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Original Article

^{201}Tl 게이트 심근관류 SPECT 및 심초음파의 좌심실 구혈률 상관관계 비교

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The Correlation Analysis of Ejection Fraction: Comparison of ^{201}Tl gated Myocardial Perfusion SPECT and Echocardiography

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Purpose : Gated myocardial perfusion SPECT provides not only myocardial perfusion status, but various functional parameters of left ventricle (LV). The purpose of this study was to analyze ejection fraction (EF) for correlation and difference between ^{201}Tl gated myocardial perfusion SPECT and echocardiography depending on extent of perfusion defect, gender and LV volumes. **Materials and Methods :** From April 2011 to May 2012, we analyzed 291 patients (male:female =165:126; mean: 64.6±10.8 years) who were examined both ^{201}Tl gated myocardial perfusion SPECT and echocardiography at less than 7 days apart in our hospital. 101 patients showed perfusion defect and the rest of the people without any defect. We applied automatic analysis (Quantitative gated SPECT, QGS), and calculated EF, End-diastolic volume (EDV) and End-systolic volume (ESV) from Stress (G-Stress) and Rest (G-Rest) studies. And we analyzed the correlation and difference for EF between ^{201}Tl gated SPECT and echocardiography. **Results :** The correlation of LVEF among G-Stress, G-Rest and echocardiography was quite a good (G-Stress vs. G-Rest: r=0.909, G-Stress vs. echocardiography: r=0.833, G-Rest vs. echocardiography: r=0.825). And there were significant differences in EDV, ESV and EF in total patients (p<0.01). The normal group showed significant difference in EF (p<0.01) and the group with perfusion defect also demonstrated significant difference (a group with reversible defect: p<0.01, fixed defect: p<0.01) depending on extent of perfusion defect. We analyzed difference in normal group by gender. In normal group, there was no significant difference (p>0.05) in EF from men. However, there was a significant difference (p<0.01) from women. When we classified two groups by average size of EDV in Korean women, there was no significant difference in a group of above average size of EDV (p>0.05). **Conclusion :** When compared among Stress and Rest of ^{201}Tl gated SPECT and echocardiography, we confirmed that there was a good correlation for LVEF. But there were significant differences among three studies. And extent of perfusion defect, gender and LV volumes are independent determinants of the accuracy of LVEF. So, it is hard to compare and interchange quantitative indices among modalities. We should take additional researches to prove results of our study. **(Korean J Nucl Med Technol 2012;16(2):49-56)**

Key Words : Myocardial perfusion SPECT, Echocardiography, Quantitative gated SPECT, Ejection fraction

Introduction

Gated SPECT provides important diagnostic and prognostic information over SPECT alone by using electrocardiographically linked myocardial perfusion images to provide ventricular wall motion and thickening information. This additional information allows both regional perfusion and glob-

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al function to be assessed simultaneously at no extra cost in terms of acquisition time.[1)] an accurate assessment of left ventricular function is important in the diagnosis and management of several cardiac disease states such as heart failure and post-myocardial infarction.[2)]

The perfusion information obtained by the gated SPECT acquisition reflects the perfusion at the time of injection, ventricular function information is that occurring at the time of the acquisition. As a result, the ventricular function generally reflects the resting condition of the myocardium whether the patient is injected at rest or stress.[3)] The time after stress that the SPECT acquisition is commenced is one factor that may determine whether the functional information is considered resting or post-stress.[4)] A large proportion of nuclear medicine departments perform gated SPECT only on the stress myocardial perfusion data.[5)] DePuey reports that there is significant evidence to suggest that functional information acquired at rest. Consequently, the American Society of Nuclear Cardiology recommends that gated SPECT is performed on both stress and rest studies.[6)]

^{201}Tl is suboptimal for use with gated SPECT because of a large amount of scattered photons and low myocardial count densities.[7)] However, gated ^{201}Tl SPECT enables clinicians to assess both post-stress and rest left ventricular volume and function, which is advantageous for detecting transient dilatation induced by stress or multivessel coronary artery disease.[8,9)]

There are many factors affecting accuracy of LVEF. According to several study, gender, extent of perfusion defect, Age, LV volume and thickness are independent determinants of the accuracy.[10)] Attenuation from the left hemi-diaphragm can reduce photon counts in the inferior wall. It occurs mainly in case of men. But for women, main problem is breast attenuation, it decreases counts in the anterior wall. Women often have smaller LV volumes. It has been shown that gender related differences in normal limits exist.[11,12,13)] It is known that in patients with small sized hearts, LV volumes, especially ESV, are often overestimated because of partial volume effect. In general, this phenomenon occurs more in woman than in man because woman tend to have smaller volumes. And also, accuracy of LVEF depends on the extent of perfusion defect. Gated SPECT relies on demonstration of the regional contractile function in a hypoperfused area as an indication of the viability. Whereas preservation of function is clearly proof of viability, absence of function does not necessarily indicate absence of viability. This is because chronically ischemic myocardium, so-called hibernating myocardium, may have greatly reduced or absent systolic function.[14)]

The purpose of this study was to analyze EF for correlation between ^{201}Tl gated myocardial perfusion SPECT and echocardiography depending on extent of perfusion defect, gender and LV volumes.

Materials and Methods

1. Study population

Between April 2011 and May 2012, we prospectively studied consecutive 291 patients who underwent adenosine stress gated ^{201}Tl SPECT and echocardiography within a 7 days period for the evaluation of chest pain or dyspnea for clinical reasons. The age range was 30-86 years (mean = 64.6±10.8). The study population consisted of 165 men and 126 women.

2. Gated ^{201}Tl myocardial SPECT

Gated ^{201}Tl SPECT images were acquired after adenosine stress testing (post-stress SPECT) and again 4 hrs after the injection of ^{201}Tl chloride (redistribution SPECT). Adenosine was intravenously administered at a rate of 0.14 $\mu g \cdot kg^{-1} \cdot min^{-1}$ for 6 min. Three minutes after the initiation of the adenosine infusion, a dose of ^{201}Tl (range, 92.5-148 MBq) determined by the subject's body weight was injected intravenously. Five minutes after adenosine infusion, post-stress myocardial perfusion images were acquired with a 2-head gamma camera (Infinia, GE Healthcare, USA) equipped with a low-energy-general-purpose collimators (64 × 64 matrix, 30 projections over 180 degrees, 8 frame per cardiac cycle, 50 sec per projection). A zoom factor of 1.38 was used. The pixel size was 6.4 mm. Transaxial slices were reconstructed by filtered backprojection with a Butterworth filter (power, 10; critical frequency, 0.37). No attenuation or scatter correction was applied. Left ventricular volume and ejection fraction were calculated from gated ^{201}Tl SPECT by commercially available quantitative gated SPECT (QGS) software (Cedars Sinai Medical Center, Los Angeles, CA). When automatic reconstruction or reorientation failed, we were excluded that patients from study population.

3. Echocardiography

The two-dimensional echocardiograms were acquired at rest with standard short axis, apical 2-chamber and 4-chamber views by IE33 echocardiography system (Philips, Netherlands) (Fig. 1). The cinematic frames corresponding to end-diastole and end-systole were selected from the 2-chamber and 4-chamber views. Left ventricular end-diastolic volume, end-systolic volume and ejection fraction were derived via the previously validated modified Simpson's biplane disc method.[15]

4. Statistical Analysis

The difference between gated ^{201}Tl SPECT and echocardiographic results was examined by repeated-measures ANOVA.

Fig. 1. IE33 echocardiography system (Philips Healthcare, Netherlands).

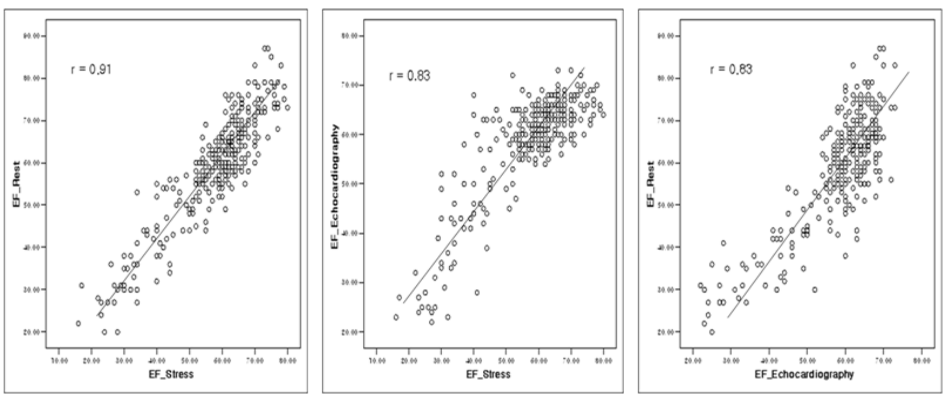

Fig. 2. Correlation of EF (%) between methods.

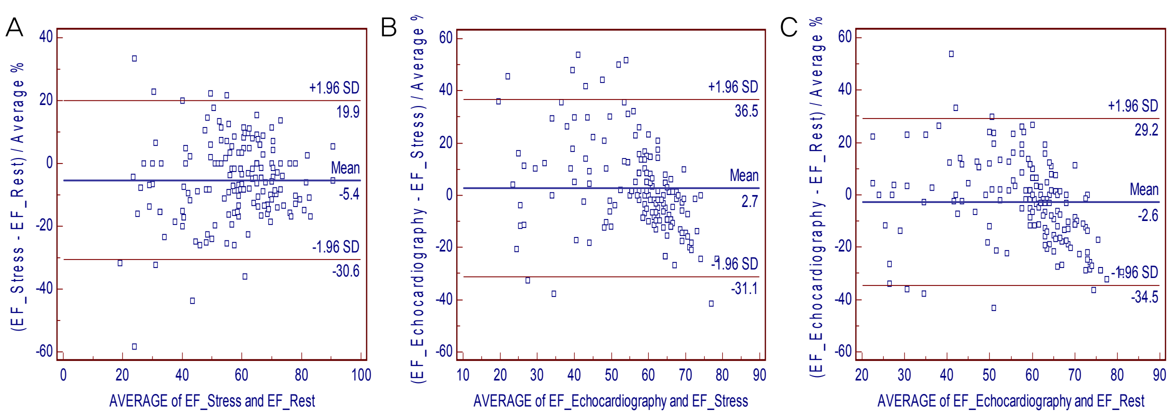

Fig. 3. The Bland-Altman graphs of agreement for EF between Stress / Rest (A), Echocardiography / Stress (B) and Echocardiography / Rest (C).

And Pearson's correlation coefficient was used for the statistical analysis of the relationships between methods. Bland-Altman analysis was used to assess agreement between studies.[16)]

Results

Two-hundred and ninety-one patients were followed. 101 patients showed perfusion defect. When divided extent of perfusion defect, 58 patients had reversible defect and 43 patients showed fixed defect. And the rest of the people, normal 190 patients, represented without any defect.

The correlation of LVEF among Stress, Rest and echocardiography was quite a good (Stress vs. Rest: r=0.909, Stress vs. echocardiography: r=0.833, Rest vs. echocardiography: r=0.825) (Fig. 2).

There was no significant difference in EF from Stress / Rest and Rest / Echo, and we confirmed that there were more significant differences from Stress / Echo because a few values were out of 95% confidence interval(Fig. 3).

In total patients, there were statistically significant differences in EF, EDV and ESV (p<0.01) (Table 1).

We classified groups by extent of perfusion defect, normal patients, patients with reversible perfusion defect and fixed defect. When divided groups by extent of perfusion defect, there were statistically significant differences in EF, EDV and ESV (p<0.01) (Table 2, 3, 4).

When assorted two groups by gender, men was not significant difference in EF (p>0.05) (Table 5). However, in women, we could find that women's EF was significantly

Table 1. LV volumes and LVEF by gated SPECT and echocardiography in total patients (n=291)

	Stress	Rest	Echo	p value
	Mean±SD	Mean±SD	Mean±SD	
EDV (ml)	44.8±39.6	40.1±36.4	45.1±30.3	<0.01
ESV (ml)	93.8±48.5	86.0±46.0	102.1±39.1	<0.01
EF (%)	57.3±13.0	58.8±13.2	58.3±10.5	<0.01

LV = left ventricle; LVEF = left ventricular ejection fraction; Echo = echocardiography; EDV = end-diastolic volume; ESV = end-systolic volume.

Table 2. LV volumes and LVEF by gated SPECT and echocardiography in normal patients (n=190)

	Stress	Rest	Echo	p value
EDV (ml)	76.1±31.9	69.4±28.4	91.1±30.0	<0.01
ESV (ml)	29.4±21.5	26.2±18.9	35.2±17.9	<0.01
EF (%)	63.2±8.1	64.1±8.9	62.0±6.0	<0.01

LV = left ventricle; LVEF = left ventricular ejection fraction; Echo = echocardiography; EDV = end-diastolic volume; ESV = end-systolic volume.

Table 3. LV volumes and LVEF by gated SPECT and echocardiography in patients with reversible perfusion defect (n=58)

	Stress	Rest	Echo	p value
EDV (ml)	108.1±53.2	96.1±49.1	105.3±36.8	<0.01
ESV (ml)	57.6±46.6	48.2±38.9	48.1±31.5	<0.01
EF (%)	51.3±12.6	55.1±12.9	56.8±11.8	<0.01

LV = left ventricle; LVEF = left ventricular ejection fraction; Echo = echocardiography; EDV = end-diastolic volume; ESV = end-systolic volume; Reversible = patients with reversible perfusion defect.

Table 4. LV volumes and LVEF by gated SPECT and echocardiography in patients with fixed perfusion defect (n=43)

	Stress	Rest	Echo	p value
EDV (ml)	152.9±50.6	145.9±51.3	146.3±46.0	<0.01
ESV (ml)	95.6±43.3	90.4±44.2	84.6±38.6	<0.01
EF (%)	39.4±11.1	40.4±11.6	43.7±11.6	<0.01

LV = left ventricle; LVEF = left ventricular ejection fraction; Echo = echocardiography; EDV = end-diastolic volume; ESV = end-systolic volume; Fixed = patients with fixed perfusion defect.

different (p<0.01) (Table 5).

To find out differences in LV volumes, we classified two groups above 70 ml and below 70 ml by an average size of EDV in Korean women.[17] When compared three studies, there were statistically significant differences in below an average size of EDV (Table 6). But in case of above 70 ml for EDV by an average size, there was no significant difference in EF (p>0.05) (Table 6).

Discussion

Hachamovitch et al. reported that the addition of gated information provided statistically incremental prognostic value.[18] Using an automated gated SPECT algorithm, Sharir et al. showed that a left ventricular systolic volume of ≤ 70 ml was related to a low mortality rate even in patients with severe perfusion abnormalities.[19] These conclusions rely on the determination of function Information - including the EF and ventricular volumes - to be robust between rest and stress studies, for the gamut of coronary pathologies and through procedural variations.[20] Gayed et al., however, concluded that myocardialperfusion defects, regardless of size and extent, seem to affect the accuracy of left ventricular EF calculation using QGS.[21] DePuey reported that there is significant evidence to suggest that functional information acquired after stress is different from that acquired at rest; however, this investigation demonstrated no statistical difference between stress and rest in terms of functional information (p _ 0.15 for EF).[5]

Stress volumes were not shown to be predictive of a negative ΔEF, whereas rest volumes were shown to be predictive. One might postulate that the stress volumes have suffered the impact of stunning and, thus, are not predictive. It follows that the rest volumes within the normal range are most likely to demonstrate a negative ΔEF. One speculates that this resulted from less reliable calculations in smaller hearts, whereas resting pathology may be present in larger hearts, each confounding the outcome of interest. Transient dilatation, therefore, predicts a negative ΔEF because it presents the possibility of both stress-induced stunning and inadequate time after stress for recovery of function.[20]

Independent predictors of variations in _EF include the presence of ischemia or increased heart rate during the stress acquisition compared with the rest.[22] There are several causes of increased heart rate during the stress study that are not related to stress-induced ischemia.[23]

A stress EF alone may be an unreliable tool for evaluating cardiac function in the patient with stress-induced stunning. Moreover, stress-induced stunning cannot be readily identified without the rest EF. Performing both a rest EF and a stress EF on patients may allow identification of poststress stunning that may aid in diagnosis, particularly in multivessel disease.[20]

Because of low spatial resolution and partial volume effect, gated SPECT does not define endocardial borders with high accuracy. Endocardial border with QGS was determined in correspondence of 65% of the inner standard deviation of the Guassian count profile. 4D-MSPECT also uses Gaussian fit to determine the peak activity and an estimate of the myocardial thickness. Because the SPECT value represents the true activity only when the object size is larger than twice the spatial resolution and partial volume effect affects the observed radioactivity in the endocardial border zone, errors in border determination can occur with variations in the left

Table 5. Comparison of LVEF by gender (F:M=86:104)

		Stress	Rest	Echo	p value
EF (%)	Men	60.6±5.9	60.8±5.9	61.5±4.6	0.08
	Women	65.4±9.0	66.9±10.0	62.4±6.9	<0.01

LVEF = left ventricular ejection fraction; Echo = echocardiography.

Table 6. Comparison of LVEF by LV volumes in women (70 ml≤: 70 ml>= 41:63)

		Stress	Rest	Echo	p value
EF (%)	70 ml≤	61.4±11.2	61.6±10.6	60.2±9.5	0.30
	70 ml>	68.1±6.0	70.3±7.9	63.9±3.8	<0.01

LV = left ventricle; LVEF = left ventricular ejection fraction; Echo = echocardiography; EDV = end-diastolic volume.

ventricular thickness.[24] In accordance with our data, a previous study revealed that hypertensive patients with left ventricular hypertrophy manifested a significantly higher left ventricular volume and a lower ejection fraction on gated SPECT.[10,25]

This study revealed that sex was independent determinants as well. Our results of sex-specific difference in left ventricular volume and ejection fraction are consistent with those of previous studies; they revealed higher normalized end-diastolic volume and end-systolic volume, and a lower ejection fraction in men with gated SPECT.[25-28]

Gender may be related to the low resolution of nuclear cardiology images, which causes the apparent shrinkage of the left ventricular cavity in patients with small ventricles; i.e., in women or patients with a smaller body surface area. Gender was still independent determinants in patients with an end-diastolic volume of more than 70 ml, which suggests that other mechanisms unrelated to partial volume effect in small ventricle exert an effect. Women may have a low myocardial count density or contrast because of breast attenuation, a low coronary flow reserve, and a high washout of ^{201}Tl after vasodilator stress.[29-32]

This study revealed that an extent of perfusion defect, sex and left ventricular volume were independent determinants of the difference in left ventricular volume and ejection fraction between gated SPECT and echocardiography. Our results suggest that end-diastolic volume, end-systolic volume and ejection fraction measured from gated SPECT have systemic errors determined by individual patient characteristics.

Conclusion

When compared among Stress and Rest of ^{201}Tl gated SPECT and echocardiography, we confirmed that there was a good correlation for LVEF. But there were significant differences among three studies.

And extent of perfusion defect, gender and LV volumes are independent determinants of the accuracy of LVEF.

So, it is hard to compare and interchange quantitative indices among modalities. We should take additional researches to prove results of our study.

요　　약

좌심실 용적 및 구혈률은 관상동맥질환 환자의 치료에 있어 예후예측 및 경과 관찰에 매우 중요한 지표이며, 현재 게이트 심근관류 SPECT (Myocardial perfusion SPECT)를 이용하여 심근관류 이상을 진단하는 동시에 좌심실 용적 및 구혈률(Ejection fraction, EF)을 측정하는 방법이 널리 사용되고 있다. 게이트 심근관류 SPECT와 심초음파(Echocardiography)로 산출한 좌심실 용적 및 구혈률이 높은 상관성을 가진다는 많은 보고들이 있으나 심근관류결손의 유무와 정도에 상관없이 비교되었으며, 제한된 환자들에서 비교 분석이 시행되었다.

이에 본 연구에서는 ^{201}Tl 게이트 심근 관류 SPECT에서 부하기(G-Stress) 및 휴식기(G-Rest) 좌심실 구혈률을 관류 결손 여부와 성별, 심실 용적에 따라 심초음파와 비교하여 그 상관성을 알아보고자 하였다. 2011년 4월부터 2012년 5월까지 본원에서 ^{201}Tl 게이트 심근관류 SPECT 검사와 심초음파를 일주일 내 시행한 환자 중 성인 291명(남:여=165:126, 평균나이 64.6±10.8세)을 대상으로 하였다. 이 중 정상으로 진단받은 환자 190명과 가역성 관류결손, 고정 관류결손으로 판정 받은 환자 58명, 43명을 대상으로 연구 분석하였다. 데이터 분석에는 QGS (Quantitative gated SPECT) 소프트웨어를 이용하였고, 자동화된 방식으로 EF, 확장기말 용적(End-diastolic volume, EDV), 수축기말 용적(End-systolic volume, ESV)을 산출하였다. 본 연구에서는 심근관류결손의 가역성 여부와 성별을 기준으로 게이트 심근 관류 SPECT에서의 부하기/휴식기와 심초음파에서의 EF, EDV, ESV를 반복측정 분산분석(repeated-measures anova)과 Bland-Altman 분석을 이용하여 차이를 비교하고, pearson 상관계수를 구하여 각각의 상관관계를 분석 하였다. 전체 환자 중 부하기와 휴식기, 심초음파에서의 EF는 높은 상관관계(G-Stress와 G-Rest r=0.909, G-Stress와 EC r=0.833, G-Rest와 EC r=0.825)를 나타냈으나, 전체 환자 중 EF, EDV, ESV는 통계적으로 유의한 차이를 보였다(p<0.01). 관류 결손 여부에 따른 EF값의 차이는 정상 군에서 통계적으로 유의한 차이를 보였고(p<0.01), 관류 결손이 있는 환자 군에서 통계적으로 유의한 차이를 보였다(가역성 관류결손, 고정 관류결손 p<0.01). 성별에 따라 차이를 분석한 결과, 정상 군 중 남성에서의 EF는 통계적으로 유의한 차이를 보이지 않았고(p>0.05), 여성에서의 EF는 통계적으로 유의한 차이를 보였다(p<0.01). 여성환자 중, 좌심실용적으로 분류하였을 때 평균 확장기말 용적보다 적은 군에서 유의한 차이를 보였고,

평균 보다 큰 군에서는 통계적으로 유의한 차이를 보이지 않았다. ^{201}Tl 게이트 심근 관류 SPECT 중 부하기 및 휴식기에서의 좌심실 구혈률과 심초음파와의 상관관계는 전체적으로 높은 것으로 나타났다. 하지만 EF, EDV, ESV는 통계적으로 유의한 차이를 보였다. 관류 결손의 정도, 성별, 좌심실 용적은 LVEF의 정확성에 영향을 미칠 수 있을 거라 사료되며, 이에 대한 추가적인 연구가 필요할 것이다.

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