Mid-Term Follow-Up after Arterial Switch Operation for Complete Transposition of the Great Arteries

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Abstract: *Purpose*: Transposition of the Great Arteries has to be surgically corrected by an arterial switch operation. This complex surgical procedure has the potential for significant short- and long-term complications like dilation of the neo-aortic root, coronary and pulmonary artery (PA) stenosis. The aim was to determine a suitable follow-up algorithm for mid-term follow-up.

Material and Methods: 26 patients (mean age 10±2 years) were examined using echocardiography, ECG-gated Computed Tomography Angiography (CTA) and functional Magnetic Resonance Imaging (MRI) with flow, cine and pulmonary perfusion measurements.

Results: CTA was capable to visualize coronary arteries in all cases. Coronary stenosis did not occur. Echocardiography failed to visualize the coronary arteries in 81%. CTA revealed moderate PA stenosis (25-50% lumen reduction) in 41% and severe stenosis (>50%) in10%. Visualization of pulmonary arteries was possible by echocardiography in only 45%. Correlation between MR-pulmonary perfusion abnormalities and PA stenosis were not present. Doppler-echocardiography showed mild flow acceleration in the main PA (mean pressure gradient 34mmHg) in 4 patients, while MRI found an increased velocity in 9 patients. 10 patients had neo-aortic root dilatation detected with CTA. On echocardiography 8 patients had mild, 4 had moderate aortic valve insufficiency. On MRI amount of aortic valve insufficiency was too small to be quantified.

Conclusion: Branch stenosis of the PA was the leading complication 10 years after surgery, coronary stenosis did not occur. Value of Echocardiography is minor in the visualization of coronary arteries and PA morphology and it is recommended only for the assessment of cardiac and valvular function. Additionally, CTA is method of choice for visualization of coronary arteries and PA morphology. In this study the value of MRI for assessment of the complete morphology was limited, but improves with technical advance.

Keywords: Transposition of Great Arteries, arterial switch, follow-up, Magnetic Resonance Imaging, Pediatric, Multi-Detector Computer Tomography, Echocardiography.

INTRODUCTION

Dextro-Transposition of the great arteries (TGA) is a cyanotic congenital heart disease found in approximately 5% of all newborns [1]. It is characterized by ventriculoarterial discordance with the aorta originating from the right ventricle and the pulmonary artery from the left ventricle. Arterial switch operation (ASO) restores the normal anatomic arrangement of the circulation and, as such, promises a lifelong perfect postoperative anatomy and physiology. From its first description by Jatene in 1976 [2], it has steadily become the procedure of choice when the anatomy is appropriate and is usually performed in the first month of life [3]. Outcome of ASO is usually uneventful [4] and a number of studies showed excellent results concerning general health status [5-10]. Early follow-up strategies, using invasive cardiac catheter with angiography and pressure measurement (so far still the gold-standard), have been left in most departments. Over the last years transthoracic echocardiography and Magnetic Resonance Imaging (MRI) have emerged as the preferred methods, being least invasive and readily available [11-13].

Despite, excellent early outcome, ASO still remains a complex surgical procedure with the potential for significant short-, mid- and long-term complications [14]. These are: Coronary and pulmonary stenoses in

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the early- and mid-term and aortic root dilation with aortic regurgitation (AR) in the long-term [3, 15, 16]. The incidence of coronary stenosis, leading to impaired ventricular function, ranges from 2-20 % [4, 17]. The incidence of pulmonary arterial stenosis is between 3 – 30%. It is usually a branch stenosis, which is characterized by its oval shape [18]. The development of aortic root dilation leading to progressive AR is an evolving problem, still not fully understood. De Koenig and co-workers reported that 70% of the children after ASO had dilation 10 years after corrective surgery [19]. They also quoted that exercise capacity in TGA patients after ASO was diminished to about 85% of normal values, while cardiac function was unimpaired. This problem, also described by other groups [20, 21], is fostered by pulmonary stenosis [20] or abnormal aortic elasticity [22, 23].

As a consequence, follow-up strategies must be created that comprise morphological and functional imaging. The utilizable methods are: cardiac catheterization (gold-standard), echocardiography, multi-detector computer tomography (MDCT) and MRI. Because of its invasiveness, cardiac catheterization has its limitation in all patients. Echocardiography is frequently insufficient in visualizing the localisation of the neo-pulmonary trunk, its branches and the coronary arteries. Recently MDCT showed very good results in adults and children with congenital heart disease [24-26]. MDCT allows for excellent 3D morphological imaging of the pulmonary and aortic anatomy [27] as well as the coronary arteries [28, 29]. Still the amount of radiation is a matter of debate, especially in children. MRI also provides a less invasive alternative for assessment of cardiac morphology and function as well as pulmonary perfusion. It has a big amount of additional possibilities, such as measurement of the through-plane blood flow of the main pulmonary arteries and the ascending aorta. This allows quantification of blood flow [30, 31] and detection of stenotic flow. On the other hand imaging of very small structures with standard T2-HASTE or SSFP sequences such as coronary arteries is still a major challenge for this method.

Investigating the mid-term result of our patients using echocardiography, MDCT and MRI (triple investigation), we aimed to find out which method is most suitable at this certain point of time. As a consequence we wanted to differentiate which method should be preferred for follow-up examinations after ASO for TGA.

PATIENTS AND METHODS

Patients

Overall 26 consecutive paediatric patients treated with ASO for TGA between 1991 and 1998 were enrolled in this prospective study (18 male, 8 female). Patients were included in the study during their regular scheduled follow-up examinations (basic examination including ECG and echocardiography) between 2005 and 2007.

The study was carried out according to the institutional ethical guidelines and in conformity with the Declaration of Helsinki. The study was approved by the local Ethics Committee (IRB number: 135/2005) and all patients/parents gave informed consent.

For MDCT and MRI, both performed at the same day, no β-blockers or sedatives were given. A 20 to 22 G needle was placed in an antecubital or more peripheral vein for contrast media injection. At the day of examination the patient's demographics were: mean age 10 ± 2 years (range 7 – 15 years), mean height 141 ± 17 cm (range 117 – 175 cm), and mean weight 35 ± 13 kg (range 20 – 63 kg).bv

Surgical Procedure

21 of 26 patients were operated at the local department of cardiothoracic surgery. They were operated between days 3 to 241 of life (mean 5 ± 56 days). Additional cardiovascular anomalies were present in all patients. 14 patients showed simple TGA with associated atrium septal defect (ASD) and/or persistent ductus arteriosus PDA). The remaining patients had additional anomalies like ventricular septal defect and/or hypoplastic aortic arch and/or coronary artery anomalies.

Echocardiography

Image Acquisition

Echocardiographic data were obtained in 26/26 patients using a General Electrics Vivid 7 system (GE Vingmed Ultrasound, Horten, Norway) equipped with a M3S Octave phased-array transducer (transducer frequency 2.0/4.3 Mhz). Echo studies included M-Mode and two dimensional studies of the right and left heart, the atrioventricular- and semilunar valves, the entire pulmonary artery and the aorta. Additionally coronary vessels were investigated.

Color-, pulsed wave- and continuous wave - Doppler studies were performed over the tricuspid-, mitral, pulmonary and aortic valve. Additionally the main, left and right pulmonary arteries were examined.

Image Processing and Quantitative Analysis

Digitally stored data were reviewed by two readers (blinded) blinded to MRI and MDCT findings. General Electrics EchoPAC software was used for the interpretation of M-Mode, 2D and Doppler studies.

M-Mode, 2D and Conventional Doppler Echocardiography

The left ventricular volumes and ejection fraction were calculated by the method of Simpson from biplane imaging. Left ventricular mass was calculated from M-Mode studies using the Devereux method. It was normalized to the body surface area. Coronary arteries, aortic valve, aortic arch and the pulmonary arteries were visualized from the parasternal view.

Doppler studies included maximum and mean velocity across the aortic valve. Further the main, left and right pulmonary arteries were examined. A range between 0.5 – 1.5 m/s was taken as a normal value for the peak velocity in the main pulmonary artery [32]. In addition, mitral and tricuspid valve peak flow velocity in the early diastole (E) and peak velocity at atrial contraction (A) were measured. The ratio between A and E wave was calculated.

Multi-Detector Computed Tomography (MDCT)

Image Acquisition

MDCT was performed in 21/26 patients on a 16 row detector scanner (Toshiba Aquilion 16, Toshiba Medical Systems, Tokyo, Japan). For retrospective cardiac gating the scanner integrated ECG unit was used. The scanner did not allow for ECG-pulsing or ECG based tube current modulation. Mean heart rate was 84 ± 18 beats / min (range 44 – 125 beats/min). Contrast media was injected automatically (Injektron CT2, Medtron®, Saarbrücken, Germany). MDCT parameters were (no dose modulation): 120 KVp, 15 – 61 mAs, gantry rotation time 0.4 s (n=13) or 0.5 s (n=8), beam pitch 5.6 (n=1), 4 (n=8), or 3.2 (n=12). The mean length of the scan was 118 ± 23 mm. The reconstructed field-of-view (FOV) was adjusted to the individuals' heart size (235 ± 28 mm). The iodine concentration used was 250 mg/dl in 2 patients or 300 mg/dl in 19 patients, depending on the patients' age and needle size. A 30 ml saline flush was injected after application of contrast media. The injection rate for contrast media and saline was 2 (in 18 patients) or 1 ml/sec (in 3 patients).

Image acquisition was started manually with contrast media arriving in the ascending aorta. For examination, patients were instructed to hold their breath in inspiration. 1 mm thin slices with a 20% overlap were reconstructed. Gated MDCT datasets were reconstructed every 10% of the cardiac cycle and

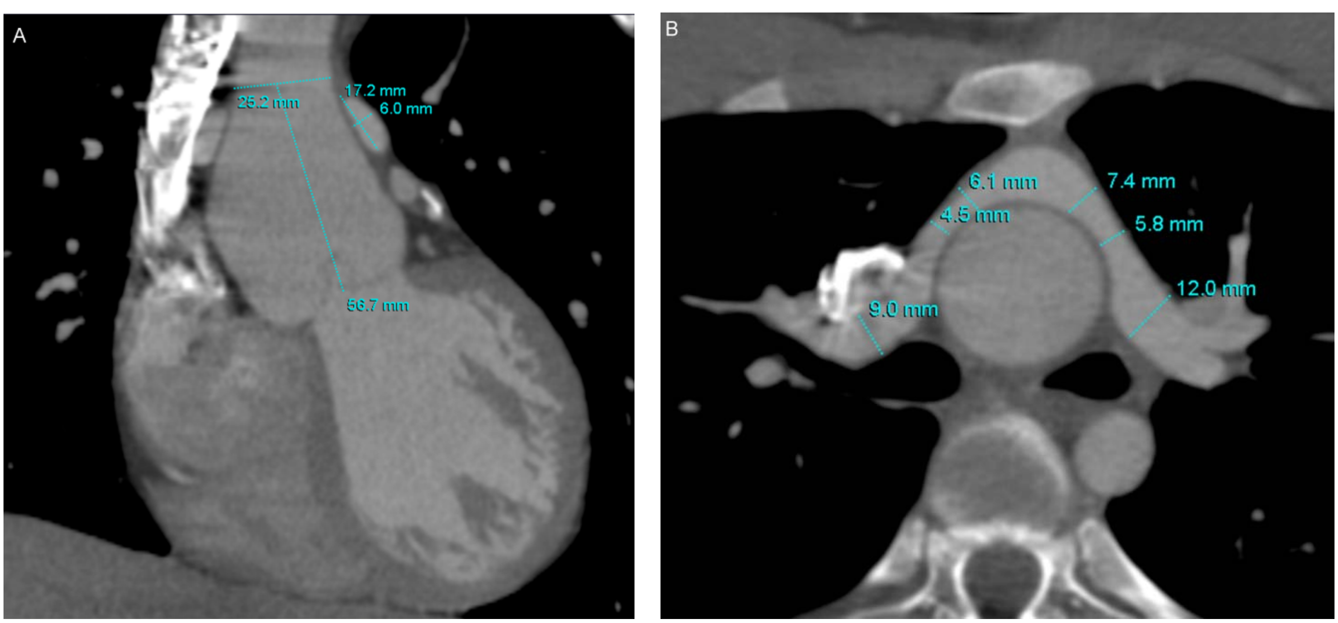

Figure 1: CT angiography of a 15 year old boy after arterial switch operation. (**A**) Diameters and length of the aortic root were assessed in an angulated coronal slice. (**B**) Measurements of the right and left pulmonary artery were taken at three positions, proximal, in the middle section and distal to the neoartic root.

all 10 resulting 3D datasets were transferred to a picture archiving and communication system (PACS) and dedicated visualization workstation (Vitrea V. 3.5, Vital images Inc, Plymouth, MN, USA).

Image Analysis

MDCT images were reviewed in consensus with three readers (one cardiologist (blinded), two radiologists (blinded). The proximal diameters of the coronary arteries were assessed. Image analysis comprised position of the main pulmonary artery in relation to the aorta. Diameters and length of the aortic root, the main pulmonary artery and the right and left pulmonary artery were measured in diastole (Figure **1**).

In those 5 patients who did not get a MDCT examination an ECG- and respiratory gated MRI sequence was applied with an isotropic resolution of 1 mm [33]. Values were compared to known standard scores (z-scores, derived by echocardiography). The z-score of a measurement is the distance of this measurement from the mean of the population, expressed in units of the standard deviation [34].

MRI

Image Acquisition

Studies were performed on a commercial 1.5 T whole-body MR system (Magnetom Avanto, Siemens Medical Systems, Erlangen, Germany) with a slew rate of 30 mT/m and 125 T/m/s. 26/26 patients were examined by MRI. The scanner's ECG gating unit was used for triggering during the cardiac measurements. For MR signal detection one body array coil (anterior) and the two spine array elements (posterior) were used. Three techniques were applied for assessment of the cardiovascular status.

CINE Examination of the Left Ventricle

The left ventricle was examined from the basis to the apex in the short axis view with a retrospective ECG gated 2D steady state free precession (SSFP) Cine (TE: 1.19 ms, α: 80°, slice thickness: 4 mm, in-plane resolution: 1.8 x 1.8 mm^2) was acquired. Using retrospective ECG gating the temporal resolution was 20 ms. Images were visually assessed by two readers (blinded) for regional wall motion abnormalities of the right or left ventricle and the interventricular septum.

Phase-Contrast Flow Measurements (pc-Flow)

One to two cm above the aortic valve a 2D Fast low-angle shot (FLASH) pc-flow measurement was performed (time of echo (TE): 2.8 ms, repetition time (TR): 46 ms, α: 30°, slice thickness: 6 mm, in-plane resolution: 1.4 x 1.4 mm^2, expiratory breath-hold, no view sharing). The temporal resolution of the retrospective ECG gated sequence was 23 ms per frame. For evaluation of flow measurements the software "Flow quantification" (part of ARGUS®, Version VA50C, Siemens Medical Solutions, Erlangen, Germany) was used. The aorta and main pulmonary artery were outlined manually on the magnitude images at all timepoints by an experienced observer blinded to all patients' information. The resulting parameters were forward and backward volume [ml/R-wave to R-wave (RR)-interval] (allowing for calculation of the regurgitation fraction [%]), cardiac output (and, peak velocity [cm/s]. The ejection fraction could not be assessed by this technique.

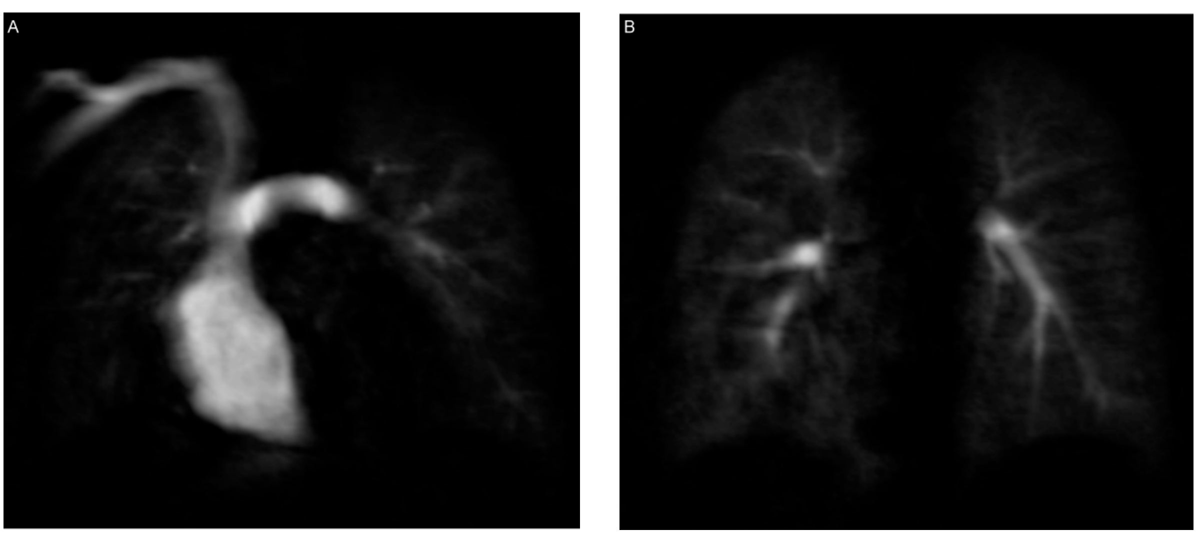

Figure 2: MR perfusion images of a 13 year old boy. (**A**) shows a ventral slice and (**B**) a more dorsal slice. A homogenous pulmonary perfusion was found.

As reference normal values for peak velocities in the main pulmonary artery in children a study by Abolmaali *et al.* was used [35], describing a normal value of 96 ± 15 cm/s. Based on this publication, our values were transferred into z-scores like: z-score 1 = <111 cm/s, z-score 2 = < 126 – 141 cm/s, z-score 3 = > 141 cm/s.

Pulmonary Perfusion

Visualization of lung perfusion was done using 0.1 mmol Gadopentetic acid (Gd-DTPA), injected with a flow rate of 3 ml/s. Images were acquired in an inspiratory breath-hold (Flash 3D, 1x1x2.5 mm3, TR 2.36, TE 0.89, Flip angle (FA) 25°, 4s/3D dataset) (Figure **2**). Pulmonary perfusion was evaluated visually (blinded) and rated as normal, delayed and absent on a lobar basis (lingula was counted as separate lobe).

RESULTS

Echocardiography

The ejection fraction of the left ventricle was 49 ± 10 % and the left ventricular mass index 73 ± 18 g/m^2. The origin and proximal part of the right coronary artery was visualized in 4/26 patients, the left coronary artery in 6/26 patients.

The main pulmonary artery was assessable in 19/26 patients (73%), while it failed in 7/26 (27%). 15/19 (79%) patients showed an increased velocity of more than 1.5 m/s in the main pulmonary artery, only 4/19 (21%) patients showed normal velocities. Pulmonary arterial valve insufficiency was not found. The proximal right pulmonary artery was seen and evaluated in 16/26 (62%) patients, the proximal left pulmonary artery in 18/26 (69%) patients. Evaluation of the middle and distal part of the pulmonary arteries was possible in 5/26 (19%) of pulmonary arteries.

Aortic valve insufficiency was observed in 12/26 (46%) patients (8 times mild, 4 times mild to moderate), while there was no insufficiency in 14/26 (54%) patients.

MDCT

Twenty-one patients underwent MDCT. Coronary arteries were visualized in the entire population, ostial or proximal coronary stenosis was absent (Figure **2**). The mean diameter of the left coronary artery was 3.5 ± 0.7 mm (range 2.0 – 4.9 mm) and of the right coronary artery 3.3 ± 0.7 mm (range 2.0 – 4.7 mm). In three patients (14%) an anomalous origin of the right circumflex from the right coronary artery was observed.

The pulmonary root was located directly anterior to the neo-aortic root 3 times, in 19 (73%) patients it was located to the right side, and in 4 patients it was located on the left.

The right pulmonary artery was normal in 17/26 patients (65%). 7 patients showed a mild stenosis (reduction of the lumen to 25-50%), and 2 patients showed a severe stenosis (>50%). Normal left pulmonary artery was found in 9/26 (37%) patients. 14 patients showed mild stenosis and 3 patients showed a severe stenosis.

The neo-aortic root diameter was within normal ranges in two patients (z-score 1), moderately enlarged in 14 patients (z-score 2) and significantly enlarged in 10 patients (38%) (z-score 3). The length of the neo-aortic root was 34 ± 8 mm (21 – 53 mm).

MRI

The evaluation of the CINE measurements of the left ventricle showed a normal ejection fraction (50%) and myocardial mass (41 g/m^2).

By visual evaluation the right ventricle showed a good function in all patients and no regional wall motion abnormalities were detected.

Evaluation of the pulmonary perfusion images showed a normal perfusion in 138/156 lobes (88%). 7/156 (5%) lobes showed a delayed perfusion and 11/156 (7%) lobes demonstrated perfusion defects.

In two patients, flow measurements were not assessed due to ECG gating problems. Flow measurements in the ascending aorta did not reveal aortic valve stenosis but moderate aortic valve insufficiency in 2/25 (8%) patients. The peak velocity in the pulmonary artery was 150 ± 50 cm/s. Based on the z-scores 12/24 (50%) patients showed a normal peak velocity. 12/24 (50%) showed peak velocities larger than 141 cm/s (z-score 3). Two patients had a moderate insufficiency of the pulmonary valve.

DISCUSSION

In our cohort, the main mid-term complication at 10 years follow-up was pulmonary arterial stenosis (50%). It was mild in 21/52 (40%) and severe in 5/52 (10%) of all pulmonary arteries. The second observation was an increased velocity in the main pulmonary artery in more than 50% of the patients. Third, a significant neo-aortic root dilatation was observed in 10/26 patients (38%). Coronary artery stenosis or severe wall motion abnormalities of the left ventricle were not observed.

This is the first study comparing different techniques in the mid-term follow-up for complete investigation of all anatomic sites that can be affected after ASO. Left ventricular function was investigated by echocardiography and MRI with similar results, both methods did not reveal severe pathologies. No clinical relevant septal or myocardial dyskinesia was observed. Even the proximal parts of the coronary arteries were not assessed sufficiently by echocardiography. Therefore this technique is not an appropriate tool for the detection of coronary stenosis, a life-threatening complication after ASO. Using new ECG and respiratory gated sequences [36] MRI today has the potential to investigate the coronary arteries. At the time of the study, between 2005 and 2007, only work-in-progress sequences were available, so it was not possible to use this technique. Despite of recent technical advance, we still consider MRI not to be the optimal method for coronary artery visualization before adolescence. ECG-gated CTA however allowed for clear visualization of the coronary arteries in all patients (Figure **3**). It is therefore the only method comparable to cardiac catheterization.

The major finding at mid-term follow-up is stenosis of the branch pulmonary arteries. This is in accordance with previous reports [18, 31]. Therefore, the focus of the investigation must be in coverage of this area. Echocardiography did not allow for reliable visualization of the complete left and right pulmonary arteries. Thus, most of the pulmonary stenosis were overseen on Echocardiography. Additionally, there is discussion in the literature, that downstream vasculature is also affected with reduced vascular diameter, if there is central pulmonary arterial obstruction. MR perfusion imaging of the lung parenchyma aims at the visualization of this phenomenon. Furthermore, MRI perfusion can be performed easily without determination of patient's individual circulation time and long breath-hold. Therefore, this approach seemed to be the most feasible. However, we did not find a perfusion difference between the right and left lung, there was severe branch stenosis of the pulmonary arteries. A time resolved angiography could have been another possible method. However, the spatial resolution of this technique is still limited, i.e. 1.3 x 1.5 x 10 mm^3 [37], and furthermore the pulmonary arteries are subject of large pulsatile changes due to the close anatomic relation to the neo-aorta. One possible solution would be again the use of the ECG and respiratory gated technique (Figure **4**). In case of upstream flow turbulences, like observed in our study in 50% of patients, these steady-state-free precession based techniques are hampered due to signal loss post stenosis. Our latest experience confirms these problems. MDCT however allows for nice and sharp visualization of the pulmonary arteries, as seen in this study.

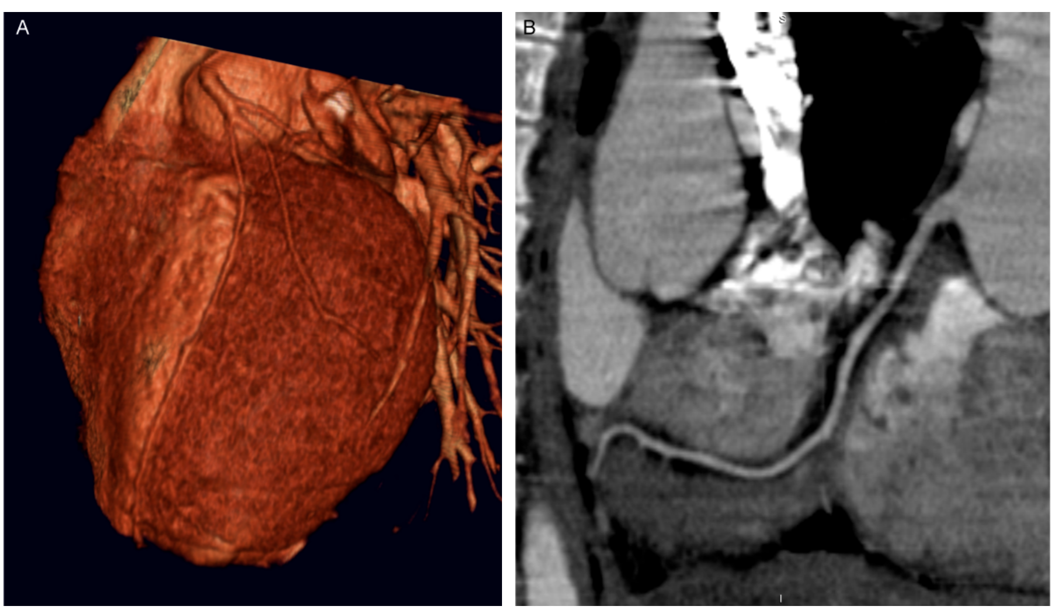

Figure 3: Visualization of the left coronary artery in the same patient as shown in Figure **1**. Due to the ECG gated CT angiography acquisition the coronary arteries can be followed down to the periphery in 3D (**A**) and as a curved multiplanar reconstruction (**B**).

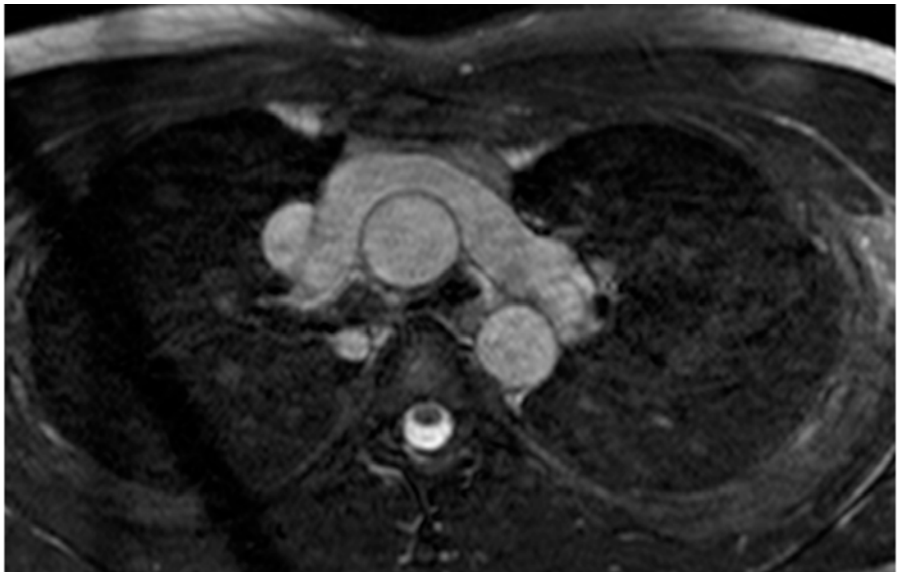

Figure 4: Same patient as shown in Figure **3**. This image shows a transversal view to the pulmonary arteries using a 3D ECG and respiratory gated steady-state-free precession sequence. In this patient no severe increase in blood velocity in the main neopulmonary trunk was present. Therefore, this technique could be applied with excellent image quality.

Increased flow-velocity in the neo-pulmonary trunk is a common finding after ASO and can be explained by the discrepancy in size between the neo-pulmonary root and the distal pulmonary bifurcation. This is accompanied by a mild pressure gradient of 20 mmHg, which is taken as normal [38]. A velocity increase was found in 50% of the patients of our cohort, which is in accordance with the reported data of Bove *et al.* [11]. Temporary pulmonary vessel compression, caused by expansion of the neo-aortic root and ascending aorta in systole, is reported to be another factor for pulmonary flow acceleration and flow turbulence [40].

After ASO, the neo-aortic root is usually larger sized in comparison with a matched control population. This enlargement of the neo-aortic root itself is not a clinical problem as long as it is not associated with aortic valve dysfunction [11] or pulmonary artery compression. In our series 24/26 patients had a dilated neo-aortic (z-score +2 and larger), this number correlates with other studies (32, 40). Additional aortic insufficiency was only mild (Grade I) and found in 14/26 (54%). While this is no actual problem, the individual development has to be followed closely as this is a condition boosting further neo-aortic root dilatation.

As mentioned in the beginning, most deaths in the first year following ASO are attributed to myocardial ischemia or infarction associated with the relocation of the coronary arteries during surgery. Taylor *et al.* used MRI to assess the coronary arteries and late-enhancement for assessment of myocardial viability mid-term after ASO [39]. The patients were 11 years old, similar to our patients, and did not have coronary stenosis or positive late-enhancement (other than known at the time of surgery). These results support our findings that at mid-term the coronary arteries are not an issue. In the later course, if the neo-aortic root dilates further, this can lead to a kinking of the proximal parts of the coronary arteries with subsequently reduced myocardial perfusion. Additionally, with increase in size, the neo-aortic root looses its windkessel function with reduced diastolic blood flow to the coronary arteries. Interesting flow patterns with abnormal vortex and helix flow are described by Geiger and co-workers, highlighting the influence of flow disturbance on the progression of aortic disease and dysfunction [31]. Their patients were a bit older, but still comparable to our group in which more than 50% of the patients present with aortic dilation and regurgitation. At mid-term, echocardiography is sufficient to assess aortic regurgitation and able to visualize pathologic flow in the aortic root. Combination with MDCT, providing for excellent visualization of the anatomy is a reasonable approach. Modern MR sequences such as 4D-phase contrast flow [31, 40] still are not available in general, have limited spatial resolution and therefore fail to provide with sufficient anatomic information.

RECOMMENDATION

Patients with congenital cardiovascular malformation are exposed to examinations with radiation on a regular basis [41]. Therefore, special care should be taken to avoid radiation and use radiation free techniques. Despite knowing this fact, at mid-term follow up a MDCT angiography is recommended to complement routine echocardiography. MDCT should be performed as prospective ECG-gated angiography (diastolic phase), or if available with a latest technology high rotation CT (like Siemens FLASH). In older patients a contrast enhanced MR angiography should be offered in combination with flow measurements in the neo-aorta and neo-pulmonary artery. While the coronary arteries are not an issue at mid-term, they are again problematic in the long-term [6]. Therefore, late enhancement images should be acquired to assess any myocardial damage.

LIMITATIONS

The major limitation of this study is that the MR protocol did not include modern MRI sequences such as 3D-True-Fisp and 4D phase contrast flow. However, at time of investigation, these methods were not available – and are not yet routinely available on every scanner. On the other hand, with recent reduction of radiation dose on MDCT [42], our recommendations are still reasonable and not out of date. Further, MDCT and echocardiography are less time consuming and reproducible as, for example 4D phase contrast flow measurements.

CONCLUSION

This is the first study comparing different techniques in the mid-term follow-up after ASO. In general, ASO showed good results without residual findings that deserved re-operation or intervention. The main complication at mid-term was neo-pulmonary or branch pulmonary arterial stenosis. However, this central obstruction was not associated with reduced pulmonary perfusion or increased perfusion defects. For optimal investigation of morphology and function at mid-term, a combination of CTA and echocardiography is recommended.

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