Sestamibi SPECT in the detection of myocardial viability in patients with chronic ischemic left ventricular dysfunction: Comparison between visual and quantitative analysis

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Background. **Technetium 99m sestamibi cardiac scintigraphy is widely used as a means of predicting myocardial viability in patients with chronic ischemic left ventricular (LV) dysfunction. No data are available comparing the results of visual and quantitative analysis of tomographic imaging in the assessment of myocardial viability. The aim of this study was to directly compare visual and quantitative analysis of resting sestamibi single photon emission computed tomography in the identification of viable myocardium in patients with chronic LV dysfunction.**

Methods and Results. **Sixty-five patients with an earlier myocardial infarction and LV dysfunction that had occurred within 1 week underwent echocardiography and resting sestamibi SPECT. In each patient, regional tracer distribution was visually assessed and quantitatively measured in 13 segments. Regional LV function was evaluated in corresponding segments by means of echocardiography. All patients underwent revascularization, and echocardiography was repeated 12 months later as a means of assessing the recovery of regional LV function. Among all akinetic or dyskinetic revascularized segments, 66 of 112 viable segments (59%) and 85 of 100 nonviable segments (81%) were identified by means of visual analysis. Eighty-two of 112 viable segments (73%; $P < .05$ vs visual analysis) and 74 of 100 nonviable segments (74%; $P = .3$ vs visual analysis) were identified by means of quantitative analysis, with a threshold of 55%. Receiver operating characteristic curve areas constructed by using visual and quantitative analyses for the detection of myocardial viability in all 212 akinetic or dyskinetic segments were 0.79 ± 0.04 and 0.81 ± 0.03, respectively (*P* = not significant). Overall concordance in the detection of myocardial viability between visual and quantitative analysis was observed in 165 of akinetic or dyskinetic dysfunctional segments (78%), with a κ value of 0.6.**

Conclusions. **The results of this study demonstrate that, in patients with chronic myocardial infarction and LV dysfunction, visual and quantitative analysis of sestamibi tomographic images at rest have similar overall accuracy in predicting the recovery of LV function after coronary revascularization procedures. (J Nucl Cardiol 2000;7:406-13.)**

Key Words: Technetium 99m sestamibi • left ventricular function • receiver operating characteristic curve • single photon emission computed tomography

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Technetium 99m sestamibi cardiac imaging at rest is widely used as a means of predicting myocardial viability in patients with regional or global left ventricular (LV) dysfunction.[1-4] Several studies used either visual or quantitative analysis of single-photon emission computed tomography (SPECT) as a means of evaluating myocardial viability.[5,6] However, it has been suggested that quantitative analysis of regional tracer activity may improve the diagnostic accuracy of sestamibi cardiac imaging in the identification of patients with dysfunctional, but still viable, myocardium who may benefit from coronary revascularization procedures.[6] Thus, the identification of the most effective quantitative criteria for the detection of myocardial regions with reversible LV dysfunction by using sestamibi SPECT has been addressed in recent studies.[7,8] To date, there has been no systematic comparison of visual and quantitative methods in the assessment of myocardial viability that demonstrates the superior value of the quantitative versus the visual method. This information may be clinically important, because in most laboratories the evaluation of the images is performed visually. Therefore, the present study was designed to compare directly the visual and quantitative analysis of resting sestamibi myocardial SPECT in the detection of dysfunctional but viable myocardium in patients with chronic ischemic LV dysfunction undergoing coronary revascularization. In addition, in a separate group of patients, the interobserver and intraobserver reproducibility for both visual and quantitative analysis was assessed.

MATERIALS AND METHODS

Patient Population

Sixty-five patients (7 women and 58 men; mean age, 53 ± 10 years) with an earlier myocardial infarction and impaired regional or global LV function were included in this study. All patients had a significant stenosis (≥ 50% of maximal luminal diameter) of at least 1 epicardial coronary vessel. Cardiac medications, except nitrates and antiplatelet drugs, were discontinued 72 hours before imaging studies. Patients with unstable angina or recent myocardial infarction (< 8 weeks) were excluded from the study. In all patients, baseline studies included coronary angiography, radionuclide angiography, two-dimensional echocardiography, and rest sestamibi imaging. All patients gave informed consent as part of a protocol approved by the Institutional Clinical Research Subpanel of our university.

Coronary Angiography

Coronary angiography was performed by means of Judkin's technique. It was reported by 2 independent, experienced observers. Stenoses of coronary vessels were coded according to American Heart Association criteria.[9] The presence of significant (50% coronary diameter reduction) stenosis in the proximal coronary arteries or their major branches was assessed by using caliper measurement.

Radionuclide Angiography

All patients underwent equilibrium radionuclide angiography within 1 week of echocardiography and sestamibi imaging. In all patients, in vivo labeling of red blood cells was performed with 555 MBq of Tc-99m. Radionuclide angiography was performed at rest in the 45-degree left anterior projection, with the patient in the supine position. A small field-of-view gamma camera (Starcam 300 A/M, General Electric, Milwaukee, Wis) equipped with a low-energy all-purpose collimator was used. Data were recorded at a frame rate of 24 frames per cardiac cycle on a dedicated computer system. Radionuclide angiographic studies were analyzed by using a standard commercial software (General Electric). The reproducibility of ejection fraction measurements in our laboratory has been reported previously.[10] In particular, the assessment of the ejection fraction within the same patients under steady-state conditions on different days of observation showed a significant correlation ($r = 0.97$, $P < .01$), and the standard deviation rate of the reproducibility of the measurements was 1.5%.

Echocardiography

Echocardiographic studies were performed under resting condition. Standard tomographic views of the left ventricle were obtained from the parasternal long-axis and short-axis views and from the apical 4- and 2-chamber views, with particular attention paid to the optimization of regional function. All studies were performed on a Hewlett-Packard Sonos 1000 ultrasound system (Andover, Mass) equipped with a 2.5-MHz transducer and were recorded on half-inch VHS tape. Echocardiograms were analyzed by 2 independent readers who were unaware of clinical and angiographic data. Discrepancies were resolved by means of consensus. For the analysis of wall motion, the left ventricle was divided into 13 segments corresponding to the scintigraphic regions (Figure 1). For each segment, wall motion was scored according to the recommendations of the American Society of Echocardiography,[11] on a scale of 1 to 3, in which 1 indicated normal, 2 indicated hypokinesia (reduced wall thickening and inward motion), and 3 indicated akinesia (absence of wall motion and of systolic thickening) or dyskinesia (paradoxical outward motion in systole). For the purpose of the present investigation, we focused on akinetic or dyskinetic segments, those that should be evaluated for the assessment of myocardial viability.[12] To assess the recovery of function, resting and follow-up echocardiograms were compared in all patients. For each segment, recovery of function was defined as an improvement of 1 or more point after revascularization.

Sestamibi Tomography

At baseline, all patients underwent resting sestamibi SPECT. Cardiac medications, except nitrates and antiplatelet drugs, were discontinued at least 72 hours before the study. All patients were intravenously injected at rest with 740 MBq of Tc-99m sestamibi. Imaging was performed 60 minutes after tracer injection, as described previously,[13] by using a rotating large field-of-view gamma camera (Elscint SP4HR, Haifa, Israel) equipped with a low-energy, all-purpose, parallel-hole collimator and connected with a dedicated computer system. Thirty-two projections (30 sec/projection) were obtained over a semicircular 180-degree arc, which extended from the 30-

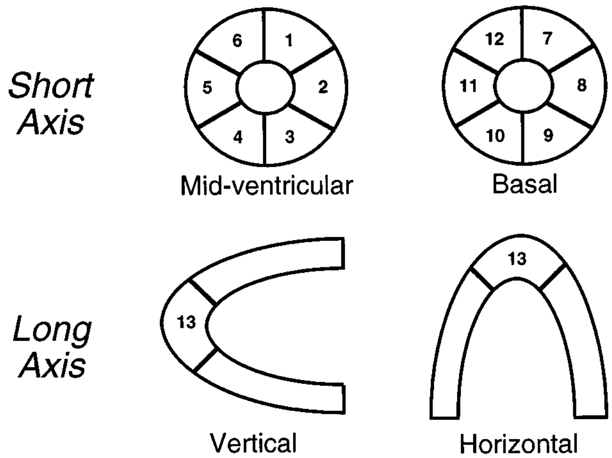

Figure 1. Diagram of the standard segmentation scheme used for regional analysis of Tc-99m sestamibi tomography and echocardiography.

degree right anterior oblique to the left posterior oblique position. A 20% symmetric energy window centered on the 140-keV peak was used. Filtered backprojection was then performed by using a low-resolution Butterworth filter with a cutoff frequency of 0.5 cycles/pixel, order 5.0. No attenuation or scatter correction was applied.

Image Analysis

In each patient, scintigraphic studies were analyzed by 2 independent observers who were unaware of clinical, angiographic, and echocardiographic findings for both quantitative and visual analyses. Discordance in the evaluation was resolved by means of a consensus. Regional sestamibi distribution was visually and quantitatively assessed on 2 short-axis tomograms with a semiautomatic circumferential profile method, as reported previously.[14] Each short-axis tomogram was divided into 6 sectors of equal arc, representing the anterolateral, lateral, inferior, posteroseptal, septal, and anterior myocardium. Apical activity was measured in a single region from vertical and horizontal long-axis tomograms. Therefore, in each patient, 13 anatomic segments were evaluated (Figure 1), and each segment was assigned to one of the major vascular territories, as described previously.[15] Briefly, the left anterior descending artery territory included the anterior wall, septum, and apex. The inferior wall was assigned to the right coronary artery. The lateral wall was assigned to the left circumflex artery.

A separate group of 6 patients was analyzed for the evaluation of intraobserver and interobserver reproducibility for both visual and quantitative analyses. Intraobserver reproducibility was measured, comparing the images interpreted twice for visual analysis and processed twice for quantitative analysis by the same reader. Interobserver reproducibility was measured, comparing the images interpreted for visual analysis and processed for quantitative analysis by 2 different readers.

For visual analysis, a side-by-side comparative display of the short- and long-axis slices was performed by the readers, who were blinded to the quantitative scintigraphic findings, with a 4-point scoring system (0, absent tracer uptake; 1, severe reduction of tracer uptake; 2, moderate reduction of tracer uptake; 3, normal tracer uptake). To assess myocardial viability by means of visual analysis, a segment was considered viable when it showed normal tracer uptake or moderate reduction of tracer uptake. Alternatively, a segment was considered to be nonviable when it showed absent or severe reduction of tracer uptake. For quantitative analysis, in each tomogram, the myocardial region with the maximum counts was considered to be the normal reference region. Tracer uptake in all other segments was then expressed as a percentage of the activity measured in the reference region. A segment was considered abnormal when the tracer uptake was more than 2 SD below the mean observed in the same region in healthy volunteers.[16] To assess myocardial viability quantitatively, a different analysis was performed, which considered both 50% as the cutoff point and the best threshold of 55%, as previously assessed in our laboratory.[7]

Functional Outcome

Within 3 weeks of the baseline studies, all major epicardial coronary arteries with significant stenosis were subjected to revascularization. In all patients, coronary revascularization was performed (35 patients underwent coronary artery bypass grafting surgery, and the remaining 30 patients underwent percutaneous transluminal coronary angioplasty with stent implantation). Successful dilatation, as defined by means of a diameter of the residual stenosis of the target vessel not exceeding 30% of luminal diameter, was obtained in all these latter cases. No patient had major complications associated with the revascularization procedure. Twelve months after coronary revascularization, all patients underwent repeat echocardiography to assess the recovery of regional LV function.

Statistical Analysis

Data are expressed as the mean plus or minus 1 SD. Differences between mean values were assessed by means of the Student unpaired *t* test, with Bonferroni's correction when appropriate. Sensitivity, specificity, and diagnostic accuracy were based on their standard definitions. Frequency data were compared by means of the McNemar or chi-square test. The Spearman rank correlation coefficient was used as a means of assessing the relationship between myocardial viability and the magnitude of regional sestamibi activity at both visual and quantitative analyses. A P value less than .05 was considered to be statistically significant. Receiver operating characteristic curve (ROC) areas were expressed as the mean plus or minus the SE.[17] The κ statistic was used as a measure of agreement between visual and quantitative sestamibi analysis.[18] A value of 1 denotes perfect agreement, and 0 indicates no agreement beyond chance.[19] In general, κ values of 0.6 or greater are considered to be indicative of good agreement. The intraclass coefficient of correlation (ICC) was used as a means of assessing intraobserver and interobserver reproducibility for both visual and quantitative analysis.[20,21] The ICC was calculated as ICC = $S_{t2}/(S_{t2} + S_{02})$, in which S_{02} is taken to be the within-subject mean square and is a measure of the variance within subjects. S_{t2} is calculated as S_{t2} = (BMS – WMS)/K_0, in which BMS is the between-subject mean square, WMS is the within-subject mean square, and K_0 is the number of replicate measurements, which, in this case is 2.[20,21] Finally, when appropriate, ICC is tested with F = BMS/WMS and testing it on (n-1) and n (k-1) degrees of freedom.[20]

RESULTS

General Findings at Baseline and Follow-up

In all 65 patients examined, the 70 earlier myocardial infarctions were located in the anterior wall in 44 cases, in the inferior wall in 24 cases, and in the lateral wall in 2 cases. At the time coronary angiography was performed, 32 patients had single-vessel disease, 21 patients had 2-vessel disease, and 12 patients had 3-vessel disease. LV ejection fraction at baseline was 40% ± 10%. Clinical baseline data of patient population are reported in Table 1. A total of 845 segments (13 per patient) were evaluated. Before revascularization, 453 myocardial segments (54%) showed normal LV function, and 392 myocardial segments (46%) had abnormal wall motion. In particular, 165 segments (42%) were hypokinetic, and 227 segments (58%) were akinetic or dyskinetic. Of the 227 akinetic or dyskinetic segments at baseline, 15 (7%) were not revascularized, whereas the remaining 212 (93%) received revascularization procedures. Of these latter segments, 112 (53%) showed functional improvement after revascularization and were considered to be viable, and 100 (47%) did not change at the follow-up study and were considered to be nonviable. Of all the revascularized akinetic or dyskinetic segments analyzed, 16% were supplied by vessels with a 50% to 70% luminal diameter stenosis, 28% were supplied by vessels with a more than 70% luminal diameter stenosis, and 56% of segments were supplied by an occluded artery. After revascularization, all 65 patients studied underwent a stress test follow-up examination (physical exercise in 49 patients and a pharmacological test with dobutamine in 16 patients), and in all patients, there was no evidence found by means of electrocardiography suggesting recurrent ischemia.

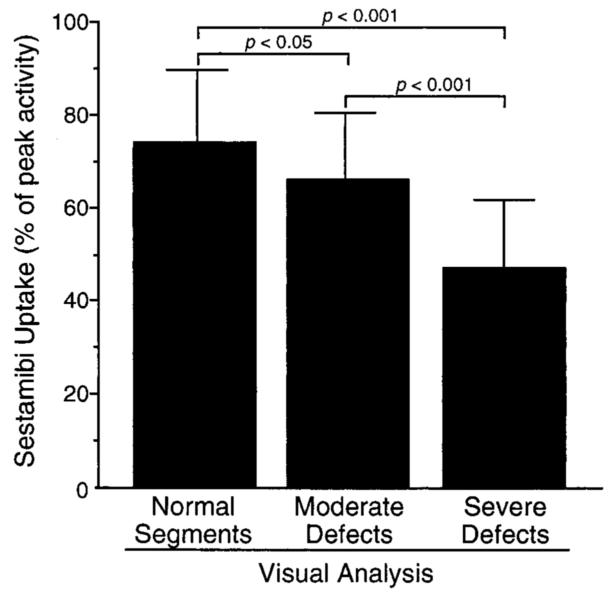

Figure 2. Bar graph showing Tc-99m sestamibi uptake in akinetic or dyskinetic segments classified as normal, with moderate defects, and with severe defects by means of visual analysis.

Table 1. Clinical characteristics of the study population

	Study population (n = 65)
Clinical characteristics	
Age (years)	53 ± 10
Male sex (%)	58 (89)
Site of previous myocardial infarction	
Anterior wall (%)	44 (63)
Inferior wall (%)	24 (34)
Lateral wall (%)	2 (3)
Coronary angiography	
Single-vessel disease (%)	32 (49)
2-vessel disease (%)	21 (32)
3-vessel disease (%)	12 (18)
Radionuclide angiography	
LV ejection fraction (%)	40 ± 10

Intraobserver and Interobserver Reproducibility

For this analysis, 6 patients were examined twice by the same observer (intraobserver reproducibility) and interpreted by 2 different observers (interobserver reproducibility). The observers were blinded to the patient's

Table 2. Intraobserver and interobserver reproducibility of visual and quantitative analyses in a separate group of 6 patients

	Intraobserver reproducibility			Interobserver reproducibility		
	ICC	F	*P* value	ICC	F	*P* value
Visual analysis	0.9	61.5	< .001	0.8	9.54	< .001
Quantitative analysis	0.8	11.32	< .001	0.7	5.1	< .001

Table 3. Detection of myocardial viability by means of visual and quantitative analyses

		Quantitative analysis	
	Visual analysis	Cutoff ≥ 50%	Cutoff ≥ 55%
Sensitivity (%)	59	82*†	73*
Specificity (%)	81	61*†	74
Accuracy (%)	69	72	74
Positive predictive value (%)	78	70	76
Negative predictive value (%)	64	75	72

**P* < .05 versus visual analysis
†*P* < .05 versus cutoff of 55% or more

clinical data and to each other's results. The results of this analysis are listed in Table 2. The correlation for intraobserver and interobserver reproducibility were high ($P < .001$) for both visual and quantitative analyses.

Visual and Quantitative Analysis

Akinetic or dyskinetic revascularized segments were classified on sestamibi images according to visual score. Of the 212 segments analyzed, 27 (13%) were classified as normal, 58 (27%) were classified as moderate, and 127 (60%) were classified as severe defects. At quantitative analysis, the mean sestamibi activity was 74% ± 15% in normal segments, 66% ± 14% in moderate segments, and 47% ± 14% in severe defects (Figure 2).

Differentiation of Reversible From Irreversible Dysfunction

Among all akinetic or dyskinetic revascularized segments, 66 of 112 viable segments (59%) and 85 of 100 nonviable segments (81%) were identified by means of visual analysis (Table 3). Ninety-two of 112 viable segments (82%) and 61 of 100 nonviable segments (61%) were identified by means of quantitative analysis, with 50% as the cutoff. By using the best threshold of 55%, 82 of 112 viable segments (73%) and 74 of 100 nonviable segments (74%) were identified (Table 3). Significantly higher sensitivity ($P < .05$) but lower specificity ($P < .05$) was shown by means of quantitative analysis with 50% as a cutoff, as compared with that shown by means of visual analysis (Table 3). However, when comparing quantitative analysis with the best threshold of 55% to visual analysis, sensitivity was significantly higher ($P < .05$), whereas specificity was not different ($P = .3$). Moreover, significant differences in both sensitivity and specificity were found when comparing the 2 methods of quantitative analysis (Table 3).

The probability of akinetic or dyskinetic segments representing viable myocardium, defined as improved wall motion after revascularization, was significantly related to the level of regional tracer activity for both visual ($P < .0001$) and quantitative ($P < .0001$) analyses (Figure 3). ROC curve areas constructed by using visual and quantitative analyses for the detection of myocardial viability in all 212 akinetic or dyskinetic segments were 0.79 ± 0.04 and 0.81 ± 0.03, respectively (P = not significant; Figure 4).

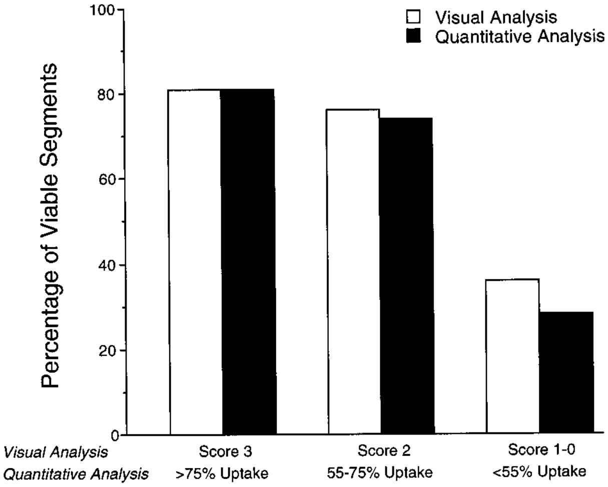

Figure 3. Bar graph showing the percentage of akinetic or dyskinetic segments that represent viable myocardium (defined as improved wall motion after revascularization) in normal segments (score 3 by means of visual and > 75% uptake by means of quantitative analysis), moderate (score 2 by means of visual and 55% to 75% uptake by means of quantitative analysis), and severe (score 1 and 0 by means of visual and < 55% uptake by means of quantitative analysis). The probability of dysfunctional segments at baseline to represent viable myocardium is related to the magnitude of regional sestamibi activity by means of both visual and quantitative analysis.

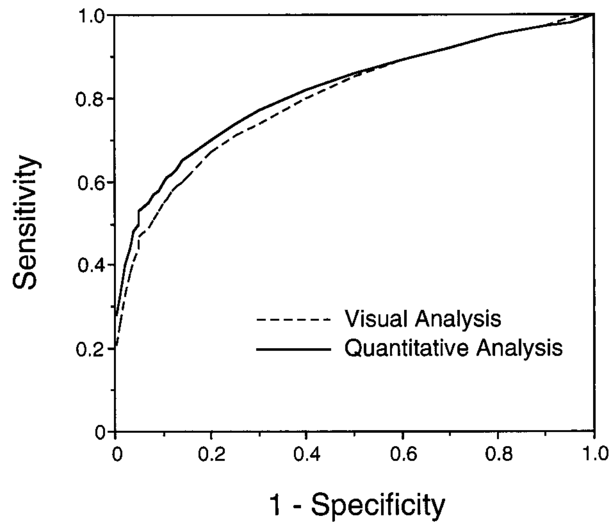

Figure 4. Receiver operating characteristic curves of diagnostic accuracy of visual and quantitative analysis of Tc-99m sestamibi tomography to differentiate akinetic or dyskinetic segments with or without functional recovery after revascularization.

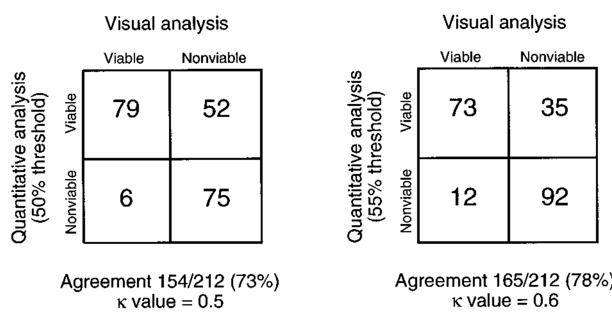

Figure 5. Concordance data of classification of akinetic or dyskinetic segments as viable or nonviable between visual and quantitative analysis.

Agreement in the Detection of Myocardial Viability

Overall concordance in the detection of myocardial viability between visual and quantitative analyses with 50% as the cutoff point was observed in 154 of the 212 akinetic or dyskinetic segments (73%), with a κ value of 0.5 (Figure 5). By comparing the results of the visual and quantitative analyses with 55% as cutoff point, the agreement was observed in 165 of the segments analyzed (78%), with a κ value of 0.6 (Figure 5).

DISCUSSION

The results of this study indicate that, in patients with chronic myocardial infarction and mild-moderate LV dysfunction, visual analysis shows good overall accuracy in predicting the recovery of regional LV function after revascularization. No overall differences in discriminating reversible from irreversible LV dysfunction were demonstrated by means of a direct comparison between visual and quantitative analyses. Our findings further demonstrate high intraobserver and interobserver reproducibility of both visual and quantitative measurements. Reproducibility of visual and quantitative analyses of sestamibi imaging was assessed by using the intraclass correlation coefficient, typically a ratio of the variance of interest over the sum of the variance of interest plus error, providing measures of reliability.[20,21]

The potential reversibility of LV dysfunction is one of the most important issues to be addressed in patients with an earlier myocardial infarction and severe coronary artery disease. In such cases, myocardial imaging at rest with thallium or Tc-99m–labeled agents has been demonstrated to provide clinically relevant data for clinical decision-making. It has also been suggested that quantitative analysis of tracer content may enhance the ability of myocardial SPECT studies in predicting the recovery of severe regional wall motion abnormalities after coronary revascularization.[5,6] Moreover, in the present investigation, all radionuclide studies were performed in patients receiving nitrate treatment; it has been reported that nitrate administration improves the accuracy of ses-

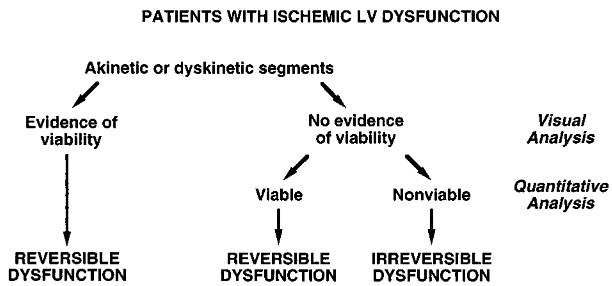

Figure 6. Flow diagram proposed to use visual inspection and quantitative analysis of sestamibi tomographic imaging efficiently to predict the recovery of akinetic or dyskinetic segments in patients with ischemic LV dysfunction.

tamibi imaging in detecting myocardial viability.[22] In this study, we directly compared visual and quantitative tomographic methods in the detection of myocardial viability in the same patients with chronic ischemic LV dysfunction. Our results show that there is a good correlation between visual and quantitative analysis in the evaluation of defect severity in akinetic and dyskinetic myocardial segments (Figure 2). However, in our study, the sensitivity was significantly lower with visual analysis than with quantitative analysis. In fact, 36% of akinetic or dyskinetic segments classified as nonviable at the time of the preoperative visual scoring improved after revascularization; however, only 24% of akinetic or dyskinetic segments with a preoperative threshold less than 50% and 28% of segments with a preoperative threshold less than 55% at quantitative analysis showed functional recovery after revascularization. These findings show that sestamibi SPECT with quantitative analysis provides important information to identify correctly akinetic or dyskinetic segments that will recover their function after coronary revascularization. Moreover, by using the best threshold for quantitative analysis (55%), as compared with 50% as the cutoff point, there was an increase in specificity, with preserved good sensitivity. These observations, according to the results of previously published data,[7] underline the importance of using the most appropriate threshold for sestamibi SPECT to identify preserved myocardial viability in the presence of severe LV dysfunction. By comparing the results of visual analysis with those of quantitative analysis with the best cutoff point, sensitivity was significantly higher at quantitative analysis, but there was no statistical difference in specificity. However, higher specificity was shown by means of visual analysis than by means of quantitative analysis with a cutoff point of 50%. Moreover, the overall concordance in the classification of segments between visual and quantitative analysis was higher by using the best cutoff point than by using the cutoff point of 50%.

The results of the present study also support the concept that the analysis of regional sestamibi activity, performed by means of either visual or quantitative analysis, provides important data about myocardial viability and the potential for recovery of akinetic or dyskinetic segments after revascularization. Therefore, in regions with severe functional impairment, the probability of reversibility of LV dysfunction is related to the amount of sestamibi uptake across a wide spectrum of activity on both visual and quantitative approaches.

This study demonstrated that computer quantification with the most appropriate threshold for myocardial perfusion imaging enhances the sensitivity of sestamibi SPECT in the assessment of myocardial viability. Quantification should be used as a means of confirming the impression derived from visual analysis of tomographic images. However, the computer does not recognize artifacts. Potential artifacts are identified by means of the inspection of the analog images. Thus, the process of integrating visual and quantitative information, defined by Wackers as "quantitative analysis with visual overread,"[23] may be the best approach to characterize a myocardial region when the issue of myocardial viability has to be addressed. Myocardial quantification with the most appropriate threshold for sestamibi imaging provides similar results when compared with visual analysis for specificity. Not only high sensitivity, but also good specificity in detecting viable myocardium are needed to help in patient treatment and in the selection of patients who will be submitted to the risks and costs of a revascularization procedure.

In the present investigation, myocardial SPECT was performed under resting conditions, and the presence of reversible thallium defects on stress in an asynergic region has recently been demonstrated to more accurately predict recovery of function after revascularization.[24] Furthermore, in our study, patients did not undergo coronary angiography at the follow-up examination; therefore, restenosis or graft occlusion after revascularization or a progression of coronary impairment cannot be completely excluded. However, all patients were carefully observed until the final study, and no clinical evidence or electrocardiography stress test results suggested recurrent ischemia.

CONCLUSIONS

The results of this study demonstrate that, in patients with chronic myocardial infarction and mild-moderate LV dysfunction, visual analysis of sestamibi tomographic images at rest has good overall accuracy as a means of predicting recovery of regional LV function after revascularization. The comparison between visual and quantitative analysis methods demonstrates no overall important differences in performance to discriminate reversible from irreversible dysfunction. However, quantitative analysis with the most appropriate threshold of tracer activity shows higher sensitivity in the identification of dysfunctional viable myocardium. These findings may be helpful in using myocardial perfusion imaging efficiently in the detection of myocardial viability. As shown in Figure 6, quantitative analysis seems unnecessary in patients with evidence of viability shown by means of visual analysis. In fact, most of the akinetic or dyskinetic segments with preserved sestamibi activity shown by means of visual analysis demonstrate functional recovery after revascularization. However, quantitative analysis may provide important information in identifying viable myocardium in regions with a severe reduction of tracer uptake on visual inspection. In fact, a substantial number of dysfunctional segments with no evidence of viability shown by means of visual analysis exhibit preserved tracer uptake with quantitative analysis and improved wall motion after revascularization. Finally, in the presence of an intermediate level of tracer uptake at rest (defined as being in the 40% to 60% range of peak activity), the probability of a favorable outcome is also intermediate, and further information may be needed to make an appropriate clinical decision.[25] This may include a stress study to determine whether inducible ischemia is present or a metabolic study evaluating the presence of a mismatch between reduced flow and preserved or enhanced glucose metabolism.

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