A comparison and validation of blood-pool imaging and ECG-gated SPET myocardial perfusion imaging to assess left ventricular ejection fraction

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Abstract

The aim of this study was to validate the accuracy of left ventricular ejection fraction (LVEF) obtained by quantitative gated single photon emission tomography (QGS) perfusion imaging in comparison with gated blood-pool imaging. *Resting gated myocardial perfusion imaging* was performed in 269 patients with suspected or known coronary artery disease, and followed by equilibrium nuclear cardiac blood-pool imaging in one week. The later was considered as the reference standard. The LVEF from both methods were analyzed. The LVEF were calculated with QGS using Cedars Cardiac Quantification software. *We found that* LVEF from QGS and blood-pool (Bp)-LVEF were highly correlated (r=0.819, <0.001). Taken into consideration that QGS-LVEF was significantly different from Bp-LVEF (mean±SD: 57.77%±19.28% vs 54.23%±15.41%, P<0.05), data were further analyzed by grouping participants based on end-systolic ventricular volume (ESV). QGS-LVEF was not significantly different from Bp-LVEF in the group where that ESV was larger than 15m, (mean±SD: 52.71%±16.11% vs 51.83%±15.33%, P>0.05), whereas when ESV was smaller than 15mL, QGS-LVEF was significantly higher than Bp-LVEF (mean±SD: 80.53%±7.01%vs 65.06%±10.37%, P<0.05). *Our findings* demonstrate that when ESV values are larger than 15mL, QGS-LVEF could replace Bp-LVEF. However, when ESV value is smaller than 15mL, LVEF should be assessed in combination with blood-pool imaging.

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Introduction

Nowadays radionuclide imaging exerts great effect in clinic practice. The importance of nuclear myocardial imaging was evidenced by being a functional no-wounded and repeated diagnose method. The major goal of myocardial perfusion imaging is the mapping of the relative myocardial perfusion at stress and rest. Thallium-201 chloride (^{201}Tl-Cl) was used initially in planar imaging. Although it just provides significant noninvasive information about the heart, incremental advancements in gamma camera technology, computers, and radiopharmaceuticals now allow additional information to be obtained effectively. Although the additional information is clinically important, non perfusion data were ignored previously because they were neither technically nor economically feasible to be obtained routinely. With the approval of the ^{99m}Tc-based agents, quantification of left ventricular ejection fraction (LVEF) and left ventricular volumes became practical. This in turn stimulates the development of automated quantification software of left ventricular function and its subsequent commercial release. The Cedars-Sinai quantitative gated single photon emission tomography (SPET) (QGS) software package provides a standardized automated method for rapidly determining the LVEF and volume as well as other parameters in a consistent and reproducible manner in the clinical setting. Although this software application is a significant advancement, limitations are apparent in routine use. These include inappropriate regions of interest (ROI) when there is overlapping bowel activity and less well-documented, falsely elevated LVEF measurements in patients with small hearts. In this article, we compared LVEF measured with QGS myocardial perfusion and blood-pool imaging which is the current clinical "gold standard" [1] and investigated the underlying reasons of discrepancies.

Subjects and methods

Study population

Two hundred and sixty nine patients were recruited (115 men, 154 women; aged 42-93yr; mean age 72.91yrs). A hundred and sixty three patients had coronary artery disease, 85 had hypertension and 29 had valvular disease. Patients abstained from all cardiac medications for 24h prior to the procedure.

Each patient was subject to the SPET study and blood-pool imaging in one week. All patients were given the informed consent.

Gated SPET and data analysis

Gated acquisition (64×64 matrix) was done on a single-head SPET (E.CAM, Siemens Gammasonics, Inc. Germany) 90min after intravenous injection of 925±37MBq ^{99m}Tc-MIBI, with 20 views, at 60s per view, and a zoom factor of 1.23. The cardiac cycle was divided into 8 equal intervals according to signals provided by electrocardiogram (ECG). All gates were reconstructed using filtered backprojection (Butterworth filter, third order; critical frequency, 0.5). Both reorientation and data analysis were done by observer G.W. The datasets were transferred to an ICON system (Siemens Gammasonics Inc. Germany), where they were reoriented on the transversal planes, first parallel to the septum and then parallel to the inferior wall. The reoriented short-axis datasets (voxel size, 5.8×5.8×5.8mm^3) were stored for analysis. Gated SPET images were analyzed for the same functional variables with QGS (version 5.0) on a Siemens ICON system. All SPET datasets were evaluated by observer 1, who was unaware of the blood-pool results. All algorithms used automatic processing. End-diastolic volume (EDV) and ESV were in milliliters and LVEF were present in percentage.

Gated blood-pool imaging and data analysis

Conventional ECG gated planar equilibrium radionuclide angiography studies was done on a single-head SPET (E.CAM, Siemens Gammasonics, Inc. Germany) and ECG 30min after intravenous injection of 740±37MBq (mean ± SD) ^{99m}Tc-RBC. It was realized in the best septal LAO 30°-45°projection with a caudal tilt for 400 kilocounts per frame, 24 frames per cardiac cycle, 128x128 matrix, a ±10% R–R acceptance window, image magnification of 2.67, and an energy window of 20% centered on 140keV. The size of 1 pixel after magnification was 3.38mm. The data were processed on a dedicated workstation (Siemens Gammasonics Inc. Germany), and the LVEF was obtained with a previously validated algorithm included in the standard software package. All operations and datasets were evaluated by observer H.C, who was unaware of the SPET results.

Statistical analysis

All statistical analyses were done using SPSS 12 (SPSS Inc.). Data are expressed as mean±SD. The level for statistical significance was set at $P<0.05$. Bonferroni–Holm correction was selected for multiple comparisons [2]. The degree of agreement was evaluated according to Bland and Altman [2]; Bland–Altman limits (mean of the differences±2SDs of the differences) were shown in the figures. Pearson correlation coefficient was also calculated.

Results

Linear correlation was observed between QGS and Bp-LVEF ($r=0.819$, $P<0.001$) (Fig. 1), but a significant difference was also observed between them ($t=5.51$, $P<0.05$) (Table 1).

Table 1. *Comparison of LVEF calculated with QGS and blood-pool imaging*

LVEF	Mean±SD	t	P
QGS(n=269)	57.77±19.28	5.517	0.000
Blood-pool(n=269)	54.23±15.41		

When ESV was larger than 15mL, linear correlation was observed between QGS-LVEF and Bp-LVEF ($r=0.885$, $P<0.001$) (Fig. 2), and no significant difference was observed between them. ($t=1.53$, $P>0.05$) (Table 2).

Table 2. *Comparison of LVEF calculated with QGS and blood-pool imaging when ESV was larger than 15mL*

LVEF	Mean±SD	t	P
QGS (n=220)	52.71±16.11	1.53	0.128
Blood-pool (n=220)	51.83±15.33		

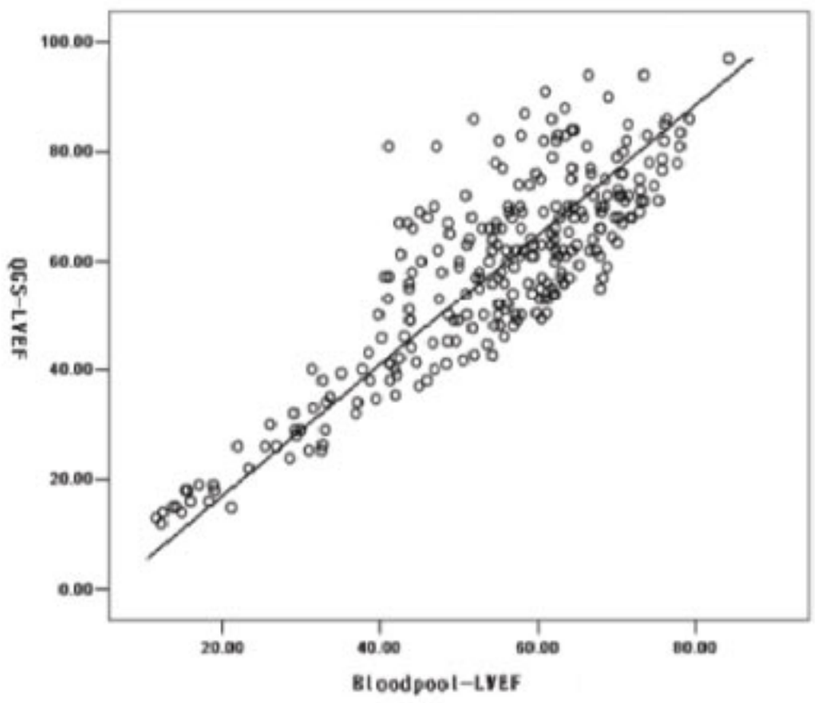

Figure 1. Linear correlation of QGS methods vs. gated blood-pool imaging method for LVEF calculation. $r=0.819$, $P<0.001$.

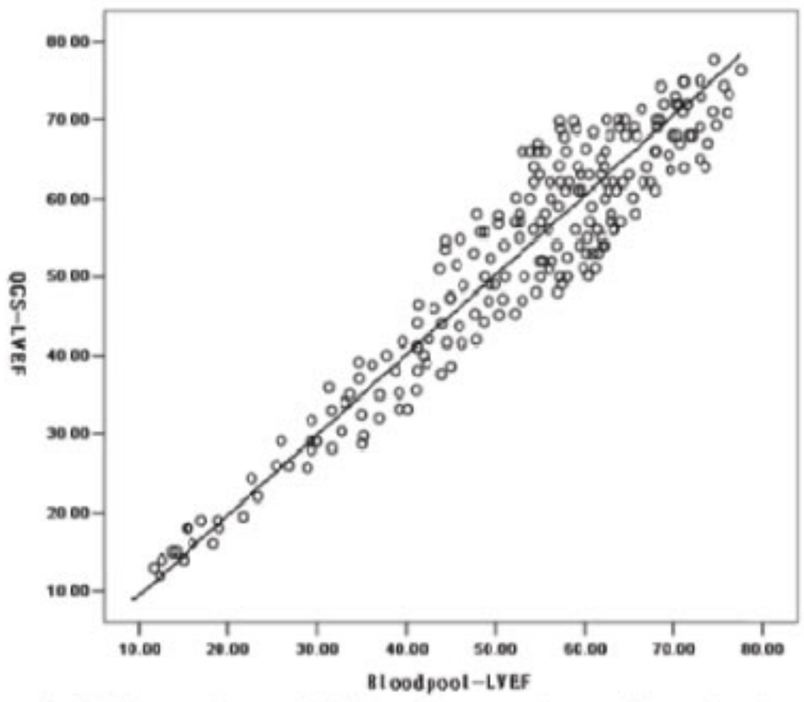

Figure 2. When the ESV is larger than 15mL, the linear correlation of QGS methods vs. gated blood-pool imaging method for LVEF calculation. $r=0.885$, $P<0.001$.

When ESV was smaller than 15mL or equal to 15mL, linear correlation was not observed between QGS-LVEF and Bp-LVEF ($r=0.282$, $P=0.05$) (Fig. 3),and a significant difference was observed between them ($t=10.07$, $P<0.001$) (Table 3).

Table 3. *Comparison of LVEF calculated with QGS and blood-pool imaging when ESV is smaller than 15mL*

LVEF	Mean±SD	t	P
QGS (n=49)	80.53±7.01	10.07	0.000
Blood-pool (n=49)	65.06±10.37		

Patients were in New York Heart Association (NYHA) functional class II or III and had echocardiographic LVEF < 50%.Using 50% as the cut-off in this study, the positive rate of LVEF, which LVEF is less than 50%, is 27.14% and 31.23% in all patients by QGS and blood-pool imaging, respectively. No significant difference was observed between them (P>0.05).

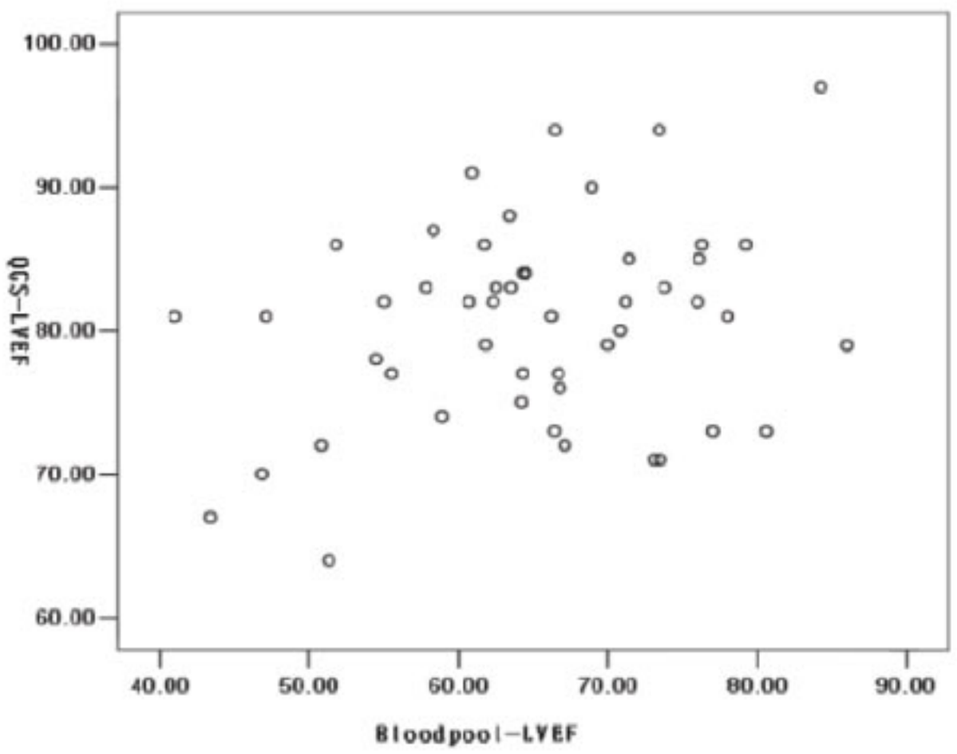

Figure 3. When the ESV is smaller than 15mL, no linear correlation of QGS-LVEF with Bp-LVEF was observed (r=0.282, P=0.05)

When the ESV is larger than 15mL, the positive rate respectively is 32.73%, 35%, and no significant difference was observed (P>0.05). However, when ESV is smaller than 15mL or equal to 15mL, the positive rate respectively was 2%, 14.29%, significant difference was observed between them(P<0.01) (Table 4). In group with ESV>15mL, only five patients' LVEFs were smaller than 50% by BP, whereas they were larger than 50% by QGS. The five patients had serious arrhythmia and their BP LVEFs were larger than 45%.

Table 4. *LVEF positive rate using 50% as the cut-off in all patients by QGS and blood-pool imaging*

	QGS		Blood-pool		t	P
	Case	Rate	Case	rate		
All (n=269)	73	27.14 %	84	31.23 %	1.098	>0.05
ESV>15 mL (n=220)	72	32.73 %	77	35.00 %	0.516	>0.05
ESV≤15 mL (n=49)	1	2.00 %	7	14.29 %	4.657	<0.01

The QGS-LVEF increased as EDV and ESV decreased (Fig. 4). The r value of LVEF and ESV is higher than that of LVEF and EDV (r 0.835 vs.0.776). As ESV value became smaller, the r value of LVEF and ESV ascended, on the contrary, the r value of LVEF and EDV descended (Fig. 5). It indicated that evaluating reliability of LVEF based on ESV was better than that based on EDV.

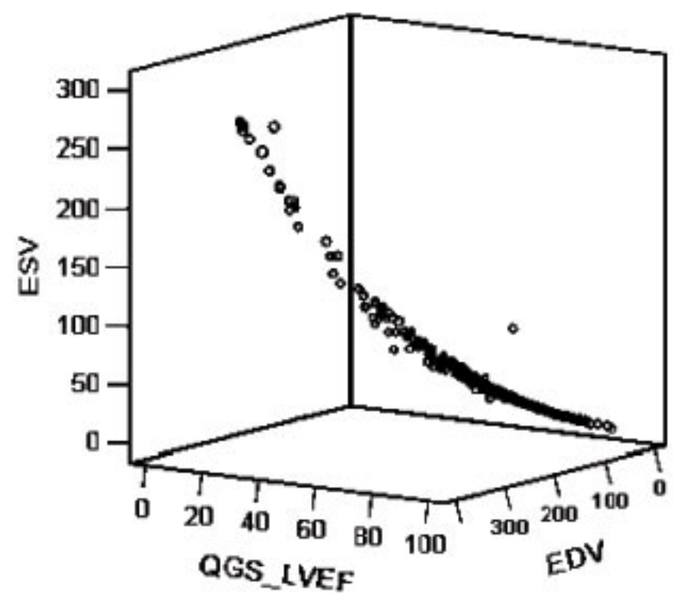

Figure 4. QGS-LVEF increased as EDV and ESV decreased.

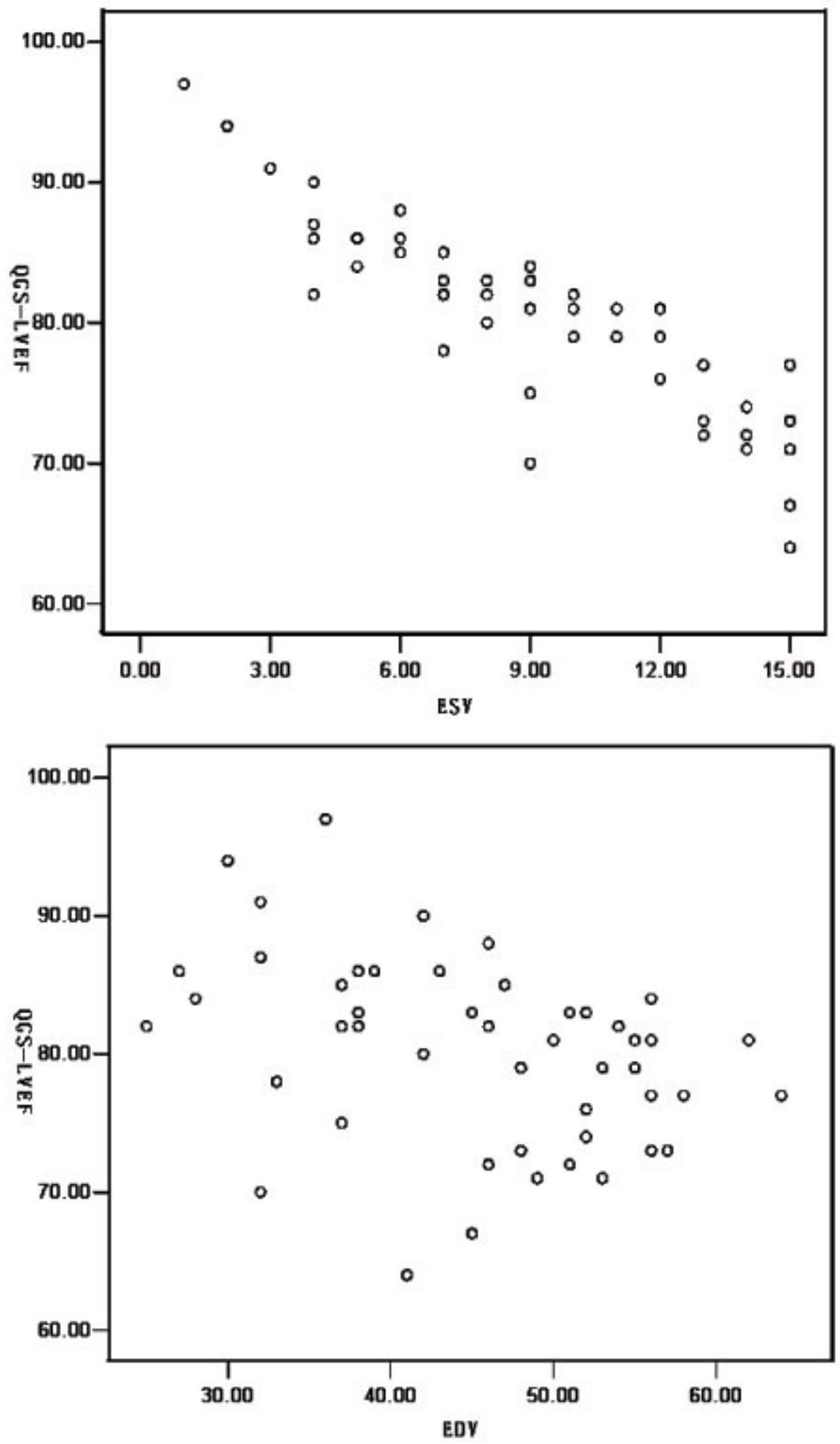

Figure 5. When ESV is smaller than 15mL or equal to 15mL, the r value of correlation between LVEF and ESV is 0.886 (P<0.001), the r value of correlation between LVEF and EDV is 0.411(P=0.003).

Discussion

Undoubtedly, LVEF and myocardial perfusion are important factors for evaluating a great deal of diseases associated heart [3-5]. The ECG-gated SPET allows simultaneous assessment of both perfusion and function.

Several approaches for analysis of left ventricular volume and LVEF using ECG-gated SPET have been developed. Although the automated program, QGS has been extensively evaluated, there is still some controversy about the reliability of LVEF and several conditions may affect the accuracy of the program [6-8]. Some researchers reproted that good correlation existed between QGS-LVEF and LVEF measured by other techniques [9-11]. Conversely, in our study, we found that the mean value of QGS LVEF was significantly higher than the Bp-LVEF in 269 patients. In accordance with our results, LVEF was overestimated by QGS have been recently described [12]. Unlike them, we found the phenomenon was not existed in all patients but only in a few patients with small hearts. Simultaneously, our results showed the mean value was not significantly different and the correlation became stronger between the QGS LVEF and blood-pool LVEF in 220 patients when the patients with ESV≤15mL were excluded. On the contrary, the QGS LVEF was elevated in patients with small hearts. This phenomenon is based on the limited spatial resolution of the system in which, in a small heart, each voxel represents a considerable portion of the LV volume [13-15]. As the myocardium moves inward, there can be an abrupt change because the LV endocardial edge is either represented by a voxel or not represented, in effect quantizing its value. As in a patient's heart, the less distinct boundaries, or partial volume effect, may contribute to overestimation of the LVEF because the edges may be smeared together at end systole [16]. Others reported this phenomenon, stating that the elevated LVEFs were associated with the filtering during reconstruction [17], and others that a significant problem in commercially available software is caused by the partial-volume effect with inaccurate determination of the inner boundary at the apex on the end-systolic images [18].

Other researchers reported that QGS would overestimate the LVEF when EDV<70mL. In this study, it was observed that the correlation of LVEF and ESV was stronger than that of LVEF and EDV, especially in patients with small hearts [6, 19]. We observed that the r values of the two correlation was 0.886 and 0.441 respectively when ESV≤15mL. This phenomenon is the result of that the partial volume effect become larger and the spatial resolution becomes less with the volume descending. Thus we believe that the ESV should be better reference than the EDV when we evaluate the reliability of QGS LVEF.

Generally, it is presumed that the person has good LV systolic function when his/her LVEF is ≥50% [20]. According to this, using a threshold value of 15mL for ESV to determine the accuracy of QGS LVEF, in this study, we noticed no significant difference between the QGS LVEF and blood-pool LVEF on determining LV systolic function when ESV is >15mL. However, there was a significant difference between them when ESV is ≤15mL. Additionally, there were 5 patients (5/220, 2%) with serious arrhythmia whose QGS LVEFs were disparity with Bp-LVEF when ESV is >15ml. Moreover, these patients' Bp-LVEFs were slightly less than 50%. The disparity may be resulted from the decreased time resolution due to influence of arrhythmia. There were 6 patients in group of ESV≤15mL (6/49, 12%) whose QGS LVEF were different from Bp-LVEF . Then, we compared the six patients' LVEF to LVEF measured by echocardiogram, and data showed that the later matched the Bp-LVEF. So we supposed that QGS LVEF were overestimated when ESV ≤15mL.

Although the introduction of automated quantitative analysis programs such as QGS has been a major advancement in clinical practice, problems still exist. The end-user needs to be aware of the system's limitations when reporting clinical information. There is the potentiality that in patients with small hearts, such as small women and children, a significant drop in the LVEF could be missed when the QGS LVEF is normal. A fake increase of the LVEF in patients with small hearts, in our study with an ESV of <15mL, can occur when measurements are made with the QGS software. These data argue against using QGS LVEF for monitoring the LVEF in patients with small hearts. Our data imply that a patient may have a mildly decreased LVEF that still appears to be normal by the QGS LVEF.

In conclusion, this study showed the accuracy and reproduction of QGS LVEF in patients with ESV >15mL. But it is incompetent in patients with small hearts. So QGS-LVEF should be combined with blood-pool imaging to assess LEVF in patients with small hearts of ESV <15mL.

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Sent by Dr A. Zissimopoulos. The ancient sanctuary of the island of Samothrace, where king Philip B', father of Alexander the Great married his wife Olympiad.