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Using Quantitative Coronary Arteriography to Redefine SPECT Sensitivity and Specificity

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ABSTRACT **Previous studies looking at the sensitivity, specificity, and predictive accuracy of single photon emission computed tomography (SPECT) have been based upon the results obtained by visual interpretation of coronary arteriograms. Since the results of visual and quantitative determination of percent diameter stenosis have been shown to be statistically different, the results obtained from SPECT imaging when compared to quantitative methods for assessing coronary artery disease would be expected to provide a more correct assessment of sensitivity, specificity, and predictive accuracy. To determine the "true" sensitivity, specificity, and predictive accuracy of SPECT in diagnosing coronary artery disease, this study compared the results obtained in 44 SPECT images (20 thallium and 24 teboroxime) with the results obtained when quantitative coronary arteriography was used to analyze the coronary arteriograms. These 44 cases were then compared against 8 different definitions of significant coronary artery disease, varying from 30 to 80%, to yield 352 comparisons.**

The maximum specificity and predictive accuracy was found when 45% diameter stenosis was used to define the presence or absence of significant disease. At 45% diameter stenosis, SPECT imaging demonstrated an 86% sensitivity, 78% specificity, and 94% predictive accuracy with only 6% false positives. In 100% of the cases where 45% diameter stenosis was used to define the presence of disease and exercise failed to demonstrate ST segment changes or angina, when SPECT imaging demonstrated a perfusion defect(s), quantitative coronary arteriography agreed with SPECT imaging results. Regardless of whether 45, 50, or 55% diameter stenosis was used to define significant disease, excluding one equivocal (47% diameter stenosis) result, when exercise testing demonstrated a positive result and SPECT demonstrated no perfusion abnormalities, quantitative coronary arteriography revealed no significant coronary artery disease.

Key words: Single photon emission tomography, teboroxime, PET

INTRODUCTION

Considerable controversy has occurred over the proposed sensitivity and specificity of both single photon emission computed tomography (SPECT) and positron emission tomography (PET) imaging. The use of newer technetium tracers and rubidium-82 have added to the debate. However, despite several reports on sensitivities and specificities dating from the mid-1970s [1–3] through the mid-1980s [4,5], and studies looking at the results of intravenous pharmacologic stressors [6], the discussions to date have focused on the visual interpretation of coronary arteriograms as the principal method for determining the presence or absence of significant coronary artery disease, against which SPECT and PET imaging are compared.

In a recently published study [7], Fleming et al. looked at SPECT imaging comparing thallium-201 and technetium-99m teboroxime. When results obtained using the two nuclides were compared with results obtained using automated quantitative coronary arteriography (QCA), teboroxime while better than thallium, was not statistically better. The same study, however, demonstrated a statistical difference ($P < 0.005$) between the two tracers when compared with the "visual" interpretations of coronary arteriograms. This pointed out a major problem when using visual interpretations of coronary arteriograms to make comparisons between nuclides, or imaging modalities. Furthermore, it has been shown [8] that there are patterns in visual reporting of coronary arteriograms that can lead to erroneous conclusions

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about the number of coronary arteries "truly" diseased, the results of angioplasty, and the relative merit of nuclear tracers and imaging modalities.

In order to remove the biasing results of visual interpretation of coronary arteriograms, this study looked at the results of 44 SPECT images, which were compared with results obtained from QCA. These 44 images were then compared against 8 arbitrarily determined definitions of "significant" percent diameter stenosis to determine the "true" sensitivity, specificity, and predictive accuracy of SPECT imaging. These eight arbitrary definitions were 30, 40, 45, 50, 55, 60, 70 and 80% diameter stenosis, resulting in 352 comparisons (44 images × 8 definitions of disease). The predictive accuracy was then analyzed using Bayes' theorem. Finally, the results of exercise treadmill testing were compared with the results obtained by SPECT imaging, and flow sheets developed for 45, 50, and 55% diameter stenosis respectively.

METHODS

Study population

Subjects were enrolled if they were suspected of having coronary artery disease, and they and their private physicians agreed to participation in the study. All patients signed a consent form approved by the Institutional Review Board for the Protection of Human Subjects. The average age was 56.6 ± 11.2 years, with 62% of the subjects being male. Patients who had a history of cardiomyopathy, severe valvular disease, unstable angina, recent myocardial infarction, morbid obesity, or who were pregnant were not eligible for enrollment into the study.

Coronary arteriograms and quantitative coronary arteriography

All subjects underwent conventional coronary arteriography via a Judkins approach. The images were obtained using a Philips Poly Diagnost C/Lateral ARC system with pincushion and magnification correction as previously described by Brown et al. [9]. The films were analyzed by a DEC VAX 11/780 computer and Tektronics 4207 graphics computer as previously described [7]. The percent diameter reduction in the most severely stenotic region of each of the three major coronary arteries (including branches) was reported as the percent diameter stenosis for that artery.

Exercise protocol

Each of the 44 SPECT images were acquired after individuals completed a Bruce protocol exercise treadmill study. Exercise was stopped after subjects reached 85% of their maximum predicted heart rate or when fatigue occurred. Exercise results were reported as positive if there was an ST segment depression of 1 mm, or if the subject had anginal symptoms, which were relieved with sublingual nitroglycerin. All regions of ST depression had to be recorded in two contiguous leads. Furthermore, each patient with a 1-mm ST segment depression subsequently developed 2-mm depression before stopping exercise.

SPECT imaging

Each SPECT image was obtained after the injection of either thallium-201 or technetium-99m teboroxime. SPECT imaging protocols for both thallium and teboroxime are shown in Figure 1. Image reconstructions were done in conventional short, horizontal, and vertical-long axis views. Figure 2A demonstrates the vertical long axis images for both stress and redistribution images using thallium. Figure 2B reveals vertical long axis images for teboroxime at stress and rest.

Images were analyzed by two observers blinded to clinical and QCA data. Perfusion of regions were scored on a continuous scale from 0 to 5, where 0 equaled "normal"

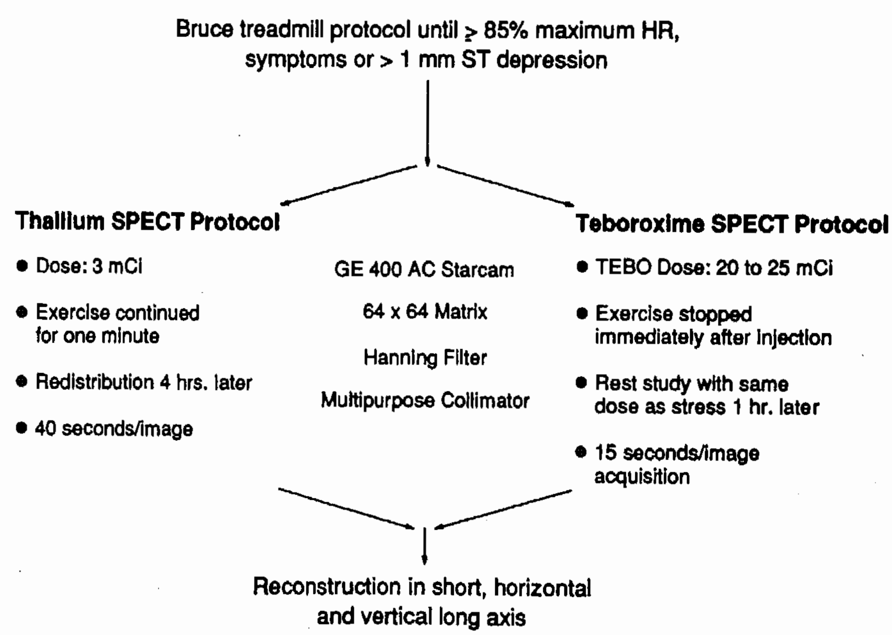

Fig. 1. Exercise and SPECT protocol. The **left side** of the diagram explains the approach used for those SPECT studies where thallium-201 was used. The **right side** of the diagram compares the method for performing teboroxime SPECT imaging with exercise treadmill testing.

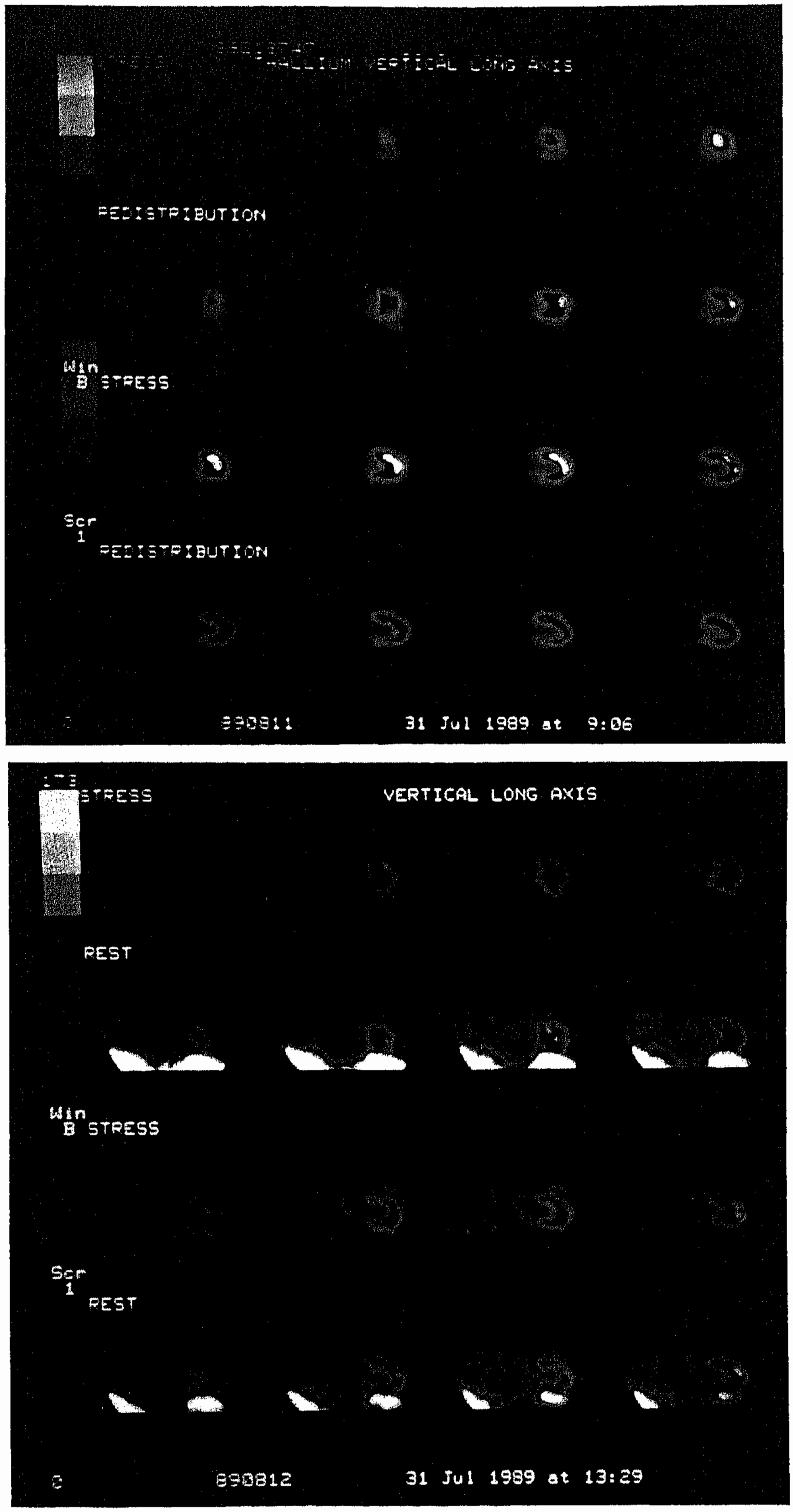

Fig. 2. **A.** Stress and redistribution SPECT images of thallium-201 using reconstructed vertical long axis views. The images are graded qualitatively **(on a gray scale)** on a continuum from regions of highest tracer uptake (white), to regions of lowest uptake (black). **B.** Stress and rest SPECT images of technetium-99m teboroxime using reconstructed vertical long axis views. The images are quantitatively graded in a manner identical to the thallium images in **A.** Note the hepatobiliary uptake of teboroxime on the rest images associated with the relatively short biologic half-life of 5.3 min.

perfusion, 1 represented "probably normal" perfusion, 2 was "equivocal," and 3 to 5 defined "mild," "moderate," and "severe" defects. Eight regions were analyzed per image including anterior, anterolateral, posterolateral, posterior, inferior, posteroseptal, anteroseptal, and apex. Averaged values from two observers ranging from 0 to 2 were reported as not significant for perfusion abnormalities. Mean values from 3 to 5 were reported as remarkable for the presence of perfusion deficits. Segments were matched to the region of arterial distribution as described previously [7].

Order of testing

The order of QCA and SPECT imaging occurred randomly to prevent any biasing of entry into the study. Studies were completed without any intervening changes in the patients condition or electrocardiogram.

Statistical analysis

SPECT sensitivity and specificity were determined for each of the 44 images using different levels of percent diameter stenosis, ranging from 30 to 80%, to define the presence of significant disease. Chi-square analyses were done to determine differences in SPECT imaging results at 45, 50, and 55% diameter stenosis. The predictive accuracy was subsequently determined for 45, 50, and 55% diameter stenosis using Bayes' theorem. Three flow sheets demonstrating the results obtained through a combination of treadmill testing and SPECT imaging for 45, 50, and 55% diameter stenosis were then developed.

RESULTS

Exercise results

As outlined in Table I, approximately 48% of the individuals demonstrated significant ST segment changes during or after exercise. No individuals demonstrated ST segment changes "only" after exercise and no dysrhythmias occurred. Angina occurred in 43% of subjects and was relieved with one (0.4 mg) or two sublingual nitroglycerin. The maximum rate-pressure product and heart rate achieved were comparable to those reported in other studies. All subjects exercised to fatigue or symptom limitation, and no one was stopped at the arbitrary 85% of maximum predicted heart rate.

Interobserver variability

The variability noted between observer interpretation of SPECT imaging is noted in Table II, with results listed for both stress and rest/redistribution readings. As previously reported [7], there are no statistically significant differences in the ability of observers to read SPECT thallium and SPECT teboroxime images. These results demonstrate complete agreement, or a difference of only one observer score

TABLE I. Results of exercise testing in 44 SPECT studies

Maximum heart rate (beats/min)	134 ± 13.5
Rate-pressure product[a]	22,710 ± 4,018
Exercise ECG response	
Positive (%)	21 (47.7%)
Negative (%)	23 (52.3%)
Angina during exercise (%)	19 (43.2%)

[a]Maximum systolic blood pressure × maximum heart rate. Values are mean ± standard deviation.

TABLE II. Interobserver variability in SPECT image interpretation

Interobserver difference[a]	Stress	Rest redistribution	Statistical difference
0 (no difference)	58%	59%	NS[b]
1	21%	21%	NS
2	10%	10%	NS
3	4%	4%	NS
4	4%	4%	NS
5	3%	2%	NS

[a]Observer scores differed from 0 to 5 based upon a 0 to 5 scale of severity of perfusion defects. Abbreviations: NS, not statistically significant.

TABLE III. SPECT sensitivity and specificity as determined by varying percent diameter stenosis necessary to define significant coronary artery disease

	Percent diameter stenosis							
	30	40	45	50	55	60	70	80
Percent sensitivity	77	81	86	90	93	93	100	100
Percent specificity	60	71	78	69	59	59	57	44

(on a scale of five) in approximately 80% of the segments read. Observers agreed within two scores in approximately 90% of the segments. As pointed out in Table II, there were no differences in interobserver variability scoring of stress versus rest/redistribution images.

SPECT sensitivity and specificity

The calculated sensitivity and specificity of varying levels of percent diameter stenosis are reported in Table 3. When 30% diameter stenosis was used as the arbitrary definition of disease, SPECT sensitivity was 77% and specificity was 60%. Sensitivity increased as the definition of a significantly diseased vessel increased from 30 to 80% diameter reduction. Sensitivity reached 90% when stenosis was defined as 50% diameter stenosis or greater. The specificity reached a maximum of 78%, when 45% diameter stenosis was used to define significant disease. In this case, seven of nine individuals defined as free of significant disease by QCA were free of perfusion abnormalities. These results are depicted in Figure 3.

The results of chi-square analysis shown in Table IV demonstrate no statistical differences between the results obtained by defining disease as either 45 or 50% diameter stenosis and no differences between results obtained by defining disease as either 50 or 55% diameter stenosis. However, there was a statistical difference ($P < 0.025$) between the sensitivity and specificity obtained by SPECT when disease was defined as 45 versus 55% diameter stenosis. This was due to the significantly higher specificity associated with 45% diameter stenosis. When disease was defined as being present with a 45% diameter narrowing or greater, there were 9 cases by QCA where disease was absent and SPECT imaging reported normal perfusion in 7 of these 9. At 50%, there were 13 cases free of disease, with 9 having normal studies. For 55% diameter narrowing, there were 17 cases free of significant disease, with 7 having normal SPECT perfusion images.

SPECT predictive accuracy

As shown in Table V, when the prevalence of disease is taken into account, Bayes' theorem can be applied to the

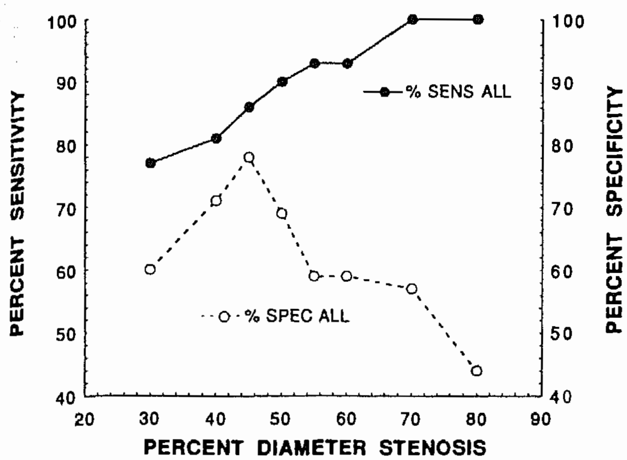

Fig. 3. Comparison of percent sensitivity and specificity to percent diameter stenosis. The percent sensitivity (●) and percent specificity (○) are plotted against percent diameter stenosis. Percent diameter stenosis represents a varying definition of significant disease e.g., at 30% diameter stenosis, the results of SPECT imaging provides a sensitivity of 77% and a specificity of 60%. When the definition of significant disease is changed to 70% diameter stenosis, the reported sensitivity and specificity of SPECT imaging become 100% and 57%, respectively. Note that the best specificity occurs at 45% diameter stenosis.

results obtained in this study, and sensitivity, specificity, and predictive values for SPECT imaging can be determined based upon the results of quantitative analysis of coronary arteriograms. From this, the number of false positives obtained using SPECT imaging can be determined. The highest predictive value, like specificity, was obtained when disease was defined as 45% or greater reduction in diameter. This resulted in a 6% false positive rate. As expected, the number of false positives increased as the percent diameter stenosis used to define significant disease increased.

Treadmill testing and SPECT

From this study, three flow sheets were developed (Figs. 4–6) which demonstrate the results obtained from both the treadmill and SPECT components of the study. Each figure represents a different result using the arbitrary definitions (45, 50, or 55% diameter stenosis) of significant disease.

Figure 4 shows the results of treadmill and SPECT imaging studies in which significant disease was defined as 45% diameter stenosis or greater. In 92% of the cases, where both treadmill and SPECT studies were positive, QCA indicated anatomic disease. In only one case, where the treadmill test

TABLE IV. Chi-square values of different sensitivity and specificity

	50% diameter stenosis	55% diameter stenosis
45% diameter stenosis	2.92 (P = NS)	9.97 ($P < 0.025$)
50% diameter stenosis	NA	3.02 (P = NS)

Abbreviations: NA, not applicable; NS, not statistically significant.

was positive and the SPECT image was equivocal, did QCA indicate disease. In that case, the lesion had a 47% diameter stenosis in the anterior descending artery. In all cases where the treadmill study was negative and the SPECT image revealed a perfusion defect, anatomic disease was present.

In Figures 5 and 6, the results are shown for treadmill and SPECT studies in which significant disease was defined as 50 and 55% diameter stenosis, respectively. In 88% of the cases where treadmill and SPECT studies were positive, anatomic disease was present. In 100% of the cases where the treadmill was positive and the SPECT image was normal, significant coronary disease was absent. The presence of a positive finding during the exercise portion of the study added no additional information. When the treadmill study revealed no electrocardiographic changes and/or there were no anginal symptoms, and the SPECT image demonstrated a perfusion defect, QCA detected anatomic disease in 88% (Fig. 4) and 75% (Fig. 5) of the cases.

DISCUSSION

Previous discussions focusing on the sensitivity and specificity of SPECT (including those comparing it to PET imaging) have looked at results obtained from comparisons with visual reporting of disease from arteriograms. However, as previously demonstrated [8], the results of visual estimates follow patterns that can result in potential errors in interpreting results obtained with nuclear images. The use of reproducible and accurate methods to measure coronary arteriograms is one way in which these errors may be reduced and was used in this study to determine the "true" sensitivity, specificity, and predictive accuracy of SPECT imaging. Another recent study [10] pointed out that the use of electrocardiographic criteria may be of "minimal" value in the clinical determination of myocardial area at risk and can be influenced by multiple factors, giving "large" standard errors.

In this current study, 352 comparisons (44 SPECT images × 8 different definitions of significant disease) were

TABLE V. Determination of predictive value of SPECT using varying percent diameter stenosis to define significant disease

	Percent prevalence of disease present by QCA	Percent SPECT sensitivity	Percent SPECT specificity	Predictive value of SPECT study by Bayes' theorem	Number of false positives per 100 studies
45% diameter stenosis[a]	80	86	78	0.94	6
50% diameter stenosis[a]	73	90	69	0.89	11
55% diameter stenosis[a]	61	93	59	0.78	22

[a]Percent diameter stenosis as defined by quantitative coronary arteriography (QCA).

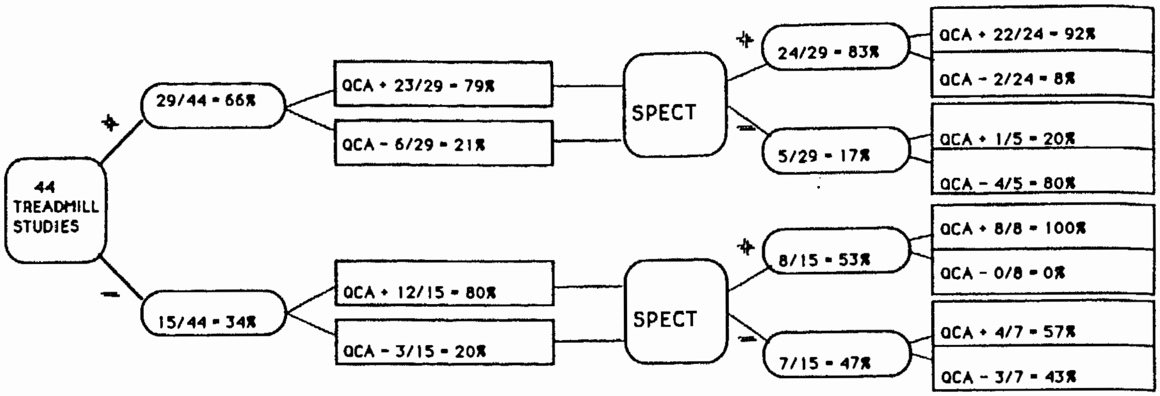

Fig. 4. Results of exercise treadmill testing and SPECT imaging. The results depicted in this diagram reveal the results of exercise treadmill and SPECT studies, using 45% diameter stenosis as the definition of significant anatomic disease. Notice that, with the exception of one equivocal study, if SPECT and treadmill studies had varying results, then results of QCA were consistent with results obtained by SPECT imaging.

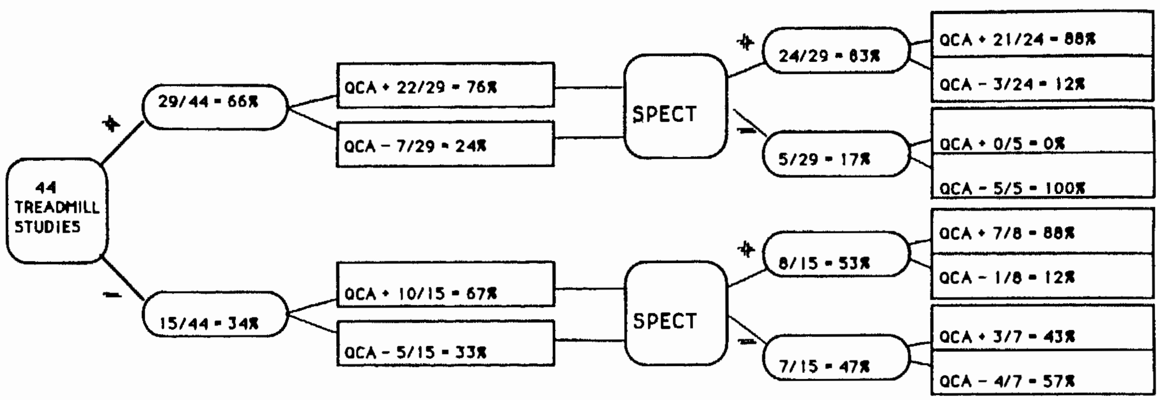

Fig. 5. Results of exercise treadmill testing and SPECT imaging. The results depicted in this diagram reveal the results of exercise treadmill and SPECT studies, using 50% diameter stenosis as the definition of significant anatomic disease.

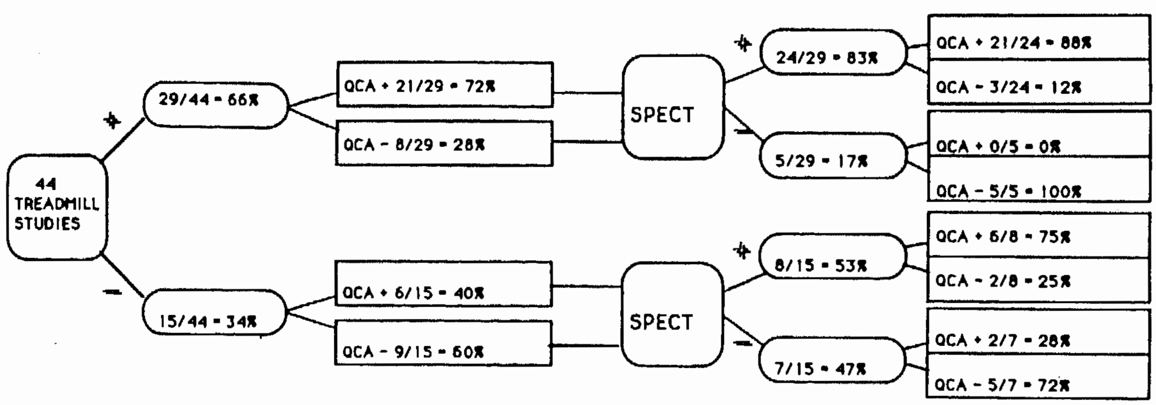

Fig. 6. Results of exercise treadmill testing and SPECT imaging. The results depicted in this diagram reveal the results of exercise treadmill and SPECT studies, using 55% diameter stenosis as the definition of significant anatomic disease.

made with results obtained from coronary arteriograms as analyzed by QCA. The definition of significant coronary artery disease by percent diameter stenosis was varied to determine the impact of results obtained by SPECT perfusion imaging studies over a wide range of arbitrarily defined disease. The maximum predictive value and specificity occurred when significant disease was defined as a 45% or greater reduction in arterial diameter. With the exception of one equivocal study, using 45% diameter stenosis as the definition of significant disease, when results of the exercise component of the study and the SPECT perfusion image disagreed, QCA always agreed with the results obtained with SPECT imaging. The result of a positive exercise stress test adds little if any benefit to the study, and increases the potential risk to the patient, when compared to pharmacologic stressors.

The results obtained using 45% diameter stenosis as the definition of disease were not statistically different from those obtained using 50% diameter stenosis, but were different ($P < 0.025$) from results obtained using 55% diameter stenosis. This may in part be due to the smaller number of normals present when disease was defined as 45% diameter stenosis. It may, however, also represent the "true best" definition for the ability of SPECT imaging to provide specificity and predictive accuracy. The resultant predictive value of the SPECT images was 94%, with a 6% false-positive rate. The number of false positives increased to 11 and 22% when significant disease was defined as 50 and 55% diameter stenosis respectively.

CONCLUSIONS

The use of arbitrary definitions can sometimes be confusing, and it may be better to remind ourselves that coronary atherosclerosis is a continuum, not a finite phenomenon. However, in the realm of clinical decision-making, some point is frequently necessary at which action must be taken or disease is considered to be "significant." Since decisions about patient care, as well as comparisons of imaging modalities and nuclear tracers, are based upon such definitions of disease, we must be certain of the accuracy and reproducibility of these terms.

This study used the accuracy and reproducibility of QCA to redefine the sensitivity, specificity, and predictive accuracy of SPECT imaging. This study suggests that the best results for SPECT imaging occurred when disease was defined as the presence of a lesion with 45% diameter stenosis or greater, and that such a definition gives SPECT imaging a 94% predictive accuracy. SPECT imaging may play a more important role in the screening of individuals with "moderate" coronary artery disease, since its highest predictive accuracy with least false negatives appears to be in the 45 to 50% diameter stenosis range in this study. A comparison study using a quantitative method to assess coronary artery disease is necessary for comparing other nuclides or other imaging modalities. Further work needs to be done including sensitivity, specificity and predictive accuracy of SPECT using pharmacologic stressors, IPPA, and PET imaging.

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Detecting Coronary Artery Disease Using SPECT Imaging: A Comparison of Thallium-201 and Teboroxime

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ABSTRACT **Thirty subjects underwent single photon emission computed tomography (SPECT) imaging with technetium-99m teboroxime (TEBO). Of these, 26 underwent thallium SPECT imaging and 25 underwent quantitative coronary arteriography (QCA). Twenty-one of the subjects underwent all three studies. SPECT images were reviewed by two independent observers blinded to the clinical data. Stenoses were considered significant if there was a ≥ 50% diameter narrowing as defined by QCA analysis of the coronary arteriograms. The overall sensitivity and specificity was 78% and 78%, respectively, for thallium-201. The overall sensitivity and specificity for teboroxime was 72% and 80%, respectively. The results obtained for these two tracers were not statistically different. Some of the false-positive results obtained from teboroxime imaging appear to have been due to the 10-min acquisition protocol and can be reduced with the use of new software programs using a continuous 3-min acquisition and dipyridamole. Teboroxime's rapid biologic half-life allows completion of SPECT imaging within 60–90 min, compared with the minimum of 4 h required for thallium SPECT imaging.**

Key words: Quantitative coronary arteriography (QCA), SPECT imaging, teboroxime, thallium-201

INTRODUCTION

The use of thallium imaging as a tracer of myocardial perfusion has been limited by a low photon energy of 80 KeV with resultant attenuation problems. Additionally, thallium's relatively long half-life of 73 h reduces the amount of thallium that can be given to overcome these artifact problems. Technetium-99m (Tc-99m) is essentially a monoenergetic (89%) radionuclide with a higher photon energy (140 KeV) and less compton scatter than thallium, making it ideally suited for single photon emission computed tomography (SPECT). Because Tc-99m has a physical half-life of 6 h and a biological half-life of 5.3 min, the patient can receive up to 20–30 mCi without receiving excessive amounts of the radioisotope.

The lipophilic character of Tc-99m teboroxime (TEBO) provides greater than 90% extraction by myocardial tissue over a wide range of coronary blood flow [1]. This is greater than uptake obtained by tracers that behave like microspheres [2,3] and do not appear to be dependent on the sodium–potassium ATPase pump. As previously demonstrated [4] the results of visual interpretation of coronary arteriograms can lead to erroneous conclusions about the results obtained with different nuclear tracers. To reduce these errors, this study was designed to look at the overall sensitivity, specificity, predictive values, and accuracy of thallium and teboroxime using quantitative coronary arteriography (QCA).

METHODS

Study population

Thirty subjects who were suspected of having coronary artery disease were enrolled in the study. These subjects received approval to enter the study from their primary care physicians and signed a consent form approved by the Institutional Review Board for the Protection of Human Subjects. Patients were excluded from the study if they had a history of cardiomyopathy, severe valvular disease, unstable angina, morbid obesity, pregnancy, or had a recent myocardial infarction that would preclude them from undergoing the exercise portion of the SPECT studies. Additionally, subjects were excluded if they had continuing angina, myocardial infarction, or underwent angioplasty or coronary artery bypass surgery between SPECT studies and coronary arteriography.

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Of the 30 patients, 40% were women and 60% were men, with an average age of 55 years. All 30 subjects underwent SPECT teboroxime imaging, 26 underwent SPECT thallium imaging, and 25 underwent coronary arteriography with QCA analysis of coronary arteriograms as previously described [4].

Coronary arteriography and quantitative coronary arteriography

All subjects underwent conventional coronary arteriography via a Judkins approach. The images were obtained using a Philips Poly Diagnost C/Lateral ARC system with magnification and pincushion correction as previously described by Brown.[5] The films were analyzed with a DEC VAX 11/780 mainframe computer. Hardcopy reports were generated by a Tektronics 4207 graphics computer. The most severe percent diameter reduction for each of the major coronary arteries (including branches) was reported as the percent diameter stenosis for each artery.

Exercise protocol

SPECT images were obtained after subjects exercised using the Bruce protocol. Subjects were exercised until symptom (angina, fatigue) limitation, or 2-mm depression occured in two continuous leads on their electrocardiograms. Thallium was given intravenously 1 min prior to cessation of the exercise period. Teboroxime was given at peak exercise and the subject immediately transferred to the SPECT table for imaging.

SPECT imaging

Each SPECT image was obtained using a General Electric 400 AC Starcam, using a 64 × 64 matrix, Hanning Filter (0.83 Hz cutoff), and a multipurpose collimator, with image reconstruction along short, horizontal, and vertical long axis. Thallium images were acquired after 3 mCi of thallium-201 were injected during the exercise period of the study. Each of the 32 images required 40 sec for acquisition. Subjects were returned 4 h later for redistribution images using the same protocol.

Teboroxime image acquisition began within 2 min of intravenous injection of 20 to 25 mCi of teboroxime. The same SPECT camera, matrix, filter, and collimator was used. Subjects returned 1 h later for a second injection of teboroxime, using the same dose used during the stress component of the study. Each teboroxime image was acquired over 15 sec.

SPECT images interpretation

Images were analyzed by two observers blinded to clinical and QCA data. Perfusion of regions were scored on a continuous scale from 0 to 5, where 0 equaled "normal" perfusion, 1 represented "probably normal" perfusion, 2 was "equivocal," and 3 to 5 defined "mild," "moderate," and "severe" defects. Eight regions were analyzed per image including anterior, anterolateral, posterolateral, posterior, inferior, posteroseptal, anteroseptal, and apex. Averaged values from two observers ranging from 0 to 2 were reported as not significant for perfusion abnormalities. Mean values from 3 to 5 were reported as remarkable for the presence of perfusion deficits. Segments were matched to the region of arterial distribution. The anterior and anteroseptal regions were matched to the left anterior descending artery. The anterolateral and posterolateral were matched with the circumflex artery. The inferoposterior region was matched to the right coronary artery. Assignment of the posterior and apical regions was determined by reviewing individual coronary arteriograms.

Order of testing

The order of QCA and SPECT imaging occurred randomly to prevent any biasing of entry into the study. Studies were completed without any intervening changes in the patients' condition or electrocardiogram.

Statistical methods

Chi-square analysis with correction for continuity was used to determine whether there were statistical differences between the two tracers as compared with results obtained by QCA analysis of the coronary arteriograms. Differences between thallium and teboroxime stress tests were compared by Student's t-test for paired data.

RESULTS

Exercise results

When results of maximum heart rate were achieved, and rate–pressure product (maximal systolic blood pressure × maximal heart rate), angina pectoris, and electrocardiographic changes were compared, there were no differences between results obtained during thallium and teboroxime components of the study. All subjects were exercised to fatigue or symptom limitation. No subject was arbitrarily discontinued at 85% of maximum predicted heart rate.

Interobserver variability

There were no statistical differences in the interpretation of SPECT thallium and teboroxime images. Perfusion scores differed by one or were in total agreement between 75% and 83% of the time.

Comparison of thallium and teboroxime

Table I shows the overall results obtained when all 30 subjects were studied using the previously described protocols. Significant coronary artery disease was present in all three arteries in 36% of those studied by thallium and in 33% of those studied by teboroxime. The sensitivity and specificity for thallium was 78% and 78%, respectively, with an accuracy of 78%. For teboroxime, the overall sensitivity and specificity was 72% and 80%, with an accuracy of 77%.

The best results, regardless of tracer, were obtained when there was a greater prevalence of disease in that region. For example, with thallium there was a 57% prevalence of disease in the left anterior descending (LAD) artery, with a sensitivity of 75%, specificity of 89%, and an accuracy of 81%. The same findings were present in the teboroxime images where there was significant disease in 52% of the LAD arterial distributions studies. Here the sensitivity was 69%, specificity 92%, and the accuracy was 80%. There

TABLE I. Detection of Overall Disease and the Ability to Discriminate Specific Regions of Coronary Blood Flow*

	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Disease prevalence	Accuracy
Thallium-201						
All regions	78%	78%	67%	86%	36%	78%
LAD	75%	89%	90%	73%	57%	81%
LCx	67%	89%	50%	94%	14%	86%
RCA	88%	54%	54%	88%	38%	67%
Teboroxime						
All regions	72%	80%	64%	85%	33%	77%
LAD	69%	92%	90%	73%	52%	80%
LCx	50%	81%	33%	89%	16%	76%
RCA	88%	71%	58%	92%	32%	76%

*LAD, left anterior descending artery; LCx, left circumflex artery; RCA, right coronary artery.

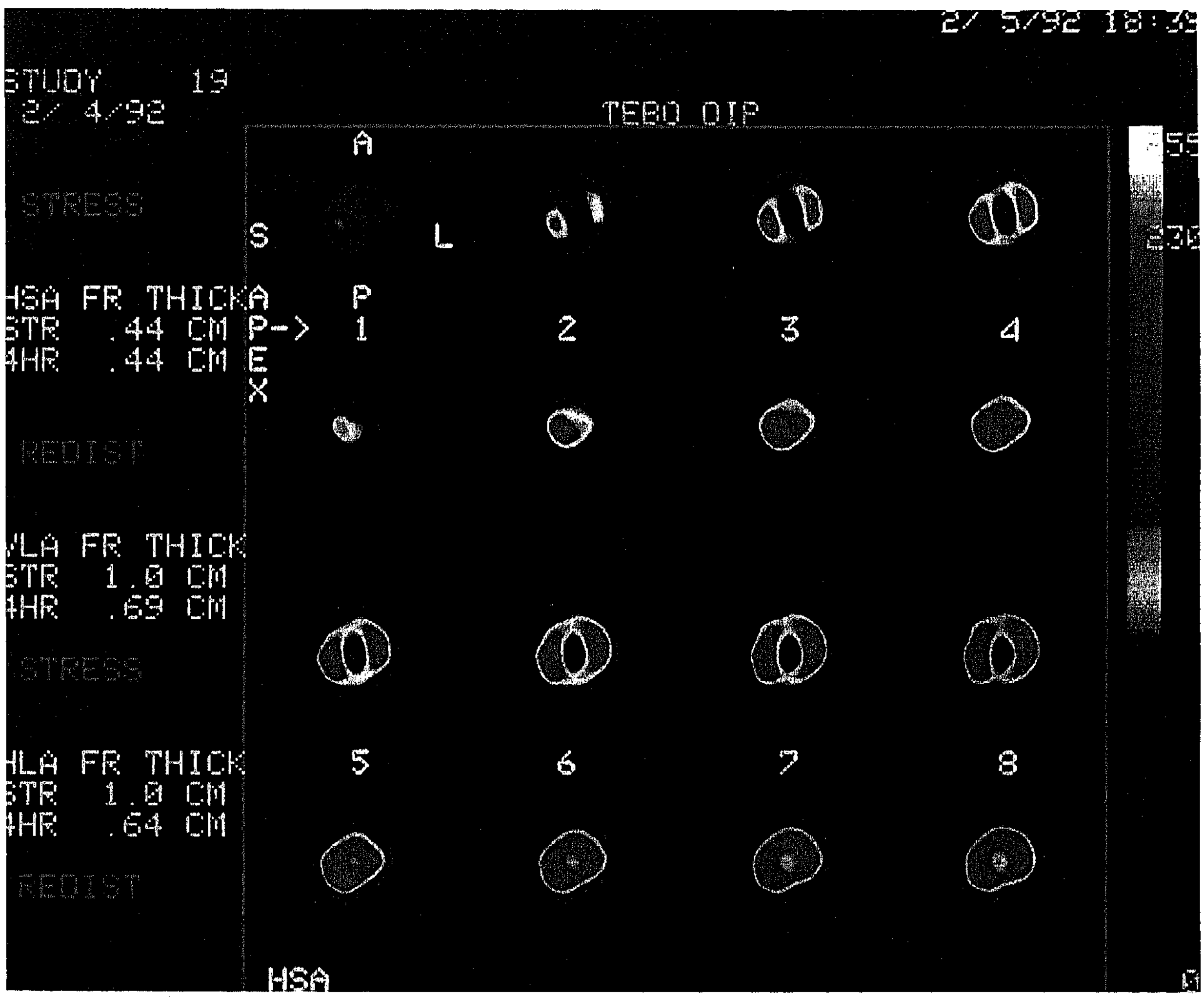

Fig. 1. Stress and rest dipyridamole teboroxime SPECT images. Image reconstruction in the short axis view reveals dipyridamole stress images in rows 1 and 3. Rest images are represented in rows 2 and 4. Slices begin at the apex (slice 1) and proceed toward the base (slice 8). The anterior wall is located at the top of each image, the inferior wall at the bottom, septum to the left, and lateral wall to the right. Note the decreased teboroxime activity in the anterior and inferior regions during dipyridamole stress, with normal perfusion during the rest study 1 h later.

were no statistical differences between results obtained with thallium and those obtained with teboroxime.

DISCUSSION

The use of technetium-99m teboroxime SPECT imaging has recently been investigated as a possible alternative to thallium-201 imaging. Teboroxime has several advantages over thallium, including a shorter half-life of 6 h, the monoenergetic photon peak of 140 KeV ideally suited for SPECT imaging, and the ready availability of technetium-99m from molybdenum–technetium generators. The results of this study using a 10-minute acquisition protocol demonstrated that results obtained from thallium and teboroxime are comparable with no statistical differences. Given the reduced amount of time necessary to obtain stress/rest images with teboroxime (60–90 min) as compared with thallium stress/redistribution (4 h) images, a considerable amount of time can be saved for the patient. Additionally, only 20 min of table time are required to image a patient with teboroxime as compared with 40 to 80 min for thallium.

Despite the higher photon energy available with Tc-99m, there continued to be a problem with false positives inferolaterally, as was previously seen with thallium. This rate of false positives inferiorly and laterally appear to be due to the original protocol, which acquired images over 10-min and began in the right anterior oblique (RAO) position and rotated to the left posterior oblique (LAO) position. Given teboroxime's biologic half-life of 5.3 min, only 25% of the activity was left by the time imaging was completed in the lateral regions of the myocardium. Additionally, if the left circumflex was not significantly diseased, washout resulted in low counts being present by the time the SPECT camera was laterally located. False-positive defects in the inferior wall appear to be due to liver uptake of the tracer interferring with result interpretation. Also, with the step and shoot approach, approximately 25% of the data were lost. These problems may have been minimized in this study given the relatively high prevalence of disease in the population. Two-thirds of the patients had significant disease in at least one coronary artery.

In an attempt to overcome these limitations, a new protocol was written using dipyridamole and teboroxime. The patient was administered 0.568 mg of dipyridamole per kilogram body weight over 4 min. At 6 min 25 mCi of teboroxime was administered, immediately followed by a 10 cm^3 flush of normal saline. Forty-five seconds later a 250 mg bolus of aminophylline was administered to reverse the effects of dipyridamole and prevent the rapid washout of teboroxime. Continuous image acquisition then began in LAO and rotated to the RAO position during a 3-min acquisition time. Imaging was completed with an Elscint Apex SP-4 γ camera with reconstruction in short axis, vertical, and horizontal long axis views after software removal of the liver was accomplished. The patient was reimaged 1 h later at rest with 30 mCi of teboroxime and a continuous 3-min acquisition. The patient experienced no adverse effects.

Fig. 1 demonstrates the results of this new protocol in a clinical study with a patient who had a 26% diameter narrowing of the left circumflex, 64% narrowing of the proximal left anterior descending, and 72% narrowing of the mid right coronary artery, as determined by quantitative coronary arteriography (QCA). There was no collateral circulation noted on the coronary arteriogram. The results of the QCA and the dipyridamole teboroxime study using this new protocol matched without giving false positive defects laterally.

CONCLUSION

Teboroxime SPECT imaging provides equivalent results to that obtained with conventional thallium SPECT imaging. These results can be obtained in one-quarter of the time (1 h) with considerably less time spent lying on the SPECT table. Given the current changes in the imaging protocol, the number of false positives should be considerably reduced, making teboroxime not only faster, but potentially more accurate. Additionally, given the rapid washout of teboroxime, rest images can probably be acquired in 30 min rather than 1 h after stress/dipyridamole images. The use of adenosine may reduce the washout of teboroxime and eliminate the need for aminophylline.

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