ORIGINAL ARTICLE

Impact of Valve Plane Alignment on the Repeatability of Left Ventricular Ejection Fraction in ECG-gated Myocardial SPECT Using Corridor 4DM

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Abstract

***Background*: In myocardial gated single-photon emission computed tomography (GSPECT), to differentiate true changes of left ventricular ejection fraction (LVEF) from inherent methodical variability is clinically relevant; however, data about repeatability of GSPECT LVEF in the same patients are rather inconsistent in literature. The aim of this study was therefore to determine repeatability coefficient (RC) of GSPECT LVEF at rest and to investigate the effect of the introduction of processing constraints in left ventricular edge detection.**

***Methods*: Thirty-five patients referred for one-day myocardial GSPECT stress-rest scan were included. After the routine stress-rest study, patients were completely repositioned on the imaging table for a second rest acquisition using the same acquisition parameters. LVEF was computed using Corridor 4DM software without and with manual alignment of valve plane. Repeatability was assessed using the Bland-Altman method.**

***Results*: RC of LVEF from unaligned datasets was 7.6% with upper and lower limits of agreement of 7.4% to -7.8%. After valve plane and ventricular long-axis length alignment, RC improved to 3.6% with upper and lower limits of agreement of 3.4% to -3.8%.**

***Conclusions*: RC using unaligned determination of GSPECT LVEF was comparable to that from previous publications. However, RC using valve plane alignment could be improved to below 4% on 95% confidence level.**

Keywords: ^{99m}Tc-Sestamibi, Coefficient of repeatability, Ejection fraction, Gated-SPECT, Left ventricular function

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Myocardial perfusion single-photon emission computed tomography (SPECT) is one of the most frequently used diagnostic procedures in nuclear medicine (1). Electrocardiographically (ECG)-gated acquisition makes extraction of information about the ventricular function feasible and is considered to be a useful extension of myocardial SPECT (2).

In daily clinical practice, end diastolic (EDV), end systolic (ESV) ventricular volumes and left ventricular ejection fraction (LVEF) are considered to be relevant and may provide additional diagnostic and prognostic information in selected groups of patients (3, 4).

Several studies have shown that the values of the above-mentioned parameters calculated from gated single-photon emission computed tomography (GSPECT) correlate well with estimates from already established and validated procedures (3).

However, reliable detection of relatively small changes of ventricular function in the same patient remains challenging (5). In this context, different working groups reported on their experience comparing post stress and resting values of LVEF, ESV and EDV. It could be convincingly demonstrated that the decrease of LVEF after stress correlates with the extent of

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stress induced ischemia and that the post-stress dysfunction is more pronounced in patients with severe multivessel coronary heart disease (3).

In order to interpret changes of parameters of left ventricular function in the individual patient correctly, data about reproducibility and repeatability of GSPECT is essential. While numerous publications documented excellent reproducibility of GSPECT processing, information about repeatability is still limited. Furthermore, investigations addressing repeatability are methodically heterogeneous (6–9).

The aim of our study was the prospective determination of the repeatability coefficient (RC) of LVEF by repeated GSPECT data acquisition at true resting conditions. Secondary aim was to investigate the effect of geometrically identical definition of the valve plane in repeated investigations.

Materials and methods

Study population

The study was approved by the Ethics Committee of the Medical Association of Hamburg (ID-Number PV7133). Between December 2019 and April 2020 all potentially eligible patients who were referred to a clinically indicated 1-day myocardial stress-rest GSPECT were informed about the study and asked to participate.

Primary exclusion criteria were atrial fibrillation, frequent ectopic beats, body mass index (BMI) >36, difficult stable positioning and limited general conditions probably preventing prolonged acquisition time.

Study protocol

For the stress study 200 MBq ^{99m}Tc-Sestamibi was injected after administration of 400 μg Regadenoson. The resting dose of 800 MBq ^{99m}Tc-Sestamibi was injected at least two hours after the stress activity injection.

Imaging was started 60 minutes after tracer injection both after stress and at rest. GSPECT data were acquired using a three-detector gamma camera (Anyscan Trio SC, Mediso ltd. Budapest, Hungary) equipped with a parallel hole LEHRHS (low energy high resolution high sensitivity) collimator in two detector 180° arc mode, circular orbit, 32 projections per detector, 20 seconds per projection, 12 frames per R-R cycle with a gating window of 30%. Acquisition matrix size was 128 × 128 (pixel size 4.9 × 4.9 mm).

The second rest-scan was performed after removing the patient from the scanning bed, a 5 minute break, and subsequent complete repositioning.

Image processing

Raw image data was sent from the acquisition computer to a dedicated processing workstation (SyngoMMWP VE61A, Siemens Hoffman Estates, IL, USA), with integrated Corridor 4DM software (Invia Medical Solutions, Ann Arbor, MI, USA; 4DM version 2013.1.2.63).

Images were reconstructed by filtered back projection using Butterworth filter with cut-off of 0.30 cycles/pixel order of 5 for gated images and cut-off of 0.45 cycles/pixel for non-gated images.

All reconstructed images were processed using Corridor 4DM software, with manual adjustment of the orientation of the ventricular axes if needed (unaligned processing) and with identical definition of ventricular valve plane and the distance between valve plane and apex (aligned processing). For the aligned processing, the automatically processed first study served as reference. In the second study the length of the end-diastolic (when necessary also the end-systolic) ventricular axis (distance between the apical ventricular border and the valve plane) was manually adjusted to the length automatically determined in the first study (Figure 1).

Correct masking of ventricular border was visually checked after each processing. Reoriented slices with contours definitely outside of the ventricular wall were repeatedly reconstructed, reoriented and submitted to the processing software.

Using ungated data, values of summed stress (SSS), rest (SRS) and difference scores (SDS) of regional myocardial perfusion were determined. Score values of at least 4 were considered to be pathologic. Finally, LVEF, EDV and ESV were computed from gated data. LVEF >55% was considered to be normal, 35–55% moderately reduced and <35% markedly reduced. Left ventricles with ESV < 20 ml were considered to be “small hearts” (10, 11).

Statistical analysis

Statistical analysis was performed using Excel (Microsoft Corporation, version 16.36). Continuous variables are expressed as mean ± standard deviation. Differences of LVEF between serial measurements are given in absolute LVEF units. Results of repeated acquisitions were compared using Bland-Altman method including visualization of upper and lower limits of agreement at a 95% confidence level. RC was determined according to the method of Bland and Altman (12).

Results

Study subjects

A total of 35 patients (20 males, 15 females) underwent repeated rest acquisitions. No patient had to be retrospectively excluded. The mean age of the population was 70 ± 10 years ranging from 41 to 83 years. Average body mass index (BMI) was 26.2 ± 3.5 ranging from 20.7 to 33.1 and median BMI was 25.8.

Coronary artery disease (CAD) was suspected in 23 of 35

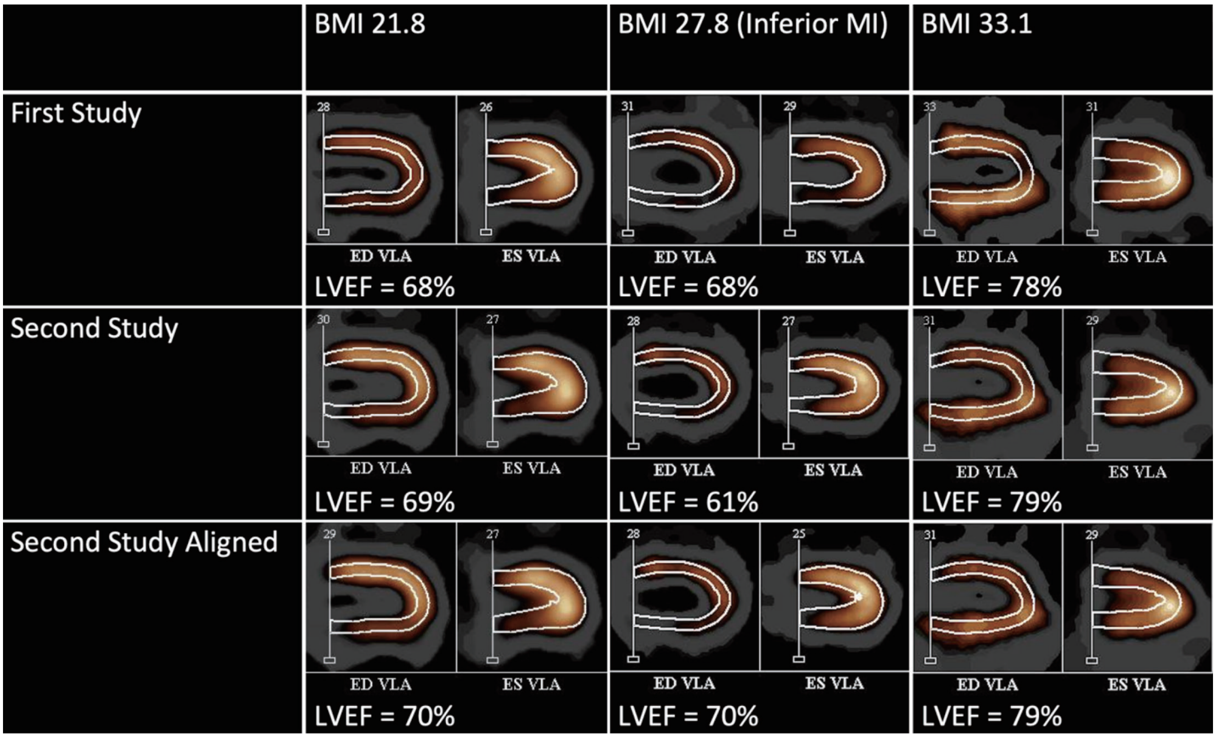

Figure 1 Unaligned and aligned processing of the valve plane.
All reconstructed images were processed automatically (first two rows) and with additional manual alignment of the ventricular length (third row) using the automatically processed first study as reference (aligned processing).

patients, while 12 patients had documented CAD including 4 patients with documented myocardial infarction (MI).

SSS and SDS were abnormal in 15 and 9 patients, respectively. In the resting study 5 patients had abnormal score values. Three patients had mildly abnormal, one patient moderately and one patient severely abnormal summed resting score.

Quality of 4DM-contouring

In one of 35 patients contouring of the inferior wall was visually suboptimal probably due to inherent instability at handling of a perfusion defect (SRS = 4) in this region and increased gastrointestinal tracer accumulation. This problem could be solved by repeated reconstruction under exclusion of the gastrointestinal region adjacent to the inferior wall.

Ventricular function

Based on the first resting study and unaligned processing, mean EDV was 106 ± 57 ml ranging from 36 to 388 ml, mean ESV was 43 ± 48 ml ranging from 9 to 301 ml. LVEF was normal in 30 patients, moderately reduced in 4 and markedly reduced in 1 patient. Average unaligned LVEF was 65 ± 11% ranging from 22% to 84%. Average aligned LVEF was 65 ± 12% ranging from 22% to 81%. There was no significant difference between the mean values of unaligned and aligned LVEF.

Repeatability of unaligned LVEF data

Bland-Altman-analysis demonstrated a mean difference of -0.2% with limits of agreement of 7.4% to -7.8% (Figure 2). RC was 7.6%.

Repeatability of aligned LVEF data

Comparison of the LVEF values after aligned processing demonstrates the stabilizing effect of valve plane alignment. Bland-Altman-analysis documented an unchanged mean difference of -0.2% with a narrower 95% confidence interval in comparison to unaligned processing (Figure 3). RC was 3.6%.

RC in small hearts

Based on unaligned data of the first resting study, 8 patients had an ESV ≤20 ml (“small heart”) and 27 patients had an ESV >20 ml. Considering the unaligned data LVEF was 77 ± 4% in patients with small hearts and 62 ± 11% in the others ($p<0.0004$).

RC in patients with a “small heart” using unaligned and aligned data was 7.8% and 4.5% respectively. In patients with ESV above 20 ml RC using unaligned data was 7.6%, with aligned data 3.4%.

Discussion

Myocardial perfusion SPECT is usually performed in ECG-gated mode with subsequent data processing using dedicated commercial software solutions. LVEF, EDV and ESV

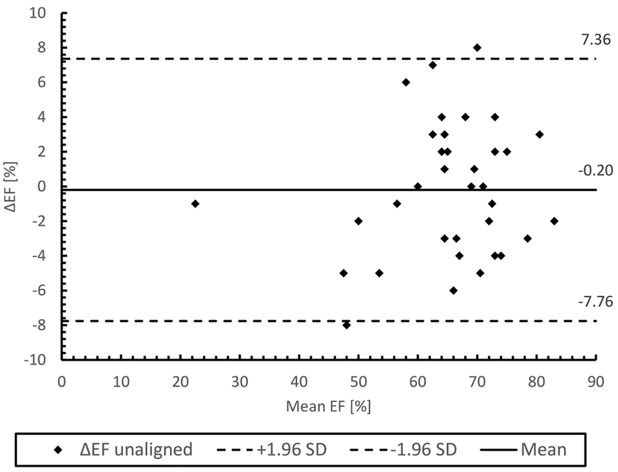

Figure 2 Bland-Altman plot of serial LVEF measurement using unaligned data.

Bland-Altman-analysis demonstrated a mean difference of -0.2% with limits of agreement of 7.4% to -7.8%. RC was 7.6%.

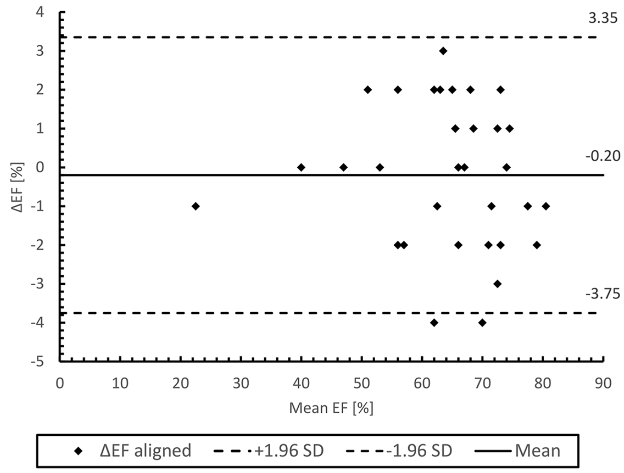

Figure 3 Bland-Altman plot of serial LVEF measurement using valve plane-aligned data.

Bland-Altman-analysis documented a mean difference of -0.2% with limits of agreement of 3.4% to -3.8%. RC was 3.6%.

determined by GSPECT correlate well with reference methods with some statistically significant systematic differences (3). This is also true for the comparison of different processing software (13).

In daily clinical practice, detection of changes in left ventricular functional parameters as well as gender differences may be relevant and have been discussed in the past (5, 14). In this context, in order to differentiate real differences of ventricular function from methodical uncertainty information about the repeatability of the method is essential (15).

Most important parameter of the inherent methodological variability is the RC, which can be determined by repeated data acquisition of the same patient (16).

In order to ensure stable cardiac function, we determined the RC after the resting study, which is started at least 3 hours after stress in our institution. We can assume, that in this late post-stress phase physiological changes of left ventricular functional parameters are negligible.

Using unaligned processing and Corridor4DM, the RC of LVEF in our study was 7.6% with limits of agreement of 7.4% to -7.8%. These results are in good concordance with previous publications.

Using Quantitative Gated SPECT Software (QGS) and repeated post stress data acquisition with complete repositioning of the patients, Kliner et al. reported a RC of LVEF of 7.5% with limits of agreement of +9.1% to -6.0% (6). Also using QGS, Xu et al. achieved RC of LVEF of 6.4% and 8.7%, for high activity stress and low activity rest myocardial perfusion GSPECT respectively. In this setting, patients were not repositioned between repeated studies, and studies requiring operator adjustment of the left ventricular contour were excluded from the analysis (8). Using the same processing software Hyun et al. repeated image acquisition of the same patient undergoing high count stress MPI. In this study, RC was 5.4% with limits of agreement of 5.4% to -5.5% (17). In the adenosine versus regadenoson comparative evaluation for myocardial perfusion imaging (ADVANCE-MPI) study the RC for post stress LVEF assessment was 6.9% in 259 patients undergoing repeated adenosine MPI within 4 weeks (18).

Effect of constraints in same patient evaluation

When processing sequential data sets of the same patient, it is helpful to deal with images as a group rather than individually (19). In order to implement this idea into practice, Germano et al. developed a shape quality control score in the GSPECT processing using QGS software. Processing results with low score values were considered to be algorithmic failure and reprocessed based on the knowledge of the left ventricular mask location in the other data set (19). Using this "same patient processing" procedure, stress and rest RC values for LVEF could be reduced substantially (4.5% vs 6.5% and 4.7% vs. 8.2% respectively) (16).

Another important aspect with possible influence on the repeatability of GSPECT is the precise definition of the mitral valve plane during segmentation of the left ventricle. This step often requires manual adjustment, which affects the quantification of left ventricular function (20–22).

Using simple valve plane alignment and identical lengths of left ventricular long axes in our study, the coefficient of repeatability could be reduced below 4% on a 95% confidence level.

Patients with small systolic ventricles

Limited geometric resolution results in underestimation of left ventricular volumes in myocardial GSPECT. It is more pronounced in end-systolic ventricles below 20-30 ml and called "small heart effect" in the literature (23, 24). However, the impact of ventricle size on the RC of LVEF has not been investigated in the past. Using aligned processing, we observed a tendency to higher RC (4.5% vs 3.4%) of LVEF in systolic ventricles below 20 ml.

Limitations

In our study we used only one commercially available program, Corridor 4DM. Most patients had normal ventricular function without significant perfusion defects at rest. Furthermore all patients had sinus rhythm without significant number of premature heart beats. The transferability of our observations to other processing software or to different patient collectives needs further investigations.

When acquiring two studies on the same day a good repeatability could be demonstrated, which supports the validity of comparison between post-stress and rest conditions. However, marked differences in the level and regional distribution of hepatobiliary and gastrointestinal tracer activity in separate day investigations may influence the repeatability of left ventricular contouring.

Conclusions

Using manual valve plane alignment in Corridor 4DM serial myocardial GSPECT processing coefficient of repeatability can be reduced below 4%.

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Conflicts of interest

None.

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