Assessment of Agreement between Gated SPECT Myocardial Perfusion Imaging and Gated SPECT Blood Pool Imaging for Measurement of Left Ventricular Ejection Fraction in Coronary Artery Disease

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ABSTRACT

Objective: **Quantitative assessment of left ventricular ejection fraction (LVEF) from radionuclide cardiac imaging study has both diagnostic and prognostic value in coronary artery disease (CAD). Gated SPECT blood pool imaging (GSBPI) and gated SPECT myocardial perfusion imaging (GSMPI) are two technically comparable radionuclide methods for non-invasive measurement of LVEF. While the former is a gold standard the latter is popular as it provides a wider array of information. This study was carried out to bridge the lack in the existing body of evidence regarding assessment of agreement of between GSBPI and GSMPI for measurement of LVEF in CAD. The objective of this study was to validate the LVEF measurements from routine GSMPI as a valuable parameter for clinical decision making through assessment of agreement between GSMPI and GSBPI performed in a short interval, in same patient having CAD.**

Patients and Methods: **A total of 28 patients (three female) was observed with a mean age of 54.2 ± 8.5 years during February to May 2012. All patients underwent GSBPI and GSMPI with a gap of three to seven days in between. LVEF measured by GSBPI performed at rest was compared with LVEF measured in rest phase of one day stress-rest GSMPI. Agreement analysis was done with Bland Altman plot.**

Results: **Mean LVEF measurements show an apparent overall slight underestimation by GSBPI (54.8 ± 25.3) in comparison to GSMPI (56.9 ± 25). Bland Altman plots show that the differences between GSBPI and GSMPI for measurement of LVEF at rest in same patient fall within two SD of the mean difference. This finding remained similar while further categorization of study patients was done on basis of ranges of LVEF, end diastolic volume (EDV), end systolic volume (ESV), infarct size and regional wall motion abnormality (RWMA).**

Conclusions: **There was overall significant agreement between GSMPI and GSBPI for measurement of LVEF in CAD in this small study. This agreement remains significant irrespective of ranges of LVEF, EDV, ESV, infarct size and RWMA.**

Key Words: **LVEF, Agreement, Correlation, Gated SPECT, myocardial perfusion, blood pool imaging.**

INTRODUCTION

The coronary artery disease (CAD) has been evolving as a major contributor to mortality and disability in Bangladesh (1, 2, 3). Risk stratification in CAD is based on estimates of myocardial ischemia (4) and left ventricular ejection fraction (LVEF) (5, 6). Quantitative assessment of the LVEF through its diagnostic and prognostic value has been guiding clinicians and surgeons to device medical and interventional therapies in patients with CAD. An accurately estimated LVEF is therefore a crucial expectation from a non-invasive radionuclide cardiac imaging study.

Equilibrium radionuclide ventriculography (ERNV), a planar technique, since its inception in 1970 has gained reputation of being a gold standard technique for measurement of LVEF (7). It was in early eighties when nuclear cardiology emerged as a partner in CAD management in Bangladesh with the advent of multi gated radionuclide ventriculography (MUGA), a planar variety of ERNV.

Electrocardiogram (ECG) gated SPECT blood pool imaging (GSBPI) being a tomographic variety of ERNV is technically superior than planer techniques for estimation of LVEF, EDV, ESV and LV regional wall motions (8). ECG gated SPECT myocardial perfusion imaging (GSMPI) provides quantifications of LVEF, LV cavity end systolic volume (ESV), end diastolic volume (EDV), regional myocardial perfusion, regional wall motion and regional wall thickening. GSMPI has become a popular technique in the management of CAD in Bangladesh since 2001(9).

There are reports of validation of GSMPI against planer and SPECT blood pool techniques with good inter method correlation for measurements of LVEF and LV volumes (10). However, interchangeable use of these two methods are either opposed or kept conditional by a number of recommendations. Sole reliance on correlation coefficient is not appropriate for analysis of measurement method comparison (11). A high correlation can falsely come out of a data containing wide range of value and can conceal considerable lack in agreement. Existing literatures lack study regarding assessment of agreement of LVEF measurement by two tomographic radionuclide techniques, GSMPI and GSBPI. Thus an assessment of agreement between GSMPI and GSBPI for measurement of LVEF in CAD appeared to have important clinical value. The objective of this study was to validate the LVEF measurements from routine GSMPI as a valuable parameter for clinical decision making through assessment of agreement between GSMPI and GSBPI performed in a short interval, in same patient having CAD.

PATIENTS AND METHODS

A total of 27 adult male and female patients were included by non-random sampling technique who were referred either for screening of suspected CAD or for clinical evaluation of known CAD under medical treatment or post coronary revascularization. All patients underwent GSMPI and GSBPI within a span of three to seven days. No patient has any intervening cardiac event. Left ventricular parameters were measured in rest phase of routine one day standard stress-rest GSMPI and compared against those obtained from GSBPI performed at rest on a separate day.

This cross sectional analytical study was carried out over a period of one year from July 2011 to June 2012 at the former Institute of Nuclear Medicine & Ultrasound (INM & U), which is currently known as National Institute of Nuclear Medicine & Allied Sciences (NINMAS). The study population consisted of patients referred to the institute for GSMPI. The sample size was calculated for discordance rate (α) of 0.10 and tolerance probability (β) of 95% for agreement of two measurement methods assuming no discordant pair of measurement ($k = 0$) allowed (12). The academic Committee of INM & U approved the study protocol. Informed written consent was obtained from all patients.

For the pre procedure counseling and evaluation of patients there was a face to face interview session between each patient and a nuclear medicine physician. Best possible attempts were made to maintain adherence to quality control recommendations from renowned authorities (10,13) at all levels of patient preparation, radiopharmaceutical preparation and dispensing, image acquisition, image processing and image interpretation. Image acquisition for both the GSMPI and GSBPI were conducted with Siemens E cam dual head gamma camera.

SPECT acquisition with ECG gating at rest phase was done 45-60 minutes after rest injection of 25 mCi of Tc-99m-sestamibi on the same day following the post-stress scan (done 15-30 minutes after stress injection of 10 mCi of tracer). Both the detector heads were placed at 76° to each other. A zoom of 1.45 was used. A symmetric 15% energy window around the 140 keV 99mTc photo-peak was set. Data was stored

in 64 x 64 matrices (pixel size 6.59 cmm and 21-27 slices in short axis). ECG gating was done with three limb leads and acquisition was set to eight frames per R-R interval (about 153ms/frame). Framing method configuration was with 60% width and forward backwards by thirds. The auto-centre set to average of 10 beats with pick bin of 10 bits and auto-tracking on. Reject PVC (Premature Ventricular Contraction) beat mode was set with PVC threshold of 300 msec. Rotation of camera heads were set to counter clock wise with starting angle at 52°. The detectors took 32 views over 104° of rotation in a non circular orbit using a step-and-shoot method, progressing from 45° right anterior oblique to 45° left posterior oblique projections. During acquisition the patient was in supine position with 'head out' orientation. Acquisition time was 20 seconds per projection (about 450-750 k counts/detector/view) requiring about 14 minutes per patient per scan. Butterworth filtering with cutoff of 0.5 cycles/sec and order 7 was used.

In vivo method for labeling of stannous pyrophosphate with Tc-99m pertechnetate was used. After 20 minutes of intravenous injection of 15-20 mg pyrophosphate, 15-20 milli Curie of Tc-99m-pertechnatate was injected in a different vein of contra-lateral arm. Immediately thereafter gated blood pool SPECT images was acquired. Standard protocol was followed for image acquisition which was same in all aspects with the GSMPI acquisition protocol as mentioned earlier, except in the frame rate with ECG gating. For three limb leads ECG gating the acquisition was set to 16 frames per R-R interval that took about 45-48 millisecond/frame and 300-350 kilo counts/detector/view and the time of scan took 12 minute per patient per scan.

The measurements of LV volumes and EF were generated by software after manual processing of raw data had been done at a dedicated work station (Siemens e.soft). Quantitative assessment of SPECT perfusion was done by 4D-MSPECT v4.2 software (Invia, LLC 2007). SPECT blood pool data was quantified with QBS 2007 (Quantitative Blood-pool SPECT, Cedars cardiac quantification software 6.5.9.1 Cedars Sinai Medical Centre, Los Angeles, California).

Statistical analysis of data was done using IBM SPSS statistics (Statistical Package for Social Sciences) version 20 (IBM corporation 2011) for windows. Descriptive statistics viz. frequency, percentage, mean, SD, range were calculated for the basic demographic characteristics and LVEF of the study patients. For analysis of agreement between GSMPI and GSBPI derived measurements of LVEF at rest, Bland-Altman plots were constructed to observe if the differences of LVEF plotted against respective geometric means of LVEF falls within two standard deviations (SD) of difference.

In this study, in addition to an overall agreement analysis, further assessment of agreement were done in the study patients among different ranges of LVEF, EDV, ESV, infarct size and wall motion. Cut offs for LVEF ranges and cut offs for EDV and ESV limits for SPECT measurements were adopted from available published literature (14-21). LVEF was categorized as 'less than 35%', '35 to less than 55%' and '55% or greater'. EDV was categorized as below 85 ml, 85 to 140 ml and above 140 ml. ESV was categorized as below 15 ml, 15 to 60 ml and above 60 ml. While assessing agreement in absence or presence of infarct, quantitative estimation of fixed defect on 17 LV segments were assigned in to qualitative categories. For qualitative infarct size assumption, fixed defect involving up to five out of 17 LV myocardial segments was considered as small LV infarct. Fixed perfusion defect size of more than five segments was considered as large infarct. For assessment of agreement in absence or presence of regional wall motion abnormality (RWMA), summed motion score (SMS) at rest obtained from GSMPI images were qualitatively assigned into three categories. A SMS at rest of up to

10 were considered as normal if there was no RWMA that is visually detectable in cine views of 4D reconstruction images. A resting SMS of 10 to 25 was considered as mild to moderate RWMA while SMS at rest more than 25 was considered as gross RWMA.

RESULTS

Among the 27 study patients there was 24 males (88.9%) and 3 females (11.1%).The age range of the patients were 32 to 68 years, with a mean ± SD of 54.19 ± 6.15 years. The reasons for referral for GSMPI was evaluation of myocardial viability after old myocardial infarction in 15, assessment post coronary revascularization in four and evaluation of chest pain in eight patients (Table 1).

Table 1: Demographic characteristics of study patients

Demographic characteristics	Male	Female	All patients
Age(Mean±SD)	53.5±8.6	59.3±7.5	54.2±8.5
Weight (Mean±SD)	64.9±6.9	70±10	65.5±7.2
Height(Mean±SD)	163.3±3.3	162±3.8	163.2±3.3
BMI(Mean±SD)	24.4±2.6	26.6±4.0	24.6±2.8
Old MI (n)	15	0	15
Post PCI (n)	3	1	4
Evaluation of chest pain (n)	6	2	8

BMI, Body mass index; MI, Myocardial infarction; PCI, Percutaneous coronary intervention

Table 2: Summary of LV parameters measured by GSMPI and GSBPI

LV parameters at rest (Mean±SD)	GSMPI			GSBPI		
	Male	Female	All patients	Male	Female	All patients
LVEF	55.1±24.5	71.3±29.7	56.9±25.0	53.1±24.6	68.3±32.6	54.8±25.3
EDV	98.6±55.3	75.0±57.2	95.9±54.9	109.9±46.1	105.7±66.1	109.5±47.1
ESV	55.9±53.3	38.0±58.0	53.9±52.9	59.7±50.8	45.3±63.0	58.1±51.1
Summed perfusion score	12.1±11.4	5.7±8.9	11.4±11.2	-	-	-
Summed motion score	22.9±17.0	14.7±15.5	21.9±16.8	-	-	-

LVEF, Left ventricular ejection fraction; EDV, End diastolic volume; ESV, End systolic volume.

A comparison of estimates of LVEF were between two methods at different ranges of LVEF, EDV, ESV, infarct size and RWMA is further summarized in Table 3.

Table 3: Comparison of LVEF between two methods at different ranges of LVEF EDV, ESV, infarct size and RWMA

Study patients	LVEF GSMPI Mean±SD	LVEF GSBPI Mean±SD	Difference Mean±SD
LVEF 55% and above(n=14)	78.1±12.2	76.2±9.7	1.9±8.9
LVEF below 55 to 35% (n=7)	41.7±6.3	40±12.9	1.7±14
LVEF below 35% (n=6)	25±3	22±3.6	3±5.9
EDV <85ml (n=16)	74.3±15.7	72.6±13.9	1.8±10.3
85ml< EDV <130ml(n=3)	39.7±5	32.3±7.5	7.3±9.5
EDV >130ml (n=8)	28.5±7	27.6±13	0.9±8.9
ESV <15ml (n=9)	85.6±7.7	81.2±6.5	4.3±8.2
15ml<ESV <60ml(n=8)	58±10.7	57.3±16.9	0.8±13.2
ESV >60ml (n=10)	30.2±7.2	29±12.2	1.2±8.1
No LV infarct (n=13)	79.5±11.6	77.3±9.1	2.2 ± 9.2
Small LV infarct (n=8)	38.9±13.9	35±16.2	3.8 ± 10.9
Large LV infarct (n=6)	31.8±7.6	32.3±14.8	0.5 ± 9.9
No RWMA (n=10)	83.6±9.7	79.9±8.2	3.7 ± 9.9
Mild to moderate RWMA (n=6)	59.5±9.1	55.5±18.8	4 ± 10.6
Gross RWMA (n=11)	31.2±7.6	31.6±14.4	0.4 ± 9.3

LVEF, Left ventricular ejection fraction; EDV, End diastolic volume; ESV, End systolic volume; RWMA, regional wall motion abnormality

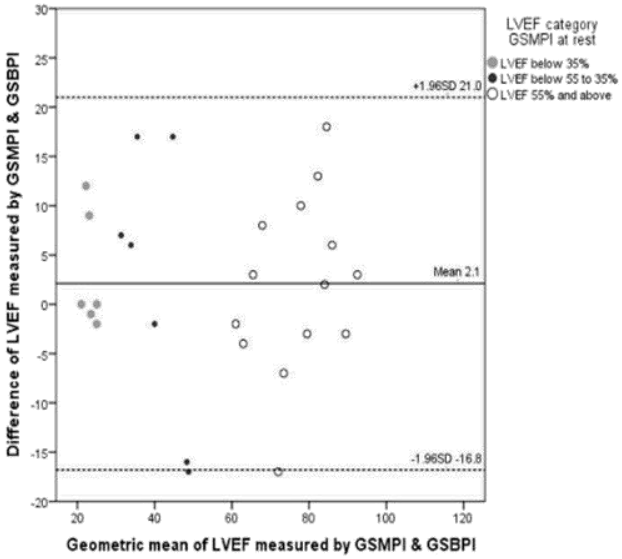
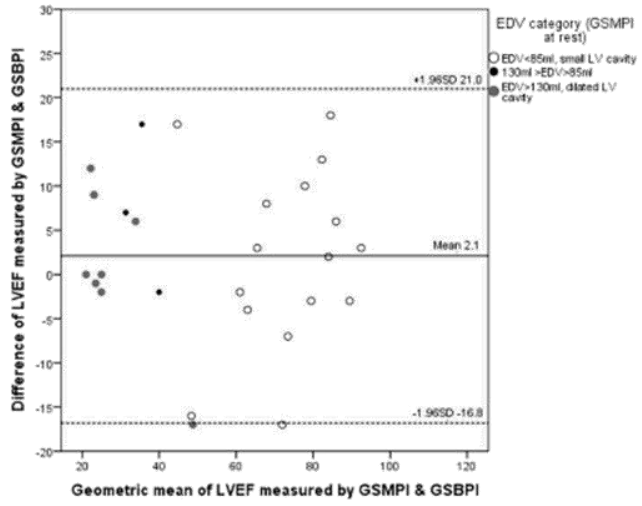


Figure 1(a)



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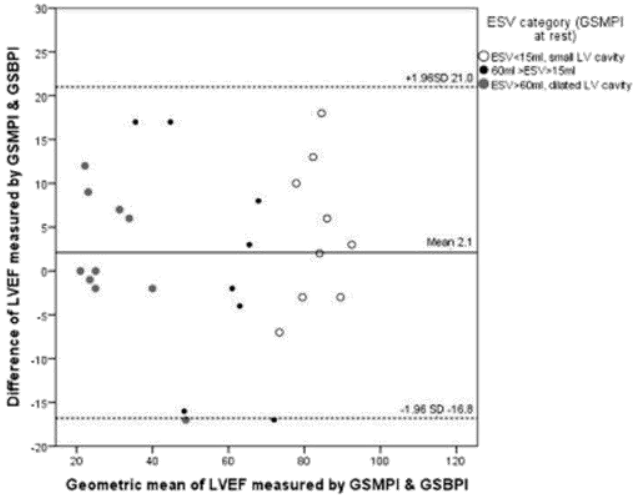

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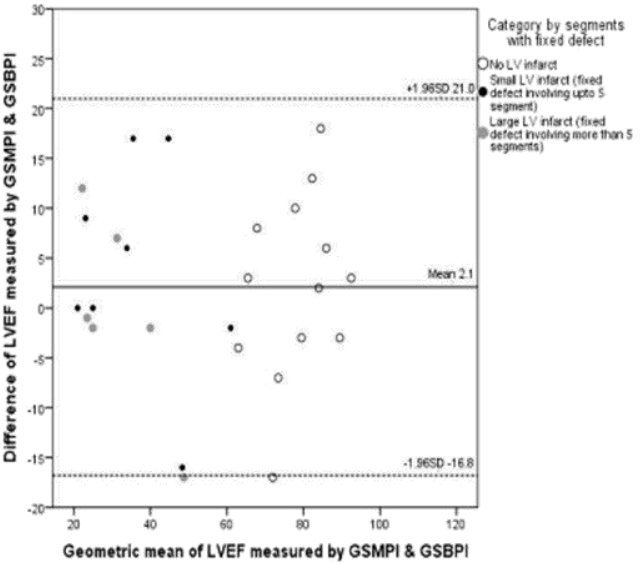

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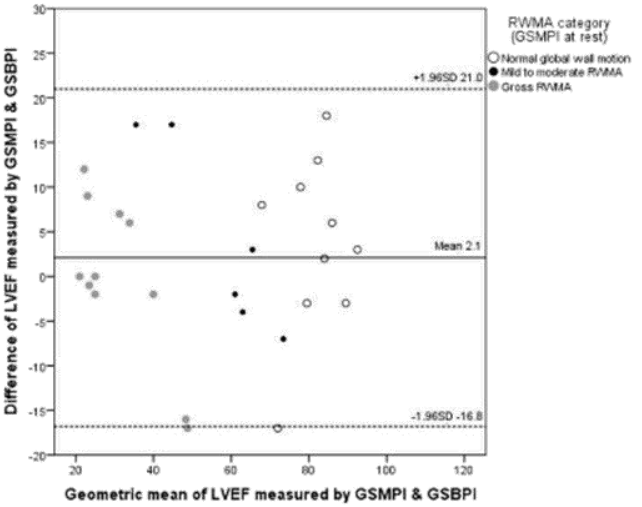

Figure 1(e)

Figure 1: Bland Altman plot showing agreement between GSMPI and GSBPI for measurement of LVEF at rest among ranges of LVEF (a), EDV (b), ESV (c), LV infarct size (d), RWMA (e) based on GSMPI results. Geometric means of LVEF measurements by GSMPI and GSBPI both at rest in each patient are plotted in X axis and difference between LVEF measurements by GSMPI and GSBPI both at rest in each patient are plotted in Y axis. The central line represents mean difference of LVEF measurements by two radionuclide methods. The outer pair of lines represents ±1.96 SD of difference.

DISCUSSION

The current study with Bland-Altman plots show that there was no significant difference between GSMPI and GSBPI for measurement of LVEF at rest in 27 patients with CAD i.e. the agreement between GSMPI and GSBPI for measurement of LVEF were significant. This finding was in concordance with findings by Paul et al. who reports no significant difference in the mean difference from zero for measurement of LVEF by GSMPI and GSBPI, both done with a frame rate of 10 per cardiac cycle (22). In addition Paul et al. in their study demonstrates underestimation of LVEF by GSMPI in comparison to GSBPI with a mean difference of 2.3 (±5.1). On the

contrary current study showed slight overestimation of LVEF at rest by GSMPI in comparison to GSBPI with an overall mean difference of 2.1 (± 9.6). In some recent case series similar overestimation of LVEF by GSMPI is claimed relative to planar blood pool radionuclide techniques (17,19, 23, 24). While on contrary some groups report underestimation of LVEF by GSMPI compared with that by gated planar blood pool radionuclide techniques (7, 20, 25, 26).

All of these investigators who report underestimation of LVEF by GSMPI had used lower frame rates in GSMPI (eight frames/cardiac cycle) in comparison to blood pool techniques (16, 18 & 24 frames). However, Kumita et al. (25) who report an underestimation of LVEF by GSMPI had used frame rate of 32 for GSMPI and 25 frames/cardiac cycle for ERNV. All of the investigators who report overestimation of LVEF by GSMPI had used a gating of eight frames per cardiac cycle for GSMPI and higher frame rates (16 to 24) for blood pool technique. The current study too used a lower frame rate (eight frames/cardiac cycle) for GSMPI in comparison to GSBPI (16 frames/cardiac cycle) and discovered an underestimation of LVEF by GSMPI in comparison to GSBPI. Thus the postulated explanation of temporal under sampling of LV volumes in lower frame rate which has been suggested as a reason of underestimation of LVEF by gated radionuclide techniques may not stand true. In this study, agreement was also assessed after categorization of patients on basis of different ranges of LVEF, EDV, ESV, infarct size and wall motion. The agreement was however significant in all ranges.

The small sample size reduces the weight of inferences from this study. The sample size was small due to facts like interrupted supply of technetium generator, limited availability of pyrophosphate kit and busy patient schedule. This study, first in Bangladesh was attempted to assess if GSMPI agrees with gold standard GSBPI for measurement of LVEF. The result also shows an overall agreement between 4DMSPECT and QBS software for measurement of LVEF that matched with some earlier studies done using planar blood pool technique and QGS. Finally, results from this study may add confidence to put LVEF on MPI reports in most of the cases. Fact regarding frame rate may raises quest for explanations of underlying mechanisms. Need for determination of reference ranges and normal limit for SPECT measurement of LVEF, EDV, ESV, infarct size and RWMA is also warranted through larger trials in future.

DISCLOSURE

No competing financial interests exist

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