Comparison of gated SPECT, echocardiography and cardiac magnetic resonance imaging for the assessment of left ventricular ejection fraction and volumes

Hakan Demir,* Yusuf Z. Tan,* Guliz Kozdag,† Serkan Isgoren,* Yonca Anik,‡ Dilek Ural,† Ali Demirci,‡ Fatma Berk*

From the *Department of Nuclear Medicine, †Department of Cardiology, ‡Department of Radiology, Kocaeli University School of Medicine, Kocaeli, Turkey

Correspondence and reprint requests: Hakan Demir, MD · Nuclear Medicine · Kocaeli University School of Medicine · Umuttepe Yerleskesi · Kocaeli TR-41380 · Turkey · hakandemir99@yahoo.com · Accepted for publication May 2007

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BACKGROUND: Left ventricular ejection fraction (LVEF), end-diastolic volume (EDV) and end-systolic volume (ESV) can be determined non-invasively by two-dimensional echocardiography (ECHO), gated single photon emission computed tomography (GSPECT) and cardiac magnetic resonance imaging (CMRI). This study was designed to analyze the concordance between LVEF, EDV and ESV values derived from ECHO, GSPECT and CMRI.

METHODS: ECHO, GSPECT and CMRI were performed in a group of 21 patients with suspected coronary artery disease. LVEF, EDV and ESV values were calculated.

RESULTS: The mean LVEF measured with GSPECT, ECHO and CMRI were 55.9±17.8%, 55.7±16.4% and 56.4±15.7%, respectively. The mean EDV measured with GSPECT, ECHO and CMRI were 109.2±42.4 mL, 127.5±42.2 mL and 91.1±38.0 mL, respectively. The mean ESV measured with GSPECT, ECHO and CMRI were 54.2±41.2 mL, 59.9±37.6 mL and 41.8±26.9 mL, respectively. The results of linear regression analysis showed very good correlation between LVEF and ESV values derived from GSPECT, ECHO and CMRI (r=0.91, r=0.92, r=0.97 for LVEF and r=0.86, r=0.91, r=0.91 for ESV, P<0.01). Good correlations were found between EDV values obtained from GSPECT, ECHO and CMRI (r=0.71, r=0.68, r=0.73, P<0.01). Agreement between these techniques in LVEF values was also good, but not in LV volumes, according to Bland-Altman plots.

CONCLUSIONS: This study showed good overall correlations between LVEF, EDV and ESV values derived from GSPECT, ECHO and CMRI. LVEF obtained from any of these three imaging modalities could be used interchangeably. However, care should be taken in comparing LV volumes.

Left ventricular function and volumes have major diagnostic and prognostic importance in patients with various cardiac diseases. Nowadays several noninvasive techniques are available for this purpose, including 2- or 3-dimensional echocardiography (ECHO), cardiac magnetic resonance imaging (CMRI), radionuclide ventriculography (RNV) and myocardial gated SPECT (GSPECT). Since all of these techniques have some advantages or limitations none of them is considered a gold standard. Recently, GSPECT has been proposed for the determination of left ventricular ejection fraction (LVEF), end-diastolic volume (EDV) and end-systolic volume (ESV). GSPECT offers the potential advantage of combining information on myocardial function and perfusion without any extra cost, discomfort and radiation risk to patient.

According to previously published studies, GSPECT correlates well with both ECHO and CMRI with respect to LVEF, LV volumes and wall motion. The aim of this prospective study was to analyze the concordance between LVEF, EDV and ESV values derived from GSPECT, ECHO, and CMRI in the same group of patients.
METHODS
Twenty-one patients with known or suspected coronary artery disease, referred for routine GSPECT imaging, were included in the study. All patients underwent ECHO and CMRI. All investigations were completed within 4 weeks. There were no cardiac events between the three studies. Cardiac medications were not changed during the study. Patients who had a history of severe valvular disease, morbid obesity, pregnancy or who had myocardial infarction, angioplasty or bypass surgery during the 6 weeks before participation in the study were excluded.

GSPECT acquisition was started after 45 minutes of the intravenous injection of 555 MBq of 99mTc-methoxyisobutyl-isonitrile (99mTc-MIBI) at resting condition. Data acquisition was performed with a single-head SPECT system (ADAC Laboratories, Milpitas, California, USA) equipped with a low-energy, high-resolution collimator. A 20% window around the 140 keV energy peak of 99mTc-MIBI was used. The acquisition matrix size was 64×64×16. A total of 64 projections (step-and-shoot mode, 30 s per projection) were obtained over a 180° circular orbit. Acquisitions were gated for eight frames per cardiac cycle. The images were reconstructed using filtered back-projection. The resulting transaxial slices were re-oriented perpendicular to the heart’s long axis, yielding long- and short-axis tomograms. The LVEF and left ventricular volumes were calculated using previously validated and commercially available automated software (Auto SPECT, Autoquant, ADAC Laboratories, Milpitas, California, USA) from the GSPECT images.

ECHO was performed with a Toshiba SSA-390-A ultrasound machine (Toshiba Medical Systems, Nasu, Japan) by one experienced cardiologist blind to the results of the GSPECT study. All images were obtained with a second harmonic mode. Two-dimensionally guided M-mode recordings were taken from the parasternal long-axis view according to the criteria of the American Society of Echocardiography. EDV, ESV and LVEF were derived from apical four-chamber and two-chamber views with the previously validated modified Simpson’s biplane discs method.20,21

All CMRI studies were performed on a 1.5-T MR scanner (Philips Gyroscan Intera Master, Eindhoven, Netherlands) with a 30 mT/m maximum gradient strength and a 150 mT/m per millisecond slew rate using a synergy body coil. Our routine CMRI protocol started with the reference images of Balanced Turbo Field Echo (B-TFE) in sagittal, axial and coronal planes, and was followed by coil sensitivity (SENSE) reference images. ECG gated, breath hold of T2 weighted B-TFE sequence (TR/TE=3.1/1.5, matrix: 256×256) in four chambers, left ventricle short axis and long axis planes were performed.

Values of LVEF, EDV and ESV derived from all three investigations were compared. Continuous data were expressed as the mean±SD. The agreement between LVEF, EDV and ESV derived from GSPECT, ECHO and CMRI data was determined with linear regression (Pearson’s correlation coefficient) and Bland-Altman analysis.22 The differences between GSPECT, ECHO and CMRI measurements of LVEF, EDV, and ESV were tested for significance using a t-test for paired samples and P<0.05 was considered significant. For linear regression analysis P<0.01 was considered significant. Our University Hospital’s Scientific and Ethics Committee for Human Clinical Research approved this protocol, and all patients provided informed consent prior to enrollment into the study.

RESULTS
Twenty-one patients (15 male and 6 female, mean age 55±9 years, range 38-74 years) were included in the study. Fifteen patients were hypertensive. One had diabetes mellitus. Five patients had a history of myocardial infarction. No patient was excluded from the study because of the poor image quality of any imaging modality.

Comparison of LVEF Results
The LVEF measured with GSPECT was in the range 23% to 80%, with a mean of 55.9±17.8%. The corresponding values in ECHO were similar: the LVEF was in the range 23% to 77%, with a mean of 55.7±16.4% (Table 1). The linear regression analysis showed very good correlation (r=0.91, P=0.000) between LVEF assessed with ECHO and with GSPECT. The mean difference in LVEF measured with ECHO and GSPECT was 0.2±7%, with limits of agreement of -13.8% to 14.4% (P=0.883, 95% confidence interval, -3.6 to 3.0), as shown by Bland-Altman analysis. These limits of confidence contained 95.2% (20/21 samples) of the data points. No systematic under- or overestimation of LVEF was found with GSPECT as compared with ECHO.

The LVEF measured with CMRI was in the range 23% to 74%, with a mean of 56.4±15.7% (Table 1). The linear regression analysis showed very good correlation (r=0.97, P=0.000) between LVEF assessed with ECHO and with CMRI. The mean difference in LVEF measured with ECHO and CMRI was -0.74±4.1%, with limits of agreement of -8.9 to 7.4% (P=0.412,
95% confidence interval, -2.6 to 1.1), as shown by Bland-Altman analysis. These limits of confidence contained 95.2% (20/21 samples) of the data points. There was no systematic under- or overestimation of LV EF with ECHO compared with CMRI. There was also very good correlation \((r=0.92, P=0.0001)\) between LV EF assessed with GSPECT and with CMRI. The mean difference in LV EF measured with GSPECT and CMRI was -0.5±7%, with limits of agreement of -14.7 to 13.7% \((P=0.749, 95\% \text{ confidence interval, -3.7 to 2.7})\), as shown by Bland-Altman analysis. These limits of confidence contained 95.2% (20/21 samples) of the data points. Also no systematic under- or overestimation of LV EF was found with GSPECT compared with CMRI. In none of the patients was LV EF measured as definitely abnormal (<40%) with one method and as definitely normal (>50%) with other method.

Comparison of EDV Results
The EDV measured with GSPECT was in the range 46 to 198 mL with a mean of 109.2±42.4 mL. The corresponding values in ECHO were similar: the EDV was in the range 51.9-249 mL with a mean of 127.5±42.2 mL (Table 1). The results of linear regression analysis showed a very good correlation \((r=0.86, P=0.000)\) between EDV assessed with ECHO and with GSPECT. The mean difference in EDV measured with ECHO and GSPECT was 5.7±20.8 mL with limits of agreement of -36.0 to 47.3 mL \((P=0.228, 95\% \text{ confidence interval, -3.8 to 15.1})\), as shown by Bland-Altman analysis. These limits of confidence contained 95.2% (20/21 samples) of the data points. The EDV was not under- or overestimated by GSPECT compared with ECHO.

The EDV measured with CMRI was in the range 6.2 to 98 mL with a mean of 41.8±26.9 mL (Table 1). The results of linear regression analysis showed a very good correlation \((r=0.91, P=0.000)\) between EDV assessed with ECHO and with CMRI. The mean difference in EDV measured with ECHO and CMRI was 18.1±17.3 mL with limits of agreement of -16.5 to 52.7 mL \((P=0.000, 95\% \text{ confidence interval, 10.2 to 25.9})\), as shown by means of Bland-Altman analysis. These

Table 1. Measurement of left ventricular volumes and ejection fraction with the three imaging methods.

| Method | Mean LVEF (%±SD) n=21 | Mean EDV (ml±SD) n=21 | Mean ESV (ml±SD) n=21 |
|--------|------------------------|------------------------|------------------------|
| GSPECT | 55.9±17.8 (23-80) | 109.2±42.4 (46–198) | 54.2±41.2 (9–149) |
| ECHO   | 55.7±16.4 (23–77) | 127.5±42.2 (51.9–249) | 59.9±37.6 (14.8–184) |
| CMRI   | 56.4±15.7 (23–74) | 91.1±38.0 (18.4–151) | 41.8±26.9 (6.2–98) |

The mean difference in EDV measured with GSPECT and CMRI was 18.1±32 mL, with limits of agreement of -46.5 to 82.1 mL \((P=0.018, 95\% \text{ confidence interval, 3.4 to 32.8})\), as shown by means of Bland-Altman analysis. These limits of confidence contained 95.2% (20/21 samples) of the data points. The EDV was slightly overestimated by GSPECT compared with CMRI.

Comparison of ESV Results
The ESV measured with GSPECT was in the range 9 to 149 mL with a mean of 54.2±41.2 mL. The corresponding values in ECHO were similar: the ESV was in the range 14.8-164 mL with a mean of 59.9±37.6 mL (Table 1). The results of linear regression analysis showed a very good correlation \((r=0.86, P=0.000)\) between ESV assessed with ECHO and with GSPECT. The mean difference in ESV measured with ECHO and GSPECT was 5.7±20.8 mL with limits of agreement of -36.0 to 47.3 mL \((P=0.228, 95\% \text{ confidence interval, -3.8 to 15.1})\), as shown by Bland-Altman analysis. These limits of confidence contained 95.2% (20/21 samples) of the data points. The ESV was not under- or overestimated by GSPECT compared with ECHO.
limits of confidence contained 95.2% (20/21 samples) of the data points. The ESV was underestimated by CMRI compared with ECHO. Also there was a very good correlation ($r=0.91, P=0.000$) between ESV assessed with GSPECT and with CMRI. The mean difference in ESV measured with GSPECT and CMRI was $12.4\pm 19.9$ mL, with limits of agreement of $-27.4$ to $52.2$ mL ($P=0.010$, 95% confidence interval, 3.3 to 21.5), as shown by means of Bland–Altman analysis. These limits of confidence contained 95.2% (20/21 samples) of the data points. The ESV was underestimated by CMRI compared with GSPECT.

**DISCUSSION**

Left ventricular function and volumes have major diagnostic and prognostic importance in patients with various cardiac diseases. Nowadays several noninvasive techniques are available for this purpose, including ECHO, CMRI, RNV and GSPECT. In recent years all of these imaging techniques have become more available, and clinicians could be faced with LVEF and LV volume results obtained with various imaging techniques during a long follow-up period. Therefore, cardiologists need to know the exact correlation and agreement between these techniques. Another concern is whether measurements of LV volume and ejection fraction derived from different techniques could be used interchangeably. In contrast to most studies, which included only two imaging modalities (GSPECT vs. ECHO or CMRI; ECHO vs. GSPECT or CMRI) we performed three imaging methods in the same group of patients. The present study is, to our knowledge, only the second one to compare left ventricular functions (LVEF, EDV and ESV) derived from GSPECT, CMRI and ECHO in the same group of patients. In the first study, Yamamura et al performed multi-detector row CT and magnetic resonance imaging in 50 patients, two-dimensional ECHO in 41 patients and GSPECT in 27 patients. They found that the standard deviation of the EF difference between multi-detector row CT and MR imaging was significantly less than that between echocardiography and MR imaging ($P<0.001$) or that between GSPECT and MR imaging ($P<0.001$). According to previous studies that compared GSPECT and ECHO there was very good agreement between LVEF, EDV and ESV values. Fleming found a high correlation ($r=0.76$) between resting echocardiographic EFs and SPECT resting gated sestamibi images in patients with single-vessel disease, and a moderate correlation ($r=0.68$ and $r=0.68$) in patients with 2- and 3-vessel disease, respectively. In a recently published study, we compared left ventricular function and volumes of GSPECT and ECHO in patients with dilated cardiomyopathy. We found good correlations for the assessment of LVEF, EDV and ESV ($r=0.72$, $r=0.71$ and $r=0.71$, respectively). In the present study, when we compared the results of GSPECT and ECHO, the values for LVEF, EDV and ESV correlated strongly ($r=0.91, r=0.81$, $r=0.71$, respectively). Also no systematic under- or overestimation of LVEF and ESV values was found with GSPECT as compared with ECHO according to Bland–Altman plots. However, EDV was slightly overestimated by ECHO compared with GSPECT.

A number of studies have compared GSPECT and CMRI. Thorley et al. compared GSPECT with CMRI measurements of LVEF and EDV in 50 patients and found a good correlation ($r=0.82$ and $r=0.90$). In another study, Bavelaar-Croon and colleagues also found a good correlation for LVEF, EDV and ESV ($r=0.85$, $r=0.94$, $r=0.95$, respectively). In our study, LVEF, EDV and ESV results of GSPECT were also correlated very well with CMRI results ($r=0.92$, $r=0.68$, $r=0.91$, respectively). LVEF was not under- or overestimated by GSPECT compared with CMRI. But, EDV and ESV were slightly underestimated by CMRI compared with GSPECT. Interestingly, most previous studies have reported that volumes were underestimated by GSPECT compared with CMRI. Because of high spatial resolution, excluding papillary muscles and trabeculations from volumes in CMRI was easier than in either GSPECT and ECHO. In our study, to exclude major vascular structures and valves from ventricular volume slices of CMRI were minimally repositioned to midventricular region at the base of the heart. So, inclusion or exclusion of the most basal slice, which consists of parts of LV myocardium, outflow tract, and left atrium, could be the main reason for the difference between previous studies and the present study. In addition, the frame numbers per cardiac cycle were different in CMRI and GSPECT (16 vs. 8 frames for CMRI and GSPECT, respectively). We used 8 frames for GSPECT images to obtain sufficient count statistics. This could be the technical reason for the conflict in volume results.

Direct comparison of CMRI and ECHO was made using different protocols and imaging techniques, in some previous studies. Hoffmann et al, in a
multi-centre study, assessed the agreement of LVEF derived from cineventriculography, cardiac magnetic resonance imaging, unenhanced and contrast-enhanced echocardiography in 120 patients. They reported that the correlation for EF between MRI and unenhanced echocardiography was 0.60. In most of those studies that compared CMRI and ECHO, measurements of CMRI were larger than ECHO results. In the present study, LVEF, EDV and ESV values from CMRI and ECHO correlated very well. While LVEF was not under- or overestimated by CMRI compared with ECHO, the values of EDV and ESV were underestimated. We think the reasons for the difference between CMRI and GSPECT results (exclusion of basal portions of left ventricle and high spatial resolution of CMRI) also account for the difference between ECHO and CMRI results.

In addition to very good correlations and agreements between the LVEF values for these three imaging modalities, in none of the patients was LVEF measured as definitely abnormal (<40%) with one method and as definitely normal (>50%) with the other method. This result is in agreement with the study by Bavelaar-Croon and colleagues. Thus, LVEF results obtained from any of these three imaging modalities could be used interchangeably.

In conclusion, we found overall very good correlations and agreements between LVEF derived from GSPECT, CMRI and ECHO as shown both linear regression and Bland-Altman analysis. Even though we found good correlations between EDV and ESV values derived from all of these imaging modalities, agreements between these results were not as good as between LVEF results. Therefore, care should be taken in comparing LV volumes derived from these three imaging methods.
RESEARCH

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