Comparative Values of Gated Blood-Pool SPECT and CMR for Ejection Fraction and Volume Estimation

Right and left ventricular functions

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Abstract:

Objective: Gated blood-pool single photon emission computed tomography (GBPS) was compared with cardiac magnetic resonance (CMR) for the measurement of left ventricular (LV) and right ventricular (RV) ejection fractions (EF) and volumes (end-diastolic volume: EDV or end-systolic volume: ESV) in a mixed population. **Methods:** Thirty patients (70% male; mean age 61 ±14 year) referred for various symptoms or heart diseases, predominantly ischemic, were included. GBPS data were analyzed using previously described segmentation software based on the watershed algorithm. CMR images were acquired for both ventricles at the same time using an SSFP sequence and short-axis views. No compensation for papillary muscles was used. LV and RV EF and volumes were assessed with GBPS and CMR and compared. **Results:** LV EF and volumes were correlated ($p<0.001$). The difference in LV EF between GBPS and CMR was not significant ($p=0.063$). Limits of agreement were close for LV EF (-11 to 15%) and wider for LV volumes (-82 to 11 mL for EDV and -52 to 15 mL for ESV), with higher

volume values obtained with CMR (mean differences of 36 ±24 mL for EDV and 19 ±17 mL for ESV). The RV EF and volumes assessed by GBPS and CMR were correlated (p<0.001). The difference in RV ESV between GBPS or CMR was not significant (p=0.136). Limits of agreement were relatively close for all RV parameters (-15 to 8% for EF; -44 to 22 mL for EDV and -25 to 21 mL for ESV). In 24 patients without valvulopathy or shunt, the difference between LV stroke volume (SV) and RV SV was lower with GBPS than CMR (respectively, 9 ±14 mL and 18 ±13 mL with p=0.027). **Conclusion:** GBPS is a simple and widely available technique that can assess both LV and RV EF and volumes with slight differences compared with CMR.

Keywords: Gated blood-pool imaging; SPECT; magnetic resonance imaging; ejection fraction; ventricular volume

INTRODUCTION

Accurate quantification of ventricular function and volumes is important in the management of patients with cardiovascular disease. In patients with coronary artery disease, left ventricular (LV) ejection fraction (EF) at rest or stress, end-diastolic volume (EDV) and end-systolic volume (ESV) are strong independent predictors of cardiovascular morbidity and death [1,2]. Even patients without prior myocardial infarction or valvular disease are at high risk of congestive heart failure and death when only a mild impairment of LV EF is present [3]. Right ventricular (RV) EF is also a very important parameter, which, independently of pulmonary hypertension, improves the accuracy of the prognostic stratification of patients with heart failure [4].

Several imaging techniques can be used to assess EF and ventricular volumes. Availability, innocuousness and cost made echocardiography the most frequently used technique in spite of high interobserver variability and the requirement of a geometrical assumption to define LV and RV volumes. Several factors may affect the measurement of LV function in gated SPECT perfusion imaging, such as areas of marked hypoperfusion [5-8]. The limitations of planar gated blood-pool are overlapping structures and difficult assessment of RV function using the first-pass technique [9].

Thanks to the combination of excellent spatial, contrast, and temporal resolution, cardiac magnetic resonance imaging (CMR) has become a useful tool to assess cardiac performance in an accurate and reproducible way [10-13]. A new steady state-free precession (SSFP) sequence has improved the contrast between myocardium and cavity, allowing significantly better detection of the endocardial border *[14]*. Simpson's rule as a geometrical model is far more accurate than those used in contrast ventriculography, echocardiography (M-Mode and 2D) or myocardial perfusion scintigraphy. [15,16] This approach is usually more time-consuming for both image acquisition and post-processing, and it also requires highly qualified staff. Likewise, CMR is not widely available and is of limited feasibility for patients with implanted devices or claustrophobia.

Gated blood-pool SPECT (GBPS) is a technically simple and widely available count-based method that is independent of geometry. Thus, it may permit simultaneous assessment at equilibrium of the LV and RV parameters [9,17,18]. Regional ventricular function measurements like local EF or local times of end-systole are also available with this technique [19-22].

In this study, we investigated the correlation and agreement between LV and RV EF and volume measurements derived from GBPS data and those obtained with the CMR method as the correlative standard.

MATERIALS AND METHODS

Patients

Thirty consecutive patients [aged 61 ±14 years (range 34-87 years); 70% male] were prospectively included in the study. All had clinical indications for CMR studies and isotopic evaluation of EF to diagnose cardiac disease or as follow-up. Reasons for referral were coronaropathy (n=16), myocarditis (n=4), arrhythmogenic right ventricular dysplasia (n=2), constrictive pericarditis (n=2), pulmonary hypertension (n=4), cardiac involvement in scleroderma (n=1) and adrenergic cardiomyopathy (n=1). All subjects were prospectively recruited from inpatient and outpatient populations at the Montpellier University Hospital between August 2, 2008, and June 15, 2009.

All correlative GBPS and CMR studies were performed within a mean interval of 12 ±21 days (median: 2 days, range: 0-81 days). No patient had any significant cardiac event between studies, and none had changes in medical or surgical therapy. All patients gave their informed consent prior to inclusion in the study.

CMR Data Acquisition

CMR data were collected on a 1.5-T scanner (Magnetom Sonata; Siemens Medical Solutions, Erlangen, Germany). Breath-hold TrueFISP cine CMR was used [23]. The integrated parallel acquisition technique (iPAT) was required in 6 cases.

Multiplane localizers identified the cardiac position and the usual cardiac imaging planes using a standard iterative scouting technique. Retrospective ECG-gated cine CMR images were then acquired using a segmented steady-state precession sequence: TrueFISP. Ten to twelve short-axis views that encompassed the entire left and right ventricles were acquired using the following parameters

from the Society for Cardiovascular Magnetic Resonance (SCMR) [24]: slice thickness 8 mm with 2-mm interslice gaps to equal 10 mm, matrix 128 x 256, temporal resolution 40 ms or less, and field of view of 30-40 cm^2 depending on the patient's chest size. Breath-hold duration was 15-20 s per image sequence. To improve patient comfort and compliance, data were acquired during the patient's end inspiration (moderate inspiration). The same acquisition was used to determine left and right ventricular parameters. Total data acquisition time was 20 min for cooperative patients with regular pacing and able to hold their breath.

CMR Calculations

Images were examined off-line using commercially available software (ARGUS, Siemens Medical Solutions). End-systole and end-diastole were not predefined, but contours were drawn on all phases and end-systole and end-diastole were automatically defined as the phases with the highest and lowest volumes.

CMR values were derived independently by modified Simpson's rule from semiautomated SA regions that were modified manually to conform to endocardial borders [15,16]. Ventricular basal limits were defined as proposed by Alfakih et al. [25]. In line with the SCMR recommendations, no corrections were performed to compensate for papillary muscles, so as to simplify the CMR measurements for optimal reproducibility, saving post-processing time, and to use local institution normal reference ranges [24,26].

GBPS Data Acquisition

Patients were injected with 740–925 MBq (20–25 mCi) of in vitro labeled erythrocyte solution. Data were acquired using a dual-head γ-camera (Sopha DST-

XL or Infinia Hawkeye 1; GE Healthcare) in a 90° configuration with low-energy high-resolution parallel-hole collimators. Tomographic gated blood-pool scintigraphy was performed with the following acquisition parameters: 5.6°-6° per step (15-16 steps over 90° per head) for 180° according to the american and european guidelines [27,28], 40-s acquisition per step, 10% R-R interval acceptance window, 8 gated intervals, and 64*64 (pixel size: 5.9-6.8 mm). With these acquisition parameters, the examination time was 10-11 min for patients with regular pacing.

GBPS Processing

For all the patients in this study, 16 transverse slices were reconstructed for each time frame using filtered backprojection reconstruction. The projection data underwent compensation for scatter using the Jaszczak method [29]. Transverse slices were reoriented into the usual cardiac axis and processed with in-house semiautomatic GBPS software based on the watershed immersion algorithm (Tompool®: freely available on the net at *http://www.scinti.etud.univ-montp1.fr*).

The previously described GBPS algorithm [9,18,19,30] was modified and adapted to be run on standard desktop personal computers running under Windows operating systems (Microsoft Corp.). Iterative thinnings that were used to produce a skeleton by influence zones [9] were replaced by a full 3D immersion approach taking adjacent slices into consideration. This approach produced less over-segmentation of the ventricular cavities. In order to identify each segmented structure as belonging to the LV, the RV or the vascular structure behind the valve plane, septal, atrioventricular and pulmonary infundibulum planes were defined beforehand. Time-activity curves were generated using deformation of a reference

curve as described by Caderas De Kerleau et al. [31]. These improvements led to a fully automatic algorithm, except for the precise location of the 3 aforementioned planes.

Statistics

Statistical analysis was performed with commercially available software (SPSS for Windows, version 13.0; SPSS Inc., Chicago, IL; and GraphPad Prism for Windows, version 5, GraphPad Software Inc., La Jolla, CA). The mean ± standard deviation (SD) characterizes the distributions of the parameters for the data. Continuous data were compared with a paired Student's t test or a paired Wilcoxon test, as appropriate. Correlation between continuous variables was determined using linear regression and Spearman's rank order correlation coefficient (r_S). Bland-Altman analyses of measurement differences plotted versus mean values were used to assess biases (mean difference), trends, and 95% limits of agreement [32]. For all statistical testing, a two-tailed p value of less than 0.05 was considered statistically significant. The interoperator variability (V) of the semiautomatic tomographic method is expressed as the coefficient of variation of the paired measurements of ejection fractions and volumes made by each of the two nuclear medicine physicians who used the program and analyzed the results of the segmentation procedure [33]:

$$V(\%) = 100 \times \frac{\frac{\sqrt{\sum_{i=1}^{n}(EF_{1,i} - EF_{2,i})^2}}{2n}}{\frac{\overline{EF_1} + \overline{EF_2}}{2}},$$

where $EF_{1,I}$ and $EF_{2,I}$ are the i^{th} ejection fractions (or volumes) measured by the first and second physicians, respectively, EF_1 and EF_2 are the mean ejection fractions

(or volumes) measured by the first and second physicians, respectively, and n is the number of measurements.

RESULTS

GBPS was performed successfully in all patients and no complications occurred, whereas one patient was excluded from the CMR database on the basis of inadequate CMR gating (arrhythmia). The mean heart rate of the 29 remaining subjects during the GBPS (66±12 bpm) was not significantly different (p=0.31) from that observed during the CMR (67±12 bpm). All GBPS and CMR images were of sufficient image quality and suitable for analysis.

Algorithms were run for GBPS data for all 30 subjects. Calculations of right and left EF and volumes using Tompool® took less than 1 min per patient. CMR post-processing was more time-consuming: semi-manual endocardial drawings required more than 30 min per patient (10 min for LV drawings and 20 min for RV drawings).

Using CMR as the reference, left ventricular function was impaired in 13 (45%) patients and right ventricular function was impaired in 5 (17%) patients.

Left Ventricle

Main results are presented in **TABLE 1**.

TABLE 1: Left and right ventricular parameters assessed by GBPS and CMR (n=29).

	Left Ventricle		Right Ventricle	
	GBPS	CMR	GBPS	CMR
EDV (mL)	104±57*	140±59*	92±31*	103±37*
ESV (mL)	50±51*	69±58*	45±22	47±25
SV (mL)	54±18*	71±19*	47±15*	56±21*
EF (%)	58±19	56±17	52±10*	56±11*

End-diastolic volume (EDV); end-systolic volume (ESV); ejection fraction (EF);

* significant differences in measurements ($p<0.05$)

Ejection Fraction

TABLE 2: Comparisons between gated blood-pool SPECT (GBPS) and CMR (cardiac magnetic resonance) measurements of left and right ventricular ejection fractions (LV EF and RV EF).

		LV EF	RV EF
Correlation	r_S	0.92	0.92
	p	<0.001	<0.001
Regression line	slope	1.05	0.78
	y_0	0.55	8.92
Difference (GBPS-CMR)	mean ±SD	2.40 ±6.67	-3.63 ±6.00
	95% LA	[-10.68 ; 15.48]	[-15.39 ; 8.12]
	SEM	1.24	1.11
	95% CI	[-0.08 ; 4.88]	[-5.86 ; -1.40]
	bias	no	yes

95% limits of agreement (95% LA); standard error of the mean difference (SEM); 95% confidence interval (95% CI)

LV EF assessed with GBPS and CMR were correlated (r_s=0.92; p<0.001; standard error of estimate (SEE) =6.73%) **(FIGURE 1)**. Mean LV EF values for GBPS and CMR were not different (respectively, 58±19% and 56±17%; p=0.063). **FIGURE 2** shows a Bland-Altman plot of LV EF measurements by GBPS and CMR. The results of the Bland-Altman analysis are summarized in **TABLE 2**, showing for EF a mean difference of 2.4% and 95% limits of agreement of -10.7% to 15.5%.

FIGURE 1

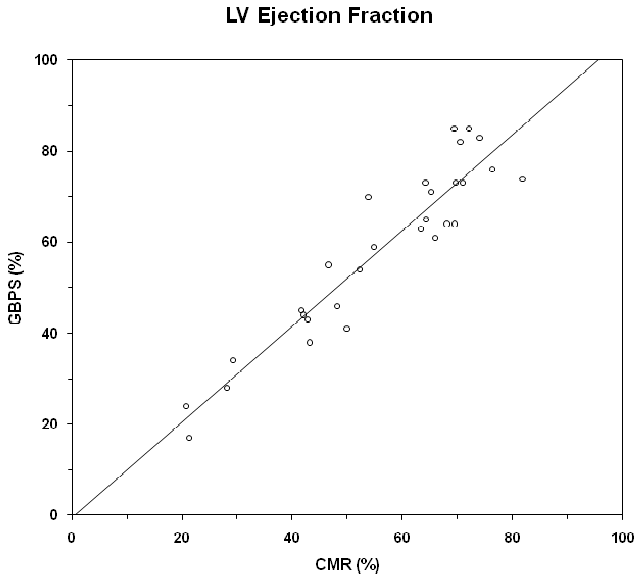

FIGURE 1: Correlation between gated blood-pool SPECT (GBPS) and cardiac magnetic resonance (CMR) measurements of left ventricular (LV) ejection. $LVEF_{GBPS}$=1.05 $LVEF_{CMR}$ – 0.55; R^2=0.88; SEE=6.73; r_S=0.92; p<0.001.

FIGURE 2

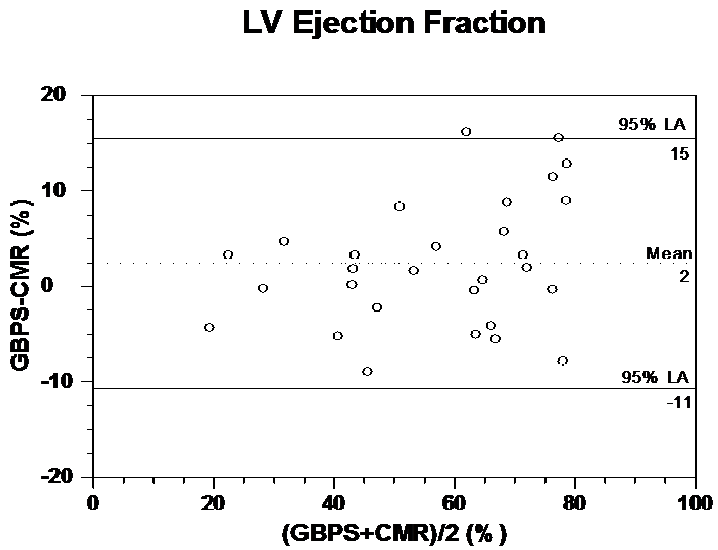

FIGURE 2: Left ventricular (LV) ejection fraction by Bland-Altman plotting. Horizontal lines indicate the mean difference and 95% limits of agreement (95% LA).

Volumes

LV EDV and ESV assessed with GBPS and CMR were correlated (respectively, r_s=0.82; p<0.001; SEE=6.73 mL and r_s=0.82; p<0.001; SEE=23.27 mL) **(FIGURE 3).** The mean LV EDV and ESV values for GBPS and CMR were different (respectively 104±57; 140±59 mL; p<0.001 and 50±51; 69±58 mL; p<0.001)**. FIGURE 4** shows a Bland-Altman plot of LV EDV and ESV measurements by GBPS and CMR. The results of the Bland-Altman analysis are summarized in **TABLE 3**, showing for EDV a mean difference of -35.88 mL and 95% limits of agreement of -82.42 mL to 10.67 mL and for ESV a mean difference of -18.68 mL and 95% limits of agreements of -51.86 mL to 14.51 mL.

TABLE 3: Comparisons between gated blood-pool SPECT (GBPS) and CMR (cardiac magnetic resonance) measurements of left and right ventricular (LV and RV) end-diastolic and end-systolic volumes (EDV and ESV).

		LV EDV	LV ESV	RV EDV	RV ESV
Correlation	r_S	0.84	0.89	0.80	0.86
	p	<0.001	<0.001	<0.001	<0.001
Regression line	slope	0.89	0.84	0.75	0.78
	y_0	-20.61	-7.62	14.01	8.44
Difference (GBPS-CMR)	mean ±SD	-35.88±23.75	-18.68±16.93	-11.24±16.91	-1.92±11.53
	95% LA	[-82.42; 10.67]	[-51.86; 14.51]	[-44.39; 21.90]	[-24.52; 20.69]
	SEM	4.41	3.14	3.14	2.14
	95% CI	[-44.69; -27.06]	[-24.96; -12.39]	[-17.53; -4.96]	[-6.20; 2.37]
	bias	yes	yes	yes	no

95% limits of agreement (95% LA); standard error of the mean difference (SEM); 95% confidence interval (95% CI)

FIGURE 3

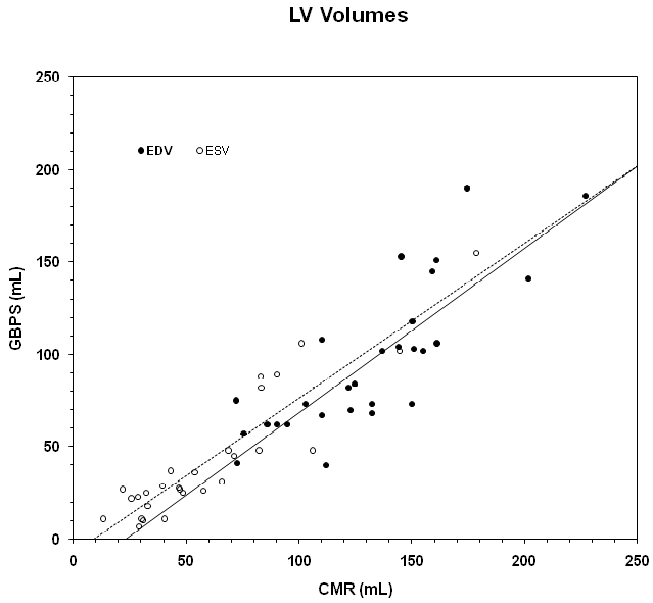

FIGURE 3: Correlation between gated blood-pool SPECT (GBPS) and cardiac magnetic resonance (CMR) measurements of left ventricular (LV) end-diastolic (EDV) and end-systolic volumes (ESV).

EDV_{GBPS}=0.89 EDV_{CMR} – 20.61; R^2=0.84; SEE=23.27; r_S=0.82; p<0.001.

ESV_{GBPS}=0.84 ESV_{CMR} – 7.62; R^2=0.92; SEE=14.37; r_S=0.89; p<0.001.

FIGURE 4

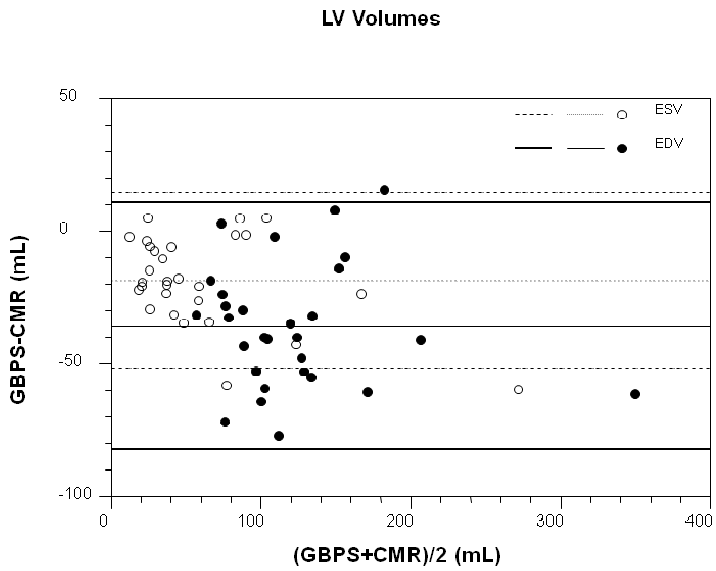

FIGURE 4: Left ventricular (LV) end-diastolic (EDV) and end-systolic volumes (ESV) by Bland-Altman plotting. Horizontal lines indicate mean difference and 95% limits of agreement (95% LA).

Right Ventricle

The main results are presented in **TABLE 1.**

Ejection Fraction

RV EF assessed with GBPS and CMR were correlated (r_s=0.74; p<0.001; SEE=5.52%) **(FIGURE 5)**.The mean RV EF values for GBPS and CMR were different (respectively, 52 ±10% and 56 ±11%; p=0.003)**. FIGURE 6** shows a Bland-Altman plot of the RV EF measurements by GBPS and CMR. The results of

the Bland-Altman analysis are summarized in **TABLE 2,** showing for EF a mean difference of -3.63% and 95% limits of agreement of -15.39% to 8.12%.

FIGURE 5

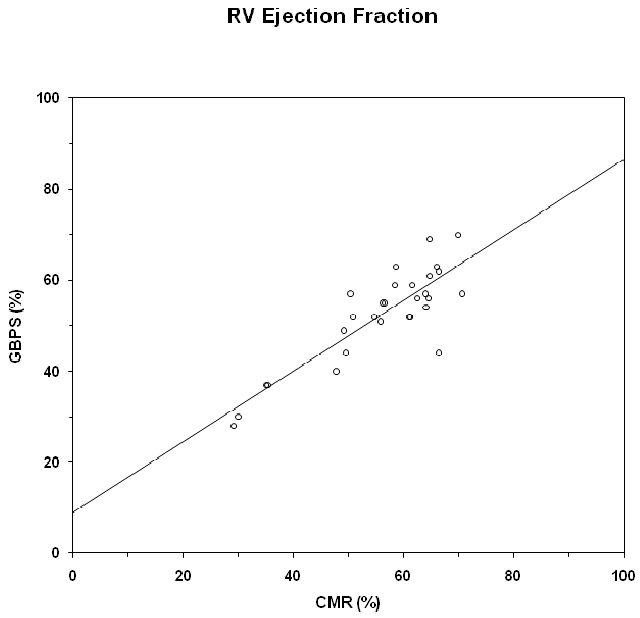

FIGURE 5: Correlation between gated blood-pool SPECT (GBPS) and cardiac magnetic resonance (CMR) measurements of right ventricular (RV) ejection fraction. $RVEF_{GBPS}$=0.78 $RVEF_{CMR}$ + 8.92; R^2=0.73; SEE=5.52; r_S=0.74; p<0.001.

FIGURE 6

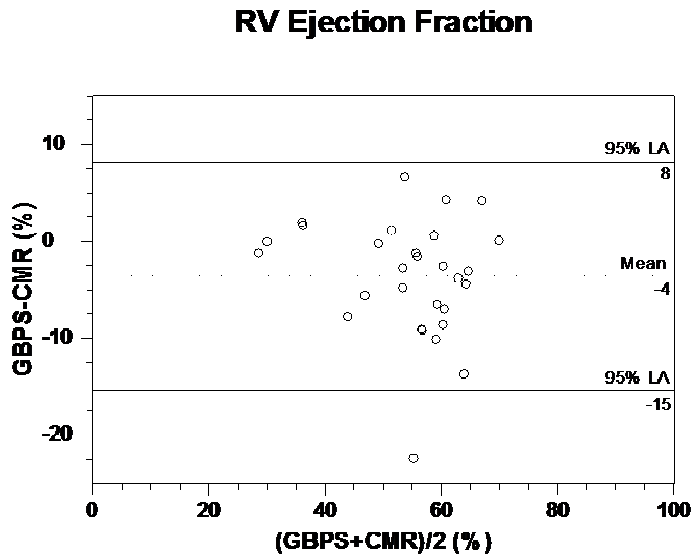

FIGURE 6: Right ventricular (RV) ejection fraction by Bland-Altman plotting. Horizontal lines indicate the mean difference and 95% limits of agreement (95% LA).

Volumes

RV EDV and ESV assessed with GBPS and CMR were correlated (respectively, r_s=0.80; p<0.001; SEE=14.55mL and r_s=0.86; p<0.001; SEE=10.26mL) **(FIGURE 7).** The mean RV EDV values for GBPS and CMR were different (respectively, 92 ±31 and 103±37mL; p=0.001). The mean RV ESV values for GBPS and CMR were not different (respectively, 45±22 and 47 ±25 mL; p_w=0.136). **FIGURE 8** shows a Bland-Altman plot of RV EDV and ESV measurements by GBPS and CMR. The results of the Bland-Altman analysis are

summarized in **TABLE 3**, showing for EDV a mean difference of -11.24 mL and 95% limits of agreement of -44.39 mL to 21.90 mL and for ESV a mean difference of -1.92 mL and 95% limits of agreement of -24.52 mL to 20.69 mL.

FIGURE 7

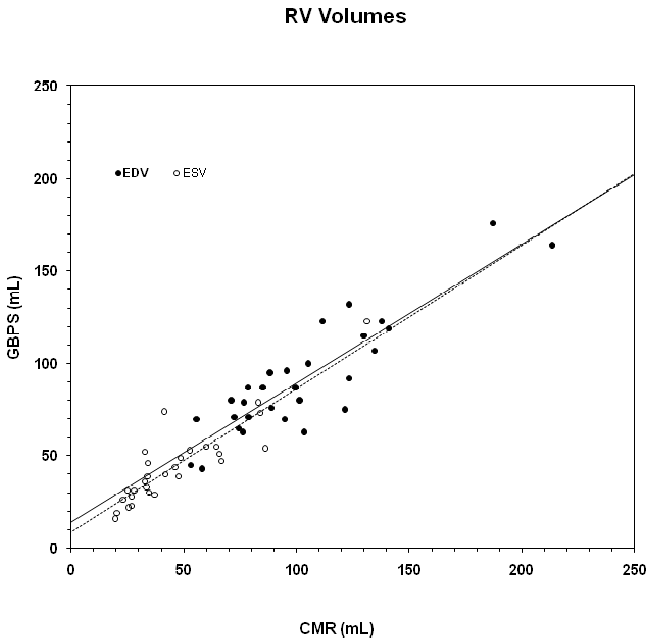

FIGURE 7: Correlation between gated blood-pool SPECT (GBPS) and cardiac magnetic resonance (CMR) measurements of right ventricular (RV) end-diastolic (EDV) and end-systolic volumes (ESV).

EDV_{GBPS}=0.75 EDV_{CMR} +14.01; R^2=0.79; SEE=14.55; r_S=0.80; p<0.001.

ESV_{GBPS} 0.78 EDV_{CMR} +8.44; R^2=0.79; SEE=10.26; r_S=0.86; p<0.001.

FIGURE 8

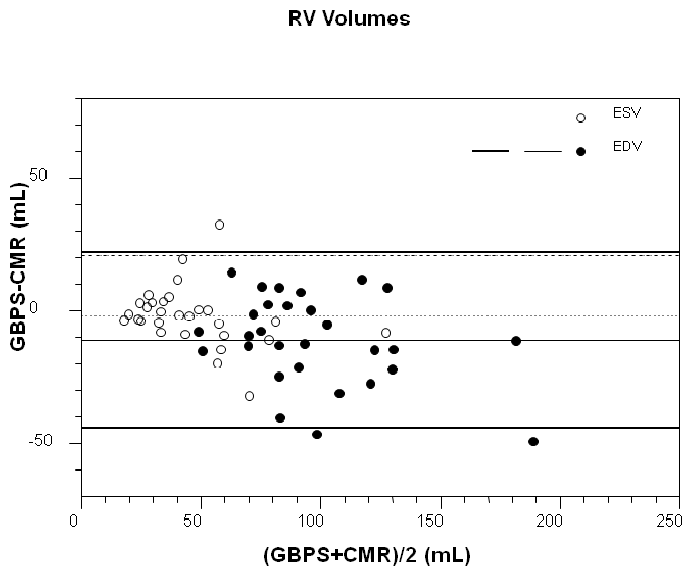

FIGURE 8 : Right ventricular (RV) end-diastolic (EDV) and end-systolic volumes (ESV) by Bland-Altman plotting. Horizontal lines indicate mean difference and 95% limits of agreement (95% LA).

Stroke Volumes

For the 24 patients without valvulopathy or shunt, LV SV and RV SV were respectively 54±18 mL; 47±15 mL for GBPS and 71±19mL; 56±21mL for CMR (**TABLE 1**). LV SV was significantly higher than RV SV with GBPS and CMR (respectively, p=0.003 and p<0.001). Means were significantly different between GBPS and CMR with, respectively, 9 ±14 mL and 18 ±13 mL (p=0.027).

Interoperator variability

GBPS interoperator variability is, respectively, 0.6%, 1.1% and 1.7% for the LV EF, EDV and ESV and 0.9%, 1.8% and 2.5% for the RV EF, EDV and ESV.

DISCUSSION

A few reports have compared GBPS with CMR measurements using current SSFP sequences [21,34-36]. Our investigation demonstrates that both left and right ventricular function can be simultaneously, easily and rapidly obtained using GBPS with a count-based method whose results are in close agreement with those provided by CMR. Correlations were found between GBPS and CMR for all parameters. Using only 8-frame GBPS, we did not find systematic underestimation of EF, confirming the results from previous reports [31,37]. The wider limits of agreement between GBPS and CMR for RV EF can be partly explained by the increased variability in the post-processing data for the RV using CMR *[13]* as well as GBPS [9,18]. With regard to CMR, this was mainly due to the difficulty of defining the most basal slice in the short-axis view and the upper limit of the RV between the ventricle and the pulmonary artery. Concerning GBPS, the pulmonary valve plane was chosen by detecting the changes in shape at the superior border of the RV at end-diastole. This inevitably introduced uncertainty but seemed to be more appropriate for patients with cardiac dilatation than the method used by Chin et al., who defined the upper border of the RV as the transverse slice above the superior border of the LV at end-diastole [38]. However, the clinical impact of such low variability has not been shown.

In spite of their totally different approaches (count-based for GBPS and based on modified Simpson's rule for CMR), the volume measurements were in quite close agreement. However, bias, trends and wider limits of agreement were found for the highest LV and RV volumes. Several factors may explain this finding. One is the self-attenuation by the blood pools of radiation emanating from ventricles. This assumption may be correct especially in patient with dilated cardiomyopathy. As large volumes are more influenced than smaller volumes by

radiation attenuation, this might partially explain the increasing volumes differences between GBPS and CMR. Volumes obtained by GBPS are probably slightly underestimated because of radiation attenuation; further study using CT based attenuation correction is necessary. Another factor is the inclusion of papillary muscles and trabeculations in performing CMR cavity drawings. Trabeculae significantly affect quantifications of LV volume [39]. Higher mean percentage differences between CMR and GBPS in ESV measurements than in EDV are in support of this hypothesis. Last, the use of the short axis in performing CMR measurements leads to the problem of determining atrioventricular planes on most basal slices. This generates more variability than the horizontal long-axis method for the RV [40] or the radial long-axis method for the LV [41].

Twenty-four subjects without any significant valvulopathy or ventricular communication were included in further analysis of SV. For these patients, it was clear that no difference between LV and RV SV should exist. Using CMR and GBPS independently to assess LV and RV SV, we found a significant difference for both techniques, with higher LV SV than RV SV. This confirmed previously published results comparing GBPS and thermodilution measurements [18]. The mean differences between SV were two times smaller using GBPS than CMR. However, Alfakih et al. found a smaller difference of 7.4 ±10.8 mL between LV and RV SV using CMR with the exclusion of two papillary muscles from the LV cavity (18 ±13 mL in our study) [40]. This result is in close agreement with our GBPS finding, thus indicating that a similar degree of accuracy in volume measurements can be obtained, with a more sophisticated and therefore less reproducible analysis of MRI studies.

CMR is often used for quantifying LV or RV EF and volumes. In this CMR, which does not use ionizing radiation, has one major advantage over scintigraphic techniques. Nevertheless, CMR is not widely available and has limited feasibility in

patients with implanted devices or claustrophobia. It also requires considerable expertise and involves time-consuming data processing (more than 30 minutes for both ventricles) because of the lack of a commercially available segmentation method. Cost should also be considered in the overall evaluation of the technique [42]. Manual or semiautomatic processing of CMR data also leads to decreased reproducibility, with a mean interobserver difference of -2.5 ±2.5% for LV EF and 2.9 ±5.8% for RV EF in healthy patients [43]. Our study demonstrates close correlation and agreement between EF and volumes assessed by GBPS and CMR. The results could be improved by modifications to both techniques and they need to be validated further in a larger number of patients with a greater frequency of severe dysfunction.

CONCLUSION

EF and volume measurements by GBPS showed correlation and close agreement with CMR calculations, with no need for a highly qualified physician and rapid procedures for data analysis. This suggests that this simple and widely available technique is a clinically useful tool for assessing both LV and RV functions.

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