The Influence of Left Ventricular Volume and Wall Motion on Myocardial Images

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SUMMARY We studied 10 dogs to determine if changes in myocardial images could result from alterations in left ventricular (LV) geometry independent of any change in tracer distribution. All dogs received 20 mCi of $^{99m}$Tc-labeled albumin microspheres (10–45 μ) via the left atrium, after which control multigated, gated and ungated myocardial perfusion images were obtained. Next, five dogs were sequentially imaged 1) during partial aortic occlusion to increase LV volume; 2) after release of the aortic occlusion; 3) after ligation of the coronary vasculature of the apex of the LV to produce regional dyskinesis; and 4) after nitroprusside induced hypotension to decrease ventricular volume. Only ligation and nitroprusside studies were done in the remaining five dogs. We gave 1.5 mCi of thallium-201 intravenously to two other dogs and obtained sequential ungated control, ligation, and nitroprusside images.

At postmortem exam, tracer activity was equivalent at the apex and base for both microspheres and thallium. Nevertheless, partial aortic occlusion caused defects in the apex and anterior wall in four of five dogs. Coronary ligation caused new defects in eight of 10 dogs given microspheres and in both dogs given thallium. With nitroprusside, microsphere and thallium defects generally decreased in size. Gated images showed that defects caused by ligation tended to be larger in end-systole than in end-diastole, while all partial aortic occlusion-induced defects were equal or greater in size in end-diastole compared with end-systole.

These results indicate that changes in LV geometry or contraction pattern may cause defects on myocardial images without any change in tracer distribution.

SERIAL IMAGING after administration of $^{201}$Tl has been used by several investigators to differentiate between myocardial ischemia and infarction. Defects related to ischemia eventually fill in, while those related to infarction persist. Sometimes regions which initially demonstrate normal or reduced activity appear to lose $^{201}$Tl activity over time. Such changes, when they occur, have usually been ascribed to concomitant changes in tracer concentration related to alterations in regional blood flow. However, alterations in hemodynamics during ischemia may produce important changes in left ventricular volume or regional wall motion or both. The influence that ventricular volume and regional wall motion might have on $^{201}$Tl images, independent of changes in actual tracer distribution, has not been systematically investigated. Therefore, we undertook the present study to assess the effect of these geometric factors on the appearance of myocardial images.

Materials and Methods

Ten mongrel dogs (mean weight 23 kg, range 21–28 kg) were anesthetized with sodium pentobarbital (45 mg/kg i.v.), intubated, and ventilated with a Harvard respirator. We adjusted tidal volume, respiratory frequency, and $F_{O_2}$ as needed to maintain arterial $P_{O_2}$ above 100 mm Hg and arterial $pH$ and $P_{CO_2}$ within the physiologic range (pH 7.38–7.42; $P_{CO_2}$ 35–45 mm Hg). We exposed the heart through a left thoracotomy and suspended it in a pericardial cradle. Through a

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stab wound, we placed a 50-cm polyethylene catheter (1.67 mm i.d.) in the left atrium and secured it with a pursestring suture. Next, we cannulated the right internal mammary artery using a polyethylene catheter like the one described above. Left atrial and systemic arterial pressures were continuously monitored using Statham P231D transducers and recorded using a Hewlett-Packard model 7758-A eight-channel recorder. Heart rate (ECG lead II) was also continuously monitored. We cannulated the femoral veins for administration of drugs.

Figure 1 shows the experimental protocol. After obtaining control hemodynamic measurements, we injected 20 mCi of $^{99mTc}$-human serum albumin microspheres (about $10^6$ microspheres, 95% of which were 10–45 μ in diameter) via the left atrium; 5 minutes later we recorded control multigated and ungated images.

In five dogs, we placed a snare around the proximal aorta just above the coronary arteries. We then tightened the snare to induce left ventricular dilation. We tried to adjust the degree of dilation by adjusting the snare so that mean atrial pressure would rise by 1.5–3 times control levels. Two to three minutes later, after a steady state for LAP and heart rate were attained, we recorded repeat multigated and ungated images. Next, we released the snare and after equilibration of LAP and mean arterial pressure (MAP) we recorded new images. Then we ligated the coronary vasculature to the apex of the left ventricle to induce apical dyskinesis and systolic wall thinning, as would occur during an ischemic event. We gave lidocaine — 40 mg i.v. followed by a 2-mg/kg drip — to prevent ventricular ectopic activity, and obtained images 5 minutes later. Next, to decrease left ventricular volume, we gave sodium nitroprusside i.v. until MAP was lowered to 45 ± 5 mm Hg. When a steady state had been achieved for 5 minutes, we again recorded images. The dogs were then sacrificed and the hearts removed and sectioned for counting. In the remaining five dogs, we omitted the aortic snare intervention and performed only ligation and nitroprusside studies.

To a third group of eight dogs (controls) we gave only microspheres. These dogs were sacrificed 2 hours later. The hearts from the control dogs were sectioned and counted in the same way as those from the intervention dogs (see below).

Finally, we gave 1.5 mCi $^{201Tl}$ i.v. to two additional dogs and recorded control ungated images as described above. We then ligated multiple apical vessels and obtained repeat ungated images 10 minutes later. Next, nitroprusside was infused as previously described and repeat ungated images were obtained after a steady state had been attained for 5 minutes. The dogs were then sacrificed and myocardial thallium activity determined.

**Postmortem Materials — Counting Methods**

The hearts were first washed thoroughly in tap water, blotted dry and carefully trimmed to remove all fat and epicardial blood vessels. Next, the atria and free wall of the right ventricle were removed and the left ventricle was divided into five equal subsections and counted in a gamma well counter (Searle Model 1185, Searle Analytic, Inc, Des Plaines, Illinois). After appropriate background subtraction, activity in each sample was calculated and expressed as counts/g/min. A representative nonischemic zone of myocardium was similarly removed, sectioned and counted. An apex (ischemic zone)-to-base (nonischemic zone) count ratio was calculated for each experiment.

**Imaging Methods**

We used an Ohio-Nuclear Series 420 mobile gamma camera equipped with a high-resolution, parallel hole collimator to obtain the nuclear images, and an MDS PAD computer system (Medical Data Systems, Ann Arbor, Michigan) to collect and display them. The detector was aligned over the exposed heart to obtain a lateral view before the first imaging study and was not moved until the final images were obtained at the end of the experiment. The ungated images were collected in the memory of the computer with

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**Figure 1.** Schematic diagram of the study protocol. Control multigated and ungated images were obtained after injection of 20 mCi of $^{99mTc}$-labeled microspheres (MS) via the left atrium (LA). Repeat multigated and ungated images (Images 2–5) were obtained after partial aortic (Ao) obstruction, after release of the aortic obstruction, after coronary artery apical ligations, and after nitroprusside-induced (NP) hypotension, respectively.
128 × 128 matrix (2 mm) resolution. The gated images were acquired with 64 × 64 matrix (4 mm) resolution using software. We obtained 100 thousand to 200 thousand counts in each multigated image, and a minimum of 400 thousand counts in each ungated scan. Both gated and ungated images were later displayed on a cathode ray tube, matched for contrast and peak intensity and then photographed on polaroid film. End-systole and end-diastole were determined by visual inspection of the image sequence.

Image Analysis

The images were divided into three zones (anterior, apical and inferior) for purposes of analysis. Each zone was graded independently by three observers for absent, reduced or normal activity. Differences of opinion regarding segmental activity were resolved by consensus.

Statistical Analysis

All data are expressed as mean ± SEM. We assessed the significance of differences between the means using the t test for paired data.

Results

Hemodynamic Data

The coronary ligation intervention induced no significant change in heart rate (158 ± 6 to 153 ± 9 beats/min) or LAP (8 ± 1 to 9 ± 1 mm Hg), but MAP declined from 116 ± 6 to 103 ± 7 mm Hg (p < 0.05).

The nitroprusside intervention (based on eight dogs because two died at the start of the intervention) induced no significant change in heart rate (148 ± 10 to 145 ± 9 beats/min), while LAP declined slightly (10 ± 1 to 8 ± 1 mm Hg; p < 0.05) and MAP decreased markedly (103 ± 7 to 45 ± 5 mm Hg; p < 0.01).

Finally, in response to the aortic snare intervention, there was no significant change in heart rate (158 ± 16 to 151 ± 11 beats/min), but LAP increased from 7 ± 1 to 15 ± 2 mm Hg (p < 0.01). Since we placed the arterial pressure cannula distal to the aortic occluder, the observed MAP dropped substantially in each study. After we released the snare, heart rate (150 ± 8 beats/min), MAP (107 ± 9 mm Hg) and LAP (8 ± 1 mm Hg) returned to levels that were not significantly different from preobstruction values.

In Vitro Myocardial Microsphere Activity

The apex-to-base count ratios were not significantly different in the nine study dogs (0.96 ± 0.05) and in the eight control dogs (0.97 ± 0.02).

Imaging Data

$^{99m}$Tc-Labelled Microsphere Images

Ligation Intervention. Figures 2 and 3 show the effect of multiple apical coronary ligations on the ungated control perfusion images in four dogs. Two of these had partial aortic occlusion before ligation (fig. 2) and two did not (fig. 3). In all four cases, a new defect appeared on the image after ligations were applied. Moreover, the gated images from dog 1 (fig. 4) showed that the defect was larger in end-systole than in end-diastole. Overall, eight of 10 dogs had similar new or enlarged apical defects on ungated images in response to coronary ligation. In the two remaining dogs, the control image did not change appreciably after coronary ligation. Visual analysis of gated images revealed that six of eight defects were larger in end-systole than in end-diastole. The defects

![Image of images showing control, AoS, Control II, Ligation, and Np for Dog 1 and Dog 2.]
were the same size in both end-systole and end-diastole in the remaining two cases.

Nitroprusside Intervention. Three examples of the effect of nitroprusside on ligation-induced apical defects are shown in figures 2 and 3. The ungated images show that each of the three ligation-induced defects became smaller or resolved (note dog 3) after this intervention. The overall size of the left ventricle on each of the perfusion images decreased after nitroprusside administration. The gated images from dog 1 (fig. 4) showed no significant defect in end-diastole but a large defect in end-systole. Overall, five of seven dogs that had a defect on ungated images after ligation also had a decrease in the size of the defect after nitroprusside infusion. All five of these dogs had a decrease in size of the left ventricle on ungated images as well. Although left ventricular size also decreased in the remaining two dogs, there was no obvious change in the size of the defect on the ungated scans.

Aortic Snare Intervention. Figure 2 shows the effect of partial aortic obstruction on the ungated myocardial images from two of the dogs. The control ungated images showed uniform tracer distribution throughout the myocardium. However, the scans obtained during partial aortic occlusion revealed obvious defects involving the apex and anterior wall of the left ventricle in both dogs. The scans also show that the size of the left ventricular cavity clearly increased during this intervention. After release of the snare (control II), defects in both regions essentially returned to pre-occlusion, control appearance, and the left ventricular cavity size also decreased. The gated images from dog 1 (fig. 4) showed that the end-systolic and end-diastolic size of the defect was essentially the same. Of five dogs studied, four had apical and anterior wall defects on ungated scans similar to those described above. In each of these dogs, the left ventricle showed a moderate-to-marked increase in size on the ungated scan during this intervention. In contrast, the one dog that had no defect during the partial occlusion had only a slight increase in the size of the left ventricle on its ungated scan. These defects were of equal or greater size in end-diastole compared with end-systole. In addition, in each of these dogs, release of the aortic snare resulted in the resolution of the intervention-induced defects and a clear-cut decrease in the size of the left ventricle on the nuclear images.

Thallium Images

Figure 5 shows myocardial images obtained in one of the two dogs that received thallium. The control image shows uniform tracer distribution. After coronary ligation, a defect in the apex of the left ventricle was apparent, but decreased in size during nitroprusside infusion. Similar changes in response to both interventions occurred in the second dog. In these two

**Figure 3.** The effects of coronary artery apical ligations and nitroprusside-induced (NP) hypotension on ungated 99mTc microsphere images is shown in two dogs in which partial aortic occlusion was not performed. Coronary ligations caused prominent apical defects. After NP, these apical defects decreased in size, and virtually disappeared in dog 3.

**Figure 4.** End-systolic and end-diastolic images obtained from a representative study (dog 1) during the ligation, nitroprusside (NP), and partial aortic occlusion (Ao) interventions. After the coronary ligations, an apical defect is apparent at end-systole but not at end-diastole. After NP, the apical defect persists at end-systole, but appears smaller. During partial aortic occlusion both anterior and apical defects are present and comparable in size at end-systole and end-diastole.
Figure 5. The effects of apical coronary artery ligation and nitroprusside-induced (NP) hypotension on ungated thallium-201 images are shown in scans obtained from one of the two dogs studied with thallium. Again, coronary ligations caused an unequivocal apical defect which decreased in size after NP.

Discussion

Our study indicates that changes in left ventricular volume and regional wall motion may have an important influence on myocardial images independent of changes in myocardial tracer distribution. Dilation of the left ventricle may cause defects to appear on myocardial scans, but these defects tend to resolve as the ventricle returns to its normal size. Similarly, defects may also be caused by the production of apical dyskinesis and associated systolic wall thinning. Furthermore, a decrease in left ventricular volume may cause such defects either to disappear or to decrease in size. These myocardial image changes occurred despite the constancy of myocardial tracer distribution per unit mass of tissue documented by postmortem scintillation well counting.

The mechanism by which these changes occur is most likely related to an alteration in the actual density of radioactivity projected onto the detector crystal when the heart is imaged. Thus, although radioactivity per gram of tissue does not change during ventricular dilation or during induced regional wall abnormalities (apical dyskinesia), the projected surface area over which the counts were distributed does increase. The aortic snare intervention induces ventricular dilatation which results in stretching of the anterior and apical walls, and the resultant defects are usually most prominent during diastole. In contrast, coronary ligation has its most prominent effect in systole, when the apical wall is thinnest. The response to nitroprusside-induced hypotension illustrates the potential interplay between changes in cavity size and regional wall motion. Although systolic wall thinning and dyskinesia persist in each case, the size of the defect appears to change only when overall cavity size decreases sufficiently to cause the surrounding walls with normal activity to project over the dyskinetic zone. The defects occur when counts per unit area increase, even though activity concentration remains constant.

This study has several clinical implications. First, the interpretation of serial myocardial images in the setting of acute ischemia must consider not only alterations in tracer distribution but also changes in left ventricular cavity size and wall motion as causes for an apparent change in the size of a defect. These geometric factors may be particularly important in assessing the effects of agents such as vasodilators on regional activity of a myocardial tracer. By reducing left ventricular volume, any of the vasodilators may lead to improvement or disappearance of a perfusion defect suggesting, perhaps erroneously, reversal of ischemia. Second, an increase in size or even the appearance of a new defect may not be related to loss of tracer from the myocardium. This is particularly relevant to the interpretation of serial thallium images. Enlarging defects on thallium scans may be associated with infarct extension. The mechanism for these changes has been presumed to be loss of myocardial tracer from previously normal zones. The results of the present study suggest that geometric factors also may account for such changes. Moreover, thallium clearance from the myocardium seems to be unaffected by 2 hours of coronary occlusion and resultant ischemia. When defects increase in size on serial thallium scans after extension of myocardial infarction, alterations in left ventricular geometry rather than loss of thallium from the affected zone is more likely to be responsible. Third, changes in left ventricular volume which may occur during exercise could obscure serial changes in tracer distribution on thallium scans.

In conclusion, the results of the present study indicate that the appearance of myocardial images may be significantly influenced by factors other than the actual distribution of the tracer within the myocardium (i.e., by left ventricular volume and regional wall motion). Images made during or after acute myocardial ischemia appear most likely to be affected by such factors. In addition, the apex of the left ventricle appears most susceptible to these factors, although the anterolateral wall may also be affected. Thus, when patients are imaged under conditions in which geometric factors are likely to vary, attention should be directed toward identifying and where possible minimizing such influences to avoid potentially inaccurate interpretations of the scans. Furthermore, because the apex and to a lesser extent the anterolateral wall of the left ventricle appear to be most susceptible to changes induced by geometric factors, particular caution should be exercised when interpreting changes in these zones. Finally, we do not imply that conventional myocardial imaging cannot supply meaningful information regarding the underlying status of the myocardium and the coronary circulation. On the contrary, by identifying a potential pitfall in this method we feel that inappropriate and misleading conclusions can be more easily avoided, thereby increasing the diagnostic reliability of the procedure.
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