# Verification of the left ventricular ejection fraction from gated myocardial perfusion studies (GSPECT)

# Anna Teresińska, Jacek Wnuk, Stefania Konieczna, Arkadiusz Dąbrowski

Nuclear Medicine Division, National Institute of Cardiology, Warsaw, Poland

# Abstract

**Introduction:** The perfusion study (which may be obtained using SPECT or GSPECT technology within six hours of administration of the radionuclide Tc-99m-MIBI) reflects the regional blood supply to the left ventricular [LV] myocardium at the time of radionuclide administration (i.e. at rest, at peak exercise, or at peak vasodilatation), while the values of EF, EDV, and ESV measured using GSPECT are parameters of LV contractility at the time of image acquisition (i.e. at rest or in a near-resting state following exercise or vasodilatation). Planar radionuclide ventriculography [RNV] is, however, considered to be the most accurate method for calculating LVEF.

**Aims:** The main goal of the study was to compare the values of EF obtained by the most frequently used method, GSPECT-QGS, and the reference method, RNV – taking into consideration various clinical scenarios (presence or absence of LV dilatation) and various conditions under which GSPECT was recorded (at rest, post-exercise, or post-dipyridamole).

**Methods:** Two hundred patients (145 males) aged 58±11 (18-80) with previously confirmed (n=166, of whom 108 had a history of myocardial infarction) or suspected (n=34) coronary artery disease were included in the study. Ranges of normal values for EF, EDV, and ESV were established based on a group of 26 'normal' subjects. LV dilatation was defined as an EDV >127 ml (at rest, measured by QGS) – this was present in 88 patients. Myocardial perfusion studies were obtained using GSPECT following administration of Tc-99m-MIBI at rest (all patients), as well as one hour after treadmill exercise (138 patients) or dipyridamole administration (48 patients). The resting RNV was conducted within three weeks of the GSPECT exam. The EF values obtained by QGS and RNV were compared for patients with and without LV dilatation. EF, EDV, and ESV values obtained by QGS were compared for resting patients, post-exercise, and post-dipyridamole.

**Results:** 1. The GSPECT EF values calculated using QGS software, at rest or one hour after treadmill exercise or dipyridamole administration, demonstrated, for the study population as a whole, a significant, strong correlation with the results obtained by the reference method, RNV (correlation coefficient,  $r \ge 0.86$ ). The correlation was stronger in patients with LV dilatation than in those without. Both in patients with and without LV dilatation the correlation of EF with RNV was slightly weaker for post-exercise (relative to resting) and post-dipyridamole (relative to post-exercise) measurements. 2. QGS tended to underestimate the absolute values of EF, as compared to RNV. 3. In post-exercise and post-dipyridamole measurements, relative to the resting measurements (in patients with previously diagnosed or suspected coronary artery disease) the mean values of EF were lower while EDV and ESV were higher.

**Conclusions:** In order to complement data on myocardial perfusion, the GSPECT-QGS technique should be optimally used to calculate LV contractility parameters at rest (as opposed to post-exercise or post-dipyridamole), and include a range of normal values for EF, EDV, and ESV, obtained using QGS. Of note, EF measurements by GSPECT are more accurate for dilated than non-dilated ventricles.

Key words: Tc-99m-MIBI, SPECT, GSPECT, radionuclide ventriculography, left ventricle, ejection fraction

Kardiol Pol 2005; 63: 465-475

#### Address for correspondence:

Dr. Anna Teresińska, Samodzielna Pracownia Medycyny Nuklearnej, Instytut Kardiologii, ul. Alpejska 42, 04-628 Warszawa, tel.: +48 22 343 42 81, fax: + 48 22 815 40 03, e-mail: annateresinska@ikard.waw.pl **Received:** 12 January 2005. **Accepted:** 22 August 2005.

# Introduction

Myocardial perfusion scintigraphy (SPECT) plays a diagnostic and prognostic role by providing information on the extent and character of disturbances in blood supply to the left ventricular myocardium. Thanks to the additional option of ECG 'gating' the study (Gated SPECT, GSPECT), which creates the possibility of measuring perfusion in the various phases of the cardiac cycle, perfusion scintigraphy can be currently used to simultaneously assess the functional parameters of the left ventricle (LV) - ejection fraction (EF), end-systolic volume (ESV), and end-diastolic volume (EDV). The assessment of both perfusion and functional parameters - most notably EF - plays a significant role in diagnosis and prognosis in patients with coronary artery disease (CAD), as well as in selecting the most appropriate therapy for a given patient; using GSPECT perfusion studies to acquire reliable data on LV function can significantly shorten and simplify this process. One must keep in mind that the perfusion image (which can be recorded within six hours of administration of the radionuclide Tc-99m-MIBI) reflects the regional blood flow to LV myocardium at the time of radionuclide administration (i.e. at rest, at peak exercise, or at peak vasodilatation), while the obtained values of EF, EDV, and ESV are parameters of the LV at the time of image acquisition (i.e. at rest or in a near-resting state following exercise or vasodilatation).

Most laboratories with GSPECT-capable gamma cameras use *Quantification Gated SPECT* (QGS)

**Table I.** Clinical characteristics of the studypopulation

Gender	
female	55 (28%) 145 (72%)
Indic	140 (7270)
Age (years, range, mean ±SD)	18-80 (58±18)
LVEF (%, range, mean±SD)	
in echocardiography*	17-82 (42.4±15.5)
in contrast ventriculography**	20-70 (43.0±15.8)
History of myocardial infarction	108 (54%)
Confirmed CAD without history of MI	58 (29%)
Suspected CAD	34 (17%)
Post-CABG/PTCA	63 (32%)
Diabetes mellitus	24 (12%)
Hypertension	85 (43%)

\*available for 52 patients

\*\*available for 25 patients

CAD – coronary artery disease

LVEF – left ventricular ejection fraction

software, developed at Cedars-Sinai Medical Center, which allows for the assessment of LV function [1]. Our initial experience indicated a certain variation between the values of LV function parameters obtained by this method and other GSPECT methods [2, 3], which inclined us to test these methods on a large group of patients, using planar radionuclide ventriculography (RNV), which our laboratory has extensive experience with and which is often considered the most accurate method of assessment of LVEF, as a reference method.

The primary aim of this study was to assess the degree of correlation and compare the absolute values of LVEF obtained using GSPECT-QGS with those obtained using the reference method, resting RNV, in patients with various degrees of CAD, in two different clinical situations (with and without LV dilatation), and under three different conditions (at rest, post-exercise, post-dipyridamole). The establishment of normal values of EF, ESV, and EDV in GSPECT-QGS was an additional goal.

# Methods

#### Patient characteristics

Two hundred patients, undergoing myocardial perfusion studies in order to either assist in the diagnosis of CAD (34 patients), or evaluate the effects of treatment or myocardial viability (166 patients with confirmed CAD, of whom 108 had a history of myocardial infarction), were included in the study. The characteristics of the study population are presented in Table I.

A 'normal' group, comprising 26 patients with suspected CAD, without LBBB or arrhythmia, whose resting and post-exercise (or post-dipyridamole, in 3 patients) perfusion studies were normal, was simultaneously examined, in order to establish a range of normal values for EF in QGS studies. This group consisted of 18 women and 8 men, aged 26-74 (mean, 50±7), selected from the group of patients not taking part in the programme of EF verification using RNV.

#### Assessment of EF using GSPECT

With the exception of 14 patients, who had only resting exams performed, all study participants underwent GSPECT examination at rest and one hour post-exercise or post-dipyridamole (standard procedure in Tc-99m-MIBI perfusion studies), according to a two-day (0.3 mCi/kg injections at rest and during exercise) or one-day protocol (0.11 mCi/kg injection at rest, followed four hours later by a 0.3 mCi/kg injection during exercise or vasodilatation) [4]. Exercise was performed on a treadmill, according to a modified Bruce protocol. Pharmacological strain was induced by intravenous administration of 0.56 mg/kg dipyridamole over a period four minutes, followed by four minutes of stationary walking; the injection of Tc-99m-MIBI was administered after the third minute of walking. The cardiac cycle was divided into eight phases during GSPECT acquisition. Parameters of GSPECT acquisition: matrix – 64x64; gamma camera rotation angle – 180°; number of projections - 68; collimator - low-energy, high-resolution. The acquisition time of a single projection was 25s for the two-day protocol, 52 s at rest and 13 s during exercise for the one-day protocol. Parameters of GSPECT reconstruction: Butterworth filter; cutoff frequency – 0.4; order – 7. The MIBI used in the study was produced by OBRI-POLATOM (Świerk, Poland). Image acquisition was performed using a rotating dual-head AXIS camera and ODYSSEY computer system (PICKER-PHILIPS).

#### Assessment of EF using RNV

RNV was performed within three weeks of the GSPECT examination in all patients, with the exception of those who had experienced exacerbation of CAD in that period. Radionuclide ventriculography was performed using Tc-99m, according to the standard procedure [5]. The cardiac cycle was divided into 24 phases. Acquisition in a given projection was performed until 6 million impulses were recorded. The LAO 45° projection was used to determine EF. Image acquisition was performed using an ORBITER 75 gamma camera and MaxDELTA 2000 computer system (Siemens).

A dilated (*large*) LV was defined as having an end-diastolic volume greater than 127 ml in the QGS examination (this value was equal to the mean + 2 standard deviations of EDV values in the *normal* group – see Results).

All patients expressed written consent to take part in an additional RNV examination. The study protocol and patient information and consent forms were approved by the Local Bioethics Committee at the Cardiology Institute in Warsaw, Poland.

#### Statistical methods

Continuous variables are presented as a range of values and mean  $\pm$  standard deviation. Mean values in a given subgroup of patients were compared using a two-sided paired t-test (p<0.05). Mean values of different subgroups of patients were compared using a bilateral non-paired t-test (p<0.05). EF values from RNV and QGS were compared by linear regression analysis (the Pearson correlation coefficient, r, was considered significant if p<0.05; two given values of r were considered discrete if the 95-percent confidence intervals, <Cl<sub>0.95</sub>>, for these

467

values did not overlap). The consistency of EF from RNV and QGS was assessed using the Bland-Altman method, analysing the difference between two values, in relation to their mean value [6].

### Results

# Values of EF, EDV, and ESV in the *normal* group (Table II)

The mean resting values in the group of 'normal' patients were:  $62.3\pm8.0\%$  (EF),  $86.0\pm20.4$  ml (EDV), and  $33.1\pm12.1$  ml (ESV). The lower limit of normal (LLN; mean – 2SD) for EF was 46%, while the upper limits of normal (ULN; mean + 2SD) were 57 ml for ESV and 127 ml for EDV; a dilated LV was thus defined as having an EDV greater than 127 ml. The mean values of EF at rest in *normal* women were significantly higher than in men ( $64.2\pm7.2\%$  and  $57.3\pm8.3\%$ , respectively), while the mean values of EDV and ESV were significantly lower than in men (EDV:  $78.8\pm16.8$  ml and  $104.7\pm17.1$  ml, respectively; ESV:  $28.7\pm10.0$  ml and  $44.4\pm9.9$  ml, respectively) (Table II).

The mean post-exercise values in the group of 'normal' patients were:  $63.8\pm7.8\%$  (EF, NS with respect to resting values),  $86.5\pm20.6$  ml (EDV, NS with respect to resting values), and  $32.0\pm12.1$  ml (ESV, NS with respect to resting values).

# Comparison of mean values of EF obtained by RNV and GSPECT-QGS (Table III)

The values of EF in resting RNV studies of the patient population ranged from 16 to 82% (mean, 50.8±14.9%).

Table III presents the mean values and correlations between EF values obtained by RNV at rest and GSPECT-QGS at rest and one-hour post-exercise (or post-dipyridamole) – in the study population as a whole and in subgroups of patients with large or small LV. Table III also compares the mean values of end-diastolic and end-systolic volumes obtained by QGS – at rest, post-exercise, and post-dipyridamole.

Mean values of EF in QGS examinations were significantly lower than those in RNV in almost all cases (in the study population as a whole and patients with large LV – at rest, post-exercise, and post-dipyridamole; in patients with small LV – post-exercise and post-dipyridamole).

Mean values of post-exercise EF in QGS examination were significantly lower than resting values in all patients groups; post-dipyridamole values were significantly lower than resting values in the study population as a whole and patients with small LV, and non-significantly lower in patients with large LV. Mean values of post-exercise EDV and ESV were significantly higher than resting values in the study population as a whole and patients with large left ventricles, and non-significantly higher in patients with small LV. Post-dipyridamole values were non-significantly higher than resting values in all patient groups.

# Linear correlation of results (Table III, Figures 1 and 2)

The values of EF obtained by RNV (at rest) correlated well with the values obtained by GSPECT ( $0.86 \le r \le 0.91$ , Table IIIa) for the entire population, both at rest (Figure 1), one hour post-exercise, and one hour post-dipyridamole. The correlation between EF values obtained by RNV and GSPECT was stronger in the group of patients with dilated LV ( $0.76 \le r \le 0.92$ , Table IIIb) than in the group with non-dilated LV ( $0.43 \le r \le 0.62$ , Table IIIc; the correlation between the values obtained by

RNV and post-dipyridamole QGS was especially weak). In patients with non-dilated LV, the values of EF calculated based on the resting GSPECT study demonstrated a stronger correlation with EF values obtained by RNV than values of EF calculated based on the GSPECT study one hour post-exercise.

# Consistency of results (Figures 1 and 3)

Bland-Altman analysis of the study population revealed that 95% of the differences between RNV and QGS values of EF fell within the range from -10.9% to +17.5% (limits of consistency:  $3.3\%\pm14.2\%$ ) (Figure 1). The limits of consistency for differences in post-exercise ( $4.3\%\pm15.6$ ) and post-dipyridamole ( $5.5\%\pm14.1\%$ ) EF were similar.

Bland-Altman analysis also demonstrated that the limits of consistency for differences in EF were narrower in the group of patients with dilated LV than in those

**Table II.** Normal values of global parameters of left ventricular function obtained by resting GSPECT using QGS – comparison of our results with data published in literature

Study (number of normal patients)		Total			Female			Male	
	mean EF [%] SD [%]	mean EDV [ml] SD [ml]	mean ESV [ml] SD [ml]	mean EF [%] SD [%]	mean EDV [ml] SD [ml]	mean ESV [ml] SD [ml]	mean EF [%] SD[%]	mean EDV [ml] SD [ml]	mean ESV [ml] SD [ml]
Our results (26: 18F i 8M)	62 8 LLN: 46	86 20 ULN: 127	33 12 ULN: 57	64 7 LLN: 49	79 17 ULN: 112	29 10 ULN: 49	57* 8 LLN: 41	105* 17 ULN: 139	44* 10 ULN: 64
Ababneh 2000 [10] (884: 519F and 365M)	63 9 LLN: 55#			66 8 LLN: 50	57 17 ULN: 91	19 11 ULN: 40	58* 8 LLN: 42	74* 22 ULN: 119	29* 13 ULN: 55
Sharir 2001 [11] (64: 31F and 33M)	66 8 LLN: 50#								
de Bondt 2001 [12] (102: 59F and 43M)	63 9 LLN: 55 <sup>#</sup>	88 28 ULN: 144 <sup>#</sup>	34 16 ULN: 66 <sup>#</sup>	66 9 LLN: 48 <sup>#</sup>	75 23 ULN: 121 <sup>#</sup>	27 14 ULN: 55#	59* 6 LLN: 47 <sup>#</sup>	106* 25 ULN: 156#	44* 14 ULN: 72 <sup>#</sup>
Bavelaar-Croon 2001 [13] (23: 10F and 13M)	55 5 LLN: 45#	100 18 ULN: 136#	45 11 ULN: 67#						
Nichols 2002 [14] (50: 23F and 27M)	62 9 LLN: 44	84 26 ULN: 137	33 17 ULN: 67	69 8 LLN: 53	63 17 ULN: 97	20 10 ULN: 40	57* 7 LN: 44	101* 20 ULN: 141	44* 13 ULN: 70
Druz 2004 [15] (43: 14F and 29M)	62 10 LLN: 42 <sup>#</sup>	70 25 ULN: 120 <sup>#</sup>	28 14 ULN: 56 <sup>#</sup>						

\* p<0.05, relative to female patients

LLN, lower limit of normal

ULN, upper limit of normal

# – approximate value

F – female

M – male

Table III. Values (mean±SD) of ejection fraction (EF), end-diastolic volume (EDV) and end-systolic volume (ESV) obtained by various methods in the study population as a whole (a) and subgroups of patients with large (b) and small (c) left ventricles. SD, standard deviation; r, correlation coefficient between EF value obtained by GSPECT-QGS and EF value obtained by RNV; <CI<sub>0.95</sub>>, 95% confidence interval for correlation coefficient

# III a. Entire study population

		RNV at rest	QGS at rest	QGS post-exercise	QGS post-dipyridamole
all patients (n=200)	<b>EF</b> ±SD [%] r <cl<sub>0.95&gt; EDV±SD [ml] ESV±SD [ml]</cl<sub>	<b>50.8</b> ±14.9 1	<b>47.9</b> *±15.9 0.89 <0.86-0.92> 150±93 90±86		
patients who underwent an exercise study (n=138)	<b>EF</b> ±SD [%] r <cl<sub>0.95&gt; EDV±SD [ml] ESV±SD [ml]</cl<sub>	<b>52.9</b> ±14.5 1	<b>50.1</b> *±15.6 0.88 <0.84-0.91> 143±85 82±80	<b>48.6</b> *, <sup>†</sup> ±15.2 0.86 <0.81-0.90> 148±88 <sup>†</sup> 88±84 <sup>†</sup>	
patients who underwent a dipyridamole study (n=48)	<b>EF</b> ±SD [%] r <cl<sub>0.95&gt; EDV±SD [ml] ESV±SD [ml]</cl<sub>	<b>46.0</b> **±16.3 1	<b>42.5</b> **±16.9 0.91 <0.84-0.95> 172±116 115±106		<b>40.5</b> *, <sup>†</sup> ,**±16.5 0.90 <0.83-0.94> 176±112 118±102

#### III b. Patients with dilated left ventricles

		RNV at rest	QGS at rest	QGS post-exercise	QGS post-dipyridamole
all patients (n=88)	<b>EF</b> ±SD [%] r <cl<sub>0.95&gt; EDV±SD [ml] ESV±SD [ml]</cl<sub>	<b>39.8</b> ±13.6 1	<b>35.1</b> *±13.3 0.91 <0.87-0.94> 221±101 154±97		
patients who underwent an exercise study (n=56)	<b>EF</b> ±SD [%] r <cl<sub>0.95&gt; EDV±SD [ml] ESV±SD [ml]</cl<sub>	<b>42.7</b> ±15.1 1	<b>37.4</b> *±14.8 0.92 <0.87-0.95> 214±94 144 ±95	<b>36.0</b> *, <sup>†</sup> ±13.2 0.91 <0.85-0.95> 221±98 <sup>†</sup> 154±99 <sup>†</sup>	
patients who underwent a dipyridamole study (n=26)	EF±SD [%] r <cl<sub>0.95&gt; EDV±SD [ml] ESV±SD [ml]</cl<sub>	<b>33.3</b> **±8.8 1	<b>29.2</b> *,**±8.1 0.81 <0.62-0.91> 239±122 179±108		<b>28.1</b> *,**±8.9 0.76 <0.53-0.89> 243±112 181±102

#### III c. Patients with non-dilated left ventricles

		RNV at rest	QGS at rest	QGS post-exercise	QGS post-dipyridamole
all patients (n=112)	<b>EF</b> ±SD [%] r <cl<sub>0.95&gt; EDV±SD [ml] ESV±SD [ml]</cl<sub>	<b>59.5</b> ±8.8 1	<b>58.0</b> ±9.0 0.60 <0.47-0.71> 94±20 41±14		
patients who underwent an exercise study (n=82)	<b>EF</b> ±SD [%] r <cl<sub>0.95&gt; EDV±SD [ml] ESV±SD [ml]</cl<sub>	<b>59.9</b> ±9.1 1	<b>58.7</b> ±8.7 0.62 <0.47-0.74> 94±20 40±14	<b>57.1</b> *, <sup>†</sup> ±9.4 0.57 <0.40-0.70> 99±23 43±17	
patients who underwent a dipyridamole study (n=22)	<b>EF</b> ±SD [%] r <cl<sub>0.95&gt; EDV±SD [ml] ESV±SD [ml]</cl<sub>	<b>61.0</b> ±6.9 1	<b>58.2</b> ±9.2 0.43 <0.01-0.72> 92±21 40±14		<b>55.1</b> *, <sup>†</sup> ±10.1 0.54 <0.15-0.78> 95±25 44±18

\* – p<0.05, relative to RNV

 $\dagger$  – p<0.05, relative to resting values \*\* – p<0.05, relative to patients who underwent an exercise study



**Figure 1.** Comparison of RNV EF and QGS EF at rest in the study population as a whole (n=200). Left: correlation between RNV EF and QGS EF (r, correlation coefficient [see Table III]). Right: Bland-Altman consistency plot of RNV EF and QGS EF

with non-dilated LV (4.7%±11.5% vs 1.5%±15.5% at rest, 6.7%±12.1% vs 2.7%±17.0% post-exercise, and 5.2%±11.9% vs 5.8%±16.9% post-dipyridamole, Figure 3).

# Discussion

According to our knowledge, the 200 CAD patients taking part in this study constitute the largest group of any study comparing GSPECT-QGS to RNV to date, so the results presented in Table III can be considered statistically reliable; earlier comparisons in patients with CAD dealt with 30- to 62-patient groups (and often yielded inconsistent results) [7-10].

# Normal values for EF, EDV, and ESV obtained by GSPECT-QGS [11-16] (Table II)

The lower limit of normal (LLN) for EF in the group of 26 patients was 46%. This value does not differ significantly from those obtained in other QGS studies on 'normal' patients, which ranged from 42 to 55%. The upper limits of normal (ULN) for EDV and ESV in the group of *normal* patients were also consistent with findings from previous studies (127 ml *vs* 120-140 ml for EDV, 57 ml *vs* 56-67 ml for ESV).

As has been the case in previous studies [11, 13, 15], significant differences were found between the genders – women had a significantly higher mean EF and significantly lower mean EDV and ESV. Thus, the LLN for EF was 49% (*vs* 41% for men), the ULN for EDV was 112 ml (*vs* 139 ml for men), and the ULN for ESV was 49 ml (*vs* 64 ml for men). These values were consistent with those reported in previous studies.

The mean resting values of EF, EDV, and ESV in this patient group did not differ significantly from the postexercise or post-dipyridamole values, similarly to other studies which compared: [14] post-exercise, post-dipyridamole, and post-dobutamine values, and [16] post-adenosine values. Only DeBondt et al. produced different results: the mean value of EF in patients with a low CAD risk was found to be significantly higher following exercise on a stationary bicycle than at rest (due to a marked decrease in ESV), while the post-dipyridamole value was similar to the resting value [13]. This is, however, an isolated finding, and it appears that, in healthy individuals, the values of EF, EDV, and ESV obtained by GSPECT post-exercise and post-vasodilatation do not differ significantly from resting values.

Our *normal* group is relatively small, which makes it impossible to reliably assess the relationship between LV contractility parameters and age. It is, however, worth noting that DeBondt et al. reported that EF rises, while EDV and ESV decline, with age [13]. It is thus plausible that the assessment of cardiac function by GSPECT and QGS should be based on variable normal values, dependent on gender and age.

# Comparison of mean values of EF obtained by RNV and GSPECT-QGS

The mean resting values of EF obtained by QGS in our study population were found to be lower than the mean resting values of EF obtained by RNV; this relationship was not reported in previous studies [8, 10]. Our results are, however, similar to those published by Manrique et al. [7]: mean EF in RNV (R-R cardiac cycle divided into 16 phases) was significantly higher than EF in QGS (R-R divided into 8 phases). The underestimation of EF in QGS may be the result of the division of the cardiac cycle into only eight phases (the only acquisition



**Figure 2.** Correlation between RNV EF and QGS EF in the subgroups of patients with non-dilated left ventricles (left) and dilated left ventricles (right). Top: QGS EF from resting GSPECT. Middle: QGS EF from post-exercise GSPECT. Bottom: QGS EF from post-dipyridamole GSPECT; r, correlation coefficient (see Table III)

option available in our GSPECT system) – since EDV and ESV, the parameters used to calculate EF, are approximated from an eight-point graph of the LV volume [9]. Our RNV system, on the other hand, divides the R-R cardiac cycle into 24 phases, yielding a 24-point graph of LV radioactivity, which allows for the moments of ED and ES to be identified more accurately – EDV can therefore be greater, and ESV smaller, than in GSPECT.

Our RNV software does not, however, allow for the measurement and analysis of numerical values of EDV and ESV.

It is thus likely that the observed underestimation of EF in QGS, relative to RNV, can be decreased or entirely eliminated by dividing the cardiac cycle in GSPECT into a larger number of phases. However, the application of



**Figure 3.** Bland-Altman consistency plot of RNV EF and QGS EF in the subgroups of patients with non-dilated left ventricles (left) and dilated left ventricles (right). Top: QGS EF from resting GSPECT. Middle: QGS EF from post-exercise GSPECT. Bottom: QGS EF from post-dipyridamole GSPECT

a different quantitative analysis program ('Emory Cardiac Toolbox' [2]) to the same eight-phase division of the R-R cycle in GSPECT yields values of EF that are significantly higher than those in RNV [3] – it is thus the algorithm used to calculate EDV and ESV that has a significant effect on the absolute value of EF in GSPECT.

The mean post-exercise and post-dipyridamole values of EF in QGS were significantly lower, while the mean values of EDV and ESV were significantly higher, than resting values in our study population. Previous studies produced similar results [14, 16, 17]. At least two plausible explanations exist: 1) severe ischaemia induced by exercise (or irregularities in blood flow

induced by vasodilatation) renders the endocardial border difficult to define in scintigraphic imaging [7, 18]; 2) myocardial stunning of the cardiomyocytes (i.e. an actual decline in EF) induced by ischaemia during the exercise or dipyridamole test persists for a longer period of time following completion of the test [14, 16]. The application of GSPECT-QGS to calculate the resting left ventricular contractility parameters should be limited to the resting portion of the perfusion study (and not the post-exercise and post-dipyridamole portions, which yield left ventricular volumes different from those obtained when both radionuclide administration and image acquisition are performed in a true resting state).

#### Linear correlation and consistency of results

Our results indicate that the values of LV EF obtained by GSPECT-QGS correlate strongly with the values of EF obtained using the reference method, RNV. The correlation coefficients of resting values for the study population as a whole (0.89) and subgroup of patients with large LV (0.91) at rest are consistent with the results (0.82-0.94) of previous studies using QGS [7-10].

Our results also indicate that the correlation between EF values obtained by QGS and RNV is clearly weaker for patients with non-dilated LV. Non-dilated LV were defined as having an EDV ≤127 ml (this value corresponds to our upper limit of normal for EDV). We decided to study the dependency of QGS results on LV size based on reports of such a problem (especially the overestimation of EF in patients with small LV) [10, 19, 20]. Our study did not confirm the overestimation of EF in patients with small LV; we did, however, confirm that in the group of patients with small LV, the correlation of EF with the reference method was weaker (Vallejo et al. observed this when EDV in QGS was found to be less than the mean value for the patient population, 104 ml [19]) and the values of EF were less consistent with the reference method (wider limits of consistency, determined by Bland-Altman analysis).

The demonstration of a strong correlation between and relatively high degree of consistency of EF in QGS and RNV, especially in patients with dilated LV, has significant implications for the diagnosis and monitoring of EF in patients at a high risk of acute coronary complications – post-MI, with heart failure. Our results seem to justify replacing the RNV examination (which places the patient at additional risk while costing both money and time) with GSPECT in this group of patients, provided that: 1) a perfusion study is planned for the patient, independently of assessment of contractility (which is most often the case – to assess myocardial viability), and 2) the clinical question does not include the assessment of right ventricular contractility – where RNV remains unsurpassed (the application of SPECT technology in cardiology is currently limited to the study of the LV). Gating the SPECT examination only slightly increases acquisition time (unless patients have frequent arrhythmias). It is worth noting, however, that the additional processing of a gated study, following the assessment of perfusion (which essentially is performed on a composite, ungated image) significantly increases the time required for computer processing.

### Methodological limitations of the study

Our 'normal' group was relatively small, with women constituting a significant majority. We compared our values of lower limits of normal for EF and upper limits of normal for EDV and ESV for the *normal* population as a whole and the subgroups of women and men, and found that they do not differ significantly from the values reported in other studies. Our goal is to continue to expand the group of *normal* patients, which will allow us, among other things, to refine our ranges of normal values and verify the relationship between EF in QGS and age, as described in [13].

The lack of verification of EDV and ESV values obtained by QGS constitutes a further limitation of the study. Our current RNV software could not provide numerical values of EDV or ESV (only EF).

There were also no analyses of the effect on results of: 1) the number of phases into which the cardiac cycle was divided in GSPECT (since our GSPECT system permits only eight-phase acquisition – see Discussion); 2) the administered dose of radionuclide (this problem was addressed by Vallejo et al. [19]) – the effect of radionuclide dosage is eliminated in our study by adjusting the GSPECT protocols so that the total number of counts registered is constant (in the one- and two-day protocols, at rest, post-exercise, and post-dipyridamole).

#### Conclusions

In order to complement data on myocardial perfusion, the GSPECT-QGS technique should be optimally used to calculate LV contractility parameters at rest (as opposed to post-exercise or post-dipyridamole), and include a range of normal values for EF, EDV, and ESV, obtained using QGS. Of note, EF measurements by GSPECT are more accurate for dilated than non-dilated ventricles.

#### References

- Germano G, Kiat H, Kavanagh PB, et al. Automatic quantification of ejection fraction from gated myocardial perfusion SPECT. J Nucl Med 1995; 36: 2138-47.
- Faber TL, Cooke CD, Folks RD, et al. Left ventricular function and perfusion from gated SPECT perfusion images: an integrated method. J Nucl Med 1999; 40: 650-9.
- Wnuk J, Szumilak B, Dąbrowski A, et al. Weryfikacja wartości frakcji wyrzutowej lewej komory, uzyskiwanej z badań perfuzji mięśnia sercowego wykonywanych bramkowaną techniką SPECT (GSPECT). Doniesienie wstępne. *Probl Med Nukl* 2002; 32: 193-200.
- Teresińska A, Królicki L, Potocka J, et al. Standaryzacja radioizotopowych badań perfuzji mięśnia sercowego. Probl Med Nukl 2000; 14: 133-46.
- Teresińska A, Królicki L, Potocka J, et al. Standaryzacja angiokardiografii radioizotopowej po równomiernym wyznakowaniu krwi. *Probl Med Nukl* 2000; 14: 147-58.
- Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; 1: 307-10.
- Manrique A, Faraggi M, Vera P, et al. 201Tl and 99mTc-MIBI gated SPECT in patients with large perfusion defects and left ventricular dysfunction: comparison with equilibrium radionuclide angiography. J Nucl Med 1999; 40: 805-9.
- 8. Chua T, Yin LC, Thiang TH, et al. Accuracy of the automated assessment of left ventricular function with gated perfusion SPECT in the presence of perfusion defects and left ventricular dysfunction: correlation with equilibrium radionuclide ventriculography and echocardiography. *J Nucl Cardiol* 2000; 7: 301-11.
- Kumita S, Cho K, Nakajo H, et al. Assessment of left ventricular diastolic function with electrocardiography-gated myocardial perfusion SPECT: comparison with multigated equilibrium radionuclide angiography. J Nucl Cardiol 2001; 8: 568-74.
- Nakajima K, Higuchi T, Taki J, et al. Accuracy of ventricular volume and ejection fraction measured by gated myocardial SPECT: comparison of 4 software programs. J Nucl Med 2001; 42: 1571-8.
- 11. Ababneh AA, Sciacca RR, Kim B, et al. Normal limits for left ventricular ejection fraction and volumes estimated with gated myocardial perfusion imaging in patients with normal exercise test results: influence of tracer, gender, and acquisition camera. *J Nucl Cardiol* 2000; 7: 661-8.
- Sharir T, Berman DS, Waechter PB, et al. Quantitative analysis of regional motion and thickening by gated myocardial perfusion SPECT: normal heterogeneity and criteria for abnormality. J Nucl Med 2001; 42: 1630-8.
- De Bondt P, Van de Wiele C, De Sutter J, et al. Age- and gender-specific differences in left ventricular cardiac function and volumes determined by gated SPET. *Eur J Nucl Med* 2001; 28: 620-4.
- 14. Bavelaar-Croon CD, America YG, Atsma DE, et al. Comparison of left ventricular function at rest and post-stress in patients with myocardial infarction: Evaluation with gated SPECT. *J Nucl Cardiol* 2001; 8: 10-8.
- Nichols K, Santana CA, Folks R, et al. Comparison between ECTb and QGS for assessment of left ventricular function from gated myocardial perfusion SPECT. J Nucl Cardiol 2002; 9: 285-93.

- 16. Druz RS, Akinboboye OA, Grimson R, et al. Postischemic stunning can affect left ventricular ejection fraction and regional wall motion on post-stress gated sestamibi tomograms. J Am Coll Cardiol 1997; 30: 1641-8.
- 17. Johnson LL, Verdesca SA, Aude WY, et al. Postischemic stunning can affect left ventricular ejection fraction and regional wall motion on post-stress gated sestamibi tomograms. *J Am Coll Cardiol* 1997; 30: 1641-8.
- 18. Bonow R. Gated myocardial perfusion imaging for measuring left ventricular function. *J Am Coll Cardiol* 1997; 30: 1649-50.
- 19. Vallejo E, Dione DP, Sinusas AJ, et al. Assessment of left ventricular ejection fraction with quantitative gated SPECT: accuracy and correlation with first-pass radionuclide angiography. J Nucl Cardiol 2000; 7: 461-70.
- 20. Hambye AS, Vervaet A, Dobbeleir A. Variability of left ventricular ejection fraction and volumes with quantitative gated SPECT: influence of algorithm, pixel size and reconstruction parameters in small and normal-sized hearts. *Eur J Nucl Med Mol Imaging* 2004; 31: 1606-13.

# Weryfikacja wartości frakcji wyrzutowych lewej komory, uzyskiwanych z badań perfuzji mięśnia sercowego wykonywanych bramkowaną techniką SPECT (GSPECT)

#### Anna Teresińska, Jacek Wnuk, Stefania Konieczna, Arkadiusz Dąbrowski

Samodzielna Pracownia Medycyny Nuklearnej, Instytut Kardiologii, Warszawa

#### Streszczenie

**Wstęp:** Obraz perfuzji (który może być rejestrowany techniką SPECT lub GSPECT w okresie do 6 godz. od podania pacjentowi radioizotopu Tc-99m-MIBI) odzwierciedla regionalne ukrwienie mięśnia lewej komory [LV] w momencie podania radioizotopu (czyli w spoczynku, na szczycie wysiłku lub na szczycie efektu wazodylatacyjnego), natomiast uzyskiwane w GSPECT wartości EF, EDV i ESV są parametrami kurczliwości LV w momencie rejestracji obrazu (czyli w spoczynku lub w stanie bliskim spoczynkowi po wysiłku lub po zastosowaniu wazodylatatora). Za najdokładniejszą metodę obliczania LVEF uznawana jest jednak planarna wentrykulografia radioizotopowa [RNV].

**Cel:** Podstawowym celem pracy było porównanie wartości EF uzyskiwanych najczęściej stosowaną metodą GSPECT-QGS i metodą referencyjną RNV – z uwzględnieniem różnych sytuacji klinicznych (LV powiększona lub nie powiększona) i różnych stanów pacjenta podczas rejestracji GSPECT (w spoczynku, po wysiłku lub po obciążeniu dipirydamolem).

**Metodyka:** Badaniami objęto 200 pacjentów (145 mężczyzn) w wieku 58±11 (18–80) lat z rozpoznaną chorobą naczyń wieńcowych (n=166, w tym 108 po przebytym zawale serca) lub z jej podejrzeniem (n=34). Ustalono zakres wartości prawidłowych EF, EDV i ESV w oddzielnej 26-osobowej grupie pacjentów. Na tej podstawie powiększoną LV zdefiniowano jako komorę o EDV >127 ml (w spoczynku, wg QGS) – jej obecność stwierdzono u 88 pacjentów. Badania perfuzji mięśnia sercowego po podaniu Tc-99m-MIBI zarejestrowano techniką GSPECT w spoczynku u wszystkich pacjentów oraz 1 godz. po wysiłku na bieżni (u 138 pacjentów) lub po obciążeniu dipirydamolem (u 48 pacjentów). Spoczynkowe badanie RNV przeprowadzono w odstępie czasu nie przekraczającym 3 tyg. Porównano wartości EF uzyskane metodami QGS i RNV u pacjentów z komorą powiększoną i nie powiększoną. Porównano wartości EF, EDV i ESV uzyskiwane metodą QGS po rejestracjach w spoczynku, po wysiłku i po dipirydamolu.

Wyniki: 1. Wartości EF uzyskane techniką GSPECT przy użyciu oprogramowania QGS w rejestracji spoczynkowej lub dokonywanej 1 godz. po wysiłku na bieżni lub 1 godz. po obciążeniu dipirydamolem, w uogólnionej grupie pacjentów wykazały istotną, wysoką korelację z wynikami uzyskanymi w referencyjnym badaniu RNV (współczynnik korelacji r ≥0,86). Korelacja i zgodność była lepsza w przypadku komór powiększonych niż niepowiększonych. Zarówno w grupie komór powiększonych, jak i niepowiększonych korelacja z RNV EF była nieistotnie gorsza w przypadku rejestracji powysiłkowych (w porównaniu do spoczynkowych) oraz rejestracji podipirydamolowych (w porównaniu do powysiłkowych). 2. W stosunku do RNV, QGS zaniżała bezwzględne wartości EF. 3. W rejestracjach po wysiłku lub po dipirydamolu, uzyskiwane średnie wartości EF były niższe a wartości EDV i ESV były wyższe niż w rejestracjach spoczynkowych (w populacji pacjentów z rozpoznaną chorobą wieńcową lub z jej podejrzeniem).

Wnioski: Dla uzupełnienia informacji o perfuzji mięśnia sercowego, optymalne wykorzystanie techniki GSPECT-QGS do obliczania spoczynkowych parametrów kurczliwości LV powinno dotyczyć spoczynkowej (a nie powysiłkowej lub podipirydamolowej) części badania perfuzji oraz powinno obejmować dołączenie do wyniku EF, EDV i ESV zakresu wartości normalnych uzyskiwanych metodą QGS. Należy przy tym mieć świadomość, że EF w GSPECT jest wyznaczana dokładniej w przypadku komór powiększonych niż nie powiększonych.

Słowa kluczowe: Tc-99m-MIBI – SPECT – GSPECT, wentrykulografia radioizotopowa, lewa komora, frakcja wyrzutowa

Kardiol Pol 2005; 63: 465-475

#### Adres do korespondencji:

dr n. med. Anna Teresińska, Samodzielna Pracownia Medycyny Nuklearnej, Instytut Kardiologii, ul. Alpejska 42, 04-628 Warszawa, tel.: +48 22 343 42 81, faks: + 48 22 815 40 03, e-mail: annateresinska@ikard.waw.pl **Praca wpłynęła:** 12.01.2005. **Zaakceptowana do druku:** 22.08.2005.