

Gated Myocardial Perfusion Tomography for the Assessment of Left Ventricular Function and Volumes: Comparison with Echocardiography

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The purpose of this study was to evaluate left ventricular volumes and function by gated SPECT using different tracers and protocols in comparison with quantitative echocardiography. Gated myocardial perfusion scintigraphy permits simultaneous assessment of left ventricular perfusion, function and volumes. Information is scanty regarding the accuracy of absolute left ventricular volumes measurements by this technique. **Methods:** We performed gated SPECT and echocardiography within 15 d of each other in 109 consecutive patients (53 men, 56 women; mean age 63 ± 14 y). Gated tomographic data, including left ventricular volumes and ejection fraction, were processed using an automatic algorithm, whereas echocardiography used standard techniques. **Results:** The correlations between gated tomography and echocardiography with respect to end-diastolic volume, end-systolic volume and left ventricular ejection fraction were good to excellent (all $P < 0.001$, r values ≥ 0.68), regardless of the use of poststress or rest/redistribution images, ^{201}Tl or $^{99\text{m}}\text{Tc}$ tracers. End-systolic volume was similar with gated tomography and echocardiography ($P = \text{ns}$), but end-diastolic volume and left ventricular ejection fraction were significantly higher with echocardiography ($P \leq 0.05$). **Conclusion:** Quantitative gated tomography, using either ^{201}Tl or $^{99\text{m}}\text{Tc}$ tracers, has a good correlation with echocardiography for the assessment of left ventricular volumes and ejection fraction. These results support the clinical use of this new technique.

Key Words: myocardial perfusion imaging; gated SPECT; left ventricular volumes; left ventricular function

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Left ventricular (LV) function and volumes, along with myocardial perfusion, have major diagnostic and prognostic importance in patients with coronary artery disease (1–9). Myocardial perfusion scintigraphy is a well-established technique for evaluation of myocardial perfusion (9). Recently, with electrocardiographic gating during the acquisition of SPECT perfusion images, it has become possible to simultaneously assess LV perfusion, function and volumes. Both $^{99\text{m}}\text{Tc}$ and ^{201}Tl , the most commonly used tracers for

perfusion scintigraphy, can be used for gated SPECT purposes (10–16).

The aim of this study was to compare gated SPECT, using different protocols and tracers, with two-dimensional echocardiography, with respect to determination of LV volumes and LV ejection fraction (EF).

MATERIAL AND METHODS

Study Population

Consecutive patients who underwent both a myocardial perfusion SPECT and a two-dimensional echocardiogram within a 15-d period were selected for the study. Exclusion criteria were any change in clinical status between acquisition of the gated SPECT and two-dimensional echocardiography studies, acute myocardial infarction or unstable angina occurring less than 7 d before the study, and percutaneous coronary angioplasty, coronary artery bypass graft surgery or other surgical procedures occurring within 30 d of the study. Overweight patients (more than 250 lb) and patients with significant arrhythmia that compromised the gating technique were also excluded.

Gated SPECT Protocols

The criteria used in our laboratory for selection of the perfusion agent were the following: (1) ^{201}Tl (111 MBq [3.0 mCi]) stress 4-h redistribution was used in patients who weighed less than 200 lbs and women with breast cup sizes A or B; (2) 1-d protocol using $^{99\text{m}}\text{Tc}$ sestamibi or $^{99\text{m}}\text{Tc}$ tetrofosmin (8–12 mCi stress / 24–30 mCi rest) was used in patients weighing more than 200 lbs or with breast cup sizes C or D; and (3) dual isotope protocol (^{201}Tl 111 MBq [3.0 mCi] rest/ $^{99\text{m}}\text{Tc}$ agent 888–1110 MBq [24–30 mCi] stress) was used for studies initiated late during the daily workload. Fifty-eight (53%) patients underwent pharmacologic stress with adenosine, 33 (30%) with exercise and 18 (17%) with dobutamine. Arterial blood pressure and heart rate were measured immediately before the stress.

Gated myocardial SPECT images were acquired in a 90° configuration dual-head SPECT system, equipped with a low-energy, high-resolution collimator. Sixty-four projections (32 per each detector, matrix size 64×64) were acquired over a 180° anterior arc, divided into 8 frames per cardiac cycle. Acquisition commenced 30–60 min after injection of $^{99\text{m}}\text{Tc}$ -labeled agents and within 10 min after ^{201}Tl injection (peak stress) and again 4 h later (redistribution images). The acquisition lasted 30 s per projection for studies performed with ^{201}Tl or a low dose of a $^{99\text{m}}\text{Tc}$ tracer, and 25 s per projection for studies performed with a high dose of a $^{99\text{m}}\text{Tc}$ tracer.

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Nongated Images

Nongated projection data were created by summing the gated data at each projection into a nongated raw data. The data were then reconstructed with the standard filtered backprojection algorithm. Images were qualitatively and quantitatively interpreted by an expert nuclear cardiologist (17–19). Patients with normal stress perfusion images did not undergo rest or redistribution images.

Gated Images

Gated myocardial SPECT images with ^{201}Tl and $^{99\text{m}}\text{Tc}$ sestamibi or tetrofosmin and a matrix size of 64×64 pixels were reconstructed using backprojection algorithm with three-dimensional Butterworth filter of cutoff frequency 0.35 cycles per pixel (Nyquist frequency) and order 5. The transaxial gated tomographic slices were then reoriented into short, horizontal long axis and vertical long axis views.

The LVEF, end-diastolic volume (EDV) and end-systolic volume (ESV) were assessed with the commercially available automatic “Cedars Quantitative Gated SPECT” software (Cedars Sinai, Los Angeles, CA). The algorithm operates in three-dimensional space. It segments the left ventricle, estimates and displays endocardial and epicardial surfaces for all eight images in the cardiac cycle, calculates the relative LV volumes and derives the LVEF. In cases when the LV contour contained organs other than the heart or jagged irregularities that did not correspond to ventricular structures, a semiautomatic algorithm was used. In this mode, the operator defines the center of the left ventricle and resizes the LV mask.

Echocardiographic Technique

The two-dimensional echocardiograms were acquired at rest with standard short axis, apical and parasternal views. Arterial blood pressure and heart rate were measured immediately before starting the study. Images were analyzed on a computerized off-line station by consensus between two experienced echocardiographers who were unaware of clinical and laboratorial data.

LV volumes were derived with the modified Simpson's method (20) or a previously derived equation validated in our laboratory ($\text{EDV} = [3.42 \times D_{\text{max}} \times L_{\text{max}}] - 6$) (21). LVEF was computed by the modified Simpson's method (20) or the multiple diameter method (22).

Internal Reproducibility of Gated SPECT

To evaluate the reproducibility of the algorithm used in the measurement of absolute volumes and LVEF, 34 gated SPECT studies were randomly selected. The raw data were reprocessed by the same observer who had processed the original studies and volumes and LVEF calculations were recalculated.

Statistical Analysis

Data are represented as mean \pm SD or frequency. Two-tail *t* test was used when appropriate. Correlations between two-dimensional echocardiography and gated SPECT variables after stress, and at rest or redistribution, were assessed by linear regression analysis (Pearson's *r*).

RESULTS

Study Patients

One hundred and eleven patients qualified for the study. Two patients were excluded because of an uninterpretable gated SPECT (low count statistics) in one, and an uninterpretable echocardiogram in the other. Thus, 109 patients consti-

tuted the study cohort. The patients' mean age was 63 ± 14 y (range 19–98 y), 53 were men and 56 were women. Twenty-two patients (20%) had a history of myocardial infarction, 15 (14%) had a history of congestive heart failure, 30 patients (28%) had previous revascularization (19 had coronary artery bypass grafting and 11 had percutaneous transluminal coronary angioplasty) and 5 (5%) had a left bundle branch block on the electrocardiogram.

All 109 patients had a gated SPECT study after stress and a rest two-dimensional echocardiogram. Seventy-three patients also had rest or redistribution images. Fifty-five patients underwent the stress part of a 1-d protocol with a $^{99\text{m}}\text{Tc}$ tracer, of whom 31 also had a rest gated SPECT study. A stress ^{201}Tl gated SPECT study was performed in 42 patients, 30 of whom also had a redistribution ^{201}Tl gated SPECT study. A dual isotope protocol was used in 12 patients. In 2 patients, 1 with a rest ^{201}Tl gated SPECT study from a dual isotope protocol and 1 with a ^{201}Tl redistribution gated SPECT, the images were technically poor and were excluded from the analysis (Fig. 1). Thus, a total of 180 gated SPECT studies were available for comparison with two-dimensional echocardiography. Six gated SPECT studies were processed with the semiautomatic technique. The time difference between the first gated SPECT acquisition and the echocardiographic study was 1.5 ± 4.9 d; it was less than 6 h in 55 patients (50%) and less than 36 h in 89 patients (82%). The mean heart rates before SPECT and before echocardiography were 71 ± 13 beats/min and 70 ± 13 beats/min ($P = \text{ns}$), whereas the respective values for systolic blood pressure were 136 ± 26 mm Hg and 136 ± 21 mm Hg ($P = \text{ns}$). The results of the perfusion part of the SPECT studies are shown in Table 1.

Left Ventricular Function and Volumes in the Total Cohort

In the total cohort, there were significant linear correlations between poststress gated SPECT studies and the rest echocardiograms with respect to EDV, ESV and LVEF. The Pearson's correlation coefficients were $r = 0.87, 0.86$ and 0.72 , respectively ($P < 0.001$) (Fig. 2A–C). The absolute LV volumes and EF are shown in Table 2. The EDV was significantly larger by two-dimensional echocardiography than by poststress gated SPECT (118 ± 32 mL versus 103 ± 52 mL, $P = 0.01$). The LVEF was also significantly higher by echocardiography ($59\% \pm 16\%$ versus $52\% \pm 15\%$, $P = 0.001$), but the ESV was similar by both techniques (52 ± 35 mL versus 55 ± 44 mL, $P = \text{ns}$) (Table 2).

Analysis of the 71 patients who had both echocardiograms and gated SPECT after rest or redistribution yielded similar results. There were good correlations between the two techniques with respect to determinations of EDV, ESV and LVEF ($r = 0.89, 0.90$ and 0.78 , respectively, $P < 0.001$ for all comparisons) (Fig. 3A–C). The EDV was larger by echocardiography than by gated SPECT (119 ± 35 mL versus 104 ± 49 mL, $P = 0.03$). The ESV was similar (57 ± 38 mL versus 58 ± 45 mL, $P = \text{ns}$) and the LVEF was

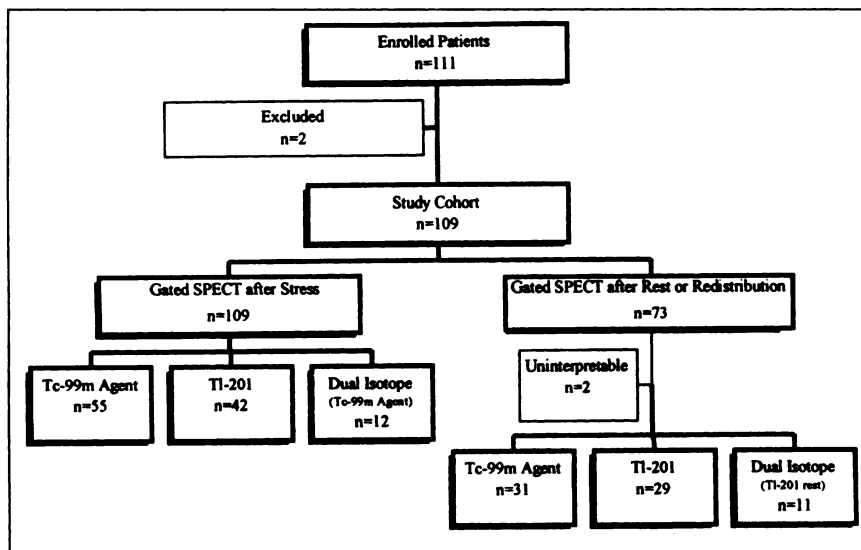


FIGURE 1. Study population.

higher by echocardiography (56 ± 16 mL versus 49 ± 16 mL, $P = 0.02$) (Table 2).

Correlations between the poststress and the rest or redistribution gated SPECT studies in the 71 patients with complete available data were excellent for EDV ($r = 0.98$), ESV ($r = 0.98$) and LVEF ($r = 0.90$) (Fig. 4A–C). There were no systematic differences in the absolute measurements of EDV, ESV and LVEF between the poststress and the rest/redistribution studies (Table 2).

Left Ventricular Function and Volumes in Studies Performed with ^{99m}Tc Agents

Among the 55 patients with poststress gated SPECT studies using a ^{99m}Tc tracer, there was a good linear

correlation with echocardiography with respect to EDV, ESV and LVEF (Table 3). The absolute volumes and LVEFs are shown in Table 2. Echocardiography resulted in larger EDV than poststress gated SPECT (116 ± 30 mL versus 101 ± 47 mL, $P = 0.05$), similar ESV and a tendency for a higher LVEF ($60\% \pm 14\%$ versus $56\% \pm 14\%$, $P = 0.07$).

There were 31 patients who had rest gated SPECT and echocardiography. In these patients, there was good correlation between the two techniques with respect to EDV, ESV and LVEF ($r = 0.86, 0.86$ and 0.72 , respectively) (Table 3). The absolute volumes and LVEF were similar with both techniques (Table 2). The correlation between poststress and rest gated SPECT among these 31 patients was excellent (Table 3). The absolute volumes and LVEF were similar comparing poststress and rest gated SPECT (Table 2).

TABLE 1
Myocardial Perfusion SPECT Data

	No. of patients	%
Perfusion agent		
^{99m}Tc (one-day protocol)	55	50
^{201}Tl	42	39
Dual isotope (^{201}Tl and ^{99m}Tc)	12	11
Type of stress		
Adenosine	58	53
Treadmill	32	30
Dobutamine	19	17
Normal perfusion	55	51
Abnormal perfusion	54	49
Fixed defect	9	8
Reversible defect	20	18
Partially reversible defect	25	23
Defect vascular territory		
LAD	26	24
RCA	35	32
CFX	15	14
Perfusion defect size (mean \pm SD) = $10\% \pm 15\%$		

LAD = Left anterior descending coronary artery; RCA = right coronary artery; CFX = circumflex coronary artery.

Left Ventricular Function and Volumes During ^{201}Tl Gated SPECT

There was a good correlation for volumes and EF measurements ($r = 0.84, 0.79$ and 0.68 for EDV, ESV and LVEF, respectively) in the 42 patients with poststress ^{201}Tl gated SPECT and echocardiography (Table 3). The absolute volumes and LVEF were consistent with the results for the total cohort, as well as for the subgroup of patients who had poststress ^{99m}Tc gated SPECT. The absolute values were higher by echocardiography for determination of EDV (116 ± 28 mL versus 98 ± 45 mL, $P = 0.03$) and LVEF ($59\% \pm 17\%$ versus $50\% \pm 14\%$, $P = 0.01$), and similar regarding ESV (Table 2). In this subgroup of patients, there was an excellent linear correlation between poststress gated SPECT and redistribution gated SPECT (Table 3). Absolute volumes and LVEF were equivalent with the two techniques (Table 2).

In the 29 patients who had ^{201}Tl redistribution imaging, the correlation of redistribution gated SPECT and echocardiography was good (Table 3). The absolute values for EDV were higher by echocardiography (117 ± 28 mL versus 98 ± 40 mL, $P = 0.03$), but the ESV and LVEF were similar (Table 2).

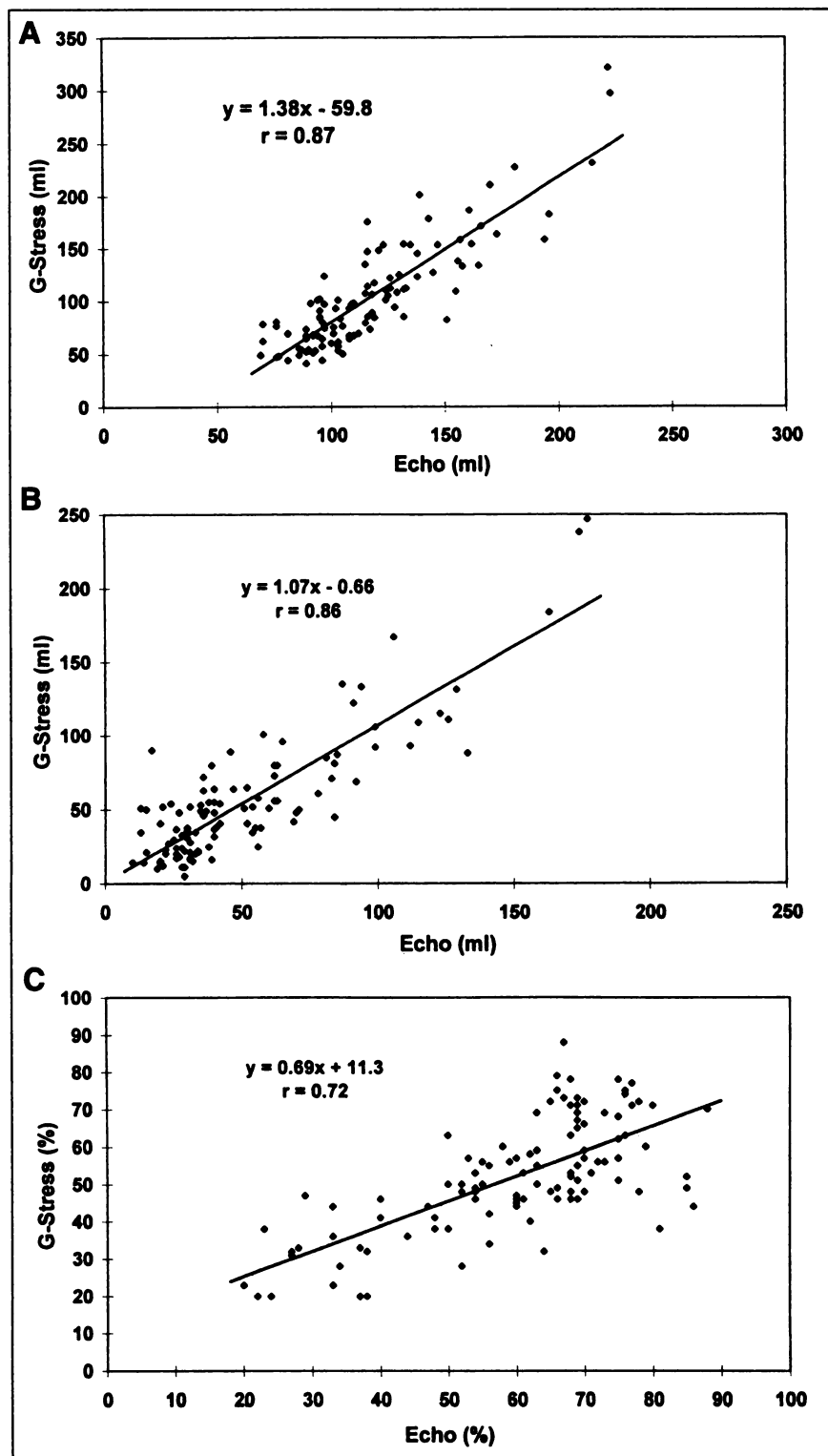


FIGURE 2. Correlation, in 109 cases, between EDV (A), ESV (B) and LVEF (C) values measured by gated SPECT after stress and two-dimensional echocardiogram. G-stress = gated SPECT after stress; ECHO = two-dimensional echocardiography.

Internal Reproducibility of Measurements

The reproducibility of gated SPECT was excellent. There were no differences in absolute measurements of EDV (96 ± 33 mL versus 96 ± 34 mL), ESV (48 ± 28 mL versus 48 ± 27 mL) and LVEF ($53\% \pm 14\%$ versus $54\% \pm 14\%$). The correlations between these three variables were excellent (all with $r = 0.99$, $P < 0.001$).

DISCUSSION

Assessment of LV volumes and function has major clinical importance in the management of patients with known or suspected coronary artery disease (1-9,23-25). This study examined the performance of automatic quantitative gated SPECT in the evaluation of LV absolute volumes and LVEF using different protocols, tracers and dosimetry.

TABLE 2
LV Volumes and LVEF by Gated SPECT and Two-Dimensional Echocardiography

	Echo × G-stress			Echo × G-rest			G-stress × G-rest		
	Echo	G-stress	P	Echo	G-rest	P	G-stress	G-rest	P
All cases	(n = 109)			(n = 71)			(n = 71)		
EDV (mL)	118 ± 32	103 ± 52	0.01	119 ± 35	104 ± 49	0.03	110 ± 55	104 ± 49	ns
ESV (mL)	52 ± 35	55 ± 44	ns	57 ± 38	58 ± 45	ns	63 ± 47	58 ± 45	ns
LVEF (%)	59 ± 16	52 ± 15	0.001	56 ± 16	49 ± 16	0.02	48 ± 15	49 ± 16	ns
^{99m} Tc	(n = 55)			(n = 31)			(n = 31)		
EDV (mL)	116 ± 30	101 ± 47	0.05	118 ± 33	105 ± 48	ns	113 ± 53	105 ± 48	ns
ESV (mL)	49 ± 31	50 ± 39	ns	54 ± 35	56 ± 41	ns	63 ± 44	56 ± 41	ns
LVEF (%)	60 ± 14	56 ± 14	0.07	57 ± 14	52 ± 13	ns	50 ± 14	52 ± 13	ns
²⁰¹ Tl	(n = 42)			(n = 29)			(n = 29)		
EDV (mL)	116 ± 28	98 ± 45	0.03	117 ± 28	98 ± 40	0.04	100 ± 42	98 ± 40	ns
ESV (mL)	51 ± 31	53 ± 36	ns	56 ± 33	55 ± 38	ns	57 ± 36	55 ± 38	ns
LVEF (%)	59 ± 17	50 ± 14	0.01	55 ± 17	49 ± 15	ns	47 ± 15	49 ± 15	ns

LV = left ventricular; LVEF = left ventricular ejection fraction; echo = two-dimensional echocardiogram; G-stress = gated SPECT after stress; G-rest = gated SPECT after rest or redistribution; EDV = end-diastolic volume; ESV = end-systolic volume.

Echocardiography is a well validated (20) and widely used technique for assessment of LV function and volumes, thus we chose this technique to validate our measurements. Our group has recently reported good to excellent correlations between gated SPECT and MR angiography (26), as well as between sestamibi gated SPECT, ²⁰¹Tl gated SPECT and first-pass radionuclide angiography (27). Other investigators have compared LVEF assessed by gated SPECT and radionuclide angiography (12,13,28,29) or contrast angiography (14,28). Good correlations were found among all these methods.

Correlation Between Gated SPECT and Echocardiography

In our study, the correlation between gated SPECT and echocardiography with respect to EDV, ESV and LVEF ranged from good to excellent whether we used the post-stress or a separate rest acquisition. Achtert et al. (30), using a digital phantom model, found that quantitative gated SPECT overestimated the true EF by 3%–7% when the myocardial tracer activity was normal and underestimated it by up to 9% when the myocardial tracer activity was very low. The accuracy for determining LV volumes had an average error of 12%. Germano et al. (12), using a phantom model, found that volumes estimated by a quantitative gated SPECT algorithm were within 10% of the true known volume. Recently the same group of investigators (27) observed a good correlation between sestamibi gated SPECT and first-pass radionuclide angiography with respect to estimation of EDV and ESV. Zanger et al. (28) reported a good agreement between echocardiography and gated SPECT for determination of LVEF and volumes. Other investigators reported a good correlation between gated SPECT and cardiac MRI for the assessment of LV volumes and EF (14,26). In all these previous studies ^{99m}Tc sestamibi was the tracer used. Recently, Germano et al. (13) and He et al. (27) validated the accuracy of gated SPECT for the measurement

of LVEF in patients who underwent ²⁰¹Tl myocardial gated SPECT. In this study, we used both ^{99m}Tc and ²⁰¹Tl. However, independent of the tracer selection, the results of absolute volumes and LVEF estimates correlated well with two-dimensional echocardiography. Even in the worst possible scenario, that is, gated SPECT performed during ²⁰¹Tl redistribution, the performance was still good.

Generally, our patients had smaller EDV, similar ESV and consequently lower LVEF by gated SPECT than by echocardiography. One exception was in the subgroup of rest gated SPECT studies using ^{99m}Tc agents. When a high dose of ^{99m}Tc was used, there was no significant difference between gated SPECT and echocardiography regarding EDV, ESV and LVEF. This suggests that studies using a high dose of a ^{99m}Tc agent may be ideal for gated SPECT studies, but more studies are necessary to define if there is indeed an advantage of using higher doses of ^{99m}Tc agents.

Correlations Between Poststress and Rest/Redistribution Gated SPECT

In our study, the correlations between poststress and rest or redistribution gated SPECT studies for assessment of LV volumes and EF were excellent. These results are in agreement with other recent studies using either ^{99m}Tc agents (27–33) or ²⁰¹Tl (27,34). Other investigators, however, have demonstrated that gated SPECT performed immediately after exercise may manifest postischemic stunning in some patients (33–36). In our patient cohort, where pharmacologic stress was used in approximately two-thirds of the patients, myocardial stunning was uncommon.

Reproducibility of Gated SPECT

The reproducibility of measurements of gated SPECT after stress and after rest or redistribution were excellent. The internal reproducibility of the algorithm was, in fact, nearly perfect. Recently, Berman et al. (37), using the same automatic quantitative gated SPECT algorithm, reported

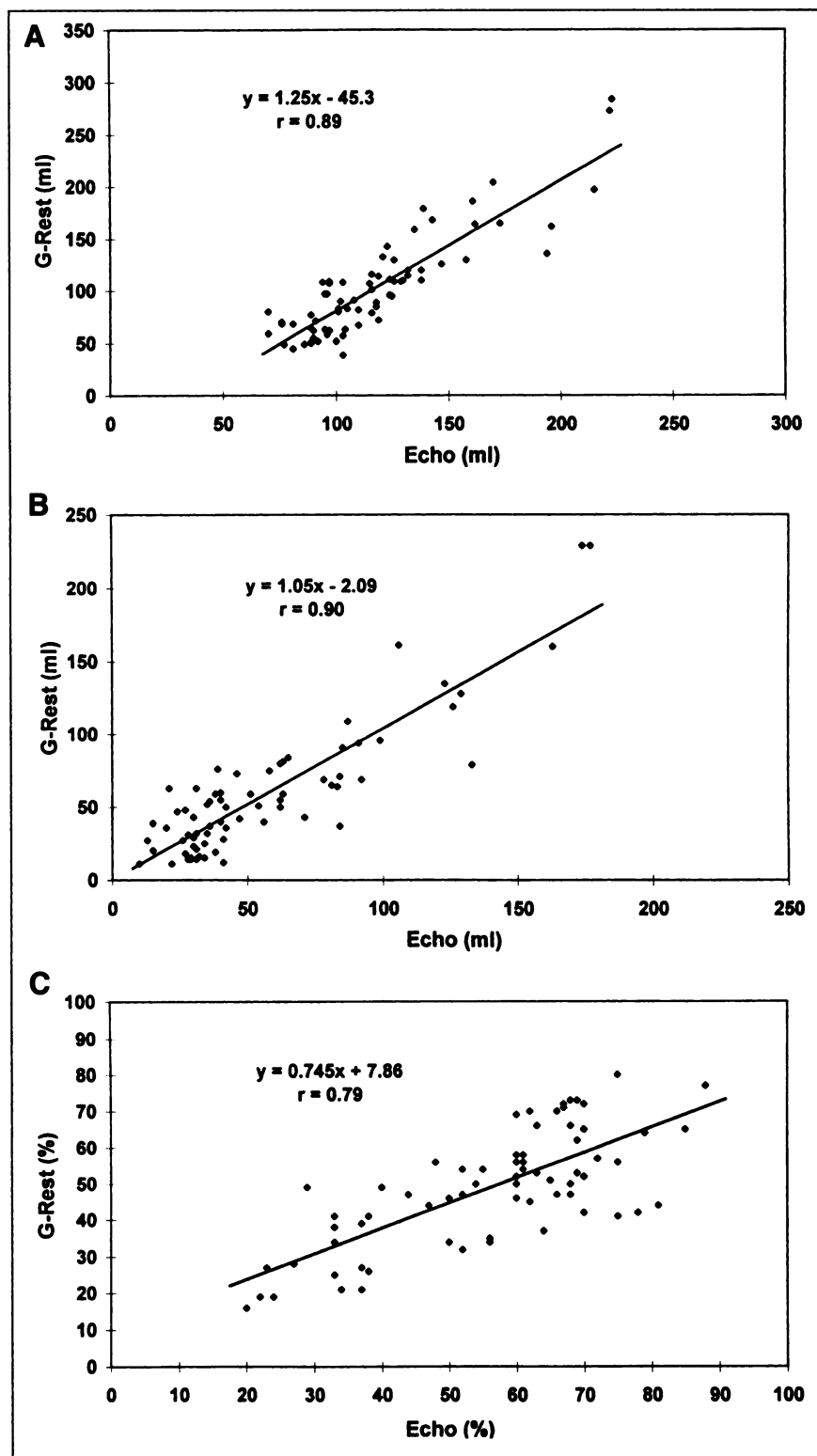


FIGURE 3. Correlation, in 71 cases, between EDV (A), ESV (B) and LVEF (C) values measured by gated SPECT after rest or redistribution and two-dimensional echocardiography. G-rest = gated SPECT after rest or redistribution; ECHO = two-dimensional echocardiography.

excellent interstudy repeatability of LV volumes when studies were acquired in two different positions (prone and supine).

Pitfalls of Automatic Gated SPECT

The use of only 8 frames per cardiac cycle by necessity reduces the time resolution for calculation of LVEF. Al-

though 16 frames per cycle does improve the time resolution, it leads to either fewer counts per frame or prolongation of the acquisition. Moreover, an excellent agreement has been found between acquisitions with 8 or 16 frames (12), albeit with slightly lower values for the LVEF calculated from the 8 frame studies (3.7%). In keeping with these

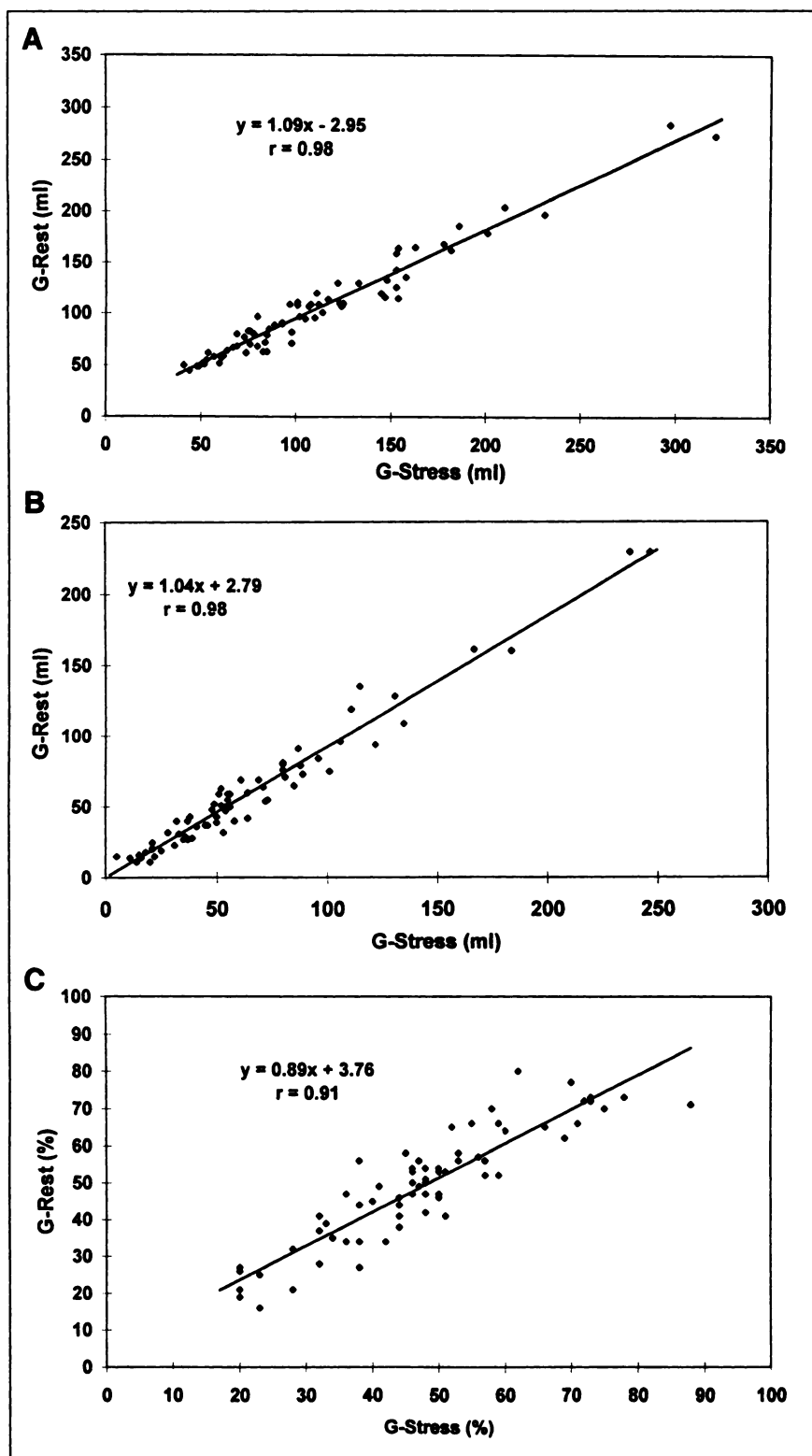


FIGURE 4. Correlation, in 71 cases, between EDV (A), ESV (B) and LVEF (C) values measured by gated SPECT after stress and gated SPECT after rest or redistribution. G-stress = gated SPECT after stress; G-rest = gated SPECT after rest or redistribution.

observations, we found slightly lower values for LVEF calculated by gated SPECT than by two-dimensional echocardiography (4%–9%).

In patients with small ventricles, the LVEF may be overestimated because of underestimation of volumes, particularly in end-systole, secondary to use of smoothing

filters (13). Typically, these patients have a normal heart but their LVEF may be falsely elevated.

Occasionally, the algorithm may fail to correctly track the LV edges; this occurs when a severe defect with very low tracer activity is present. Rarely we have seen the presence of excessive visceral activity to also compromise tracking of

TABLE 3
Correlations Between Gated SPECT and Two-Dimensional Echocardiography for LV Volumes and LVEF*

	Echo × G-stress		Echo × G-rest		G-stress × G-rest	
	r	SEE	r	SEE	r	SEE
All cases	(n = 109)		(n = 71)		(n = 71)	
EDV (mL)	0.87	26.2	0.89	22.8	0.98	12.1
ESV (mL)	0.86	22.2	0.90	19.9	0.98	9.5
LVEF (%)	0.72	10.7	0.79	9.8	0.91	6.4
^{99m} Tc	(n = 55)		(n = 31)		(n = 31)	
EDV (mL)	0.83	26.9	0.86	25.2	0.97	13.0
ESV (mL)	0.83	22.1	0.86	21.4	0.98	9.6
LVEF (%)	0.69	10.5	0.72	9.3	0.90	6.1
²⁰¹ Tl	(n = 42)		(n = 29)		(n = 29)	
EDV (mL)	0.84	15.3	0.86	20.7	0.97	9.7
ESV (mL)	0.79	19.4	0.85	19.9	0.98	8.3
LVEF (%)	0.68	12.4	0.75	10.6	0.89	6.8

* $P < 0.001$ for all correlations.

LV = left ventricular; LVEF = left ventricular ejection fraction; echo = two-dimensional echocardiogram; G-stress = gated SPECT after stress; G-rest = gated SPECT after rest or redistribution; EDV = end-diastolic volume; ESV = end-systolic volume.

LV edges. In these unusual instances, the observer may visually adjust the LV edges.

Limitations of the Study

Because the standard policy in our laboratory is that obese patients and women with large breasts are imaged with ^{99m}Tc agents, this policy leaves patients with the most favorable body build to be imaged with ²⁰¹Tl. Thus, our good results with this tracer may not necessarily apply to larger patients.

Another limitation of the study is that we cannot be certain that preload and afterload, both of which modulate the LV function, were the same during the poststress, the rest SPECT studies and the rest echocardiograms, because these were performed at different times. However, about 50% of the studies were performed within 6 h of each other and arterial blood pressure and heart rate were similar before the stress SPECT studies and before the acquisition of the echocardiographic images.

CONCLUSION

In conclusion, quantitative gated SPECT, using a variety of protocols and with either ²⁰¹Tl or ^{99m}Tc tracers, has a good correlation with echocardiography for the measurements of absolute LV volumes and LVEF. This automatic technique is highly reproducible and thus can be used clinically for those measurements, with the added advantages that the ventricular performance parameters are obtained from the perfusion images. Moreover, contrary to echocardiographic techniques used to assess LV volumes and LVEF, which are quite labor intensive and more observer dependent, the gated SPECT technique is nearly totally automatic, fast and highly reproducible.

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