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Routine breath-hold gradient echo MRI-derived right ventricular mass, volumes and function: accuracy, reproducibility and coherence study

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Abstract

Right ventricular (RV) dysfunction is a predictor of poor outcome in patients with heart disease. Conventional imaging modalities fail to assess RV volumes accurately. We sought to assess the accuracy and reproducibility of routine breath-hold gradient echo magnetic resonance imaging (MRI)-derived RV mass, volumes and function. We assessed: (1) The accuracy of in vivo MRI-derived RV mass in comparison to the RV weight in 9 minipigs. (2) Intra- and inter-observer reproducibility of RV mass, end-diastolic (EDV) and end-systolic (ESV) volumes and ejection fraction (EF) in 15 normal volunteers and 10 patients with heart disease. (3) Inter-study reproducibility of the former parameters in 25 coronary artery disease patients. (4) The correlation between right and left ventricular stroke volumes in the total population. Strong statistically significant correlations were found between: (1) MRI-derived RV mass and RV weight ($r = 0.98$, bias = 2.5 g), (2) Intra-observer measurements of RV mass ($r = 0.96$, bias = 0.5 g), EDV ($r = 0.99$, bias = −1.5 ml), ESV ($r = 0.98$, bias = 0.1 ml) and EF ($r = 0.92$, bias = −1.4%), (3) Inter-observer measurements of RV mass ($r = 0.95$, bias = 1.1 g), EDV ($r = 0.98$, bias = −1.1 ml), ESV ($r = 0.98$, bias = 1.2 ml) and EF ($r = 0.87$, bias = −1.9%), (4) Inter-study measurements of RV mass ($r = 0.91$, bias = −0.1 g), EDV ($r = 0.96$, bias = 3.8 ml), ESV ($r = 0.98$, bias = 0.3 ml) and EF ($r = 0.90$, bias = 0.9%), (5) MRI-derived right and left ventricular stroke volumes ($r = 0.87$). The assessment of the RV mass, volumes and function by routine breath-hold gradient echo MRI is accurate and highly reproducible. The correlation between left and RV MRI-derived stroke volumes indicates excellent coherence of simultaneous bi-ventricular volume measurements.

Abbreviations: EDV – end-diastolic volume; ESV – end-systolic volume; EF – ejection fraction; LV – left ventricular; MRI – magnetic resonance imaging; RV – right ventricular

Introduction

The major prognostic value of the left ventricular (LV) dimensions and function in diverse diseases of the heart is widely established [1, 2]. More recently the prognostic impact of right ventricular (RV) involvement in classically left side pathologies has become of interest, especially in the setting of coronary heart disease underlining the need for accurate imaging modalities of the right ventricle [3–5].

The assessment of RV mass, volumes and function by standard invasive or non-invasive imaging techniques is limited by the complex 3D shape of the RV, especially in patients with deformed or dilated RV.

Cine magnetic resonance imaging (MRI) is commonly used for the anatomic and functional assessment of the heart [6–9]. Nevertheless, while its accuracy and reproducibility have been widely demonstrated for the LV measurements [10–12], few studies have assessed the in vivo validity and reproducibility of the RV dimensions and function using routine cine-MRI methods.

We sought to assess the validity of in vivo MRI-derived RV mass, the intra-observer, inter-observer and inter-study reproducibility of the method and the coherence of the right and left ventricular MRI-derived volumes.

Methods

The study was approved by the ethics committee of the University Hospital of Angers and all patients gave informed consent. The animal investigation was conform to the position of the American Heart Association on research animal use.

Study population

Animal group

The animal population consisted of nine Yucatan male minipigs weighing 25 ± 16 kg (10–55 kg) who underwent MRI [13]. The animals were sacrificed immediately after the MRI. The ventricles were separated from the atria, great vessels and valves. The RV free wall was then dissected free from the left ventricle and the interventricular septum, and weighed at autopsy.

Human group

For the assessment of intra- and inter-observer reproducibility, 15 healthy young adults (6 female, 9 male, age 27 ± 8 years), 3 patients with aortic valvular stenosis (1 female, 2 male, age 67 ± 13 years) and 7 patients with a past history of AMI (all male, age 53 ± 11 years) gathered with the animal group were studied.

The inter-study reproducibility was assessed on 25 patients with a past history of anterior wall AMI (2 female, 23 male, age 54 ± 12 years) who underwent two MRI studies within 2 ± 1 months, without any clinical event during the interval.

Patients with intra- or extra-cardiac shunts or significant valvular regurgitation were not included in the study.

The coherence of left and right ventricular volumes was assessed in the global, animal and human population.

Imaging technique

Short axis MR studies were performed at 1.5 T (Signa Horizon release 5.7, GE Medical Systems, Milwaukee, Wisconsin, USA) after three pilot acquisitions as recommended [14]. Both ventricles were entirely imaged with a segmented K-space, breath-hold (15–25 s per slice) electrocardiogram-gated fast gradient echo sequence, using a cardiac phased array coil.

The study was performed with the following parameters: TR = 10.2 ms, TE = 2.7 ms, 1 excitation, partial echo, flip angle = 30°, 256 × 128 matrix, 32 cm square field of view, spatial resolution 1.25 × 2.5 mm^2, 8 views per segment, 12–26 phases per cardiac cycle, effective temporal resolution = 40.8 ms, slice thickness = 10 mm, inter-slice gap = 0 mm. The imaging technique is more widely detailed elsewhere [15].

Image analysis

For all studies, images were analysed on a multi-modality station (HP 715-50, Hewlett-Packard, Palo Alto, California, USA) with UNIX environment. The window and level settings were optimized for best contrast between myocardium and ventricular cavity on a mid-ventricular image and then appointed to all images. The identification of ventricles, atria and valves was supported by cine loop movies. The LV end-systolic – phase with smallest LV cavity- and end-diastolic – phase with

largest LV cavity-borders were drawn using a previously validated computer-assisted contour detection in-house software [16]. RV free wall was identified using images with the LV contours. RV end-diastolic and end-systolic endocardial and epicardial borders were manually drawn on each slice by two trained observers. The RV was separated from the right atrium on the most basal slice. The identification of the right atrioventricular ring was supported by the visualization of the right coronary artery. Both RV inflow and outflow were included in the quantification of volume up to the most basal slice in diastole but not in systole. Papillary muscles and moderator band were included in the mass and excluded from the volume. RV trabeculations were included in the mass only when attached to the RV free wall without interposition of cavity. The global RV mass, measured at end-diastole, and global volumes were calculated by the sum of slice's mass and volumes (Figure 1).

Statistical analysis

Continuous variables are presented as means ± SD. The correlation between anatomic and MRI-derived measurements and, the intra-observer, inter-observer and inter-study measurements was analysed using Student's paired *t* test and linear regression analysis. The variability of measurements was estimated by the variability index defined as the ratio of the absolute value of the difference between the measurements on the average of the measurements. The degree of agreement between measurements was assessed by Bland–Altman's repeatability analysis [17]. A p value of less than 0.05 was considered statistically significant.

Results

Validation study

The RV weight measured at autopsy (18.7 ± 9.1 g) was not different from any of the MRI-derived mass measurements (Table 1). There was a strong correlation (MRI-derived mass = $0.74 \times$ RV weight + 2.4, $r = 0.98$, $p < 0.001$) between MRI-derived mass and the weight of the RV free wall (Figure 2a). The Bland–Altman agreement analysis is shown in Figure 2b.

Reproducibility study

Intra-observer reproducibility

The two measurements of all RV parameters, performed by observer 1, were comparable, in the global group and all subgroups (Table 1). The two measurements of RV mass, EDV and ESV performed by observer 1 were strongly correlated

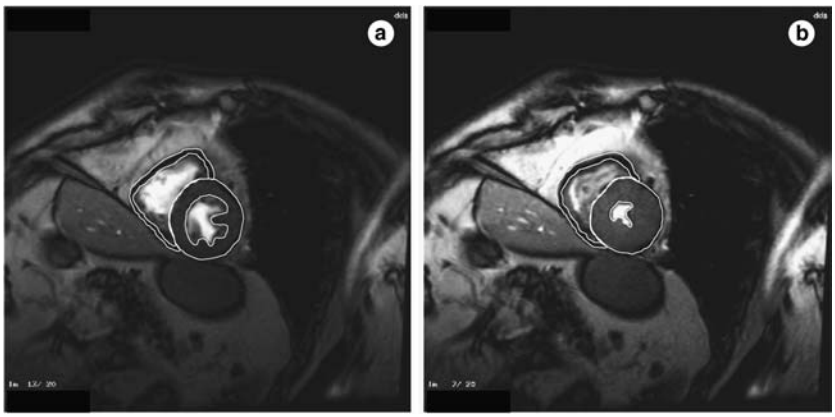

Figure 1. Representative short-axis mid-ventricular end-diastolic (a) and end-systolic (b) images in a normal volunteer.

Table 1. Intra- and inter-observer magnetic resonance imaging-derived right ventricular parameters

	Autopsy	Animal study (n = 9)			Healthy human adults (n = 15)			Heart disease patients (n = 10)		
		Obs 1 Measure 1	Obs 1 Measure 2	Obs 2	Obs 1 Measure 1	Obs 1 Measure 2	Obs 2	Obs 1 Measure 1	Obs 1 Measure 2	Obs 2
Mass, g	18.7 ± 9.1	16 ± 7	17 ± 7	15 ± 6	30 ± 6	29 ± 6	29 ± 6	33 ± 5	32 ± 4	32 ± 4
Volumes, ml										
End diastolic	–	39 ± 19	37 ± 17	40 ± 18	97 ± 27	100 ± 29	95 ± 23	116 ± 30	118 ± 30	122 ± 26
End systolic	–	15 ± 8	14 ± 7	16 ± 7	52 ± 19	52 ± 21	48 ± 19	56 ± 18	56 ± 22	56 ± 17
Ejection fraction, %	–	61 ± 11	62 ± 11	61 ± 9	47 ± 10	48 ± 10	50 ± 10	52 ± 6	54 ± 7	54 ± 8

Obs. – observer.

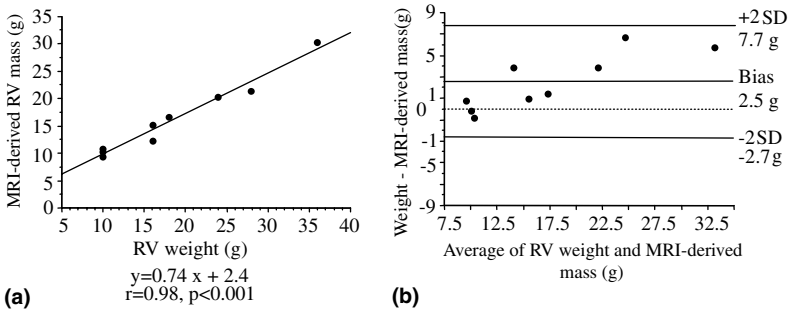

Figure 2. Comparison of MRI-derived right ventricular mass and right ventricular weight at autopsy in minipigs MRI: magnetic resonance imaging, RV: right ventricular. (a) Correlation study. (b) Bland–Altman agreement analysis.

($r = 0.96$, 0.99 and 0.98 respectively, $p < 0.0001$ for all). The measurements of the RV EF were significantly but less strongly correlated ($r = 0.92$, $p < 0.0001$). The intra-observer variability indexes were 8.1, 6.6, 8.1, and 6.7% for mass, EDV, ESV and ejection fraction (EF), respectively. The Bland–Altman intra-observer repeatability analysis is summarized in Table 2.

Inter-observer reproducibility

The measurements of all RV parameters, performed by observers 1 and 2, were comparable, in

Table 2. Bland–Altman repeatability analysis for right ventricular parameter

	Interobserver reproducibility (n = 34)			Intraobserver reproducibility (n = 34)			Interstudy reproducibility (n = 25)		
	Bias	Limits of agreement	SDD	Bias	Limits of agreement	SDD	Bias	Limits of agreement	SDD
Mass, g	0.5	−4.7 to 5.7	2.6	1.1	−4.5 to 6.7	2.8	−0.1	−8.5 to 8.3	4.2
Volumes, ml									
End-diastolic	−1.6	−16.2 to 13	7.3	−1.1	−18.1 to 15.9	8.5	3.8	−18.2 to 25.8	11
End-systolic	0.1	−10.1 to 10.3	5.5	1.2	−9.2 to 11.6	6	0.3	−12.1 to 12.7	24.8
Ejection fraction, %	−1.5	−10.1 to 7.1	4.3	0.5	−12.3 to 8.5	5.2	0.9	−10.7 to 12.5	5.8

SDD – standard deviation of the difference.

the global group and all subgroups (Table 1). As for the intra-observer reproducibility, the measurements of RV mass, EDV and ESV performed by the two observers were strongly correlated ($r = 0.95$, 0.98 and 0.98, respectively, $p < 0.0001$ for all) while the measurements of the RV EF were less strongly correlated ($r = 0.87$, $p < 0.0001$). The inter-observer variability indexes were 8.9, 7.9, 9.6 and 8.3% for mass, EDV, ESV and EF, respectively. The Bland–Altman inter-observer repeatability analysis is summarized in Table 2.

Inter-study reproducibility

The MRI derived RV mass (36 ± 9 vs. 36 ± 10 g), EDV (117 ± 38 vs. 114 ± 42 ml), ESV (65 ± 29 vs. 65 ± 36 ml) and EF (45 ± 13 vs. 44 ± 11%) were comparable between the two studies. The correlation between the measurements was statistically significant for all parameters but stronger for the measurements of EDV and ESV ($r = 0.96$ and 0.98 respectively, $p < 0.0001$ for both) compared to the measurements of mass ($r = 0.91$, $p < 0.0001$) and EF ($r = 0.90$, $p < 0.0001$). The inter-study variability indexes were 8.5, 8.1, 9.4 and 9.4% for mass, EDV, ESV and EF, respectively. The Bland–Altman analysis for the inter-study repeatability is summarized in Table 2.

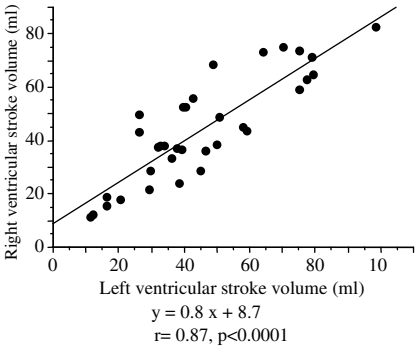

Figure 3. Correlation between right and left ventricular stroke volumes.

Comparison of left and right ventricular stroke volumes (Figure 3)

Left and right ventricular stroke volumes were comparable (45.3 ± 21.2 vs. 45 ± 19.8, $p = \text{NS}$) and strongly correlated ($r = 0.87$, $p < 0.0001$).

Discussion

Our data show that: (1) The in vivo measurement of RV mass by routine gradient echo MRI is highly accurate. (2) The assessment of RV mass, volumes and EF are reproducible between measurements, operators and studies. (3) The quantification of RV volumes by MRI is coherent with LV volumes as indicated by similar and strongly correlated right and left ventricular stroke volumes.

RV hypertrophy, dilatation and dysfunction are commonly observed as a consequence of pressure or volume overload in patients with congenital heart disease, valvular heart disease and congestive heart failure [18, 19]. Direct alteration of RV myocardium in the setting of acute myocardial infarction is also associated with RV enlargement and dysfunction. The involvement of the right ventricle in these settings is a strong and independent predictor of mortality [4, 5, 20, 21].

Various invasive – conventional angiography- and non-invasive methods – echocardiography and radionuclide angiography – have been used to assess the RV dimensions and function. The complex 3-dimensional anatomy of the RV is a major obstacle to the accurate assessment of the RV with such methods, using geometric assumptions of the RV anatomy. Such methods are poorly accurate in normal hearts and invalid in deformed hearts [22–25].

While breath-hold segmented *k*-space gradient echo MRI is commonly used for the assessment of the heart, our study is the first to report the validity of this method in the assessment of RV mass and its reproducibility. Other MRI sequences could be used for the assessment of the RV. However, breath-hold segmented *k*-space acquisition provides a better spatial and temporal resolutions and reduced motion artifacts compared to

standard gradient echo imaging and spin echo imaging [26, 27]. Newer sequences such as steady-state free precession (SSFP) MRI with enhanced contrast between blood and myocardium, especially on the long axis images, have been recently developed [28]. Such sequences need extremely fast gradients available only on very recent MRI machines and are associated with reduced myocardial signal to noise ratio and increased specific absorption rates. Compared to SSFP imaging, gradient echo imaging is reported to underestimate volumes and overestimate mass [29]. Nevertheless, gradient echo imaging is widely validated and used for the assessment of LV dimensions and function. Our study extends its use to routine assessment of RV mass, dimensions and function. Furthermore, the clinical relevance of the superiority of SSFP imaging compared to gradient echo imaging is doubtful. Finally the assessment of ventricular dimensions and function appears not to be totally interchangeable between imaging modalities and MRI sequences [29]. Hence disposing of easily accessible, reproducible, accurate imaging modalities of ventricles is of clinical importance. Breath-hold gradient echo imaging provides accurate, widely accessible and reproducible images of right and left ventricles that could be used for the assessment and follow-up of ventricular dimensions and function in all patients with heart disease.

In our study, the intra-observer, inter-observer and inter-study variability of the method in the assessment of the RV parameters is extremely low and comparable to those reported for the LV parameters [10, 11, 25]. This results not only in an accurate assessment of RV dimensions in clinical routine, but also in a reduction of the sample size in clinical trials [12].

We studied the reproducibility of RV parameters in healthy adults and patients with various heart diseases and a wide range of mass and volume values. The absence of systematic error in this heterogeneous population confirms the robustness of MRI-derived RV mass and volumes (Table 3).

The less strong correlation between RV mass and EF measurements compared to volume quantification is predictable as the variability is logically increased when more than one volume measurement is used for the assessment of mass and EF.

Table 3. Inter-study magnetic resonance imaging-derived right ventricular parameters

	Study 1 (n = 25)	Study 2 (n = 25)
Mass, g	36 ± 9	36 ± 10
Volumes, ml		
End diastolic	117 ± 38	114 ± 42
End systolic	65 ± 29	65 ± 36
Ejection frction, %	45 ± 13	44 ± 11

A previous study [30] has shown poor correlation between right and left ventricular EFs both in normal volunteers and patients. RV EDV and ESV are highly variable depending on position, respiratory phases, pre-load status and diverse heart or lung pathologies. This explains the expected difference between right and left ventricular EFs and also underlines the difficulties to determine normal RV EF values. In absence of significant intra or extra cardiac shunts, the right and left stroke volumes are almost equivalent, as the bronchial circulation physiologic shunt could be considered as non-significant. Our study demonstrates the coherence of MRI-derived volumes, between left and right ventricles, by showing the equivalence of right and left ventricular stroke volumes.

Study limitations

The drawbacks to the MRI technique used in our study concern patients with severe cardiac or pulmonary disease unable of keeping an apnea of about 15–25 s, those with cardiac arrhythmia disturbing the ECG synchronization, and more generally patients who present a contraindication to MRI.

Another limitation to the method is the time consuming manual contour detection. Our software used for the computer-assisted detection of the LV contours failed to detect accurately the RV contours, because of the complex shape of the RV. To our knowledge, there are no commercially available accurate RV contour detection software. Future effort might be done to develop such software. Newer imaging sequences such as SSFP,

providing enhanced contrast between blood and myocardium might facilitate automated RV contour detection.

Finally our experimental study on animals might be underpowered to reveal a systematic error in the measurement of the RV mass. Nevertheless the correlation between MRI-derived mass and RV weight remains highly significant.

Conclusions

Our study shows that breath-hold segmented *k*-space MRI is highly accurate in the quantification of the RV mass. It provides highly reproducible measurements of RV mass, volumes and function. We also demonstrated the equivalence and the correlation of left and right ventricular MRI-derived stroke volumes indicating the coherence of simultaneous left and right ventricular volume quantifications. Future studies using this routine imaging modality, available on almost all MRI systems, might be done to assess the prognostic value of MRI-derived RV parameters not only in right but also in left side pathologies.

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