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Prediction of functional recovery in patients with chronic coronary artery disease and left ventricular dysfunction combining the

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09 May 2026

Prediction of Functional Recovery in Patients With Chronic Coronary Artery Disease and Left Ventricular Dysfunction Combining the Evaluation of Myocardial Perfusion and of Contractile Reserve Using Nitrate-Enhanced Technetium-99m Sestamibi Gated Single-Photon Emission Computed Tomography and *Dobutamine* Stress

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This study aimed to assess whether contractile reserve evaluation using dobutamine gated single-photon emission computed tomography (SPECT) improves the capability of quantitative perfusion analysis to predict functional recovery of viable hibernating myocardium. Resting and dobutamine nitrate-enhanced technetium-99m sestamibi (sestamibi) gated SPECT studies were performed in patients with coronary artery disease who had left ventricular dysfunction. Tracer activity was quantified, and wall motion and thickening visually scored. Reversible dysfunction was identified with gated SPECT repeated after coronary revascularization. Using the best activity threshold, perfusion quantification achieved 85% sensitivity and 55% specificity. Contractile reserve detection was significantly less sensitive (64%, p <0.0005), but more specific (88%, p <0.00001) than perfusion quantification. However, in the subgroup of hypokinetic segments, the sensitivity of contractile reserve assessment was just slightly lower than perfusion quantification (72% vs 91%, p = NS), whereas specificity was significantly higher (94% vs 23%, p <0.00001). Conversely, in the adyskinetic segments, perfusion quantification was significantly more sensitive than contractile reserve (82% vs 59%, p <0.005), but similarly specific (76% vs 85%, p = NS). Therefore, the identification of reversible dysfunction based on perfusion quantification in adyskinetic segments and on contractile reserve detection in hypokinetic segments was significantly more specific (83% vs 55%, p <0.00001) than standard quantitative perfusion SPECT, without major loss in sensitivity (78% vs 85%, p = NS). In conclusion, contractile reserve evaluation using dobutamine gated SPECT enhances the reliability of nitrate-enhanced sestamibi SPECT when used to predict reversible dysfunction in hypokinetic segments, whereas perfusion quantification remains superior in adyskinetic segments.
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Quantitative technetium-99m sestamibi (sestamibi) single-photon emission computed tomography (SPECT) is a reliable method for the detection of myocardial viability, particularly when nitrate-enhanced imaging is used.[1–6] Perfusion imaging with technetium-labeled agents, however, is increasingly acquired using the gated SPECT modality, which offers advantages in terms of artifact detection and additional functional data.[7,8] Great interest has been given to the implications of gated SPECT for viability detection, but no definitive results have been reached.[9–12] An interesting proposal has been to associate gated SPECT with low-dose dobutamine infusion to assess the contractile reserve of asynergic segments.[13] The feasibility of this procedure has been demonstrated,[14,15] but its predictive value for postrevascularization outcome and its optimal combination with quantitative perfusion imaging are still unclear. In this study, we used dobutamine gated SPECT to evaluate the contractile reserve of asynergic segments with the aim to verify the contribution of functional data to perfusion quantification for the prediction of postrevascularization recovery.

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METHODS

Patient population: We studied 33 consecutive patients (31 men, mean age 65 ± 9 years) who fulfilled the following inclusion criteria: prior myocardial infarction (anterior in 23, inferior in 10 cases), impaired left ventricular function (mean left ventricular ejection fraction 33.3 ± 9.6% (range 15% to 49%; 17 patients <35%), and scheduled to undergo revascularization. Exclusion criteria were: recent (<1 month) myocardial infarction or unstable angina, heart disease other than coronary artery disease, atrial fibrillation, or history of sustained ventricular tachycardia. There were 11 patients with 1-vessel, 12 patients with 2-vessel, and 10 patients with 3-vessel coronary artery disease.

Study protocol: All patients underwent in a single-session nitrate-enhanced resting and dobutamine sestamibi gated SPECT. To assess functional outcome, baseline resting sestamibi gated SPECT was repeated after revascularization: ≥3 months for bypass grafting (13 patients) and ≥1 month for coronary angioplasty (20 patients). Nitrates and β-adrenergic blocking agents were discontinued 48 hours before the tests. All patients gave informed consent to participate in the study, which was approved by the Ethics Committee of our institution.

Sestamibi SPECT: The modality of nitrate infusion has been previously described.[4] After 1 hour, baseline resting gated SPECT was acquired. Immediately thereafter, dobutamine infusion (5 μg/kg body weight/min) was started, and increased after 5 minutes to 10 μg/kg/min. Early interruption criteria were hypotension, angina, or significant ventricular arrhythmia. Gated SPECT acquisition was started after 3 minutes of the 10-μg dose that was maintained until acquisition was completed.[16] For the postrevascularization study, the same dose of sestamibi (1,111 MBq, 30 mCi) was injected, followed 1 hour later by SPECT acquisition. A dual-head gamma camera (ADAC Vertex, ADAC Laboratories, Milpitas, California) with high-resolution collimators and a 15% window centered on the 140-keV photopeak of technetium-99m was used. SPECT was performed with 32 projections over a 180° elliptical orbit at 45 s/projection, 64 × 64 matrixes, 8-frames/cardiac cycle. The studies were reconstructed using filtered back-projection without attenuation or scatter correction. The reconstructed slices were realigned along the heart axis and short-, horizontal long-, and vertical long-axis views were obtained. For tracer activity quantification, the gated SPECT images were summed, obtaining a standard perfusion study.

Data analysis: The left ventricle was divided into 16 segments and each of the segments assigned to the related coronary territory.[17] For tracer activity quantification, the mean uptake of each segment was calculated, the activity of the segment with peak uptake equated to 100%, and the other segments scaled in percent of peak activity.[6] Regional wall motion and thickening were assessed visually by consensus of 2 experienced observers, who were blinded to the data, and scored using a 4-point scale (1 = normal, 2 = hypokinesia; 3 = akinesia; 4 = dyskinesia).[18] Previous data indicated a good reproducibility of these evaluations in our laboratory.[15] Baseline dysfunctional segments (score > 1) that exhibited a decrease ≥1 grade in regional score during dobutamine administration were considered to have contractile reserve.[19] Similarly, functional recovery was defined on the basis of decrease ≥1 grade in regional score at follow-up.[19,20] However, a change from dyskinesia to akinesia was not considered to be significant.[21]

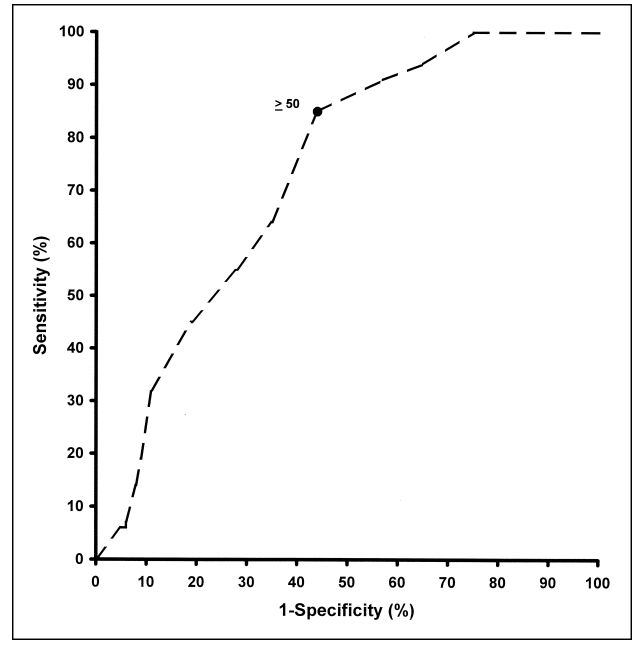

FIGURE 1. Receiver operating characteristics curve constructed using different sestamibi activity thresholds to define reversible dysfunction in asynergic segments.

Statistical analysis: Receiver operating characteristics curve analysis was used to identify the best cut-off value of sestamibi activity for predicting functional recovery. The comparison of proportions was made using the Fisher's exact test or the chi-square test with Yates' correction, as appropriate. A p value <0.05 was considered statistically significant.

RESULTS

Baseline and follow-up gated SPECT: Fifty-one vascular territories including 356 segments were successfully revascularized. Baseline resting gated SPECT classified 86 segments as normokinetic, 107 as hypokinetic, and 163 as adyskinetic. After revascularization, 109 of 270 dysfunctional segments (43 hypokinetic) showed functional recovery, whereas 161 (64 hypokinetic) showed no functional changes.

Myocardial perfusion: According to receiver operating characteristics curve analysis, the optimal cut-off value to identify reversible dysfunction in asynergic segments was ≥50% of peak activity (Figure 1). Using this threshold, perfusion imaging predicted functional recovery in 93 of 109 segments (85% sensitivity), and excluded it in 89 of 161 segments (55% specificity), with 67% global accuracy. In hypokinetic segments, sensitivity, specificity, and accuracy of ses-

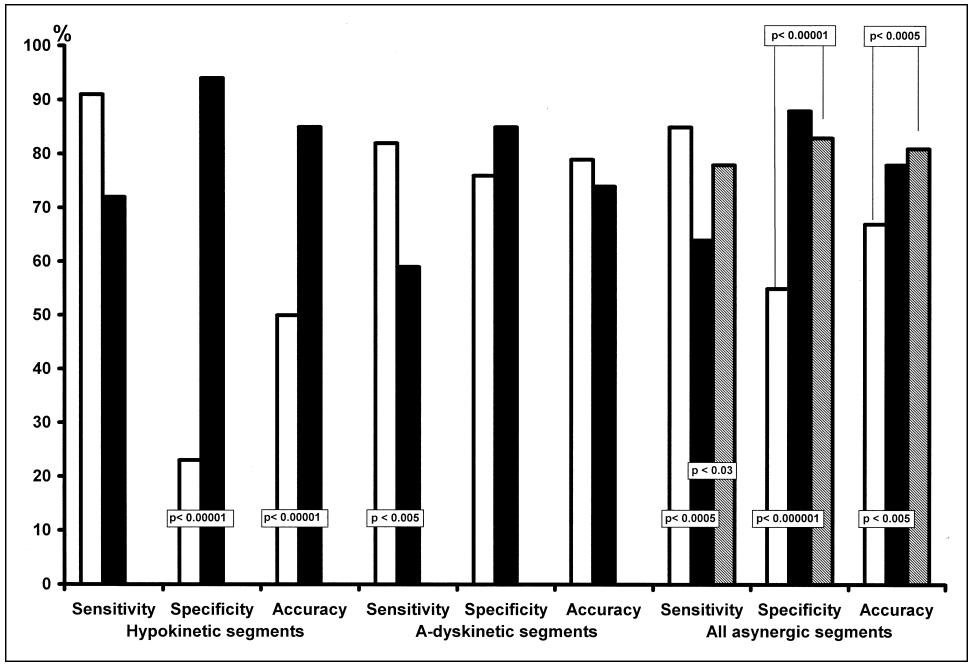

FIGURE 2. Sensitivity, specificity, and accuracy for recovery of segmental function in hypokinetic segments, adyskinetic segments, and all asynergic segments using perfusion imaging *(white bars)*, contractile reserve *(black bars)*, and using activity quantification in adyskinetic segments and contractile reserve detection in hypokinetic segments *(hatched bars)*.

tamibi SPECT were 91% (39 of 43 segments), 23% (15 of 64 segments), and 50% (54 of 107 segments), respectively. In adyskinetic segments, sensitivity, specificity, and accuracy were 82% (54 of 66 segments) (p = NS vs hypokinetic segments), 76% (74 of 97 segments) ($p < 0.00001$ vs hypokinetic), and 79% (128 of 163 segments) ($p < 0.00001$ vs hypokinetic), respectively (Figure 2).

Dobutamine gated SPECT: Dobutamine stimulation elicited contractile reserve in 89 dysfunctional segments (35 hypokinetic). Of these, 70 segments (31 hypokinetic) showed reversible dysfunction at follow-up (sensitivity 64%, $p < 0.0005$ vs perfusion quantification). Only 39 of 181 segments (12 hypokinetic) without response to dobutamine showed functional improvement after revascularization (specificity 88%, $p < 0.00001$ vs perfusion quantification). In hypokinetic segments, contractile reserve showed higher specificity (94% vs 23%, $p < 0.00001$) and global accuracy (85% vs 50%, $p < 0.00001$) than perfusion quantification, and similar sensitivity (72% vs 91%, p = NS). In adyskinetic segments, contractile reserve showed lower sensitivity (59% vs 82%, $p < 0.005$) than sestamibi activity, without significant differences in specificity (85% vs 76%, p = NS) or overall accuracy (74% vs 79%, p = NS) (Figure 2).

Combination of perfusion quantification and contractile reserve: When adyskinetic segments were considered to be viable if they had nitrate sestamibi activity $\geq$50%, and hypokinetic segments were considered to be viable if they had contractile reserve independently of tracer activity, the specificity (134 of 161 segments, 83%; $p < 0.00001$) and the global accuracy (219 of 270 segments, 81%; $p < 0.0005$) improved significantly compared with perfusion quantification alone, whereas sensitivity did not change significantly (85 of 109 segment, 78%), but remained higher than using contractile reserve alone (70 of 109 segments, 64%, $p < 0.03$) (Figure 2).

DISCUSSION

For detecting viable hibernating myocardium, the role of functional imaging, mainly echocardiography, is to recognize the contractile reserve of asynergic regions under dobutamine.[16,19,21–23] Most recently, gated SPECT has also been shown to be reliable for contractile reserve evaluation.[14,15] Thus, the simultaneous assessment of myocardial cellular integrity using perfusion imaging and of contractile reserve using dobutamine gated SPECT has been suggested as a new approach to viability detection.[13] In general, the demonstration of contractile reserve has a higher specificity than myocardial perfusion imaging.[19,24,25] The latter approach is usually more sensitive, particularly in the clinically most important subgroup of akinetic segments.[19] In our series, the higher specificity of contractile reserve versus perfusion quantification was confirmed. This finding was particularly conspicuous in the hypokinetic segments, where the low specificity of perfusion imaging was explained by tracer uptake within the layer of viable tissue that sustained contractility. Despite preserved tracer activity, if this tissue coexists with scarred myocardium, contractile reserve is absent and functional recovery cannot be expected. Conversely, hypokinetic segments including normal tissue and viable hibernating myocardium will show both contractile reserve during dobutamine and reversible dysfunction after revascularization. Tracer activity quantification, however, was significantly more sensitive than contractile reserve evaluation, especially in the more severely dysfunctional segments, as shown by other studies.[19] Based on these observations, we used combined criteria to identify the segments with reversible dysfunction. Regional dysfunc-

tion was assessed on the basis of gated SPECT evaluation at rest. If a segment was adyskinetic, it was classified according to the sestamibi activity value, using the best cut-off for viability. If a segment was hypokinetic, it was examined for the presence or absence of contractile reserve in dobutamine gated SPECT and classified accordingly as probably viable or nonviable, respectively. This approach achieved high sensitivity, specificity, and overall accuracy, and was significantly superior to perfusion imaging or contractile reserve evaluation applied separately. These results support the proposal of taking advantage of the combination of perfusion and contractile reserve data made possible by dobutamine gated SPECT.[13] In contrast, prior studies about the use of baseline gated SPECT to improve the detection of viable hibernating myocardium have failed to demonstrate major diagnostic gains over perfusion images alone.[9–12]

The results of the present study must be evaluated cautiously because of several limitations. As in many other studies using functional recovery as the reference standard to define myocardial viability, the patient population is quite small.[9,11,12] A limitation of gated SPECT compared with echocardiography is the impossibility to monitor changes during dobutamine infusion, and so to differentiate between lack of improvement and biphasic response, which is considered the most reliable marker of preserved viability in dobutamine echocardiography.[26,27] Conversely, we did not perform a quantitative analysis of wall motion and thickening on gated SPECT images.[28,29] This approach could increase the reliability and reproducibility of gated SPECT functional assessment and represents a potential advantage of this method. Finally, we did not consider the global left ventricular ejection fraction data, neither to establish the outcome of the revascularization nor to identify a possible relation between dobutamine-induced and postrevascularization changes. Recent echocardiographic data suggest a very good accuracy of the dobutamine ejection fraction to predict global functional response after the intervention.[30] Taking into account the good reproducibility of gated SPECT measurements,[7] further studies are warranted to establish the predictive value of the ejection fraction response to dobutamine.

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