COMPARISON OF BLOOD POOL GATED SPECT WITH THREE DIFFERENT GATED MYOCARDIAL PERFUSION SPECT PROGRAMS FOR LEFT VENTRICULAR FUNCTIONAL PARAMETERS IN PATIENTS WITH LOW LIKELIHOOD FOR CAD

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ABSTRACT:

Purpose: To compare several gated myocardial perfusion SPECT (gMPS) programs with blood pool gated SPECT (BPGS) for the evaluation of left ventricular (LV) functional parameters and further investigate the effect of heart size in a population with low coronary artery disease (CAD) risk.

Materials and Methods: Forty patients whose gMPS were seen to be normal were included. Rest blood pool studies were performed in patients 3 days after the evaluation of gMPS, and the data were processed with 3 different programs: Emory Cardiac Toolbox (ECT), Quantitative Gated SPECT (QGS), and 4D-MSPECT. The results of each program were evaluated using BPGS as the reference method and all programs were compared with each other. Patients were also grouped according to their end systolic volumes (ESV) with BPGS; the ESV < 30 ml (small heart) group was compared to group 2 (ESV >30 ml) for functional parameters. Repeated measures ANOVA, linear regression, and Bland-Altman analysis were used to compare the methods.

Results: All gMPS programs were well correlated with BPGS, while 4D-MSPECT had the best correlation. Mean differences in EF between gMPS programs and BPGS were not significant, except for ECTb, with which EF values were significantly higher from BPGS. No statistically significant differences were observed between BPGS and gMPS programs for mean end diastolic volume (EDV) values. However, ESV values from ECT and 4D MSPECT programs were significantly lower than those from BPGS. EF values were significantly higher in patients with small hearts for all methods. The closest EF values to the reference method values were calculated with 4D MSPECT in group 1 and with QGS in group 2.

Conclusion: gMPS programs yield accurate and reliable results in the assessment of myocardial function in addition to myocardial perfusion. In all patient groups and the small heart group, the closest LVEF values to those of the reference method were calculated with 4D-MSPECT. Overestimation of LVEF in small hearts is the major problem of gMPS methods and also ERNA and BPGS. In this study the lowest overestimations of LVEF values were obtained with QGS in small hearts.

Keywords: EF, Blood-Pool Gated SPECT, Gated MPS

KORONER ARTER HASTALIĞI RİSKİ DÜŞÜK OLAN HASTALARDA SOL VENTRİKÜL FONKSİYONLARININ DEĞERLENDİRİLMESİNDE GATED KAN HAVUZU SPECT İLE ÜÇ FARKLI GATED MYOKARDİYAL PERFÜZYON SPECT PROGRAMININ KARSILASTIRILMASI

ÖZ:

Amaç: Bu çalışmanın amacı koroner arter hastalığı (KAH) riski düşük olan hastalarda sol ventrikülün fonksiyonel parametrelerini belirlemede farklı gated miyokardiyal perfüzyon SPECT (gMPS) programlarını gated kan havuzu SPECT (BPGS) ile karşılaştırmaktı. Ayrıca kalp boyutunun fonksiyonel parametreler üzerine etkisini araştırmaktı.

Gereç ve Yöntem : KAH riski düşük olan ve gMPS incelemesi normal olarak değerlendirilen 40 hastaya gMPS incelemesini takip eden 3 gün içinde istirahat kan havuzu görüntülemesi yapıldı. 3 farklı gMPS programına (Emory Cardiac Toolbox (ECT), Quantitative Gated SPECT (QGS) ve 4DMSPECT) ait sonuçlar BPGS referans alınarak değerlendirildi ve tüm programlar birbiri ile karşılaştırıldı. Ayrıca hastalar sistol-sonu hacimlerine (SSH) göre gruplandı; SSH< 30 ml olan hastalar (grup 1) SSH> 30 ml olan hastalar (grup 2) ile fonksiyonel parametreler açısından karşılaştırıldı. Karşılaştırmada tekrarlayan ANOVA ölçümü, doğrusal regresyon analizi ve Bland- Altman metodu ile yapıldı.

Bulgular: Tüm gMPS programları BPGS ile iyi korele olup 4D-MSPECT programı en iyi korelasyonu gösterdi. ECT dışında diğer gMPS programları ile BPGS arasındaki ortalama EF farkı istatistiksel olarak anlamlı bulunmadı. ECT programı ile ise belirgin yüksek ejeksiyon fraksiyonu (EF) değerleri hesaplandı. BPGS ve gMPS programları arasında ortalama diyastol sonu hacmi (DSH) değerleri açısından istatistiksel farklılık saptanmamış olup, ECT ve 4D-MSPECT ile hesaplanan ortalama SSH değerleri BPGS'den anlamlı derecede düşüktü. Tüm programlar ile küçük hacimli kalplerde EF değerleri istatiksel olarak anlamlı ölçüde yüksek olarak hesaplandı ve BPGS yöntemine en yakın sonuçlar grup 1 de 4D-MSPECT ile grup 2 de ise QGS ile bulundu.

Sonuç: Sol ventrikül fonksiyonlarını belirlemede gMPS programları ve BPGS iyi korele ve uyumludur. Tüm hasta grubunda ve küçük kalpli hasta grubunda referans yönteme en yakın sonuçlar 4D-MSPECT ile hesaplandı. Küçük kalplerde EF değerlerinin olduğundan yüksek hesaplanması gMPS programlarının yanında ERNA ve BPGS için de önemli bir problemdir. Bu çalışmada küçük kalplerde en düşük EF değerleri QGS ile hesaplandı.

Anahtar Kelimeler EF, Kan Havuzu SPECT, Gated MPS

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INTRODUCTION

Left ventricular (LV) function is an important prognostic factor in patients with coronary artery disease (CAD). Tomographic methods are used for the assessment of LV function via volumes and ejection fraction (EF) from blood pool or myocardial perfusion studies. Electrocardiographically gated myocardial perfusion SPECT (gMPS) is widely used to evaluate myocardial perfusion, LV function, regional wall motion, and wall thickening. Different gMPS programs are available in clinical practice. These include ECT (Emory Cardiac Toolbox; Emory University, Atlanta, GA, USA)[1], QGS (Quantitative Gated SPECT; Cedars-Sinai Medical Center, Los Angeles, CA, USA)[2], and 4D-MSPECT (University of Michigan Medical Center, Ann Arbor, MI, USA)[3]. All these programs have shown good correlation among each other and with other conventional methods for the estimation of EF[4-11] but an overestimation of EF has been reported by several investigators in the setting of small hearts [12-15]. Blood pool gated SPECT (BPGS), the three dimensional analogue of the conventional gated blood pool method (Equilibrium radionuclide angiography: ERNA), by its tomographic perspective, has the benefit of isolating the left and right ventricles without overlap of other cardiac chambers, which improves the assessment of regional wall motion[16-24].

Only a few studies have compared several gMPS programs using BPGS as the reference method [25-27]. The aim of the present study was to compare several gMPS programs in reference to BPGS for the evaluation of LV functions and further investigate the effect of heart size, if any, on the outcome of these methods in a population with low CAD risk.

METHOD:

Patient population: A total of 40 patients, 19 females and 21 males (ages 25-64, mean: 47±9), with clinical suspicion of CAD were included in our study from among those admitted to our department for gMPS and whose myocardial perfusion was seen to be normal with the same day rest-stress 99mTc-MIBI gMPS protocol. Cardiac risk factor determinations for the subjects were assessed according to European Heart Associations 3rd Combined Study Group [28] and Framingham heart studies [29]. All subjects had risk scores under 5%, and were regarded as the low risk group (Table 1). Subjects with known contraindications for exercise testing and with left bundle branch block were excluded from the study. Furthermore, patients with high gastrointestinal activity, movement or soft tissue attenuations on SPECT images and patients with body mass index higher than 35 were excluded in case those affected cardiac counts. Moreover, none of the subjects had cardiac valvular disease, pulmonary hypertension, or pulmonary parenchymal disease.

Tablo 1: Cardiac risk factors of patients

Patient	Age	Gender	Symptom	Family history	DM	HT Systolic (mmHg)	Smoking	Cholesterol mg/dl	EKG changing (STd)	SCOR %
Aİ	48	M	NA	+			+	250		3
DG	39	M	NA	+			+	300		2
EKP	54	M	AAP				+	300	1mm	4
EKY	46	M		+					1mm	1
Eİ	32	M	AAP				+			1
FA	58	F			+	160				2
FAT	63	F	NA				+	300		5
FS	40	M	NA			160		300		2
FY	60	F	NA			140		250	1mm	3
GU	46	F		+						1
GE	64	F						250		3
HS	40	M					+			1
HU	56	F		+		140		250		2
HB	40	M	NA	+		160				2
KA	39	F	AAP			180			1mm	1
KD	61	M						250		4
KN	52	F					+	250		2
MB	35	M	AAP				+			1
MT	52	M					+	300		4
MTN	44	F		+					1mm	1
MK	42	M				160	+			2
NO	34	F	NA	+						1
NE	37	F		+		140				1
NT	47	F				160	+			2
RG	46	M	AAP							1
RA	44	M		+		160				1
RGN	43	M	NA			140				1
RS	48	M			+			300	1mm	3
SE	50	M	AAP				+			2
SK	35	M	AAP					300		1
ST	36	F					+		1mm	1
SB	38	M					+		1mm	1
SKR	40	F	AAP				+			1
ŞE	53	F		+		160				2
ŞM	64	F			+			300		3
TB	54	F	AP			160				2
UO	51	F	NA			180				2
YS	41	M		+		160	+			2
YK	59	M						300	2mm	5
ZO	62	F				140			1mm	2

M: Male, F: Female, NA: Nonanginal chest pain, AAP: Atypic angina pectoris, AP: Angina pectoris, DM: Diabetes mellitus, HT: Hypertension, STd: ST segment deviation

gMPS imaging protocol and data processing: 99mTc-MIBI gMPS was performed using a one day rest-stress protocol following overnight fasting. A dose of 8 mCi 99m 99mTc- MIBI was injected while the patients were at rest and SPECT images of the myocardium were obtained in 60 minutes. After approximately 3 hours, exercise testing with a symptom limited standard Bruce protocol was performed on a treadmill. When the heart rate was over 85% of the targeted heart rate, 25 mCi

99mTc-MIBI was injected and stress gated SPECT images were taken in 15-20 min. Gated acquisition was done on a dual head gamma camera (Optima NX-General Electric) equipped with high resolution collimators. The acquisition parameters were as follows: 20 seconds per projection for a total 64 projections, 8 frames per cardiac cycle and an acceptance window of 50-150% of the mean pre-acquisition heart rate. The energy peak was 140 keV with a 20% window. The acquisition matrix was 64x64. Gated SPECT images were analysed for the same functional parameters with three different quantification packages: ECT, QGS, and 4D- MSPECT.

Each program uses a different algorithm to compute LV parameters. The model for the ECT software applies a 3-dimensional hybrid sampling technique that uses cylindrical coordinates to sample from the basal wall to the distal wall and spherical coordinates to sample the apex. QGS software uses a full set of short-axis images. After a full set of short-axis images was selected, fully automatic sampling of 3-dimensional data was performed, providing the final results. Fitted to a 3-dimensional ellipsoid, a Gaussian function was applied to determine the myocardial borders. The 4D-MSPECT model also uses a cylindrical–spherical coordinate system, with cylindrical coordinates to sample from the basal wall to the distal wall and spherical coordinates to sample the apex. Weighted spline and thresholding techniques were used to refine surface estimates. Fitted to a Gaussian function, wall position and thickness were estimated.

Rest blood pool studies were performed in patients in 3 days after the evaluation of gMPS.

Blood pool study: The gated blood pool procedure was performed using in-vivo 99m-Tc labelled red blood cells with a pyrophosphate (PYP) commercial kit. For the in-vivo labelling, PYP was injected into patients via an IV line. After 15-20 min, 25-30 mCi 99mTc-pertechnetate was injected through the same IV line and the IV line was washed with 10 ml of SF.

SPECT imaging was performed with the same dual-head gamma camera (Optima NX-General Electric) equipped with two low energy high resolution (LEHR) parallel hole collimators. Data were acquired from 32 projection views over 180 degrees, with 30 seconds per view, on 64x64 matrices, 16 frames per cardiac cycle with ECG gating, ±35% R-R acceptance window, and 20% energy window centered at 140 keV. The data were processed on the computer (Xeleris, GE Electric) with the BPGS program, an automatic software algorithm defined by Van Kriekinge-Germano et al. (Cedars-Sinai Medical Center) (17). BPGS automatically fits left and right ventricular ROIs and calculates left and right ventricular ejection fractions and volumes. Only the left ventricular values were used in this study.

The patients were also grouped according to their heart size with BPGS. We grouped patients according to end systolic volume (ESV), like Hambye et al.[14], and regarded ESV<30 ml as small hearts, as they did. The ESV < 30 ml (small heart) group was compared to group 2 (ESV >30 ml) for functional parameters. There were 18 patients in group 1, 12 females and 6 males (ages 32-64, mean: 49±9), and there were 22 patients in group 2, 7 females and 15 males (ages 25-64, mean: 46±10).

Statistics: Statistical analysis was performed using SPSS version 11.5 (SPSS Inc, Chicago, IL, USA). Continuous data were reported as mean ± SD. Correlation coefficients were calculated using Pearson's and Spearman's tests amongst all the methods for LVEF, EDV, and ESV. Linear regression analysis between gMPS values of different programs and the reference method was performed, along with Bland-Altman analysis (30). p<0.05 was considered statistically significant.

RESULTS

Table 2 shows the LVEF, EDV, and ESV values calculated using different methods and Table 3 shows the correlation matrix for all parameters.

Table 2: LVEF, EDV and ESV values calculated by using different methods (mean ± SD)

	ECT	QGS	4D-MSPECT	BPGS
LVEF (%)	69.4±7.4	61.4±8.1	66.2±8.6	63.1±8.7
EDV (ml)	91.6±22.1	84.7±21.6	85.7±21.7	87.6±24.3
ESV (ml)	28.9±12.7	33.9±15.1	30.2±14.4	33.3±15.4

Table 3: Correlation Matrix for different gMPS methods.

	ECT-QGS	ECT-4D M	QGS-4D M	BPGS-ECT	BPGS-QGS	BPGS-4D M
EF	r: 0,823	r: 0,746	r: 0,821	r: 0,609	r:0,672	r:0,703
EDV	r: 0,853	r :0,876	r: 0,939	r: 0,779	r:0,803	r:0,804
ESV	r: 0,943	r:0,930	r:0,937	r:0787	r:0,784	r:0,799

EF: 4D-MSPECT had the best correlation with the reference method (r: 0.703). There was also a good correlation between QGS and BPGS (r: 0.672). Mean differences of EF values were 3% and 2%, respectively, and they were not statistically significant. When compared with BPGS, EF values of the ECT method were significantly higher and the mean difference was 6% (p<0.001). In the Bland-Altman plots, as the ventricle performance gets better, the difference decreases (Figure 1). Ventricular Volumes: All three gMPS methods had good correlations with BPGS in terms of ventricular volumes (p<0.001). No statistically significant differences were observed between the BPGS and gMPS methods for mean EDV values. However, lower ESV values were calculated with the ECTb and 4D MSPECT methods compared with BPGS and the differences were statistically significant for both (p<0.01). The Bland-Altman plots revealed an increase in difference for the ECTb method when ESV values were higher (Figure 2).
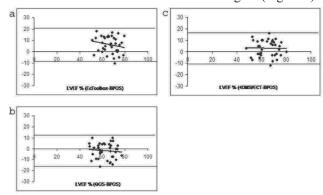

Figure 1: Bland-Altman analysis of LVEF with respect to a ECTbox vs. BPGS, b QGS vs. BPGS, c 4D-MSPECT vs. BPGS.
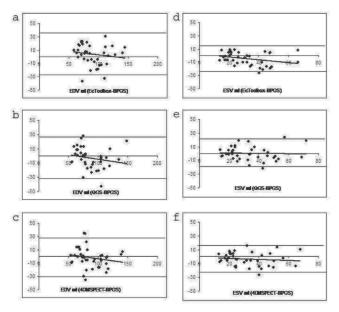
Figure 2. Bland-Altman analysis of EDV with respect to ECTbox vs. BPGS, b QGS vs. BPGS, c 4D-MSPECT vs. BPGS and ESV with respect to d ECTbox vs. BPGS, e QGS vs. BPGS, f 4D-MSPECT vs. BPGS

Inter-gMPS Comparison: Correlations for all parameters among the gMPS methods were higher when compared with the reference method individually (Table 2). The highest EF values were calculated with ECTb, and the lowest values were calculated with QGS. The mean EF difference between QGS and ECT was 8% and between QGS and 4D MSPECT was 5% (p<0.001). ECTb showed the highest EDV and lowest ESV values. The difference between ECTb and the other two methods was statistically significant in terms of EDV (p<0.001). QGS showed the lowest EDV and highest ESV values and the difference between QGS and other two methods was statistically significant in terms of ESV (p<0.001).

Subgroups: Patients were grouped according to their ESV values with BPGS. Group 1 had 18 patients with an ESV lower than 30 ml (small heart) and group 2 had 22 patients with an ESV higher than 30 ml. These two groups had statistically significant differences in terms of EF with all methods. EF values were higher in patients with small hearts.

Group 1:

The closest EF values to those of the reference method were calculated with 4D MSPECT and no statistically significant differences were shown between gMPS and BPGS. In the inter-gMPS comparison, QGS showed the lowest values and this difference was significant (p<0.001).

Group 2:

The closest EF values to those of the reference method were calculated with QGS and no statistically significant difference was shown between them. However, EF values obtained by the other two methods were significantly higher than those obtained with BPGS (p<0.01).

For each group, mean LVEF values are summarized in table 4.

Table 4: Correlation Matrix for different gMPS methods.

	ECTb	QGS	4D-MSPECT	BPGS
LVEF %(Group 1)	73.9±5.9	66.6±6.6	71.5±6.2	70.3±5.7
LVEF %(Group 2)	65.6±6.4	57.1±6.6	61.9±7.9	57.2±5.8

EDV:

For all methods, EDV values were significantly different between groups 1 and 2. For both groups, the highest EDV was calculated with ECTB, and in hearts of normal size this value was the closest value to that of BPGS. In small hearts, the closest value to that of BPGS was calculated with QGS.

ESV:

MPS programs cause overestimation in small hearts but underestimation in normal volume hearts. There was a statistically significant difference between group 1 and group 2 values for all methods.

The highest ESV value was calculated with QGS in both groups and also it was the value closest to that of BPGS in group 2. For the small heart group the closest value to that of BPGS was calculated with ECTb.

DISCUSSION

In this study we compared three different gMPS programs in reference to BPGS for the evaluation of LV functions in a group of patients with low CAD risk. Our results showed that BPGS and the three different gMPS methods were well correlated in calculating left ventricle volumes and determining the ventricle function. Furthermore, the correlation of gMPS between each other was also high. Good agreement was observed between the gMPS methods and BPGS for the measurement of LVEF and volumes. The highest EDV values, lowest ESV values, and, as a result of these calculations, highest LVEF values were calculated with ECT among the gMPS programs. The highest ESV values and lowest LVEF values were calculated with QGS.

In previous studies, there are results suggesting that lower LVEF values are calculated with QGS, and higher LVEF values are calculated with ECT (9,31,32). Lum et al. calculated lower LVEF values with QGS when compared with 4D MSPECT (mean 6%) and ECT (mean 4%) (p<0.001). Our study revealed this difference to be 5% and 8%, respectively (p<0.001). Nakajima et al. (9) calculated this LVEF difference between QGS and ECT to be 6% in a patient group with normal perfusion (p<0.001). They took ERNA as the reference and the closest values to those of the reference method for LVEF and EDV were calculated with QGS. Moreover, the results of QGS and 4D MSPECT were similar and the mean difference between ECT and ERNA was 9% (p<0.0001). In our study, when BPGS was taken as the reference, the closest LVEF values were calculated with QGS, with a mean difference lower than 2%. Between ECT and BPGS, the mean difference was 6% (p<0.001). Yamada et al.[33] compared QGS and Segami programs in their study

and QGS calculated higher values for LVEF, but the difference between the two programs were lower than 2%. In a study by Odagiri et al.[27], there were no statistically significant differences between the results of QGS and QBS (Quantitative blood pool SPECT) programs when calculating EF values. Vanhove et al.[25] also calculated lower LVEF values with QGS compared to QUBE (Quantitative blood pool SPECT developed by Free University of Brussels) with a mean difference of 6% (p<0.01).

When volumes are considered, we calculated the highest EDV values with ECT, similar to the study by Nakajima et al., who did not show any significant differences. Lum et al. [31] calculated the highest EDV values with the 4D MSPECT method and they showed significant differences between different methods (p<0.001). Neither study gave ESV data, and so we were unable to compare our results with theirs by means of ESV. Yamada et al.[33] calculated smaller volumes with QGS compared to Segami (p<0.001).

Nakajima et al.[12] showed in a study performed with a mathematical digital phantom that as the left ventricle volume gets smaller gMPS methods tend to underestimate the volumes and overestimate LVEF values. This difference is more prominent with QGS; in smaller hearts, LVEF difference between ECT and QGS increases from 5% to 10% when compared with normal sized hearts. In a phantom study by Ford et al. (13), for QGS this difference gets more prominent when EDV < 70 ml and LVEF >40%. We also grouped patients according to ESV, like Hambye et al. (14), and regarded ESV<30 ml as small hearts, as they did. They calculated the difference between ECT and QGS in small hearts as 14.5% and this difference was reported as 9% in the other group. In this study we also calculated higher LVEF values in small hearts with all methods (p<0.01). In small hearts, the highest EF values were calculated with ECT and the lowest values were calculated with QGS among the gMPS programs, but the difference between gMPS methods and BPGS was not statistically significant, similar to the study by Lum et al.[31]

CONCLUSION:

Our study showed that the ECT, QGS, and 4D-MSPECT methods correlated well with one another and BPGS. Despite small systematic differences, agreement between gMPS and BPGS was good for LVEF and volumes.

In all patient groups and the normal heart sized group, the closest LVEF values to those of the reference method were calculated with QGS. Overestimation of LVEF in small hearts is the major problem of gMPS methods and BPGS. In this study the closest LVEF values to those of BPGS were calculated with 4DM SPECT in the small heart group, but the lowest overestimation of LVEF values was obtained with QGS.

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