The Diagnostic and Prognostic Value of ECG-Gated SPECT Myocardial Perfusion Imaging

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Since the development of gated SPECT imaging approximately 10 y ago, this technique is now almost universally used as an adjunct for radionuclide perfusion imaging, enabling the assessment of perfusion along with determination of regional and global left ventricular function in the same examination. The gated SPECT determination of the left ventricular ejection fraction and volumes has been extensively validated. Additionally, this method allows for the improved identification of soft-tissue artifacts and enhances the detection of multivessel coronary artery disease. Furthermore, gated SPECT provides powerful information for the risk assessment of patients with known or suspected coronary artery disease and aids in the assessment of myocardial viability. Gated SPECT imaging has clearly become an integral part of radionuclide myocardial perfusion imaging.

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Electrocardiographically (ECG)-gated myocardial perfusion SPECT was developed in the late 1980s and has rapidly evolved into a standard for myocardial perfusion imaging in the United States. The American Society of Nuclear Cardiology in its position paper from March 1999 recommended the routine incorporation of ECG gating during SPECT cardiac perfusion scintigraphy (*1,2*). Gated SPECT studies allow simultaneous assessment of perfusion and function in a single-injection, single-acquisition sequence.

The development of new radioisotopes and improvements in imaging hardware and computer technology have contributed significantly to the growth of gated SPECT. The ^{99m}Tc-based perfusion tracers, because of their higher count rates and stable myocardial distribution with time, permit evaluation of regional myocardial wall motion and wall thickening throughout the cardiac cycle. The development of automated algorithms to quantitatively measure left ventricular (LV) volume and ejection fraction (EF), and even regional myocardial wall motion and thickening from gated SPECT, rapidly and accurately, and with minimal operator interaction, has also contributed to its widespread use. These innovations have made SPECT imaging a premier method of noninvasive evaluation of myocardial blood flow and cardiac function in a variety of clinical situations (*3*).

GATED SPECT ACQUISITION AND PROCESSING

In a gated acquisition, a 3-lead ECG provides the R wave trigger to the acquisition computer, with 2 successive R wave peaks on the ECG defining a cardiac cycle. Counts from each phase of the cardiac cycle are associated with a temporal frame within the computer (*4*). Gating of myocardial perfusion is usually performed at 8 frames per R–R interval per projection, although most manufacturers have the capability to acquire 16 frames per R–R interval. The acquired data are then reconstructed and displayed in a cinematic or multiframe format, allowing the reader to assess wall motion in all areas of the myocardium, including the left and right ventricles (Fig. 1) (*5*).

Changes in heart rate due to a variety of factors can result in temporal blurring—that is, mixing of counts from adjacent frames. To minimize temporal blurring, a beat rejection
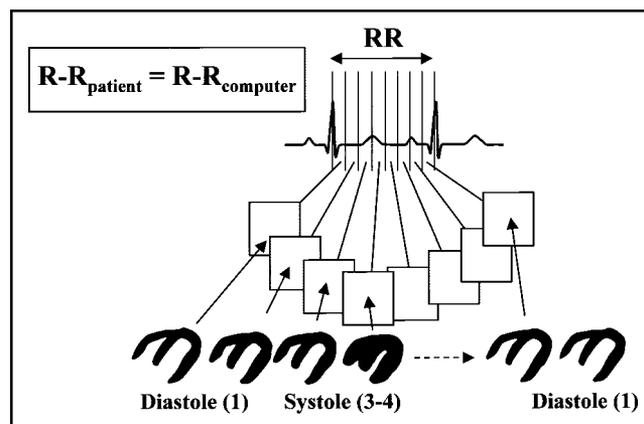
FIGURE 1. ECG-gated SPECT acquisition. Separate temporal frames corresponding to different phases of cardiac cycle are acquired for each angular projection. Perfusion images are obtained from summation of individual frames. (Reprinted with permission of (*5*).)

window is set by specifying the acceptable deviation of each R–R interval from the expected value. A 20% window has historically been applied, although in patients with highly variable heart rates, up to a 100% acceptance window can be set. In patients with arrhythmias, it is important to check for gating errors, as it has been demonstrated that EF fluctuations, perfusion differences, and, in particular, wall thickening discordance may occur with arrhythmias (*6*). Thus, in cases of extreme variation in heart rate or rhythm, an ungated SPECT study may be the most appropriate test.

There are a variety of single-day and 2-d protocols that may be used in conjunction with gated SPECT. Either ^{201}Tl or ^{99m}Tc perfusion tracers may be used. Most commonly used is the high-dose technetium stress study because of its superior myocardial count density. ^{99m}Tc-Sestamibi provides more reproducible volume and LVEF measurements than [201]Tl (*7*). In addition, when low- versus high-dose

technetium was compared there was less variability of LVEF in the high-dosage cohort (*8*).

Either or both of the acquisitions composing the stress/rest or rest/stress sequence can be gated. Although the common practice is to gate only the poststress image, a small study by Johnson et al. reports that, in 36% of patients with reversible perfusion defects, the poststress LVEF was >5% lower than at rest (*9*). This implies that global and regional LV function obtained from poststress gated acquisitions are not representative of basal LV function in patients with stress-induced ischemia and that perhaps both rest and stress images should be gated routinely, as long as counts are sufficient.

Overall ventricular function and regional cardiac function (myocardial wall motion and thickening) are calculated separately using computer software requiring minimal operator input (Fig. 2). Most of these programs use an edge
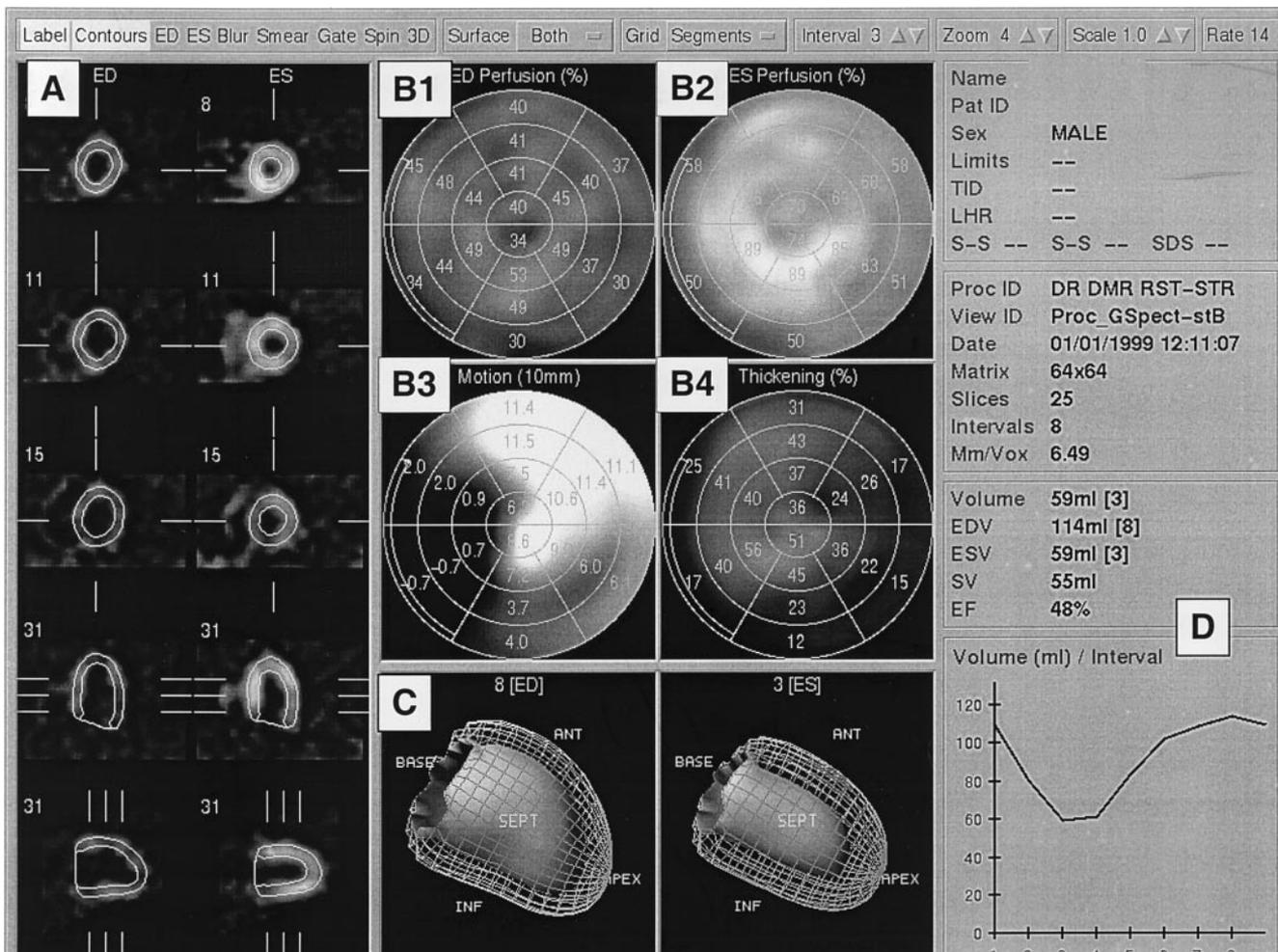
FIGURE 2. Quantification of EF, regional myocardial wall motion, and thickening from gated myocardial perfusion SPECT (QPS; Cedars-Sinai). (A) Myocardial contours displaying endocardial and epicardial surfaces overlying end-diastolic (ED) and end-systolic (ES) frames display 3 short-axis images, a midcavity horizontal image, and a midcavity vertical long-axis image. (B) Quantitative polar plots measuring regional myocardial wall perfusion (B1, B2), motion (B3), and wall thickening (B4) from gated SPECT. (C) Three-dimensional display of endocardial (solid) and epicardial (grid) LV surfaces calculated by automatic algorithm. (D) Endocardial time–volume curve and calculated LVEF from end-systolic and end diastolic volumes.

detection method using endocardial and epicardial surface points and make geometric assumptions (gaussian fit) to calculate LV end-systolic and end-diastolic volumes. Other methods seek definition of the same points using the percentage systolic count increases because of the partial-volume effect. Newer programs are usually a hybrid of edge detection and count-based methods and are 3-dimensional (10–12). Visually the ventricular wall thickening can be accentuated with thermal or hot body imaging options.

CLINICAL APPLICATIONS

Ventricular Function

The 3 most widely distributed software packages for LV function analysis from gated myocardial perfusion scans are QGS (Cedars-Sinai), 4D-MSPECT (University of Michigan), and the Emory Cardiac Toolbox or ECTb (Emory University). The QGS methodology uses gaussian fit to determine endocardial and epicardial offsets, whereas ECTb is a count-based method. Although both programs have, in general, compared favorably with other modalities for determining LVEF and volumes (Tables 1 and 2), it is important to keep in mind that the choice of gold standard, as well as degree of rigorousness in comparing the different methodologies in these validation studies, may vary. Some modalities used for comparison, including 2-dimensional echocardiography, radionuclide ventriculography, and first-pass radionuclide angiography have their own inherent inaccuracies. It is also important to note that not all reports provided the statistical analysis of the variability around the correlation line, such as the SE of estimates, which indicates the likelihood that the EF measured by the new technique will be within a certain range of the EF measured by the gold standard. If there is a large range, this usually indicates that a study is not as reliable. Perfusion defects, background activity, time after injection, and the injected dose may have a confounding effect on the quantitative determination of LVEF and LV volumes, as demonstrated by a small study done in canines by Vallejo et al., which showed that the automated QGS program consistently overestimated LVEF and LV volumes when compared with MRI (13). Furthermore, since this was a canine study, it is postulated that perhaps in smaller hearts, the limited spatial resolution of SPECT makes endocardial border recognition problematic and that perhaps a count-based method would be more appropriate. A larger human study by the same author, comparing gated SPECT with first-pass radionuclide angiography, showed a better correlation in studies with low extracardiac activity, higher counts, and larger hearts (14). This emphasizes the critical importance of quality control and optimizing image acquisition, as well as awareness on the part of the reader to recognize the presence of such variables. A study by Nakajima et al., specifically examining pediatric hearts (age, 2 mo to 19 y) with correspondingly small LV volumes (14–326 mL), also emphasized that in patients with small ventricular volumes gated SPECT is valid if appropriate image acquisition parameters are used (15).

Several studies have directly compared the performance of gated SPECT software packages. A comparison between QGS and ECTb showed that QGS consistently provided significantly lower volumes and EFs compared with the ECTb algorithm for both coronary artery disease (CAD) and low-likelihood patients (Table 3) but that both methods showed close correlation with each other ($r = 0.91$–0.94) (16). Lum and Coel demonstrated a correlation coefficient of >0.9 in estimating EF and end-diastolic volume among QGS, ECTb, and 4D-MSPECT (17). Nakajima et al. compared QGS, ECTb, and 4D-MSPECT with gated blood pool and observed correlation coefficients of 0.89, 0.85, and 0.90, respectively (18). Although several studies have shown high correlation between various gated SPECT software programs in estimation of ventricular volume, since each program uses a different algorithm, their LV function data should be interchangeable only with caution. In the situation in which the same gated SPECT software application is used twice consecutively on the same patient, there is high correlation for both wall motion ($r = 0.95$) and systolic thickening ($r = 0.88$) (19).

Artifact Identification

Initially, the clinical role of gated SPECT lay in its ability to enhance artifact identification. Soft-tissue attenuation artifacts often appear as fixed defects and are difficult to differentiate from infarct, thereby reducing the test specificity of SPECT myocardial perfusion imaging. Gated acquisitions may help differentiate scar from artifact as fixed defects with decreased function likely represent a myocardial infarction (MI), whereas attenuation artifacts will have a fixed defect with normal or relatively normal wall motion. DePuey and Rozanski demonstrated that false-positive perfusion studies could be reduced from 14% to 3% by incorporating regional wall motion data in the interpretation of perfusion imaging (20). In women, where the false-positive rate of stress ECGs is relatively high and breast soft-tissue attenuation artifact is common, ECG gating was shown to further enhance the diagnostic specificity of ^{99m}Tc perfusion imaging from 84% to 94% (21). Subsequently, Smanio et al. demonstrated that the addition of gated SPECT for the assessment of regional systolic function reduces the degree of uncertainty in the interpretation of ^{99m}Tc-sestamibi perfusion studies. The number of "borderline-normal" or "borderline-abnormal" interpretations was significantly reduced. In patients with a low likelihood of CAD, the normalcy rate increased from 74% to 93% (Fig. 3). In patients with a high likelihood of CAD, the trend was also toward a higher number of unequivocally abnormal interpretations (22).

Diagnosis of CAD

The detection of CAD, particularly multivessel disease, is also enhanced by the capability to obtain functional information through gating. Though proven in various studies that SPECT myocardial perfusion imaging reliably detects

TABLE 1
Validation of Quantitative Measurements of LVEF by Different Software Programs for Gated Myocardial Perfusion SPECT

Authors	Year	Software	Gold standard	No. of patients	r	Isotope	Reference
Ioannidis et al.	2002	QGS	MRI		0.89		62
Baba et al.	2002	QGS	Contrast ventriculography	20	0.80	[201]Tl	63
Itti et al.	2001	QGS	ERNA	50	0.88–0.92	[201]Tl	64
Vourvouri et al.	2001	QGS	2D Echo	32	0.83		65
Higuchi et al.	2001	QGS	ERNA		0.90		66
Germano et al.	1995	QGS	FPRNA	65	0.90	^{99m}Tc-Sestamibi	10
Faber et al.	1999	ECTb	MRI	10	0.88	^{99m}Tc-Sestamibi	67
			FPRNA	79	0.82		
Vallejo et al.	2000	QGS	MRI	16 (canine)	0.51	^{99m}Tc-Sestamibi	13
Tadamura et al.	1999	QGS	MRI	20	0.92	[201]Tl	68
					0.94	^{99m}Tc-Sestamibi	
Yoshioka et al.	1999	QGS	FPRNA	21	0.91	^{99m}Tc-Tetrofosmin	69
					0.87		
Vallejo et al.	2000	QGS	FPRNA	400	0.66		14
Nichols et al.	1998		LV angiography	58	0.86	^{99m}Tc-Sestamibi	70
Nichols et al.	1997		FPRNA	22	0.90	^{99m}Tc-Sestamibi	71
Atsma et al.	2000	QGS	Contrast ventriculography	74	0.84	^{99m}Tc-Tetrofosmin	72
Wright et al.	2000	QGS	ERNA	70	0.70–0.71	[201]Tl (low dose)	73
Bax et al.	2000	QGS	MRI	22	0.90	^{99m}Tc-Tetrofosmin	74
Bavelaar-Croon et al.	2000	QGS	MRI	21	0.85		75
Cwajg et al.	2000		2D Echo	109	≥0.68	[201]Tl [99m]Tc	76
Nichols et al.	2000	SPECT EF QGS ECTb	2D Echo	33	0.92 overall 0.82 SPECT EF 0.75 QGS 0.72 ECTb		77
He et al.	1999		FPRNA	63	0.84–0.85	^{99m}Tc-Sestamibi [201]Tl	78
Vaduganathan et al.	1999		MRI	25	0.93	[99m]Tc	79
Inubushi et al.	1999	QGS	FPRNA	44	0.919	^{99m}Tc-Sestamibi	80
Nichols et al.	1996		ERNA	75	0.87	^{99m}Tc-Sestamibi	81
			FPRNA	65	0.87		
Nakajima et al.	2001	QGS ECTb 4D-MSPECT pFAST*	ERNA	30	0.82 QGS 0.78 ECTb 0.69 4D-MSPECT 0.84 pFAST*		18
Everaert et al.	1997	QGS Stanford	ERNA	40	0.89 QGS 0.93 SU	^{99m}Tc-Tetrofosmin	82
Chua et al.	2000	QGS	ERNA	62	0.94	[99m]Tc	83
Abe et al.	2000	QGS	Contrast ventriculography	229	0.78	^{99m}Tc-Tetrofosmin	84
Manrique et al.	2000	QGS	ERNA	55	0.71–0.94	[201]Tl	85
Williams and Taillon	1996	University of Chicago image inversion	FPRNA	38	0.83	^{99m}Tc-Sestamibi	86
			Contrast ventriculography	54	0.93		

* Perfusion and function analysis for gated SPECT.
ERNA = equilibrium radionuclide angiography; 2D Echo = 2-dimensional echocardiography; FPRNA = first-pass radionuclide angiography.

CAD, the question of underestimating ischemia in the case of multivessel disease or left main disease because of balanced global hypoperfusion comes into question. According to several reports, only 13%–50% of patients with 3-vessel CAD or left main disease actually have perfusion abnormalities in multiple territories (23–25). This could potentially lead clinicians to underestimate risk or incorrectly predict prognosis. Several studies have clearly demon-

TABLE 2
Assessment of LVEF by 5 Methods: Range and Lower Normal Limits

Method	Gated SPECT (QGS)	Echocardiography	MRI	Angiography	ERNA
Mean LVEF ± SD (%)	63 ± 10	60 ± 5	65 ± 5	67 ± 8	55 ± 7
Lower normal limit (%)	44	48	57	51	43

ERNA = equilibrium radionuclide angiography.
Data are from (87).

strated the incremental value of using both functional and perfusion data in detecting multivessel disease or high-grade stenoses over perfusion data alone, although there are some conflicting data on sensitivity and specificity. Sharir et al. examined a population of 99 patients who underwent dual-isotope resting ^{201}Tl/exercise gated ^{99m}Tc-sestamibi SPECT with normal resting perfusion. Multivariate regression analysis showed that both extensive perfusion abnormalities and the presence of wall motion abnormalities in multiple territories were independent predictors of severe multivessel CAD but that the addition of wall motion variables to perfusion data resulted in a significant increase in the global χ^2 for predicting severe proximal left anterior descending as well as severe multivessel CAD. For perfusion alone, sensitivity was 49%, whereas combined perfusion and wall motion abnormality yielded a sensitivity of 82% (26). Lima et al. demonstrated that evaluation of segmental poststress thickening abnormalities on gated SPECT better identified patients with severe angiographic triple-vessel disease. The addition of functional data derived from gated SPECT to perfusion data improved detection of multivessel disease from 46% to 60% ($P < 0.05$) and triple-vessel disease from 10% to 25% ($P < 0.001$) (27).

The use of rest and stress LVEF may also assist in the detection of multivessel coronary disease, as demonstrated in a study by Yamagishi et al., wherein the combination of perfusion data and worsening of the LVEF significantly increased sensitivity in detecting multivessel CAD over ^{201}Tl perfusion defects or rest LVEF and postexercise LVEF alone (43.3% vs. 26.9%, 25.4%, and 25.4%, respectively). In this study, though sensitivity increased, there was also a significant decrease in specificity, although this remained

TABLE 3
Comparison of 2 Software Programs for Quantitation of LV Function and Volumes in Normal or Low-Risk Subjects

Parameter	QGS	ECTb
EF (%)	62 ± 9	67 ± 8
EDV (mL)	84 ± 26	105 ± 33
ESV (mL)	33 ± 17	35 ± 17

EDV = end-diastolic volume; ESV = end-systolic volume.
Values are mean ± SD. Data are from (16).

acceptable at approximately 90% (28). Another study sought to correlate the degree of angiographic stenosis with the presence of regional wall motion abnormalities (RWMA) on exercise stress/rest gated ^{99m}Tc SPECT studies (29). Reversible RWMA were found to be highly specific for angiographic stenoses of >70%, both overall and for specific vascular territories (94%–100%). Furthermore, when patients were stratified according to the severity of angiographic stenoses (50%–79% and 80%–99%), the presence of reversible RWMA distinguished a higher angiographic severity with positive predictive values between 77% and 88% for specific vascular territories. Of note, these improvements in specificity were at the expense of sensitivity, which were much less compared with perfusion alone (53% for reversible RWMA vs. 89% for perfusion alone).

In addition, diastolic dysfunction on poststress gated SPECT imaging has been shown as an indicator of CAD (30,31). Poststress diastolic dysfunction is though to be a manifestation of myocardial ischemia causing increased early filling pressures. Indices of diastolic dysfunction include peak filling rate (PFR) and time to PFR of the left ventricle. PFR computed by gated SPECT using 8 frames per R–R interval has a poor correlation of 0.51 compared with equilibrium radionuclide angiography (ERNA) (30). The correlation improves if more frames are used. Paul et al. measured diastolic parameters through gated SPECT and found that PFR was lower in post-stress patients with severe reversible scintigraphic perfusion defects compared with rest images (2.23 s^{-1} and 2.94 s^{-1}; $P < 0.005$) (31). Yet, other parameters such as LVEF, end-diastolic volume, and end-systolic volume were also all significantly lower in the same patient groups. Although gated SPECT allows observations of diastolic dysfunction, this parameter does not currently have incremental diagnostic value over existing standards.

Prognosis and Risk Stratification

As with the case with perfusion imaging in general, gated SPECT imaging has also found an important role in the risk assessment of patients with known or suspected CAD. This is not surprising, given the well-recognized prognostic role of LV function with regard to long-term survival, as has been shown using a variety of techniques for LV functional assessment. Among a large series of 1,690 consecutive patients who underwent dual-isotope gated SPECT imaging, those whose EFs were <45% were associated with
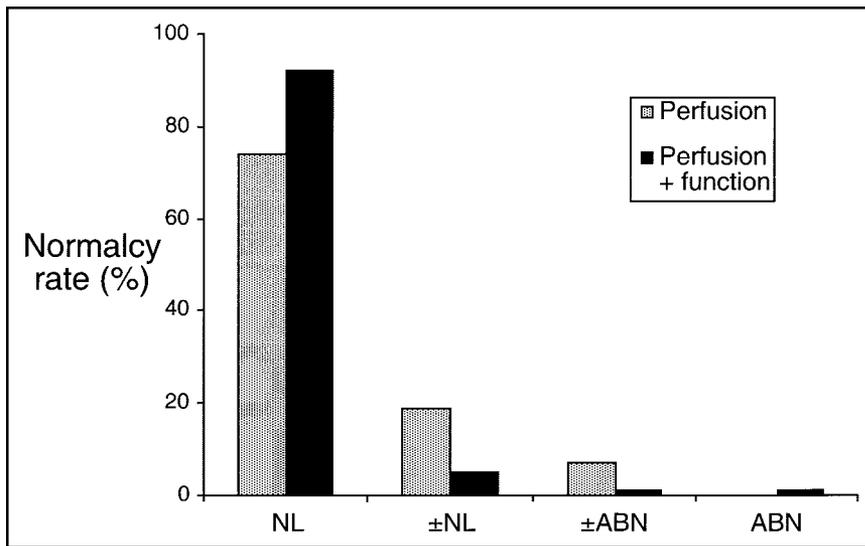
FIGURE 3. In patients with low likelihood of CAD, normalcy rate increased from 74% to 93%, and borderline readings decreased from 32% to 10% when functional data from gating are incorporated into study interpretation. NL = normal; ±NL = borderline normal; ±ABN = borderline abnormal; ABN = abnormal. (Modified and reprinted with permission of (22).)

reduced survival, irrespective of the perfusion defect size or severity. Additionally, those patients with normal end-systolic volumes of <70 mL or an EF of >45% had a very low cardiac mortality rate, despite severe perfusion abnormalities (Fig. 4) (32). This group also examined the relative value of perfusion and function in the risk stratification in 2,686 patients into low-, intermediate-, and high-risk categories for cardiac death and MI (33). LVEF was most predictive of death and the amount of ischemia (summed difference score on perfusion imaging) was the best predictor of nonfatal MI. Functional information was found to be of incremental value in the prediction of cardiac death beyond the perfusion imaging parameters. Interestingly, the presence of ischemia did not influence prognosis in patients with LVEFs of <30%, due to the already high mortality rate.

After an acute MI, LV function has long been a key determinant for survival. Recently, a study of 128 postinfarct survivors confirmed the value of gated SPECT imaging for risk stratification in post-MI patients, as an LVEF of <40% with this method was found to increase the risk of a subsequent cardiac event by almost 3-fold

(34). Interestingly, neither the presence of a fixed or reversible defect had independent predictive value in this study, although the latter finding may be a result of the censoring of high-risk patients who underwent early revascularization.

ECG-gated SPECT is also commonly used for preoperative risk stratification for noncardiac surgery. A study done by Hashimoto et al. assessed the relationship between perioperative cardiac events and various predictors, including clinical factors, perfusion, and functional assessment using the QGS program to assess LV function and estimate regional wall motion. Multivariate analysis demonstrated functional analysis to be an independent predictor of perioperative cardiac events. Function and wall motion assessment proved especially useful in patients with normal perfusion scans (35).

Ischemic Cardiomyopathy and Viability Determination

In patients with dilated cardiomyopathy, the distinction between an ischemic and nonischemic etiology has clinical relevance and may greatly affect management decisions.
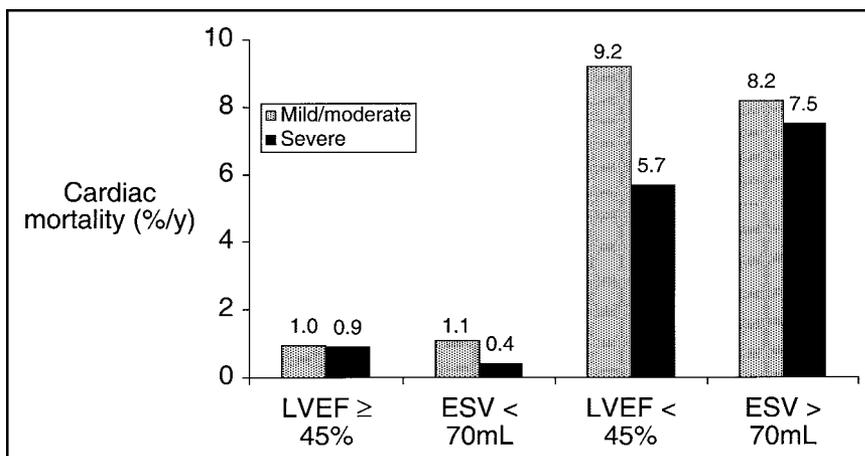
FIGURE 4. Annual cardiac death rates stratified by LV volume and EF. Patients with LVEF of ≥45% or end-systolic volume (ESV) of <70 mL have low mortality rate regardless of severity of perfusion defects. Similar findings are noted for patients with low EF (<45%). (Modified and reprinted with permission of (32).)

Danias et al. demonstrated that ischemic and nonischemic cardiomyopathy can be reliably distinguished from each other noninvasively with gated SPECT imaging. Summed stress scores and the amount of regional variability in function are greater in ischemic cardiomyopathies than in nonischemic cardiomyopathies and this is an important parameter in distinguishing between these broad categories (*36*).

In patients with CAD and LV dysfunction, the issue of myocardial viability is often highly relevant in the decision-making process regarding revascularization. Several modalities have been studied and used for the assessment of viability, including ^{201}Tl stress–redistribution, rest–redistribution, or reinjection scintigraphy with either ^{201}Tl or ^{99m}Tc-sestamibi (*37–44*), low-dose dobutamine echocardiography (*45*), contrast-enhanced MRI, and ^{18}F-FDG PET (*46–48*). Although ^{18}F-FDG PET is widely considered the gold standard, with sensitivities ranging from 71% to 100%, a recent meta-analysis by Bax et al. showed no clear advantage of one technique over another (*49*). The principal limitation of ^{18}F-FDG PET is the fairly high cost of the equipment, thus limiting its availability in all medical centers. Other modalities are usually used to determine viability before using PET. The addition of functional information provided by ECG gating is thought to have an incremental value for the prediction of viability over perfusion studies alone. In a small study by Levine et al., perfusion and wall motion combined significantly improved the sensitivity and accuracy for the prediction of viability, as defined by an ≥20% improvement in perfusion or function when compared with perfusion imaging alone (95% vs. 86% sensitivity, 91% vs. 85% accuracy). Specificity remained the same at 55% (*50*). In another trial, gated SPECT ^{99m}Tc-tetrofosmin assessment of wall thickening (rather than wall motion) combined with perfusion data increased the sensitivity for assessment of viability, using ^{18}F-FDG PET as the gold standard, from 79% to 85% but decreased the specificity from 79% to 56% (*51*). Other investigators have demonstrated that the assessment of wall thickening on gated SPECT may have its impact on improved specificity with regard to postrevascularization recovery of regional function, depending on tracer

activity on perfusion. When segments with >50% tetrofosmin activity have detectable wall thickening, there is a higher likelihood of functional improvement when compared with segments with no contractile function; however, in segments with <50% tracer activity, there was no significant difference (*52*). It is important to note that though these particular studies demonstrate an advantage of combined function and perfusion assessment, the actual sensitivities and specificities are not significantly different from the weighted mean sensitivities and specificities of the meta-analysis (*49*), and most of these studies have small populations and varied study designs.

Low-dose dobutamine has been used successfully to demonstrate contractile reserve for many imaging modalities, including echocardiography (*45*), radionuclide angiography (*53*), MRI (*54*), and, most recently, gated SPECT imaging (*55–57*). Gated SPECT has shown the increase in contractile function that accompanies low-dose dobutamine, with the LVEF increasing from 14% to 46% at baseline to 23%–71% and 25%–85% at 5 and 10 µg/kg/min of dobutamine infusion (*58*). Viability measurements based on contractile reserve have higher specificity than perfusion imaging overall; this finding has been confirmed for gated SPECT imaging as well. In a study by Leoncini et al., the use of low-dose dobutamine gated SPECT significantly improved the specificity and overall accuracy for predicting functional recovery after coronary revascularization. The visual assessment of regional function after low-dose dobutamine was especially useful for hypokinetic segments, where the specificity for postrevascularization functional improvement increased to 94% as compared with 23% for perfusion imaging. However, the sensitivity for prediction of improvement in akinetic regions was inferior with dobutamine gated SPECT compared with quantitative perfusion imaging (Fig. 5). This study suggests a combined approach, using data from both contractile reserve and quantitative tracer activity (*55*). In the same series, they also assessed global LV function with low-dose dobutamine infusion as a predictor of postrevascularization functional improvement and found that gated SPECT had a predictive

FIGURE 5. Prediction of functional recovery with nitrate-enhanced ^{99m}Tc-sestamibi dobutamine gated imaging. For all asynergic segments, using combination of tracer activity and contractile reserve (black bars; combined) improved specificity and overall accuracy significantly when compared with perfusion quantification alone (stippled; perfusion). Sensitivity was not altered significantly with combined approach but was higher than using contractile reserve alone (hatched bars; CR). (Modified and reprinted with permission of (*55*).)
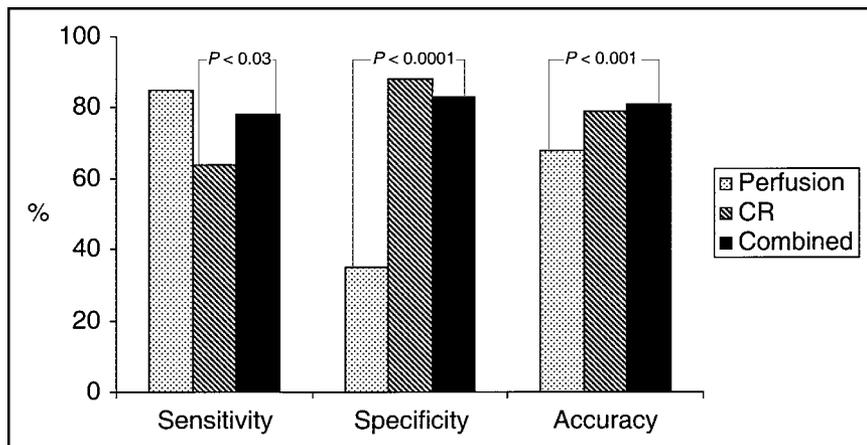
value similar to that of echocardiography (*59*). An increase in the LVEF of >5 EF units was found to be a good predictor of improvement in EF after revascularization (*56*). Again, it is important to note that the main limitation of these studies, as well as other studies looking at functional recovery, is the small population size.

Other Diagnostic Applications

Aside from its well-studied applications in determining systolic function, attempts have been made to expand the clinical applications of ECG-gated SPECT imaging. Echocardiography has been the most commonly used method for assessing LV diastolic function. Radionuclide techniques, specifically equilibrium radionuclide angiography, have more recently been applied as well. Several diastolic parameters have been used, including PFR, which measures the most rapid change in ventricular counts in early-to-mid diastole, the time to peak filling (the time interval from the nadir of LV counts to the moment of the PFR), and the filling fraction (percentage of filling that has occurred at one third, one half, and two thirds of diastole). A small study has applied ECG-gated SPECT to assess the same diastolic parameters (specifically PFR), and found a close correlation between PFR generated by and gated SPECT using a higher frame rate of 32 frames per cardiac cycle (the most commonly used frame rate is 8 frames per cycle) (*30*). In another study, the diastolic parameters of a small group of patients with systemic sclerosis were examined using gated SPECT, and again a closer correlation and higher accuracy was found when using 16 frames per cycle (*60*). Both of these studies used 3-detector SPECT systems. These findings are consistent with the concept that accurate assessment of diastolic function by radionuclide techniques requires a high temporal resolution and reliability of the diastolic filling phase of the time–activity curve. In addition, the fidelity of the diastolic filling phase of the time–activity curve is also affected by the traditional problems associated with gating based on R–R interval, such as arrhythmias or premature ventricular contractions, and thus alternative acquisition modes (such as list mode acquisition) or "bad-beat rejection" filters have to be applied. These technical considerations have currently limited the usefulness of gated SPECT for assessment of diastolic function.

Another potential underdeveloped application of gated SPECT is the assessment of right ventricular size and wall motion. In a case report, an unsuspected pulmonary embolism was diagnosed when unexplained right ventricular dilatation and hypokinesis was detected on gated SPECT imaging (*61*). More studies are definitely warranted for this application, but routine examination of right ventricular size and motion when interpreting studies may provide additional clinical information.

CONCLUSION

Gated SPECT imaging has attained widespread use because it provides a wealth of additional information that is useful not only to the reader interpreting myocardial perfusion imaging studies but also to the referring clinician. Although the major benefit of perfusion imaging has been its ability to improve artifact recognition, the use of functional information also improves the detection of severe and extensive coronary disease, provides independent and incremental prognostic information, and aids in the evaluation of myocardial viability. Novel applications have also been described and unique values of this technique will undoubtedly continue to evolve.

REFERENCES

1. Bateman TM, Berman DS, Heller GV, et al. American Society of Nuclear Cardiology position statement on electrocardiographic gating of myocardial perfusion SPECT scintigrams. *J Nucl Cardiol.* 1999;6:470–471.
2. Anonymous. Imaging guidelines for nuclear cardiology procedures. Part 2. American Society of Nuclear Cardiology. *J Nucl Cardiol.* 1999;6:G47–G84.
3. Hida S, Chikamori T, Usui Y, Yanagisawa H, Morishima T, Yamashina A. Effect of percutaneous coronary angioplasty on myocardial perfusion, function, and wall thickness as assessed by quantitative gated single-proton emission computed tomography. *Am J Cardiol.* 2003;91:591–594.
4. Germano G, Nichols K, Cullom SJ. Gated perfusion SPECT: technical considerations. In: DePuey EG, Garcia EV, Berman DS, eds. *Cardiac SPECT Imaging.* 2nd ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2001:103–115.
5. Cullom SJ, Case JA, Bateman TM. Electrocardiographically gated myocardial perfusion SPECT: technical principles and quality control considerations. *J Nucl Cardiol.* 1998;5:418–425.
6. Nichols K, Dorbala S, DePuey EG, Yao SS, Sharma A, Rozanski A. Influence of arrhythmias on gated SPECT myocardial perfusion and function quantification. *J Nucl Med.* 1999;40:924–934.
7. Hyun IY, Kwan J, Park KS, Lee WH. Reproducibility of Tl-201 and Tc-99m sestamibi gated myocardial perfusion SPECT measurement of myocardial function. *J Nucl Cardiol.* 2001;8:182–187.
8. Vellejo E, Chayo H, Plancarte G, Victoria D, Bialostozky D. Variability of serial same-day left ventricular ejection fraction using quantitative gated SPECT. *J Nucl Cardiol.* 2002;9:377–384.
9. Johnson LL, Verdesca SA, Aude WY, et al. Postischemic stunning can affect left ventricular ejection fraction and regional wall motion on post-stress gated sestamibi tomograms. *J Am Coll Cardiol.* 1997;30:1641–1648.
10. Germano G, Kiat H, Kavanagh PB, et al. Automatic quantification of ejection fraction from gated myocardial perfusion SPECT. *J Nucl Med.* 1995;36:2138–2147.
11. Germano G, Erel J, Lewin H, Kavanagh PB, Berman DS. Automatic quantitation of regional myocardial wall motion and thickening from gated technetium-99m sestamibi myocardial perfusion single-photon emission computed tomography. *J Am Coll Cardiol.* 1997;30:1360–1367.
12. Nichols K, DePuey EG. Regional and global ventricular function analysis with SPECT perfusion imaging. In: Zaret BL, Beller GA, eds. *Nuclear Cardiology: State of the Art and Future Directions.* 2nd ed. St. Louis, MO: Mosby; 1999: 216–234.
13. Vallejo E, Dione DP, Bruni WL, et al. Reproducibility and accuracy of gated SPECT for determination of left ventricular volumes and ejection fraction: experimental validation using MRI. *J Nucl Med.* 2000;41:874–882.
14. Vallejo E, Dione DP, Sinusas AJ, Wackers FJ. Assessment of left ventricular ejection fraction with quantitative gated SPECT: accuracy and correlation with first-pass radionuclide angiography. *J Nucl Cardiol.* 2000;7:461–470.
15. Nakajima K, Taki J, Higuchi T, et al. Gated SPECT quantification of small hearts: mathematical simulation and clinical application. *Eur J Nucl Med.* 2000;27: 1372–1379.
16. Nichols K, Santana CA, Folks R, et al. Comparison between ECTb and QGS for assessment of left ventricular function from gated myocardial perfusion SPECT. *J Nucl Cardiol.* 2002;9:285–293.
17. Lum DP, Coel MN. Comparison of automatic quantification software for the measurement of ventricular volume and ejection fraction in gated myocardial perfusion SPECT. *Nucl Med Commun.* 2003;24:259–266.
18. Nakajima K, Higuchi T, Taki J, Kawano M, Tonami N. Accuracy of ventricular volume and ejection fraction measured by gated myocardial SPECT: comparison of 4 software programs. *J Nucl Med.* 2001;42:1571–1578.
19. Paeng JC, Lee DS, Cheon GJ, Lee MM, Cung JK, Lee MC. Reproducibility of an automatic quantitation of regional myocardial wall motion and systolic thick-

ening on gated ^{99m}Tc-sestamibi myocardial SPECT. *J Nucl Med.* 2001;42:695–700.

20. DePuey EG, Rozanski A. Using gated technetium-99m-sestamibi SPECT to characterize fixed myocardial defects as infarct or artifact. *J Nucl Med.* 1995;36:952–955.

21. Taillefer R, DePuey EG, Udelson JE, Beller GA, Latour Y, Reeves F. Comparative diagnostic accuracy of Tl-201 and Tc-99m sestamibi SPECT imaging (perfusion and ECG-gated SPECT) in detecting coronary artery disease in women. *J Am Coll Cardiol.* 1997;29:69–77.

22. Smanio PE, Watson DD, Segalla DL, Vinson EL, Smith WH, Beller GA. Value of gating of technetium-99m sestamibi single-photon emission computed tomographic imaging. *J Am Coll Cardiol.* 1997;30:1687–1692.

23. Chae SC, Heo J, Iskandrian AS, Wasserleben V, Cave V. Identification of extensive coronary artery disease in women by exercise single-photon emission computed tomographic (SPECT) thallium imaging. *J Am Coll Cardiol.* 1993;21:1305–1311.

24. Rehn T, Griffith LS, Achuff SC, et al. Exercise thallium-201 myocardial imaging in left main coronary artery disease: sensitive but not specific. *Am J Cardiol.* 1981;48:217–223.

25. Christian TF, Miller TD, Bailey KR, Gibbons RJ. Noninvasive identification of severe coronary artery disease using exercise tomographic thallium-201 imaging. *Am J Cardiol.* 1992;70:14–20.

26. Sharir T, Bacher-Stier C, Dhar S, et al. Identification of severe and extensive coronary artery disease by postexercise regional wall motion abnormalities in Tc-99m sestamibi gated single-photon emission computed tomography. *Am J Cardiol.* 2000;86:1171–1175.

27. Lima RS, Watson DD, Goode AR, et al. Incremental value of combined perfusion and function over perfusion alone by gated SPECT myocardial perfusion imaging for detection of severe three-vessel coronary artery disease. *J Am Coll Cardiol.* 2003;42:64–70.

28. Yamagishi H, Shirai N, Yoshiyama M, et al. Incremental value of left ventricular ejection fraction for detection of multivessel coronary artery disease in exercise: [201]Tl gated myocardial perfusion imaging. *J Nucl Med.* 2002;43:131–139.

29. Emmett L, Iwanochko RM, Freeman MR, Barolet A, Lee DS, Husain M. Reversible regional wall motion abnormalities on exercise technetium-99m-gated cardiac single photon emission computed tomography predict high-grade angiographic stenoses. *J Am Coll Cardiol.* 2002;39:991–998.

30. Kumita S, Cho K, Nakajo H, et al. Assessment of left ventricular diastolic function with electrography-gated myocardial perfusion SPECT: comparison with multigated equilibrium radionuclide angiography. *J Nucl Cardiol.* 2001;8:568–574.

31. Paul AK, Kusuoka H, Hasegawa T, Makikawa M, Nishimura T. Prolonged diastolic dysfunction following exercise induced ischaemia: a gated myocardial perfusion SPECT study. *Nucl Med Commun.* 2002;23:1129–1136.

32. Sharir T, Germano G, Kavanagh PB, et al. Incremental prognostic value of post-stress left ventricular ejection fraction and volume by gated myocardial perfusion single photon emission computed tomography. *Circulation.* 1999;100:1035–1042.

33. Sharir T, Germano G, Kang X, et al. Prediction of myocardial infarction versus cardiac death by gated myocardial perfusion SPECT: risk stratification by the amount of stress-induced ischemia and the poststress ejection fraction. *J Nucl Med.* 2001;42:831–837.

34. Kroll D, Farah W, McKendall GR, Reinert SE, Johnson LL. Prognostic value of stress-gated Tc-99m sestamibi SPECT after acute myocardial infarction. *Am J Cardiol.* 2001;87:381–386.

35. Hashimoto J, Suzuki T, Nakahara T, Kosuda S, Kubo A. Preoperative risk stratification using stress myocardial perfusion scintigraphy with electrocardiographic gating. *J Nucl Med.* 2003;44:385–390.

36. Danias PG, Ahlberg AW, Clark BA 3rd, et al. Combined assessment of myocardial perfusion and left ventricular function with exercise technetium-99m sestamibi gated single-photon emission computed tomography can differentiate between ischemic and nonischemic dilated cardiomyopathy. *Am J Cardiol.* 1998;82:1253–1258.

37. Inglese E, Brambilla M, Dondi M, et al. Assessment of myocardial viability after thallium-201 reinjection or rest-redistribution imaging: a multicenter study—the Italian Group of Nuclear Cardiology. *J Nucl Med.* 1995;36:555–563.

38. Bonow RO, Dilsizian V, Cuocolo A, Bacharach SL. Identification of viable myocardium in patients with chronic coronary artery disease and left ventricular dysfunction: comparison of thallium scintigraphy with reinjection and PET imaging with ^{18}F-fluorodeoxyglucose. *Circulation.* 1991;83:26–37.

39. Udelson JE, Coleman PS, Metherall J, et al. Predicting recovery of severe regional ventricular dysfunction: comparison of resting scintigraphy with ^{201}Tl and ^{99m}Tc-sestamibi. *Circulation.* 1994;89:2552–2561.

40. Ragosta M, Beller GA, Watson DD, Kaul S, Gimple LW. Quantitative planar rest-redistribution ^{201}Tl imaging in detection of myocardial viability and prediction of improvement in left ventricular function after coronary bypass surgery in patients with severely depressed left ventricular function. *Circulation.* 1993;87:1630–1641.

41. Maes AF, Borgers M, Flameng W, et al. Assessment of myocardial viability in chronic coronary artery disease using technetium-99m sestamibi SPECT: correlation with histologic and positron emission tomographic studies and functional follow-up. *J Am Coll Cardiol.* 1997;29:62–68.

42. Sinusas AJ, Bergin JD, Edwards NC, et al. Redistribution of ^{99m}Tc-sestamibi and ^{201}Tl in the presence of a severe coronary artery stenosis. *Circulation.* 1994;89:2332–2341.

43. Galassi AR, Centamore G, Fiscella A, et al. Comparison of rest-redistribution thallium-201 imaging and reinjection after stress-redistribution for the assessment of myocardial viability in patients with left ventricular dysfunction secondary to coronary artery disease. *Am J Cardiol.* 1995;75:436–442.

44. Dilsizian V, Smeltzer WR, Freedman NM, Dextras R, Bonow RO. Thallium reinjection after stress-redistribution imaging: does 24-hour delayed imaging after reinjection enhance detection of viable myocardium? *Circulation.* 1991;83:1247–1255.

45. Afridi I, Kleiman NS, Raizner AE, Zoghbi WA. Dobutamine echocardiography in myocardial hibernation: optimal dose and accuracy in predicting recovery of ventricular function after coronary angioplasty. *Circulation.* 1995;91:663–670.

46. Tamaki N, Yonekura Y, Yamashita K, et al. Positron emission tomography using fluorine-18 deoxyglucose in evaluation of coronary artery bypass grafting. *Am J Cardiol.* 1989;64:860–865.

47. Schelbert HR. Positron emission tomography for the assessment of myocardial viability. *Circulation.* 1991;84(3 suppl):I122–I131.

48. Gould KL. Clinical cardiac positron emission tomography: state of the art. *Circulation.* 1991;84(3 suppl):I22–I36.

49. Bax JJ, Wijns W, Cornel JH, Visser FC, Boersma E, Fioretti PM. Accuracy of currently available techniques for prediction of functional recovery after revascularization in patients with left ventricular dysfunction due to chronic coronary artery disease: comparison of pooled data. *J Am Coll Cardiol.* 1997;30:1451–1460.

50. Levine MG, McGill CC, Ahlberg AW, et al. Functional assessment with electrocardiographic gated single-photon emission computed tomography improves the ability of technetium-99m sestamibi myocardial perfusion imaging to predict myocardial viability in patients undergoing revascularization. *Am J Cardiol.* 1999;83:1–5.

51. Maruyama A, Hasegawa S, Paul AK, et al. Myocardial viability assessment with gated SPECT Tc-99m tetrofosmin % wall thickening: comparison with F-18 FDG-PET. *Ann Nucl Med.* 2002;16:25–32.

52. Stollfuss JC, Haas F, Matsunari I, et al. ^{99m}Tc-Tetrofosmin SPECT for prediction of functional recovery defined by MRI in patients with severe left ventricular dysfunction: additional value of gated SPECT. *J Nucl Med.* 1999;40:1824–1831.

53. Zafrir N, Vidne B, Sulkes J, Sclarovsky S. Usefulness of dobutamine radionuclide ventriculography for prediction of left ventricular function improvement after coronary artery bypass grafting for ischemic cardiomyopathy. *Am J Cardiol.* 1999;83:691–695.

54. Baer FM, Voth E, Schneider CA, Theissen P, Schicha H, Sechtem U. Comparison of low-dose dobutamine-gradient-echo magnetic resonance imaging and positron emission tomography with [^{18}F]fluorodeoxyglucose in patients with chronic coronary artery disease: a functional and morphological approach to the detection of residual myocardial viability. *Circulation.* 1995;91:1006–1015.

55. Leoncini M, Marcucci G, Sciagra R, et al. 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. *Am J Cardiol.* 2001;87:1346–1350.

56. Leoncini M, Sciagra R, Maioli M, et al. Usefulness of dobutamine Tc-99m sestamibi-gated single-photon emission computed tomography for prediction of left ventricular ejection fraction outcome after coronary revascularization for ischemic cardiomyopathy. *Am J Cardiol.* 2002;89:817–821.

57. Yoshinaga K, Morita K, Yamada S, et al. Low-dose dobutamine electrocardiograph-gated myocardial SPECT for identifying viable myocardium: comparison with dobutamine stress echocardiography and PET. *J Nucl Med.* 2001;42:838–844.

58. Everaert H, Vanhove C, Franken P. Effects of low-dose dobutamine of left ventricular function in normal subjects as assessed by gated single-photon emission tomography myocardial perfusion studies. *Eur J Nucl Med.* 1999;26:1298–1303.

59. Leoncini M, Marcucci G, Sciagra R, et al. Comparison of baseline and low-dose dobutamine technetium-99m sestamibi scintigraphy with low-dose dobutamine

echocardiography for predicting function recovery after revascularization. *Am J Cardiol.* 2000;86:153–157.

60. Nakajima K, Taki J, Kawano M, et al. Diastolic dysfunction in patients with systemic sclerosis detected by gated myocardial perfusion SPECT: an early sign of cardiac involvement. *J Nucl Med.* 2001;42:183–188.

61. Soudry G, Dibos PE. Gated myocardial perfusion scan leading to diagnosis of unsuspected massive pulmonary embolism [letter]. *Ann Intern Med.* 2000;132:845.

62. Ioannidis JP, Trikalinos TA, Danias PG. Electrocardiogram-gated single-photon emission computed tomography versus cardiac magnetic resonance imaging for the assessment of left ventricular volumes and ejection fraction: a meta-analysis. *J Am Coll Cardiol.* 2002;39:2059–2068.

63. Baba A, Hano T, Ohmori H, et al. Assessment of left ventricular function by thallium-201 quantitative gated cardiac SPECT. *Kaku Igaku.* 2002;39:21–27.

64. Itti E, Rosso J, Damien P, Auffret M, Thirion JP, Meignan M. Assessment of ejection fraction with Tl-201 gated SPECT in myocardial infarction: precision in a rest-redistribution study and accuracy versus planar angiography. *J Nucl Cardiol.* 2001;8:31–39.

65. Vourvouri EC, Poldermans D, Bax JJ, et al. Evaluation of left ventricular function and volumes in patients with ischaemic cardiomyopathy: gated single-photon emission computed tomography versus two-dimensional echocardiography. *Eur J Nucl Med.* 2001;28:1610–1615.

66. Higuchi T, Nakajima K, Taki J, Kinuya S, Bunko H, Tonami N. Assessment of left ventricular systolic and diastolic function based on the edge detection method with myocardial ECG-gated SPET. *Eur J Nucl Med.* 2001;28:1512–1516.

67. Faber TL, Cooke CD, Folks RD, et al. Left ventricular function and perfusion from gated SPECT perfusion images: an integrated method. *J Nucl Med.* 1999;40:650–659.

68. Tadamura E, Kudoh T, Motooka M, et al. Use of technetium-99m sestamibi ECG-gated single-photon emission tomography for the evaluation of left ventricular function following coronary artery bypass graft: comparison with three-dimensional magnetic resonance imaging. *Eur J Nucl Med.* 1999;26:705–712.

69. Yoshioka J, Hasegawa S, Yamaguchi H, Tokita N, Paul AK, Xiulu M. Left ventricular volumes and ejection fraction calculated from quantitative electrocar-diographic-gated ^{99m}Tc-tetrofosmin myocardial SPECT. *J Nucl Med.* 1999;40:1693–1698.

70. Nichols K, Tamis J, DePuey EG, Mieres J, Malhotra S, Rozanski A. Relationship of gated SPECT ventricular function parameters to angiographic measurements. *J Nucl Cardiol.* 1998;5:295–303.

71. Nichols K, DePuey EG, Rozanski A, Salensky H, Friedman MI. Image enhancement of severely hypoperfused myocardia for computation of tomographic ejection fraction. *J Nucl Med.* 1997;38:1411–1417.

72. Atsma DE, Bavelaar-Croon CD, Germano G, et al. Good correlation between gated single photon emission computed myocardial tomography and contrast ventriculography in the assessment of global and regional left ventricular function. *Int J Card Imaging.* 2000;16:447–453.

73. Wright GA, McDade M, Keeble W, Martin W, Hutton I. Quantitative gated SPECT myocardial perfusion imaging with ^{201}Tl: an assessment of the limitations. *Nucl Med Commun.* 2000;21:1147–1151.

74. Bax JJ, Lamb H, Dibbets P, et al. Comparison of gated single-photon emission computed tomography with magnetic resonance imaging for evaluation of left ventricular function in ischemic cardiomyopathy. *Am J Cardiol.* 2000;86:1299–1305.

75. Bavelaar-Croon CD, Kayser HW, van der Wall EE, et al. Left ventricular function: correlation of quantitative gated SPECT and MR imaging over a wide range of values. *Radiology.* 2000;217:572–575.

76. Cwajg E, Cwajg J, Keng F, He ZX, Nagueh S, Verani MS. Comparison of global and regional left ventricular function assessed by gated-SPECT and 2-D echo-cardiography. *Rev Port Cardiol.* 2000;19(suppl 1):I39–I46.

77. Nichols K, Lefkowitz D, Faber T, et al. Echocardiographic validation of gated SPECT ventricular function measurements. *J Nucl Med.* 2000;41:1308–1314.

78. He ZX, Cwajg E, Preslar JS, Mahmarian JJ, Verani MS. Accuracy of left ventricular ejection fraction determined by gated myocardial perfusion SPECT with Tl-201 and Tc-99m sestamibi: comparison with first-pass radionuclide angiography. *J Nucl Cardiol.* 1999;6:412–417.

79. Vaduganathan P, He ZX, Vick GW 3rd, Mahmarian JJ, Verani MS. Evaluation of left ventricular wall motion, volumes, and ejection fraction by gated myocardial tomography with technetium 99m-labeled tetrofosmin: a comparison with cine magnetic resonance imaging. *J Nucl Cardiol.* 1999;6:3–10.

80. Inubushi M, Tadamura E, Kudoh T, et al. Simultaneous assessment of myocardial free fatty acid utilization and left ventricular function using ^{123}I-BMIPP-gated SPECT. *J Nucl Med.* 1999;40:1840–1847.

81. Nichols K, DePuey EG, Rozanski A. Automation of gated tomographic left ventricular ejection fraction. *J Nucl Cardiol.* 1996;3:475–482.

82. Everaert H, Bossuyt A, Franken PR. Left ventricular ejection fraction and volumes from gated single photon emission tomographic myocardial perfusion images: comparison between two algorithms working in three-dimensional space. *J Nucl Cardiol.* 1997;4:472–476.

83. Chua T, Yin LC, Thiang TH, Choo TB, Ping DZ, Leng LY. Accuracy of the automated assessment of left ventricular function with gated perfusion SPECT in the presence of perfusion defects and left ventricular dysfunction: correlation with equilibrium radionuclide ventriculography and echocardiography. *J Nucl Cardiol.* 2000;7:301–311.

84. Abe M, Kazatani Y, Fukuda H, Tatsuno H, Habara H, Shinbata H. Left ventricular volumes, ejection fraction, and regional wall motion calculated with gated technetium-99m tetrofosmin SPECT in reperfused acute myocardial infarction at super-acute phase: comparison with left ventriculography. *J Nucl Cardiol.* 2000;7:569–574.

85. Manrique A, Koning R, Cribier A, Vera P. Effect of temporal sampling on evaluation of left ventricular ejection fraction by means of thallium-201 gated SPET: comparison of 16- and 8-interval gating, with reference to equilibrium radionuclide angiography. *Eur J Nucl Med.* 2000;27:694–699.

86. Williams KA, Taillon LA. Left ventricular function in patients with coronary artery disease assessed by gated tomographic myocardial perfusion images: comparison with assessment by contrast ventriculography and first-pass radionuclide angiography. *J Am Coll Cardiol.* 1996;27:173–181.

87. Rozanski A, Nichols K, Yao SS, Malholtra S, Cohen R, DePuey EG. Development and application of normal limits for left ventricular ejection fraction and volume measurements from ^{99m}Tc-sestamibi myocardial perfusion gates SPECT. *J Nucl Med.* 2000;41:1445–1450.