

Comparison of left ventricular functional parameters measured by gated single photon emission tomography and by two-dimensional echocardiography

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Abstract

The aim of the present study was to evaluate the correlation amongst left ventricular (LV) functional parameters estimated by gated single photon emission tomography (GSPET) and two-dimensional (2D) M-mode, echocardiography (ECHOC). GSPET was performed in a single day stress/rest protocol by using either technetium-99m methoxy-isobutyl-isonitrile (^{99m}Tc-MIBI) or technetium-99m tetrofosmin (^{99m}Tc-myoview) in 36 consecutive patients, 21 males and 15 females; mean age 57.6±11.8 y, range 32-82 y. The various LV parameters studied were: ejection fraction (EF), end systolic volume (ESV), end diastolic volume (EDV), stroke volume (SV) and LV mass (LVM). The GSPET data were reconstructed using an automatic algorithm employing filtered back projection (FBP) and further analyzed by Emory cardiac (EC) toolbox versions EO-00369 and EO-00733 for the quantitative determinations of these parameters. All patients underwent ECHOC within 1-2 h of the post-stress data acquisition of GSPET. Our results showed that the LV volumes and the LVM showed good correlation ($r=0.749$ to 0.952 , $P=0.01$). These values could thus be used interchangeably. The assessment of these parameters by GSPET therefore does not seem to be affected by the dose of the radioactivity administered as the dose of the ^{99m}Tc-labeled myocardial agents for acquiring rest study was approximately four times higher than that for the stress study. Our results also showed that the mean ± SD values of the volumes and the EF of the LV evaluated by the two techniques, differed significantly except significant correlations for ESV, EDV and LVEF were observed between the two methods: $r=0.574$ to 0.954 ; 0.347 to 0.952 and 0.516 to 0.876 respectively. On the other hand, a wide disagreement was observed in estimating the LVM by the two techniques. The LVM measurements by 2D ECHOC were approximately double the values estimated by GSPET. Despite the large disagreement, a small correlation ($r=0.33$, $P=0.05$) was observed for LVM between the two techniques. *In conclusion*, although we observed a good correlation for LV volumes and LVM between the GSPET and the ECHOC techniques, yet these two techniques cannot be used interchangeably.

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Introduction

The quantitative assessment of the left ventricular (LV) functional parameters has major prognostic as well as diagnostic and therapeutic significance in the management of patients with coronary artery disease (CAD) [1-6]. Echocardiography (ECHOC) is the technique most commonly used for the measurement of LV parameters. An important achievement in nuclear cardiology is coupling the LV myocardial perfusion to function in a single-injection, single acquisition study with electrocardiogram by using gated single photon emission tomography (GSPET). GSPET imaging allows for the simultaneous assessment of myocardial perfusion, LV cavity volumes and LV functional parameters [7-12]. This technique applies either thallium-201 (²⁰¹Tl) or technetium-99m (^{99m}Tc) labeled radiopharmaceuticals. Several studies have reported a good correlation in studying LV functional parameters by using ²⁰¹TlCl and (technetium-99m-labeled methoxy-isobutyl-isonitrile) ^{99m}Tc-MIBI radiopharmaceuticals in GSPET studies [13-15]. However, the GSPET technique has the inherent limitation of low spatial resolution as opposed to the other imaging modalities such as ECHOC, computed tomography (CT) and magnetic resonance imaging (MRI), which determine systolic function directly from high resolution anatomical images [16]. Also, GSPET

technique faces different degrading factors related to the deterioration of depth-dependant collimator resolution, the partial volume effect, scatter and attenuation. The derived LV functional parameters may thus be affected by the accuracy of the applied reconstructed methods i.e. filtered backprojection (FBP) and ordered subsets expectation maximization (OSEM). Some commercially available quantitative software packages for GSPET processing provide good LV mass (LVM) measurements [17]. However, the validity of these softwares has not been established.

The aim of this study was to evaluate LV functional parameters measured by GSPET and using two different ^{99m}Tc -labeled agents as compared to the 2D, M-mode ECHOC.

Patients and methods

Thirty-six patients, 21 males and 15 females, mean age 57.6 ± 11.8 years, range 38-82 years, referred to the Department of Nuclear Medicine for the diagnosis of myocardial perfusion defects were enrolled in the study. All the patients enrolled in the study were suspected or documented for having coronary artery disease (CAD) and were included. The patients who developed infarction or signs of myocardial ischemia or cardiac insufficiency during the study were excluded from the study. After being fully informed, all patients gave their consent for the participation in the present study. The protocol of this study was approved by the Ethical Committee of the Postgraduate Institute of Medical Education and Research, Chandigarh, India. All patients included in this study underwent at our Department a diagnostic stress and rest myocardial perfusion scintigraphy. If during the acquisition of the GSPET data and/or the ECHOC study patients developed chest pain or any change in their clinical status, they were excluded from this study.

Thirteen patients underwent GSPET study with ^{99m}Tc -MIBI (cardiolite, Bristol Myers Squibb, Medical Imaging Inc, USA). The remaining 23 patients were subjected to GSPET with technetium ^{99m}Tc -tetrofosmin (^{99m}Tc -myoview, Amersham plc, UK). Each patient after fasting overnight, was intravenously (iv) injected with 185-250 MBq of either ^{99m}Tc -MIBI or ^{99m}Tc -myoview at peak stress. Physical-Bruce protocol or dobutamine stress was used. Physical stress was given on Medical Treadmill (CardioTrace-900 XL, Whispermill, Bangalore, India coupled with 12 leads ECG Monitor, MAC 1200 ST, Marquette, Germany, operational at 230 V and 50 MHz). Dobutamine stress was given by using a syringe infusion pump (EMCO, Infusor 850+, Bangalore, India). The stress test was considered at its peak when either the patient's heart rate reached 85% of the predicted maximum heart rate (frequently defined as 220 beats/min minus the patient's age in years) or when the heart rate-blood pressure product (maximum heart rate achieved multiplied by the maximum systolic blood pressure reached), exceeded a value of 20,000. If none of these conditions was met, the stress was considered as sub-maximal. Post-stress myocardial SPET acquisition was performed under a dual headed gamma camera (E Cam, Siemens, Erlangen, Germany) using

the low energy-high resolution parallel hole collimator. The patients who received ^{99m}Tc -MIBI were instructed to take a fatty meal after the stress test. The post-stress GSPET data were acquired at 45-60 min later in supine position, with R-R gating (8 frames /RR interval) in 64×64 matrix and in 64 projections (20 sec/projection) each throughout the 180° arc. Similarly four hours later, rest GSPET data was acquired after 45-60 min following reinjection of 555-740 MBq activity of ^{99m}Tc -labeled myocardial perfusion agents. Transaxial reconstruction of SPET images was achieved by FBP using Butterworth filter of order 7 and cutoff 0.6. These transaxial images were further processed to generate oblique sections reoriented along the horizontal and vertical long and short axes of the LV. Emory cardiac (EC) toolbox versions EO-00369 and EO-00733, was applied to acquired stress (gated/nongated data), rest (non gated) raw data and reoriented oblique stress/rest images using five sets of images. Quantitative evaluation of the left ventricular ejection fraction (LVEF), end diastolic volume (EDV), end systolic volume (ESV), stroke volume (SV) and LVM was done using EC toolbox. Two nuclear medicine specialists did the processing of GSPET data for the evaluation of these parameters considering only the mean \pm SD values. The difference in the mean values of the various quantitative parameters calculated by two individuals was less than $\pm 3.0\%$.

All patients were also subjected to 2D-ECHOC at rest by using M Mode and four chamber views Simpson's formula [18,19] performed within one hour of the acquisition of GSPET post stress data and the same as above quantitative parameters of LV functions were estimated. To compare the parameters estimated by the two GSPET and ECHOC techniques, the non-parametric test (2-related samples) employing Wilcoxon signed ranks test and two-tailed Pearson's correlation analysis were applied using SPSS version 10.0 for windows. The same cardiologist carried out all the ECHOC procedures. In order to evaluate the intraoperative variations, 10/36 of the patients underwent a second ECHOC at random. Deviations between these two ECHOC studies were less than 5%.

Results

The mean \pm S.D. values of the LV volumes and mass as computed by the GSPET (stress and rest) and the 2D ECHOC methods are presented in Table 1. Figures 1a and 1b present the histographic comparison of the GSPET and ECHOC results. Table 2 shows the results of Pearson's correlation analysis. The GSPET (post-stress and rest) mean \pm SD values for LVEF, EDV, ESV, SV, and LVM and the corresponding ECHOC values are shown in Table 1. Specifically, Table 1 shows that GSPET parameters at rest and at stress differ significantly with the corresponding ECHOC parameters. The 2-tailed Pearson's correlation-SPSS version 10.0 for Windows revealed that a significant correlation ($r=0.344-0.598$; $P=0.01-0.05$) was observed for all LV parameters studied by GSPET at post-stress as compared to the same parameters studied at rest and also between the above parameters studied by GSPET and by ECHOC (Table 2).

Table 1. Comparison of LVEF, EDV, ESV, SV and LVM values by the GSPET and ECHOC techniques

Technique	LVEF (%) (mean ± SD)	EDV (mL) (mean ± SD)	ESV (mL)	SV (mL)	LVM (g)
A: Stress GSPET	64.4 ± 19.4	77.2 ± 38.4	32.0 ± 30.5	45.0 ± 15.7	104.1 ± 38.9
B: Rest GSPET	67.1 ± 17.3	74.4 ± 36.3	28.7 ± 27.4	45.3 ± 16.2	98.7 ± 29.7
C: 2D-ECHOC	56.4 ± 10.1	74.1 ± 34.7	52.8 ± 23.8	61.2 ± 20.0	213.0 ± 77.0
t-test	Significance (p) as evaluated by Wilcoxon non-parametric test				
A vs C	0.008	<0.0001	0.0001	0.0001	<0.0001
B vs C	0.0001	<0.0001	<0.0001	<0.0001	<0.0001
A vs B	0.082	0.156	0.042	0.042	0.099

Table 2. Pearson’s correlation analysis amongst various functional parameters evaluated by the GSPET and ECHOC techniques in all patients studied

Techniques	LVEF	EDV	ESV	SV	LVM
A versus C	r=0.589 (P=0.01)	r=0.429 (P=0.01)	r=0.574 (P=0.01)	r=0.344 (P=0.05)	r=0.337 (P=0.05)
B versus C	r=0.516 (P=0.01)	r=0.347 (P=0.05)	r=0.598 (P=0.01)	r=0.134 (P=N.S.)	r=0.335 (P=0.05)
A versus B	r=0.876 (P=0.01)	r=0.952 (P=0.01)	r=0.954 (P=0.01)	r=0.749 (P=0.01)	r=0.926 (P=0.01)

Techniques: A: Stress GSPET, B: Rest GSPET, C: ECHOC

Discussion

Berman et al (1998), using the Cedars quantitative gated SPET software, reported excellent interstudy repeatability for LV volumes when patients were studied both in prone and in supine positions [19]. Our results are in agreement with those of other investigators who used either ^{99m}Tc agents or ²⁰¹TlCl. They reported an excellent correlation between post-stress and rest or redistribution GSPET studies for the estimation of both LV volumes and LVEF [20]. Other studies however, have demonstrated that GSPET performed immediately after exercise, may in some patients manifest post-ischemic myocardial stunning [21-23]. This could not apply to our patients because none had infarction or signs of myocardial ischemia during this study. As the stress GSPET with ^{99m}Tc-labeled radiopharmaceuticals acquisition is performed at 45-60 min after the radiopharmaceutical administration, the evaluated LV functional parameters at this point of time signify measurements at rest. This may explain the fact that in our study GSPET parameters at rest and at stress did not differ. This result implies that for the comparison between GSPET and ECHOC parameters, the GSPET-LV functional measurements at 3-4 h at rest, could also be a good estimate to be used for routine purposes. However, for the ²⁰¹TlCl stress studies with acquisition performed at the peak stress activity, the GSPET stress and rest LV values, would be different from one another because in that situation of cardiac stress, the heart rate, arterial blood oxygen content and stroke volume, all increase. Therefore, in ²⁰¹TlCl-GSPET studies, only LV para-

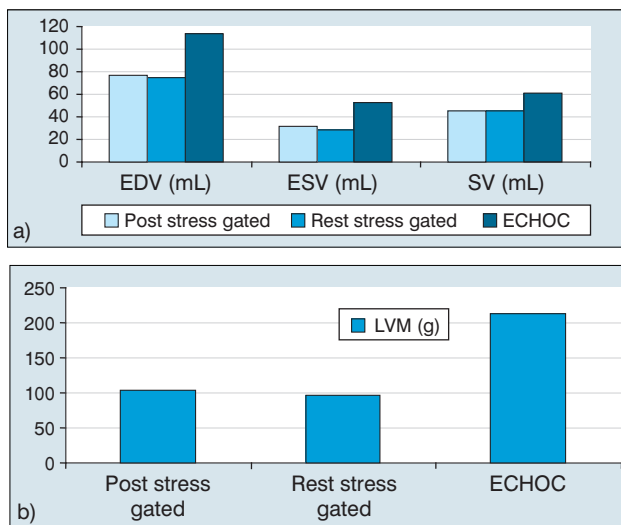


Figure 1a. The graphic presentation of EDV, ESV and SV derived by the GSPET and ECHOC techniques; cumulative results from 36 patients

Figure 1b. The LVM (g) as compared by the GSPET and ECHOC techniques

eters derived from the rest data could be compared with the same GSPET parameters at rest or at post-stress to be considered for comparison with the rest ECHOC values.

Our GSPET study by using either ^{99m}Tc-MIBI or ^{99m}Tc-myoview, overestimated LVEF by 14% in comparison with the ECHOC values. However there was a good correlation (r=0.59, P=0.01) amongst the two techniques for the measurement of LVEF. Achtert et al (1997) by using a digital phantom found that quantitative GSPET when a regular dose was used overestimated LVEF by 3%-7% and when a low radioactivity dose was used, GSPET underestimated LVEF up to 9% [24]. However, in the present study, we used a rather low or intermediate amount of radioactivity of the tracer. Achtert et al (1997) have also reported that the accuracy in determining LV volumes had an average error of 12% [24].

In this study, our patients had lower EDV, ESV, SV and consequently higher LVEF values by GSPET than by ECHOC. However, we have observed a good correlation of the above values by these two techniques. Germano et al (1995) by using a phantom model, found that volumes estimated by a quantitative GSPET algorithm were within 10% of the true volume

[25]. Zanger et al (1997) reported a good agreement between GSPET and ECHOCardiography for the determination of LVEF and LV volumes [26]. Cwajg et al (1999) reported that independent of the tracer selection, the results of absolute volumes and LVEF estimates correlated well with the 2D ECHOC results [21]. They further indicated that using high doses of the ^{99m}Tc -agent might be ideal for GSPET studies although more work is necessary on this aspect. Interestingly, in the present study, we observed that the corresponding values for various LV volumes and mass as evaluated by GSPET –stress and GSPET-rest using lower (185-250 MBq) and higher doses (555-740 MBq) of ^{99m}Tc -labelled agents (cardiolite or myoview) respectively did not differ significantly from each other (Tables 1 and 2). In view of this observation, the different radioactivity doses of the two ^{99m}Tc -agents used for GSPET studies are not expected to induce any statistical difference in the LV-functional measurements.

In the present study, we have observed a big disparity for LVM measured by the post-stress and rest GSPET versus the ECHOC technique. The ECHOC values were higher by a factor of two (Table 1) and no significant correlation ($r=0.33$) was observed between the two techniques (Table 2). In view of the limitation, that gamma camera cannot determine actual myocardial thickness [27], the GSPET technique has adopted different assumptions for the definition of myocardial wall boundaries for calculating myocardial mass. Some techniques assume that the myocardial thickness at the end of diastole is uniform (1 cm) for all patients and all territories [28]. Others rely on physicians' definition of the endocardial and epicardial boundaries [29,30]. It was recently reported that LVM values were not significantly different between GSPET and 3D-ECHOC studies (153 ± 39 g versus 146 ± 35 g) [31] and that the GSPET-LVM correlated significantly ($r=0.63$, $P<0.0001$) with the 3D ECHOC with a mean difference of 7.0 ± 32 g. On the contrary, the above values in our study between the GSPET and the 2D-ECHOC techniques did not correlate. The above mentioned authors derived GSPET-LV parameters by quantitative gated software (QGS), developed by Cedars Sinai Medical Center, LA, CA, USA and compared these values with the values calculated by 3D-ECHOC [31]. It is obvious that in our study GSPET data analysis by the currently available version of Emory Cardiac Toolbox (EO-00369 and EO-00733) underestimated the LVM as compared with the 2D-ECHOC. The absolute 2D-ECHOC values (213.0 ± 77.0 g) for LVM in our study were significantly higher than the 3D-ECHOC values (146 ± 35 g) reported by Akinboboye et al (2003) [31]. Although these two studies used different ethnic patients' population, this wide variation could not be attributed to ethnic diversity. The difference in LVM estimated by 2D and 3D-ECHOC techniques, could be ascribed to inter technique variations, as 3D-ECHOC techniques are supposed to give more accurate measurements for LVM. It has been reported that conventional ECHOC methods used for the calculation of LVM in M-mode have overestimated these results [32]. Also that the most compatible to the 3D-ECHOC results are the 2D-ECHOC results because they both employ the

area-length method for LVM measurements [32]. The said method uses the epicardial (A_{Epi}) and the endocardial (A_{Endo}) areas from the short-axis slice as the M-mode calculations, just basal to the papillary muscles. Further, the ventricular long axes (epicardial- L_{Epi} and endocardial- L_{Endo} are measured from the horizontal long-axis slices), thereby maximizing accuracy of the apex position. The LVM by this method is calculated by the formula:

$$\text{LVmass (g)} = 1.05 \times \{5/6 (A_{\text{Epi}} \times L_{\text{Epi}}) - (A_{\text{Endo}} \times L_{\text{Endo}})\}.$$

This method has been reported to give LVM measurements very close to the true LVM as compared to other 2D methods [33,34]. In yet another study, the estimation of LV functional parameters was more accurate with a multi-detector row CT scanner than with the 2D-ECHOC or the ECG-GSPET [35]. It has also been reported that contemporary M-mode 2D-ECHOC provided consistent values for LV size or function and did not seem to be affected by ethnic diversities, i.e. by urban or rural populations of differing ethnicity [36].

Conclusive remarks

Results of our study suggest that for the estimation of LV-volumes, EF and mass, in patients having no evidence of prior myocardial infarction or myocardial ischemia during the study, GSPET data cannot be interchanged with 2D-ECHOC due to the wide variation between the two techniques. The large difference in values of LVM derived by these two techniques, and closer approximation of GSPET derived value with 3D-ECHOC, suggest that there needs to be a study comparing GSPET, 2D-ECHOC and 3D-ECHOC to establish the 'gold standard' for quantitative assessment of LV parameters. However, in view of the excellent reproducibility and the repeatability of the GSPET technique for the assessment of various LV volumes, LVEF and LVM in our study, this technique has a good prognostic utility. The assessment of these parameters by GSPET does not seem to be affected by the dose of the radioactivity administered (^{99m}Tc -labeled myocardial agents) as no significant difference was noticed between the GSPET post-stress and rest studies.

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