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Phase Contrast MR Quantification of Aortic Regurgitation in Patients with Turbulent Aortic Flow

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Abstract

OBJECTIVE: To assess variability in measurements and accurately quantify aortic regurgitation in patients with coexisting turbulent aortic flow using phase contrast MR (PC-MR).

METHODS: All patients (n=21) underwent PC-MR at 2 sites: ascending aorta, sinuses of Valsalva and left ventricular outflow tract. The net flow/minute (NF), forward flow/minute (FF), regurgitant flow/minute (RF) and regurgitant fraction (RF%) were compared to the sum of superior vena cava and descending aortic flow/minute (SVC+DA), left ventricular cardiac output, difference between the two and percentage difference, respectively.

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RESULTS: NF, FF and RF were significantly different between each site. The combination of FF in the left ventricular outflow tract and NF from SVC+DA provided the best reliability of RF and RF% [ICC 0.881; 95% CI: 0.882–0.878 and 0.838; 95% CI: 0.837–0.838]).

CONCLUSION: Combining flow measurements from more than one site provides the most accurate quantification of aortic regurgitation in patients with turbulent aortic flow.

Introduction

Patients with aortic regurgitation may remain asymptomatic until the left ventricle begins to fail and symptoms of heart failure develop [1]. Serial monitoring is typically performed with transthoracic echocardiography (TTE), although cardiac magnetic resonance (CMR) can be a useful adjunct to TTE [2, 3]. CMR is established as the gold standard for quantification of left ventricular volumes and function and may provide more reproducible data for aortic regurgitation quantification [4–8]. Furthermore, CMR does not suffer from limited acoustic windows which may be compromised in patients with prior intervention or thoracic surgery.

Phase contrast MR (PC-MR) allows for direct quantification of forward and regurgitant flow [9]. However, no dedicated imaging guidelines exist which recommend exactly where PC-MR should be performed. Often local institutional protocols use the ascending aorta (AA) near the sinotubular junction for quantification of aortic valvular disease. There is growing evidence that the exact site selected to perform PC-MR e.g. ascending aorta (AA) at the level of the right pulmonary artery, aorta at the level of sinotubular junction, sinuses of Valsalva, or left ventricular outflow tract (LVOT), can lead to variability in the obtained aortic flow parameters [10–13]. The accuracy of flow estimates is further jeopardized in patients with turbulent flow [14, 15]. Hence, our study focuses on patients with turbulent flow in the aorta due to aortic stenosis and/or proximal aortic dilation where determination of accurate flow quantification parameters is the most challenging. We aim to further evaluate the variability in aortic flow measurements obtained by PC-MR from different sites as well as determine the most reliable measure of regurgitant flow in this subset of patients. We hope that this knowledge can guide the imager in deciding the best location(s) to perform PC-MR sequence and thus provide the most accurate data for clinical decision making.

Materials and Methods

This HIPAA compliant retrospective study was approved by the Institutional Review Board with waiver of informed consent.

Patients:

Consecutive patients with aortic stenosis on echocardiography and/or aortic root and proximal AA dilation who underwent CMR with PC-MR at two or more levels within the LVOT and AA were included. Patients were identified by an electronic search of our congenital imaging database for the period January 1, 2008 to November 1, 2016. Those with more than minimal mitral regurgitation as defined by echocardiography or a shunt of any severity were excluded. Demographic data were collected from the electronic medical

record and the severity of aortic stenosis and aortic dimensions were determined from prior echocardiography within 1 year of the MRI study.

MR Imaging:

All examinations were performed on a 1.5 Tesla scanner (Achieva or Ingenia, Philips, Best, The Netherlands) under the direct supervision of a cardiothoracic radiologist and a pediatric cardiologist. PC-MR was performed using a free breathing, vector-cardiographic gated, velocity-encoded sequence with 40 phases per cardiac cycle taking care to ensure orthogonal orientation to the target site. Imaging was performed in at least two of the following sites (Figure 1):

- Mid AA: Near the level of pulmonary arterial bifurcation to avoid the flow turbulence near the aortic valve leaflets.
- Sinuses of Valsalva (SoV)
- LVOT: Just below the aortic annulus.

The AA and LVOT PC-MR locations were chosen to avoid the areas of maximum flow turbulence and velocity encoding (VENC) was carefully adjusted to be close to but just higher than the peak velocity as determined by echocardiography. The plane used for the AA PC-MR also included the superior vena cava (SVC) and descending thoracic aorta (DA) in all subjects (Figure 2). For SoV where flow turbulence was high, only regurgitant flow was obtained by deliberately setting a low VENC of 100 m/s (leading to aliasing in systole). The forward and net flows were not analyzed at the SOV level given the marked flow turbulence in this location.

Cine short axis imaging was performed using breath hold, vector-cardiographic gated, segmented k-space, steady-state free precession sequence, with 30 phases per cardiac cycle.

Post processing and Flow parameters:

Post processing of all MR data was performed on commercially available software (QMass and QFlow, Medis, Leiden, The Netherlands) using a dedicated work station by a single individual. The following parameters were estimated at various sites and compared to the gold standards described below:

1. Forward flow/minute (FF) at the AA and LVOT were compared to the gold standard left ventricular cardiac output (LV_{CO}). This was obtained from cine volumetry, where $LV_{CO} = (\text{End Diastolic Volume} - \text{End Systolic Volume}) \times \text{heart rate}$.
2. Net flow/minute (NF) at AA and LVOT were compared to the gold standard obtained by summation of flow per minute in SVC and DA (SVC+DA). The DA was used as a surrogate for IVC flow thereby allowing for quantification of the net systemic flow: SVC + IVC[16].
3. Regurgitant flow/min (RF) at AA, SoV and LVOT were compared to the gold standard $LV_{CO} - (\text{SVC} + \text{DA}) \text{ flow/minute}$. In addition, RF was also estimated

using combination data (LVOT FF –(SVC+DA)) and compared to the gold standard.

4. Regurgitant fraction ($RF\% = RF \times 100 / FF$) single site estimates from AA, and LVOT were compared to $\{LV_{CO} - (SVC + DA)\} \times 100 / LV_{CO}$. For measurements at SoV (where only RF was estimated), calculation of RF% required combination of data with FF calculated as $(SVC+DA)+SoV_{RF}$ to enable estimation of RF%. In addition, RF% was also obtained using another set of combined data i.e. $(LVOT\ FF - (SVC+DA)) \times 100 / LVOT\ FF$ and compared to gold standard.

Statistical analysis:

Continuous data was summarized with means and standard deviations and categorical data was summarized using counts and percentages. Based on the distribution of the data, either paired t-test or signed rank test was used to compare the FF and NF in the LVOT and AA. Analysis of variance (ANOVA) was used to compare RF and RF% in the AA, SOV and LVOT. Intraclass Correlation Coefficients (ICC) and Bland Altman plots were used to assess the reliability and agreement between FF, NF, RF and RF% at the three locations with the gold standards. For Bland-Altman plots, horizontal lines were drawn at the mean difference and at the limits of agreement (defined as the mean difference ± 1.96 times the standard deviation of the differences). The bias was calculated as the difference between the flow values at different locations from the gold standard. Depending on normality, either a one-sample t-test or Wilcoxon signed rank test was used to test the significance of the observed bias in flow estimates between locations.

A p-value of less than 0.05 was considered statistically significant for all hypothesis tests. Statistical analysis was performed with SAS software version 9.4 (SAS Institute, Cary, North Carolina).

Results

A total of 25 studies of 21 patients met our inclusion and exclusion criteria. Demographic data are shown in Table 1. Summary statistics for measurements of FF, NF, RF and RF% at various sites are displayed in Figures 3A-C.

Forward Flow

FF in the AA and LVOT were significantly different from one another ($p = 0.01$). Though the FF at AA and LVOT were both underestimated compared to LV_{CO} , the mean difference in flow (bias) was significantly larger for the AA than the LVOT ($p=0.01$) (Table 2). LVOT also provided superior reliability with LV_{CO} compared to the AA with excellent ICC of 0.946 (95% CI 0.944–0.949) (Table 3).

Net Flow

NF in the AA and LVOT were also statistically different ($p= 0.02$). Although NF in the LVOT and AA both had good ICC compared to SVC+DA (Table 3), the net flow in the LVOT was overestimated compared to gold standard SVC+DA while flow was underestimated in the AA (Table 2).

Regurgitant Flow

Regurgitant flow (RF) was significantly different between the AA, SoV and LVOT ($p=0.04$). The values of RF were all significantly underestimated compared to the gold standard and had moderate reliability with ICC of 0.651, 0.745 and 0.510 for AA, SoV and LVOT respectively (Table 2, and Table 3). Among the three direct estimates of RF, SoV had superior reliability and smallest bias. This bias for RF at SoV was statistically significantly lower than LVOT ($p=0.01$) but not significantly lower than AA.

We also evaluated whether a combination of flow data provided improved reliability for RF compared to direct estimation at a single level. In view of the excellent reliability of LVOT for FF measurement, we assessed the performance of LVOT FF – (SVC +DA) flow. Though RF using this combination of data was significantly lower than the gold standard ($p=0.02$), it had good reliability (ICC 0.88) which was superior to any other single estimate.

Regurgitant Fraction (RF%)

The regurgitant fraction (RF%) directly obtained from single site measurements at AA and LVOT was also underestimated compared to the gold standard and had only moderate reliability with ICC of 0.440 and 0.355 respectively (Table 2, and Table 3).

When using combination of data, LVOT FF combined with SVC+DA had the best performance (ICC 0.838) compared to any single site estimate and compared to SoV_{RF} combined with SVC+DA (Table 3). Also, the observed bias using this method was the smallest in magnitude compared to the gold standard. There were significant differences in mean bias between the estimated RF using combination data and single flow estimates from AA and LVOT ($p=0.01$ & $p=0.002$); though this bias did not reach significance level compared to SoV flow.

Discussion

PC-MR is widely used for quantification of valve regurgitation, but the slice location of flow imaging can affect the accuracy of measurements. This has been suggested in some prior studies as well [10–15]. Our study adds to the existing data by assessing patients with turbulent flow including concomitant aortic regurgitation and aortic stenosis and/or aortic dilatation and suggests that the best estimate for regurgitation is obtained by using a combination of data (FF from the LVOT and NF from the sum of SVC and DA flow) in this particularly challenging subset of patients.

Chaturvedi *et al*, assessed patients with aortic regurgitation and found statistically significant differences in the NF between three different sites (sinuses of Valsalva, sinotubular junction and AA)[10]. In their study, RF was underestimated to a greater degree the further away PC-MR was performed in the ascending aorta with respect to the aortic valve. This implies that the best estimate of aortic regurgitation is obtained closer to the valve, which is consistent with the usual clinical practice of performing PC MR at the level of the sinotubular junction. However, this approach can be problematic in patients with aortic valve stenosis as seen in our study, since sites closer to the valve have the most flow turbulence and are therefore more prone to errors in estimation.

The issue of flow turbulence and its effects on PC-MR is substantiated by Muzzarelli *et al.*, who showed that forward flow in patients with bicuspid aortic valve is underestimated to a greater degree than controls[13]. In such patients, the preferred clinical practice is to avoid turbulent flow, though the best location for data acquisition and what combination of data provide the best estimate of regurgitant flow was not assessed.

Variability in PC-MR was also studied in pediatric patients with aortic regurgitation by Iwamoto *et al.* PC-MR performed at multiple sites was compared to LV_{CO} and PC-MR in the main pulmonary artery[12]. Similar to our study, RF measured by PC-MR was found to be variable depending on the location. In this study, PC measurements were performed at 3 locations: ascending aorta, valve hinge points in diastole (similar to SOV in our study) and valve hinge points in systole (similar to LVOT in our study). Our study differs in that we have focused on a unique subset of patients with aortic stenosis and aortic dilatation which leads to turbulent flow making PC-MR even more challenging. Also, instead of using main pulmonary artery as a surrogate for NF, we used SVC+DA since this is readily available on routine AA flow acquisitions (and therefore does not require a separate acquisition). We have tried to determine the combination of data providing the best estimate of regurgitant fraction in this complex patient population.

Based on our results, we propose using FF estimate from LVOT and NF estimate from SVC +DA to provide the most accurate estimate of regurgitant fraction, although this is also slightly underestimated based on our study. Single site estimation of regurgitant fraction has only moderate reliability therefore multiple sites are required to obtain the most accurate data. Future large scale prospective studies can help confirm these results. Though we feel this method is fairly robust, an important caveat is that in certain situations (e.g. aortopulmonary collaterals or venous obstruction with collateral flow), SVC+ DA may not be representative of ascending aortic stroke volume. Hence, unique hemodynamics of a particular case should be considered before using combined data.

Limitations of our study include its retrospective nature and the relatively small sample size. In view of the retrospective nature of the study various sites of measurements were obtained in different patients depending on user preference. This limitation reflects the current uncertainty about where the most accurate phase contrast measurements in this challenging population should be obtained. Because of the small sample size, further subgroup analysis depending on the degree of aortic stenosis, aortic dilatation and valve morphology is not feasible in this study. Larger studies would be helpful in determining, how the measurements obtained from PC-MR vary with the degree of stenosis and morphology of aortic valve (unicuspid, bicuspid, tricuspid). Our small sample size also creates a heterogeneous study population (consisting of aortic valve stenosis of varying severity and ascending aortic dilatation) which could limit the generalizability of results.

This study provides data and informs future studies, which can focus on patients with normal valves, stenosis and valve morphology and determine the impact of each of these factors on the accuracy of measurements and validate our results. We hope that our study will provide guidance to imagers and pave the way for future larger prospective studies.

Conclusion

PC-MR allows for direct quantification of aortic flow, however these measurements are subject to variability depending on slice location, particularly in the setting of underlying turbulent flow from valvular disease or aortic dilation. Obtaining flow measurements at more than one site provides the most accurate quantification to guide clinical decision-making. Based on our study, the combination of forward flow at the LVOT and NF from SVC+DA provides the most precise quantification.

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Ascending Aorta

Sinus of Valsalva

Left Ventricular Outflow Tract

Figure 1:
Anatomic sites for PC-MR imaging

Figure 2:
PC-MR of the ascending aorta (red circle) at the level of pulmonary arterial bifurcation.
Note that the superior vena cava (blue circle) and descending aorta (yellow circle) are also
included in the same acquisition.

A

B

C

D

Figure 3: Box and whisker plot with Mean (diamond), median (bar), upper and lower quartile (box), and maximal and minimal (whisker) values for forward flow (FF) (3A), net flow (NF) (3B), regurgitant flow (RF) (3C) and regurgitant fraction (RF%) (3D).

Left ventricular cardiac output: LV_{CO}

Left ventricular outflow tract: LVOT

Ascending aorta: AA

Sinuses of Valsalva: SoV

SVC+DA: sum of superior vena cava and descending aorta

Table 1:

Demographic data

Sex	11 males (52%) 10 females (48%)
Age at the time of the study	21.8 years $\pm$ 9.8 Range 10–54 years
Aortic stenosis	17 (81%)
-Mild	11 (52%)
-Moderate	5 (24%)
-Severe	1 (5%)
Dilated aortic root or proximal AA	
AA Z score	
Root Z score	3.7 $\pm$ 2.5 2.8 $\pm$ 1.8
Aortic valve morphology	
<i>Native aortic valve</i>	
Unicuspid	2 (10%)
Bicuspid	13 (62%)
Tricuspid	2 (10%)
Post Surgical	
Bioprosthetic	1 (5%)
Status post Ross procedure	3 (14%)

Data presented as mean $\pm$ SD or number (percent)

Table 2:

Mean differences (bias), standard deviations ($\pm$), 95% CI and limits of agreement between gold standards and flow values at different locations.

	Total N=25	Mean Difference	95% Lower CI	95% Upper CI	Limits of Agreement
Forward Flow					
AA	15	1316.73 $\pm$ 1082.61	717.20	1916.26	-805.2/3438.6
LVOT	19	543.11 $\pm$ 743.09	184.95	901.26	-913.4/1999.6
Net Flow					
AA	15	423.47 $\pm$ 883.469	-65.78	912.715	-1308.1/ 2155.1
LVOT	15	-558.73 $\pm$ 794.30	-998.60	-118.86	-2115.6/998.1
Regurgitant Flow					
AA	15	1029.74 $\pm$ 979.04	487.57	1571.91	-1100.9/2967.9
SoV	13	815.38 $\pm$ 958.29	236.29	1394.47	-1062.8/2693.6
LVOT	15 [*]	1205.49 $\pm$ 1272.76	500.66	1910.32	-1289.1/3700.1
Combined flow data using FF(LVOT) and SVC+DA	19	543.11 $\pm$ 743.09	184.95	901.26	-919.7/ 2021.4
Regurgitant Fraction %					
AA	15	9.937 $\pm$ 10.542	4.100	15.775	-10.72/30.60
LVOT	15 [*]	12.411 $\pm$ 10.81	6.425	18.398	-8.78/33.60
Combined flow data using SoV and SVC+DA	13	7.437 $\pm$ 10.323	1.199	13.675	-12.80/27.67
Combined flow data using FF(LVOT) and SVC+DA	19	5.355 $\pm$ 7.096	1.935	8.776	-8.55/19.26

^{*} LVOT phase contrast imaging was performed in 19 patients. However, the regurgitant flow aliased in 4 subjects. Hence LVOT FF was estimated in 19, but single site RF and RF% from LVOT were estimated in 15.

Table 3:

Intraclass Correlation Coefficient

	ICC	95% Lower CI	95% Upper CI
Forward Flow			
AA	0.813	0.801	0.819
LVOT	0.946	0.944	0.949
Net Flow			
AA	0.801	0.790	0.805
LVOT	0.825	0.812	0.831
Regurgitant Flow			
AA	0.651	0.631	0.697
SOV	0.745	0.732	0.751
LVOT	0.510	0.457	0.636
Combined flow data using FF(LVOT) and SVC+DA	0.881	0.882	0.878
RF %			
AA	0.440	0.346	0.746
LVOT	0.355	0.249	0.750
Combined flow data using SoV and SVC+DA	0.601	0.576	0.658
Combined flow data using LVOT FF and SVC+DA	0.838	0.837	0.838