



RESEARCH ARTICLE

COMPARISON OF EJECTION FRACTION VALUES CALCULATED BY TC-99M MIBI GATED SPECT, F-18 FDG CARDIAC GATED PET, MUGA SPECT AND ECHOCARDIOGRAPHY METHODS IN VIABILITY PATIENTS

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ABSTRACT

Objective: In our study, we aimed to investigate the correlation between left ventricular ejection fraction (LVEF) values measured by four modalities. **Materials and methods:** Among the patients who underwent myocardial perfusion scintigraphy for ischemia/infarct detection and cardiac PET for cardiac viability evaluation, MUGA imaging was performed in patients who agreed to participate in our study. 12 patients, 10 males (83.3%) and 2 females (16.7%), were included in the study (age: 64.66±9.76 (51-81)). LVEF values were measured in all 3 methods. In addition, LVEF values obtained by ECHO performed in the cardiology clinic were also obtained from the patient file. A value of $p < 0.05$ was considered statistically significant. **Results:** LVEF calculated by MUGA SPECT method was found to be statistically significantly higher than LVEF calculated by Tc-99m MIBI GATED SPECT and F-18 FDG cardiac GATED PET ($p=0.01$; $p=0.01$). In the Spearman's correlation test, the LVEF value measured in MUGA SPECT showed a positive high correlation with the LVEF values measured in Tc-99m MIBI GATED SPECT and F-18 FDG cardiac GATED PET ($p=0.01$, $r=0.80$; $p=0.01$, $r=0.95$). A moderate positive correlation was detected between the LVEF value measured in MUGA SPECT and the LVEF value measured in ECHO ($p=0.03$, $r=0.62$). **Conclusion:** Each of the four methods was able to measure LVEF in correlation with each other. LVEF values measured by Tc-99m MIBI GATED SPECT and F-18 FDG GATED cardiac PET showed a high positive correlation with MUGA SPECT. It can be inferred that these examinations can be used interchangeably for LVEF measurement.

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INTRODUCTION

The frequency of cardiovascular diseases is increasing all over the world. Left ventricular failure is most important cause of heart-related mortality. Left ventricular ejection fraction (LVEF) is one of the parameters that best reflects left ventricular systolic function. LVEF is the ratio of the stroke volume to the end diastolic volume. Low LVEF is associated with ventricular arrhythmia and sudden cardiac death. Therefore, accurate measurement of LVEF is of great importance. Coronary angiography, echocardiography (ECHO), gated single photon emission tomography (GATED SPECT), multigated acquisition (MUGA), magnetic resonance imaging (MRI) are the main methods used to measure LVEF (1). Although the gold standard method for measuring LVEF is coronary angiography, it cannot be performed on every patient, because it is an invasive procedure. Therefore, noninvasive methods are needed (2).

Left ventricular functions and LVEF can be determined with MUGA. Systolic and diastolic images of the ventricles can be evaluated visually and quantitatively. Since MUGA was found to be correlated with invasive angiography for LVEF measurement, it was frequently used for a while (3). While being less user-dependent and accurate is an advantage, two-dimensional imaging is a disadvantage. Therefore, three-dimensional nuclear imaging methods have been developed. With GATED SPECT, taken in addition to myocardial perfusion scintigraphy to determine ischemia/infarct, and cardiac positron emission tomography (PET) imaging to investigate cardiac viability, cardiac cavities are evaluated three-dimensionally and LVEF can be measured. In our study, we purposed to investigate the correlation between LVEF values measured by four different methods such as MUGA SPECT, Tc-99m MIBI GATED SPECT, F-18 FDG cardiac GATED PET and ECHO.

MATERIALS AND METHODS

Among the patients who underwent myocardial perfusion scintigraphy for ischemia/infarction detection and cardiac PET for cardiac viability evaluation, MUGA SPECT imaging was performed in those who agreed to participate in the study. In all 3 methods, LVEF values were measured automatically. In addition, LVEF values measured by ECHO were also obtained from the patient file. We included 12 patients in the study, 10 males (83.3%) and 2 females (16.7%) (age: 64.66±9.76 (51-81)). Our study received approval from XXXXX Noninterventional Clinic Studies Ethics Committee. All patients included in the study signed the informed consent form.

MUGA SPECT imaging: After 2 hours of fasting, pyrophosphate cold kit containing 10-20 micrograms/kg tin was administered IV. After 5-10 minutes, 3 ml of blood was taken with a heparinized syringe, incubated with 30 mCi Tc-99m for 5-10 minutes, then injected into the patient again under a gamma camera and imaging was performed. For MUGA imaging, ECG electrodes were connected to the patient. 180-degree SPECT-GATED images were obtained starting from the left anterior oblique projection. 16 frames/cycle images were taken for 2 minutes. SPECT images were obtained in a 64x64 matrix, rotating 64 frames for 20 seconds in each projection. Images were reconstructed by backprojection filtered with a Butterworth filter (cutoff:0.5; order:6) (AutoSPECT Pro, Philips -Intellispace Portal). Attenuation correction was performed using CT. Cardiac imaging was performed on the SPECT-CT device, which was created by combining a double-headed hybrid gamma camera and flat panel CT containing a low-dose X-Ray tube in the same gantry (Philips Brightview X-BT; Ohio, Cleveland, USA). Each image was obtained in a 64x64 matrix, with a zoom of 1.46, using a low energy high resolution (LEHR) collimator (140 keV photoelectric peak, 20% energy window). CT images were obtained with low-dose flat-panel CT (X-ray tube; 2.5 mA, 120 kVp), with a section thickness of 1 mm, using 512X512 matrix, without IV contrast. Reconstructed SPECT and CT images were transferred to a nuclear medicine workstation. It was processed with the CARDIAC-OSEM program and the EF value was obtained automatically.

Tc-99m MIBI GATED SPECT-CT imaging: Patients underwent rest and rest-GATED imaging 40 minutes after 20 mCi MIBI IV injection. In the supine position, 180-degree SPECT images starting from the RAO (right anterior oblique) and thorax images were obtained with flat panel CT. Additionally, ECG-triggered GATED images were taken.

Cardiac imaging was performed on a SPECT-CT device (Philips, Brightview XBT; Ohio, Cleveland, USA), which was created by combining a dual-headed hybrid gamma camera and flat panel CT containing a low-dose. Each image was obtained in a 64x64 matrix, with a zoom of 1.46, using a low energy high resolution (LEHR) collimator (140 keV photoelectric peak, 20% energy window). CT images were obtained with low-dose flat-panel CT (X-ray tube; 2.5 mA, 120 kVp), with a section thickness of 1 mm, using 512X512 matrix, without IV contrast. SPECT images were obtained in a 64x64 matrix, rotating 64 frames for 20 seconds in each projection. Images were reconstructed by back projection filtered with a Butterworth filter (cutoff: 0.5; order: 6)

(AutoSPECT Pro, Philips-Intellispace Portal). CT images were obtained with low-dose flat-panel CT (X-ray tube; 2.5 mA, 120 kVp), with a section thickness of 1 mm, using 512X512 matrix, without IV contrast. Reconstructed SPECT and CT images were transferred to a nuclear medicine workstation. It was processed with the CARDIAC-OSEM program and the EF value was obtained automatically.

F-18 FDG cardiac GATED PET imaging: Fasting blood sugar (FBG) was measured in non-diabetic patients after a 12-hour fast, and oral glucose solution and IV insulin were administered according to the FBG level. From diabetic patients; for those with FBG less than 150 mg/dl, 25 mg oral glucose solution; for those with FBG higher than 150 mg/dl, oral glucose solution and IV insulin were administered. When the blood sugar level was 150 mg/dl at the 30th minute, 10 mCi F-18 FDG IV was administered. Imaging was performed at the 60th minute. Cardiac PET imaging was performed with a hybrid system PET-CT device (Philips Gemini TF Release 3.5.2, Ohaio, Cleveland, USA), which combines a PET camera and a 16-slice CT device. PET images were obtained (512x512 matrix, 1.00 zoom, 3.5mm/sound speed, TOF=16, 368 MBq energy peak, 15% energy window). Tomography images taken with 120 Kev energy, 116 mAs/slice, 600 FOV and 3 mm slice thickness were processed using the ECToolbox program. GATED images were taken with ECG triggering. The EF value was obtained automatically.

Statistical analyses: The mean, standard deviation (SD), minimum and maximum values of LVEF values were calculated. Since the variables were not normally distributed, nonparametric tests were used. Friedman and Wilcoxon tests were applied to determine the difference between groups. Spearman's correlation test was applied to evaluate the correlation. A value of $p < 0.05$ was considered statistically significant. In the correlation analysis, Spearman's correlation coefficient (r) was obtained and the correlation levels between the groups were determined accordingly. Additionally, we evaluated the agreement between LVEF values calculated by different methods with the Bland-Altman plot. All statistics were performed with the SPSS 23 program (IBM SPSS Statistics 25 software).

RESULTS

The mean ± standard deviation (minimum-maximum) values of LVEF measurements obtained by MUGA SPECT, Tc-99m MIBI GATED SPECT, F-18 FDG cardiac GATED PET and ECHO were calculated as follows, respectively: 37.5±12.05% (23-59%), 29.1±13.67% (12-54%), 33.3±12.22% (20-54%) and 39.2±11.26% (25-55) (Figure 1). We found that the LVEF calculated by the MUGA SPECT method was statistically significantly higher than the LVEF calculated by Tc-99m MIBI GATED SPECT and F-18 FDG cardiac GATED PET. ($p=0.01$; $p=0.01$). We also found that LVEF calculated by the ECHO method was statistically significantly higher than LVEF calculated by Tc-99m MIBI GATE SPECT ($p=0.01$). There was no statistically significant difference between the LVEF value calculated by the ECHO method and MUGA SPECT and F-18 FDG cardiac GATED PET ($p=0.56$; $p=0.09$), and between the LVEF values calculated by the Tc-99m MIBI GATED SPECT and F-18 FDG cardiac GATED PET method ($p=0.07$) (Table 1).

Table 1. Relationship between LVEF values calculated in different examinations

Test	Mean±SD (%)	Range (%)	P
LVEF Tc-99m MIBI GATED SPECT	29.1±13.7	12-54	0.01
LVEF MUGA SPECT	37.5±12.1	23-59	
LVEF F-18 FDG cardiac GATED PET	33.3±12.2	20-54	0.01
LVEF MUGA SPECT	37.5±12.1	23-59	
LVEF ECHO	39.2±11.3	25-55	0.56
LVEF MUGA SPECT	37.5±12.1	23-59	
LVEF F-18 FDG cardiac GATED PET	33.3±12.2	20-54	0.07
LVEF Tc-99m MIBI GATED SPECT	29.1±13.7	12-54	
LVEF ECHO	39.2±11.3	25-55	0.01
LVEF Tc-99m MIBI GATED SPECT	29.1±13.7	12-54	
LVEF ECHO	39.2±11.3	25-55	0.09
LVEF F-18 FDG cardiac GATED PET	33.3±12.2	20-54	

LVEF: Left ventricular ejection fraction; SPECT: Single photon emission tomography; PET: Positron emission tomography; ECHO: echocardiography

Table 2. Spearman's correlation analysis results of LVEF values calculated in different examinations

	P	R
LVEF Tc-99m MIBI GATED SPECT and LVEF MUGA SPECT	0.01	0.80
LVEF F-18 FDG cardiac GATED PET and LVEF MUGA SPECT	0.01	0.95
LVEF ECHO and LVEF MUGA SPECT	0.03	0.62
LVEF F-18 FDG cardiac GATED PET and LVEF Tc-99m MIBI GATED SPECT	0.01	0.85
LVEF ECHO and LVEF Tc-99m MIBI GATED SPECT	0.01	0.75
LVEF ECHO and LVEF F-18 FDG cardiac GATED PET	0.04	0.58

LVEF: Left ventricular ejection fraction; SPECT: Single photon emission tomography; PET: : Positron emission tomography; ECHO: echocardiography; r: correlation coefficient

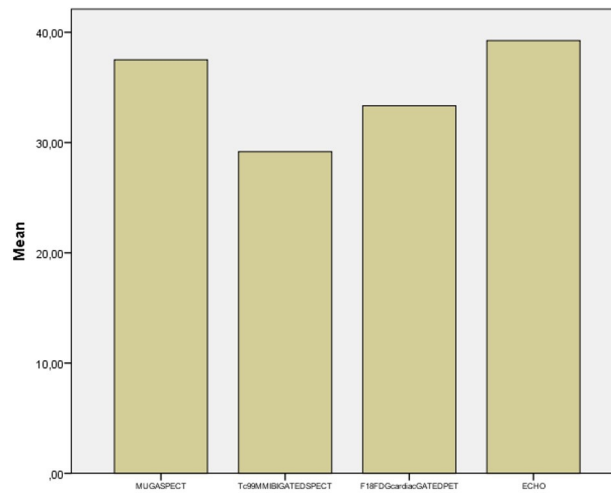
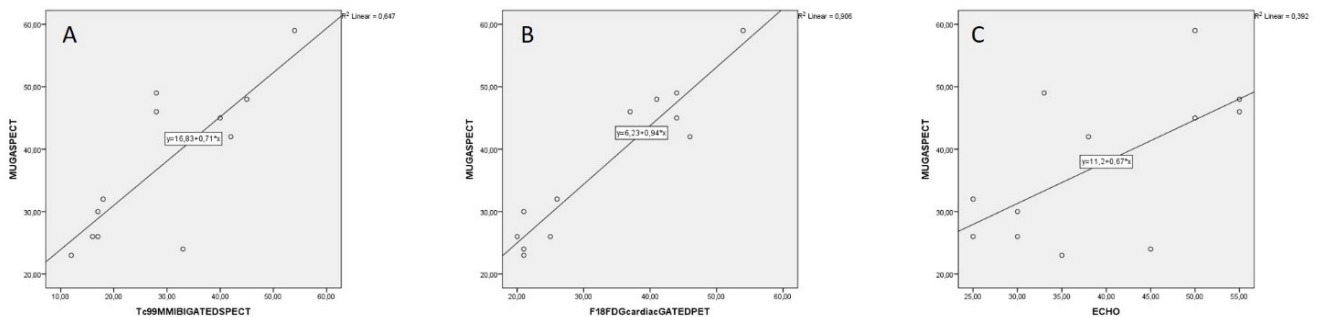
**Figure 1. Comparison of LVEF measurements of different examinations with Bar diagram**

Figure 2. In terms of LVEF values; The correlation between MUGA SPECT and Tc-99m MIBI GATED SPECT is shown with a Bland-Altman graph (A), the correlation between MUGA SPECT and F-18 FDG cardiac GATED PET is shown with a Bland-Altman graph (B), the correlation between MUGA SPECT and ECHO is shown with a Bland-Altman graph (C).

In the Spearman's correlation test, the LVEF value measured in MUGA SPECT showed a positive high correlation with the LVEF values measured in Tc-99m MIBI GATED SPECT and F-18 FDG cardiac GATED PET ($p=0.01$, $r=0.80$; $p=0.01$, $r=0.95$). A moderate positive correlation was detected between the LVEF value measured in MUGA SPECT and the LVEF value measured in ECHO ($p=0.03$, $r=0.62$) (Table 2, Figure 2). Linear correlation graphs of LVEF values are given in Figure 2.

DISCUSSION

Although invasive angiographic methods are the gold standard for LVEF calculation, their use in clinical practice is not always possible. Therefore, LVEF measurements made with noninvasive methods are expected to be highly accurate. MUGA is considered the gold standard among radionuclide methods. MUGA has been accepted as a reference in many studies comparing LVEF measurements of different examinations (4-7). In our study, we compared the LVEF values measured by three different radionuclide methods, MUGA SPECT, Tc-99m MIBI GATED SPECT, F-18 FDG PET/CT GATED and the standard noninvasive cardiological method ECHO. While two-dimensional MUGA examination is generally used as the reference standard in the literature (1, 7, 8), we used the MUGA SPECT method in our study. While heart areas are determined manually in the standard MUGA examination, this is done automatically thanks to the SPECT method. For this reason, errors that may arise from manual drawing can be prevented (9). Additionally, it is effective in evaluating right ventricular functions (10). For this reason, the fact that we used MUGA SPECT in our study increases the value of the study.

In our study, the mean MUGA SPECT LVEF was found to be significantly higher than Tc-99m MIBI GATED SPECT and F-18 FDG PET/CT GATED LVEF, and these three examinations were found to have a high positive correlation with each other. The SPECT parameters of both MUGA SPECT and Tc-99m MIBI GATED SPECT imaging are exactly the same. In both cases, attenuation correction was performed with low-dose CT using the same parameters. In this way, we prevented measurement differences due to method and processing. In the literature, some studies show that LVEF measurements of MUGA and Tc-99m MIBI GATED SPECT are correlated. The largest of these studies is the study of Godkar (1) et al., conducted with 5558 patients, and in this study, it was found that MUGA and Tc-99m MIBI GATED SPECT showed a high correlation in LVEF measurement. However, the mean LVEF measured by SPECT was found to be significantly higher than MUGA. This is attributed to the high number of patients with small hearts and the overestimation of LVEF measurement by SPECT in these patients. A similar high correlation was found in our study. In our study, unlike this study, MUGA SPECT was used instead of MUGA and there were no patients with small hearts. For this reason, exaggerated LVEF measurement values in Tc-99m MIBI GATED SPECT were not obtained. F-18 FDG PET/CT distinguishes between infarct and live tissue thanks to the cardiac GATED PET/CT protocol. In this way, it is used to determine patients who will benefit from coronary surgery. LVEF value can also be measured with this method. In LVEF measurement, we found that F-18 FDG cardiac GATED PET showed a high correlation with MUGA SPECT and Tc-99m

MIBI GATED SPECT. Additionally, there was no significant difference between the LVEF values of Tc-99m MIBI GATED SPECT and F-18 FDG cardiac GATED PET. Although there are studies on the use of F-18 FDG cardiac GATED PET in LVEF measurement (11, 12), we have not found any studies on its correlation with other examinations other than MRI. Therefore, our study is important in this aspect. Our study group consists of patients with suspected infarct and hibernated tissue and those expected to have low LVEF values. This is the reason why LVEF values are lower in our study compared to the literature. We predicted that there might be errors in the automatic drawing of heart walls and determination of areas due to infarction in our study group. However, the results showed high correlation between the three radionuclide imaging methods. It is thought that this correlation will be more evident in normal patients. Although ECHO is a more user-dependent method, unlike radionuclide imaging methods, it is used more in routine practice in measuring LVEF because it is easier to implement and does not provide radiation. There are studies in the literature showing that there is a correlation between ECHO, MUGA and Tc-99m MIBI GATED SPECT (1, 13, 14). In our study, a moderate positive correlation was detected between ECHO and MUGA SPECT, and the average LVEF was close to each other. In the study of Godkar (1) et al., LVEF values were higher in Tc-99m MIBI GATED SPECT than ECHO, while in some other studies, SPECT measured lower LVEF values than ECHO, as in our study (2).

In the literature, it has been thought that the differences between LVEF values may be due to variations in the SPECT method. It has been emphasized that differences in the processing phase, such as the filter used, projection method, cutoff and order values, attenuation correction method, and GATED parameters, rather than the shooting method, may cause these variations (1, 9, 10). Our study has some limitations. First, our number of patients is low compared to the literature. However, considering that we included patients who could undergo three different radionuclide imaging in the study group, we think that our number of patients can be considered sufficient. Secondly, our patient group consists of patients with infarcted tissue and low LVEF values. Therefore, there is a need to confirm our findings with a higher number of patients and patients with normal cardiac findings. However, the high correlation obtained in this group with coronary artery disease, where heart borders may be difficult to determine, should be considered a remarkable finding. As a result, each of the four methods was able to measure LVEF in correlation with each other. LVEF values measured by Tc-99m MIBI GATED SPECT and F-18 FDG GATED cardiac PET showed a high positive correlation with MUGA SPECT. It can be inferred that these examinations can be used interchangeably for LVEF measurement. This is the first study to show that F-18 FDG GATED cardiac PET correlates with MUGA SPECT for LVEF measurement.

Declaration of Ethical Code: In this study, we undertake that all the rules required to be followed within the scope of the "Higher Education Institutions Scientific Research and Publication Ethics Directive" are complied with, and that none of the actions stated under the heading "Actions Against Scientific Research and Publication Ethics" are not carried out. The present study was approved by XXXXXX Noninterventional Clinical Studies Ethics Committee with the

decision number E-60116787-020-443406 (date:02/11/2023). All principles of Declaration of Helsinki were followed.

Conflict of interest: No conflict of interest was declared by the authors.

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