ORIGINAL ARTICLE

Comparative Evaluation of Flow Quantification across the Atrioventricular Valve in Patients with Functional Univentricular Heart after Fontan's Surgery and Healthy Controls: Measurement by 4D Flow Magnetic Resonance Imaging and Streamline Visualization

Hoi Lam She, MBBS,* Arno A.W. Roest, MD, MBBS, BSc,† Emmeline E. Calkoen, MD,† Pieter J. van den Boogaard, PhD,‡ Rob J. van der Geest, PhD,‡ Mark G. Hazekamp, MD, PhD,§ Albert de Roos, MD, PhD,‡ and Jos J.M. Westenberg, PhD‡

*Department of Radiology, Princess Margaret Hospital, Hong Kong SAR; †Division of Pediatric Cardiology, Department of Pediatrics; ‡Department of Radiology; §Department of Thoracic Surgery, Leiden University Medical Center, Leiden, The Netherlands

ABSTRACT

Purpose. To evaluate the inflow pattern and flow quantification in patients with functional univentricular heart after Fontan's operation using 4D flow magnetic resonance imaging (MRI) with streamline visualization when compared with the conventional 2D flow approach.

Method. Seven patients with functional univentricular heart after Fontan's operation and twenty-three healthy controls underwent 4D flow MRI. In two orthogonal two-chamber planes, streamline visualization was applied, and inflow angles with peak inflow velocity (PIV) were measured. Transatrioventricular flow quantification was assessed using conventional 2D multiplanar reformation (MPR) and 4D MPR tracking the annulus and perpendicular to the streamline inflow at PIV, and they were validated with net forward aortic flow.

Results. Inflow angles at PIV in the patient group demonstrated wide variation of angles and directions when compared with the control group ($P < .01$). The use of 4D flow MRI with streamlines visualization in quantification of the transatrioventricular flow had smaller limits of agreement (2.2 ± 4.1 mL; 95% limit of agreement −5.9–10.3 mL) when compared with the static plane assessment from 2DFlow MRI (−2.2 ± 18.5 mL; 95% limit of agreement agreement −38.5-34.1 mL). Stronger correlation was present in the 4D flow between the aortic and transatrioventricular flow (R^2 correlation in 4D flow: 0.893; in 2D flow: 0.786).

Conclusions. Streamline visualization in 4D flow MRI confirmed variable atrioventricular inflow directions in patients with functional univentricular heart with previous Fontan's procedure. 4D flow aided generation of measurement planes according to the blood flood dynamics and has proven to be more accurate than the fixed plane 2D flow measurements when calculating flow quantifications.

Key Words. 4D Flow; Magnetic Resonance Imaging; Fontan

Introduction

Functional univentricular hearts comprise of a spectrum of complex congenital cardiac malformations, where most are managed surgically in view of an ultimate Fontan's operation.[1] With advancement in surgical techniques, the survival of these patients has greatly improved over the past decades, and lifelong follow-up entails where gradual attrition from heart failure occurs in 6.7% of these patients.[2] There has been increasing use of cardiovascular magnetic resonance imaging (MRI) in addition to echocardiography for early recognition of single ventricular dysfunction and atrioventricular (AV) regurgitation.[3] Flow analysis with conventional two-dimensional (2D) single-directional velocity-encoded cine magnetic resonance imaging (VEC MRI) of the atrioventricular valves is limited due to cardiac motion and angulation of the inflow to the valve annulus.[4] The acquisition plane remains static throughout the cardiac cycle and is not adapted to dynamically changing flow direction, both during diastolic inflow as well as regurgitation during systole, which had been shown to result in overestimation of flow volume.[5–7] The use of four-dimensional (4D) VEC MRI, also known as 4D flow, can overcome these limitations as it measures all three directional components of the velocities of blood flow relative to the three spatial dimensions of a specific volume throughout the cardiac cycle. Retrospective manual adjustment of the measurement plane is therefore feasible taking into account to the inflow angle (i.e., perpendicular to the flow direction) and movement throughout the cardiac cycle.[8–11] Furthermore, flow patterns can be characterized and highlighted by streamlines, which are lines tangent to the local velocity vectors representing the blood flow direction at one instant in time, allowing assessment of complex flow patterns.[12,13]

Complex flow patterns are anticipated in patients with functional univentricular heart, prior to and after completion of Fontan circulation. We hypothesize that with the use of 4D flow MRI streamline visualization, flow quantification across the AV valve can be improved. The purpose of this study is to evaluate the inflow pattern in patients with functional univentricular heart after Fontan's operation when compared with healthy controls. With streamline visualization in 4D flow MRI, we performed flow quantification across the AV valve at the level of peak inflow velocity (PIV) and perpendicular to the inflow direction as well as perpendicular to regurgitant jets. This flow assessment is compared with the flow assessed from a static plane at the location of the AV annulus, i.e., 2D flow.

Materials and Methods

Study Population

The study was approved by the local Ethics Committee. Due to the retrospective observational nature of this study, the need for informed consent was waived by the local Ethics Committee. All the patient identifications were anonymized. Between May 2013 to January 2015, seven consecutive patients with functional univentricular heart after Fontan's operation who underwent MRI with 4D flow, as part of the standard imaging protocol, were retrospectively identified. For comparison as the control arm, 4D flow data from 23 healthy subjects with similar age and no history of heart disease were included from a previously reported study.[4]

MRI Technique

4D flow MRI was obtained using a 3T-MRI scanner (Ingenia, Philips Medical Systems, Best, The Netherlands) with maximal gradient amplitude of 45 mT/m for each axis and a slew rate of 200 T/m/s. A combination of FlexCoverage Posterior coil in the tabletop with a dStream Torso coil was used, providing up to 32 coil elements for signal reception. Gadolinium contrast agent (0.15 mmol/kg body weight, Dotarem, Guerbet, Aulnay-sous-Bois, France) was administrated in the patients group for the purpose of evaluation of late gadonilium delayed enhancement prior to 4D flow acquisition. Instead, 4D flow acquisition per se did not require any contrast administration. The MRI scanning commenced 1 minute after contrast administration.[14] For control subject, no contrast was administered. Velocity encoding was performed three-directionally with maximal velocity encoding (Venc) of 150 cm/s in all directions. Images were acquired with free breathing, without respiratory compensation and using retrospective ECG-gating. The 4D flow series were principally acquired with a T1-weighted sequence. All acquisitions were reconstructed into 30 phases and representing one average cardiac cycle. The heart rates of the all scanned patients ranged from 54 to 103 bpm with an average of 72.1 ± 13.2 bpm (mean $\pm$ SD); average heart rate of the control group was 71.8 ± 13.1 bpm while that of the patient group was 73.4 ± 14.6 bpm. Sequence parameters were adapted to individual patient's anatomy: spatial resolution $= 2.3 \times 2.3 \times 3.0$–$4.2$ mm; flip angle $= 10°$; time to echo (TE) = 3.2 ms; time to repetition (TR) 7.7 ms. The nominal temporal resolution was therefore $4 \times \text{TR} = 31$ ms. Parallel imaging was performed with sensitivity encoding (SENSE) using a factor of 2 and echo planar imaging with factor 5 was used for acquisition acceleration. The commercially available concomitant gradient correction and local phase correction filter on the MRI software platform were applied. The 4D flow acquisition time with a typical heart rate of 60–80 beats per minute was between 8 and 10 minutes. Two orthogonal two-chamber views were obtained in the patients group using two separate acquisitions rather than reconstruction from a single acquisition; while a two-chamber view of the left ventricle, and another four-chamber view were obtained for the healthy controls. Furthermore, a short axis stack of slices fully covering the heart was acquired for both groups for assessing the left ventricular volumes. These acquisitions were obtained using a steady-state free-precession sequences with scan parameters: spatial resolution = 1.0 × 1.0 × 8.0 mm; TE = 1.5 ms; TR = 3.0 ms; field of view = 350 mm field of view; section thickness = 8 mm; flip angle = 45°. The MRI technique adopted in this study had been detailed in previous studies and in accordance with the consensus statement.[14,15]

Image Analysis—Characterization of the AV Inflow

Images were analyzed using in-house developed Mass software.[4,16] 2D streamlines were generated and projected on the cardiac chambers. Image pixels within the cardiac chambers with a minimal in-plane velocity of 10 cm/s were defined as candidate seed points. Streamlines were generated by applying a simple Euler integration method in both forward and backward directions, with a step size of 1 pixel dimension and using bilinear image interpolation. Integration was terminated when either the velocity was below 10 cm/s, or when the trace length reached beyond the length of 80 screen pixels.

To delineate the inflow patterns with streamlines, two orthogonal two-chamber views, which were obtained by two separate acquisitions utilizing 2D cine steady-state free-precession sequences, in the patient group generated from perpendicular planes placed at the midpoint of AV valve to the ventricular apex were used to measure the two inflow angles relative to the long-axis. This was obtained by measuring angle 1: angle between the annulus to the long-axis at E peak where annulus plane was manually identified at the lateral and septal attachment of the AV valve, and long axis as the line through the middle of annulus to the ventricular apex; and angle 2: angle between the annulus and inflow direction at PIV at E peak, as the highest velocity occurs at E peak. We calculated the inflow angle at PIV-level by angle 2 minus angle 1 (Figure 1). Timing of the E peak was determined according to the flow-time curve obtained from velocity mapping. For patient 5, who was diagnosed to have double inlet left ventricle, we measured the angle of the inflow over the left AV valve as we observed negligible flow through the right AV orifice. The same measurements were performed on the two-chamber and four-chamber imaging planes at the left cardiac chamber in the healthy controls. For each patient, the reformatting procedure and the subsequent image analysis required 15 minutes to accomplish. The measurements were performed by a radiologist with 4 years of experience in cardiovascular MRI (S.H.L) and repeated measurements were done 1 week apart for intraobserver variation. Image analysis was also repeated by an experienced MRI technician with over 20 years of experience (P.v.d.B.) who was blinded to the results from the first observer.

Image Analysis: Characterization of the AV Forward Flow

To correlate with the conventional 2D approach, a static fixed multiplanar reformation (MPR) was reconstructed with velocity reformatted perpendicular to the MPR, statically positioned at the annulus retrospectively at end systole by an MRI technician (P.v.d.B.) with over 20 years of experience. For 4D flow quantification, during diastole MPR measurement planes were generated at the level of PIV distal to the annulus, using streamline visualization to ensure that the imaging plane is perpendicular to the inflow in two orthogonal planes in the 4 and 2 chamber orientation (Figure 1). The 4D flow quantification analysis was performed by a radiologist (S.H.L) with 4 years of experience in cardiovascular MRI. During systole, the reformatted measurement planes were placed at the annulus perpendicular to the streamline inflow. In case of valvular regurgitation, the measurement planes were placed perpendicular to the regurgitant jet visualized with the streamlines, approximately 1cm proximal to the valve. In diastole, a reformatted measurement plane was placed perpendicular to the streamlines at PIV-level during early filling, and remained aligned perpendicular to the inflow vectors of the highest velocity throughout the ventricular filling of the cardiac cycle.

Transvalvular flow volume was measured by integrating the transvalvular velocity over the inflow area and was integrated throughout the cardiac cycle. Net forward flow at aortic valve level was assessed from the same 4D flow MRI data for internal validation and calculation of agreement and correlation measurements with the trans-AV effective forward flow.

Image Analysis: Ventricular Volume and Ventricular Function

Manual contour segmentation of the ventricular volume in end systole and end diastole was

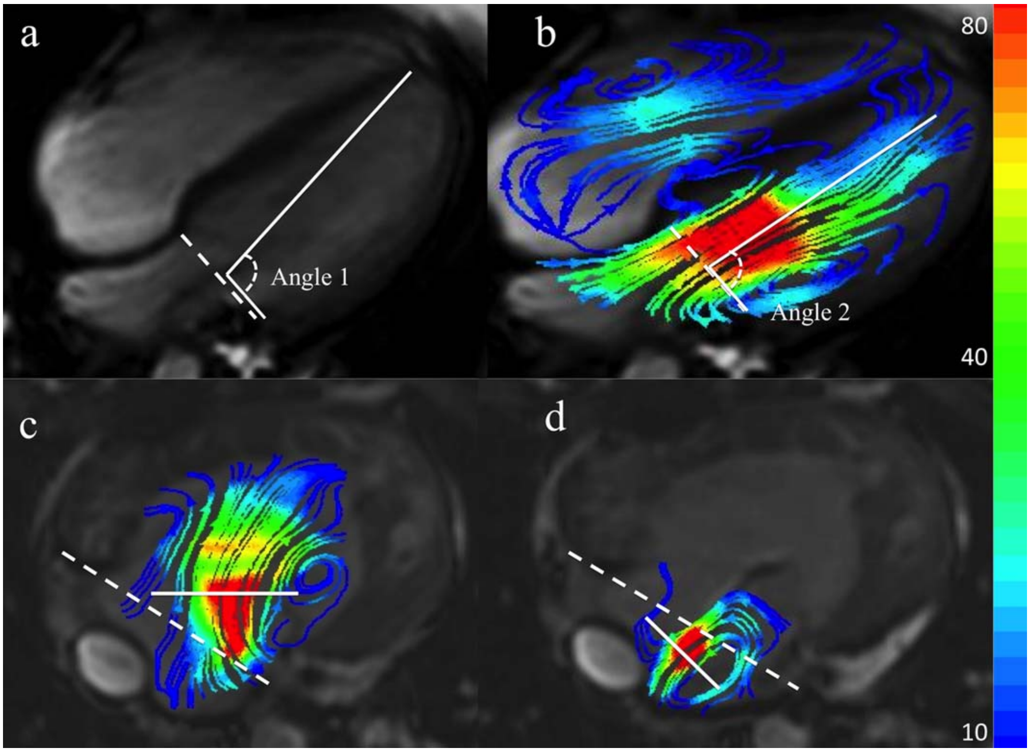

Figure 1. MRI 4D flow with streamline visualization. (A) Healthy volunteer four-chamber view. Angle between long-axis and annulus (angle 1) where annulus (dashed line) was manually identified as the lateral and septal attachment of left AV valve, and long axis as the line through the middle of annulus to the ventricular apex. (B) Healthy volunteer four-chamber view with streamline visualization by velocity encoding (color scale in cm/s). Angle between annulus and peak inflow velocity at E peak (angle 2). (C) A patient with functional univentricular heart, two-chamber view with streamline visualization at diastole phase of cardiac cycle. Positioning of the reformat plane is shown at peak inflow velocity (PIV)-level, angulated perpendicular to the inflow direction (solid line). (D) Same patient during systole of cardiac cycle. Regurgitation jet was observed at the AV valve, and reformat plane was placed perpendicular to the regurgitation jet. [Color figure can be viewed at wileyonlinelibrary.com]

performed on the short-axis stack using the in-house developed Mass software.[4,16] Ejection fraction (EF) was computed (EF = ventricular end diastolic volume − ventricular end systolic volume/ ventricular end diastolic volume).

Statistical Analysis

The data were analyzed with SPSS Statistics (v. 22.0 IBM SPSS, Chicago, IL) software. A *P* value of less than .05 was considered to indicate statistically significant differences. Continuous variables were presented as mean ± standard deviation or median with interquartile range (IQR) where appropriate. Variables were tested for normal distribution using the Shapiro–Wilk test. Demographic data differences between the patient group and healthy controls were evaluated by unpaired *t*-tests or Mann–Whitney *U*-test. E peak angles were analyzed with paired t-tests. Intraobserver and interobserver variations for repeated angle measurements were evaluated by intraclass correlation coefficient (ICC) and coefficient of variation. To evaluate the agreement between the conventional fixed plane 2D and 4D flow acquisition, the trans-AV flow in patients with univentricular heart physiology and healthy controls were evaluated by Bland-Altman plot analysis and Pearson correlation coefficients were reported. Mean signed differences and confidence intervals (i.e., the limits of agreement) and the mean relative unsigned difference

Table 1. Clinical Characteristics and Primary Diagnosis of Functional Univentricular Heart Patients

Subject	Gender	Age at Time of MRI (years)	Diagnosis
1	F	16	HLH, TGA
2	M	9	HLH
3	F	28	AVSD, DORV
4	F	15	TA, HRH
5	F	16	DILV
6	F	11	HLH
7	F	15	HLH

Table 2. Summary of the Patients' and Healthy Controls' Demographic Data

	Controls (N = 23)	Patients (N = 7)	*P* Value
Age (years)	16 (IQR 11–27)	15 (IQR 11–16)	.6
Male (N, %)	15 (65)	1 (14)	<.01
BSA (m^2)	1.6 ± 0.3	1.4 ±0.2	.09
EDV/BSA (mL/m^2)	87.1 ± 11.3	113.3 ± 42.8	<.01
EF (%)	60.5 (IQR 57–65.6)	49.0 (IQR 47–51)	<.01

F, female; M, male; HLH, hypoplastic left heart syndrome; HRH, hypoplastic right heart syndrome; TGA, transposition of great arteries; DILV, double inlet left ventricle; TA, tricuspid atresia; AVSD, atrioventricular septal defect; DORV, double outlet right ventricle; BSA, body surface area; EDV, ventricular end-diastolic volume; EF, ejection fraction.
Data are presented as mean ± standard deviation or median ± interquartile range whenever appropriate.

were determined, and their significance determined by paired sample *t*-tests.

Results

Baseline Characteristics

Baseline characteristics are summarized in Tables 1 and 2. There was no statistically significant difference in the age of the patient and control groups. The median age of the patient group was 16 (IQR 11–27), with a mean body surface area (BSA) of 1.4 ± 0.2 m^2, ventricular end diastolic volume to body surface area (EVD/BSA) of 113.3 ± 42.8 mL/m^2 and median ejection fraction of 49% (IQR 47–51).

Atrioventricular Inflow Angulation

Table 3 summarizes the inflow measurements. In both orthogonal two-chamber views in the patient group, there were statistically significant differences when compared with the control group in the annulus-long-axis angle (angle 1) (image plane 1: $P = .02$; image plane 2, $P < .01$). There were also statistically significant differences in the PIV angle (angle 2) at E peak for the patient group when compared with control group (image plane 1: $P = .03$; image plane 2: $P = .01$). All healthy controls had an inflow angle at PIV posterior to the long-axis at two-chamber plane (9.8 ± 7.6°) and lateral to the long axis at four-chamber plane (5.3 ± 6.9°). In the patient group, both orthogonal two chamber planes demonstrated wide variation of inflow angles at PIV, ranging from anterior to posterior position with respective to the long axis (image plane 1: −8.4 ± 17.9°; image plane 2: −8.2 ± 25.3°). Interobserver coefficient of variation for angle measurements was 10%, with an intraclass correlation coefficient higher or equal to 0.86 ($P < .01$). Intraobserver coefficient of variation for angle measurements was 3.8%, with an intraclass correlation coefficient higher or equal to 0.96 ($P < .01$).

Flow Quantifications across Atrioventricular Valve

Flow across the AV valve in the patient group and across the left AV valve in healthy controls was presented in Table 4. In the healthy population, strong correlation with aortic flow was present in both the 4D flow and the 2D flow measurements (R^2 correlation for 4D flow: 0.976; 2D flow: 0.986). In the patient group, strong correlation was present in the 4D flow while good correlation was observed in the 2D flow (R^2 correlation in 4D flow: 0.893; in 2D flow: 0.786). Absolute error of transmitral flow from aortic flow in the healthy group was statistically significant when comparing 4D flow with 2D flow (4D flow: 0.9 ± 3.6 mL; 2D flow: 10.4 ± 8.5 mL; $P \leq .01$). In the patient group, absolute error of trans-AV flow in 4D flow and 2D flow were not statistically different, but the measurements with the 2D flow did vary from vast underestimation to overestimation resulting in wide limits of agreement (4D flow: 2.2 ± 4.1 mL; 2D flow −2.2 ± 18.5 mL, $P = .5$). Agreement between the AV net forward flow in the patient and control groups are illustrated in the Bland-Altman graphs (Figure 2). For the healthy controls, mean difference between aortic flow and trans-AV flow when using 4D flow at PIV-level was 0.9 ± 3.6 mL; 95% limit of agreement −6.1 − 8.1 mL while using 2D

Table 3. Inflow Angles at E Peak

	Image plane 1			Image plane 2		
	Controls	Patients	*P* Value	Controls	Patients	*P* Value
Annulus—long axis (angle 1)	94.8 ± 2.9	81.0 ± 7.4	.02	94.2 ± 6.0	90.8 ±18.3	<.01
Peak inflow velocity angle (angle 2)	85.6 ± 8.1	99.1 ± 14.1	.03	88.9 ± 7.4	89.5 ± 17.4	.01
Inflow at PIV level (angle 1–2)	9.8 ± 7.6	−8.4 ± 17.9	<.01	5.3 ± 6.9	−8.2 ± 25.3	<.01

All the angles in the table were measured in degrees.
Angle measurements in two-chamber (image plane 1) and orthogonal two-chamber (image plane 2) in patients group obtained through perpendicular planes placed at midpoint of atrioventricular (AV) valve to ventricular apex. For healthy controls, two-chamber (image plane 1) and four-chamber (image plane 2) angles were measured. Data are presented as mean ± standard deviation.

Table 4. Comparison of Flow Volumes and Quantifications

	Control			Patients		
Reformat Plane	Static 2D	4D PIV with Angulation	*P* Value	Static 2D	4D PIV with Angulation	*P* Value
AV flow volume (mL/heart beat)	85.5 ± 26.3	76.1 ± 19.6		75.4 ± 14.0	79.8 ± 14.9	
Absolute error AV flow with aortic flow (mL)	10.4 ± 8.5	0.96 ± 3.6	<.01	−2.2 ± 18.5	2.2 ± 4.1	.5
Correlation coefficient of AV flow with aortic flow (R^2)	0.986	0.976		0.786	0.893	
Aortic flow (mL/heart beat)		75.1 ± 20.2			77.6 ± 38.5	

Comparison of transatrioventricular (AV) velocity mapping flow volume measurements using the static two-dimension (2D) multiplanar reformation (MPR) and four-dimension (4D) MPR tracking the annulus and peak inflow velocity (PIV) in the control and patient groups. Net forward flow at aortic valve level was assessed from the same 4D flow MRI data for internal validation and calculation of agreement and correlation measurements with the trans-AV effective forward flow. Data are presented as mean ± standard deviation.

flow mean difference was 10.4 ± 8.5 mL; 95% limit of agreement −6.2 − 27.0 mL. For the functional univentricular heart group, mean difference between aortic flow and trans-AV flow was smaller when PIV level measurement plane at PIV-level was used (2.2 ± 4.1mL; 95% limit of agreement −5.9 − 10.3 mL) when compared with using the 2D flow (−2.2 ± 18.5 mL; 95% limit of agreement −38.5 − 34.1 mL). Two of the patients had mild AV regurgitation (Subject 2, regurgitation fraction: 12.2%, net forward trans-AV flow: 60.7 mL, net forward aortic flow: 61.3 mL; Subject 6, regurgitation fraction: 8.8%, net forward trans-AV flow: 63.4 mL, net forward aortic flow: 67.3 mL).

Discussion

In this small pilot study, flow quantification over the atrioventricular valve in patients with a univentricular heart after Fontan's procedure was evaluated by comparing 4D flow MRI with streamline visualization and 2D flow MRI. A total of seven post-Fontan patients were included in the study and the main findings of our study were as follows: There was a significant difference in the inflow angle at PIV when comparing the patients with functional univentricular heart after Fontan's procedure with the healthy control groups. The PIV inflow angle in the patient group demonstrated wide variations of angles and directions. Second, the use of 4D flow MRI with streamlines visualization improved the positioning and angulation of measurement planes, thus allowing better quantification of the trans-AV flow, with smaller limits of agreement when compared with the static plane assessment from 2D flow MRI. The limits of agreement for 2D flow was −2.2 ± 18.5 mL, implying that 2D flow measurement can be anything from important underestimation to overestimation of flow. In fact, the wide limits of agreement in assessing atrioventricular flow minus aorta flow with 2D flow vs. 4D flow demonstrated the inappropriateness of using 2D flow in evaluating regurgitation. 2D flow might over or underestimate flow volumes up to 50%, which implies that regurgitation could not be accurately quantified.

A previous study by Calkoen et al.[4] has demonstrated a higher accuracy in trans-left AV flow quantification in patients after atrial septal defect repair when measurements were performed at the PIV-level angulated to the inflow with the use of streamline visualization by 4D flow MRI. In our study, annulus-inflow to PIV angle ranges from −8.4 ± 17.9 to −8.2 ± 25.3 in the two orthogonal two-chamber planes, signifying the flow directions can be extended to both anterior and posterior of the ventricular long-axis with high degree of variability, most likely due to the underlying abnormal anatomy. The healthy controls however, demonstrated uniform flow patterns with inflow projected more posterior to the long-axis during E peak in the two chamber view, and more lateral inflow direction in the four-chamber view. To have high accuracy in flow quantification, alignment of the measurement plane should be perpendicular to the flow.[6] With the complex and unpredictable flow patterns in our patients with functional univentricular heart, through-plane measurement by conventional static 2D VEC MRI would be deemed challenging and 4D flow MRI is superior as the

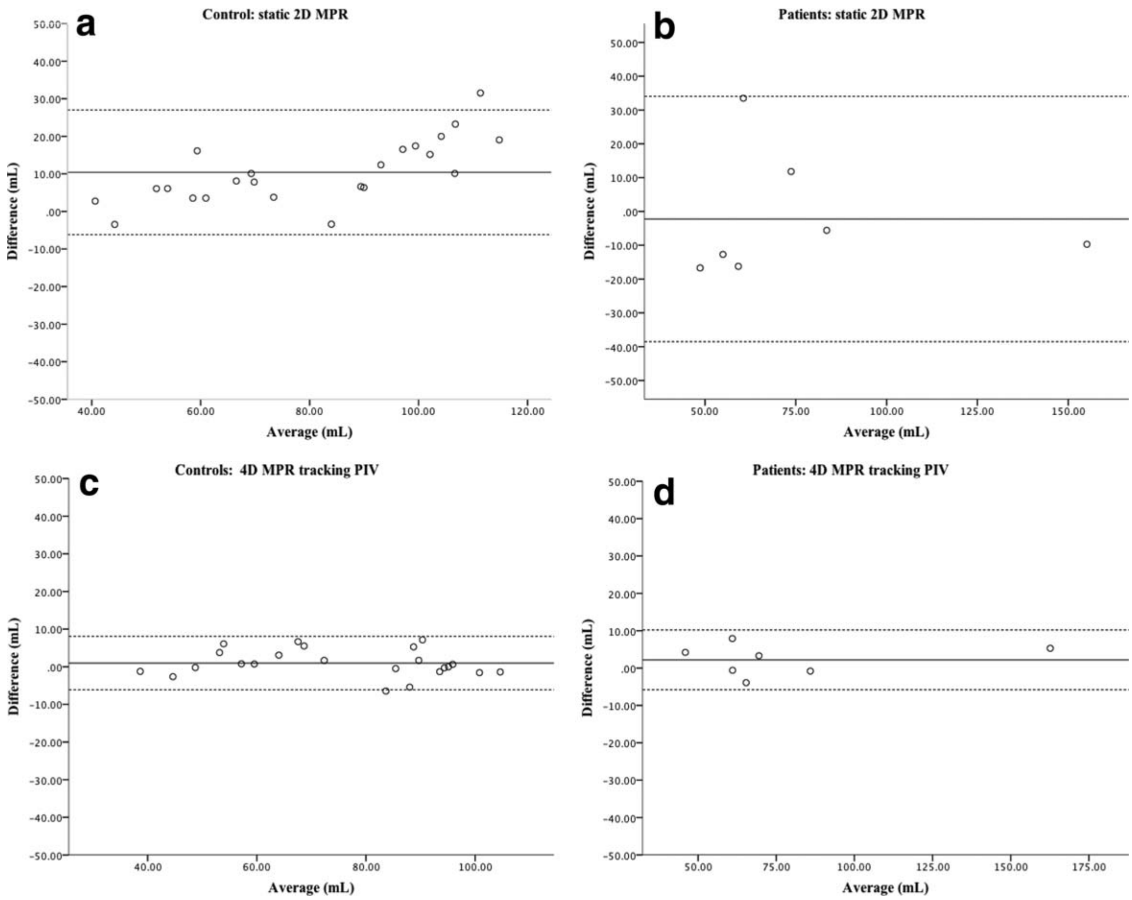

Figure 2. Agreement between atrioventricular valve forward flow and aorta. Bland–Altman graphs depicting agreement between aortic flow and effective forward flow over left AV valve in healthy patients with static 2D MPR (A), 4D MPR (B) tracking the peak inflow velocity (PIV) level in healthy controls and 2D MPR (C), 4D MPR (D) in patients with functional univentricular heart.

measurement plane can be adjusted retrospectively to align with the inflow direction at peak inflow.

In our study, a static measurement plane with through-plane encoded velocity, as used for 2D VEC MRI, was shown to be comparable in accuracy with 4D flow MRI in the healthy controls. This is in line with the previous study by Westenberg et al. that 2D VEC MRI can be comparable to 4D VEC MRI when assessment takes place at a plane that does not show through-plane motion.[17]

The higher flow volumes in the healthy controls with 2D VEC MRI were in line with previous studies reporting an overestimation of trans-left AV volume when measurements are carried out on a static plane inside the ventricle.[18] However, this was not observed with the 2D VEC MRI in our patients with functional univentricular heart. This may be explained by the increased misalignment of the flow directions in the patient group, where there may be less longitudinal motion of the AV groove due to operation, different anatomy, or myocardial dysfunction and hence leading to increased number of voxels of inaccurate velocity, resulting in overall underestimation in total volume.

The most important finding of the current study is the finding of higher correlation and agreement of the trans-AV flow in patients with functional univentricular heart using the 4D flow MRI when compared with 2D flow MRI (4D flow MRI R^2: 0.893; 2D flow MRI R^2: 0.786). Smaller limits of agreements were observed for 4D flow MRI than 2D VEC MRI in both healthy controls and patients with functional univentricular heart. The results consolidated the use of streamline visualization in adjustment of measurement plane for both atrial inflow and regurgitation jets.

In current practice of measurement of AVV-inflow with MRI, the image plane should be apical to the valve throughout the cardiac cycle and positioned at the annular level on an endsystolic image position.[4,19] Unfortunately, this is practically very difficult if not impossible in patients with post-Fontan patients to make this alignment during inflow measurement, thus potentially leading to under- or overestimation of inflow with 2D flow measurement. Our results showed that, with the technique of 4D flow MRI, patients with complex congenital heart defects such as post-Fontan patients with functional univentricular heart can be more accurately assessed as skewed anatomy is commonly encountered in these condition. The more accurate measurement by 4D flow might have positive clinical impacts on patients in evaluating the severity of the regurgitation, in particular benefiting children who could not always accurately quantify their own symptoms. Theoretically, the technique can also be extended to quantify flow in patients with other cardiac conditions, for instance, valvular heart disease.

Study Limitation

This is a single-centered retrospective study with small sample size. Second, 4D velocity acquisitions are subjected to error from non–flow-related local phase shifts, limited spatial and temporal resolution and respiratory motions.[20,21] However, transvalvular velocities were assessed with respect to the velocity sampled in nearby myocardium, eliminating the possible effects of phase offset errors. Second, the MPR planes used for flow quantification were planned using streamline visualization as projected onto the two- and four-chamber views, which were generated from different scans. Heart rate and respiratory rate variability may have an effect on the streamline data.

Conclusion

Streamline visualization in 4D flow MRI showed wide variation in peak AV inflow directions in patients with various functional univentricular hearts with previous Fontan's procedure. Furthermore, 4D Flow aided in generation of measurement planes according to the blood flood dynamics and this approach proved to be more accurate to assess AVV-flow as compared to the fixed plane 2D flow measurements.

Author Contributions

Concept/design: Hoi Lam She and Arno A.W. Roest. Data analysis/interpretation: Hoi Lam She, Arno A.W. Roest. Drafting article: Hoi Lam She, Emmeline E. Calkoen, Pieter J. van den Boogaard, Arno A.W. Roest. Critical revision of article: Hoi Lam She, Emmeline E. Calkoen, Pieter J. van den Boogaard, Rob J. van der Geest, Mark G. Hazekamp, Albert de Roos, Jos J.M. Westenberg, Arno A.W. Roest. Approval of article: Hoi Lam She, Emmeline E. Calkoen, Pieter J. van den Boogaard, Rob J. van der Geest, Mark G. Hazekamp, Albert de Roos, Jos J.M. Westenberg, Arno A.W. Roest. Statistics: Hoi Lam She, Arno A.W. Roest. Data collection: Hoi Lam She, Emmeline E. Calkoen, Pieter J. van den Boogaard, Rob J. van der Geest, Mark G. Hazekamp, Arno A.W. Roest

Corresponding Author: Hoi Lam She, MBBS, Department of Radiology, Princess Margaret Hospital, Hong Kong. Tel: +852 2990 2711; Fax: +852 2990 3276; E-mail: helenshe1025@gmail.com

Funding: The current study did not receive any funding support.

Ethical approval: All human and animal studies have been approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Due to the observational nature of the current study and all patient identification were anonymized, informed consent was waived by the local Ethics Committee.

Conflict of interest: All authors have no conflict of interest to declare.

Accepted in final form: June 21, 2016.

References

1 Khairy P, Poirier N, Mercier LA. Univentricular heart. *Circulation* 2007;115:800–812. Feb 13;

2 Khairy P, Fernandes SM, Mayer JE Jr, et al. Long-term survival, modes of death, and predictors of mortality in patients with fontan surgery. *Circulation* 2008;117:85–92. Jan 1;

3 Kilner PJ, Geva T, Kaemmerer H, Trindade PT, Schwitter J, Webb GD. Recommendations for cardiovascular magnetic resonance in adults with congenital heart disease from the respective working groups of the european society of cardiology. *Eur Heart J* 2010;31:794–805.

4 Calkoen EE, Roest AA, Kroft LJ, et al. Characterization and improved quantification of left ventricular inflow using streamline visualization with 4DFlow MRI in healthy controls and patients after atrioventricular septal defect correction. *J Magn Reson Imaging* 2015;41:1512–1520.

5 van der Hulst AE, Roest AA, Westenberg JJ, Kroft LJ, de Roos A. Cardiac MRI in postoperative congenital heart disease patients. *J Magn Reson Imaging* 2012;36:511–528. Sep;

6 Lotz J, Meier C, Leppert A, Galanski M. Cardiovascular flow measurement with phase-contrast MR imaging: basic facts and implementation. *Radiographics* 2002;22:651–671. May-Jun;

7 Rebergen SA, van der Wall EE, Doornbos J, de Roos A. Magnetic resonance measurement of velocity and flow: technique, validation, and cardiovascular applications. *Am Heart J* 1993;126:1439–1456.

8 Brix L, Ringgaard S, Rasmusson A, Sorensen TS, Kim WY. Three dimensional three component whole heart cardiovascular magnetic resonance velocity mapping: comparison of flow measurements from 3D and 2D acquisitions. *J Cardiovasc Magn Reson* 2009;11:3

9 Markl M, Frydrychowicz A, Kozerke S, Hope M, Wieben O. 4D flow MRI. *J Magn Reson Imaging* 2012;36:1015–1036.

10 Markl M, Kilner PJ, Ebbers T. Comprehensive 4D velocity mapping of the heart and great vessels by cardiovascular magnetic resonance. *J Cardiovasc Magn Reson* 2011;13:7

11 Nordmeyer S, Riesenkampff E, Messroghli D, et al. Four-dimensional velocity-encoded magnetic resonance imaging improves blood flow quantification in patients with complex accelerated flow. *J Magn Reson Imaging* 2013;37:208–216.

12 Napel S, Lee DH, Frayne R, Rutt BK. Visualizing three-dimensional flow with simulated streamlines and three-dimensional phase-contrast MR imaging. *J Magn Reson Imaging* 1992;2:143–153. Mar-Apr;

13 Bogren HG, Buonocore MH. 4D magnetic resonance velocity mapping of blood flow patterns in the aorta in young vs. Elderly normal subjects. *J Magn Reson Imaging* 1999;10:861–869.

14 Dyverfeldt P, Bissell M, Barker AJ, et al. 4D flow cardiovascular magnetic resonance consensus statement. *J Cardiovasc Magn Reson* 2015;17:72

15 Calkoen EE, Roest AA, van der Geest RJ, de Roos A, Westenberg JJ. Cardiovascular function and flow by 4-dimensional magnetic resonance imaging techniques: new applications. *J Thorac Imaging* 2014;29:185–196.

16 Roes SD, Hammer S, van der Geest RJ, et al. Flow assessment through four heart valves simultaneously using 3-dimensional 3-directional velocity-encoded magnetic resonance imaging with retrospective valve tracking in healthy volunteers and patients with valvular regurgitation. *Invest Radiol* 2009;44:669–675.

17 Westenberg JJ, Roes SD, Ajmone Marsan N, et al. Mitral valve and tricuspid valve blood flow: accurate quantification with 3D velocity-encoded MR imaging with retrospective valve tracking. *Radiology* 2008;249:792–800.

18 Kilner PJ, Gatehouse PD, Firmin DN. Flow measurement by magnetic resonance: a unique asset worth optimising. *J Cardiovasc Magn Reson.* 2007;9:723–728.

19 Fratz S, Chung T, Greil G, et al. Guidelines and protocols for cardiovascular magnetic resonance in children and adults with congenital heart disease: SCMR expert consensus group on congenital heart disease. *J Cardiovasc Magn Reson* 2013; 15:51

20 Uribe S, Beerbaum P, Sorensen TS, Rasmusson A, Razavi R, Schaeffter T. Four-dimensional (4D) flow of the whole heart and great vessels using real-time respiratory self-gating. *Magn Reson Med.* 2009;62:984–992.

21 Gatehouse PD, Rolf MP, Graves MJ, et al. Flow measurement by cardiovascular magnetic resonance: a multi-centre multi-vendor study of background phase offset errors that can compromise the accuracy of derived regurgitant or shunt flow measurements. *J Cardiovasc Magn Reson* 2010;12:5