression between the two sets of values.

Our study utilizes methods that are quite different from those reported previously. Investigators (3) who have used threshold measurements as a means for determining the endocardial and epicardial borders of reconstructed 201TI tomographic images have reported intraobserver variabilities (8%) that are higher than our present interstudy variability (3.3%). The small mean difference (4 g) between two 201TI tomographic studies performed 10 days to 2 wk apart indicate a high degree of reproducibility when our reconstruction technique and automated method for determining LV mass is utilized. When control data are compared from all ten

mass would offer the possibility of serial noninvasive evaluations of interventions designed to affect myocardial mass in either the experimental canine model or in patients undergoing therapy for disorders associated with myocardial hypertrophy.

Our study findings are consonant with those of Wolfe and co-workers (3) who found a good correlation between in vivo 201TI SPECT determined LV mass and postmortem LV mass in normal dogs. Other investigators using an in vitro method for evaluating the amount of infarcted myocardium by 201TI SPECT imaging have likewise demonstrated a good correlation between the noninvasive estimation of LV mass and actual measured heart weight (4,5).

TABLE 1
Interstudy Variability in LV Mass Determinations with 201TI SPECT

<table>
<thead>
<tr>
<th>Dog no.</th>
<th>201TI SPECT #1*</th>
<th>201TI SPECT #2</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>155 g</td>
<td>149 g</td>
</tr>
<tr>
<td>2</td>
<td>119 g</td>
<td>117 g†</td>
</tr>
<tr>
<td>3</td>
<td>99 g</td>
<td>96 g</td>
</tr>
<tr>
<td>4</td>
<td>112 g</td>
<td>117 g†</td>
</tr>
<tr>
<td>Mean</td>
<td>(121.25) g</td>
<td>(119.75) g</td>
</tr>
</tbody>
</table>

* The SPECT #1 study preceded the second study (SPECT #2) by 10–14 days.
† Study performed using 2 mCi of 201TI correlation coefficient = 0.98.

FIGURE 5
The 201TI SPECT estimate of infarct mass is compared with infarct weight in grams determined from planimetry of the triphenyltetrazolium chloride defined myocardial infarct. The correlation coefficient was 0.94; p < 0.001. A small 4-g apical myocardial infarct was not identified by the SPECT infarct detection routine. The weight of one subendocardial infarction was overestimated by SPECT, possibly due to areas of peri-infarct ischemia.
animals with two studies (those with a second study without an intervention and those with a postinfarction study), the reproducibility of the data remains high. There was an absolute mean difference of 4.1 ± 2.4 g (3.6%) despite the comparison of normal and infarcted hearts.

Despite the known alterations that occur in LV geometry after an acute myocardial infarction (8), the boundary detection and reconstruction algorithms successfully identified the myocardial volumes of a control study and a subsequent acute infarct study with an average absolute difference of 4.2 g (3.8%). The actual volume of infarcted tissue may be affected by edema and the entrance of other components into the infarcted tissue (9), hence the apparent increase in weight after infarction (+2.8 g) noted in this study could be real.

The calculated normal and infarcted myocardial volumes in this study correlated well with those measured at autopsy (r = 0.94) and suggest that the present 201TI tomographic technique can be used to estimate weight in normal as well as acutely infarcted tissue. It is possible that this technique could be extended to evaluate interventions which are designed to alter acute infarct size, although this possibility requires further investigation.

The apparent thickness of the LV wall on a tomographic slice is determined by the actual thickness of the myocardium as well as by the wall thickening and wall motion that occurs during ventricular systole (10). A study of an arrested heart (or a gated end-diastolic image) should provide a more crisp visual definition of the endocardium and epicardium. However, with our present boundary detection technique, the detected edges were virtually equivalent and therefore the estimated LV myocardial volume (and mass) varied by <2%. Hence, accurate estimation of LV myocardial volumes and mass could be obtained with our method in the nongated, spontaneously breathing canine model. This finding suggests a potential advantage of the SPECT technique when compared with other recently reported methods for determining LV mass, including "cine" computed tomographic scanning (11) and magnetic resonance imaging (12–14). Both of the latter modalities require electrocardiographic gating which may be cumbersome or may be difficult to perform in the face of arrhythmias.

Other imaging techniques have been utilized to estimate LV mass. Two-dimensional echocardiography has been used to estimate mass in animal models (15) and in selected patients. However, the echocardiographic technique makes certain assumptions about LV geometry, and the sensitivity of the technique varies from patient to patient (16). Mass can be determined by computed tomography and magnetic resonance imaging. However, both techniques require expensive facilities and the former does not distinguish between normal and infarcted tissue easily. Hence, 201TI SPECT imaging can provide estimates of normal and infarcted LV mass at a relatively low cost, using equipment that is readily available at many medical centers.

We used large doses of 201TI in most animals in this study to ensure adequate counting statistics. The use of 2 mCi in five of the dogs reported herein did not affect estimates of LV mass. In addition, we have used 3 mCi doses of 201TI in patient studies of LV mass and have found correlation coefficients of 0.96 when compared with data obtained from contrast ventriculography (17).

Despite the encouraging results of our present study, the technique has several limitations. The resolution of the system is limited and attenuation correction has not been addressed. The overestimation of LV mass, particularly in smaller hearts, may be a consequence of these problems. Since the average weight of the canine left ventricles studied in this investigation is near the lower limits of normal for an adult human population, this technique may not be applicable to studies of young patients. However, the linearity of our tomographic mass estimates when compared to postmortem data, suggests the possibility of using a simple regression equation to provide an accurate estimate of LV mass in adult patients.

In summary, we conclude that we can accurately and reproducibly estimate the volume and mass of both normal and infarcted myocardium in the canine model. This technique requires a minimum of operator interaction. It may be useful in future studies to quantitate both hypertrophy and infarction in clinical and experimental studies.

NOTES

1. Technicare Omega 500, Solon, OH.
2. Informatek SIMIS-5, Sophia, Baltimore, MD.

ACKNOWLEDGMENTS

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REFERENCES

4. Holman BL, Moore SC, Shulkin PM, et al. Quantita-