The systemic right ventricle
Winter, M.M.

Citation for published version (APA):
Winter, M. M. (2010). The systemic right ventricle

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: http://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.

Download date: 13 Dec 2018
Cardiac CT provides a reliable alternative for cardiac MRI in adult patients with a systemic right ventricle


Submitted
ABSTRACT

Background: Twenty percent of patients with a systemic right ventricle (RV) is pacemaker dependent, and unsuitable to undergo Cardiovascular Magnetic Resonance (CMR) imaging. The aim of this study was to evaluate whether Multidetector Row Computed Tomography (MDCT) could provide a reliable alternative for CMR in these patients.

Methods: Thirty-five patients with a systemic RV underwent MDCT (n=15; 47% male; 32±8 yrs), or CMR (n=20; 80% male; 35±12 yrs). Systemic RV end diastolic volume, end systolic volume, stroke volume, and ejection fraction were obtained. Intra- and interobserver variability for both modalities were assessed and compared.

Results: We found the intra-, and the interobserver variability of volumes and function measurements of the systemic RV obtained with MDCT to be higher compared to those obtained with CMR. However, these differences in variability did not reach statistical significance, the only exception being the interobserver variability of systemic right ventricular stroke volume (12% with CMR vs. 32% with MDCT; p<0.01).

Conclusions: MDCT provides a reliable alternative for CMR for volumes and function assessment in patients with a systemic right ventricle, although larger variability between measurements should be taken into account. However, patient selection should be restrictive, to avoid unnecessary exposure to radiation and contrast agents.
BACKGROUND
Patients with a complete transposition of the great arteries (TGA) who underwent an atrial switch operation in the past and patients with a congenitally corrected transposition of the great arteries (ccTGA) have a morphologic right ventricle (RV) supporting the systemic circulation. Due to improvements in palliative cardiac surgery early in life, the number of adult patients with a systemic RV has increased dramatically over the past few decades. Although long-term outcome in these patients is unknown, morbidity is worrisome, with tricuspid valve regurgitation, arrhythmias, and RV dysfunction being the main constituents.

Reliable assessment of systemic right ventricular volumes and function is important for clinical decision making, to follow-up therapeutic intervention, and to properly execute clinical research. Currently, Cardiovascular Magnetic Resonance (CMR) is considered the gold standard for accurate and reproducible systemic right ventricular volumes and function assessment. However, 20% of patients with a systemic RV is pacemaker dependent, and an increasing number of patients with a failing systemic RV benefits from cardiac resynchronization therapy. As most intra-cardiac devices are considered to be CMR incompatible, these patients are unsuitable to undergo CMR. Multidetector Row Computed Tomography (MDCT) could provide a reliable alternative for CMR in these patients.

Although the accuracy of MDCT measurements is relatively well documented, no studies have been performed on the reproducibility of measurements. Therefore, the objective of our study was to evaluate intra- and interobserver variability of systemic right ventricular volumes and function measurements by MDCT, in comparison to CMR, in patients with a systemic RV.

METHODS
Patient characteristics
A cross-sectional study was performed among 35 consecutive patients with a systemic RV, 23 patients with an atrially switched TGA, and 12 with a ccTGA.
The Human Research Committees of all participating institutions approved of the study protocol, and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki. Written informed consent was obtained from all patients prior to participation in the study.

**Image acquisition**

For Multidetector Row Computed Tomography (MDCT) image acquisition, we used a Philips Brilliance-64 Computed Tomography scanner (120 kV; average 400 mAs). All scans were obtained in the cranio-caudal direction, during inspiratory breath-hold. Patients received 90 mL of a contrast medium (70 ml at a flow rate of 5.0 mL/s, followed by a 20 ml bolus at a flow rate of 3.5 mL/s, and a 40 ml bolus of saline at a flow rate of 3.5 mL/s) containing 300 mg of iodine (Iomeron 300, Bracco Imaging SpA, Milan, Italy). The scan was automatically commenced after contrast detection in the systemic RV and the descending aorta. The contrast detection threshold was set at 150 Hounsfield Units. A standard scan protocol was observed in all patients. To cover the whole heart 60-80 slices were made, each with a 2 mm thickness and no interslice gap. Ten sets of reconstructions at every 10% (0-90%) of the RR-interval were performed. From these axial images, multiplanar reformations in the short-axis orientation, with a slice-thickness of 6 mm, and no interslice gap, were made. This resulted in 12 to 15 short-axis reconstructions, which were used for functional analysis. Short-axis reconstructions were made after the MDCT was performed. Figure 1.

For Cardiovascular Magnetic Resonance (CMR) image acquisition we used a 1.5 Tesla scanner (Siemens Avanto, Erlangen, Germany), using standardly available sequences to assess ventricular volumes. After visualizing the long and short axes of the heart, a multi-phase steady-state free precession sequence (SSFP) with retrospective electrocardiographic triggering was applied to visualize 2-chamber, 3-chamber and 4-chamber views. Guided by these views, a multislice and multiphase SSFP sequence was applied perpendicular to the ventricular septum, encompassing the total heart.
Figure 1. Short axis view in end diastole obtained in a patient with an atrially switched TGA, by a). Multidetector Row Computed Tomography, and b). Cardiovascular Magnetic Resonance.

These sequences were individually adjusted to acquire short axis slices with optimal spatial and temporal resolution. Typical parameters were: flip angle: 50-70 degrees; repetition time: 3-4 msec; echo time: 1-2 msec; temporal resolution: 40 msec, 1-2 X 1-2 mm / pixel in-plane spatial resolution, 8 mm slice thickness, and 1 mm interslice gap. This resulted in 9 to 15 slices to cover the whole heart. CMR images were acquired during repeated end-expiratory breath holds.

Image analysis
For MDCT and CMR image analysis we used MASS Analytical Software System (Medis, Leiden, the Netherlands). Cine loops were used to choose end-diastole and end-systole. End diastole was defined as the phase with the largest right ventricular (and left ventricular (LV)) volume and end systole as the phase with the smallest right ventricular (and LV) volume. The slices at the base of the heart were considered to be in the ventricle if the blood was at least half surrounded by ventricular myocardium. To optimize differentiation between ventricle and atria and vessels in the basal slices, 4-chamber views in phase with short-axis views...
were available in the CMR group. Trabeculations and papillary muscles were considered part of the ventricular cavity. The sums of the traced contours in end diastole and end systole were used to calculate end diastolic volume and end systolic volume using a disc summation technique. End diastolic volumes and end systolic volumes were used to calculate stroke volume and ejection fraction. Stroke volume was defined as end diastolic volume – end systolic volume, and ejection fraction as \( \frac{(\text{end diastolic volume} - \text{end systolic volume})}{\text{end diastolic volume}} \times 100\% \).

Contours were traced 3 times by 2 independent observers (SR, MW). The first observer analyzed all scans twice, with a minimal interval of 2 weeks between the first and second scan analysis, and blinded to the previous results. The second observer analyzed the scans once, blinded to the results of the first observer.

**Statistics**

For statistical analyses SPSS 16.0 (SPSS Inc., Chicago, Illinois) for Windows was used. P values <0.05 were considered statistically significant. The descriptive data are presented as mean with standard deviation if normally distributed, or as median with range as appropriate. Intra- and interobserver measurement variability was determined from the mean values and the differences between the 2 measurements, and visualized with the methods and plots as described by Bland and Altman. The coefficient of variability was calculated as the standard deviation of the difference of the paired measurements divided by the mean of the average of the paired measurements, and expressed as a percentage. The statistical comparison of any differences in reproducibility of MDCT and CMR measurements was assessed with an extension of the Bland-Altman methods. Therefore, a log transformation of the squared differences between the 2 measurements was performed. If the squared difference was 0, we replaced the value by the next smallest value multiplied by 0.5, before log transformation. A 2-tailed paired t-test of the logged squared differences of MDCT versus CMR was performed thereafter. 20, 21
RESULTS

Patient characteristics
A total of 35 adult patients (66% male, mean age 33.6 ± 10.7 years) with a systemic RV were included in the study, 23 patients with an atrially switched TGA, and 12 patients had a ccTGA.

CMR was performed in 20 patients, whereas 15 patients underwent MDCT (14 patients with a permanent pacemaker, 1 patient with an implantable cardioverter-defibrillator). There were no statistically significant differences in age, type of TGA, and NYHA functional class between patients who underwent CMR and MDCT. All CMR and MDCT scans were undertaken without complications. Patient characteristics are summarized in table 1.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All patients* (n=35)</th>
<th>CMR* (n=20)</th>
<th>MDCT* (n=15)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>33.6 ± 10.7</td>
<td>34.8 ± 12.5</td>
<td>31.9 ± 8.0</td>
<td>N.S.</td>
</tr>
<tr>
<td>Male</td>
<td>23 (66%)</td>
<td>16 (80%)</td>
<td>7 (47%)</td>
<td>0.06</td>
</tr>
<tr>
<td>NYHA Class I</td>
<td>77%</td>
<td>75%</td>
<td>80%</td>
<td>N.S.</td>
</tr>
<tr>
<td>II</td>
<td>14%</td>
<td>20%</td>
<td>7%</td>
<td>N.S.</td>
</tr>
<tr>
<td>III</td>
<td>9%</td>
<td>5%</td>
<td>13%</td>
<td>N.S.</td>
</tr>
<tr>
<td>IV</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>N.S.</td>
</tr>
<tr>
<td>Atrially switched TGA</td>
<td>23 (66%)</td>
<td>13 (65%)</td>
<td>10 (67%)</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

* Data are mean value ± standard deviation, or as number of patients (percent). CMR = cardiovascular magnetic resonance; MDCT = multidetector rowcomputed tomography; TGA = transposition of the great arteries; p value indicates the difference between patients who underwent CMR vs. MDCT.

Systemic right ventricular volumes and function assessment
Systemic right ventricular volumes and function assessment by CMR and MDCT was performed 3 times; twice by a single observer, and once by a second observer. We found no statistically significant differences in intra-observer variability of end diastolic volume, end systolic volume, stroke volume and ejection fraction between measurements obtained by CMR, compared to MDCT. Moreover,
we found no statistically significant differences in interobserver variability of end diastolic volume, end systolic volume, and ejection fraction between measurements obtained by CMR, compared to MDCT. However, CMR had superior interobserver reproducibility for stroke volume measurements compared to MDCT (12% variability with CMR vs. 32% variability with MDCT; p<0.01). Figure 2. Although these differences were statistically non-significant, the coefficient of variability was higher for all measurements performed with MDCT, except for the inter-observer variability of end systolic volumes (13% with CMR vs. 12% with MDCT; p=N.S.). Intra- and interobserver variability data are summarized in table 2.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Average</th>
<th>Difference</th>
<th>CV</th>
<th>Average</th>
<th>Difference</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDV (ml)</td>
<td>212</td>
<td>-5 ± 13</td>
<td>6%</td>
<td>294</td>
<td>-11 ± 36</td>
<td>12%</td>
</tr>
<tr>
<td>ESV (ml)</td>
<td>139</td>
<td>-4 ± 9</td>
<td>7%</td>
<td>200</td>
<td>-19 ± 35</td>
<td>18%</td>
</tr>
<tr>
<td>SV (ml)</td>
<td>74</td>
<td>-1 ± 7</td>
<td>9%</td>
<td>96</td>
<td>5 ± 15</td>
<td>16%</td>
</tr>
<tr>
<td>EF (%)</td>
<td>36</td>
<td>0.1 ± 2</td>
<td>6%</td>
<td>35</td>
<td>5 ± 9</td>
<td>25%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Average</th>
<th>Difference</th>
<th>CV</th>
<th>Average</th>
<th>Difference</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDV (ml)</td>
<td>213</td>
<td>-7 ± 21</td>
<td>10%</td>
<td>277</td>
<td>-22 ± 34</td>
<td>12%</td>
</tr>
<tr>
<td>ESV (ml)</td>
<td>139</td>
<td>-5 ± 18</td>
<td>13%</td>
<td>189</td>
<td>-5 ± 22</td>
<td>12%</td>
</tr>
<tr>
<td>SV (ml)</td>
<td>74</td>
<td>-2 ± 9</td>
<td>12%</td>
<td>89</td>
<td>-17 ± 29</td>
<td>32%</td>
</tr>
<tr>
<td>EF (%)</td>
<td>36</td>
<td>-0.1 ± 3</td>
<td>8%</td>
<td>35</td>
<td>-6 ± 7</td>
<td>20%</td>
</tr>
</tbody>
</table>

Data are mean values ± standard deviation of the average and the difference of the paired observations. CV = coefficient of variability; EDV = end diastolic volume; EF = ejection fraction; ESV = end systolic volume; SV = stroke volume. P-value indicates difference in coefficient of variability between CMR and MDCT.
Figure 2. Bland-Altman plots demonstrating the intra-observer (left side), and inter-observer (right side) variability of right ventricular a). end diastolic volume, b). end systolic volume, c). stroke volume, and d). ejection fraction. On the X-axis the mean value of both measurements, and on the Y-axis the difference between measurements. The ▲ represent measurements performed with MDCT, the --- represent the mean of the differences between MDCT measurements. The * represent measurements performed with CMR, the --- represent the mean of the differences between CMR measurements.
DISCUSSION

In the current study, we found no statistically significant differences in reproducibility of systemic right ventricular volumes and function measurements performed by MDCT, compared to CMR. Our findings indicate that MDCT provides a reliable alternative for volumes and function assessment in patients with a systemic RV, who are unsuitable to undergo CMR.

In patients with normal cardiac anatomy MDCT is already considered to be a reliable alternative for CMR for measurements of ventricular volumes and function measurements. However, the feasibility of routine use of MDCT in patients with a systemic RV cannot simply be extrapolated from these data, as the morphology of the systemic RV differs substantially from the subpulmonary RV. The complex geometric shape of the systemic RV, its extensive trabeculations and poor acoustic windows, make standard geometric assumptions impossible, and function assessment challenging. Subsequently, quantitative assessment of the systemic RV with frequently used diagnostic modalities, such as echocardiography, is difficult. MDCT, similar to CMR, has the ability to provide any desired imaging plane and do not rely on geometric assumptions to calculate right ventricular volume. However, its role in patients with a systemic RV had not yet been established.

The establishment of MDCT as a reliable alternative for CMR is important, as 20% of patients with a systemic RV is pacemaker dependent, and an increasing number of patients is receiving cardiac resynchronization therapy, or implantable cardiac defibrillators (ICD). Although data on CMR compatibility and safety of intra-cardiac devices remain limited and controversial, most intra-cardiac devices are currently considered to be CMR incompatible. One study reports encouraging results on device safety when scanning patients with certain devices, if the right precautions are taken. However, others have described a variety of mechanisms by which CMR could affect pacemaker- and ICD-function. The magnetic forces could attract and displace the pacemakers and ICDs, and could lead to reed switch activation in sporadic cases. Moreover, radiofrequent energy could cause
heating of the intra-cardiac leads. In summary, whether scanning patients with pacemakers and ICD is contraindicated remains disputable, as contraindications are predominantly theoretical, and clinical data are limited. To obtain valid and accurate information on CMR compatibility and safety of intra-cardiac devices further research is warranted.

There are several restrictions that should be taken into account before MDCT is performed. Firstly, we found remarkable differences in reproducibility between MDCT and CMR, although they were not statistically significant. These differences are most likely due to differences in image acquisition and image analysis between the 2 modalities. In MDCT temporal resolution remains limited in comparison with CMR, making MDCT more sensitive to cardiac motion and making the definition of end systolic and end diastolic time points less precise. Artificially lowering a patient’s heart rate partially overcomes this problem, but is not desirable as this could change functional parameters. On the other hand, MDCT provides excellent spatial resolution, which, in combination with the administered contrast, enhances differentiation between blood and myocardium. The lower reproducibility of MDCT parameters could also be due to differences in image analysis between MDCT and CMR. Although the protocol we used to draw contours was the same in the CMR group as in the MDCT group, the analytical software could not provide us with a 4-chamber view in phase with the short axis view in the MDCT group. This made differentiation between ventricles, atria and vessels in the basal slices challenging.

Another important difference with CMR, is patients’ exposure to radiation and contrast agents during MDCT. Although the effective radiation dose per scan was around 14 mSv in our study, effective radiation doses of up to 32 mSv per scan have been reported. The possible impact of this large quantity of radiation should not be taken lightly. Einstein et al. and Hurwitz et al. have reported that MDCT derived coronary angiography, with an effective radiation dose ranging from 12 to 32 mSv, causes a significant increase in risk of both lung and breast cancer, especially in younger and female patients. There are strategies by which
radiation dose can be reduced, without reducing image quality to an unacceptable level; patients should only be scanned when in stable sinus rhythm, tube voltage can be lowered to 100 or 80 kV in small subjects or children, and the scan volume should be accurately specified prior to scanning.\textsuperscript{36, 39} Beside radiation, the administered contrast agent imposes a risk factor for patients undergoing MDCT. The risk of contrast-induced nephropathy is significant, especially in patients with risk factors, such as pre-existing renal function impairment or diabetes mellitus.\textsuperscript{40} The risk of contrast-induced nephropathy can be reduced by prophylactic treatment with acetylcysteine and hydration, but proper risk assessment of all patients prior to MDCT remains of key importance.\textsuperscript{41, 42} However, thorough patient selection remains the best way to avoid any unnecessary exposure to radiation or contrast agents.

As with most studies on MDCT or CMR in patients with congenital heart disease, our study is limited by a relatively small number of patients. Moreover, we compared two different groups of patients; those who underwent CMR, and those who underwent MDCT. However, we found no differences in characteristics between patients who underwent CMR, compared to those who underwent MDCT, except for sex distribution. All patients who underwent MDCT were unsuitable to undergo CMR, due to the presence of intra-cardiac devices. We could have performed MDCT in patients without intra-cardiac devices to overcome this limitation, but chose not to unnecessarily expose these young patients to radiation and contrast agents.

**CONCLUSIONS**

Multidetector Row Computed Tomography provides a reliable alternative for Cardiovascular Magnetic Resonance for volumes and function assessment in patients with a systemic right ventricle, although larger variability between measurements should be taken into account. Patient selection should be restrictive, to avoid unnecessary exposure to radiation and contrast agents.
Reference List

10. van der Zedde J, Oosterhof T, Tulevski II, Vliegen HW, Mulder BJ. Comparison of segmental and global systemic ventricular function at rest and during dobutamine stress...


