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Original Article

Normal Values of Left Ventricular Functional indices in Gated ^{99m}Tc-MIBI Myocardial Perfusion SPECT

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ABSTRACT

Introduction: Although left ventricular(LV) function parameters measured by gated myocardial perfusion SPECT (GSPECT) have been validated, experimental data have revealed that the calculated the LV function parameters using GSPECT are affected by patient populations as well as particular acquisition and processing conditions. We tried to determine the normal values of GSPECT in an Iranian population.

Methods: We studied 3500 Iranian patients who underwent GSPECT in an outpatient setting. To develop normal limits of LV functional indices using GSPECT, 148 patients with a low (<5%) likelihood of coronary disease and normal tomograms were selected. No one of 148 patients had known coronary artery disease, typical angina, history of hypertension, diabetes mellitus, and smoking, any abnormality in echocardiography or hyperlipidemia. They were not taking any medication known to affect LV function at least 2 days before the study. End diastolic volume (EDV), end systolic volume (ESV) and LV ejection fraction (LVEF) were calculated in rest GSPECT using iterative reconstruction and QGS (quantitative gated SPECT) software.

Results: Mean EDV, ESV and LVEF were 53.8±20.2, 14.3±10.8 and 75.0%±9.6% respectively. These data showed a Gaussian distribution, so mean±2SD would show the upper or lower limits of normal for LV functional parameters. There were the marked sex differences in mean LVVs and LVEF measurements. BMI index had not effect on the measurement of the LV functional parameters. We noticed that 85.4% of our subjects had ESV<25 ml while most of them were women (112/123, 91%).

Conclusion: From a clinical viewpoint, each institute should use a standard protocol for the specific patient population and for the mode of SPECT acquisition and reconstruction. Normal thresholds using GSPECT, OSEM reconstruction and QGS algorithm in men and women were EDV>130, ESV>55 & LVEF<52% and EDV>77, ESV> 26 and LVEF<62% respectively.

Key words: Left ventricular volume, Ejection fraction, Myocardial perfusion, Gated SPECT, Normal limits.

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INTRODUCTION

Electrocardiography -gated mode for simultaneous assessment of myocardial perfusion and left ventricular (LV) function in gated myocardial perfusion SPECT (GSPECT) allows better clinical risk stratification using assessment of ventricular function variables in addition to perfusion findings (1-4).

Validation studies indicate that measurement of left ventricular volumes (LVVs) and ejection fraction (LVEF) by this approach are highly reproducible and accurate. Different methods and algorithms to quantify LVEF and LVVs in GSPECT have been described, all offering high reproducibility and good agreement with various non-nuclear or nuclear techniques (5-17). For the computation of LVVs and LVEF, the commercially available automated QGS (Cedars-Sinai Quantitative Gated SPECT) software has most frequently been validated using the currently established gold standard of cardiac magnetic resonance imaging (cMRI) and is currently the most widely used software in the clinical setting (5-20).

However, experimental data have revealed the sensitivity of LV function parameters measured by GSPECT to patient populations as well as particular acquisition and processing conditions, such as injected radiotracer, injected dose , time of imaging , background activity, patient position and patient–detector distance during acquisition, matrix size, temporal sampling (16 versus 8 frames per cardiac cycle), collimation system, filtering and zooming , reconstruction strategy, cut-off frequency, algorithms and softwares , perfusion defects and high liver activity, etc (5-24).

Another problem in using quantitative GSPECT for LV function parameters calculation is encountered in patients with a small heart. Indeed, due to the limited spatial resolution of gamma cameras, the opposite endocardial edges of the left ventricle overlap, so that the ventricular cavity may become almost virtual, especially at end-systole. This results in an underestimation of volumes, and hence overestimation of LVEF, particularly when using algorithms based on edge detection (5,16,19,25). QGS was shown to overestimate the ejection fraction in patients with small hearts especially when the end-diastolic volume (EDV) was <70ml or the end-systolic volume (ESV) <25ml (16,19, 25-27).

Some studies suggested that the patients with low ESV (especially less than 25 ml) should be considered as patients with small heart(16,19,25-27). In spite of these reports, in our clinic we have frequently observed patients with low likelihood of CAD and normal GSPECT that many of them have had ESV<25 and high LVEF.

Hence in this study we assessed the results of GSPECT in patients with a low likelihood of coronary artery disease (CAD) to determine normal values for both gated SPECT, LVVs and LVEF in an Iranian population.

METHODS

Study population: The study population consisted of 148 patients with normal myocardial perfusion SPECT from 3500 patients referred for GSPECT in an outpatient setting.

To develop normal limits for LVVs and LVEF, these 148 patients with a low (<5%) likelihood of CAD were evaluated. Likelihood of CAD was derived on the basis of Bayesian theory of prescan patient data. All 148 subjects did not have known coronary artery disease, typical angina, history of hypertension, diabetes mellitus, smoking, CCU admission, hyperlipidemia and were not taking any medication known to affect LV function at least 2 days before the study. All were prescreened with a 2-dimensional echocardiography to exclude any abnormality. Patients with documented CAD, a history of myocardial infarction, a history of coronary revascularization, or any abnormality in electrocardiogram were excluded.

Acquisition protocol: All patients underwent stress/rest ^{99m}Tc-sestamibi GSPECT using a 2-day protocol. Rest GSPECT was performed 90 min after intravenous injection of 740-925 MBq ^{99m}Tc-sestamibi. SPECT was performed in the supine position using a dual-head gamma-camera in the 90°-setting (Dual-Head Variable-Angle E.CAM; Siemens) equipped with high-resolution, low-energy collimators. The two heads were placed in an L-shaped configuration. Thirty two views over a 180˚ arc were obtained from the 45˚ right anterior oblique to the 45˚ left posterior oblique. Images were acquired for 25 sec per view with a zoom factor of 1.45 and gated at 8 frames per cardiac cycle using an R-wave trigger. The images were stored in a 64×64 matrix in the computer.

Data analysis: The projection data were reconstructed into tomographic transaxial images using ordered sets expectation maximization (OSEM) technique with 8 iterations and two subsets. The transverse images were reoriented into the three orthogonal slices, short, horizontal and vertical long axis, for display and

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interpretation. No attenuation or scatter correction was applied. The initial interpretation of myocardial perfusion was provided visually and semi-quantitatively. The 17-segment five point scale was used for visual semi-quantitative assessment of myocardial perfusion (Figure 1). The summed stress score (SSS), summed rest score (SRS) and the summed difference score (SDS=SSS-SRS) were calculated (28).

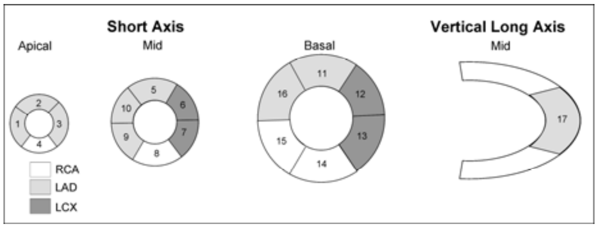

Fig. 1: 17-segment five point scale for semi-quantitative assessment of myocardial perfusion.

Measurement of LVVs and LVEF: For calculation of EDV, ESV and LVEF, we used a commercially available automated program, QGS which estimates three dimensional image volumes from gated SPECT studies. After calculation of the endocardial volumes, it derives the LVVs and LVEF. The rest phase indices were used to develop normal limits of EDV, ESV and LVEF on GSPECT.

Statistical analysis: Continuous variables are described by the mean value ± standard deviation (SD). Patients groups were compared using a *t* test for continuous variables. On-way ANOVA analysis and Tukey HSD test in post Hoc analysis were used for comparison of mean values between subgroups. A P value of less than 0.05 was considered statistically significant.

RESULTS

We evaluated 148 patients with a low (<5%) likelihood of CAD and normal tomograms to develop normal limits of the left ventricular functional indices. The population included 27(18.2%) men and 121(81.8%) women with a mean age of 52.9±11.6 (26-78). Visual calculated SSS and SRS in all patients were between 0 and 3. LV functional indices (EDV, ESV, and LVEF) calculated using rest GSPECT in our 148 subjects showed a Gaussian distribution.

Table 1 summarizes the results of rest EDV, ESV and LVEF in all 148 patients as well as in males and females.

Body mass index (BMI) had been calculated only in 73 patients. Mean calculated BMI in these patients was 28.1±5.0 (16-44.2).

Table 1: Left ventricular functional indices in rest gated myocardial perfusion SPECT.

LV Index	Sex			Total
	Females	Males	*P* value	
EDV(ml)	48.8±14.3	76.0±27.2	<0.001	53.8±20.1 (18-167)
ESV(ml)	11.4±7.2	27.9±13.7	<0.001	14.3±10.8 (2-70)
LVEF (%)	78.4±8.3	64.9±6.6	<0.001	75.0±9.6 (43-94)

The patients were classified based on BMI as obese (BMI≥30), overweight (25≤BMI<30), and normal weight (BMI<25). The LVEF was 76.7±7.6, 76.2±9.2 and 78.5±9.9 in obese, overweight and normal weight subjects respectively (Table 2). One way ANOVA with Tukey HSD test as post Hoc analysis showed no significant difference in EDV, ESV and LVEF between obese, overweight and normal weight patient groups.

Table 2: End-diastolic volume (EDV), end-systolic volume (ESV) and left ventricular ejection fraction (LVEF) in different groups based on body mass index (BMI).

LV functional index	BMI<25	25≤BMI<30	BMI≥30	*P* value ANOVA
EDV(ml)	44.1±18.8	50.3±14.9	48.9±14.0	0.4
ESV(ml)	11.1±9.4	12.8±7.8	12.0±6.5	0.7
LVEF (%)	78.5±9.9	76.2±9.2	76.7±7.6	0.7

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DISCUSSION

This is the first study describing normal values of LV functional indices using GSPECT and OSEM reconstruction in an Iranian population.

We derived normal limits for automatically measured EDV, ESV and LVEF in a population with a low (<5%) likelihood of CAD undergoing ^{99m}Tc Sestamibi GSPECT. BMI index had not effect on the measurement of the LV functional parameters.

Because of Gaussian distribution of these data, mean±2SD would show the upper or lower limits of normal for LV functional parameters (Table 3).

Table 3: Abnormal criteria for left ventricular functional indices.

Parameters	Men	Women	Overall
EDV(mL)	>130	>77	>94
ESV(mL)	>55	>26	>36
LVEF	<52%	<62%	<57%

Table 4: Frequency of patients based on End-systolic volume (ESV). (P<0.001)

Patients	ESV<25 ml	ESV≥25 ml	Total
Women	112(94.9%)	6(5.1%)	118(100%)
Men	11(42.3%)	15(57.7%)	26(100%)
Total	123(85.4%)	21(14.6%)	144(100%)

Different population and acquisition factors have effect on calculated LVVs and LVEF on GSPECT (5-24). We showed previously in a study on 60 patients using GSPECT, that heart rate, EDV, ESV and stroke volume are significantly different when the image acquisitions were performed on prone versus supine position (24). In another study, we studied thirty patients with ESV<25 ml. They underwent rest ^{99m}Tc Sestamibi GSPECT using acquisition zooms of 1.45 and 1.78 consecutively (19). Increasing in zooming or filter cut-off frequency resulted in higher EDV and ESV but lower LVEF. Differences in LVEF between two acquisition zooms were decreased by sharper cut-off frequencies (19). Gayed et al. studied 32 patients with GSPECT and echocardiography (23). They concluded that the dose of injected radiotracer can affect the result of GSPECT as well as high-dose GSPECT demonstrated better correlation with quantitative echocardiography LVEF results (23). In some studies, it is noted that there may be difference between calculated LVVs and LVEF using post-stress or rest GSPECT (21, 22). Many studies were conducted on effect of different available algorithms (QGS, ECTb, 4D-MSPECT, LMC, Multidim, LVGTF) on calculation of left ventricular functional indices(17).These software were accurate and there are good correlations between them and gold standard procedures, although the calculated values are different using these softwares. QGS has most frequently been validated using the currently established gold standard of cMRI as well as QGS is currently the most widely used in the clinical setting (1-20).

Kawano et al, studied 64 patients who underwent GSPECT. Normal range of LVEF in Japanese (mean±2SD) was 53-93 % (29). Rozanski et al. (30) studied 98 normotensive patients with a low Bayesian likelihood (<10%) of CAD using ^{99m}Tc Sestamibi GSPECT. They had LVEF, EDV and ESV 63±10, 73±29 and 28±17 respectively. They reported abnormal criteria based on mean ±2SD; in men: LVEF<41%, EDV>157 and ESV>78 and for women: LVEF<49%, EDV>106 and ESV>47.

Anyway, in our study, we derived abnormal thresholds (Table 3) in rest ^{99m}Tc Sestamibi GSPECT using acquired images in supine position with a zoom factor of 1.45, 25 sec per view, gated at 8 frames per cardiac , 64×64 matrix as well as reconstructed by OSEM and processed by QGS.

In addition to overall cut-off values, men and women were separated for these analyses, given the marked sex differences in mean LVVs and LVEF measurements. In concordance with prior observations, significant sex differences in LVVs and LVEF were noted (17,30,31). In women, resting EDV and ESV were significantly smaller and resting LVEF was significantly higher than men. Other investigators have noted a similar relationship (17,30,31). Because women in general have smaller hearts, as seen in this study, a proportionately greater mean resting LVEF could be explained simply on this basis. Increased counts of scintigraphic images at end-systole complicated the identification of LV endocardial borders. The root of this problem may be that counts from close myocardial walls spill into opposite walls,

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thereby distorting count profiles and causing their local maxima to be misregistered toward the center of the left ventricular cavity. Because the effect would be most pronounced at end-systole, the calculated LVEF is artifactually high. Because more women than men have relatively small hearts, this effect could result in skewing of normal limit calculations based on gated SPECT technique (5,16,17, 19,22,25, 30).
A few studies in other nations suggested that the patients with ESV<25 ml had a small heart (16,19,25-27). We noticed that 85.4% of our subjects had ESV<25 ml while most of them were women (Table 4, Chi-Square test: P<0.001).

CONCLUSION

Normal thresholds using GSPECT, OSEM reconstruction and QGS algorithm in men and women were EDV>130, ESV>55 & LVEF<52% and EDV>77, ESV> 26 and LVEF<62% respectively.
From a clinical viewpoint, each institute should use a standard protocol for the specific patient population and for the mode of SPECT acquisition and reconstruction.

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