Assessment of cardiac function and hemodynamics in children and adults with right ventricular pressure overload: role of cardiac magnetic resonance imaging

Romeih, Soha

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Chapter 8

Is cardiac CT a reproducible alternative for cardiac MR in adult patients with a systemic right ventricle?

Michiel M Winter [a,b], Soha Romeih [a,b,c], Berto J Bouma [a], Maarten Groenink [a,c], Nico A Blom [d], Anje M Spijkerboer [c], Barbara JM Mulder [a,b]

a. Department of Cardiology, Academic Medical Center, Amsterdam, the Netherlands.
b. Interuniversity Cardiology Institute of the Netherlands, Utrecht, the Netherlands.
c. Department of Radiology, Academic Medical Center, Amsterdam, the Netherlands.
d. Department of Paediatrics, Academic Medical Center, Amsterdam, the Netherlands.

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Abstract

Objective: 20% of patients with a systemic right ventricle (RV) are pacemaker dependent, and unsuitable to undergo cardiac magnetic resonance (CMR). Multidetector row computed tomography (MDCT) could provide a reproducible alternative for CMR in these patients. The aim of this study was to compare variability of MDCT with CMR.

Methods: Thirty-five patients with systemic RV underwent either MDCT (*n*=15), or CMR (*n*=20). Systemic RV volumes, and ejection fraction were obtained, and 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 were not significant, the only exception being the interobserver variability of systemic RV stroke volume.

Conclusions: MDCT provides a reproducible alternative for CMR for volumes and function assessment in patients with a systemic RV.

Introduction

Patients with a complete transposition of the great arteries (TGA) who had undergone 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 the palliative cardiac surgery early in life, the number of adult patients with a systemic RV has increased dramatically over the past few decades.[1] Although long-term outcome in these patients is unknown, morbidity is worrisome, with tricuspid valve regurgitation, arrhythmias, and RV dysfunction being the main constituents.[2;3]

Reliable assessment of systemic RV volumes and function is important for clinical decision making, to follow-up therapeutic intervention, and to properly execute clinical research.[4;5] Currently, cardiac magnetic resonance (CMR) is considered the gold standard for accurate and reproducible systemic RV volumes and function assessment.[5;6] However, 20% of patients with a systemic RV are pacemaker or implantable cardioverter-defibrillator (ICD) dependent,[7;8] and an increasing number of patients with a failing systemic RV benefits from cardiac resynchronization therapy.[9] As most intracardiac devices are considered to be CMR incompatible, these patients are unsuitable to undergo CMR. Multidetector row computed tomography (MDCT) may provide a reliable alternative for CMR in these patients.

Although the accuracy of MDCT measurements of cardiac volumes and function is relatively well documented, no studies have been performed on the reproducibility of measurements.[10;11] Therefore, the objective of our study was to evaluate intra- and inter-observer variability of the right ventricular volumes and function measurements by MDCT, in comparison to CMR, in patients with a systemic RV.

Patients and methods

Patient characteristics

A cross-sectional prospective study was performed among 35 consecutive patients with a systemic RV, 23 patients with an atrially switched TGA, and 12 with a ccTGA. All patients had RV volumes and function evaluation either by CMR (n = 20; mean age = 35 ± 12 yrs) in patients without, or by MDCT (n =15; mean age = 32 ± 8 yrs) in patients with a pacemaker or ICD. The Human Research Committees of all participating institutions approved the study protocol, and the study protocol conforms 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 MDCT image acquisition, Contrast- enhanced retrospective electrocardiogram–gated MDCT was performed using Philips Brilliance-64 Computed Tomography scanner. All scans were obtained during breath-hold at the end of inspiration. Patients received 90 ml of a contrast medium (70 mL at a flow rate of 5.0 mL/s, followed by a 20 mL 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). No B-Blocker preparation was used. The scan was automatically commenced after contrast detection in the systemic RV. The contrast detection threshold was set at 150 Hounsfield Units. The rotation time was 0.4 sec, and the pitch factor was 0.2. The tube current was 600 MA, and the tube voltage was 120 kV, and the effective radiation dose per scan was around 14 mSv. Two- millimeter thick contiguous slices were reconstructed in 512 x 512 matrix using a 100 mm filed of view. The whole heart was covered within 60-80 slices per cardiac phase. Data in steps of 10% of R-R interval (ranging from 0% to 90% for each investigation) were obtained using a segmental reconstruction algorithm. From these axial images, multi-planar reformations in the short-axis orientation, with a slice-thickness of 6 mm, without slice gap, were done. This resulted in 12 to 15 short-axis slices, which were used for functional analysis.

CMR was performed using 1.5 Tesla scanner (Siemens Avanto, Erlangen, Germany), 2-, 4- chamber and short-axis views covering both ventricle from the base of the heart to the apex were acquired using a retrospective electrocardiogram-gated steady-state free precession sequence during breath holding at expiration. Short-axis view is consisting of 12 to 15 contiguous slices. Scan parameters were: repetition time = 3.2 - 3.8 ms; echo time = 1.6 - 1.9 ms; flip angle = 50 - 70^{o}; slice thickness = 6 mm without slice gap; matrix = 160 x 256; field of view = 350 - 400 mm. Temporal resolution was approximately 25 ms. All the data were stored in DICOM format and transferred to a PC workstation running a MASS ® program.

Image analysis

For MDCT and CMR image analysis we used the 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 RV and left ventricular (LV) volume and end systole as the phase with the smallest RV 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, using 2- and 4-chamber views simultaneously with short-axis views was possible only in the CMR group. Trabeculations and papillary muscles were considered part of the ventricular cavity.[5] The sums of the traced contours in end diastole en 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 [(end diastolic volume – end systolic volume) / end diastolic volume] X 100%. All ventricular volumes were indexed for body surface area according to the Mosteller formula: (√ Height (cm) x weight (kg)/3600).
Contours were traced in total 3 times by 2 independent observers (M.W, S.R) 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 (CV) 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 unpaired *t*-test of the logged squared differences of MDCT versus CMR was performed thereafter.[12]

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 with a ccTGA.
CMR was performed in 20 patients, whereas 15 patients underwent MDCT due to implantation of pacemaker or ICD (14 patients with pacemakers, and 1 patient with an ICD). There were no statistically significant differences in age, type of TGA, and NYHA functional class between patients who underwent CMR and who underwent MDCT. All CMR and MDCT scans were undertaken without complications. Patient characteristics are summarized in **Table 1**.

Table 1. Baseline characteristics

Characteristics	All patients* (n=35)	CMR* (n=20)	MDCT* (n=15)	p Value
Age (years)	33,6 ± 10,7	34,8 ± 12,5	31,9 ± 8,0	N.S.
Male	23 (66%)	16 (80%)	7 (47%)	0,05
BSA (m^2)	1,9 ± 0,04	1,8 ± 0,2	1,9 ± 0,3	N.S.
Heart Rate (b/m)	71 ± 2	71 ± 16	70 ± 10	N.S.
NYHA Class				
I	77%	75%	80%	N.S.
II	14%	20%	7%	N.S.
III	9%	5%	13%	N.S.
IV	0%	0%	0%	N.S.
Atrially switched TGA	23 (66%)	13 (65%)	10 (67%)	N.S.

* 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 beteen patients who underwent CMR vs. MDCT.

Systemic RV volumes and function assessment

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 a superior interobserver variability for stroke volume measurements compared to MDCT (12% variability with CMR vs. 32% variability with MDCT; $P < 0.01$), **Figure 1.** These differences were statistically non-significant, except for the interobserver variability for stroke volume measurements. However, 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 = NS). Intra- and interobserver variability data are summarized in **Table 2**.

Figure 1. Bland-Altman plots depicting the intra- and interobserver variability between multidetector row computed tomography, and cardiac magnetic resonance.
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 represents —— the mean of the differences between MDCT measurements. The ✳ represent measurements performed with CMR,- - - - the represent the mean of the differences between CMR measurements.

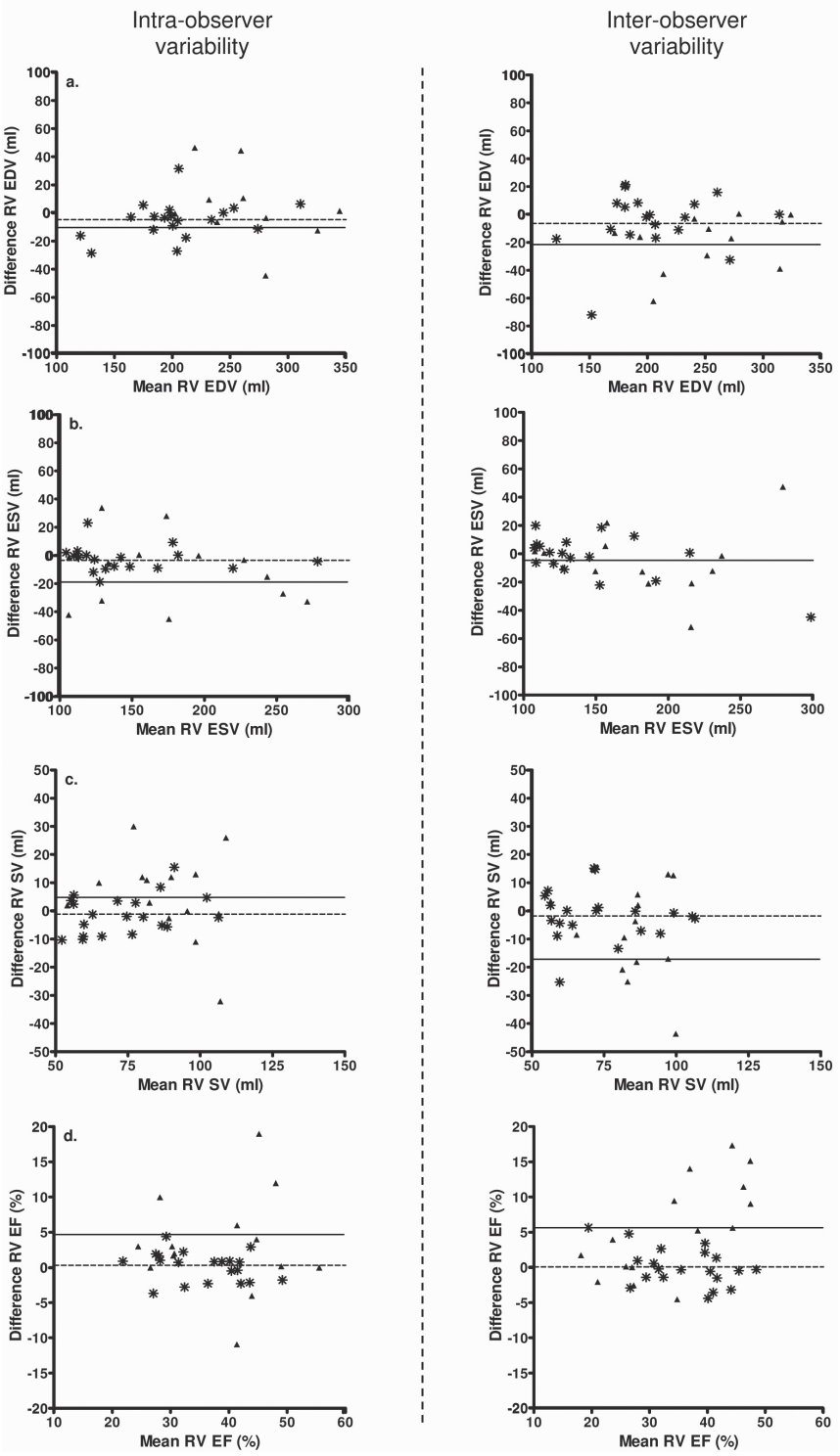
Intra-observer variability
Inter-observer variability
a.
Difference RV EDV (ml)
Mean RV EDV (ml)
b.
Difference RV ESV (ml)
Mean RV ESV (ml)
c.
Difference RV SV (ml)
Mean RV SV (ml)
d.
Difference RV EF (%)
Mean RV EF (%)

Table 2. Intra- and inter-observer variability of measurements.

	Intra-observer variability						
	CMR (n=20)			MDCT (n=15)			p-value
Parameter	Average	Difference	CV	Average	Difference	CV	
EDV (ml)	212	-5 ± 13	6%	294	-11 ± 36	12%	N.S.
ESV (ml)	139	-4 ± 9	7%	200	-19 ± 35	18%	N.S.
SV (ml)	74	-1 ± 7	9%	96	5 ± 15	16%	N.S.
EF (%)	36	0,1 ± 2	6%	35	5 ± 9	25%	N.S.
	Inter-observer variability						
	CMR (n=20)			MDCT (n=15)			p-value
Parameter	Average	Difference	CV	Average	Difference	CV	
EDV (ml)	213	-7 ± 21	10%	277	-22 ± 34	12%	N.S.
ESV (ml)	139	-5 ± 18	13%	189	-5 ± 22	12%	N.S.
SV (ml)	74	-2 ± 9	12%	89	-17 ± 29	32%	<0.01
EF (%)	36	-0,1 ± 3	8%	35	-6 ± 7	20%	N.S.

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.

Discussion

In the current study, we have shown for the first time that volumes and function measurement with MDCT is equally reproducible compared to assessment with CMR in patients with a systemic RV, and therefore provides an alternative for those patients who are unsuitable to undergo CMR.

In patients with normal cardiac anatomy MDCT is already considered to be a reliable alternative for CMR for biventricular volumes and function measurements.[10;13] 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.[14;15] Subsequently, quantitative assessment of the systemic RV with frequently used diagnostic modalities, such as echocardiography, is difficult.[16;17] MDCT, similar to CMR, has the ability to provide any desired imaging plane and does not rely on the geometric assumptions to calculate the RV volume. However, its role in patients with a systemic RV had not yet been established.

The establishment of MDCT as a reproducible alternative for CMR is important, as 20% of patients with a systemic RV are pacemaker dependent, and an increasing number of patients are receiving cardiac resynchronization therapy or ICDs.[18] 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.[19] One study reports encouraging results on device safety when scanning patients with certain devices, if the right precautions are taken.[20] 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,[21] and could lead to "reed switch activation" in sporadic cases.[22] Moreover, radiofrequent energy could cause heating of the intra-cardiac leads.[23]

In summary, whether scanning patients with pacemakers and ICD is contraindicated remains disputable, as contraindications are predominantly theoretical, and clinical data are limited.[22] 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 the 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.[24] Using beta-blockers medication to lower 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 an excellent spatial resolution which, in combination with the administered contrast, enhances differentiation between blood and myocardium.[25] 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 provide us with 4-and 2- chamber views simultaneous with the short-axis view in the CMR group but not in MDCT group. This made differentiation between ventricles, atria and vessels in the basal slices challenging in MDCT group.

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.[26] 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.[27] There are strategies by which radiation dose can be reduced, without reducing image quality to an unacceptable level; patients should only be scanned when they have a stable sinus rhythm, tube voltage can be lowered to 100 or 80 kV in the small patients or the children, ECG-controlled tube current modulation can be used, and the scan volume should be accurately specified prior to scanning.[26;28] 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.[29] The risk of contrast-induced nephropathy can be reduced by prophylactic pre-hydration, but proper risk assessment of all patients prior to MDCT remains of key importance.[30] However, reticence and thorough patient selection remain key to avoid any unnecessary exposure to radiation or contrast agents.

As with most studies on MDCT or CMR in patients with congenital heart diseases, 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 reproducible alternative for cardiovascular magnetic resonance for ventricular 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.

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