ECG Gating of Thallium-201 Myocardial Images: Effect on Detection of Ischemic Heart Disease

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Using the angiographic findings as the standard, we have examined the sensitivity and specificity of ECG-gated static thallium-201 myocardial images in 54 patients undergoing selective coronary arteriography. Gated and nongated images, each in anterior, 45° LAO, and 65° LAO projections, were processed by interpolative background subtraction. They were then analyzed separately by four independent observers who were unaware of patient identity, the results of coronary arteriography, and which studies were gated or nongated. No significant differences were observed between the gated and nongated images regarding sensitivity or specificity, the detection rate for reversible myocardial ischemia, the accuracy of prediction of arteriographic extent of disease, or the degree of inter- or intraobserver variability. We conclude that ECG-gated acquisition of T1-201 images does not produce any significant advantages, at least when interpolative background subtraction is used.

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In the usual method of acquisition, thallium-201 myocardial images contain data from all phases of the cardiac cycle, and are thus blurred to some extent by cardiac motion, with some possible loss of resolution of abnormalities. One method to overcome the effect of cardiac motion is ECG-gated acquisition of data, such as is employed in equilibrium emission angiocardiography (*1*). ECG-gated acquisition of Tl-201 images has previously been shown to be feasible (*2–4*), but when gating is used, longer acquisition times become necessary, since an image contains data from only a fraction of the cycle. The increased acquisition time must be balanced against the possible improvement in resolution with gating. This consideration is critical in stress myocardial imaging, as excessively long imaging times could produce false-negative results due to early redistribution of the tracer to ischemic but viable areas of myocardium (*5, 6*).

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Our study was designed to evaluate a method of ECG-gated acquisition that produces a static diastolic image containing data from half the cardiac cycle. In a series of patients undergoing selective coronary arteriography, ECG-gated and nongated images were compared and assessed for the following factors: (a) sensitivity and specificity for the detection of coronary artery disease; (b) frequency of detection of myocardial ischemia; (c) the accuracy with which the extent of coronary artery disease could be predicted; and (d) inter- and intra-observer variability. The coronary arteriogram that was obtained in all these patients was taken as the standard.

PATIENTS

The study group consisted of 54 consecutive patients who had both ECG-gated stress thallium-201 imaging and selective coronary arteriography. There were 16 women and 38 men, ranging in age from 29–73 years. The reasons for study were increasing angina pectoris (20 patients), atypical chest pain (25 patients), investigation preceding percutaneous coronary angioplasty (five patients), suspicion of accelerated coronary atherosclerosis after cardiac transplantation (two patients), elective assessment 3 mo after acute myocardial infarction (one patient), and a positive ECG treadmill test in an asymptomatic individual (one patient). Sixteen patients had a previously documented myocardial infarction.

METHODS

Coronary arteriography. Selective coronary arteriography was performed in multiple projections using a percutaneous transfemoral route. Coronary stenoses were considered significant if they produced 50% or more reduction in luminal diameter in any projection.

Thallium-201 myocardial imaging. *Acquisition.* Stress Tl-201 studies were performed by exercising the patient on a treadmill until 85% of the maximum predicted heart rate was attained or a limiting symptom (chest pain, extreme dyspnea, fatigue, or lightheadedness) developed. Thallium-201 monochloride (1.5 mCi) was then injected intravenously and the patient continued exercising for a further 60 sec. ST segment depression was not used as an end point, but ventricular tachycardia (more than four consecutive ectopic beats) and exercise-induced hypotension were.

Delayed images, when obtained, were acquired 4–6 hr after the stress study without further injection of tracer. Rest studies were performed after intravenous injection of 1.5 mCi Tl-201 with the patient at rest for 10 min and fasted for 4 hr.

In all patients, imaging began 10–15 min after injection of the tracer, using a portable gamma camera with converging collimator, the energy window being 20%, centered over 80 keV. In each study, 45° LAO, anterior, and 65° LAO images were acquired, in that order. For the 45° LAO image, the count was run to 900 sec or 1.3 million counts, whichever occurred first, whereas the anterior and 65° LAO images were acquired for 900 sec or 500,000 counts.

During data acquisition, the R wave of ECG was used to signal the beginning of each cycle. Every cycle was divided into 17 equal segments, and the first 16 of these stored in video memory. Corresponding data points from the remainder of the cycles in the same projection were superimposed, and the final composite cycle dumped onto the disc of a computer interfaced to the camera. Figure 1 shows the composite 16-frame cycle from the 45° LAO study of one patient.

Processing and interpretation. For purposes of processing and analysis, the first four and last four of the 16 frames in each projection were combined to produce a diastolic image. The nongated images were produced by combining all 16 frames. Figure 2 shows the diastolic gated and nongated images from the same patient as in Fig. 1. The patient's systolic gated image is also shown. Increased blurring of the myocardial edges and the

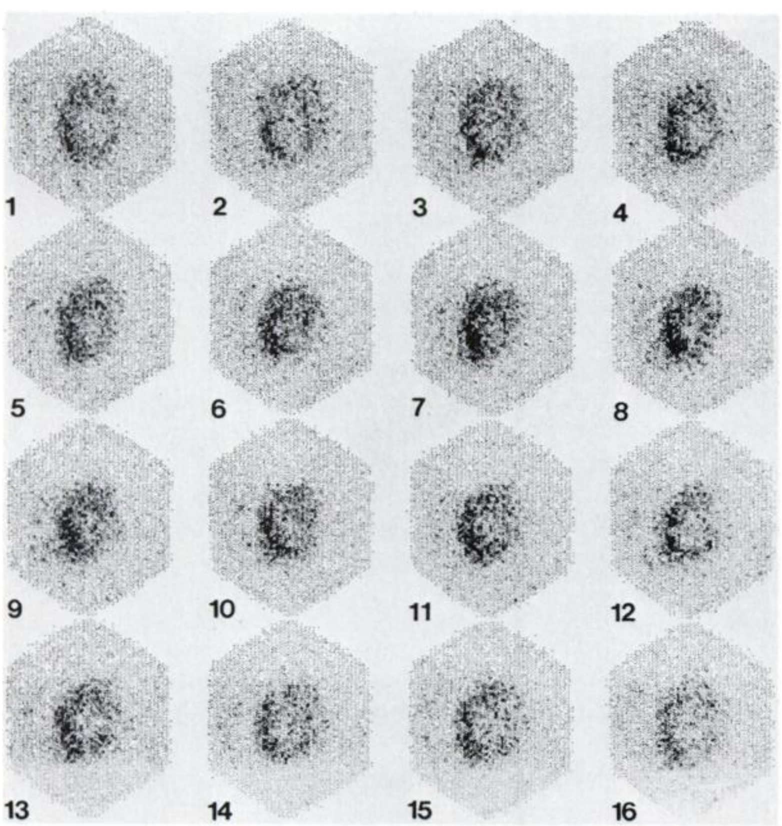

FIG. 1. Unprocessed composite cycle, 45° LAO projection, from a patient under stress, with disease of right coronary artery and left circumflex. Frame 1 occurs immediately after R wave. Beginning of systole is seen in frame 3 or 4, and diastolic filling begins in frame 11. There is a posterolateral defect, best seen in diastolic frames.

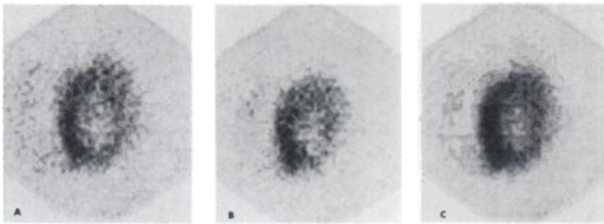

FIG. 2. (A) Gated diastolic image created by adding frames 1 to 4 and 13 to 16 from Fig. 1. (B) Gated systolic image produced by summing frames 5 to 11 from Fig. 1. (C) Nongated image produced by adding all 16 frames in Fig. 1.

smaller size of the left-ventricular cavity are readily appreciated on the nongated image. This image, however, more closely resembles the diastolic than the systolic gated image.

All studies were subjected to weighted nine-point smoothing and were processed using interpolative background subtraction (*7*). The processed images were displayed using an electrostatic plotter and a pseudo-gray scale (*8*). Figure 3 shows the processed gated and nongated images from the same patient as in Figs. 1 and 2.

For the purposes of analysis the gated and nongated studies were randomly mixed and given identification numbers. Each study was analyzed independently by four observers who were unaware of clinical details, the results of arteriography, and whether a particular set of images came from a gated or nongated study. Two of the observers were attending physicians in nuclear medicine and the other two second-year residents in nuclear medicine.

Each observer classified every stress study as normal or abnormal on a 1 to 4 scale, where 1 = normal, 2 = probably normal, 3 = probably abnormal, and 4 = abnormal. For determination of overall sensitivity and specificity, scores of 1 and 2 were considered normal and 3 and 4 as abnormal. When one observer disagreed with the other three, the majority verdict was accepted. For studies in which the observers were split equally between normal and abnormal, all four observers reviewed the images together and reached a consensus. When the stress study was abnormal and rest or delayed images were available, each observer was asked to say whether there were any reversible (ischemic) defects present. Finally, for each abnormal study, the observers were asked to predict how many abnormal vessels (1, 2, or 3) the patient would have at arteriography. The schema used for relating myocardial image abnormalities to coronary artery territories is shown in Fig. 4. Since defects in certain areas may be due to stenosis of more than one vessel, the observers were asked to predict both the minimum and the maximum number of coronary stenoses that could account for the abnormalities in the stress myocardial image.

Statistical analysis. The results from the gated and nongated images were examined for significant differences using the Chi-square test.

RESULTS

Coronary arteriography. Selective coronary arteriography was abnormal in 43 patients. Seventeen had single-vessel disease, 12 double-vessel disease, and 14 triple-vessel disease. The remaining 11 patients had normal coronary arteriograms (no stenosis ≥50% luminal diameter).

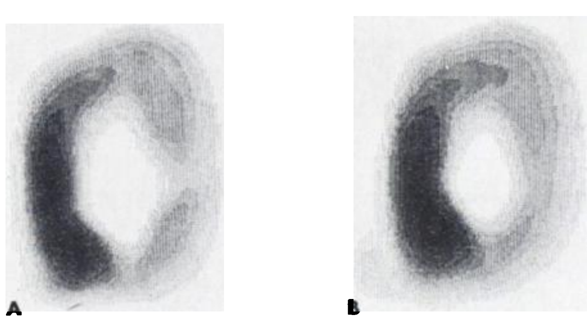

FIG. 3. (A) Gated image as in Fig. 2A, after smoothing and interpolative background subtraction. (B) Nongated image, as in Fig. 2B, after smoothing and interpolative background subtraction. Left-ventricular cavity is larger in gated image and myocardial borders sharpen. Posterolateral defect is well seen on both studies, though perhaps more obviously in the gated study.

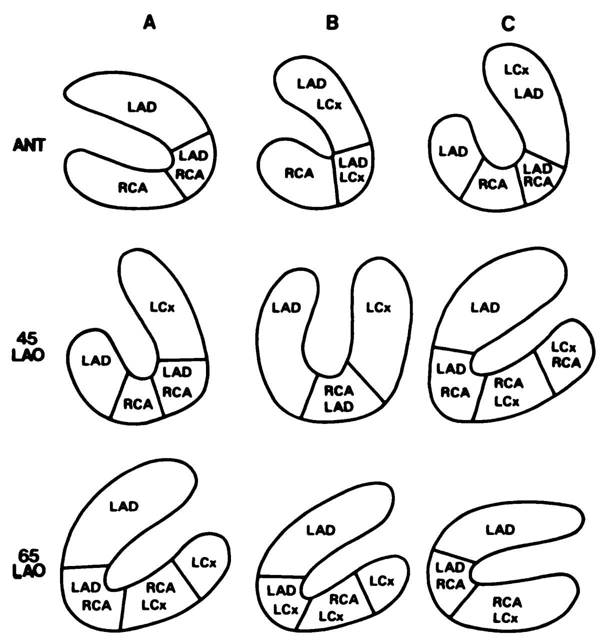

FIG. 4. Correlation between myocardial areas and coronary arteries. Observer first decided whether myocardial orientation corresponded most closely to A, B, or C "type" of heart. Defects on image were then matched to corresponding vessels, as shown. LAD = left anterior descending; RCA = right coronary artery; LCX = left circumflex.

TABLE 1. SENSITIVITY OF GATED AND NONGATED STRESS Tl-201 IMAGES FOR THE DETECTION OF CORONARY ARTERY DISEASE

Arteriographic extent of disease	Frequency of abnormal stress T1-201 images	
	Gated studies	Nongated studies
Single-vessel	14 of 17 (82%)	13 of 17 (76%)
Double-vessel	10 of 12 (83%)	10 of 12 (83%)
Triple-vessel	12 of 14 (86%)	12 of 14 (86%)
Total	36 of 43 (84%)	35 of 43 (81%)

Sensitivity and specificity of Tl-201 imaging. Interpretable stress Tl-201 images were obtained in all 54 patients, and resting or 4-hr redistribution images in 36.

Considering any abnormality of the stress image as positive, the sensitivity for the diagnosis of coronary artery disease was 36 of 43 (83.7%) for the gated images and 35 of 43 (81.4%) for the nongated images ($p > 0.05$, NS). The lack of significant difference between gated and nongated images held in patients with single-, double-, or triple-vessel disease (Table 1). There was also no significant difference in sensitivity between the two sets of studies in patients with no known previous myocardial infarction (22 of 27 against 21 of 27). Resting or 4-hr delayed images were available in 32 patients with abnormal arteriograms. Reversible ("ischemic") defects were present in 19 of 32 gated studies (59.4%) and in 17 of 32 (53.1%) nongated studies ($p > 0.05$, NS).

Of the 11 patients with no significant coronary artery disease, the gated stress images were normal in seven (63.6%), and the nongated images were normal in nine (81.8%) ($p > 0.05$, NS). Resting or delayed images were available in three of the four patients normal by arteriogram but with abnormal gated studies, and in both with abnormal nongated studies. In each situation one patient showed a reversible defect. Thus the specificity of a reversible defect in coronary artery disease was nine of ten (90%) for both gated and ten of 11 (91%) for nongated images ($p > 0.05$, NS).

When the results for individual observers were considered, no significant differences in sensitivity and specificity were found between the gated and nongated images (Table 2).

TABLE 2. COMPARISON OF SENSITIVITY AND SPECIFICITY FOR THE FOUR OBSERVERS

	Gated study	Nongated study
Resident 1		
Sensitivity	37 of 43	35 of 43
Specificity	6 of 11	7 of 11
Resident 2		
Sensitivity	38 of 43	37 of 43
Specificity	6 of 11	7 of 11
Attending physician 1		
Sensitivity	33 of 43	34 of 43
Specificity	9 of 11	9 of 11
Attending physician 2		
Sensitivity	38 of 43	36 of 43
Specificity	6 of 11	8 of 11

Prediction of extent of coronary artery disease from stress Tl-201 images. For the 43 patients with abnormal arteriograms, Table 3 compares the minimum extent of coronary artery disease predicted from the stress Tl-201 findings with the arteriographic extent of disease. The number of abnormal vessels was correctly predicted in 15 of 43 (35%) patients both on the gated and nongated images. The distinction between single and multivessel disease was correctly made from the gated images in 20 of 43 (47%) patients, both on the gated and nongated images.

The maximum predicted extent of disease is compared with the arteriographic findings in Table 4. The number of stenosed vessels was correctly predicted from the gated images in 13 of 43 (30%) patients and from the nongated images in 11 of 43 (26%) ($p > 0.05$, NS). The division between single and multivessel disease was correctly made in 22 of 43 (51%) patients from gated images and 21 of 43 (49%) from the nongated images ($p > 0.05$, NS).

Reproducibility and certainty of interpretation of Tl-201 images. Table 5 summarizes the interobserver agreement in the interpretation of the images. Complete interobserver agreement was considered to be present only when all four observers gave exactly the same score on the 1 to 4 scale for a particular set of images. Essential interobserver agreement indicates all observers giving

TABLE 3. COMPARISON BETWEEN MINIMUM EXTENT OF CORONARY ARTERY DISEASE PREDICTED FROM STRESS Tl-201 IMAGES AND EXTENT OF DISEASE AT CORONARY ARTERIOGRAPHY

No. of abnormal vessels at coronary arteriography	No. of abnormal vessels predicted from gated (G) and nongated (NG) Tl-201 images							
	None		One		Two		Three	
	G	NG	G	NG	G	NG	G	NG
One	3	4	13	13	1	0	0	0
Two	2	2	8	8	2	2	0	0
Three	2	2	7	7	5	5	0	0

TABLE 4. COMPARISON BETWEEN MAXIMUM EXTENT OF CORONARY ARTERY DISEASE PREDICTED FROM STRESS Tl-201 IMAGES AND EXTENT OF DISEASE AT CORONARY ARTERIOGRAPHY

No. of abnormal vessels at coronary arteriography	No. of abnormal vessels predicted from gated (G) and nongated (NG) Tl-201 images							
	None		One		Two		Three	
	G	NG	G	NG	G	NG	G	NG
One	3	4	5	4	9	9	0	0
Two	2	2	3	4	6	5	1	1
Three	2	2	1	1	9	9	2	2

scores of 1 and 2 (normal and probably normal) or 3 and 4 (probably abnormal and abnormal). One observer dissenting indicates essential agreement between three of the observers and the fourth giving an opposite classification to the study.

Complete interobserver agreement was present in 27 of 54 (50%) studies, both for the gated and nongated images, while there was essential agreement in 44 of 54 (82%) gated studies and 42 of 54 (78%) nongated studies. Gating against nongating caused no significant difference.

Three of the observers read 37 pairs of studies on a second occasion, with 3 mo between the two interpretations. As shown in Table 6, there was good intraobserver reproducibility, with no significant differences between gated and nongated studies.

The certainty with which the observers interpreted the studies was also examined. Of the 216 readings (54 from each observer) available for the gated images, 170 of 216 were classified as definitely normal (scale 1) or definitely abnormal (scale 4). For the nongated images the corresponding figure was 169 of 216. Once again there is no significant difference between the gated and nongated studies.

DISCUSSION

The aim of ECG-gated acquisition of Tl-201 myocardial images is to eliminate the blurring of the images produced by motion during the cardiac cycle and thus possibly to increase the accuracy of interpretation. Hamilton and colleagues (*3*) reported that when the acquisition was obtained from 50-msec segments of the cycle in diastole, the gated images differed significantly from the nongated, with the former showing clearer resolution of the myocardium, a larger ventricular cavity, and easier appreciation of areas of decreased uptake. Systolic myocardial thickening and wall motion could also be analyzed by visual inspection of a cine loop of the different segments of the cycle. The method of acquisition in the present study was similar, using 16 frames per cardiac cycle. For the purposes of analysis, however, data obtained from one half of the cycle was combined to allow adequate images to be obtained in a shorter acquisition period, thus making multiple projections possible. That this method of gating is valid is indicated by Figs. 2 and 3, which show gated and nongated 45° LAO images from the same patient. The gated image shows a larger left-ventricular cavity, more clearly defined edges to the myocardial image, and less-thick myocardium. The defect in the posterolateral wall is seen both on the gated and nongated images but is more marked on the gated study. The aim of our study was to assess whether the doubling of imaging time necessitated by our method of ECG gating could be justified by any clinical advantage the gated study might have over a nongated one.

The sensitivity of detection of coronary artery disease on the gated studies (36 of 43) was not significantly higher than that on the nongated images (35 of 43). In both cases the sensitivities were in the middle of the

TABLE 5. INTEROBSERVER AGREEMENT IN THE INTERPRETATION OF THE Tl-201 IMAGES

	Gated images	Nongated images
Complete interobserver agreement	27 (50%)	27 (50%)
Essential interobserver agreement	44 (81.5%)	42 (77.8%)
One observer dissenting	8 (14.8%)	9 (16.7%)
Observers equally divided	2 (3.7%)	3 (5.6%)

TABLE 6. INTRA-OBSERVER REPRODUCIBILITY IN INTERPRETATION OF Tl-201 IMAGES

	Gated studies	Nongated studies
Observer 1		
complete agreement	30 of 37	31 of 37
essential agreement	36 of 37	36 of 37
Observer 2		
complete agreement	32 of 37	31 of 37
essential agreement	36 of 37	36 of 37
Observer 3		
complete agreement	30 of 37	30 of 37
essential agreement	34 of 37	36 of 37

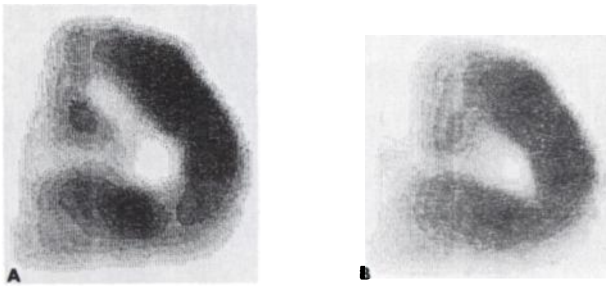

FIG. 5. Anterior images from patient with isolated disease of right coronary artery. 45° and 65° LAO images were interpreted as normal both on gated and nongated studies. (A) Gated study interpreted as abnormal. (B) Nongated study interpreted as normal.

range previously reported for stress Tl-201 imaging (*9–14*). Failure to demonstrate any improvement in sensitivity with gating could have been due to many of the patients having large defects due either to multivessel disease or to previous myocardial infarction. That this was not the case is shown by the similar sensitivity for gated and nongated images in patients with single-vessel disease (14 of 17 contrasted to 13 of 17) and in the patients with no known previous myocardial infarction (22 of 27 contrasted to 21 of 27). In two of the patients in whom both the gated and nongated images were falsely negative, exercise was stopped because of dyspnea at considerably less than 85% of the predicted maximal heart rate, a factor known to increase the likelihood of a false-negative result (*15*). In the remainder of the patients in whom both sets of studies were falsely negative, no obvious explanation could be found. Figure 5 shows the anterior images from the one patient in whom the gated study was interpreted as abnormal and the nongated study as normal.

The sensitivity reported here is significantly lower than the figure of 65 of 67 given by Buda et al. (*16*), who also used interpolative background subtraction. This difference may be due to method used to derive the sensitivity figures. Whereas the present study involved independent blind readings by four observers, Buda et al. relied on review of the clinical reports on the Tl-201 studies. Such reports were produced after discussion by a group of observers who had clinical information available. When the clinical reports from the present study were analyzed, the sensitivity for the gated images was 40 of 43, not significantly different from that of Buda et al. ($p > 0.05$). Clinical reports were not available for our nongated studies.

The specificity of detection of coronary artery disease showed no significant differences between the gated and nongated studies, though the small number (11) of patients with normal arteriograms makes the drawing of general conclusions difficult. Two patients with cardiomyopathy had abnormalities on both the gated and nongated images, including one patient who showed reversible defects, an occurrence previously described in cardiomyopathy (*17, 18*). The specificity figures we report here are lower than in many other series in the literature (*9–14*). This is a reflection of the relatively small number of patients with normal Tl-201 images who undergo coronary arteriography at this institution, and because two of the 11 we did study had noncoronary cardiac disease.

The sensitivity and specificity of interpretation were also compared for the resident physicians and attending physicians, since a previous study had suggested that image processing by background subtraction increases sensitivity of detection of coronary artery disease more in less experienced observers (*20*). The present study failed to demonstrate any significant difference in sensitivity or specificity between the gated and nongated studies for any of the observers.

Because of improvement in resolution, it was hoped that the gated study might allow detection of small areas of ischemia not visualized on the nongated images. In fact, the frequency of reversible images was not significantly different (19 of 32 against 17 of 32). The frequency of ischemic abnormalities in this study was somewhat lower than that reported for various other series of Tl-201 imaging for coronary artery disease (*9, 11, 13*). Our reduced frequency may be due to the prolongation of imaging time necessitated by gated acquisition, thus allowing early redistribution of Tl-201 to occur in transiently abnormal areas (*6*). Because the nongated images in this series were produced by combining gated images, the nongated studies would be equally affected by the prolonged imaging time.

A number of previous studies (*10, 21, 22*) have demonstrated that, in the majority of patients, the extent of coronary artery disease predicted from Tl-201 images is less than that found at arteriography. This underestimation of disease may be due to limitation of exercise by the development of ischemia in one vessel's territory before abnormalities occur in other vascular territories (*21*). Collateral circulation also appears to exert some protective effect (*23, 24*). The hope that the increased resolution potentially available from gated Tl-201 studies might allow more accurate determination of the extent of disease is not confirmed by the findings of our study. Predictions of the minimum extent of coronary artery disease that would account for the Tl-201 image findings correctly identified the number of stenosed vessels in 15 of 43 patients both on the gated and nongated studies and separated single- from multivessel disease accurately in 20 of 43 patients. Prediction of the maximum possible extent of disease from the thallium images correctly identified the number of stenosed vessels in less than one third of the patients studied and was able to distinguish single- and multivessel disease in approximately half of them. There were no significant differences between the gated and nongated studies.

The final variable examined in our study was the influence of ECG gating on the inter- and intraobserver variability in the reading of Tl-201 images. The repeatability of interpretation for each of three observers reading images on occasions 3 mo apart was high, with essential intraobserver agreement 94% or greater in each case. There was no significant difference found between the gated and nongated studies. Essential agreement between all four observers was present in 82% of the gated studies and 78% of the nongated. The difference is not significant, and the level of interobserver agreement is very similar to that found in other studies (*11, 25*). Our results indicate that ECG gating of Tl-201 images does not increase the reproducibility of interpretation of such images, either within one observer or between different observers. Moreover the certainty with which the observers read each study as normal or abnormal was not altered by gated acquisition.

CONCLUSION

This study has examined the value of ECG-gated acquisition of static Tl-201 myocardial images by comparing gated and nongated studies in three projections from 54 patients also undergoing coronary arteriography. No significant differences were found in sensitivity, specificity, detection rate for myocardial ischemia, accuracy of prediction of extent of coronary artery disease, and inter- or intraobserver agreement. It is concluded that, at least when the images are subsequently processed by interpolative background subtraction, ECG-gated acquisition of static images has no advantage over nongated acquisition.

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