Effect of a Delay in Commencing Imaging on the Ability to Detect Transient Thallium Defects

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Sixty patients, 42 with coronary disease and 18 normals, were studied to assess the impact of a delay following exercise in commencing thallium imaging on the sensitivity for detecting ischemic transient defects. Three sets of images were obtained beginning 2 min, 18 min, and 2 hr after exercise. Each patient's images were separated into two pairs of studies for analysis: 2 min–2 hr and 18 min–2 hr. Of the 42 patients with coronary disease, a greater number had transient defects detected on the 2 min–2 hr compared with the 18 min–2 hr study (22 compared with 14, p <0.05). False positives were not increased by earlier imaging. We conclude that a modest (18 min) delay obtaining the first set of images causes a significant reduction in the ability to detect transient thallium defects, and that imaging should begin several minutes after exercise.

Serial thallium-201 (^{201}Tl) imaging, in conjunction with exercise stress tests, provides useful information about regional differences in myocardial blood flow due to coronary artery disease (CAD) (1–6). Fill-in of initial defects through redistribution has been useful in detecting the presence of reversible myocardial ischemia (7). Since redistribution may begin soon after initial thallium uptake (8,9), the ability to detect transient defects may decrease when initial imaging is significantly delayed from the time of thallium injection. Such delays in commencing imaging may be due to differences in location of exercise equipment and imaging facilities, or a decision to wait for ischemic electrocardiogram (ECG) changes to disappear before imaging is begun. Furthermore, since it is customary to obtain two or more views of the heart for each set of thallium images, there will frequently be a significant delay between injection and commencement of the second or third view, even when the first view is obtained in a timely fashion.

This study was undertaken to examine the effect of a delay in commencing imaging on the ability to detect transient thallium defects.

MATERIALS AND METHODS

Patient population

Sixty patients, ranging in age from 35 to 67 yr were studied. All patients underwent selective coronary angiography. Forty-two had significant CAD, defined as at least 50% narrowing in one or more coronary arteries, and 18 were normal. Of the patients with coronary disease, 14 had one-vessel, 15 had two-vessel, and 13 had three-vessel disease. Twenty-one had a history of prior myocardial infarction.

Exercise protocol and image acquisition

An i.v. cannula was inserted into a dorsal hand vein and a baseline 12-lead ECG was recorded in the supine position prior to exercise. Patients were then exercised on a supine bicycle ergometer until either fatigue, significant chest pain, 2 mm or more of horizontal to downsloping ST segment depression, or three or more consecutive ventricular premature complexes developed. Exercise was performed in graded 3-min stages
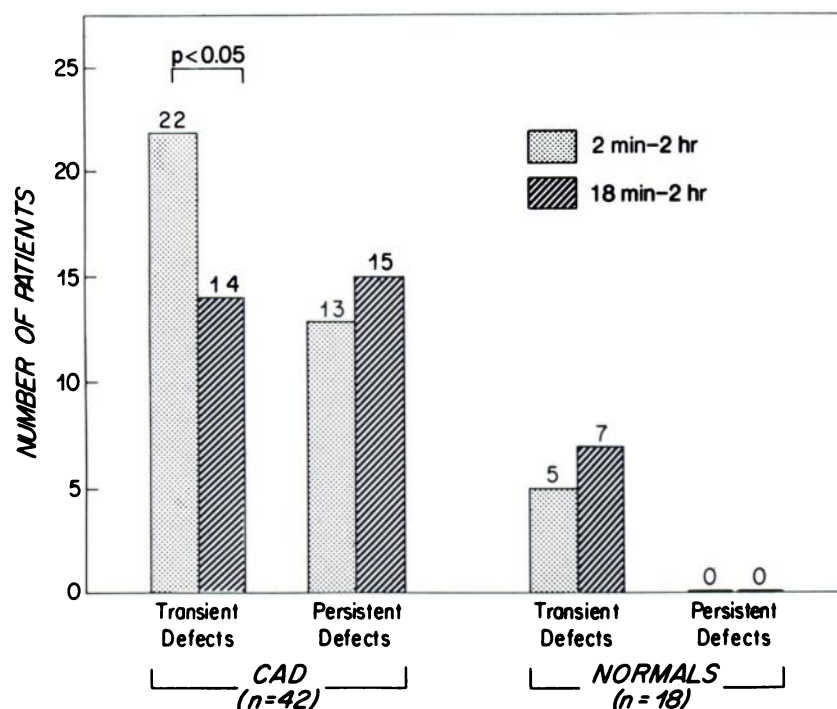
FIGURE 1
Number of patients with positive thallium scans for either transient or persistent defects in group with coronary disease and group of normals

beginning at a workload of 150 kpm/min and increasing by 150 kpm/min for subsequent stages. Heart rate, blood pressure, and a 12-lead ECG were recorded each minute, and the cardiac rhythm was monitored continuously. Approximately 60 sec prior to the anticipated completion of exercise, 1.5 mCi of ^{201}Tl was injected intravenously. Following exercise, three sets of images were obtained in the anterior and 45° left anterior oblique projections. The times from cessation of exercise to the start of each set of images were ~2 min, 18 min, and 2 hr. Images were obtained with a scintillation camera interfaced to a digital computer. An all-purpose collimater was used, and a 30% energy window centered on the 60–80 keV mercury x-ray peak of ^{201}Tl was selected. Images were collected in a 128 × 128 matrix and acquisition time was 6 min for each view.

For the first two sets of images, there was an interval of ~2 min between each view to permit reprogramming of the computer and repositioning of the camera.

Data analysis

Each patient's images were separated into two pairs of studies for analysis—2 min–2 hr and 18 min–2 hr. Four observers were shown each pair of studies in a randomized fashion and were blinded both to the patient's identity and timing of the first set of images in the study. Studies were viewed in raw, unsubtracted form on a computer cathode ray tube.

Myocardial distribution of ^{201}Tl was analyzed in each of six segments: anterolateral, apical, and inferior in the anterior view and septal, apical-inferior, and posterior on the 45° left anterior oblique view. Thallium activity was scored for each segment from 0 to 2 in

steps of 0.5, 2 representing normal uptake and 0, absent uptake. The scores for the four observers were averaged for each segment. A transient defect was defined by an increase in average score of equal to or greater than 0.5 from the initial image (2 min or 18 min) to the delayed image (2 hr). A persistent defect in the anterolateral, inferior, septal, or posterior segment was defined as a score 1.5 or less on the 2-hr image without having increased by 0.5 or greater from the 2-min or 18-min image. Since the apical and apical-inferior segments normally have less activity than the others, a persistent defect for these segments was defined as a score of 1.25 or less on the 2-hr image without having increased by 0.5 or greater from either of the two earlier images.

Statistical analysis

For each of the two pairs of studies, 2 min–2 hr and 18 min–2 hr, the total number of patients with transient defects and persistent defects alone was calculated for subjects with coronary disease as well as for normals. Differences in these numbers were analyzed by means of McNemars test for correlated proportions.

RESULTS

Figure 1 summarizes the numbers of patients with transient and persistent ^{201}Tl defects using the grading criteria previously described. Of the 42 patients with coronary disease, 22 had transient defects (with or without persistent defects) while 13 had persistent defects alone using the 2-min images as the initial thallium study. When the 18-min images were used as the initial study, there were 14 patients with transient de-

fects and 15 with persistent defects alone. The difference in the numbers of patients with transient defects using the 2-min compared with 18-min images as the initial study was statistically significant (p <0.05). There was no significant difference between the numbers of patients with persistent defects alone. Of the 18 normal patients without CAD, there was no significant difference in the number of patients with false-positive transient defects between the 2-min–2-hr study (five patients) and 18-min–2-hr study (seven patients). All of the five patients falsely positive on the 2-min–2-hr study were also positive on the 18-min–2-hr study. There were no patients with false-positive persistent defects alone using either study.

Test results for transient defects were correlated between the 2-min–2-hr and 18-min–2-hr study for the 42 patients with CAD. Twelve patients were positive using either the 2-min–2-hr or 18-min–2-hr study. An additional ten patients were positive on the 2-min–2-hr study but negative on the 18-min–2-hr study. Only two patients had positive tests with 18-min–2-hr but not with 2-min–2-hr studies.

Of the 12 patients positive for transient thallium defects on both studies, nine had evidence of ischemia during exercise by exhibiting electrocardiographic ST segment changes (three patients), by experiencing anginal chest pain (one patient) or both (five patients). Of the ten positive on only the 2-min–2-hr study, eight had ECG or subjective symptoms of ischemia (three by ECG, one by chest pain, four both), and of the two positive in only the 18-min–2-hr study, both had ECG changes and chest pain.

The group of ten patients positive for transient defects on only the 2-min–2-hr images was compared to the 12 patients positive on both the 2-min–2-hr at 18-min–2-hr sets of images with respect to certain clinical, exercise, and angiographic parameters. There were no significant differences between the groups in any of the following (values refer to group positive at 2 min compared with group positive at 2 min and 18 min; means shown are ± s.d.), (a) incidence of prior myocardial infarction (5/10 compared with 8/12); (b) use of propranolol (8/10 compared with 8/12); (c) peak exercise double product (15,000 ± 5,000 compared with 18,700 ± 7,900); (d) incidence of exercise-induced chest pain (5/10 compared with 7/12) or ischemic ECG changes (7/10 compared with 9/12); (e) initial mean score of thallium defects which showed redistribution (0.96 ± 0.32 compared with 1.12 ± 0.20); or (e) mean number of vessels diseased (1.9 ± 0.9 compared with 2.2 ± 0.9).

DISCUSSION

The results of this study show that even a modest delay (18 min) in beginning imaging after the cessation of exercise may cause a significant reduction in the ability to detect transient thallium defects. While the assumption that all patients in this study with significant coronary disease who had transient defects experienced myocardial ischemia cannot be proven, the likelihood is probably high. As noted above, eight of the ten patients with transient defects on the 2-min–2-hr but not 18-min–2-hr study experienced either anginal chest pain or ischemic ECG changes with exercise. These findings support the hypothesis that exercise-induced ischemia did in fact, develop in these patients and would have been missed if only the 18-min and 2-hr images had been obtained.

False positives did not appear to be increased by initial imaging at 2 min compared to 18 min. As previously noted, all five patients who were falsely positive for transient defects using the 2-min–2-hr image set were also falsely positive with the 18-min–2-hr images. Both sets of images on these five patients had at least one false-positive region in common. Since the scoring was done by observing either 2-min–2-hr or 18-min–2-hr studies in a random fashion (not contiguously for the same patient), these patients did appear to have consistently abnormal thallium distributions by our scoring techniques which were not related to the initial time of imaging. The overall specificity of 72% using the 2-min–2-hr set of images is lower than some reports in the literature, but similar to that of Patterson (6) in a consecutive series of patients undergoing catheterization for chest pain. Whatever the cause of false positives in our patients, early imaging did not appear to be a significant factor.

The accuracy of identifying defects on thallium images is a complex function of the size and location of the hypoperfused area, the ratio of activity in normal to abnormal regions, count densities in the images, the contribution of nontarget "background" activity and the characteristics of the imaging equipment used (10). It is also dependent on the normal range of regional variation in thallium activity in the absence of coronary disease, based on the imaging parameters used and the type of analysis performed, whether qualitative or quantitative. It will also be influenced by decisions regarding the balance of "sensitivity" compared with "specificity." When a lesion is near the threshold of detectability, using a particular type of analysis and confidence level, a small amount of redistribution may cause the original defect to become indistinguishable from normal regions, at least to the previously set degree of confidence. Therefore, it is probably not essential that redistribution be rapid or marked for defects to "disappear" between images acquired at 2 min and 18 min after exercise, but only that sufficient redistribution occur that detection criteria applied to the region in question yield a result which is just below a "diagnostic" level. This is not to imply that some patients do not show true rapid redistribution of initial defects, but that

such a phenomenon is not necessary to explain the decreased sensitivity between the 2-min and 18-min images in detecting defects. Studies in humans and animal models suggest that when rapid redistribution does occur, it probably reflects relatively mild degrees of coronary stenosis (11,12). It is also possible that some individuals experience an element of exercise-induced coronary spasm (13). The resolution of such spasm soon after exercise might be expected to produce rapid redistribution, based on animal models with transient occlusion (8). We were not able to document any statistical evidence of more mild disease in our patients with transient defects on only the 2-min–2-hr images compared to those positive on both 2-min–2-hr and 18-min–2-hr images. This may be partly due to the relatively limited number of patients in each group, but the results would not be entirely unexpected in view of the many factors noted above which play a role in the detection of "defects."

CONCLUSION

In summary, we have found that a delay of 18 min in commencing imaging after cessation of exercise significantly reduces the ability to detect transient defects, compared to a 2-min imaging time. While 18 min is probably a longer delay than exists in most facilities, even lesser delays may also cause at least some loss of sensitivity. Further, even if the first view is started in a timely fashion, the interval between exercise and the second and third view may easily be 15–20 min. We would, therefore, recommend that the delay between exercise and imaging be minimized as much as is practical, and preferably be kept to several minutes if conditions allow it.

ACKNOWLEDGMENT

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