
Echocardiographic Validation of Gated SPECT Ventricular Function Measurements

Kenneth Nichols, David Lefkowitz, Tracy Faber, Russell Folks, David Cooke, Ernest V. Garcia, Siu-Sun Yao, E. Gordon DePuey, and Alan Rozanski

Division of Cardiology, Department of Medicine, and Division of Nuclear Medicine, Department of Radiology, St. Luke's-Roosevelt Hospital and Columbia University College of Physicians and Surgeons, New York, New York; and Department of Radiology, Emory University, Atlanta, Georgia

Left ventricular (LV) volumes are valuable prognostic indicators in the management of coronary artery disease and traditionally have been obtained by x-ray contrast angiography or echocardiography. There now are several scintigraphic methods to compute volumes that are based on different LV modeling assumptions. Both the reasons that calculations from different nuclear techniques can disagree with one another and the relationship of these values to the more conventional echocardiographic measurements must be investigated thoroughly for calculations to be interpretable for individual patients. **Methods:** Echocardiographic volumes were determined in 33 retrospective subjects with coronary artery disease (mean age, 61 ± 12 y; 42% men; 70% with abnormal perfusion and 58% with abnormal segmental wall motion) using the modified Simpson's rule technique applied to digitized apical 4-chamber and apical 2-chamber views of 4 averaged heartbeats. These volumes were compared with those from 3 gated SPECT methods based on Simpson's rule LV modeling similar to standard echocardiographic algorithms (SPECT EF from St. Luke's-Roosevelt Hospital) (method 1), Gaussian myocardial count profile curve fitting (QGS from Cedars-Sinai Medical Center) (method 2), and an endocardial model based on perfusion sampling and count-based thickening (Cardiac Toolbox from Emory University) (method 3). **Results:** By ANOVA, there were no significant differences among ejection fractions (EFs), but there were for volumes. Paired *t* test analysis showed volumes from methods 2 and 3 to be significantly larger than echocardiographic volumes and larger than those of method 1. Linear regression analysis comparing gated SPECT and echocardiographic volumes showed a nearly identical strong correlation ($r = 0.92$; $P < 0.000001$) for all 3 methods. Excellent correlation also was found among gated SPECT volumes from the 3 methods ($r = 0.94$). Bland-Altman analysis and *t* tests showed that method 1 volumes (70 ± 61 mL) were the same as for echocardiography (77 ± 55 mL), but volumes were overestimated by method 2 (105 ± 74 mL) and method 3 (127 ± 92 mL), particularly for larger volumes. Pearson coefficients for EFs compared with echocardiography were $r = 0.82, 0.75,$ and 0.72 for methods 1–3, respectively. EFs correlated strongly among the 3 gated SPECT methods ($r = 0.86$ – 0.92). The Fisher *z* test showed no differences among these methods for any of the volume or EF linear correlation analyses. **Conclusion:** All gated SPECT parameters correlated well with echocardiographic val-

ues. However, the gated SPECT method for which underlying assumptions most closely resembled those commonly used in echocardiography produced mean volume values closest in agreement with echocardiographic measurements.

Key Words: ventricular volume; gated SPECT; echocardiography

J Nucl Med 2000; 41:1308–1314

For prognosis of patient outcome after myocardial infarction, ejection fraction (EF) (1), ventricular volume (2), and regional wall motion (3) have been shown to be powerful indicators. Recent studies have verified that left ventricular (LV) volumes constitute an independent marker of cardiac pathology (4,5). For some time, echocardiography has been the most widely used method for assessing regional wall motion (6) and, when angiography is not available, also is the most common means for obtaining accurate ventricular volumes (7).

In recent years, gated scintigraphy has been proposed as an alternative means for obtaining LVEF and volumes. Numerous publications have established agreement between gated SPECT EFs and those of other methods (8–10). However, EF accuracy does not prove volume accuracy because systematic volume errors tend to cancel (11). Evidence has been mounting that gated SPECT and angiographic volumes correlate well (12–14). Validation with echocardiography has not yet been as extensive, and the preponderance of these reports has appeared only as abstracts (15–18). Yet, in cases in which gated SPECT is performed without additional imaging evaluations, it is important to be able to relate calculations to values that would have been obtained had other imaging, such as echocardiography, been performed because of the history and wide experience clinicians have with echocardiography. Also, because perfusion scintigrams are discontinuous if the myocardium is scarred or ischemic and because hypoperfusion frequently is associated with regional wall motion abnormalities, it is important to determine if gated SPECT calculations are reliable under these circumstances. Because several different gated SPECT methods are available, based

Received Oct. 12, 1999; revision accepted Dec. 29, 1999.

For correspondence or reprints contact: Kenneth Nichols, PhD, Columbia University, Division of Cardiology, PH9-Rm. 993B, 622 W. 168th St., New York, NY 10032.

on different underlying assumptions, it also is necessary to determine the degree to which these agree with one another and are likely to reproduce echocardiographic test results. Therefore, this investigation undertook to establish relationships between scintigraphic and echocardiographic volumes, to ascertain whether these findings apply equally to different gated SPECT methods, and to interpret the results in the context of those found for angiography.

MATERIALS AND METHODS

Patient Population

Data for 33 patients (mean age, 61 ± 12 y; 44% men) studied from 1992 to 1998 were analyzed retrospectively on the basis of patients having had both echocardiographic and ^{99m}Tc sestamibi gated myocardial perfusion evaluations. Echocardiographic studies were performed at rest to evaluate LV function, congestive heart failure, stroke, endocarditis, valvular disease, and measurement of myocardial wall thickness for assessment of LV hypertrophy. Scintigraphic studies were performed to assess myocardial perfusion and function. All correlative studies were performed within 1 mo of each other, with a median time difference of 3 d. No patient experienced any significant cardiac event between studies nor was there any change in medical or surgical therapy.

Echocardiographic Measurements

Ventricular calculations were performed using 2-dimensional echocardiography (Sonos 1500; Hewlett Packard Co., Andover, MA; and 128XP; Acuson Corp., Mountain View, CA). Four heart cycles were averaged and digitized, with mean R-R interval sampling of 17 frames per heartbeat. Calibrations were performed separately for each patient data acquisition. Data analysis (Dextra 2000; Dextra Color Systems Inc., Long Beach, CA) was performed by an experienced cardiologist who chose the highest quality data from among 2-chamber and 4-chamber views, equivalent to SPECT vertical long-axis (VLA) and horizontal long-axis (HLA) views. The cardiologist selected the cinematic frames corresponding to end-diastole (ED) and end-systole (ES). A modified Simpson's rule (also known as the method of disks (19)) technique was used to compute volumes and EFs from orthogonally (70° - 90°) paired apical 2-chamber or 4-chamber views.

Gated Scintigraphy

^{99m}Tc sestamibi injections were performed during peak exercise following a Bruce treadmill protocol or intravenous pharmacologic coronary vasodilatation with dipyridamole (0.142 mg/kg/min infused over 4 min) using 1.11 GBq for a 1-d protocol or 814 MBq for a separate-day protocol (20). Tomograms (64×64) with a pixel size of 6.4 mm were acquired with high-resolution collimation for 20 s per projection at 64 projections over 180° with a dual-detector camera (Optima; General Electric Medical Systems, Milwaukee, WI) so that acquisitions were performed in 12 min. Tomograms of stress perfusion distribution were acquired with patients at rest, 30 min after stress, at 8 frames per R-R interval. An R-R beat window was used such that data were collected if incoming R waves fell between 50% and 150% of the mean preacquisition heart rate. All patient data were screened for arrhythmic artifacts (11).

Standard clinical data-processing parameters were used (21): Butterworth (cutoff, 0.40; power, 10.0) prefilters for gated tomograms, followed by quantitative ramp x-filtering, interslice spatial averaging, and time-filtering among gated frames. Images were reoriented into VLA, HLA, and short-axis (SA) sections using

manual choices by an observer of anterior, inferior, septal, and lateral limits and approximate LV symmetry axes. Commercially available software (21) was used to produce cinematic midventricular VLA and HLA and all SA images at all levels from apex to base.

Gated SPECT Analytic Methods

Three gated SPECT methods were used for computation of LV volumes and EFs. Method 1 (SPECTEF) was developed at St. Luke's-Roosevelt Hospital in New York, NY. Input data were paired midventricular VLA and HLA gated tomograms (8,10) and, in that sense, were the closest to echocardiographic LV modeling (19) of the 3 scintigraphic methods. Originally, this method was developed on the basis of endocardial borders drawn by cardiologists at a 35% count contrast threshold while viewing VLA and HLA mid-LV ED and ES scintigrams, for which locations of perceived borders then were corrected for the gamma camera's measured line-spread function (8). Drawings were performed on frames individually normalized to themselves to provide the most consistent myocardial shape impression to observers and to minimize potential arrhythmia artifacts (11). Subsequently, the rules used to define endocardial borders were encoded for automatic processing (10). The valve plane was defined at basal points where myocardial counts dropped below 25% of maximum myocardial counts.

Curve fitting of count profiles across myocardial walls for detection of midmyocardial points formed the basis of method 2 (QGS) from Cedars-Sinai Medical Center in Los Angeles, CA (9). This is the most widely distributed gated SPECT technique and uses the full set of SA gated tomograms to enable a fully 3-dimensional handling of data. Motivating this approach is the assumption that the greatest counts correspond to myocardial centers. Clusters of neighboring 3-dimensional points likely comprising myocardial segments were fit to a 3-dimensional ellipsoid. Count profiles were sampled in directions normal to the ellipsoid and were fit to Gaussian functions. For counts below 50% of maximum, missing wall segments were interpolated. The valve plane was defined by criteria similar to those used by method 1. Epicardial and endocardial surfaces were offset from midmyocardial points by incorporating intraframe count differences and systolic count increases, with the constraint of constant myocardial mass (22).

Method 3 (Cardiac Toolbox), originated at Emory University in Atlanta, GA, also identified midmyocardial locations with the highest regional counts. Like method 2, this technique analyzed the full set of all gated SA tomographic slices. This approach located points corresponding to LV-shaped objects imbedded within time-varying 3-dimensional input count distributions (23). Offsets to the endocardium from detected midmyocardial points at ED were defined to be half the myocardial thickness, assumed to be uniformly 1 cm, on the basis of MRI studies (24). To estimate the endocardial offsets at ES, the percentage of regional myocardial thickening was computed from polar perfusion maps formed for all sets of SA frames for each of the 8 R-R intervals. Fourier fits of the 8 time-varying counts at each polar map pixel location were performed to compute systolic count changes. The percentage of myocardial thickening was equated with these observed systolic count changes, attributed to partial-volume effects (25). The valve plane was modeled as 2 intersecting planes toward the base of the heart.

All scintigrams and echocardiograms were acquired at St. Luke's-Roosevelt Hospital. Gated SPECT computations using

TABLE 1
Gated SPECT Versus Echocardiographic LV
Aggregate Volumes

Parameter	Method 1	Method 2	Method 3
<i>r</i>	0.92	0.92	0.92
Slope	1.01 ± 0.05	1.22 ± 0.07	1.40 ± 0.07
Intercept (mL)	-7.2 ± 5.0	11.1 ± 6.3	12.4 ± 7.0
Mean (mL)	70 ± 61	105 ± 74	127 ± 92
SEE (mL)	23.9	30.0	36.9
Paired <i>t</i> test <i>P</i>	0.18	10 ⁻⁶	10 ⁻⁶

method 1 were performed without knowledge of echocardiographic results and vice versa. Original tomographic data were sent to Emory University, where methods 2 and 3 were applied without knowledge of values from method 1 or echocardiography.

Statistical Analysis

All numeric results are reported as mean values ± 1 SD. Differences among EF results are reported in absolute EF units, not as percentages of EFs. ANOVA was performed to test for differences of values among the 3 methods, for which values of *P* were considered statistically significant if <0.05/3 (i.e., for <0.016, to account for 3 degrees of freedom). For those analyses for which ANOVA values of *P* were significant, paired *t* tests were used to compute whether 2-tailed probabilities indicated statistical significance between pairs of test results, at the level of *P* < 0.05. Linear regression analysis was used to compare calculations of LV volumes and EFs between modalities. Regression analysis also was performed in conjunction with Bland-Altman analyses of differences versus averages of paired values to search for trends and systematic errors (26,27). A value of *P* generated in association with regression analysis was the probability of no association, at a level of significance of *P* < 0.05. The statistical significance of pairs of different regression results was assessed by the Fisher *z* test.

RESULTS

Of the 33 patients, 70% exhibited abnormal perfusion and 58% were judged to have segmental wall motion abnormalities on the basis of visual echocardiographic readings. The mean echocardiographic ED volume (EDV) was 98 ± 52 mL over a wide range (38–372 mL). The mean echocardiographic ES volume (ESV) was 56 ± 55 mL (range, 13–233 mL), and the mean overall echocardiographic volumes (EDV aggregated with ESV) were 77 ± 55 mL. The mean echocardiographic EF was 52% ± 17% (range, 14%–73%).

TABLE 2
Gated SPECT Versus Echocardiographic LV EDVs

Parameter	Method 1	Method 2	Method 3
<i>r</i>	0.90	0.90	0.90
Slope	0.96 ± 0.08	1.13 ± 0.10	1.38 ± 0.07
Intercept (mL)	-2.4 ± 9.5	18.4 ± 11.3	30.4 ± 13.5
Mean (mL)	91 ± 63	128 ± 75	165 ± 91
SEE (mL)	28.0	33.5	40.0
Paired <i>t</i> test <i>P</i>	0.09	10 ⁻⁶	10 ⁻¹⁰

TABLE 3
Gated SPECT Versus Echocardiographic LV ESVs

Parameter	Method 1	Method 2	Method 3
<i>r</i>	0.94	0.94	0.94
Slope	1.15 ± 0.08	1.44 ± 0.10	1.66 ± 0.13
Intercept (mL)	-13.9 ± 5.4	0.7 ± 7.2	-2.6 ± 9.3
SEE (mL)	18.6	24.8	32.1
Mean (mL)	50 ± 52	81 ± 65	90 ± 77
Paired <i>t</i> test <i>P</i>	0.06	10 ⁻⁵	10 ⁻⁵

For method 1, observers judged it necessary to manually alter automated endocardial borders to match their visual perception of endocardium 15% of the time, consistent with previous reports (10). Method 2 required manual alterations of endocardial borders 9% of the time, also consistent with previous reports (28), and method 3 required alterations in 6% of patients. The most common circumstance for which alterations were required for the 3 methods occurred for studies showing hypoperfused myocardium adjacent to unusually intense hepatobiliary counts, as reported (10).

By ANOVA, differences among LV volumes (Tables 1–3) were significant (*P* < 0.002), but differences among EFs (Table 4) were not (*P* > 0.07). ANOVA results were essentially the same with or without inclusion of echocardiographic values as a variable. For individual paired *t* test analyses, method 1 volumes were not different from those of echocardiography (*P* = 0.18), but those of methods 2 and 3 were significantly (*P* < 0.000001) larger than echocardiographic volumes (Tables 1–3). Method 3 volumes were significantly larger than those of method 2, and both methods 2 and 3 produced volumes significantly larger than those of method 1.

There was excellent and nearly identical correlation of aggregate LV volumes (EDV aggregated with ESV) for all 3 methods with echocardiographic values (Table 1 and Fig. 1). Pearson correlation coefficients for each method individually versus echocardiography were 0.90 for EDV and 0.94 for ESV. More revealing were Bland-Altman volume graphs (Table 5 and Fig. 2), which showed slopes of 0.10, 0.30, and 0.52 for methods 1–3, respectively. A slope of 0.0 constitutes an ideal result for Bland-Altman graphs. Correlation for method 1 was marginal at *P* = 0.05, and correlations for methods 2 and 3 were definitely statistically significant, also contradicting the ideal result of *P* > 0.05 for Bland-Altman graphs. Thus, methods 2 and 3 overestimated echocardiographic

TABLE 4
Gated SPECT Versus Echocardiographic LVEFs

Parameter	Method 1	Method 2	Method 3
<i>r</i>	0.82	0.75	0.72
Slope	0.91 ± 0.11	0.72 ± 0.11	0.62 ± 0.12
Intercept (%)	9.9 ± 5.5	10.2 ± 5.5	21.3 ± 5.8
Mean (%)	51 ± 16	43 ± 15	51 ± 16
SEE (%)	9.9	10.1	11.0
Paired <i>t</i> test <i>P</i>	0.002	0.20	0.006

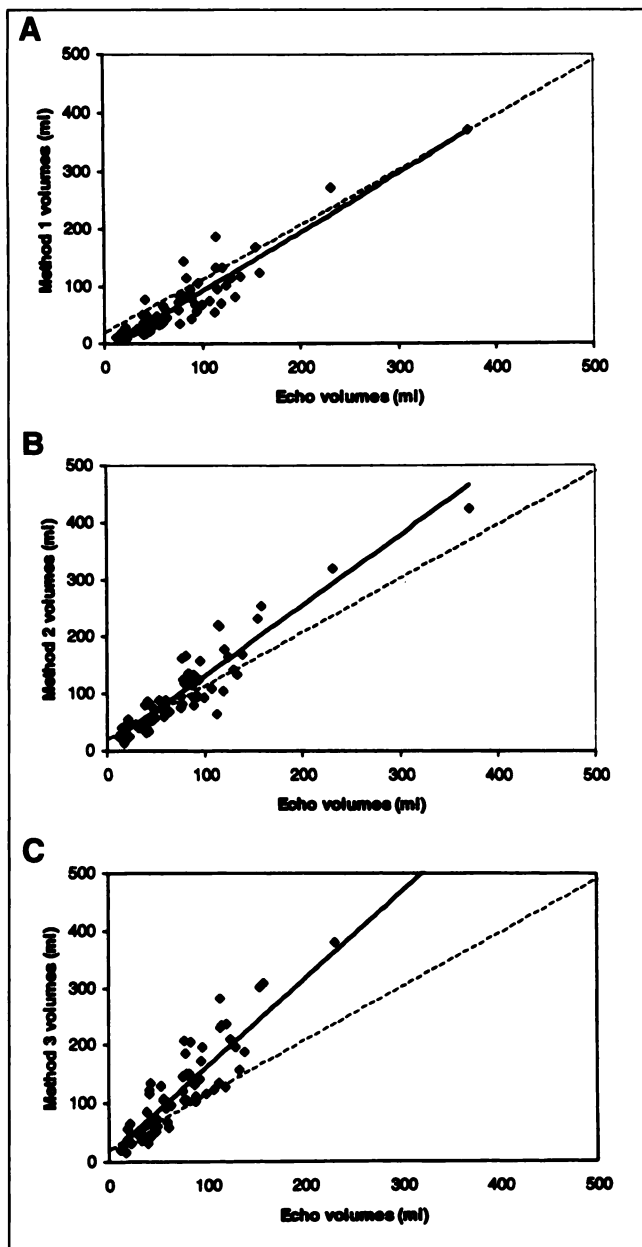


FIGURE 1. Gated SPECT LV EDV and ESV are plotted versus values computed by echocardiography for methods 1 (A), 2 (B), and 3 (C). Least-squares fits (solid lines) and lines of identity (dashed lines) are shown.

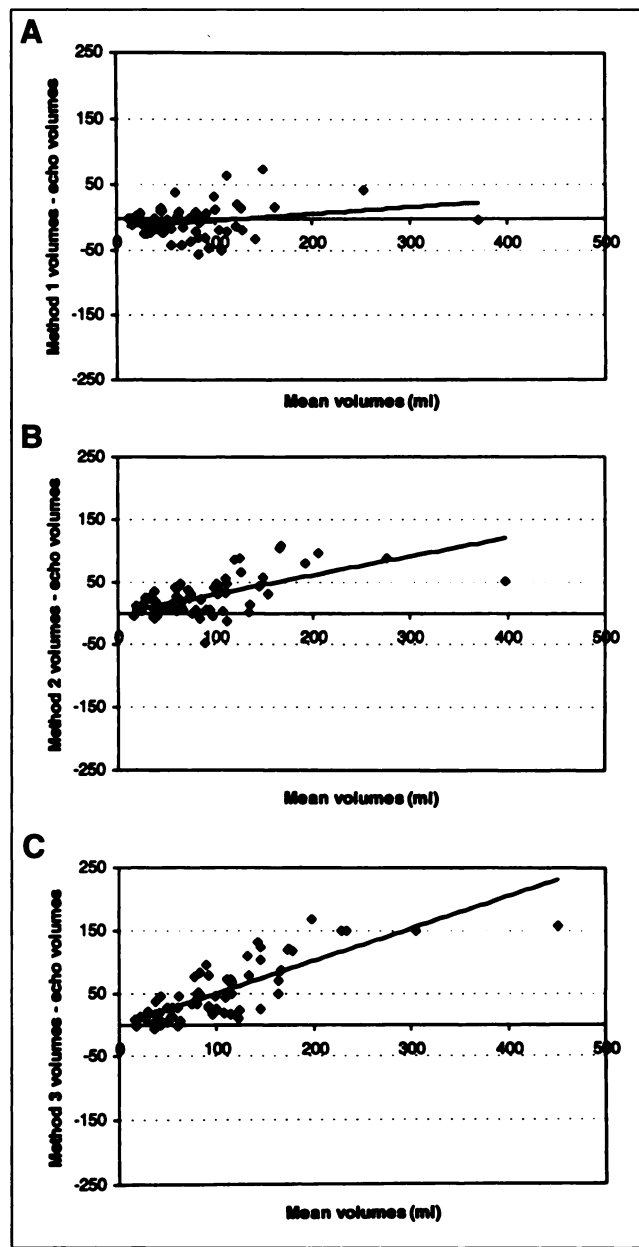


FIGURE 2. Bland-Altman graphs of differences versus means of gated SPECT and echocardiographic LV EDV and ESV are plotted for methods 1 (A), 2 (B), and 3 (C).

TABLE 5

Bland-Altman Linear Regression Results of Differences Versus Means for Gated SPECT and Echocardiographic LV Aggregate Volumes

Parameter	Method 1	Method 2	Method 3
<i>r</i>	0.24	0.56	0.80
Slope	0.10 ± 0.05	0.30 ± 0.05	0.52 ± 0.05
Intercept (mL)	-13.5 ± 5.7	1.0 ± 5.7	-1.8 ± 6.01
Regression <i>P</i>	0.05	10 ⁻⁶	10 ⁻⁶
Mean difference (mL)	-6.1 ± 23.7	28.2 ± 32.2	50.9 ± 46.7

graphic volumes, and to a greater extent for larger volumes, whereas method 1 marginally underestimated volumes for the smallest values. Essentially the same results were obtained for EDV and ESV values analyzed separately (Tables 2 and 3). Methods 1–3 correlated significantly with echocardiographic EF values, with correlation coefficients of 0.82, 0.75, and 0.72, respectively (Table 4 and Fig. 3). Bland-Altman graphs for methods 1–3 versus echocardiographic EFs yielded slopes closer to 0.0 (0.01, -0.05, and 0.13, respectively), and linear regression *P* was not significant for all 3 methods (Table 6 and Fig. 4). Linear correlation coefficients of EFs between methods were 0.89, 0.92, and 0.86 for methods 1 versus 2, 2 versus 3, and 1

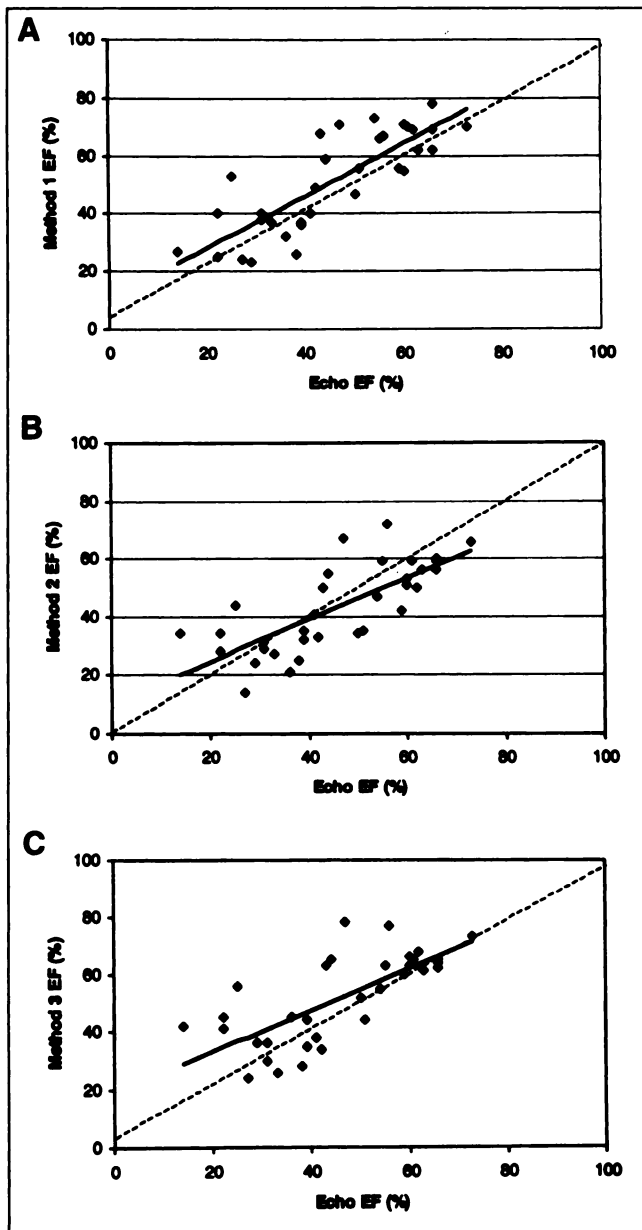


FIGURE 3. Gated SPECT LVEFs are plotted versus values computed by echocardiography for methods 1 (A), 2 (B), and 3 (C). Least-squares fits (solid lines) and lines of identity (dashed lines) are shown.

versus 3, respectively. By the Fisher z test, there was no statistically significant difference among any correlations for either EF or volume comparisons.

DISCUSSION

That excellent LV volume correlation was obtained for all gated SPECT methods versus echocardiography is encouraging, considering that the patient population studied was largely abnormal. However, the consistent volume differences among the 3 gated SPECT methods require further analysis. It is likely that the volumes of all gated SPECT methods are inherently too small for the smallest hearts (29).

The reason for this is that counts from opposite myocardial walls contribute to each other, particularly at ES, thereby distorting count profiles and causing local maxima to be misregistered toward the LV cavity center (30,31). Correction methods for this phenomenon have been proposed only recently (29). Therefore, the more relevant concern is why the 3 methods studied here diverged as LV cavity volume size increased. Part of the reason is the way in which endocardial points are offset from midmyocardial locations. Using a fixed 35% threshold and individually normalized paired VLA and HLA views, method 1 was most analogous to echocardiographic processing, which accounts for its values agreeing most closely with echocardiography. Methods 2 and 3 relied more heavily on systolic count changes to compute endocardial offsets, and some phantom and clinical studies have suggested that gated SPECT underestimates true thickening (32,33). Furthermore, method 2 adjusted ED offsets partly based on regional myocardial counts and so would have smaller endocardial offsets and larger LV cavity volumes for hypoperfused data (34). The volumes of method 3 were even larger than those of method 2 because, of the 3 methods, method 3 relied the most heavily on thickening, so that underestimation of true thickening would have the greatest overall effect in overestimating endocardial dimensions, particularly at ES. This is consistent with the observation of relatively larger slopes for ESV than for EDV regressions versus echocardiography, the largest being for method 3 (Tables 1–3). In turn, this resulted in method 3 having the smallest of the slopes for correlation of gated SPECT versus echocardiographic EF (Table 4).

None of these observations indicates which of the 3 methods ultimately produced values closest to true absolute ventricular volumes. All conventional volume methods contain their own LV modeling assumptions and limitations, a reflection of which is the fact that volumetric normal limits vary somewhat among methodologies. Some studies indicate that mean normal LV EDVs are smallest for echocardiography (35) and MRI (36) and largest for angiography (37) and cine CT (38). To date few publications have dealt with gated SPECT volumetric normal limits. Normal limits using method 1 (39) agree quite closely with those of method 2 (5,40), all of which are closest to echocardiographic normal limits (35). It is probably more meaningful to ask which gated SPECT method correlates most strongly with another

TABLE 6
Bland-Altman Linear Regression Results of Differences Versus Means for Gated SPECT and Echocardiographic LVEFs

Parameter	Method 1	Method 2	Method 3
r	0.005	0.06	0.20
Slope	0.01 ± 0.15	-0.05 ± 0.13	0.13 ± 0.11
Intercept (%)	6.0 ± 7.3	-1.0 ± 6.3	-0.5 ± 5.6
Regression P	0.99	0.54	0.34
Mean difference (%)	5.8 ± 9.9	-5.0 ± 10.0	6.0 ± 11.7

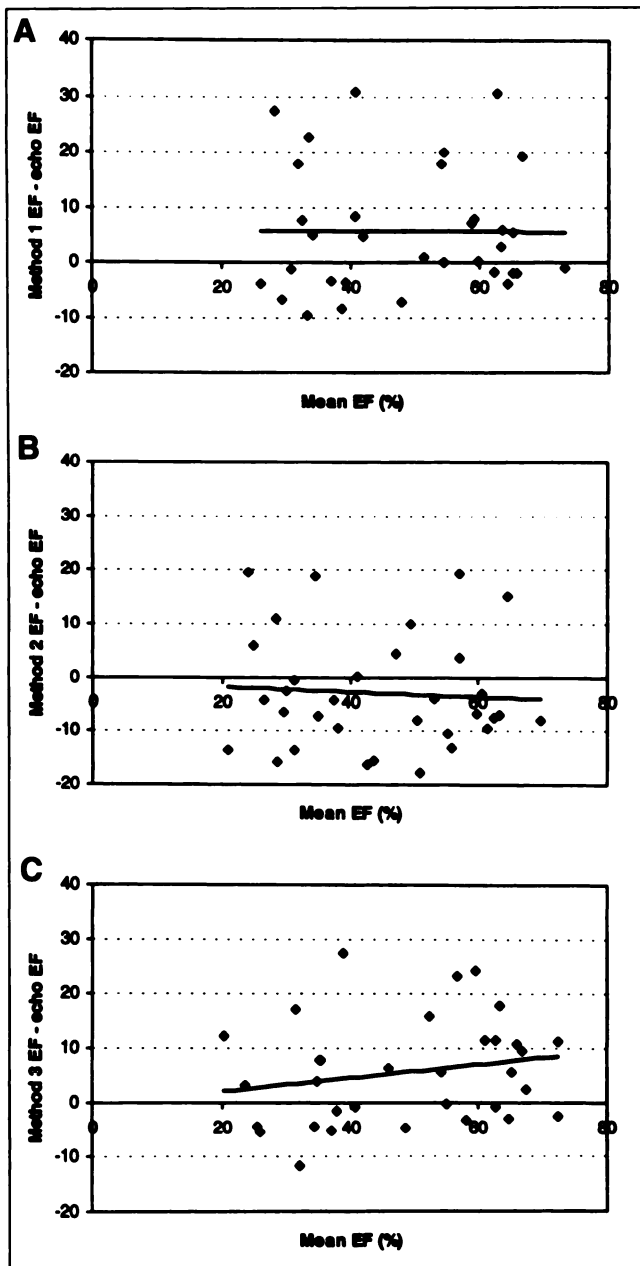


FIGURE 4. Bland-Altman graphs of differences versus means of gated SPECT and echocardiographic LVEFs are plotted for methods 1 (A), 2 (B), and 3 (C). All values are percentages.

established test, and, in this sense, all 3 methods evaluated in this investigation were equivalent. Because implementation of traditional methods may vary from one institution to another, the ideal mechanism for calibrating one of the newer gated SPECT methods versus an established technique with which clinicians are comfortable is to perform an internal validation specific to that institution. Short of that, it is reasonable to rely on published reports that show that consistent results are achievable when standard software packages are applied in a straightforward fashion, as has been found in this investigation.

The main limitation of this study is that it was based on 33

patients who were primarily abnormal subjects. Insofar as 70% of patients exhibited abnormal perfusion, a more thorough study should be performed to verify that similarly strong correlation is found among healthy subjects. Also, the results of this study were specific to the particular use of filters and filtered backprojection methods used to preprocess data before computations by methods 1–3. It is possible that use of other filters or iterative reconstruction techniques (or both) would cause methods 1–3 to produce different calculations.

CONCLUSION

The method most resembling echocardiographic modeling provided mean values closest to those of echocardiography. However, all gated SPECT volumes exhibited equally strong correlation with echocardiographic values and among methods. Therefore, it is possible to predict one method's results from the results of another for both volumes and EFs and to predict what values echocardiography would have obtained given the gated SPECT result.

ACKNOWLEDGMENTS

The authors thank Helene Salensky for extensive computer expertise in the processing of the gated SPECT data, Robyn Horowitz for the database analysis of echocardiographic patient information, and Allen Mogtader, MD, for valuable insights into the analysis of the echocardiograms. This study was supported in part by General Electric Medical Systems (Milwaukee, WI). Tracy Faber, Russell Folks, David Cooke, and Ernest V. Garcia receive royalties from the sale of CEQUAL, PerfSPECTive, and the Emory University Cardiac Toolbox, related to the research described in this article. The terms of this arrangement have been reviewed and approved by Emory University in accordance with its conflict-of-interest practice. This work was presented in part at the annual scientific meeting of the American College of Cardiology in New Orleans, LA, on March 7–10, 1999.

REFERENCES

1. Iskandrian AS, Hakki AH, Goel IP, et al. The use of rest and exercise radionuclide ventriculography in risk stratification in patients with suspected coronary artery disease. *Am Heart J*. 1985;110:864–872.
2. Fuster V, Gersh BJ, Giuliani ER, et al. The natural history of idiopathic dilated cardiomyopathy. *Am J Cardiol*. 1981;47:525–531.
3. Shiina A, Trajik AJ, Smith HC, Lengyel M, Seward JB. Prognostic significance of regional wall motion abnormality in patients with prior myocardial infarction: a prospective correlative study of two-dimensional echocardiography and angiography. *Mayo Clin Proc*. 1986;61:254–262.
4. Yao S, Palmas W, Quereshi E, Nichols K, DePuey EG, Rozanski A. Independent value of left ventricular dilatation to predict symptomatic congestive heart failure by technetium-99m sestamibi myocardial perfusion gated SPECT [abstract]. *J Nucl Med*. 1999;40:45P.
5. 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.
6. Schiller NB, Shah PM, Crawford M, et al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. *J Am Soc Echocardiogr*. 1989;2:358–367.

7. Folland EF, Parisi AF, Moynihan AF, et al. Assessment of left ventricular ejection fraction and volumes by real-time two-dimensional echocardiography. *Circulation*. 1979;60:760-766.
8. DePuey EG, Nichols K, Dobrinsky C. Left ventricular ejection fraction assessed from gated technetium-99m-sestamibi SPECT. *J Nucl Med*. 1993;34:1871-1876.
9. Germano G, Kiat H, Kavanaugh PB, et al. Automatic quantification of ejection fraction from gated myocardial perfusion SPECT. *J Nucl Med*. 1995;36:2138-2147.
10. Nichols K, DePuey EG, Rozanski A. Automation of gated tomographic left ventricular ejection fraction. *J Nucl Cardiol*. 1996;3:475-482.
11. 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.
12. Mochizuki T, Murase K, Tanake H, et al. Assessment of left ventricular volume utilizing ECG-gated SPECT with technetium-99m-MIBI and technetium-99m-tetrofosmin. *J Nucl Med*. 1997;38:53-57.
13. Nichols K, Tamis J, DePuey EG, Mieres J, Malhotra S, Rozanski A. Relationship of gated SPECT ventricular functional parameters to angiographic measurements. *J Nucl Cardiol*. 1998;5:295-303.
14. Iskandrian A, Germano G, VanDecker W, et al. Validation of left ventricular volume measurements by gated SPECT Tc-99m sestamibi imaging. *J Nucl Cardiol*. 1998;5:574-578.
15. Lefkowitz D, Nichols K, Rozanski A, Horowitz R, Mogtader A, DePuey EG. Echocardiographic validation of left ventricular volume measurements by Tc-99m sestamibi gated SPECT [abstract]. *J Am Coll Cardiol*. 1996;27:241A.
16. He ZX, Vick GW, Vaduganathan P, et al. Comparison of left ventricular volumes and ejection fraction measured by gated SPECT and by cine magnetic resonance imaging [abstract]. *J Am Coll Cardiol*. 1998;31:44A.
17. Cwajg E, Cwajg J, He ZX, et al. Comparison between gated-SPECT and echocardiography for the analysis of global and regional left ventricular function and volumes [abstract]. *J Am Coll Cardiol*. 1998;31:440A.
18. Mathew D, Zabrodina Y, Manting F. Volumetric and functional analysis of left ventricle by gated SPECT: a comparison with echocardiographic measurements [abstract]. *J Am Coll Cardiol*. 1998;31:44A.
19. Tortoleto FA, Quinones MA, Fernandez GC, Waggoner AD, Winters WL. Quantification of left ventricular volumes by two-dimensional echocardiography: a simplified and accurate approach. *Circulation*. 1983;67:579-584.
20. DePuey EG, Nichols KJ, Slowikowski JS, et al. Fast stress and rest acquisitions for technetium-99m-sestamibi separate-day SPECT. *J Nucl Med*. 1995;36:569-574.
21. Van Train KF, Areeda J, Garcia EV, et al. Quantitative same-day rest-stress technetium-99m sestamibi SPECT: definition and validation of stress normal limits and criteria for abnormality. *J Nucl Med*. 1993;34:1494-1502.
22. 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.
23. Faber TL, Cooke DC, Folks RD, et al. Left ventricular function from gated SPECT perfusion images: an integrated method. *J Nucl Med*. 1999;40:650-659.
24. Kaul S, Wismer GL, Brady TJ, et al. Measurement of normal left heart dimensions using optimally oriented MR images. *AJR*. 1986;146:75-79.
25. Galt JR, Garcia EV, Robbins WL. Effects of myocardial wall thickness of SPECT quantification. *IEEE Trans Med Imaging*. 1990;9:144-150.
26. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet*. 1986;1:307-310.
27. Bland JM, Altman DG. A note on the use of the interclass correlation coefficient in the evaluation of agreement between two methods of measurement. *Comput Biol Med*. 1990;20:337-340.
28. 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.
29. Case J, Bateman T, Cullom SJ, et al. Improved accuracy of SPECT LVEF using numerical modeling of ventricular image blurring for patients with small hearts [abstract]. *J Am Coll Cardiol*. 1999;33:436A.
30. Ford PV, Chatziioannou SN, Moore WH, Dhekne RD. The demonstration of over estimation of LVEF by quantitative gated SPECT in simulated left ventricles [abstract]. *J Nucl Med*. 1999;40:5P.
31. Lear JL, Pratt JP. Errors in automatic gated SPECT ejection fraction calculations: effects of cardiac chamber size and system resolution determined by Monte Carlo simulation [abstract]. *J Nucl Med*. 1999;40:78P.
32. Buvat I, Bartlett ML, Kitsiou AN, Dilsizian V, Bacharach SL. A "hybrid" method for measuring myocardial wall thickening from gated PET/SPECT images. *J Nucl Med*. 1997;38:324-329.
33. Fukuchi K, Uehara T, Morozumi T, et al. Quantification of systolic count increase in technetium-99m-MIBI gated myocardial SPECT. *J Nucl Med*. 1997;38:1067-1073.
34. Manrique A, Faraggi M, Vera P, et al. ²⁰¹Tl and ^{99m}Tc-MIBI gated SPECT in patients with large perfusion defects and left ventricular dysfunction: comparison with equilibrium radionuclide angiography. *J Nucl Med*. 1999;40:805-809.
35. Gordon EP, Schnittger I, Fitzgerald PJ, Williams P, Popp RL. Reproducibility of left ventricular volumes by two-dimensional echocardiography. *J Am Coll Cardiol*. 1983;2:506-513.
36. Semelka RC, Tomei E, Wagner S, et al. Normal left ventricular dimensions and function: interstudy reproducibility of measurements with cine MR imaging. *Radiology*. 1990;174:763-768.
37. Kennedy JW, Baxley WA, Figley MM, Dodge H, Blackman J. Quantitative angiocardiology. I. The normal left ventricle in man. *Circulation*. 1966;34:272-278.
38. Feiring AJ, Rumberg JA, Reiter SJ, et al. Sectional and segmental variability of left ventricular function: experimental and clinical studies using ultrafast computed tomography. *J Am Coll Cardiol*. 1988;12:415-425.
39. Nichols K, Rozanski A, Malhotra S, Cohen R, DePuey EG. Normal limits of left ventricular function parameters from myocardial perfusion gated SPECT [abstract]. *J Nucl Med*. 1996;37:105P.
40. Kang X, Berman DS, Germano G, et al. Normal parameters of left ventricle volume and ejection fraction measured by gated myocardial perfusion SPECT [abstract]. *J Am Coll Cardiol*. 1999;33:409A.