

Comparison of Gated SPECT Myocardial Perfusion Imaging with Echocardiography for the Measurement of Left Ventricular Volumes and Ejection Fraction in Patients With Severe Heart Failure

Maryam Shojaeifard¹; Tahereh Ghaedian²; Nahid Yaghoobi³; Hadi Malek³; Hasan Firoozabadi³; Ahmad Bitarafan-Rajabi³; Majid Haghjoo⁴; Ahmad Amin⁵; Nasrin Azizian⁴; Feridoon Rastgou^{3,*}

¹Echocardiography Research Center, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, IR Iran

²Nuclear Medicine and Molecular Imaging Research Center, Shiraz University of Medical Sciences, Shiraz, IR Iran

³Department of Nuclear Medicine and Molecular Imaging, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, IR Iran

⁴Cardiac Electrophysiology Research Center, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, IR Iran

⁵Department of Heart Failure and Transplantation, Rajaie Cardiovascular Medical and Research Center Iran University of Medical Sciences, Tehran, IR Iran

*Corresponding author: Feridoon Rastgou, Department of Nuclear Medicine and Molecular Imaging, Rajaie Cardiovascular Medical and Research Center, Vali-Asr St., Niayesh Blvd, Tehran, IR Iran. Tel: +98-2123922480, Fax: +98-2122042026, E-mail: f_rastgou@yahoo.com

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Background: Gated single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) is known as a feasible tool for the measurement of left ventricular ejection fraction (EF) and volumes, which are of great importance in the management and follow-up of patients with coronary artery diseases. However, considering the technical shortcomings of SPECT in the presence of perfusion defect, the accuracy of this method in heart failure patients is still controversial.

Objectives: The aim of the present study was to compare the results from gated SPECT MPI with those from echocardiography in heart failure patients to compare echocardiographically-derived left ventricular dimension and function data to those from gated SPECT MPI in heart failure patients.

Patients and Methods: Forty-one patients with severely reduced left ventricular systolic function ($EF \leq 35\%$) who were referred for gated SPECT MPI were prospectively enrolled. Quantification of EF, end-diastolic volume (EDV), and end-systolic volume (ESV) was performed by using quantitative gated spect (QGS) (QGS, version 0.4, May 2009) and emory cardiac toolbox (ECTb) (ECTb, revision 1.0, copyright 2007) software packages. EF, EDV, and ESV were also measured with two-dimensional echocardiography within 3 days after MPI.

Results: A good correlation was found between echocardiographically-derived EF, EDV, and ESV and the values derived using QGS ($r = 0.67$, $r = 0.78$, and $r = 0.80$ for EF, EDV, and ESV, respectively; $P < 0.001$) and ECTb ($r = 0.68$, 0.79 , and $r = 0.80$ for EF, EDV, and ESV, respectively; $P < 0.001$). However, Bland-Altman plots indicated significantly different mean values for EF, 11.4 and 20.9 using QGS and ECTb, respectively, as compared with echocardiography. ECTb-derived EDV was also significantly higher than the EDV measured with echocardiography and QGS. The highest correlation between echocardiography and gated SPECT MPI was found for mean values of ESV different.

Conclusions: Gated SPECT MPI has a good correlation with echocardiography for the measurement of left ventricular EF, EDV, and ESV in patients with severe heart failure. However, the absolute values of these functional parameters from echocardiography and gated SPECT MPI measured with different software packages should not be used interchangeably.

Keywords: Left Ventricular; Echocardiography; Cardiac-Gated Single-Photon Emission Computer-Assisted Tomography

1. Background

Left ventricular ejection fraction (EF) and volumes are of great prognostic value in patients with coronary artery disease, especially in those with left ventricular dysfunction, and can largely affect the management and follow-up of these patients (1, 2). Echocardiography is the most commonly used modality for the measurement of left ventricular EF and volumes, thanks to its ease of use and wide availability (1, 3). Current cardiovascular guidelines recommend echocardiography for the measurement of left ventricular EF and volumes in

the initial evaluation and management of heart failure patients (1). Among other methods for the evaluation of left ventricular EF and volumes, gated single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) has also been recognized as a feasible tool for the measurement of these parameters along with the assessment of myocardial perfusion (4). Although this technique has been validated against other techniques, such as magnetic resonance imaging and echocardiography (5), in patients with suspected

or known coronary artery diseases, it is theoretically assumed that these measurements could be more variable and less accurate in the presence of significant structural abnormality and perfusion defect, both prevalent in patients with severe heart failure. In addition, different software packages with different quantification algorithms may have more variable results in patients with left ventricular dysfunction (6, 7). Hence, more investigations are needed for a more defined application of gated SPECT MPI in heart failure patients.

2. Objectives

The aim of this study was to compare gated SPECT MPI with echocardiography for the measurement of left ventricular EF and volumes in patients with severe heart failure.

3. Patients and Methods

3.1. Patient Selection

In this study, we prospectively enrolled consecutive patients with a history of reduced left ventricular EF ($\leq 35\%$) and sinus rhythm on electrocardiogram, who were referred for gated SPECT MPI owing to clinical indication. Two-dimensional echocardiography was performed within 3 days after gated SPECT MPI.

3.2. Gated SPECT MPI

The gated SPECT MPI protocol was performed as described previously (8). In brief, 45 - 60 min after the intravenous administration of 15 - 20 mCi 99 mTc-sestamibi, 32 projections were acquired over a 180° arc from right anterior oblique to left posterior oblique view, lasting 30 seconds per projection with a step-and-shoot protocol with a dual-head gamma camera (Symbia T2; Siemens Healthcare) Chicago, IL, USA. Gated data acquisition was done with 16 frames per cardiac cycle and 30% acceptance window for the R-R interval length by using the forward-backward gating method. Then, the projections were reconstructed with filtered back-projection by using Butterworth filter (order 5, cutoff frequency 0.40), and reoriented to produce short-axis images with no attenuation or scatter correction. Then, left ventricular EF and volumes were measured by using two software packages one from Cedars-Sinai medical center (quantitative gated SPECT [QGS], version 0.4, May 2009) and another from Emory university (Emory Cardiac Toolbox [ECTb], revision 1.0, copyright 2007). The left ventricular cavity volume for each frame was calculated from the total number of voxels bounded by the endocardium and its valve plane. Among these 16 intervals, the end-diastolic volume (EDV) and end-systolic volume (ESV) were identified as the largest and smallest left ventricular cavity volume, respectively, and the left ventricular EF was derived as follows: $((EDV - ESV) / EDV) \times 100$ (9).

3.3. Quantification of EF, EDV, and ESV by Using Two Software Packages

Since the myocardial surface is not a measurable value or a quantifiable parameter and is a 3D surface which is computed and generated from connection of many different points in a 3D space, coordinated to an ellipsoidal sampling system along which unidimensional arrays were created for each spatial sampling point. These arrays contain the local maximum myocardial count at each interval. Gaussian fitting of these count profiles operates on the nonthresholded image volume. The location of the left ventricular endocardium is estimated in the three-dimensional space (10).

ECTb performs sampling on short-axis slices by using a hybrid cylindrical-spherical coordinate system, the center of which is the left ventricular long axis. The search space is limited by the left ventricular radius, apex, and base. All measurements of left ventricular function in ECTb are based on the ability to measure myocardial thickening throughout the cardiac cycle. This approach uses the myocardial location of the maximal count to determine the midpoint of the myocardial wall segment. With the assumption that at end diastole, the left ventricular myocardial thickness is 1 cm, both the endocardial and epicardial surfaces in the end-diastolic frame are defined. It then uses the regional change in counts from the end-diastolic frame to determine the change in surface location (11).

3.4. Two-dimensional Echocardiography

Echocardiographic examination was done in all subjects in the left lateral decubitus position, with the use of an echocardiography machine (vivid 7; General electric medical system Vingmed Ultrasound AS, Horten, Norway) equipped with a 3.6-MHz transducer. Measurements were performed according to the American Society of Echocardiography guidelines by an echocardiologist who was unaware of the gated SPECT results. Left ventricular dimensions (end systolic and end diastolic) were obtained from the parasternal long-axis view by using the M-mode method. Left ventricular EF, EDV, and ESV were measured by using the Simpson method with manual tracing of the endocardial border in the end-diastolic and end-systolic phases with a two-dimensional method.

3.5. Statistical Analysis

Statistical analysis was performed with SPSS software (SPSS Statistics for Windows, version 17.0; SPSS Inc., Chicago, IL, USA). Quantitative continuous variables are expressed as mean \pm standard deviation (SD), and categorical variables are presented as count (percentage). The Wilcoxon test was used for the comparison of variables measured with echocardiography and the two software packages. The correlation of left ventricular EF and volumes derived using the two software packages with

echocardiography, and with each other, was evaluated by means of Spearman's correlation analysis. Bland-Altman plots as well as scatter diagrams and regression lines were generated by using MedCalc software for Windows, version 8.0 (MedCalc Software, Ostend, Belgium). A P value of < 0.05 was considered statistically significant in all analysis.

4. Results

4.1. Patient Population

Among the 41 patients who were enrolled in the study, 28 had ischemic cardiomyopathy and 13 had nonischemic etiologies. The demographic data and clinical characteristics of the patients are shown in Table 1.

4.2. Comparison of Gated SPECT MPI and Echocardiography

The means \pm SD of EF, EDV, and ESV measured by using echocardiography and the two software packages are shown in Table 2. There was a significant difference between EF measured by using echocardiography and QGS; however, EDV and ESV showed no significant difference (Table 3). The values of EF and EDV derived by using ECTb were significantly higher than those measured by using echocardiography (Table 4). All parameters measured with the two software packages revealed a good correlation with echocardiography data and with each other (Tables 3 and 4).

Bland-Altman plots further revealed better agreement between echocardiography and gated SPECT MPI in the lower values of EDV and ESV measured with the two software packages (Figures 1 and 2). These plots also indicated that the degree of overestimation of EF and EDV with the two software packages, as compared with echocardiography,

increased along with the increase in the values of these parameters. Compared with echocardiography, there was a significant mean difference of 20.9 and 11.4 with ECTb and QGS, respectively, for the measurement of EF, and 48.0 and 16.2, respectively, for the measurement of EDV.

Table 1. Clinical Characteristics of the Study Patients (N = 41)^{a,b}

Clinical Characteristics	Values
Age, y	59 \pm 15
Male/female	28 (68.3%)/13 (31.7%)
Ischemic cardiomyopathy	28 (68.3%)
Echocardiographic findings	
EF, %	21 \pm 5
EDV, mL	187 \pm 79
ESV, mL	147 \pm 69
Perfusion findings	
TPD ^c	24 \pm 18

^a Data are represented as mean \pm SD or No. (%).

^b Abbreviations: EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; TPD, total perfusion deficit

^c Estimated by using Quantitative Perfusion SPECT software.

Table 2. Mean \pm Standard Deviation of EF, EDV, and ESV Measured with Echocardiography, QGS, and ECTb^a

Parameters	EF	EDV	ESV
Echocardiography	20.8 \pm 5.1	187.2 \pm 78.7	146.6 \pm 68.8
QGS	32.2 \pm 10.5	203.4 \pm 118.9	145.8 \pm 108.1
ECTb	41.7 \pm 14.8	235.2 \pm 115.6	150.4 \pm 107.0

^a Abbreviations: ECTb, Emory Cardiac Toolbox; EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; QGS, Quantitative Gated SPECT.

Table 3. Comparison of EF, EDV, and ESV between QGS and Echocardiography^a

	Echocardiography	QGS	P Value ^b	Spearman's Correlation Coefficient	P Value ^b
EF	20.8 \pm 5.1	32.2 \pm 10.5	< 0.001	0.678	< 0.001
EDV	187.2 \pm 78.7	203.4 \pm 118.9	0.414	0.780	< 0.001
ESV	146.6 \pm 68.8	145.8 \pm 108.1	0.197	0.809	< 0.001

^a Abbreviations: EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; QGS, Quantitative Gated SPECT.

^b $P < 0.05$ is significant.

Table 4. Comparison of EF, EDV and ESV between ECTb and Echocardiography^a

	Echocardiography	ECTb	P Value ^b	Spearman's Correlation Coefficient	P Value ^b
EF	20.8 \pm 5.1	41.7 \pm 14.8	< 0.001	0.685	< 0.001
EDV	187.2 \pm 78.7	235.2 \pm 115.6	< 0.001	0.795	< 0.001
ESV	146.6 \pm 68.8	150.4 \pm 107.0	0.592	0.806	< 0.001

^a Abbreviations: ECTb, Emory Cardiac Toolbox; EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume.

^b $P < 0.05$ is significant.

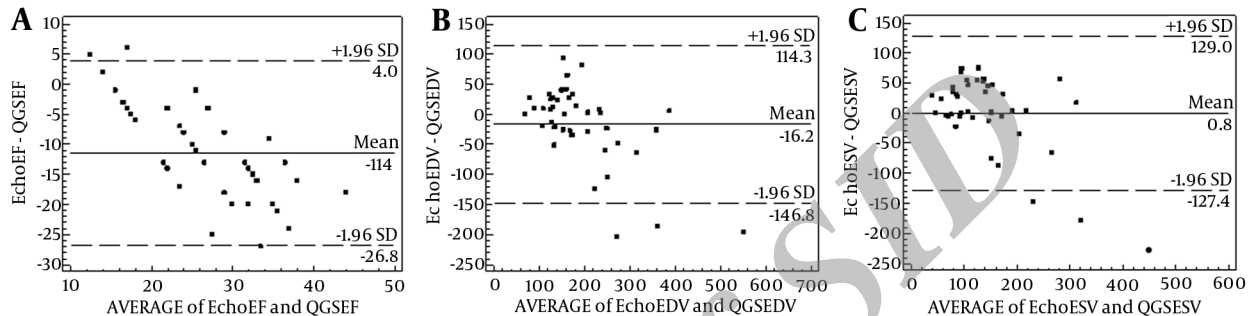
4.3. Comparison of QGS and ECTb

In the comparison between QGS and ECTb, the EF and volumes were significantly higher with ECTb, as is shown in Table 5.

The two software packages also showed excellent and significant correlation for the measurement of EF ($r=0.88$), EDV ($r=0.96$), and ESV ($r=0.97$). Bland-Altman plots for the evaluation

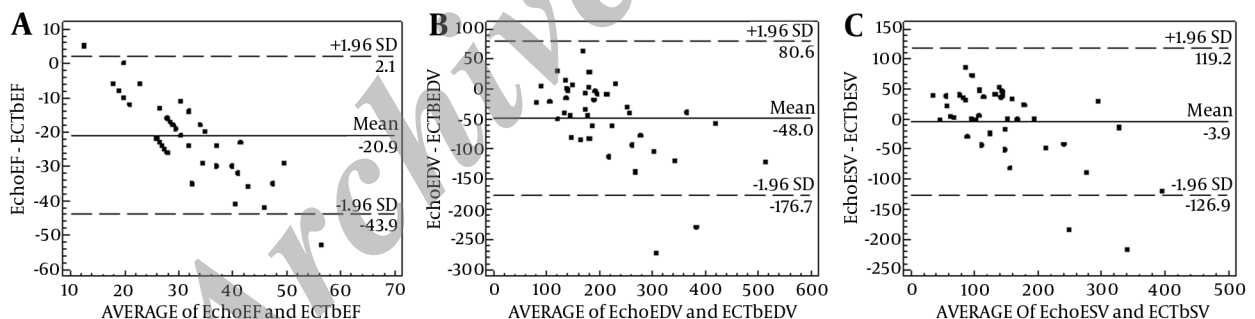
of the agreement between the two software packages are also illustrated in Figure 3. Figure 4 shows the regression equations for predicting the ECTb-derived values of these functional parameters from the corresponding QGS-derived variables. The coefficients of determinations (R^2) were 0.75, 0.95, and 0.94 for EF, EDV, and ESV, respectively.

Figure 1. Bland-Altman Plots for EF (a), EDV (b), and ESV (c) Measured by Using QGS and Echocardiography



(QGS, Quantitative Gated SPECT; EF, ejection fraction; EDV, end-diastolic volume; ESV, end-systolic volume).

Figure 2. Bland-Altman Plots for EF (a), EDV (b), and ESV (c) Measured by using ECTb and Echocardiography



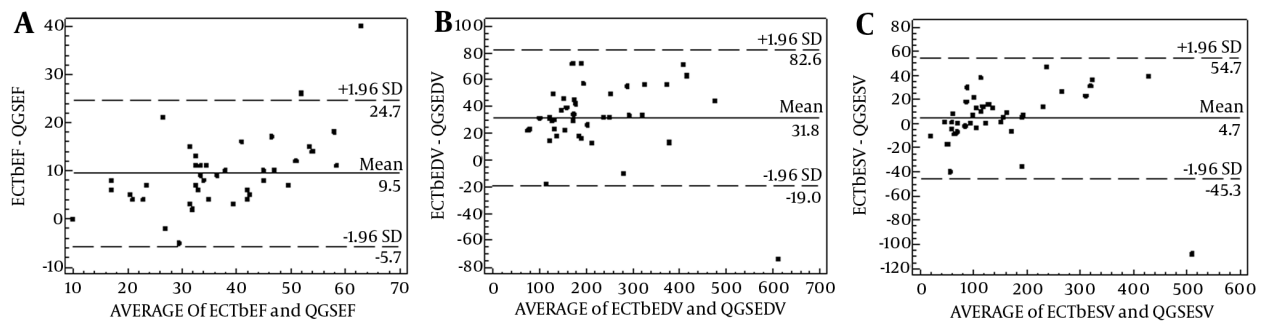
(ECTb, Emory Cardiac Toolbox; EF, ejection fraction; EDV, end-diastolic volume; ESV, end-systolic volume).

Table 5. Comparison of EF, EDV, and ESV between QGS and ECTb ^a

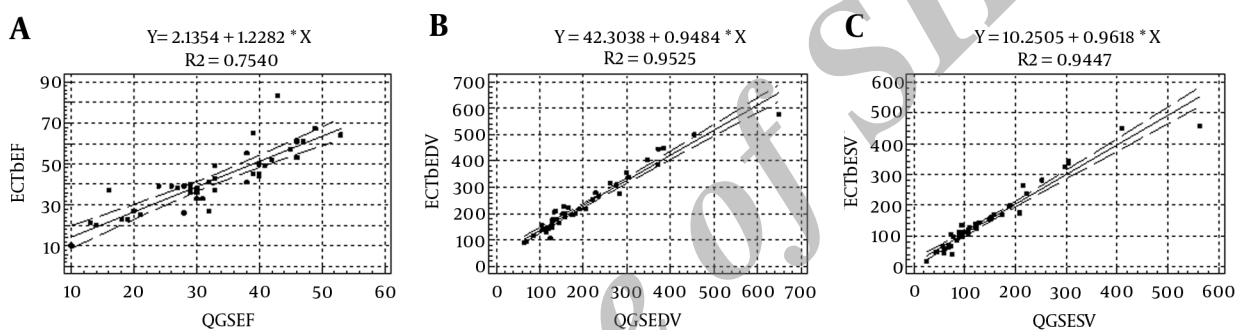
Parameters	QGS	ECTb	P Value ^b	Correlation Coefficient	P Value ^b
EF	32.2 ± 10.5	41.7 ± 14.8	< 0.001	0.887	< 0.001
EDV	203.4 ± 118.9	235.2 ± 115.6	< 0.001	0.964	< 0.001
ESV	145.8 ± 108.1	150.4 ± 107.0	0.024	0.972	< 0.001

^a Abbreviations: ECTb, Emory Cardiac Toolbox; EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; QGS, Quantitative Gated SPECT.

^b $P < 0.05$ is significant.

Figure 3. Bland-Altman Plots for EF (a), EDV (b), and ESV (c) Measured by Using ECTb and QGS

(ECTb, Emory Cardiac Toolbox; QGS, Quantitative Gated SPECT; EF, ejection fraction; EDV, end-diastolic volume; ESV, end-systolic volume).

Figure 4. Regression Lines With 95% Confidence Interval and Regression Equations for the Estimation of ECTb-Derived EF (a), EDV (b), and ESV (c) From Corresponding Variables by Using QGS Software

(ECTb, Emory Cardiac Toolbox; QGS, Quantitative Gated SPECT; EF, ejection fraction; EDV, end-diastolic volume; ESV, end-systolic volume).

5. Discussion

The measurements of EF, EDV, and ESV by using gated SPECT MPI with both QGS and ECTb are well correlated with echocardiographic data. Although echocardiography is not a gold standard tool for the evaluation of left ventricular EF and volumes, decision making in the initial evaluation, management, and follow-up of patients with heart failure is largely done on the basis of the widely available echocardiographic approach (1). A good correlation of functional parameters derived from gated SPECT MPI with echocardiography indicates that gated SPECT MPI can be reliably used for the simultaneous assessment of perfusion and function in patients with heart failure, which can provide better diagnostic and prognostic accuracy for SPECT MPI. Previous works by some authors also showed a good correlation between these two methods in these patients. Vourvouri et al. reported a good correlation between QGS and two-dimensional echocardiography in 32 patients with severe left ventricular systolic dysfunction ($r > 0.8$ for EF, and $r > 0.9$ for EDV and ESV) (12). In a study by Berk et al., a good correlation between QGS and echocardiography was also found in 33 patients with dilated cardiomyopathy, and it was noted that eight-

frame gated SPECT overestimates the values of EDV and ESV compared with echocardiography; however, EF was not statistically significant with the two methods (13). Another study by Berk et al. revealed similar results in 45 patients with dilated cardiomyopathy (14). They also reported a good reproducibility for gated SPECT MPI for the measurement of these functional parameters. Our study also revealed higher values of EF, EDV, and ESV than those measured by using echocardiography in patients with systolic heart failure, which, in contrast to the previously mentioned studies, was not statistically significant for ESV. The ESV values were statistically similar between echocardiography and gated SPECT MPI by using the two software packages. Moreover, in contrast to patients with a small heart, the ESV may be less than the EDV owing to technical variability and edge detection secondary to extensive perfusion defects and structural deformity in heart failure patients. This might be explained by better count statistics due to partial-volume effect and smaller left ventricular volume in the end-systolic frame.

Harisankar et al. also studied the accuracy of eight-frame gated SPECT MPI for the measurement of EF in 30

patients with extensive perfusion defect ($> 25\%$ of the left ventricular myocardium) (15). They reported a good agreement for the measurement of EF between radionuclide ventriculography and both QGS and ECTb; on the other hand, in comparison with echocardiography, both software packages underestimated the EF. These findings are in contrast to the results of our study and of a previous study by Berk et al. with QGS in patients with dilated cardiomyopathy (14), which showed that EF is overestimated when using gated SPECT MPI in heart failure patients. These different results between studies also further confirmed that direct translation of echocardiographic values to gated SPECT MPI for management decisions and follow-up should not be used, and each method should have a specific defined normal and abnormal limit, particularly in the presence of left ventricular systolic dysfunction.

Studies in patients with coronary artery disease and variable distribution of cardiac function status also revealed a good correlation ($r = 0.7 - 0.9$) along with such significant differences in the measurements of left ventricular EF and volumes between gated SPECT MPI and echocardiography (10, 11). Nichols et al. compared QGS and ECTb with echocardiography in 33 patients with known or suspected coronary artery diseases, and found a good correlation between each software and echocardiography (5). However, compared with echocardiography, they reported that QGS and ECTb overestimated EF values especially in the larger volumes (5).

Although gated SPECT MPI has been shown to also have a good correlation with other imaging modalities, it has been recommended that the interchangeable use of different techniques for the measurement of left ventricular EF and volumes should be avoided (16). A prospective study by Wang et al. for the comparison of gated SPECT MPI with MRI in 36 patients with dilated cardiomyopathy, for the measurement of left ventricular EF, EDV, and ESV, showed that QGS, ECTb, and 4D-MSPECT overestimated EF as compared with cardiac MRI (17). In this study, QGS showed no significant difference in the measurement of EDV and ESV, whereas ECTb and 4D-MSPECT overestimated left ventricular volumes (17). In comparison with radionuclide ventriculography, Manrique et al. reported that gated SPECT MPI significantly underestimated EF in the presence of large perfusion defect and systolic dysfunction (18).

Comparing different software packages for the measurement of left ventricular EF and volumes, Nakajima and coworkers reported a good correlation between QGS, ECTb, 4D-MSPECT, and pFAST for the measurement of EF and EDV. They also found an up to 15% error in the measurement of EDV > 74 mL (19). Another study by Hedeer et al., in 100 patients with known or suspected coronary artery diseases, also revealed a good correlation between software packages used in gated SPECT MPI; however, in comparison with MRI, these software packages (including QGS and ECTb) showed significant underestimation

of EF and volumes with significant variability between each other that was more prominent in larger volumes (6). Kakhki et al. also reported a significant overestimation of left ventricular EF and volumes with ECTb as compared with QGS (7). They also found that the difference between the two software packages increased when the perfusion defects also increased (7). Our study also showed that ECTb-derived EF, EDV, and ESV were significantly higher than the values measured with QGS. Although this intersoftware variability further emphasizes the need to use the same software for the evaluation of left ventricular EF and volumes in follow-up of patients in serial studies, with respect to the noticeable coefficient of determination (R^2) that we calculated, regression equations (Figure 4) can have a valuable role in the comparison of these variables measured using the two software packages.

Finally, it should be stated that gated SPECT MPI can be most advantageous when the simultaneous evaluation of myocardial function and perfusion are required, even in heart failure patients such as those who are candidates for cardiac resynchronization therapy, when the assessment of myocardial viability, ESV, and left ventricular dyssynchrony are needed for the evaluation of response to cardiac resynchronization therapy (20). However, the point that must be considered is the standardization of functional parameter values on the basis of the quantification software. This still needs further investigations.

We conclude that despite the presence of a good correlation between gated SPECT MPI and echocardiography for the measurement of left ventricular EF, EDV, and ESV in patients with severe heart failure, the absolute values of EF and EDV should not be used interchangeably. In this regard, ESV seems to be less affected by the type of the technique. It was also found that regression analysis can have a valuable role in the comparison of these variables between QGS and ECTb.

Authors' Contributions

All authors took part in data collection, analysis, and writing of the manuscript.

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