Right ventricular remodelling in pulmonary arterial hypertension with three-dimensional echocardiography: comparison with cardiac magnetic resonance imaging

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Aims
Right ventricular (RV) mass and volume calculations are important correlates of survival in patients with pulmonary arterial hypertension (PAH). We tested the hypothesis that RV mass, volumes and function could be measured accurately with real-time three-dimensional echocardiography (3DE) in patients with PAH and compared those against cardiac magnetic resonance (CMR).

Methods and results
Sixty consecutive PAH patients and 20 normals were examined with 3DE and CMR. RV end-diastolic volumes (EDV), end-systolic (ESV), stroke volume (SV), ejection fraction (EF), and mass were measured in all patients and in normals. Two independent observers assessed variability using the Bland–Altman analysis agreement. RV volumes (in mL) and mass were similar between 3DE and CMR in PAH patients: [EDV (in mL) 183.2 ± 38 vs. 187.3 ± 41, P = 0.32; ESV (in mL) 122 ± 33 vs. 126 ± 36, P = 0.99; SV (in mL) 63 ± 15 vs. 65 ± 19, P = 0.06; EF (in %) 33 ± 7 vs. 31 ± 9, P = 0.16 and RV mass (g) 99 ± 20 vs. 96 ± 22, P = 0.42], respectively. Interobserver variability was similar between 3DE and CMR in PAH for all variables, with CMR showing less interobserver variability for EDV compared with 3DE in both patients and normals (patients: mean bias: CMR-EDV: 0.4 ± 16 mL vs. 3DE-EDV: 6.9 ± 17.9 and in normals: CMR-EDV: 0.1 ± 9.8 vs. 3DE-EDV: 5.7 ± 16.3, respectively), whereas EF and RV mass were poorly reproducible with no correlation between observers for 3DE and CMR.

Conclusions
RV remodelling in PAH patients can be accurately assessed with both 3DE and CMR. Both modalities are robust and reproducible with CMR being more reproducible for measurements of EF and RV mass.

Keywords
Pulmonary arterial hypertension • Right ventricle • 3D echocardiography • Cardiac magnetic resonance imaging

Introduction
Right ventricular (RV) remodelling in pulmonary arterial hypertension (PAH) is characterized by dilatation and hypertrophy resulting in ventricular impairment, low cardiac output, and heart failure.1,2 Measuring RV volumes with two-dimensional echocardiography (2DE) is challenging due to its crescentic shape.3,4 In addition, the coarse trabeculations make the identification of endocardial borders hard to define with either cardiac magnetic resonance (CMR) or three-dimensional echocardiography (3DE). Many studies have used 3DE as an equivalent modality to CMR for volumetry of the left ventricle.5–8 Few studies, however, have attempted to examine the RV and those were predominantly in patients with congenital heart disease, or with left heart disease.9–14

In the present study, we hypothesized that 3DE could be used to provide reliable measurements of RV volumes and mass in PAH patients and normal individuals. To test this hypothesis,
the 3DE data were compared against CMR, both in patients and in normals.

**Methods**

Sixty consecutive newly diagnosed patients with PAH and 20 age-matched normal volunteers were examined with 3DE and CMR. Patients were diagnosed during right heart catheterization and conventional 2DE. They all had an RV systolic pressure (RVSP) more than 30 mmHg, pulmonary vascular resistance (PVR) more than 3 Wood units, and pulmonary capillary wedge pressure (PCWP) <15 mmHg, to exclude co-existing left ventricular failure. During catheterization, cardiac output was determined with the Fick principle. Thromboembolic disease was excluded during contrast-enhanced pulmonary angiography using a multidetector helical computed tomography scanner (Lightspeed Ultra, GE Medical Systems, Milwaukee, WI, USA) with a collimation of 1.25 mm, which was negative in all patients. Additionally, restrictive and obstructive lung disease, as diagnosed with lung function tests, were ruled-out from the study. None of the patients included in the study had underlying lung disease. Patients had right heart catheterization within a month of non-invasive imaging with a mean interval of 14 ± 7.2 days.

Two-dimensional, 3DE, and CMR were performed within 2 h of each other. Only patients with PAH were included, excluding those with coexistent left heart disease (impairment of systolic or diastolic function) or arrhythmia, such as atrial fibrillation. Thirty-four patients had idiopathic PAH, 9 associated with a congenital left to right intracardiac shunt, 1 had human immunodeficiency virus (HIV), and 16 patients had PAH associated with collagen vascular disease.

A comprehensive baseline 2DE examination was first performed for the detailed anatomic description and estimation of pulmonary pressures. RVSP was calculated from the maximal velocity of tricuspid regurgitation (TR) and right atrial pressure (RAP) using the Bernoulli’s equation (RVSP = 4TR² + RAP). RAP was estimated by the respiratory motion and the size of the inferior vena cava from the subcostal view.

All 60 patients and the 20 normals were assessed for RV volumes, EF and RV mass. The study was approved by the local ethics committee and the subjects gave written informed consent. The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written.

**Real-time three-dimensional echocardiography**

**Acquisition**

All examinations were performed by the same operator (3 years of experience on 2DE and 3DE with European Accreditation). 3DE acquisitions were obtained using the GE Vivid 7 scanner (Horton Norway) equipped with a central X4 transducer (frequency of 3–4 MHz, volumetric frame rate 16–24 frame/s, imaging depth 6–16 cm, rotation speed 6 Hz, and pulse length 2.5 cycles). Images were acquired from apical four-chamber views with the patient in the left decubitus position during a breath hold of 7 s. Care was taken for the views to be acquired laterally while on the apical four-chamber view, for RV optimization. In addition, the depth and width were adjusted to include the RV apex.

**Post processing**

Images were then transferred to an offline workstation (4D analysis, TomTec, Munich, Germany). Serial short-axis reconstructions of the RV volumetric data sets were then obtained, and endocardial contour was traced at 7 mm intervals with cross-reference to long-axis images for identification of the tricuspid annulus. This protocol is identical to the one used in CMR. End-diastolic phase was defined as the peak of the R-wave of the QRS complex and end-systolic as the first frame before opening of the tricuspid valve. Papillary muscles and trabeculations were excluded from endocardial mapping. End-diastolic and end-systolic RV volumes and EF were calculated offline using the method of summation of discs and semi-automated border detection. SV was calculated by the subtraction of the ESV from EDV, while EF was calculated as EDV-ESV/EDV. Valve opening and closure were identified for the accurate volume determination (Figure 1).

Using the same full-volume 3DE data set, epicardial boundaries of the RV wall were identified and traced to calculate an epicardial cast of the RV at end-diastole. The volume of this cast was then subtracted from the endocardial cast and the volume of RV myocardium was derived. By multiplying myocardial volume by the density of myocardial muscle (1.05 g/mL), RV mass was calculated. Care was taken to distinguish the endocardium of the ventricular septum with 3DE and CMR alike.

**Cardiac magnetic resonance imaging**

**Acquisition**

All acquisitions were obtained by the same radiologist at consultant level, expert in CMR imaging using a 1.5 T Philips Achieva system (Best, Netherlands). A five-element cardiac-phased array receiver coil was used and retrospective cardiac gating was achieved with a vector-ECG system. Axial slices of the RV from base to apex were planned from horizontal and vertical long-axis images of the heart in the plane of the atrioventricular groove (short axis). At the basal slice, non-trabeculated atrium was excluded from the RV cavity measurement. A balanced steady-state free precession (b-SSFP) sequence was used for image acquisition using the following parameters: matrix, 176 × 256, flip angle, 60°; field of view, 350 mm; slice thickness, 8 mm with a 2 mm gap; TE, 1.5 ms; TR, 3.0 ms; and 30 cardiac phases.

None of the patients were excluded due to claustrophobia.

**Post processing**

Images were reviewed by two observers using View Forum software (Philips). Manual delineation was used to generate areas for RV endocardium and epicardium in end-diastole and endocardium in end-systole. These time points were defined by the largest and smallest endocardial areas. The method of disk summation was then employed to provide volumetric and mass data for the RV. Trabeculations were not included in the RV myocardium, but were included in blood pool (Figure 1).

The same protocol for RV mass was used both for 3DE and CMR measurements.

**Statistical analysis**

Right ventricular volumes and mass were calculated in both patients and normals. Two observers with equal experience in both 3DE and CMR were employed for the assessment of inter-observer variability. Results were expressed as mean ± SD with 95% confidence intervals (CIs). All data were normally distributed. First, systematic differences in measurements were assessed with Student’s t-test. Analysis was performed with SPSS 13.0. A P-value of <0.05 was considered significant. Volumes, EF, and RV mass measurements obtained by 3DE and CMR were also compared using Bland–Altman method of analysis of agreement.

Mean values were used for the assessment of agreement between the two modalities. Intraclass correlation (ICC), as an absolute value, was used to measure inter-rater reliability between 3DE and CMR. Interobserver variability was expressed as an absolute value.
Figure 1 Real-time three-dimensional echocardiography and cardiac magnetic resonance analysis. (A) Three-dimensional echocardiography images were transferred to an offline workstation (four-dimensional analysis, TomTec), serial short-axis reconstruction of the right ventricular were obtained and endocardial contour was traced in end-diastole and end-systole. As a result of disk summation, the volumes and ejection fraction derived. (B) The same protocol was used for cardiac magnetic resonance analysis with View Forum Software (Philips). Manual delineation was used to generate areas for right ventricular endocardium in end-diastole and in end-systole.
For 3DE, test–retest variability was assessed by measuring two different sequences, which were obtained on the same day.

**Results**

Of the 60 PAH patients, 27 (45%) were receiving bosentan (endothelin antagonist), 31 patients (51.6%) sildenafil (PEG5 antagonist), and 2 patients (3.3%) were under prostanoid infusion, which was removed during the CMR imaging.

Forty-seven patients were women (78.3%), 45 were white (75%), 4 were Afrocaribbean (6.6%), and 11 (18.4%) were Asian. Four patients (6.6%) had body mass index

Of the 20 normals, 16 (80%) were women and all were White European.

Patients’ age was 42.8 ± 18.3 years with a heart rate of 77 ± 13 bpm, all in sinus rhythm. Mean weight was 67 ± 10.4 kg and mean height 170 ± 9.8 cm. Mean body surface area was 1.76 ± 0.18 cm² (range 1.4–2.3 cm²). In PAH patients, mean TR velocity was 4.3 ± 0.7 m/s, with mean estimated RVSP of 83.5 ± 25.3 mmHg. From the right heart catheterization, mean PCWP was 10.3 ± 2.8 mmHg and mean PVR 10.5 ± 1.9 Wood units. Mean PA pressure was 58 ± 11.6 mmHg.

In normals, the mean age was 39 ± 16.2 years, with a mean heart rate 79 ± 9.3 bpm. Mean weight was 65 ± 10.7 kg; height 171 ± 11.7 cm and body surface area 1.8 ± 0.19 cm² (range 1.4–2.2 cm²). Body surface area was matched in the two groups (P = 0.32). Mean TR velocity was 1.8 ± 0.4 m/s with a mean RVSP of 22.5 ± 6.3 mmHg.

**Volume calculations**

**Patients**

In patients, EDV, ESV, and EF were similar between 3DE and CMR. There was a trend towards SV underestimation (3%) with 3DE when compared with CMR. RV mass measured by 3DE was also similar to that measured by CMR (Table 1).

**Normal volunteers**

In normals, EDV, ESV, and EF were similar between 3DE and CMR. SV were similar, however mildly underestimated by 3DE (6%). RV mass was similar between 3DE and CMR (Table 2).

**Bland–Altman agreement between real-time three-dimensional echocardiography and cardiac magnetic resonance for right ventricular volumes in pulmonary hypertensives and normal volunteers**

**Volumes**

**Patients**

In PAH patients, EDV and ESV showed good agreement between 3DE and CMR (Figure 2) with an ICC of r = 0.74 and r = 0.75
respectively. For the SV, there was a moderate degree of agreement \((r = 0.5)\). There was also a moderate degree of agreement for 3DE and CMR for EF \((r = 0.66, \text{ Table 3})\); however, there was a discrepancy in measurements only in four patients \((6.6\%)\).

**Normals**

In normal volunteers, EDV and ESV also showed good agreement between 3DE and CMR: \(r = 0.89\) and \(r = 0.8\), respectively (Figure 3). There was also a strong agreement between 3DE and CMR for SV \((r = 0.9)\) and for EF with narrow limits of agreement \((r = 0.6)\) (Table 3).

**Bland–Altman agreement between RV mass measurement from both modalities (Table 3)**

In PAH, there was a moderate agreement \((r = 0.63, \text{ mean bias} = 1.9 \text{ g}, \text{ SD} = 18.3 \text{ g})\) for RV mass calculation between 3DE and CMR.

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**Table 1** Pulmonary arterial hypertension patients

<table>
<thead>
<tr>
<th>Measurements</th>
<th>3DE*</th>
<th>CMRa</th>
<th>P-value (Student’s t-test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDV (mL)</td>
<td>183.2 (38) (103–309, 0.9)</td>
<td>187.3 (41) (99–278.5, 0.92)</td>
<td>0.32</td>
</tr>
<tr>
<td>ESV (mL)</td>
<td>122.3 (33) (66–222.5, 0.89)</td>
<td>126.3 (36) (55–223, 0.92)</td>
<td>0.99</td>
</tr>
<tr>
<td>SV (mL)</td>
<td>63 (15) (21.5–87.5, 0.6)</td>
<td>65 (19) (31–108, 0.78)</td>
<td>0.06</td>
</tr>
<tr>
<td>EF (%)</td>
<td>33 (7) (18.5–49.0, 0.67)</td>
<td>31 (9) (18–54, 0.84)</td>
<td>0.16</td>
</tr>
<tr>
<td>RVmass (g)</td>
<td>99 (20) (54.3–149.5, 0.67)</td>
<td>96 (22) (50–181, 0.73)</td>
<td>0.42</td>
</tr>
</tbody>
</table>

Measurements of RV volumes, function, and mass calculated as mean from both observers for both 3DE and CMR.

3DE, three-dimensional echocardiography; CMR, cardiac magnetic resonance; EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; ICC, intraclass correlation coefficient; RV, right ventricle; SD, standard deviation; SV, stroke volume.

*All values are mean (SD) (range, ICC).

**Table 2** Normal volunteers

<table>
<thead>
<tr>
<th>Measurements</th>
<th>3DE*</th>
<th>CMRa</th>
<th>P-value (Student’s t-test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDV (mL)</td>
<td>88.2 (17.1) (56.2–123.4, 0.56)</td>
<td>92.8 (14.5) (64.3–111.6, 0.79)</td>
<td>0.34</td>
</tr>
<tr>
<td>ESV (mL)</td>
<td>37 (8.1) (22.5–52.7, 0.46)</td>
<td>32 (7.6) (21.8–49.7, 0.54)</td>
<td>0.47</td>
</tr>
<tr>
<td>SV (mL)</td>
<td>51.1 (8.8) (33.2–64.7, 0.63)</td>
<td>54.4 (11) (36.6–74.5, 0.71)</td>
<td>0.01</td>
</tr>
<tr>
<td>EF (%)</td>
<td>61 (3.8) (56.7–67.5, 0.12)</td>
<td>61.7 (5.6) (56.9–71.6, 0.45)</td>
<td>0.16</td>
</tr>
<tr>
<td>RVmass (g)</td>
<td>62.3 (10.6) (38.1–79.2, 0.21)</td>
<td>61 (13.2) (37.3–85.2, 0.65)</td>
<td>0.98</td>
</tr>
</tbody>
</table>

Measurements of RV volumes, function, and mass calculated as mean from both observers for both 3DE and CMR.

3DE, three-dimensional echocardiography; CMR, cardiac magnetic resonance; EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; ICC, intraclass correlation coefficient; RV, right ventricle; SD, standard deviation; SV, stroke volume.

*All values are mean (SD) (range, ICC).

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Figure 2 Bland–Altman agreement analysis between three-dimensional echocardiography and cardiac magnetic resonance for right ventricular end-diastolic volumes and right ventricular-ejection fraction.
CMR. In normals, 3DE and CMR had equally good correlations ($r = 0.64$) with a small bias (mean bias $-0.3$ g, SD $10.3$ g).

### Interobserver variability

#### Patients

For EDV, both 3DE and CMR showed low inter-observer variability (3DE: ICC = 0.89, variability: $15.1 \pm 9.8$ mL, and for CMR ICC = 0.92, variability: $11 \pm 8.4$ mL) with CMR showing less bias (Table 4). Similarly, for ESV there was low variability between 3DE and CMR (variability: $13 \pm 9$ mL, CMR-ESV: $8 \pm 10.2$ mL) but with CMR being slightly superior with less bias in measurements (3DE ICC = 0.89 and with CMR ICC = 0.92). There was a decreased variability between 3DE and CMR for SV with 3DE showing less bias (3DE: ICC = 0.59, variability: $7.1 \pm 10.6$ mL and with CMR: ICC = 0.78, variability: $9 \pm 8.6$ mL) (Figure 4). Variability of EF was better with CMR (ICC = 0.85, variability: $3 \pm 3.6$%) compared with 3DE (ICC = 0.67, variability: $3 \pm 4.3$%) (Figure 4). Finally, RV mass showed low variability for both imaging modalities (3DE ICC = 0.63, variability: $17 \pm 14.4$ g mean bias: $-16.8$ g, SD $17.9$ and for CMR ICC = 0.73, variability: $12 \pm 11.3$ g, mean bias: $-6.3$ g, SD $17.7$) with CMR having less bias and SD than 3DE.

#### Normal volunteers

EDV showed low interobserver variability with both modalities, but there was a better agreement and less bias with CMR compared with 3DE (3DE ICC = 0.56, variability: $10.7 \pm 10.6$ mL and CMR ICC = 0.79, variability: $3.8 \pm 6.7$ mL). ESV was more variable when measured with 3DE than EDV than CMR, with similar bias (Table 4) (3DE ICC = 0.46, variability: $9.2 \pm 5.2$ mL and for CMR ICC = 0.54, variability: $2.5 \pm 6.5$ mL).

### Table 3  Bland–Altman agreement analysis between three-dimensional echocardiography and cardiac magnetic resonance for right ventricular volumes, ejection fraction and mass, in pulmonary arterial hypertension patients and normal subjects

<table>
<thead>
<tr>
<th>Measurements</th>
<th>3DE, mean (SD)</th>
<th>CMR, mean (SD)</th>
<th>ICC</th>
<th>P-value</th>
<th>Mean bias</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAH (n = 60)</td>
<td></td>
<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>EDV (mL)</td>
<td>183.2 (38.2)</td>
<td>187.3 (40.9)</td>
<td>0.74</td>
<td>&lt;0.001</td>
<td>-3.7</td>
<td>28.7</td>
</tr>
<tr>
<td>ESV (mL)</td>
<td>121.8 (33)</td>
<td>125.6 (35.9)</td>
<td>0.75</td>
<td>&lt;0.001</td>
<td>-0.2</td>
<td>24.4</td>
</tr>
<tr>
<td>SV (mL)</td>
<td>62.6 (14.7)</td>
<td>64.5 (18.5)</td>
<td>0.56</td>
<td>&lt;0.001</td>
<td>-4</td>
<td>15.8</td>
</tr>
<tr>
<td>EF (%)</td>
<td>32.8 (7.1)</td>
<td>313.9 (9.3)</td>
<td>0.66</td>
<td>0.005</td>
<td>-1.3</td>
<td>7.1</td>
</tr>
<tr>
<td>RV mass (g)</td>
<td>99.3 (19.9)</td>
<td>96 (22.4)</td>
<td>0.63</td>
<td>0.001</td>
<td>1.9</td>
<td>18.3</td>
</tr>
<tr>
<td>Normals (n = 20)</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EDV (mL)</td>
<td>88.2 (17.1)</td>
<td>92.8 (14.5)</td>
<td>0.89</td>
<td>&lt;0.001</td>
<td>-1.5</td>
<td>7</td>
</tr>
<tr>
<td>ESV (mL)</td>
<td>37 (8.1)</td>
<td>32 (7.6)</td>
<td>0.8</td>
<td>&lt;0.001</td>
<td>0.8</td>
<td>4.9</td>
</tr>
<tr>
<td>SV (mL)</td>
<td>51.1 (8.8)</td>
<td>54.4 (15)</td>
<td>0.9</td>
<td>&lt;0.001</td>
<td>-2.8</td>
<td>4.8</td>
</tr>
<tr>
<td>EF (%)</td>
<td>61 (3.8)</td>
<td>61.7 (5.6)</td>
<td>0.68</td>
<td>0.0009</td>
<td>-1.3</td>
<td>4.1</td>
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<tr>
<td>RV mass (g)</td>
<td>62.3 (10.6)</td>
<td>61 (13.2)</td>
<td>0.64</td>
<td>0.0023</td>
<td>-0.3</td>
<td>10.3</td>
</tr>
</tbody>
</table>

3DE, three-dimensional echocardiography; CMR, cardiac magnetic resonance; EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; ICC, intraclass correlation coefficient; RV, right ventricle; SD, standard deviation; SV, stroke volume.

### Figure 3  Bland-Altman agreement analysis between three-dimensional echocardiography and cardiac magnetic resonance, in normal volunteers for right ventricular end-diastolic volumes and right ventricular-ejection fraction.
SV was similarly variable with both modalities (variability: 3DE-SV: 3.6 ± 6.9 mL and CMR-SV: 3 ± 6.8 mL) but with CMR showing less bias (3DE ICC = 0.63 and for CMR ICC = 0.71) (Figure 6).

There was significant variability between observers for EF with 3DE compared with CMR (3DE ICC = 0.12, P = 0.6) and for CMR ICC = 0.45, variability: 3.2 ± 5.1%) (Figure 5). Finally, RV mass was poorly reproducible with 3DE compared with CMR, which had a lower variability (3DE ICC = 0.21, P = 0.36 and for CMR ICC = 0.65, variability: 6.1 ± 8.3 g, mean bias 2.1 g, SD 12).

Test–retest reproducibility for three-dimensional echocardiography

There was high intra-class correlation between the measurements of two different sequences. The SD of bias was very low and Bland–Altman plot demonstrated no significant dispersion (Figure 6): 3DE-EDV (T): ICC = 0.96, mean bias −1.7 mL, SD 10.7 mL, 3DE-ESV (T): ICC = 0.95, mean bias −4.1 mL, SD 10.3 mL, 3DE-SV (T): ICC = 0.8, mean bias −1.1 mL, SD 10.6 mL, 3DE-EF (T): ICC = 0.83, mean bias 0.5%, SD 4.5%, 3DE-RVmass (T): ICC = 0.8, mean bias −8.8 g, SD 14.4 g.

### Table 4 Bland–Altman agreement analysis for reproducibility between two observers (inter-observer)

<table>
<thead>
<tr>
<th></th>
<th>3DE, mean bias (SD)</th>
<th>CMR, mean bias (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PAH (n = 60)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EDV (mL)</td>
<td>−6.9 (17.6)</td>
<td>−0.4 (16)</td>
</tr>
<tr>
<td>ESV (mL)</td>
<td>−5.8 (16)</td>
<td>3.1 (14.7)</td>
</tr>
<tr>
<td>SV (mL)</td>
<td>−1.9 (14.9)</td>
<td>−3.6 (13)</td>
</tr>
<tr>
<td>EF (%)</td>
<td>1.3 (6.3)</td>
<td>−1.3 (5.4)</td>
</tr>
<tr>
<td>RV mass (g)</td>
<td>−16.8 (17.9)</td>
<td>−6.3 (17.7)</td>
</tr>
<tr>
<td><strong>Normals (n = 20)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EDV (mL)</td>
<td>−5.7 (16.3)</td>
<td>−0.1 (9.8)</td>
</tr>
<tr>
<td>ESV (mL)</td>
<td>−0.9 (10)</td>
<td>−1.7 (8.3)</td>
</tr>
<tr>
<td>SV (mL)</td>
<td>−4.9 (8.5)</td>
<td>0.6 (9.3)</td>
</tr>
<tr>
<td>EF (%)</td>
<td>NC</td>
<td>0.4 (7.3)</td>
</tr>
<tr>
<td>RV mass (g)</td>
<td>NC</td>
<td>−2.1 (12)</td>
</tr>
</tbody>
</table>

3DE, three-dimensional echocardiography; CMR, cardiac magnetic resonance; EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; NC, non-significant intraclass correlation; RV, right ventricle; SD, standard deviation; SV, stroke volume.

**Figure 4** PAH patients: Bland-Altman agreement analysis for inter-observer variability for right ventricular end-systolic volumes and right ventricular-ejection fraction, as estimated with three-dimensional echocardiography and cardiac magnetic resonance.
Discussion

In this study, we have demonstrated that 3DE is a feasible method for examining RV remodelling in PAH with comparable accuracy to CMR. There is a greater degree of agreement for EDV and ESV, but less for EF and RV mass. While volumes and RV mass were similar between the two modalities in patients and normals, CMR was superior in assessing RV volumes and mass in normal subjects by showing less variability of measurements.

Three-dimensional echocardiography in pulmonary hypertension

Three-dimensional echocardiography is entering the routine echocardiographic examination and has many advantages by reducing the time of the examination, but also producing some more robust measurements for RV volumes when compared with 2DE. It is necessary, however, to fully evaluate its accuracy and understand the limitations when compared with other imaging modalities. While 3DE has proved accuracy for the assessment of LV, evaluating the RV presents many challenges. In this study, we looked at the value of 3DE in assessing RV remodelling in PAH patients against CMR.

The novelty of the present study was the evaluation of consecutive patients without excluding any patient for image quality in a large patient cohort. Despite this, an excellent agreement between 3DE and CMR was found with similar values for both volumes and RV mass. In addition, no patients or controls received contrast agents for improving endocardial border delineation, which could have further reduce the variability of volumes particularly in the smaller ventricles. There is no doubt that obesity and very large RV size can hamper image quality. In our study, all patients were included with no exceptions, reflecting our clinical practice. In another study, Tamborini et al. also showed a good correlation between 3DE and 2DE for RVEF, but they did not compare them against CMR.

Three-dimensional echocardiography images are acquired in real time. With the ultrasound system used in this study, temporal resolution was in average of 20 frames/s, which for an R–R interval of 800 ms (75 bpm) it would acquire 16 sets of images per cycle in real time. This is certainly much inferior to 2DE at present.

Figure 5 Interobserver variability of measurements for right ventricular end-diastolic volume in normal volunteers, as derive from three-dimensional echocardiography and cardiac magnetic resonance.

Figure 6 Bland Altman agreement for test retest reproducibility of three-dimensional echocardiography measurement of right ventricular mass and right ventricular-ejection fraction in pulmonary arterial hypertension patients.
which with a frame rate of >80/s, it would acquire at least 64 images per cycle for the same R–R interval. With the new ultrasound systems soon to become available, the temporal resolution of 3DE will be greatly increased.

**Cardiac magnetic resonance in pulmonary hypertension**

Cardiac magnetic resonance may be regarded as the gold standard for volumes, EF, and mass. Grothues et al.18 measured RV volumes, EF, and mass in 60 patients who underwent CMR twice (20 healthy, 20 with left heart failure, and 20 with concentric LV hypertrophy) and showed low inter-study variability (RVEDV: 6.2%). Furthermore, Helbing et al.19 demonstrated a good correlation (r = 0.86) for RVEDV between 2DE and CMR in 16 children with congenital heart disease and 17 normals with low variability and a small bias both in patients and in normals for all measurements.20 – 23

However, CMR has also some drawbacks. Data acquisition and analysis (particularly free-hand tracing) tends to be more labour intensive than in 3DE. It is not widely available; it is more expensive; and it demands significant technical support and expertise. Furthermore, CMR cannot be undertaken in patients with pacemakers, claustrophobia, or orthopnea as well as difficulties in breath-holding and patients with arrhythmia.

The temporal resolution of CMR is significantly less than that of conventional 2DE. CMR uses retrospective cardiac gating and segmented k-space techniques to allow acquisition of the whole cardiac cycle over ~12 R–R intervals. In this study, the interval between each reconstructed cardiac phase was ~27 ms which compares favourably to 3DE.

**Agreement of measurements between cardiac magnetic resonance and three-dimensional echocardiography**

In this study, we had two groups of individuals: patients with dilated and hypertrophied RV as well as normal subject with normal sized RV. Border delineation was proved easier in the dilated RV. As a result, there was good agreement between the two modalities for volumes and EF with a tight standard deviation. Nesser et al.25 also demonstrated a close correlation between 3DE and CMR for RV volumes and EF in 20 patients, while more recently Niemann et al.26 examined 14 normals and 16 patients with complex congenital heart defects with 3DE and CMR and showed excellent agreement without excluding any patients, similar to our study.

To our knowledge, this study is the largest yet in a homogenous group of PAH patients undergoing 2DE, 3DE, and CMR. Importantly, patients were consecutive with no exclusions. Despite this, an excellent agreement was demonstrated for all measurements between CMR and 3DE, particularly in PAH patients.

In a dilated RV, volumes and EF may be underestimated with 3DE—as demonstrated by the larger SD of bias, which may be explained by the disability of 3DE to visualize the entire RV apex in some very dilated RV. In agreement with our findings, Kjaergaard et al.27 showed an underestimation of RVEF with 3DE by 5.9% compared with CMR in a mixed population of 34 patients with either inferior infarct or previous pulmonary embolism. In normal subjects, endocardial mapping is more difficult in the smaller RV without intravenous contrast, which may explain the reduced reproducibility of RV mass and EF. This may be related to poor delineation of epicardial and endocardial borders as well as the thinner RV free wall. Gopal et al.27 measured RV volumes and EF in 71 normals and suggested that 3DE performed well when compared with CMR. In Gopal’s study, values for EF had a good agreement but significant variability.

Another contributor to the variability observed between modalities may be the difference in temporal resolution and the way that images are acquired with 3DE and CMR (real time vs. reconstruction). However, temporal resolution was comparable between 3DE and CMR in this study.

**Right ventricular mass**

Right ventricular mass by 3DE showed a good agreement against CMR. Variation for 3DE was 20% of the total RV mass of the hypertrophied RV, compared with 23.3% with CMR. It is likely that this small difference is due to epicardial and endocardial delineation, which occasionally may be unclear. In patients with chronic lung disease, epicardial tracing is more difficult and often intravenous injection of ultrasound contrast agents is necessary for better assessment of RV mass. In this study, no contrast agents were used. Another factor adding to the disagreements between CMR and 3DE is the unclear boundaries of the RV component of the ventricular septum.28,29 This separation, however, may be difficult to achieve with either 3DE or CMR and a standardized methodology may be required.

Measuring RV mass in the non-hypertrophied RV may be challenging, and this was demonstrated by the increased variability of measurements and the poor reproducibility of 3DE for RV mass measurement. In small ventricles, the disadvantage of small volume is added to the complex geometrical shape of the RV and the delineation of the cast becomes more difficult. Pattynama et al.22 examined 40 patients using only CMR for RV volumes and mass and showed decreased variability. In our study, however, variability for RV mass was higher in normals (r = 0.12, P = 0.6). CMR, on the other hand, proved robust for both PAH patients and normals.

**Limitations of the study**

No intravenous contrast agents were used for either 3DE or CMR. The use of intravenous contrast agents would have significantly improved RV measurements, particularly in those with smaller RV.

**Conclusion**

Three-dimensional echocardiography overcomes some of the disadvantages of CMR as it can be routinely used for serial imaging and at the bedside. RV remodelling in PAH patients can be accurately examined by both 3DE and CMR. Both are robust and reproducible with CMR being more reproducible for measurements of EF and RV mass.
References


