ORIGINAL ARTICLE

Assessment of left ventricular ejection fraction with cardiofocal collimators: Comparison between IQ-SPECT, planar equilibrium radionuclide angiography, and cardiac magnetic resonance

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Background. **IQ-SPECT has been shown to significantly reduce acquisition time and administered dose while preserving image quality in myocardial perfusion imaging. Whether IQ-SPECT provides accurate left ventricular ejection fractions (LVEF) with gated blood pool SPECT (GBPS) remains unknown.**

Methods. **Sixty patients underwent IQ-SPECT GBPS and planar imaging. Among those patients, 11 underwent both cMRI and GBPS. GBPS LVEF, LVEDV, and LVESV were calculated using 2 validated software; QBS (Cedars-Sinai Medical Center, Los Angeles, USA) and MHI (Montreal Heart Institute, Montreal, Canada). LVEF, LVEDV, and LVESV obtained with the different modalities were compared.**

Results. **Average planar LVEF was 48 ± 11% (mean ± SD), average LVEDV was 177 ± 59 mL (range 63 to 342 mL), and average LVESV was 96 ± 46 mL (range 16 to 234 mL). GBPS LVEF and their correlation coefficient with planar LVEF were 40 ± 12% ($r = 0.70$) and 44 ± 12% ($r = 0.83$) with QBS and MHI, respectively. Correlation coefficient between cMRI and planar LVEF was 0.65 and were 0.69 and 0.52 between cMRI and GBPS using QBS and MHI, respectively.**

Conclusions. **LVEF calculated with GBPS using IQ-SPECT correlates with planar measurements. Correlation is best using the MHI method and variation is independent of LVEDV. (J Nucl Cardiol 2019;26:1857–64.)**

Key Words: Radionuclide angiography • Left ventricular function • Gated blood pool imaging • Collimation

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Abbreviations

GBPS	Gated blood pool SPECT
ICD	Implantable cardioverter defibrillator
LEAP	Low energy all purpose
LEHR	Low energy high resolution
LVEDV	Left ventricular end diastolic volume
LVESV	Left ventricular end systolic volume
LVEF	Left ventricular ejection fraction
MPI	Myocardial perfusion imaging
MUGA	Multi-gated acquisition study

See related editorial, pp. 1865–1868

INTRODUCTION

Blood pool ventriculography with multigated acquisition (MUGA) allows accurate and reproducible measurements of the left ventricular ejection fraction (LVEF).[1] Because of its accuracy and reproducibility, MUGA can be used to assess LVEF prior to device implantation such as cardiac resynchronization therapy and implantable cardioverter defibrillator (ICD) as well as to monitor LVEF of patients undergoing cardiotoxic chemotherapies.[2,3] In recent years, the use of other techniques such as echocardiography and cardiac magnetic resonance imaging (cMRI) to assess LVEF has increased significantly. Yet, calculation of LVEF with these techniques can be operator dependent. Although LVEF assessment with MUGA requires operator input for contouring, the use of automatic segmentation with gated blood pool single photon emission computed tomography (GBPS) renders the method operator independent. GBPS has been shown to provide more accurate volume calculation, better assessment of wall motion, and reduction of issues related to overlapping structures when compared to planar MUGA.[4–7]

In recent years, the IQ-SPECT system (Siemens, USA) was introduced to improve myocardial perfusion imaging (MPI) performance. The system consists of cardiofocal collimators with variable-focus convergent geometry (SmartZoom), a cardiocentric detector orbit, and a dedicated ordered subset expectation maximization (OSEM) reconstruction algorithm with collimator/detector response modeling.[8,9] IQ-SPECT allows increased spatial resolution and sensitivity in the heart region compared to conventional low energy all purpose (LEAP) or low energy high resolution (LEHR) collimators.[10] In both phantom and patients studies, IQ-SPECT has been shown to preserve MPI image quality while reducing acquisition time and/or administered dose.[11–19] Recently, Erwin et al. showed that IQ-SPECT could also reduce scan time and/or injected activity of GBPS compared to conventional LEHR collimators.[20] However, the particularities of IQ-SPECT acquisition are known to produce counts inhomogeneity in the heart, especially on non-attenuation corrected images. For example, a relative increased uptake is frequently seen at the apical portion of the heart compared to the basal segments on non-corrected MPI images.[21,22] This raises the question of GBPS LVEF quantification validity with this system, particularly when used without attenuation correction or with count-based methods. The accuracy of LVEF assessment using GBPS with IQ-SPECT has not been studied. Furthermore, the effect of reduced LVEF and enlarged left ventricle (LV) on LVEF assessment with this system remains unknown. The purpose of this study is to compare the performance of IQ-SPECT GBPS to planar MUGA and cMRI.

MATERIALS AND METHODS

Patient Population

Consecutive patients who underwent LVEF assessment with both planar MUGA and IQ-SPECT GBPS imaging between August 2015 and November 2017 were retrospectively reviewed. A total of 60 patients, 12 females and 48 males, were included, with mean age of 63 years (range 24 to 86 years). All subjects were referred for LVEF assessment. 32 patients had known ischemic cardiomyopathy (CMP), 12 had dilated CMP, 6 had non-ischemic CMP of unknown etiology, 2 had myocarditis, 5 were referred with dyspnea, and 1 had a history of dextro-transposition of the great arteries status post Blalock and Rastelli procedures. Of the 60 subjects, 11 underwent cMRI within 30 days of the GBPS study and none had major procedures such as initiation of cardiac resynchronization therapy between the two studies.

Planar Equilibrium Radionuclide Angiography

Autologous red blood cells labeling was performed using the standard in vivo technique with intravenous administration of stannous pyrophosphate 20 minutes before administration of 925 to 1290 MBq of $^{99m}TcO_4^-$. Planar images were obtained for 15 minutes using a single detector camera (Digirad 2020tc) equipped with a LEAP collimator, with a 20% energy window centered on 140 keV and a 64 × 64 matrix. ECG-gated images were acquired in the best septal view with appropriate caudal tilt to optimize ventricular separation and obtained using 16 frames per R-R interval and a 15% timing acceptance window.

GBPS IQ-SPECT

Immediately after the planar acquisition, patients underwent GBPS with the IQ-SPECT system without attenuation correction on a Symbia T6 dual-head hybrid scanner (Siemens Medical Solution, USA). ECG-gated acquisitions were performed using 16 frames per R-R interval and the same 15% timing acceptance window used for planar imaging. The cardiocentric orbit was used with 34 views covering 208°, with 25 accepted beats per view. A 20% energy window centered on 140 keV was used. Images were stored in a 128 × 128 matrix. Acquisition time varied between 5 and 20 minutes, depending on heart rate and quantity of rejected beats. Image reconstruction was performed using the dedicated IQ-SPECT iterative reconstruction algorithm. A Gaussian filter (14 mm FWHM) was applied on the reconstructed gated images.

Quantitative Analysis

Planar LVEF were calculated using Corridor4DM (INVIA Medical Imaging Solutions, Ann Arbor, Michigan, USA). An experienced nuclear medicine physician outlined the initial LV contours at end systole (ES) and end diastole (ED). Fourier amplitude and phase maps were available to guide contouring. For all other time interval, the software automatically generated LV contours, which were reviewed for accuracy. A background region of interest was positioned approximately three pixels away from the lateral wall. Planar LVEF was calculated with the usual formula with background correction. GBPS LVEF was calculated automatically using two different software packages: Quantitative Blood Pool SPECT v10.0 (QBS; Cedars-Sinai Medical Center, Los Angeles, California, USA) and MHI v2.15 (Montreal Heart Institute, Montreal, Quebec, Canada).[4,23,24] The MHI segmentation software relies on an automated algorithm which creates 3D surfaces for every bin using the invariance of the Laplacian to detect the LV endocardial contours. The LVEF measurements were performed using a volume-based method with QBS software and a count-based method with the MHI software. LV end diastolic volumes (LVEDV) and LV end systolic volumes (LVESV) were also calculated with QBS and MHI software. When processing GBPS data, the operator was blind to the LVEF, LVEDV, and LVESV obtained with the other modalities and software.

cMRI

Eight patients underwent cMRI on a 1.5T scanner (Intera Achieva, Philips Medical Systems, Best, The Netherlands) and 3 on a 3T scanner (MAGNETOM Skyra, Siemens, Erlangen, Germany). The 1.5T MRI machine can operate at a maximum slew rate of 180 mT/m/ms and a maximum gradient strength of 33 mT/m. The 3T MRI machine can operate at a maximum slew rate of 200 mT/m/ms and a maximum gradient strength of 45 mT/m. For volume and function, a cardiac-gated short-axis cine steady-state free-precession sequence was acquired with enough slices to include the entire LV (repetition time = 3.4 ms; echo time = 1.2 ms; in-plane spatial resolution = 1.5 – 1.8 × 1.8 – 2.1 mm; slice = 8 mm; no gaps). Images were obtained during breath holds with acquisition of 4 slices per breath hold. Ten to twelve slices were usually acquired to cover the entire LV, resulting in an acquisition time of about 2 to 4 minutes.

LV ED and ES endocardial contours were drawn on the short-axis cine sequence using a commercially available software (CVI42 v5.2.2, Circle Cardiovascular Imaging, Calgary, AB) by a cardiothoracic radiologist blind to the MUGA and GBPS results, and following the Society for Cardiovascular Magnetic Resonance guidelines.[25]

Statistical Analysis

Statistical analyses were performed with GraphPad Prism 7 for Windows (v7.00, GraphPad Software, San Diego, California, USA). LVEF were compared using Bland-Altman analyses and linear regressions. Pearson product moment correlation coefficients were calculated to assess the correlation of LVEF between different techniques. When comparing multiple means, repeated-measure two-way analyses of variance (ANOVA) with post hoc Tukey's tests were used. Continuous variables are expressed as mean ± SD, and P value < .05 were considered statistically significant.

RESULTS

Left Ventricular Ejection Fraction

Average planar LVEF was 48 ± 11% and ranged from 23% to 70%. Average LVEF measured with GBPS methods were 40 ± 12% (range 16% to 75%) and 44 ± 12% (range 22% to 66%) with QBS and MHI, respectively (Table 1). LVEF were greater with planar MUGA compared to GBPS ($P_{ANOVA} < .0001$) with both QBS ($P < .0001$) and MHI ($P = .0003$). The average LVEF was greater with MHI compared to QBS ($P < .0001$). Correlation coefficients between planar and QBPS LVEF measurements were 0.70, and 0.83 with QBS and MHI, respectively. Correlation coefficient between QBPS LVEF measurements with QBS and MHI was 0.81. Linear regressions and Bland-Altman graphics are presented in Figure 1. Bland-Altman analysis of LVEF revealed a positive bias of planar vs IQ-SPECT for both software with mean difference of 8% (95% CI 6% to 10%) for QBS and 4% (95% CI 2% to 6%) for MHI. The bias was significantly greater with QBS compared to MHI ($P < .0001$).

Fifteen subjects had a planar LVEF between 20% and 40%, neighboring threshold values frequently used for therapy decisions. Of those 15 subjects, 3 had planar LVEF below 30% and 12 had LVEF greater or equal to 30%. For 5 subjects, LVEF measured with both QBS and MHI was below 30% but was greater or equal to 30% on planar assessment.

11 subjects underwent cMRI LVEF assessment within 30 days of their GBPS study. The average time interval between the two studies was 6 ± 6 days (range 0 to 17 days). Average LVEF on cMRI was 45 ± 10% (range 28% to 58%). Correlation coefficient between cMRI and planar LVEF was 0.69 (Table 2). Correlation coefficients between cMRI and GBPS LVEF were 0.52 and 0.65 with QBS and MHI, respectively (Figure 2).

LVEF were greater with planar MUGA compared to cMRI (P = .002, P_{ANOVA} = .0002) but not significantly different with the two software GBPS compared to cMRI (P > .16, P_{ANOVA} = .0002).

Left Ventricular End Diastolic Volume

Average LVEDV was 177 ± 59 mL (range 63 to 342 mL) as calculated by the average between QBS and MHI LVEDV. Fifty (83.3%) subjects had LVEDV greater than 120 mL. There was no significant correlation between the planar MUGA and GBPS LVEF difference vs LVEDV (Figure 3) with QBS (r = 0.03, P = .81) and MHI (r = 0.14, P = .29).

For the 11 subjects who underwent cMRI, the average LVEDV was 257 ± 78 mL (range 137 to 393 mL). Correlation coefficients between cMRI and GBPS LVEDV were 0.80 with both QBS and MHI (Figure 4, Table 2). LVEDV were greater with cMRI (P_{ANOVA} < .0001) compared to GBPS with QBS and MHI (P < .0014, P_{ANOVA} < .0001).

Left Ventricular End Systolic Volume

Average LVESV was 96 ± 46 mL (range 16 to 234 mL) as calculated by the average between QBS and MHI LVESV. There was no significant correlation between the planar MUGA and GBPS LVEF difference vs LVESV with QBS (r = 0.09, P = .48) and MHI (r = 0.17, P = .17).

For the 11 subjects who underwent cMRI, the average LVESV was 178 ± 67 mL (range 68 to 253 mL) as measured on cMRI. Correlation coefficients between cMRI and GBPS LVESV were 0.73 and 0.80 with for QBS and MHI, respectively (Figure 4, Table 2). LVESV were greater with cMRI compared to GBPS with QBS and MHI (P = .0012, P_{ANOVA} < .0001).

DISCUSSION

To our knowledge, this study is the first documentation of GBPS accuracy with IQ-SPECT for a broad range of LVEF and LV volumes. Recently, Erwin et al. showed that IQ-SPECT could reduce scan time and/or injected activity of GBPS compared to SPECT using LEHR collimators in a group of 10 subjects.[20] They also showed that IQ-SPECT GBPS correlated well with planar MUGA LVEF (r = 0.77) compared to conventional SPECT (r = 0.60 to 0.62). However, the linear regression between planar and IQ-SPECT LVEF measurements yielded a questionable slope of 1.42, which is likely related to the small sample size (10 subjects) and the relatively narrow range of LVEF in their sample (52% to 69%). This result nevertheless raised the question of accuracy and validity of IQ-SPECT GBPS LVEF for lower values LVEF.

The results of this study revealed a good correlation between IQ-SPECT GBPS and planar MUGA LVEF measurements, with correlation coefficient of 0.70 and 0.83 for the different algorithms. The MHI algorithm, which is a count-based method, yielded the highest correlation coefficient (r = 0.83). This results is nearly identical to the correlation obtained between the MHI algorithm using LEHR collimators and planar MUGA previously published by our group (r = 0.84).[23] It is also similar to results obtained by Chen et al. comparing planar MUGA and GBPS using cadmium-zinc-telluride (CZT) camera (r = 0.93).[26] With the two algorithms, the difference between planar MUGA and GBPS LVEF measurements were not correlated with LVEF and LVEDV, suggesting that the accuracy of IQ-SPECT GBPS is not significantly affected by LVEF and LV volumes. The bias between the GBPS count-based and the volume-based methods were also not significantly affected by the LVEF or LVEDV. This suggests that the heterogeneity observed in non-attenuation corrected IQ-SPECT images does not introduce a volume or LVEF dependent bias.

The average difference between planar and MHI LVEF was 4%, which represents a small absolute difference of minor clinical importance in most cases. A situation where small variations might be of clinical importance is when LVEF is used for decision making, such as for ICD implantation. For subjects with LVEF between 20% and 40%, using a cutoff value of 30% for ICD implantation, 5 subjects would be reclassified as

Table 1. Comparison of left ventricular ejection fraction (LVEF) measured with planar and IQ-SPECT

LVEF	Planar	QBS	MHI
Mean ± SD	48 ± 11%	40 ± 12%	44 ± 12%
Range	23-70%	16-75%	22-66%
Vs planar			
Average difference	-	8 ± 9%	4 ± 7%
Correlation coefficient (r)	-	0.70	0.83

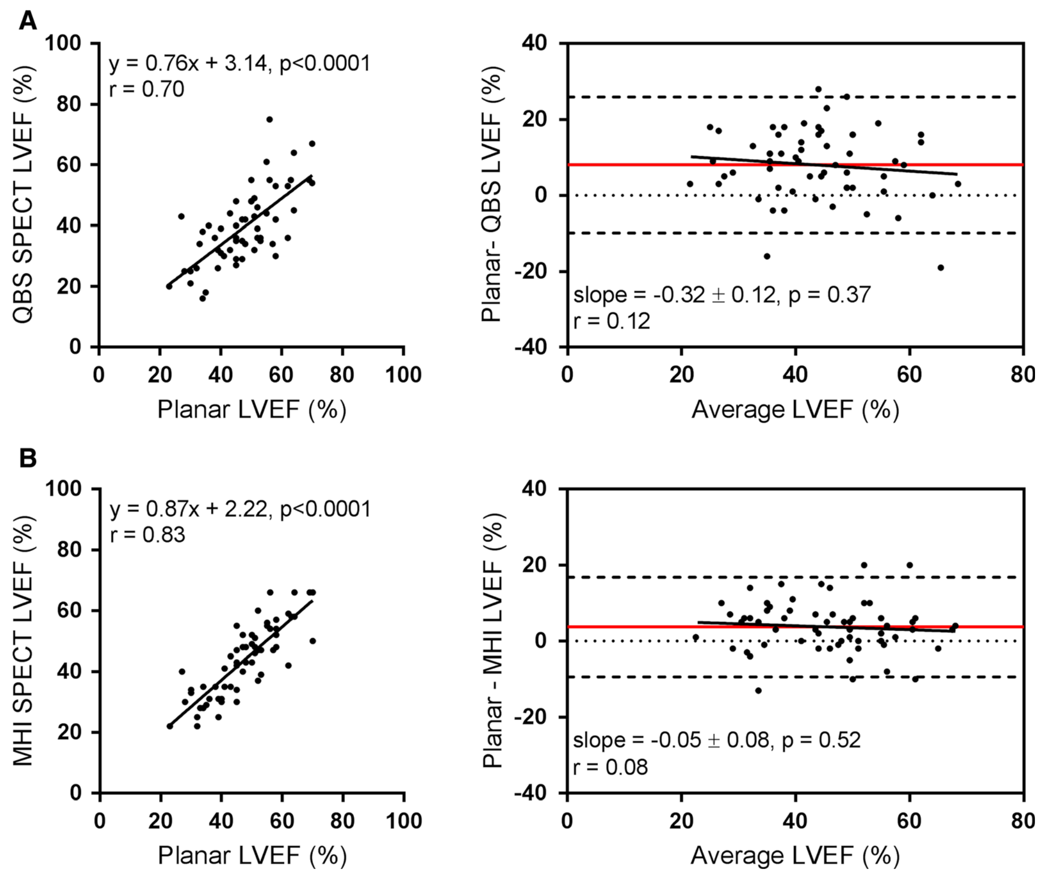

Figure 1. Correlation (left) and Bland-Altman plots (right) comparing left ventricular ejection fraction (LVEF) provided by planar multi-gated acquisition vs gated blood pool SPECT using the (**A**) the QBS algorithm and (**B**) the MHI algorithm. On the Bland-Altman plots, the red lines represent the mean difference and the doted black lines represent the 95% confidence interval of mean difference.

Table 2. Correlation coefficient (*r*) of planar and IQ-SPECT vs cardiac magnetic resonance imaging

	Planar	QBS	MHI
LVEF	0.69	0.52	0.65
LVEDV	–	0.80	0.80
LVESV	–	0.73	0.80

LVEF, left ventricular ejection fraction; *LVEDV*, left ventricular end diastolic volume; *LVESV*, left ventricular end systolic volume

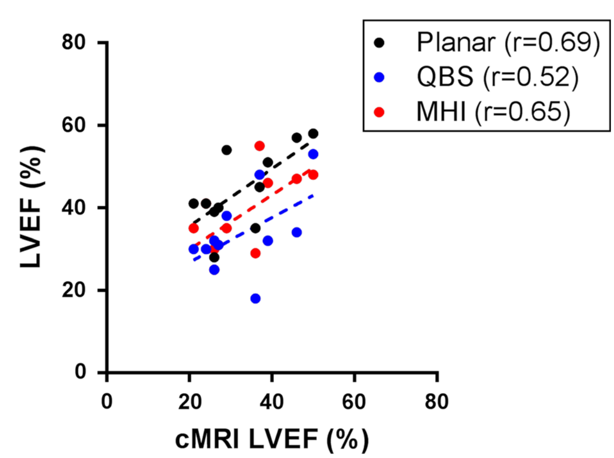

Figure 2. Correlation between left ventricular ejection fraction (LVEF) provided by cardiac magnetic resonance imaging (cMRI) vs the different radionuclide techniques.

eligible for ICD when using GBPS instead of planar LVEF. The observed LVEF differences between planar and GBPS can be in part attributed to the fact that planar LVEF assessment can be affected by several factors, including overlapping structures, suboptimal angulation,

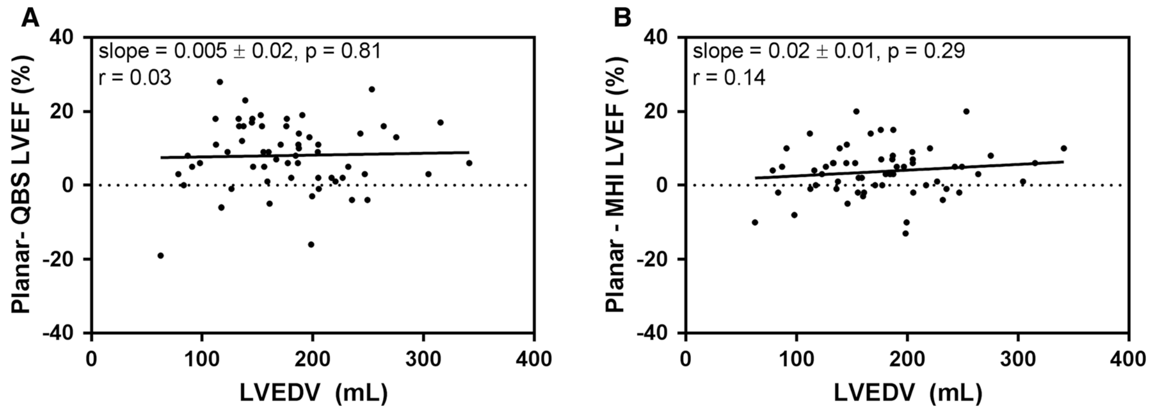

Figure 3. Correlation plots between the differences of left ventricular ejection fraction (LVEF) provided by planar multi-gated acquisition and gated blood pool SPECT vs the left ventricular end diastolic volume (LVEDV) with the (**A**) QBS algorithm, and (**B**) the MHI algorithm.

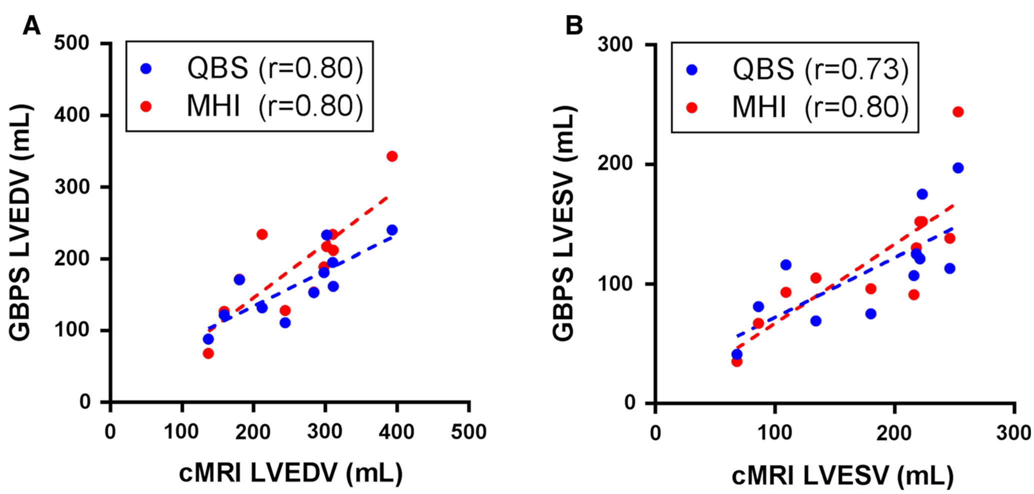

Figure 4. Correlation between (**A**) left ventricular end diastolic volume (LVEDV) and (**B**) left ventricular end systolic volume (LVESV) provided by cardiac magnetic resonance imaging (cMRI) vs gated blood pool SPECT using the QBS algorithm and the MHI algorithm.

inadequate background correction, and inaccurate basal contouring.[4–7]

In the subset of 11 subjects in which cMRI data were available, there was moderate correlation between cMRI and GBPS LVEF with the best correlation obtained with MHI ($r = 0.65$). Correlation was not as high as previously described when comparing cMRI to QBS ($r = 0.82$) and MHI ($r = 0.88$) with SPECT using LEHR collimators,[4] but was comparable to the observed correlation between cMRI and planar LVEF ($r = 0.69$). This could be related to the low sample size as well as a potential selection bias associated to the retrospective design. Indeed, patients for which the LVEF measurements were felt to be inaccurate with one modality by the clinicians might be more frequently referred to another modality, which could lead to weaker correlation. Another important consideration is the fact that the cMRI and GBPS were not performed on the same day. Although time delays between the radionuclide and cMRI studies were relatively short (6 ± 6 days), differences in pre and post-load can cause variations in the actual LVEF and lead to measurement discrepancies. Nonetheless, the delays between the radionuclide and cMRI observed in this study are similar to those of a previous work (12 ± 10 days) which demonstrated similar correlation for LVEF and LV volumes.[4]

Eighty percent of the patients' population is male, which is representative of our clinical population but not necessarily representative of most centers. For example, centers where MUGA are performed mainly to assess chemotoxicity typically have higher proportion of females. This raises the question of generalizability of the results given the potential different attenuation patterns in male and female. The gender differences observed on IQ-SPECT MPI images without attenuation correction are similar to those of conventional SPECT, with lower myocardial counts in the inferior wall of males compared to females.[13,21] This suggests that the differences in attenuation between males and females with IQ-SPECT GBPS could be similar to those observed with conventional GBPS SPECT, although the exact effects of the different attenuation patterns on LVEF assessment with IQ-SPECT GBPS remain unknown.

A limitation of this study is the retrospective design and associated potential bias. Notwithstanding this design, this study provides new data assessing the accuracy of IQ-SPECT GBPS imaging. It would have been of interest to directly compare LVEF measurements with IQ-SPECT and SPECT using LEHR collimators, which was not possible in this retrospective study. A potential limitation is that attenuation correction was not used in this study. Whether attenuation correction improves LVEF assessment with IQ-SPECT GBPS remains unknown. It is expected that the correction for attenuation would affect mostly LVEF quantification with the count-based method. Further studies are required to evaluate the effect of attenuation correction on LVEF assessment with the IQ-SPECT system. Nevertheless, many centers do not have access to hybrid SPECT/CT cameras and in that context the results of this study remain relevant. Finally, another limitation of this study is the fact that 16 frames per heart beat were used for the planar MUGA acquisitions instead of 32, which could affect the evaluation of the systolic function. Nonetheless, good correlations were found between LVEF and volumes measured with cMRI vs planar MUGA with 16 frames in larger studies.[4]

NEW KNOWLEDGE GAINED

LVEF obtained with IQ-SPECT GBPS correlated well with planar MUGA LVEF for a broad range of LVEF and LV volumes. This correlation was not affected by LVEDV or LVEF. Correlation was best with the count-based MHI software and was comparable to previously published results with conventional SPECT using LEHR collimators. The results of this study suggest that IQ-SPECT provide accurate assessment of LVEF and LV volumes.

CONCLUSION

In nuclear cardiology centers using IQ-SPECT, where MPI represents the vast majority of SPECT studies, it is desirable to perform GBPS with using the IQ-SPECT system to reduce acquisition time and/or dose as well as to avoid time-consuming collimator changes. This study demonstrates that LVEF obtained with the IQ-SPECT system correlate well with planar MUGA measurements, regardless of the analysis software. Further studies would be required to compare the accuracy of IQ-SPECT against cMRI.

Disclosure

MHI is proprietary software of the Montreal Heart Institute. Matthieu Pelletier-Galarneau, Vincent Finnerty, Stephanie Tan, Sebastien Authier, Jean Gregoire, and Francois Harel declare that they have no other conflict of interest related to this work.

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