Using Gated Technetium-99m-Sestamibi SPECT to Characterize Fixed Myocardial Defects as Infarct or Artifact

E. Gordon DePuey and Alan Rozanski

Division of Nuclear Medicine, Department of Radiology and Division of Cardiology, Department of Medicine, St. Luke's-Roosevelt Hospital Center and Columbia University College of Physicians and Surgeons, New York, New York

Perfusion-scan fixed defects may result from soft tissue attenuation, decreasing test specificity for coronary disease and myocardial infarction (MI). Gated ^{99m}Tc-sestamibi SPECT may help differentiate MI from artifact since fixed defects with decreased function (wall motion and thickening) probably represent MI, whereas attenuation artifacts either have normal function or at least do not demonstrate markedly reduced function. **Methods:** Ungated resting and gated stress ^{99m}Tc-sestamibi SPECT was performed in 551 consecutive patients referred for evaluation of coronary disease. From resting and summed gated stress images, 180 patients (33%) were identified with isolated fixed defects. Function of the defects was assessed subjectively from gated stress images and results were correlated with clinical (history and/or ECG Q-waves) evidence of MI. **Results:** Of 102 patients with fixed defects and clinical MI, 98 (96%) had abnormal defect function. Of 78 patients with no clinical MI, 18 (23%) had decreased function of the defect, possibly indicating silent MI. In 60 of the 78 patients (77%) with no clinical MI, defect function was normal. Because most (91%) of fixed defects with normal systolic function occurred in women with anterior fixed defects (48%) or men with inferior fixed defects (43%), these were most likely attenuation artifacts. By reclassifying patients with fixed defects and normal function as normal, patients with unexplained fixed defects (no clinical MI) decreased from 14% to 3%. **Conclusion:** Gating provides a valuable adjunct to ^{99m}Tc-sestamibi SPECT in characterizing fixed defects and potentially improving test specificity.

Key Words: technetium-99m-sestamibi; single-photon emission computed tomography; attenuation artifacts; myocardial infarction; fixed defects

J Nucl Med 1995; 36:952–955

Soft-tissue attenuation artifacts reduce test specificity on SPECT myocardial perfusion images (*1*). If patient positioning for image acquisition is constant in stress and rest images, and breast position and diaphragmatic height are unchanged, soft-tissue attenuation artifacts generally appear as fixed defects. Uncertainty in differentiating a fixed defect due to attenuation artifact from one due to myocardial infarction is a significant source of false-positive scans and decreased test specificity. With the high count density of ^{99m}Tc-sestamibi SPECT images, gating is possible (*2*), thereby allowing for the simultaneous assessment of resting ventricular function and either stress or rest perfusion distribution. Due to the partial volume effect, an increase in object size less than twice the resolution of the imaging system is manifested by an increase in brightness; thus, an increase in regional myocardial intensity from diastole to systole is proportional to wall thickening (*3*). We postulated that gating should differentiate scar from artifact and thereby improve test specificity since myocardial infarction fixed defects should demonstrate decreased wall motion and wall thickening (*3*), whereas attenuation artifact fixed defects should move and thicken normally.

METHODS

Patients

We prospectively performed gated ^{99m}Tc-sestamibi SPECT on 551 consecutive patients referred to St. Luke's-Roosevelt Hospital for evaluation of suspected or known coronary artery disease (CAD). For every patient, a thorough history was obtained by a cardiologist and a 12-lead ECG was performed prior to the scan to evaluate the possibility of prior myocardial infarction (MI). The conventional criterion of abnormal Q-waves in two or more leads was considered indicative of infarction.

Although the true incidence of CAD in the study population is unknown since coronary angiography was not performed, all patients were characterized as follows based upon clinical and electrographic findings. Historical and/or electrocardiographic evidence of prior myocardial infarction was evident in 102 patients who were referred for imaging because of recurrent chest pain. Eleven patients who had undergone coronary bypass surgery and two with prior transluminal coronary angioplasty were asymptomatic and referred for routine follow-up evaluation. In three patients with known cardiomyopathy, perfusion imaging was requested to evaluate the possibility of concurrent coronary ischemia as a cause of heart failure. The remaining 433 patients had no prior cardiac history and were referred for the evaluation of chest pain. Two hundred forty-two (56%) presented scintigraphic evidence of ischemia in the latter group.

Received Aug. 30, 1994; revision accepted Nov. 7, 1994.

For correspondence or reprints contact: E. Gordon DePuey, MD, Division of Nuclear Medicine, St. Luke's-Roosevelt Hospital Center, Amsterdam Avenue at 114th St., New York, NY 10025.

Gated SPECT

Eight-frame per-cardiac-cycle gated ^{99m}Tc SPECT studies were acquired on a commercially available camera and computer (XCT camera and 3000 computer, General Electric Medical Systems, Milwaukee, WI) using a 180° imaging arc, high-resolution parallel-hole collimator; and 64 stops with 20 sec per stop for a total imaging time of 25 min. All images were acquired 30–60 min after administration of 22–30 mCi of sestamibi during peak treadmill exercise or following intravenous dipyridamole infusion.

Summed gated frames were processed as 6.4-mm tomographic slices using a Butterworth filter with a 0.52 cutoff frequency and power of 5. The gated images were processed using a Hanning filter and 0.7 cutoff frequency. This processing modification was used to compensate for the lower count density in each gated frame; approximately one-eighth of that in the summed, nongated images. Resting studies were not gated and were performed either 1 to 4 days following the stress study (22 mCi), or prior to the stress study on the same day (8 mCi).

For all patients, the summed nongated SPECT studies were first interpreted. The stress and rest 6.4-mm thick short-axis, vertical long-axis and horizontal long-axis slices encompassing the extent of the left ventricle were inspected. In addition, polar maps were viewed. Perfusion defects were identified, localized to the anterior, inferior, lateral, septal or apical wall; and graded subjectively using a 0 to 3 scale (0 = normal, 1 = mild, 2 = moderate, 3 = severe). Defects were determined to be fixed or reversible, improving by one grade or more. If two or more fixed perfusion defects were identified in a single patient, only the most severe was selected for further analysis in the gated SPECT study.

The gated SPECT slices were then viewed in cinematic format at the computer console in both black and white and color. For each patient, five gated slices were viewed, including midventricular vertical long-axis and horizontal long-axis slices, and short-axis slices from the mid-, basal, and apical left ventricular regions. Regional wall motion was assessed by subjective evaluation of endocardial excursion using the black and white monitor. Regional wall motion was judged abnormal if endocardial excursion was less than approximately 50% of adjacent and contralateral segments. Regional wall thickening was subjectively assessed by image intensification from end-diastole to end-systole using the color monitor. Intensification less than approximately 50% of adjacent and contralateral segments was judged abnormal. Segmental function was ultimately judged abnormal if either wall motion or thickening was decreased. In almost all cases, however, thickening abnormalities were more readily apparent than motion abnormalities.

RESULTS

Of the 551 patients, 180 (33%) demonstrated fixed defects in the nongated stress/rest images. Of these, 116 (64%) demonstrated abnormal wall motion and/or thickening. Ninety-eight of these 116 patients (84%) had historical and/or ECG evidence of prior MI. The other 18 (16%) with a fixed defect and abnormal function were distributed among patients who had no historical or ECG evidence of prior infarction.

In 64 of the 180 patients with fixed defects (36%), function of the fixed defect was normal. Four of these patients (6%) had prior infarction, whereas the majority (94%) had no evidence of prior infarction.

From these data, it was determined that the positive predictive value of a fixed defect with abnormal function for prior MI was 85%. The negative predictive value of a fixed defect with normal function for the absence of prior infarction was 94%.

In analyzing these data differently, we observed that of the 180 patients with fixed defects, only 102 had evidence of prior infarction. Thus, the specificity of a fixed defect for prior infarction was only 57%. Of these 102 patients with documented prior infarction, 98 (96%) demonstrated abnormal function on gated sestamibi SPECT. Of the 78 patients with no evidence of prior MI, 18 (23%) nonetheless demonstrated abnormal regional function. In 60 patients (77%) regional function was entirely normal.

We investigated the possible causes of normal function in areas of fixed defects observed in the 60 patients with fixed defects, normal function and no prior MI with regard to gender and defect location. Of these, 29 (48%) were present in females and were located anteriorly. We suspected therefore that these were most likely secondary to breast attenuation artifacts. Twenty-six fixed defects with normal function (43%) occurred in the inferior wall of males. We suspected these were most likely due to attenuation by the left hemidiaphragm. Two inferior defects and one lateral defect with normal motion occurred in females. The lateral defect was present in a woman with very large, laterally positioned breasts. Also, two fixed apical defects, presumed due to physiologic apical thinning, demonstrated normal function. Overall, 91% of fixed defects with normal function could be accounted for by breast attenuation in females or diaphragmatic attenuation in males.

In general, fixed defects in the 102 patients with known myocardial infarction with (n = 98) or without (n = 4) abnormal wall thickening were more severe than those attributable to soft tissue attenuation (n = 60). In patients with MI, defect grade was 1 (mild) in 11; 2 (moderate) in 51; and 3 (severe) in 40. In patients with defects attributable to soft tissue attenuation, defects of grade 1, 2, and 3 were 19, 39, and 2, respectively (chi-square = 29.2, $p < 10^{-6}$). Severe fixed defects were more likely to represent scar, whereas mild defects were more often due to attenuation artifacts. Individual patients with defect severity alone could not differentiate scar from attenuation artifact, especially with regard to moderate defects.

Breast Attenuation

In a woman with a 44-in. chest circumference and a D brassiere cup, midventricular short-axis ungated slices and polar plots revealed a moderately extensive and moderately severe fixed anterior defect in the exercise and resting images (Fig. 1A). The patient, however, had no historical or ECG evidence of prior MI.

The end-diastolic and end-systolic midventricular short-axis and vertical long-axis slices (Fig. 1B) demonstrated normal anterior endocardial excursion and wall thickening, assessed by image intensification during systole. In this

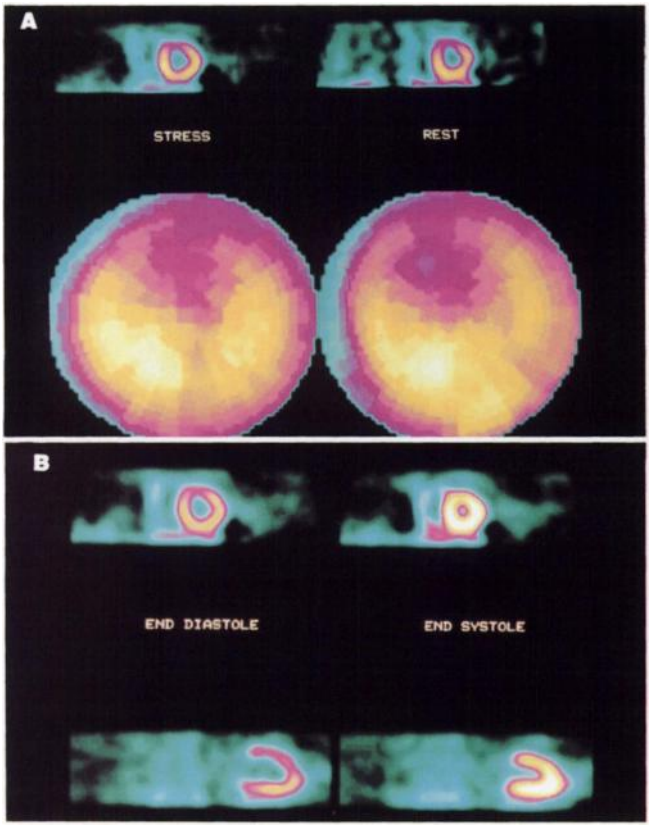

FIGURE 1. A woman with no history of myocardial infarction, a normal resting ECG and a low (<20%) pre-test likelihood of CAD. The patient has a large chest circumference. (A) Mid-ventricular exercise (top left) and resting (top right) short-axis slices and polar plots (bottom row) show a moderate, fixed anterior wall defect. (B) End-diastolic (left) and end-systolic (right) gated mid-ventricular short-axis (top row) and vertical long-axis (bottom row) slices demonstrate normal wall motion and thickening. These findings favor breast attenuation artifact rather than infarction as a cause of the fixed anterior defect.

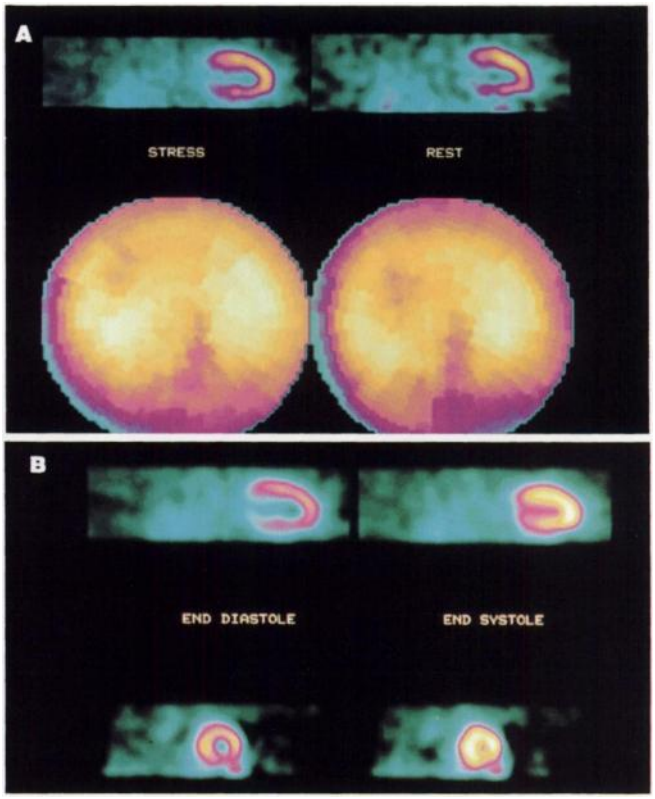

FIGURE 2. A woman with no history of myocardial infarction, a normal resting ECG, and a low (<20%) pre-test likelihood of CAD. (A) Midventricular dipyridamole (top left) and resting (top right) vertical long-axis slices and polar plots (bottom row) demonstrate a moderate, fixed inferior wall defect. (B) End-diastolic (left) and end-systolic (right) gated mid-ventricular vertical long-axis (top row) and short-axis (bottom row) slices demonstrate normal wall motion and thickening. These findings favor diaphragmatic attenuation rather than infarction as a cause of the fixed inferior defect.

patient, normal function would strongly favor breast attenuation artifact as a cause of the anterior fixed defect.

Diaphragmatic Attenuation

A dipyridamole stress/resting study was obtained in a woman of average build and no evidence of prior myocardial infarction. The scan was ordered for preoperative clearance for surgery to relieve a bowel obstruction which had distended her abdomen. Midventricular short-axis and vertical long-axis ungated slices (Fig. 2A) showed a fixed inferior defect more marked than that expected from "normal" diaphragmatic attenuation, especially for a woman.

The gated tomographic slices demonstrated normal inferior wall motion and thickening (Fig. 2B). Thus, exaggerated diaphragmatic attenuation associated with abdominal distension rather than MI is favored as a cause of the fixed inferior defect.

DISCUSSION

A recognized limitation of the present study is the lack of definitive evidence of the presence or absence of myocardial infarction in the patients studied. We recognize that historical and electrocardiographic criteria of MI are inaccurate. For example, in an autopsy series reported by Horan, the sensitivity of electrocardiographic Q-waves for MI was only 61% (*4*). In contrast, small Q-waves, particularly in the inferior wall, may be observed in patients without infarction, and poor R-wave progression is not always a reliable sign of anterior infarction. Also, in patients with conduction abnormalities, a reliable diagnosis of infarction is difficult if not impossible.

In this study, 4% of patients with prior MI demonstrated normal ventricular function. Although patient enrollment has ended, we continue to observe this phenomenon, perhaps even more frequently. There are several possible causes of normal function in the distribution of an infarct. First, the infarct may be small and may be "pulled in" by adjacent normally contracting myocardium. Second, regional ventricular function can be normal in the distribution of a subendocardial or nontransmural infarct. Finally, as

stated above, Q-waves are not 100% specific for transmural infarction.

In the present study, regional abnormalities of left ventricular function were observed in 23% of patients with fixed defects and no ECG or historical evidence of prior myocardial perfusion. Some of these defects could represent zones affected by resting ischemia, accounting for the fixed nature of the sestamibi defect and the associated wall motion abnormality (i.e., "hibernating" myocardium). There are several other possible explanations. First, silent MI with absent or atypical symptoms and no Q-waves are not infrequent. Second, both regional perfusion defects and wall motion abnormalities have been described in patients with cardiomyopathy and valvular heart disease. Also, although electrical conduction disturbances such as left-bundle branch block may result in regional asynergy, wall thickening is usually normal. By history and ECG findings, however, no patients with severe cardiomyopathy or left-bundle branch block were enrolled in the present study. Finally, visual analysis of gated studies may possibly overestimate functional abnormalities, particularly in patients with very marked attenuation artifacts. Since with marked attenuation regional count density may be noticeably decreased at end-diastole and—to a lesser degree—at end-systole, the observer may be prone to visually "overweigh" the end-systolic image and incorrectly interpret decreased wall thickening. Quantitative software to measure wall thickening objectively should obviate this potential problem (*5*).

In the present study, all gated SPECT studies were acquired following stress (exercise or intravenous dipyridamole) tracer injection, using either 22 mCi for a separate-day protocol or 30 mCi for a single-day rest/stress protocol. High count density images obtained with these doses provide good quality gated tomograms. Neither resting sestamibi scans nor low-dose (8 mCi) stress scans, however, have yet been demonstrated to provide adequate gated SPECT images.

The clinical relevance of the present study may be best gauged by the impact of gating on the specificity of ^{99m}Tc-sestamibi SPECT in the diagnosis of CAD. If all fixed defects were interpreted as infarcts and thus indicative of CAD using only nongated SPECT, the potential false-positive rate in our entire study population would be 14%. With the use of gated SPECT to help differentiate scar from attenuation artifact, however, the adjusted false-positive rate decreases to 3%.

CONCLUSION

Gated ^{99m}Tc-sestamibi SPECT potentially increases test specificity for CAD by differentiating scar from attenuation artifact as a cause of fixed defects. Of the fixed defects we observed, breast attenuation in women and diaphragmatic attenuation in men were suspected to be by far the most common cause of attenuation artifacts. When studies are interpreted, correlation of gated scan results with clinical and ECG findings is important to optimize diagnostic specificity. Finally, we feel that apart from other advantages that have been demonstrated previously in the evaluation and quantitation of global and regional ventricular function (*6*), the ability of gated ^{99m}Tc-sestamibi SPECT to improve test specificity for coronary disease warrants the use of gating routinely.

REFERENCES

1. DePuey EG, Garcia EV. Optimal specificity of thallium-201 SPECT through recognition of imaging artifacts. *J Nucl Med* 1989;30:441–449.
2. Mannting F, Mannting MGM. Gated SPECT with technetium-99m-sestamibi for assessment of myocardial perfusion abnormalities. *J Nucl Med* 1993;34:601–608.
3. Chua T, Kiat H, Germano G, et al. Gated technetium-99m-sestamibi for simultaneous assessment of stress myocardial perfusion, postexercise regional ventricular function and myocardial viability. Correlation with echocardiography and rest thallium-201 scintigraphy. *J Am Coll Cardiol* 1994; 23:1107–1114.
4. Horan LG, Flowers NC, Johnson JC. Significance of the diagnostic Q-wave of myocardial infarction. *Circulation* 1971;43:428–436.
5. Cooke CD, Garcia EV, Cullom SJ, Faber TL, Pettigrew RI. Determining the accuracy of calculating systolic wall thickening using a fast fourier transform approximation: a simulation study based on canine and patient data. *J Nucl Med* 1994;35:1185–1192.
6. DePuey EG, Nichols KN, Dobrinsky C. Left ventricular ejection fraction from gated ^{99m}Tc-sestamibi SPECT. *J Nucl Med* 1993;34:1871–1876.