Quantification of Left-Ventricular Regional Dyssynergy by Radionuclide Angiography

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To determine whether variables obtained from Fourier analysis of gated equilibrium radionuclide angiographic (RNA) images can detect and quantify changes in left-ventricular (LV) regional wall motion induced by transient ischemia, 11 chronically instrumented dogs were simultaneously studied with hemodynamic measurements and RNA during control, left circumflex (LCx) coronary artery occlusion, and postocclusion conditions. The dogs were preinstrumented with aortic and LV catheters, electromagnetic aortic and LCx coronary artery flow probes, high-fidelity LV micromanometers, LCx coronary artery occluders, and 4-mm ultrasonic transverse LV diameter and 2-mm regional LV segment crystal pairs. Radionuclide LV regional phase and amplitude variables were calculated for each condition. The absolute changes in LCx region RNA mean, median, and standard deviation of mean phase correlated with the percent changes in LCx segment crystal fractional shortening (r = −0.71, −0.64, and −0.51, respectively; all p < 0.01). Similarly, the absolute changes and percent changes in LCx region RNA mean amplitude per pixel correlated with the percent changes in LCx segment crystal fractional shortening (r = 0.89 and 0.94, respectively; both p < 0.001). When these LCx region RNA phase variables were subgrouped according to mild or severe depression or augmentation in LCx segment crystal fractional shortening, progressive differences were observed between the average values for these subgroups (p < 0.05 to p < 0.001). These data, therefore, suggest that these regional RNA phase variables may be able to detect and quantify alterations in LV contraction patterns due to transient ischemia.


Fourier analysis of gated equilibrium radionuclide angiographic (RNA) images has been reported to be useful for detecting the initiation of left-ventricular (LV) activation and emptying (I–3). This approach has been employed to identify, localize, and characterize altered ventricular electrical activation due to conduction abnormalities (4–7), Wolff–Parkinson–White syndrome (5,8), and ventricular tachycardia or pacing (7,9–13). In addition, it has been suggested that Fourier analysis of RNA images may be useful for detecting and quantifying LV mechanical dysynergy due to ischemic heart disease either at rest or during exercise (5,14–18). However, previous studies have used a subjective, visual interpretation of the RNA images as the “gold standard” against which to compare the Fourier analysis data. A subjective, visual analysis of LV images by RNA or other noninvasive and invasive techniques is limited by observer variability in the definition of the presence and extent of LV regional wall motion abnormalities; consequently, it is semiquantitative, at best. Thus, we felt that the use of regional ultrasonic segment crystal pairs, an independent and precise method for measuring changes in LV regional function (19), might be a more definitive method for determining whether or not Fourier analysis of RNA images can accurately quantify changes in LV regional wall motion. Accordingly, the purpose of this investigation was to assess whether and to what extent Fourier analysis of RNA images can identify and quantify temporary changes in LV regional wall motion induced by transient ischemia.

MATERIALS AND METHODS

Animal Instrumentation

Eleven healthy adult mongrel dogs (18–30 kg) were surgically instrumented (Fig. 1) for chronic physiologic monitoring by methods previously described from this laboratory (20).
The dogs were premedicated with xylazine and pentobarbital (15 mg/kg), intubated, and ventilated with 1.5% halothane to maintain anesthesia. The chest was opened in the fifth left intercostal space under sterile conditions, and the pericardial sac was incised and left unopposed. A polyvinyl 16-gauge catheter and precalibrated, solid state pressure transducer* were inserted into the left ventricle through the apex. In addition, polyvinyl catheters were placed in the left atrium and the ascending aorta. Electromagnetic cuff-type flow probes† were placed around the ascending aorta and the LCx coronary artery, and a hydraulic occluder was placed proximal to the LCx coronary flow probe for experimental occlusion. All dogs had two 5-MHz piezoelectric crystals, 4 mm in diameter, positioned on the endocardium in the greatest LV anteroposterior dimension. A pair of miniature regional ultrasonic segment crystals, 2 mm in diameter, was placed in the subendocardium approximately 1.5 cm apart in the distribution of the LCx coronary artery perpendicular to the LV long axis and parallel with the circumferential fibers in the central region of cyanosis observed during temporary LCx coronary artery occlusion (21). In a subgroup of dogs (n = 9), a second regional segment crystal pair was positioned in the distribution of the left anterior descending (LAD) coronary artery in a similar manner. The subendocardial location of these dimension and regional segment crystal pairs was documented at necropsy. Pacing wires were sutured to the epicardium of the left atrium in each dog. All wires and tubes were exteriorized through the third left intercostal space. The animals were allowed 10–14 days to recover from the operative procedure before undergoing investigation.

Protocol
The protocol used for this investigation consisted of the acquisition of RNA images during control, LCx coronary artery occlusion, and postocclusion conditions at hemodynamic steady state (less than 10% change in heart rate and mean aortic pressure). Each RNA acquisition required 6–10 min. Hemodynamic measurements were obtained at the beginning, middle, and end of each RNA acquisition. The LCx coronary artery occlusion time did not exceed 10 min in any animal to preclude the possibility of producing myocardial necrosis.

Hemodynamic Data Acquisition
Each animal was lightly sedated with pentobarbital and placed supine beneath the gamma scintillation camera. The LV and aortic catheters were connected to Statham P23Db pressure transducers, which were calibrated with a mercury manometer using the vertebral column as the 0 reference point and atmospheric pressure as the 0 reference. The LV pressure signal from the precalibrated high-fidelity micromanometer was then adjusted to match that obtained from the fluid-filled LV catheter. The first derivative of LV pressure was obtained electronically from the micromanometer signal using an R-C circuit with a flat frequency response to 70 Hz and 3 dB down to 100 Hz. The phasic aortic and phasic and mean LCx coronary flow were recorded using a Zepeda EDP2 flow meter. The LV anteroposterior dimension and segment length measurements from the implanted crystal pairs were obtained using a 4-channel sonomicrometer,‡ which measures the transit time of 5 MHz sound between each of the piezoelectric crystal pairs (21). This was converted to distance assuming a constant velocity of sound in blood of 1.55 mm/μsec. The resolution of this system has been reported to be 0.07 mm with the 5 MHz ultrasonic signals (22). The high-fidelity and fluid LV pressure, the first derivative of high-fidelity pressure (dp/dt), aortic pressure and flow and the LV anteroposterior dimension and segment lengths from the ultrasonic crystal pairs were recorded on an 8-channel oscillograph§ at a paper speed of 25 mm/sec. The analog signals were also digitized with an on-line analog to digital converter‡ at 5-msec intervals and stored on floppy disks utilizing a minicomputer system,§ and software developed in our laboratory.

Hemodynamic Data Processing
All hemodynamic data were analyzed by means of a computer algorithm. End-diastolic LV anteroposterior dimension and segment crystal lengths were defined as the distance between the crystal pairs at the Z-point of the high-fidelity LV pressure signal. The Z-point was defined as the LV pressure at which (+)dp/dt increased by 150 mmHg/sec with the
increase sustained for 50 msec (23). The end-systolic LV anteroposterior dimension and segment crystal lengths were measured as the minimum intercrystal distance prior to peak \((-\Delta P/dt\), which corresponds to the maximum segment shortening during LV ejection in the normal LV (19). Percent fractional shortening of the LV anteroposterior dimension and segment crystal lengths were calculated as follows:

\[
(\text{EDD} - \text{ESD})/\text{EDD} \times 100 = {}^\circ \Delta d, \text{ and }
\]

\[
(\text{EDL} - \text{ESL})/\text{EDL} \times 100 = {}^\circ \Delta L;
\]

where EDD is end-diastolic dimension and ESL is end-systolic dimension of the LV anteroposterior dimension crystal pair, and EDL is end-diastolic length and ESL is end-systolic length from the regional LV segment crystal pairs. Signals for 20 sinus beats were averaged from each hemodynamic data acquisition, excluding postventricular premature beats and beats that varied by more than 10% in cycle length from the average heart rate. Subsequently, the three mean values for the hemodynamic data obtained during each study condition were averaged to obtain values for comparison with the corresponding RNA data.

Gated Equilibrium Radionuclide Angiographic Data Acquisition

Each dog’s red blood cells were tagged with 30 mCi of technetium-99m \((^{99}\text{Tc})\) using a standard in vivo labeling technique. After light sedation with pentobarbital, the animals were positioned supine beneath a standard field of view gamma scintillation camera equipped with an all-purpose parallel hole collimator. The camera was then repositioned to the obliquity that best separated the right and left ventricles in the plane of the interventricular septum. Radionuclide angiographic image acquisitions were obtained during each study condition without altering the camera position in 64 \times 64 byte matrix into consecutive 30-msec frames to 250,000 counts per frame using an MDS A\(^2\) system* equipped with a NOVA 4 computer. The same beat exclusion criteria described for the hemodynamic data acquisitions also pertained for the RNA acquisitions.

Gated Equilibrium Radionuclide Angiographic Data Processing

The RNA images for each dog (Fig. 2, left panel) were filtered before Fourier analysis. On the filtered RNA images, the operator drew a LV region-of-interest to be used for masking both the phase and amplitude images (7). In addition, the LV region-of-interest was subdivided into septal, apical, and posterolateral regional sectors of equal size averaging approximately 90 pixels (Fig. 2, right panel). The posterolateral LV region was chosen to approximate the distribution of the LCx coronary artery. Because there was no significant change in heart rate between the three study conditions in each dog, both the global and regional LV RNA phase variables were generated using computer (MDS A\(^2\)) software programs from the same number of frames to avoid variability in late diastolic frame counts. The amplitude variables were generated using a program developed at our institution employing quantification of color-coded amplitudes.

Fourier analysis of global and regional LV RNA images is based on the mathematical technique by which a periodic wave form can be represented by the sum of cosine and sine waves of different frequencies and amplitudes (3). Because RNA images are periodic, this analysis can be used to transform pixel wave forms into their frequency related amplitude coefficients. The sinusoid that completes one cardiac cycle contains the most information about time (phase) and contraction (amplitude) during an average R-R interval. This sinusoid is known as the first Fourier harmonic or the fundamental frequency. The first harmonic amplitude coefficients are the scalars of orthogonal unit vectors, the vector sum of which yields a phase and amplitude. The Fourier transform of RNA image pixel wave forms on a pixel-by-pixel basis is given by:

\[
R(f) = \frac{2}{N} \sum_{n=0}^{N-1} C(n) \cos (2\pi fn/N) - j \sum_{n=0}^{N-1} C(n) \sin (2\pi fn/N),
\]

where \(N\) is the total number of frames in each study, \(n\) is the individual frame number, \(C(n)\) is the pixel counts in frame \(n\), \(f\) is harmonic frequency, and \(j\) is the square root of \(-1\). \(R(f)\) is the real amplitude coefficient, and \(I(f)\) is the imaginary amplitude coefficient at frequency \(f\). Therefore, at the fundamental frequency of the heart \((f = 1)\), these amplitude coefficients can be represented in polar notation as a simple amplitude expressed as

\[
A = [R(1)^2 + I(1)^2]^{1/2},
\]
and phase angle expressed as
\[ \phi = \tan^{-1} \left[ \frac{l(1)}{R(1)} \right]. \]

Amplitude is measured in counts and phase angle is measured in degrees. From the phase histograms, the RNA phase variables including mean, median, standard deviation of mean, skewness, and kurtosis of phase for the LCx region are calculated for a representative dog and appear for the control, LCx coronary artery occlusion, and postocclusion conditions in Figure 3. The MDS A² phase program was modified to group the LV amplitudes in deciles after the maximum amplitude in the LV region of interest was identified and set to 100% with all other amplitudes set relative to this value. These decile-ranked amplitudes were then summed and statistically analyzed using existing MDS A² software to obtain global and regional LV average amplitude per pixel.

Data Analysis

The average hemodynamic variables measured or calculated for the control, LCx coronary artery occlusion, and postocclusion conditions were analyzed by an appropriate analysis of variance with repeat measures and a Dunnet’s test to identify significant differences. A similar analysis was undertaken for each of the individual mean global LV and LCx region RNA phase and amplitude variables. The absolute changes and percent changes in LCx regional RNA phase and amplitude variables from control to LCx coronary artery occlusion and control to postocclusion were compared with the corresponding percent changes in LCx segment crystal %∆L to determine if absolute changes and percent changes in regional RNA phase and amplitude variables could detect and quantify changes in LCx segment crystal fractional shortening over a range of conditions. These comparisons were performed by least squares linear regression analysis to determine correlation coefficients, regression equations, standard errors of the estimate, and 95% confidence intervals for the data. In a similar manner, the intra- and interobserver variability of the LCx region RNA phase and amplitude variables were evaluated. Further, the percent changes in LCx segment crystal fractional shortening were grouped according to mildly depressed (51%–99% of control), severely depressed (<50% of control), or augmented (>100% of control) fractional shortening. The average absolute changes and percent changes in the LCx regional RNA phase and amplitude variables were grouped in this manner and compared by an analysis of variance and one sample t-test to determine differences from control (zero). A probability of 0.05 or less was considered significant (24).

RESULTS

Hemodynamic Data

There was no significant change in mean heart rate (HR), and (+)dP/dtmax between the control, LCx coronary artery occlusion, and postocclusion conditions. However, the control to LCx coronary artery occlusion condition, there was a reduction in mean aortic pressure (\( P_{AoP} \)) from 100 ± 11 to 94 ± 12 mmHg (p < 0.01) and (-)dP/dtmax from -1860 ± 255 to -1679 ± 276 mmHg/sec (p = 0.001). In addition,
there was an increase in LV end-diastolic pressure (LVEDP) from 2 ± 3 to 5 ± 4 mmHg (p<0.05). All of these parameters returned toward control during the postocclusion condition.

There was no significant change in mean LV anteroposterior dimension fractional shortening (%ΔD), LAD end-diastolic segment length (EDL1), LAD segment crystal fractional shortening (%ΔL1), and LCx end-diastolic segment length (EDL2) between the control, LCx coronary artery occlusion, and postocclusion conditions. Despite no significant change in mean LV anteroposterior end-diastolic dimension (EDD) between the control and LCx coronary artery occlusion conditions, there was a reduction in EDD during the postocclusion condition compared with control (35.6 ± 7.6 versus 36.5 ± 7.7; p<0.01). There was also a reduction (~40%) in mean LCx region segment crystal fractional shortening (%ΔL2) from the control to LCx coronary artery occlusion condition (13 ± 7 versus 7 ± 4%; p<0.05), which returned toward control during the post occlusion condition (Tables 1 and 2).

Global Left-Ventricular Radionuclide Phase Data
There was no significant change in the average mean (x) phase (φ), median phase, skewness of phase (Skφ), kurtosis of phase (Kφ), total number of pixels, and mean amplitude per pixel (x Ampl/p) in the LV region of interest. However, the standard deviation of mean phase (Sd. of xφ) did broaden from the control to LCx coronary artery occlusion condition (20 ± 7 to 32 ± 16 degrees; p<0.05). This parameter returned toward control during the postocclusion condition. In addition, the global LV ejection fraction did not differ between the three conditions (44 ± 9, 41 ± 11, and 45 ± 9%, respectively) (Table 3).

LCx Region Radionuclide Phase Data
Similar to the global LV RNA phase data, skewness and kurtosis of phase, the number of pixels, and the mean amplitude per pixel in the LCx region did not differ significantly between the control and LCx coronary artery occlusion conditions. In contrast to the global LV RNA phase data, the LCx region RNA phase data demonstrated an increase in mean phase from 25 ± 22 to 42 ± 30° (p<0.05) and median phase from 21 ± 23 to 33 ± 36° (p<0.05). Similar to the global LV RNA phase data, the LCx region RNA standard deviation of mean phase increased from 23 ± 9 to 31 ± 17 degrees (p<0.05). All three of these regional phase variables returned toward control during the postocclusion condition (Table 4).

Comparison of the Absolute Changes and Percent Changes in LCx Region RNA Phase and Amplitude Variables with the Percent Changes in LCx Segment Crystal Fractional Shortening
The absolute changes in LCx region RNA mean, median, and s.d. of mean phase from control to LCx coronary artery occlusion and from control to postocclusion are compared with the corresponding percent

TABLE 1
Hemodynamic Data (n = 11)

<table>
<thead>
<tr>
<th></th>
<th>HR (bpm)</th>
<th>xAoP (mmHg)</th>
<th>SV (ml/beat)</th>
<th>dP/dt&lt;sup&gt;1&lt;/sup&gt;</th>
<th>−dP/dt</th>
<th>LVEDP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>105 ± 18 (SD)</td>
<td>100 ± 11</td>
<td>16 ± 4</td>
<td>1746 ± 302</td>
<td>−1860 ± 255</td>
<td>2 ± 3</td>
</tr>
<tr>
<td>LCx occlusion</td>
<td>112 ± 24</td>
<td>94 ± 12&lt;sup&gt;1&lt;/sup&gt;</td>
<td>14 ± 6</td>
<td>1741 ± 319</td>
<td>−1679 ± 276&lt;sup&gt;1&lt;/sup&gt;</td>
<td>5 ± 4&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Postocclusion</td>
<td>113 ± 26</td>
<td>98 ± 17</td>
<td>15 ± 4</td>
<td>1796 ± 359</td>
<td>−1811 ± 347</td>
<td>3 ± 3</td>
</tr>
</tbody>
</table>

HR, heart rate; x, mean; AoP, aortic pressure; SV, stroke volume; LVEDP, left ventricular end-diastolic pressure.
<sup>1</sup>p < 0.05 versus control.
<sup>1</sup>p < 0.01 versus control.
<sup>1</sup>p = 0.001 versus control.
<sup>1</sup>n = 8

TABLE 2
Left-Ventricular Anteroposterior Dimension and Segment Data (n = 11)

<table>
<thead>
<tr>
<th></th>
<th>EDD&lt;sup&gt;2&lt;/sup&gt; (mm)</th>
<th>% Δ D&lt;sup&gt;2&lt;/sup&gt;</th>
<th>EDL1&lt;sup&gt;4&lt;/sup&gt; (mm)</th>
<th>% Δ L1&lt;sup&gt;4&lt;/sup&gt;</th>
<th>EDL2 (mm)</th>
<th>% Δ L2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>36.5 ± 7.7 (SD)</td>
<td>13 ± 5</td>
<td>13.9 ± 3.4</td>
<td>14 ± 4</td>
<td>12.6 ± 3.6</td>
<td>13 ± 7</td>
</tr>
<tr>
<td>LCx occlusion</td>
<td>36.8 ± 7.9</td>
<td>10 ± 6</td>
<td>14.1 ± 3.4</td>
<td>13 ± 8</td>
<td>12.8 ± 4.0</td>
<td>7 ± 4&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Postocclusion</td>
<td>35.6 ± 7.6&lt;sup&gt;1&lt;/sup&gt;</td>
<td>13 ± 7</td>
<td>13.6 ± 3.4</td>
<td>14 ± 6</td>
<td>12.5 ± 3.7</td>
<td>10 ± 4</td>
</tr>
</tbody>
</table>

EDD, end-diastolic dimension; EDL1, end-diastolic length (LAD); EDL2, end-diastolic length (LCx).
<sup>1</sup>p < 0.05 versus control.
<sup>1</sup>p < 0.01 versus control.
<sup>1</sup>n = 10.
<sup>1</sup>n = 9.
changes in LCx segment crystal fractional shortening in Fig. 4. The absolute changes in mean and median phase demonstrated negative correlations with the percent changes in fractional shortening of \( r = -0.70 \) and \(-0.64\), respectively, (both \( p<0.01\)). The absolute changes in s.d. of mean phase also demonstrated a negative correlation with the percent changes in fractional shortening (\( r = -0.51, p = 0.01\)).

The absolute changes and percent changes in LCx region RNA mean amplitude per pixel are compared with the percent changes in LCx segment crystal fractional shortening in Fig. 5. The absolute changes and percent changes in mean amplitude per pixel demonstrated positive correlations with the percent changes in fractional shortening of \( r = 0.89 \) and \(0.94\), respectively (both \( p<0.001\)). Also, the percent changes in mean amplitude per pixel from control to LCx coronary artery occlusion and control to postocclusion each correlated with the corresponding percent changes in segment crystal fractional shortening (\( r = 0.96 \) and \(0.89\), respectively, both \( p<0.001\)).

**LCx Region Radionuclide Phase and Amplitude Variables Grouped According to Changes in LCx Segment Crystal Fractional Shortening**

The LCx region RNA absolute changes in mean, median, and s.d. of mean phase were grouped according to the percent changes in LCx segment crystal fractional shortening (Fig. 6). Control was set equal to zero (100%), a mildly depressed fractional shortening was 50%–99% of control, a severely depressed fractional shortening was \(<50\%\) of control, and an augmented fractional shortening was \(>100\%\) of control. The average changes in mean phase differed from 0 when a mild or severe depression in segment crystal fractional shortening was observed (\( p = 0.01\) for both). In a similar manner, the average changes in median phase and s.d. of mean phase differed from 0 when a mild or severe depression in fractional shortening was observed (\(p<0.05\) to \( p = 0.005\)). However, there was no significant difference in the average changes in mean, median or s.d. of mean phase between these groups, nor was there a significant difference from 0 if augmented fractional shortening was noted.

The absolute changes and percent changes in LCx region RNA mean amplitude per pixel were similarly grouped according to the percent changes in LCx segment crystal fractional shortening (Fig. 7). In contrast to the mean, median, and s.d. of mean phase, the mean change in average amplitude per pixel did not differ from 0 with a mild depression in fractional shortening, but it did differ from 0 when a severe depression in fractional shortening was observed (\( p = 0.01\)). Also, as segment crystal fractional shortening was progressively depressed from mild to severe, there was a difference in the average values for the mean amplitude per pixel between these groups (\( p = 0.01\)). There was also a difference from 0 in the average change in mean amplitude per pixel when fractional shortening was augmented (\(p<0.05\)). In a similar manner, the average percent change in mean amplitude per pixel did not differ from 0 when a mild depression in segment crystal fractional shortening occurred, but it did differ from 0 when a severe depression in fractional shortening occurred (\(p<0.001\)). With a progression from mild to severe depression in fractional shortening, a difference in the average percent change in mean amplitude per pixel was observed between these groups (\(p<0.001\)).

**TABLE 3**

Global Left-Ventricular RNA Phase (\( \phi \)) Data (n = 11)

<table>
<thead>
<tr>
<th></th>
<th>( \bar{x} \phi ) (degrees)</th>
<th>Median ( \phi )</th>
<th>s.d. of ( \bar{x} \phi )</th>
<th>Sk( \phi )</th>
<th>K( \phi )</th>
<th>pixels (p)</th>
<th>( \bar{x} ) Ampl/p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>22 ± 15 (SD)</td>
<td>19 ± 15</td>
<td>20 ± 7</td>
<td>0.9 ± 0.8</td>
<td>5 ± 4</td>
<td>274 ± 74</td>
<td>273 ± 127</td>
</tr>
<tr>
<td>LCx occlusion</td>
<td>26 ± 17</td>
<td>21 ± 19</td>
<td>32 ± 16*</td>
<td>0.7 ± 0.7</td>
<td>4 ± 2</td>
<td>289 ± 85</td>
<td>249 ± 132</td>
</tr>
<tr>
<td>Postocclusion</td>
<td>20 ± 16</td>
<td>17 ± 19</td>
<td>24 ± 9</td>
<td>0.7 ± 0.8</td>
<td>5 ± 3</td>
<td>289 ± 80</td>
<td>280 ± 155</td>
</tr>
</tbody>
</table>

RNA, radionuclide angiographic; LCx, left circumflex; \( \bar{x} \), mean; s.d., standard deviation; Sk, skewness; K, kurtosis; Ampl, amplitude. \( p < 0.05 \) versus control.

**TABLE 4**

Left Circumflex (LCx) Region RNA Phase (\( \phi \)) Data (n = 11)

<table>
<thead>
<tr>
<th></th>
<th>( \bar{x} \phi ) (degrees)</th>
<th>Median ( \phi )</th>
<th>s.d. of ( \bar{x} \phi )</th>
<th>Sk( \phi )</th>
<th>K( \phi )</th>
<th>pixels (p)</th>
<th>( \bar{x} ) Ampl/p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>25 ± 22 (SD)</td>
<td>21 ± 23</td>
<td>23 ± 9</td>
<td>1.0 ± 1.1</td>
<td>6 ± 6</td>
<td>89 ± 17</td>
<td>247 ± 91</td>
</tr>
<tr>
<td>LCx occlusion</td>
<td>42 ± 30'</td>
<td>33 ± 36'</td>
<td>31 ± 17</td>
<td>0.7 ± 0.8</td>
<td>4 ± 2</td>
<td>94 ± 23</td>
<td>209 ± 118</td>
</tr>
<tr>
<td>Postocclusion</td>
<td>29 ± 23</td>
<td>26 ± 24</td>
<td>26 ± 12</td>
<td>0.6 ± 1.3</td>
<td>6 ± 5</td>
<td>86 ± 14</td>
<td>256 ± 135</td>
</tr>
</tbody>
</table>

LCx, left circumflex; RNA, radionuclide angiographic; \( \bar{x} \), mean; s.d., standard deviation; Sk, skewness; K, kurtosis; Ampl, amplitude. \( p < 0.05 \) versus control.
FIGURE 4
The correlation between the absolute changes in LCx region radionuclide angiographic (RNA) mean phase (left panel), median phase (center panel), and s.d. of mean phase (right panel), on the ordinates, and the percent changes in LCx segment crystals fractional shortening, on the abscissas, are illustrated. The solid circles represent changes from control to LCx coronary artery occlusion and the open circles represent the changes from control to postocclusion conditions for these phase parameters. The regression line, regression equation, correlation coefficient (r), standard error of the estimate (s.e.e.), and 95% confidence intervals for the data are shown for the combined comparison. Also, the correlation coefficients (r) for the individual comparisons are noted.

There was also a difference in the average percent change in mean amplitude per pixel from 0 when fractional shortening was augmented (p = 0.01).

Reproducibility
The intraobserver variability for the LCx region RNA mean, median, and s.d. of mean phase and average amplitude per pixel were r = 0.91, 0.94, 0.95, and 0.93 with mean percent differences between observations of 29%, 21%, 25%, and 8%, respectively. Similarly, the interobserver variability for these phase variables were r = 0.97, 0.98, 0.95, and 0.89 with mean percent differences between observations of 18%, 13%, 25%, and 4%, respectively.

FIGURE 5
The absolute changes in LCx region RNA mean amplitude per pixel (left panel) and the percent changes in this variable (right panel), on the ordinates, are compared with the percent changes in LCx segment crystal fractional shortening, on the abscissas. The display is similar to that in Figure 4.
DISCUSSION

Several studies have reported that Fourier analysis of RNA images can detect LV regional wall motion abnormalities due to ischemic heart disease, both at rest and during exercise (5,14,16–18). Botvinick et al examined the RNA phase analysis images of 29 patients with chronic ischemic heart disease (5). They demonstrated that the mean phase delay between normally contracting LV segments and hypokinetic, akinetic, and dyskinetic segments differed (p ≤ 0.025). The phase delay of dyskinetic segments also differed from that of akinetic segments (p<0.005). Although there was significant overlap in the phase delay between normally contracting and hypokinetic segments, this study suggested that a progressive delay in mean phase might potentially be used to quantify LV regional wall motion abnormalities. Vos et al further attempted to quantify LV regional wall motion using multiharmonic Fourier analysis in 75 patients with chronic LV wall motion abnormalities due to ischemic heart disease (18). Importantly, the posterolateral LV region multiharmonic Fourier amplitude (r = −0.65, p<0.0001) and s.d. of mean phase (r = −0.55, p<0.0001) correlated with the LV wall motion scores, while mean phase, corrected for heart rate differences between individual patients, weakly correlated with the LV wall motion scores (r = 0.21, p<0.04). Both of these initial studies used a subjective, visual interpretation of the RNA images against which the Fourier analysis data was compared rather than an independent and accurate measure of LV regional function. Thus, the ability of Fourier analysis of RNA images to identify and quantify LV regional wall motion abnormalities produced by ischemic heart disease remains uncertain.

Several investigators have applied Fourier analysis to exercise RNA studies to determine if this approach might improve the identification of acute reversible LV wall motion abnormalities due to ischemic heart disease (15–17). Ratib et al reported an increase in the s.d. of mean phase in 95% of patients with ischemic heart disease, while specificity for the exclusion of ischemic heart disease remained high (16). They postulated that Fourier analysis improved the detection of LV regional wall motion abnormalities compared with a visual interpretation of the RNA images. Subsequent studies by Turner et al (17) demonstrated that, compared with conventional RNA criteria, the skewness of phase was equally sensitive, but it was more specific for the detection of ischemic heart disease (p<0.05). Thus, these initial studies suggested that Fourier analysis of exercise RNA images may be more useful than conventional criteria for the detection of LV regional wall motion abnormalities resulting from ischemic heart disease.

The present investigation attempted to assess whether and to what extent changes in LV regional wall motion induced by transient ischemia could be detected and quantified by Fourier analysis of RNA images as previously suggested (5,14,18). Our data indicate that in this chronically instrumented dog model where the regional effects of transient ischemia can be precisely quantified by regional segment crystal pairs, the LCx region RNA absolute changes in mean (r = 0.70), median (r = −0.64), and s.d. of mean phase (r = −0.51)
correlated with the percent changes in LCx segment crystal fractional shortening. A correlation was also observed with the absolute changes and percent changes in average amplitude per pixel (r = 0.89 and 0.94, respectively). In addition, when grouped according to a mild or severe depression or an augmentation in segment crystal fractional shortening, there appeared to be less separation between groups when the absolute changes in mean, median, and s.d. of mean phase were evaluated, while a progressive difference was observed when the absolute changes and percent changes in average amplitude per pixel were compared. Furthermore, an increase in fractional shortening was detected only by the absolute changes or percent changes in average amplitude per pixel, but not the absolute changes in the mean, median, or s.d. of mean phase. These data suggest, therefore, that regional RNA phase variables may be able to detect and quantify LV wall motion abnormalities in individual patients.

Several important aspects of this study must be considered. First, the LV regional analysis proved to be essential in delineating changes in RNA phase and amplitude variables relative to the percent changes in segment crystal fractional shortening. The global LV phase analysis demonstrated a broadening of the phase histogram during LCx coronary artery occlusion compared with control, manifest by a significant increase in the s.d. of mean phase, but no significant shift in mean and median phase or reduction in average amplitude per pixel. These data may be explained in part by the observations of Wendt et al, who evaluated the first harmonic Fourier transform generated from computer phantoms that isolated motions of the left ventricle (25). The problems they observed included LV and left atrial overlap, which blurred the phase variables at the superior margin of the LV; and translational and rotational effects, which principally altered the phase variables in the septal region. They concluded that interpretation of the first harmonic global LV phase and amplitude images must be done with caution, because these phantom effects were also noted in some patient studies. Thus, in an attempt to minimize these potential confounding problems, particularly the rotational and translational effects predominating in the septal region, LV regional analysis was performed in this investigation.

A second potential concern is the importance of heart rate and its effect on the RNA phase variables. Bacharach et al reported that mean phase depended mainly on the diastolic filling period if all other factors remained constant, while its distribution, the s.d. of mean phase, was not appreciably altered (7). In addition,
although amplitude is principally determined by stroke volume, changes in diastolic filling can also alter the amplitude variable. It is important to assess heart rate changes and the number of frames used in each study, because concomitant changes in these factors may effect the phase and amplitude variables in each dog. Consequently, the changes in regional phase and amplitude variables observed in this investigation reflect predominantly those induced by transient regional ischemia. The reduction in diastolic filling rate induced by transient ischemia may explain the observed difficulty in quantifying mild reductions in segment crystal fractional shortening by the absolute changes and percent changes in average amplitude per pixel, because ischemic induced alterations in both diastolic filling and stroke volume were present (1).

Other considerations in this investigation are the masking technique, the reproducibility of the LV region-of-interest, and the correspondence of the postero-lateral LV region to the distribution of the LCx segment crystal pair. We chose to mask the RNA studies with a hand-drawn LV region-of-interest without an amplitude mask. The adequacy and reliability of this masking technique is apparent by the consistency of the mean number of pixels in the RNA LCx region for each condition and the absence of low level activity on the LCx regional phase histograms of each dog. In addition, this method of masking has been employed by Bacharach et al in assessing the effects of heart rate, systolic events, and diastolic filling on phase variables (1). The reproducibility of the LCx region RNA phase and amplitude data are important to determine the potential applicability of this method of quantitating LV regional function. The intra- and interobserver reproducibility for the phase variables demonstrated good correlation coefficients and mean percent differences between observations. Although, the mean percent differences between observations for mean, median, and s.d. of mean phase ranged from 13% to 29%, these mean percent differences represent small absolute differences, because the LV regional phase variables for the control condition were concentrated near 0°. Thus, the RNA regional phase and amplitude variable appear to be reproducible.

Finally, the RNA LCx region in some dogs probably exceeded the ischemic zone as defined by the LCx segment crystal pair. Indeed, the LCx region showed proportionally less shift in RNA phase and less reduction in average amplitude per pixel than that observed for segment crystal fractional shortening. Nevertheless, the group mean absolute changes and percent changes in the LCx regional RNA phase and amplitude variables were directional similar to those observed in segment crystal fractional shortening. There were, however, wide 95% confidence intervals for the correlations and each subgroup analysis demonstrated a wide range of individual RNA phase values. These variations may be due to the size of the region-of-interest in comparison with the transient ischemic zone. Smaller regional sectors concentrating over the maximal shift in phase may reflect more closely changes in segment crystal fractional shortening. However, the statistical reliability for this RNA technique may be approached as regional sectors are decreased in size, limiting the precision and accuracy of the method (26).

In conclusion, we have shown that several RNA phase and amplitude variables correlate with LV regional wall motion abnormalities induced by transient LCx occlusion and defined by ultrasonic LCx segment crystal fractional shortening. Also, the group mean absolute changes in phase variables and the absolute changes and percent changes in average amplitude per pixel moved directionally similar to the percent changes in LCx segment crystal fractional shortening. The application of this RNA approach to detecting and quantifying LV regional wall motion abnormalities on RNA images during exercise is problematic, because the heart rate changes observed during exercise would affect the global and regional LV phase and amplitude variables independent of the effects of transient ischemia (1,16). The data from the present investigation, however, suggest that regional RNA phase analysis may be able to detect and quantify changes in LV regional wall motion in individual patients in whom heart rate remains stable, such as following interventional angiography (27).

NOTES

* P-18, Konigsberg Instruments, Inc., Pasadena, CA.
§ Zepeda Instruments, Seattle, WA.
† Schussler and Assocs. Cardiff-by-the-Sea, CA.
‡ Beckman Instruments.
§ Dual Control Systems.
* Zobex.
* Medical Data Systems, Inc., Ann Arbor, MI.

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