Echocardiographic Definition of the Left Ventricular Centroid. II. Determination of the Optimal Centroid During Systole in Normal And Infarcted Hearts

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Although two-dimensional echocardiography is widely used in both clinical and experimental evaluations of regional cardiac wall motion, there is no established clinical method for quantitative analysis of the wall motion, not even for the normal radial motion observed in short-axis images. Measurement of radial wall motion requires determination of a centroid from which the radii emanate. Depending on its definition, the centroid is variously affected throughout systole by cardiac translation, regional wall motion and any shift of the subject position or transducer. A floating centroid is defined relative to the ventricular walls frame by frame, whereas a fixed centroid never moves with respect to the transducer. Evaluation of the best approach to definition of a centroid was previously presented (part I, this issue). The next question is how to use the centroid.

This study examines which of four centroid applications provides the best reference for quantifying regional wall motion during systole. Method 1 is a floating centroid (defined separately for every image frame), method 2 uses the end-diastolic centroid as a fixed reference for all image frames, method 3 uses the end-systolic centroid as a fixed reference and method 4 uses the average as a fixed reference. Wall motion was measured with respect to each of these centroids by determining radial wall motion from end-diastole to end-systole and correlating radial motion throughout the cardiac cycle with that in normal control hearts. Results were analyzed with respect to interobserver variance, symmetry of contraction in normal hearts (closeness of agreement of excursions for 36 equiangular radials in the short-axis view) and correlation of abnormal contraction with microsphere distribution and infarct staining.

For the normal canine heart with restricted translation, there was no significant difference in motion symmetry attributable to any method of centroid application. For the infarcted dog heart with limited translation, wall motion analysis best corresponded with microsphere distribution when a fixed reference for wall motion analysis was used (p < 0.005). The technique that best corresponded to microsphere distribution and histologic staining incorporated information throughout the cardiac cycle rather than merely analyzing end points (that is, systole versus diastole).

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may compensate to some degree for regional motion not related to regional cardiac function.

Radial measurements require definition of a centroid from which the radii emanate. There are many possible candidates for the centroid of a given image frame. In comparing the centers of endocardial coordinates, epicardial coordinates, their average and the centers of the areas subtended, we previously showed (22) that the center of endocardial area is the most reproducible between different observers for normal canine hearts.

A second major issue is how best to define the centroid throughout the cardiac cycle. The centroid may be defined separately for each image frame in the cardiac cycle (a floating centroid) or the centroid may be a fixed single reference applied to all frames. In unoperated patients with myocardial infarction, the sensitivity to identification of regional wall motion abnormalities, using the short-axis images at the mid-papillary muscle level, was better with fixed references (9). However, in postsurgical patients with increased cardiac translational movements due to pericardectomy, the fixed reference methods have been less sensitive (23). One limitation of these studies is the inability to relate the wall motion observations to the local histology, which might serve as a standard by which to assess accuracy of a particular method. A second limitation is the analysis only of “end-systolic” versus “end-diastolic” image frames, which could be problematic because of asynchrony. The timing of maximal abnormal motion does not necessarily coincide with the time when the cavity is smallest (16).

To clarify the influence of these various factors in different choices of centroid, the reproducibility, symmetry and predictive accuracy of quantified wall motion were assessed in normal and ischemically damaged canine hearts. An index of normality was derived that identifies changes in regional motion throughout the cardiac cycle.

Methods

Animal preparation. Under general anesthesia, nine mongrel dogs (mean weight 18.4 kg) underwent left lateral thoracotomy with excision of 8 cm of the fifth and sixth ribs, as previously described (24), to optimize the echocardiographic window; a pericardial cradle was formed to exclude the thoracic cavity through a subcutaneous tunnel to a pouch at the posterior nape of the neck. A silk snare with a Teflon occluder was placed around the left anterior descending coronary artery in four dogs and around the left circumflex artery in five dogs. The snares and a left atrial catheter were passed through a subcutaneous tunnel to a pouch at the posterior nape of the neck. Strings of metal spheres (3 mm diameter) were aligned on the anterior, lateral and posterior epicardial surfaces so that images and pathologic findings could be precisely correlated. In particular, three epicardial beads marked the plane for coplanar short-axis imaging and post-mortem sectioning at the mid-papillary muscle level. Any pericardial air was evacuated and the thorax was closed.

Two to 4 days after the initial operation, the dogs were prepared for echocardiography, which was performed both before and 6 h after coronary artery occlusion. The dogs were anesthetized with alpha-chloralose (60 mg/kg body weight) or sodium pentobarbital (30 mg/kg), intubated and ventilated with supplemental oxygen adjusted as needed to maintain normal blood gas test results. After recording the first set of images, radionuclide microspheres (scandium-46, strontium-85, niobium-95, rubidium-103, tin-113 or cerium-141) were injected through the indwelling left atrial catheter. Four to six million microspheres (10 to 14 μm diameter), suspended and agitated in Tween (polysorbate) and dextrose solution, were injected into the left atrium and chased with a Ringer’s lactate flush. Femoral artery blood was sampled steadily from 1 min before to 2 min after the injection at 2 ml/min for reference to calibrate flow from microsphere counts (25). The coronary snare was then tightened to occlude the coronary artery. After 6 h of occlusion, the second set of images was obtained, distinctly radionuclide microspheres were injected as before (during 2 ml/min withdrawal of arterial blood) and then the dog was killed by an overdose of pentobarbital.

Echocardiography. Images were obtained with an Advanced Technology Laboratories Mark III mechanical sector scanner with a 3.5 MHz transducer. Complete studies were performed and recorded on 0.5 in. (1.27 cm) VHS videotape. The short-axis view at the level of the midportion of the papillary muscles was required to show the three marker beads continuously and guarantee correspondence to the pathologic section.

Pathology. Immediately after death, the heart was removed, the coronary artery ostia were cannulated and the snare was removed for infusion of 1,3,5 triphenyltetrazolium chloride. The left anterior descending artery received 300 ml and the left circumflex artery 200 ml of 2 g/dl triphenyltetrazolium chloride in normal saline solution at an infusion pressure of 85 mm Hg.

The heart was fixed in formalin and frozen for cutting in 2 cm thick transverse sections aligned by the beads. The extent and location of infarction in the section at the mid-papillary muscle level were determined by planimetry from color photographs of the cut surfaces. In addition, the percent infarcted wall thickness was measured at 1° intervals around the circumference.

Radial wedges weighing about 2 g each were cut from the mid-papillary level cross section. These were then divided into endocardial and epicardial portions for radionuclide counting. Flow per gram was calculated for each of these samples by the equation F = Af/aw, where F is blood flow per gram (ml/min per g), A is specific tissue activity (counts/min), f is the reference sample blood flow withdrawal rate (ml/min), a...
is the reference sample activity (counts/min) and \( w \) is the sample weight (g).

Image analysis. Echocardiographic images containing the three beads marking the short-axis plane at the level of mid-papillary muscle were reviewed to identify examples of the complete cardiac cycle that best showed border definition. The cardiac cycle was defined functionally by a series of frames from one frame with maximal cavity size, through a minimum and back to the next maximum. Serial fields recorded at 16.7 ms intervals were digitized (with use of the PS digitizing system interfaced with a DEC VAX 11/780 computer) and myocardial borders were traced interactively on the basis of the center of the echocardiographic signal intensities representing each interface. The center of area subtended by the endocardial coordinates was used to determine a centroid for each frame (22). Images were rotated to place the anterior midpoint between the papillary muscles at 0°. At 10° increments from this reference, radial distances from the centroid to the endocardial border and the wall thicknesses were recorded for each frame. These 36 measurements per frame were repeatedly determined using the floating centroid and each of three fixed centroids: fixed end-systolic, fixed end-diastolic and fixed cycle average.

From each completed series of image frame measurements for each centroid, an index of radial wall motion was calculated. First, for a given ray, radial length to the endocardium in the sequential frames was rescaled by normalizing to unit length in the end-diastolic frame. Next, the correlation between these length changes over the cardiac cycle and comparable radial length changes in normal control hearts (17) was determined. By this method, normal inward motion yielded an \( r \) value near +1, either akinesia or otherwise uncorrelated motion yielded an \( r \) value of 0 and dyskinetic pansystolic bulging yielded an \( r \) value approaching -1. The correlation values from each of the 36 radii were then plotted serially (CORPLOT, Fig. 1).

Statistics. Three criteria were used to assess the relative value of the different centroid choices: reproducibility, symmetry of normal systolic motion (closeness of agreement of excursions for 36 equiangular radicals in the short-axis view) and correspondence of identified abnormalities with the true pathologic abnormalities as determined by microsphere-labeled flow and staining by triphenyltetrazolium chloride.

To assess interobserver and intraobserver variability and reproducibility, repeated measures analysis of variance was performed on each of the fixed centroid coordinates determined independently by repeated tracings of 10 normal cardiac cycles by two observers.

Symmetry of motion in normal hearts was assessed by multivariate analysis of variance based on the log transform of the sum of squared deviations from mean radial excursion. For each of six normal control studies, three cardiac cycles were independently digitized twice by each of two observers (72 tracings) and each tracing was analyzed with respect to each centroid definition. The centroid type was assessed as a fixed effect; observer, dog and cardiac cycle were analyzed as random effects.

The correspondence of detected wall motion abnormalities to pathologic findings was examined for each choice of centroid by two approaches to the detection of abnormal motion: fractional radial shortening (endocardial excursion) and the correlation with normal motion, with the method already discussed (CORPLOT). These measures and the results from microsphere injection and from percent transmural infarction by staining with triphenyltetrazolium chloride were plotted serially versus ray (Fig. 2 and 3). Correlations between these plots were compared after Fisher's Z transform (26) by multivariate analysis of variance with respect to centroid method as a factor. Where appropriate (27), contrasts between the centroid methods were evaluated.

Results

Reproducibility (Table 1). Reproducibility of each centroid determination was good and neither interobserver nor
intraobserver variability contributed significantly to the variance in end-systolic, end-diastolic or cycle average fixed centroid coordinates.

Normal wall motion: floating versus fixed centroids. Analysis of normal wall motion symmetry (concordance of the radial excursions from the centroid in normal dogs) demonstrated a notable contribution to variance as a result of the choice of centroid (p < 0.01, F = 5.97 with df = 3). Therefore, multiple comparisons were made using the Bonferroni correction (27): the floating centroid was compared with each of the fixed centroids and the fixed end-diastolic centroid was compared with the fixed end-systolic centroid. Although the floating centroid appeared somewhat better, none of these pairwise comparisons was significant at p =

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*These were uniformly small variances, indicating good reproducibility of the centroid determinations.

Figure 2. Relation of wall motion to microsphere distribution and staining with triphenyltetrazolium chloride in anterior infarction. This is an example of the set of plots generated comparing endocardial excursion (top), correlation with normal control wall motion or CORPLOT (second from top), blood flow determined by microsphere distribution (third from top) and percent transmural staining with triphenyltetrazolium chloride (bottom) as functions of radial position (abscissa). This heart had an anterior myocardial infarction produced by ligation of the left anterior descending coronary artery, followed by microsphere injection and subsequent infarct staining. The infarct zone shows up in rays 22 to 26 through 36 in these plots.

Figure 3. Relation of wall motion to microsphere distribution and staining with triphenyltetrazolium chloride in posterolateral infarction. This is an example of the set of plots as in Figure 2, but in a dog with a posterolateral infarction produced by ligation of the left circumflex coronary artery. The infarct zone shows up in rays 2 to 7 through 22 to 28 in these plots.

0.0125 (0.05/4). Thus, if one defines the "best" method as that which exhibits the greatest symmetry of normal contraction, there is no strong preference for any one of these paired methods.

Table 1. Interobserver and Intraobserver Variance of the X and Y Centroid Coordinates Using the Fixed End-Diastolic Centroid (ED), the Fixed End-Systolic Centroid (ES) and the Fixed Average Centroid (AVG)*
Abnormal wall motion after coronary occlusion: floating versus fixed centroids. Table 2 shows the results from analyzing the correlations between endocardial excursion using each centroid method, blood flow by microsphere counts and percent transmural infarction by staining with triphenyltetrazolium chloride (that is, comparing the apparent wall motion and the pathologic findings). With use of $p < 0.05/6 = 0.0083$ as the significance criterion for six paired comparisons, the fixed centroids proved to correlate better with blood flow and with triphenyltetrazolium chloride staining than the floating centroid. This finding was consistent by fractional excursion and by CORPLOT. However, the contrast was greater with CORPLOT, suggesting better sensitivity to the corresponding pathologic findings by that method of analysis.

### Discussion

Floating versus fixed centroids to assess wall motion. Accurate measurement of regional wall motion in the heart is a complex problem that may require different approaches in different circumstances. This study provides a systematic comparative evaluation of different methods for measuring endocardial excursion in normal and ischemically damaged canine hearts with use of a model that minimizes cardiac translation. We have previously shown (22) that the centroid determined by the center of area subtended by the endocardium has the best reproducibility when compared with centroids determined by the center of endocardial coordinates or by epicardial or mid-myocardial determinants. This study then evaluated the relative merits of the floating centroid versus three fixed centroids (end-systolic, end-diastolic and cycle average) in the assessment of normal and abnormal wall motion.

Assessing translational motions of the normal heart. In the minimally translating heart, there were symmetry of contraction and no significant differences with respect to the floating or fixed centroids: in the absence of translation, normal wall motion is concentric. Our method of symmetry analysis (comparison of the sums of squared deviations from mean radial excursion for fixed versus floating centroids) may, therefore, be used to assess the significance of cardiac translational movements and supports previous observations regarding the effects of cardiac translation. When translational freedom is increased by surgery, paradoxical septic motion has been observed in human patients (28-31) despite normal septal thickening (30,31). With use of a floating centroid, Force et al. (32) showed that there is no difference in septic motion compared with that before surgery, whereas using a fixed centroid, septic motion appeared diminished and motion of the contralateral wall appeared hyperdynamic. Similarly, Waggoner et al. (33) showed that paradoxical motion with respect to a fixed reference represents a shifting centroid. Both angiographic and echocardiographic studies in dogs and humans (9,21,34-37) suggested that normal translational motions are significant, favoring use of a floating coordinate system. Because the present study showed symmetry of normal contraction in the short-axis view with no difference between the floating and fixed centroids when translation was minimized, comparison of the symmetry of normal contraction with respect to fixed versus floating coordinates may be used to assess the significance of translational motion of the normal heart in other settings.

Assessing abnormal regional wall motion. Although the floating centroid may have advantages in monitoring the normal cardiac contraction pattern when cardiac translation is significant, it has disadvantages when assessing regional wall motion. With hypokinesia and especially dyskinesia of one region, the floating centroid is drawn toward the abnormal segment, diminishing its apparent defect and simultaneously projecting abnormal motion to the contralateral wall. In accord with this, Parisi et al. (9) showed that although the presence of an abnormality could be deter-
mined equally well with a fixed or floating reference, a fixed reference was better at localizing anterior and inferior abnormalities. Similarly, Schmittger et al. (38) found that a fixed reference was better at identifying regions of infarction in short-axis echocardiographic images. These were qualitative assessments and the present study confirms these observations quantitatively. Microsphere distribution was used in this confirmation in addition to staining with triphenyltetrazolium chloride because the latter may underestimate the infarct zone early after infarction.

In the present study, correlating radial motion throughout the cardiac cycle with normal wall motion (CORPLOT) appeared to maximize the sensitivity in localizing abnormalities of perfusion and identifying percent transmural infarction. Because the greatest wall motion abnormality in the presence of ischemic injury may occur in mid-systole, this integrated examination of motion throughout the cardiac cycle has an advantage over methods that simply compare end-systolic and end-diastolic image frames (15).

**Clinical applications.** This study does not answer the question of which method of quantitative wall motion analysis is best for all clinical settings. In postoperative patients or patients with pericardial effusion and increased transvalvular wall motion, the effects of translational motion may dominate, favoring a floating reference system despite its problems with respect to absolute quantitation of defects and localization of abnormalities. Paired with our previous study of centroids (22), this study indicates that use of a centroid based on the center of the area subtended by the endocardium minimizes intraobserver and interobserver variability and that fixed centroids are preferable when translational movement is not problematic. Also, this study provides methods for quantifying the importance of translational effects and validates the quantitative wall motion assessments with respect to the pathologic findings.

**Conclusions.** Normal cardiac contraction in a canine model with minimal translational wall motion is symmetric in the echocardiographic short-axis view and the absence of significant translational effects may be assessed by comparing the deviations in fractional radial shortening with respect to a floating versus a fixed centroid. In the absence of significant translational movement, a fixed centroid is better for localizing ischemic injury, as was demonstrated both by fractional shortening and by the CORPLOT method. The CORPLOT method of correlating normal and radial wall motion throughout the cardiac cycle appears to be more sensitive in the detection of abnormalities, most likely because it detects abnormalities of motion during the cardiac cycle that may not be evident at end-systole. When translational motion is dominant, both fixed and floating centroids have limitations. In that setting, a centroid defined only by obviously normal segments may prove better than that by any of the globally defined centroid methods.

## References


