In Vivo Assessment of Left Ventricular Wall and Chamber Dynamics During Transient Myocardial Ischemia Using Prospectively ECG-gated Computerized Transmission Tomography

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SUMMARY Seven dogs were evaluated with prospective ECG-gated computerized transmission tomography (CTT) to analyze left ventricular (LV) wall thickness and cross-sectional chamber area after acute occlusion of the left anterior descending coronary artery (LAD). ECG-gated CTT scanning during i.v. administration of contrast material was performed over the mid-left ventricle at rest, after acute occlusion of the LAD and 30 minutes after release.

The extent of systolic wall thickening (EWTh) of the anterior (potentially ischemic) segment was 39.8 ± 8.8% (SEM) in the control state and −26.0 ± 4.7% during LAD occlusion (p < 0.01). The nonischemic septum demonstrated a compensatory increase in EWTh, from 28.6 ± 3.5% to 46.4 ± 6.1% during LAD occlusion (p < 0.05). The end-diastolic LV luminal area (LVA) increased from 17.4 ± 0.8 cm² in the control state to 21.0 ± 1.1 cm² during LAD occlusion (p < 0.01). End-systolic LVA also increased, from 11.0 ± 0.9 to 15.2 ± 1.1 cm² (p < 0.01). In addition, the percent change in LVA from end-diastole to end-systole declined from 37.4 ± 3.8% during control to 28.0 ± 2.6% during LAD occlusion (p < 0.02). In conclusion, gated CTT demonstrates that the alterations in acute ischemia are characterized by changes in regional wall thickening dynamics, consisting of wall thinning during systole in the jeopardized segment and compensatory increase in the extent of systolic thickening in the normal segment, and changes in global LV function, consisting of an increase in the LVA and a decrease in the percent change of LVA during systole. Gated CTT may be useful for monitoring regional and global effects of ischemia when subjects can be studied in the supine position and with respiration suspended for 45 seconds.

EARLY DETECTION of myocardial ischemia and the quantitation of the extent of myocardial ischemic damage are important goals of noninvasive imaging techniques. Detection of myocardial ischemia by functional imaging methods requires the demonstration of regional contraction abnormalities. The availability of prospective ECG-gated computerized transaxial tomography (CTT) not only provides good discrimination of the ischemic myocardium, but can also be used to evaluate segmental function by displaying wall thickening dynamics during the cardiac cycle. Previous reports using retrospective gating have indicated the potential of this technique for assessing left ventricular (LV) dimensions, including wall thickness changes. The ability to assess wall thickening dynamics is relevant in ischemic heart disease because they are a reliable and sensitive functional indicator of seg-
mental ischemic contractile dysfunction.\textsuperscript{5-7} Equally important, the amount of infarcted myocardium and the degree of dysfunctional myocardium often differ, with contraction disturbances occurring beyond the rim of the necrotic tissue.\textsuperscript{8}

The present study was designed to document that prospective ECG-gated CTT can monitor LV wall thickness throughout the cardiac cycle and detect changes in wall thickening dynamics in the beating in situ heart after acute occlusion of the coronary artery, and to characterize these changes by analyzing LV wall thickness and LV cross-sectional area on the serial gated images of the beating heart before and within the first minutes after acute arterial occlusion.

Methods

Experimental Model

The experiments were conducted in seven conditioned mongrel dogs that weighed 18–25 kg. Under general anesthesia with pentobarbital (25 mg/kg), a left thoracotomy was performed. A hydraulic occluder was positioned around the proximal left anterior descending coronary artery (LAD) proximal to the origin of the first diagonal branch and distal to the first septal branch. Seven days later, when the dogs had recovered from surgery, ECG-gated scans were performed at the mid-LV level at rest and immediately after acute occlusion of the LAD. In six dogs, ECG-gated scans were also obtained at the same level 30 minutes after release of the LAD occlusion. The total occlusion time was 90–120 seconds. Occlusion of the LAD was selected for this study to optimize imaging of the ischemic area on CTT scans. The posterolateral wall of the left ventricle is not imaged as well on CTT scans, so circumflex occlusions were not selected as the intervention.

Before CTT, the dogs were premedicated with morphine sulfate (2 mg/kg i.m.), anesthetized with pentobarbital (20 mg/kg i.v.), paralyzed with succinylcholine (2 mg/kg i.v.) and ventilated with a Harvard respirator (15 breaths/min, tidal volume 12–15 ml/kg). The heart rate was usually 100–150 beats/min. Intravenous contrast material (Renografin 76) was infused through a leg vein at a rate of 6 ml/min for 10 minutes and then 3 ml/min for the remainder of the experiment. During the entire experiment, 100–120 ml of contrast material were administered. The first gated series was obtained after the infusion of 60 ml. Gated CTT scans were performed over the mid-LV level during breath-holding at full inspiration. The scans were initiated 10 minutes after the start of infusion of contrast media. The scanning technique was set at 120 kVp, 2-second scanning time, 50-mA, 10-mm slice thickness, and a 25-cm scanning circle. All images were reconstructed using the same algorithms with a 512 \(\times\) 512 matrix. The approximate radiation dose for a gated series of scans (approximately eight scans) was 11 rads. However, because of the precise collimation of the x-ray beam in computed tomography, this radiation dose is confined to a 1-cm thickness through the midthorax.

The Gating System

The prototype ECG-gating system consisted of a Technicare 2020 whole-body scanner, to which the gating system was added. This system allowed the scanner to accept the ECG and gating signal, which enabled the computer to reorganize the data acquired with a series of standard scans, obtained at the same anatomic level, and to reconstitute a new series of gated images depicting one composite cardiac cycle (from one end-diastole to the next end-diastole). It required approximately 40 minutes of processing time to reconstruct each gated series.

Gated CTT scanning differs significantly from standard CTT scanning. To obtain a reconstructed image of a stationary object by standard CTT, a full complement of angular x-ray data must be obtained over the full scanning circle without significant gaps (< 10\(^\circ\)) in the angular data set. To image the heart, a rapidly moving structure, over one cardiac cycle (in 10 serial images), multiple scans are required in which each scan covers multiple cardiac cycles. The standard scans (referenced to the ECG signal) must then be broken into multiple angular segments in which each segment contains the angular data acquired for each 10% of the cardiac cycle (fig. 1). The angular segments that fall within the same portion of the cardiac cycle must then be pooled together to reconstruct a new, gap-free angular data set.

The prospective gating system allows preselection of a fraction of the electrocardiographic RR interval width to be monitored; this is called the biologic window. The biologic window width sets the fraction of the cardiac cycle to be represented by each image. Prospective gating assures even distribution of the R waves throughout the scanning circle in the minimum number of scans. This is accomplished by launching

![Figure 1. The operation of the prospective ECG-gating system with the biologic window set at 10% of the RR interval. This diagram depicts the concept that when the R wave is uniformly distributed over the scanning circle, one R wave per angular segment, sufficient data are obtained to reconstruct 10 images. Each image corresponds to 10% of the cardiac cycle.](http://circ.ahajournals.org/)

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the x-ray tube at the appropriate time, relative to the R wave on the ECG input, such that one of the following R waves falls in the largest gap in the already acquired angular data (fig. 1). In this study, the width of the biologic window was set at 10% of the RR interval. Since the heart rate was 100–120 beats/min, each frame represents 0.05–0.06 second. With the biologic window set at 10% of the RR interval, approximately eight scans were required to obtain a full complement of gated angular data. This necessitated approximately 45 seconds of breath holding. The gated system requires a relatively regular cardiac rhythm. Presorting of the acquired data can be done to eliminate x-ray data acquired during premature ventricular complexes. Continuously irregular rhythms, such as atrial fibrillation, preclude successful gated reconstruction.

Wall Thickness Measurement

Each of the 10 images, comprising a single cardiac cycle, was displayed on the CTT monitor using the 512 × 512 image matrix. A 12.5 × 12.5-cm square was placed over the heart. The enclosed portion of the image was magnified to fill the entire 512 × 512 matrix. A variable region of interest was drawn over the LV wall and the average Hounsfield unit (HU) obtained. The CTT window was set at approximately 450 HU such that each 7 HU were compressed into each of the 64 gray levels. The center was set at the average Hounsfield unit measured over the LV wall. The average LV wall was approximately 60 HU and the contrast-containing LV cavity was approximately 170 HU, an approximately 15-gray-level difference. This provided a clear definition of the wall/lumen interface. The window and center, once set, were maintained constant for the entire series. LV wall thickness was measured directly on the CTT monitor by moving a cursor across the LV wall of the displayed image. The measurement is given automatically by the display program rounded to the nearest millimeter. The septum was measured directly across from the papillary muscle which was easily identified on the lateral LV wall. The anterior wall was measured at the apex of the LV lumen (fig. 2). The same position on the image was measured on every image obtained at rest, after LAD occlusion, and 30 minutes after release. This may not be precisely the same position on the LV itself during the course of a contraction because there is some longitudinal shortening and rotation of the left ventricle during systole.

Left Ventricular Luminal Measurement

The magnified images obtained while measuring the LV wall thickness, as described above, were recorded with reference markers using a multiformat camera as nine images per 11 × 14 inch film. The LV luminal area (LVA) was calculated from each of the formatted images recorded with a Hewlett-Packard computer/digitizer (9825/9874A) system by tracing manually the LV lumen (fig. 2). The computer then calculated the area contained within the closed loop.

![Figure 2](http://circ.ahajournals.org/)

**Figure 2.** Solid white lines indicate where the wall thickness of the septum (S) and anterior wall (A) were measured. White dashes outline the left ventricular lumen, traced manually, allowing the calculation of the area contained within the closed loop.

Data Analysis

The first image of the series of 10 images that represent one cardiac cycle corresponds in time with the peak of the R wave and, hence, represents the end-diastolic image. The end-systolic image was defined as the image with the least measured LVA. Since there is some shortening of the major axis during systole, it is unlikely the end-diastolic and end-systolic images are at exactly the same sagittal level of the left ventricle. The extent of wall thickening (EWTh) at rest, immediately after LAD occlusion, and 30 minutes after release was calculated for the anterior segment and septum. The EWTh was calculated by subtracting the end-diastolic wall thickness from the end-systolic wall thickness and dividing the difference by the end-diastolic wall thickness. The percent decrease in the LV luminal area (%LVA) was calculated by subtracting the end-systolic luminal area from the end-diastolic luminal area and dividing the difference by the end-diastolic luminal area.
Statistics
The wall thickness measured over the septum and anterior wall and the LVA were grouped together for each 10% of the cardiac cycle obtained at rest, full occlusion and 30 minutes after release. The calculated EWT and %LVA were grouped together for each cardiac cycle at rest, at full occlusion and after release.

All data are given as the group mean ± SEM. Group values were analyzed for overall significance using the multiple t test of significance between two means.

Results
Gated CTT Images of the Heart
Figure 3 shows a reconstructed gated series consisting of the first nine images depicting the changes through one composite cardiac cycle obtained at rest. The LV wall thickness increases in conjunction with decreases in the LVA as the cycle progresses from end-diastole (top left) to end-systole (center image). Figure 4 shows the corresponding series of images in a cardiac cycle immediately after LAD occlusion in the same dog shown in figure 3. Note the absence of thickening in the anterior segment.

Effect of LAD Occlusion on LV Luminal Area
Group data for LVA are shown in figure 5. In the control state, there was a progressive decrease in the LVA from end-diastole (17.4 ± 0.8 cm²) to end-systole (11.0 ± 0.9 cm², p < 0.05). The LVA decreased by 37.4 ± 3.8% from end-diastole to end-systole. After LAD occlusion, the LVA increased at end-diastole from 17.4 ± 0.8 to 21.0 ± 1.1 cm² (p < 0.01 vs control) and remained greater than that in the control state at each point throughout the cardiac cycle. At end-systole, the LVA was 15.2 ± 1.1 cm² (p < 0.01 compared to control). The %LVA during acute ischemia was significantly less than that during control, 28.0 ± 2.6% vs 37.4 ± 3.8% (p < 0.02). In the six dogs studied 30 minutes after release of the LAD occlusion, the %LVA returned to its preocclusion state, 36.0 ± 2.5%.

Effect of LAD Occlusion on Wall Thickness
The group data for the wall thickness across the anterior segment, destined to become ischemic, are shown in figure 6. In the control state, the LV wall thickness increased from end-diastole (7.0 ± 0.6 mm) to end-systole (9.7 ± 0.9 mm) and then decreased toward minimal thickness from end-systole to the next diastole. After LAD occlusion, the wall thickness of the anterior segment decreased from end-diastole (6.0 ± 0.2 mm) to end-systole (4.4 ± 0.3 mm). In the six dogs studied 30 minutes after release of LAD occlusion, the wall thickness of the anterior segment increased from end-diastole (7.2 ± 0.4 mm) to end-systole (9.3 ± 0.9 mm). Thus, wall thickening dynamics returned close to the values of the preocclusion state.

The changes in septal wall thickness are shown in

Figure 3. Series of gated computerized transaxial tomographic scans (approximately 60-msec images) through the mid-left ventricle depicting one composite cardiac cycle at rest. Images progress through the cardiac cycle vertically, starting at the top left and ending on the bottom right. The tenth image in the series is not shown.
FIGURE 4. Series of gated computerized transaxial tomographic scans (approximately 60-msec images) after left anterior descending coronary artery occlusion in the same dog shown in figure 3 and at the same level. The sequence is similar to that of figure 3.

Figure 7. In the control state, the septal wall thickness increased from end-diastole (9.6 ± 0.6 mm) to end-systole (12.3 ± 0.8 mm) and then decreased as it returned to its end-diastolic dimension. After LAD occlusion, the end-diastolic thickness of the septum (8.1 ± 0.6 mm) was less than that during control (9.6 ± 0.6 mm, p < 0.01), but was almost the same thickness as that in the control state at end-systole (11.9 ± 0.9 mm). The decrease in septal wall thickness in the occluded state was probably a consequence of the increase in LV luminal area and, presumably, LV volume.

Effect of LAD Occlusion on Extent of Wall Thickening

The group data for the EWTh of the anterior segment and septum are shown in figure 8. In the control state, EWTh calculated for the septal and anterior walls were approximately equivalent. After LAD occlusion, there was paradoxical thinning of the anterior segment during systole, from 39.8 ± 8.8% in the control state to -26.0 ± 4.7% in the ischemic state, p < 0.01, while the nonischemic septum demonstrated compensatory increase in EWTh, from 28.6 ± 3.5% to 46.4 ± 6.1% after occlusion (p < 0.05).
Figure 7. Mean left ventricular wall thickness (± SEM) across the septum (normal segment) through the cardiac cycle at rest and immediately after left anterior descending coronary artery occlusion.

Figure 9 shows the typical changes observed in the anterior segment, septum and LVA at rest and after LAD occlusion in one of the dogs.

Discussion

Ischemia causes alterations in LV segmental wall thickness and, particularly, in percent wall thickening. 5, 6, 9-11 Cross-sectional two-dimensional imaging modalities such as ECG-gated CTT5-7, 9, 12, 13 and sector scan echocardiography8, 10, 11, 14-16 can be used to measure ventricular wall thickness. The current study documents that ECG-gated CTT scanning of the in situ beating heart can detect segmental myocardial dysfunction by monitoring LV wall thickness throughout the cardiac cycle. With gated CTT, we could also characterize the changes in wall thickening dynamics and LVA at rest and immediately after LAD occlusion. A previous report3 demonstrated an anecdotal example of a wall thickening abnormality during acute regional ischemia in a dog using retrospectively gated CTT scans.

During acute ischemia, LV function deteriorates in conjunction with LV dilatation.17, 18 In the present study, after LAD occlusion, the ECG-gated CTT scans showed a significant increase in the end-diastolic and end-systolic LV dimensions and a smaller decrease in the LVA from end-diastole to end-systole. Gated CTT scans also showed that these variables returned to preocclusion levels at 30 minutes after release of the occlusion.

The changes in the ischemic segment after acute coronary occlusion consisted of loss of thickening during systole and, instead, paradoxical thinning. This regional myocardial response to acute ischemia is consistent with previous physiologic experiments in acutely and chronically instrumented animals. 5-8, 11, 14 After coronary artery occlusion, end-diastolic wall thickness decreased and EWTh increased in the normal segment. These results have also been observed in our laboratory and by other investigators using implanted sonomicrometer crystals. 5, 6 The increase in EWTh in the normal segment was the result of an absolute decrease in thickness at end-diastole. The end-systolic wall thickness was almost the same at rest and after occlusion. During occlusion of the coronary artery, the LV volume increases and the normal segment becomes stretched and thinned. To compensate for the lack of contraction from the ischemic zone, the normal segment probably undergoes an increase in diastolic myocardial fiber length, thereby using the Frank-Starling mechanism to maintain forward cardiac output.

Other investigators have demonstrated that monitoring wall thickness is a reliable means of assessing LV segmental dysfunction. 5, 6, 15 Some have even stated that it may be the most sensitive and accurate contractile measurement for assessing regional ischemia.6 The current study suggests that ECG-gated CTT may be used for this purpose. However, it remains to be determined if gated CTT can detect the abnormalities of wall thickening that occur with nonocclusive stenoses causing mild reductions in coronary blood flow.
Other studies have also used wall thickness measurements from CTT to assess cardiac diseases. Skioldebrand et al.,\textsuperscript{12} using nongated CTT, demonstrated that myocardial wall thickness measured from CTT scans correlated well with postmortem measurements and detected significant differences in wall thickness in normal animals compared to those with aortic coarctation. Lackner and Thunn\textsuperscript{13} demonstrated a decrease in the LV wall thickness in ischemic heart disease and an increase in LV wall thickness in aortic stenoses using CTT scans in man. In addition, CTT of the heart can detect and size irreversibly damaged myocardium by demonstrating density differences between the normal and infarcted tissue after i.v. administration of contrast material.\textsuperscript{1,3}

CTT alone provides most of the critical information needed to assess the presence and severity of ischemic heart disease. It identifies the area of critical reduction or absence of myocardial perfusion\textsuperscript{1,9} and detects the immediate onset of regional and global myocardial dysfunction. It can also define the anatomic size of the infarct by directly imaging the infarct.\textsuperscript{1,2,9} Likewise, it can define the physiologic volume of myocardial dysfunction by indicating the area that cannot thicken during systole. Although some of the information can be provided by radionuclide angiography and sector scan echocardiography, the gated CTT scan is the only method that can define and accurately measure the anatomic volume of infarcted myocardial tissue and assess the physiologic size of the myocardial infarction. However, the results in the current study were achieved under carefully controlled experimental conditions, which obviously are not applicable in the clinical assessment of acute myocardial infarction. The application of CTT in the early stages of an acute myocardial infarction is limited by the need for moving the patient from the coronary care unit to the site of the scanner and, possibly, the ability of the patient to lie flat and suspend respiration for 45–60 seconds. Once placed in the scanner gantry, the patient can be removed within a few seconds and defibrillation can be performed at the scanner.

There may also be hesitancy to administer contrast medium intravenously in the early infarction phase. Gated scans in patients will likely require the infusion of 100–150 ml of contrast media. A recent report\textsuperscript{13} of cardiac CTT scans in more than 50 patients demonstrates that many of the morphologic abnormalities associated with myocardial infarction are clearly demonstrated by CTT.

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