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Quantification of aortic flow by phase-contrast magnetic resonance in patients with bicuspid aortic valve

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Aims Bicuspid aortic valve (BAV) causes complex flow patterns in the ascending aorta (AAo), which may compromise the accuracy of flow measurement by phase-contrast magnetic resonance (PC-MR). Therefore, we aimed to assess and compare the accuracy of forward flow measurement in the AAo, where complex flow is more dominant in BAV patients, with flow quantification in the left ventricular outflow tract (LVOT) and the aortic valve orifice (AV), where complex flow is less important, in BAV patients and controls.

Methods and results Flow was measured by PC-MR in 22 BAV patients and 20 controls at the following positions: (i) LVOT, (ii) AV, and (iii) AAo, and compared with the left ventricular stroke volume (LVSV). The correlation between the LVSV and the forward flow in the LVOT, the AV, and the AAo was good in BAV patients ($r = 0.97/0.96/0.93$; $P < 0.01$) and controls ($r = 0.96/0.93/0.93$; $P < 0.01$). However, in relation with the LVSV, the forward flow in the AAo was mildly underestimated in controls and much more in BAV patients [median (inter-quartile range): 9% (4%/15%) vs. 22% (8%/30%); $P < 0.01$]. This was not the case in the LVOT and the AV. The severity of flow underestimation in the AAo was associated with flow eccentricity.

Conclusion Flow measurement in the AAo leads to an underestimation of the forward flow in BAV patients. Measurement in the LVOT or the AV, where complex flow is less prominent, is an alternative means for quantifying the systolic forward flow in BAV patients.

Keywords phase-contrast magnetic resonance • flow • aortic valve regurgitation • bicuspid aortic valve

Introduction

Cardiac magnetic resonance (CMR) imaging has become an important diagnostic tool for the evaluation and follow-up of patients with bicuspid aortic valve (BAV), because it allows a comprehensive assessment of both aortic morphology and aortic valve function. Phase-contrast magnetic resonance (PC-MR) is a non-invasive method for the measurement of blood flow that is used for the hemodynamic evaluation of the aortic valve, including the quantitative assessment of the aortic valve stenosis and regurgitation,[1–8] which was shown to have important prognostic implications.[9] Typically, the assessment of aortic regurgitation by CMR relies on the measurement of the forward and backward flow in the ascending aorta (AAo) by PC-MR, thereby quantifying the regurgitant fraction. However, conversely to patients with tricuspid aortic valve, patients with BAV have an eccentric systolic flow jet beyond the level of the aortic valve orifice (AV) that causes an abnormal flow condition in the AAo, which is characterized by an exaggerated turbulence and a helical pattern.[10] In this specific context, the flow quantification in the AAo may be inaccurate.[11–13] Therefore, we hypothesized that flow measurement at the level of the AAo in patients with BAV leads to an underestimation of the aortic forward flow. To test this hypothesis, we measured the forward flow at the level of the AAo and compared this value with the flow measurement at the level of the left ventricular outflow tract (LVOT) and the AV, where abnormal secondary flow patterns are less prominent, and with the left ventricular stroke volume (LVSV) in patients with BAV and in control patients with the normal tricuspid aortic valve.

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Methods

Patient population

Twenty-three consecutive patients with BAV and 20 control patients without aortic valve pathology who underwent a CMR examination for clinical indication at the University Hospital Lausanne (19 BAV patients and 4 controls) or at the Cardiocentro Ticino (4 BAV patients and 16 controls) were included in this study from December 2010 to January 2012. BAV patients ($n = 1$) with the evidence of mitral regurgitation on cine steady-state-free precession images of the left ventricle were excluded from this study. Therefore, the final population consisted of 22 patients with BAV and 20 controls.

CMR protocol

Scans were acquired with three different scanners: (i) 1.5-T Magnetom Symphony (Siemens Medical System), using a six-channel cardiac coil ($n = 19$), (ii) 3.0-T Magnetom Verio (Siemens Medical System), using a 36-channel cardiac coil ($n = 3$), or (iii) 3.0-T Magnetom Skyra (Siemens Medical System), using a 36-channel cardiac coil ($n = 20$). All patients underwent standard cine steady-state-free precession images of the left ventricle in the long-axis planes and a stack of short-axis images for volumetric and functional assessment of the left ventricle. Cine images in the three-chamber orientation and the LVOT were acquired to plan the acquisition of the flow images. Through-plane breath-hold segmented PC-MR were acquired at the level of the LVOT, at the level of the aortic valve, and in the proximal AAo, as shown in *Figure 1*. On the 1.5-T Magnetom Symphony, the typical flow imaging parameters were as follows: echo time (TE) = 3.8 ms, repetition time (TR) = 13.4 ms, segments 6, field of view (FOV) = 240–320 mm, matrix = 77 × 128, number of phases/cardiac cycle = 25, number of excitations (NEX) = 1, slice thickness (ST) = 6 mm. On the 3.0-T Magnetom Verio, the typical flow imaging parameters were as follows: TE = 2.0 ms, TR = 11.9 ms, segments 4, FOV = 220 × 320 mm, matrix = 132 × 192, number of phases/cardiac cycle = 20, NEX = 1, ST = 5.5 mm. Finally, on the 3.0-T Magnetom Skyra, the typical imaging parameters were as follows: TE = 2.7 ms, TR = 11.6 ms, segments 3, FOV = 240 × 350 mm, matrix = 132 × 192, number of phases/cardiac cycle = 20, NEX = 1, ST = 6 mm. The encoding velocity value was individually adjusted according to the velocity of blood flow starting from 200 cm/s. Concomitant gradient correction was performed online during the image reconstruction in all scanners.

Data analysis

Left ventricular volumetric quantification and flow analyses were performed on a dedicated workstation (Argus, Syngo, Siemens Medical System). The following measurements were performed: left ventricular end-diastolic volume, stroke volume, and ejection fraction based on the short-axis stack of cine images. The quantification was performed with the Simpson's method, manually tracing the left ventricular end-diastolic and end-systolic endocardial borders. The flow at the different locations was quantified by manually tracing the region of interest on PC-CMR images (*Figure 1*). Notably, at all levels, the 'systolic' component only of the forward flow was quantified.

The dimensions of the AAo (cross-sectional area and antero-posterior diameter) were measured on the magnitude image of the flow sequence at end-systole and end-diastole. The systolic longitudinal excursion of the aortic valve annulus was measured based on the LVOT cine image. The aortic valve area was measured by planimetry on dedicated cine images of the aortic valve (available in all but three BAV patients).

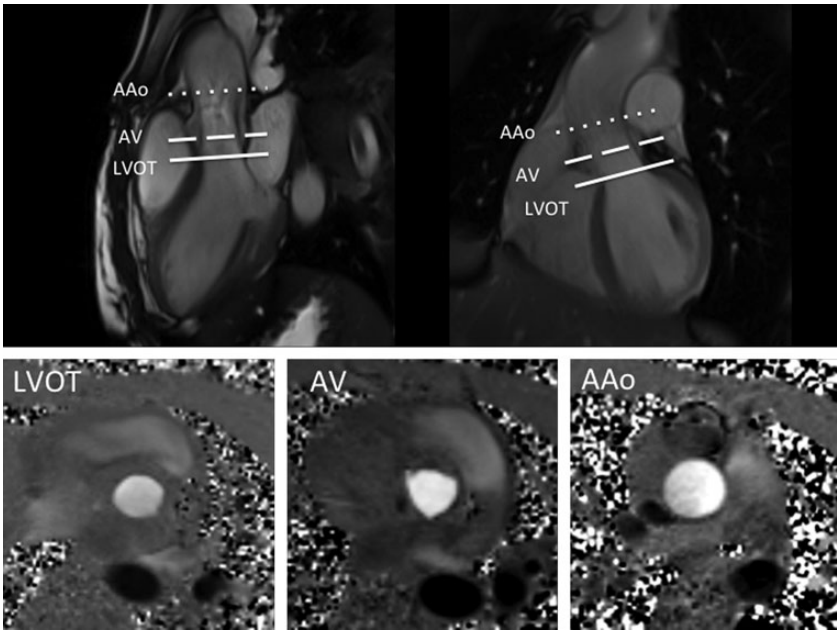

Figure 1: Illustration of the location and planning of the flow measurement by PC-MR at the level of the LVOT, the AV, and the AAo. Note that the imaging planes were prescribed in an orthogonal direction to the anatomical location, based on the systolic frame of the three-chamber long-axis and the LVOT view, respectively (see upper two figures). The inferior row of figures shows the PC-MR images at the level of the LVOT, the aortic valve, and the AAo. LVOT, left ventricular outflow tract; AV, aortic valve; AAo, ascending aorta.

Further analyses were performed to define the mechanism leading to inaccuracy of flow measurement in the AAo, because multiple factors may contribute to errors in flow measurement. The most relevant include: (i) complex flow patterns with consequent intravoxel dephasing and underestimation in velocity measurement,[7,13] (ii) longitudinal excursion of the aortic annulus with a consequent systolic change in the aortic luminal volume between the fixed plane of velocity acquisition and the moving plane of the aortic valve annulus,[11,14] and (iii) phase-offset errors.[15]

The complexity of flow pattern in the AAo was assessed by quantifying flow eccentricity according to the normalized flow displacement from the vessel centre at peak systole, as previously described.[16] Other elements of complex flow, such as turbulence and helical flow, which are known to be present in BAV patients and are related with flow eccentricity, are *per se* not available for quantification based on two-dimensional (2D) flow dataset.[10] Furthermore, to ascertain if there was any loss of signal enhancement due to increased intravoxel dephasing, the relative mean signal intensity was computed by taking the ratio of the mean signal intensity across the vessels in systole over the mean signal intensity across the vessels in diastole.[13]

The magnitude of the systolic change in the aortic luminal volume under the imaging plane was estimated by multiplying the aortic cross-sectional surface change (systolic − diastolic aortic cross-sectional area) by the longitudinal excursion in the aortic valve annulus.

In the absence of adjacent stationary tissue or an available background velocity correction method,[17,18] the mean velocity across the vessel in diastole was compared against the difference between the LVSV and the flow volumes to identify if any systematic errors were present (phase-offsets).

Statistics

Continuous data are presented as mean ± standard deviation or median (range) as appropriate. Categorical data are presented as numbers and percentages. Differences between BAV patients and controls were tested by *t*-test for continuous variables with normal distribution, Mann–Whitney *U*-test for continuous variables without normal distribution, and Fisher's test for nominal variables. The correlation between flow measurements and LVSV was assessed based on linear regression analyses and Bland–Altman plots. Linear regression analyses also were used to investigate the inter-relation between flow eccentricity, estimated magnitude of aortic luminal volume change, and the degree of flow underestimation in the AAo. A *P*-value of ≤ 0.05 was considered statistically significant (two-sided). Analyses were performed using the commercially available statistical package (SPSS version 19.0, IBM).

Results

Characteristics of the study population are summarized in *Table 1*. There were not significant differences regarding age, gender, body surface area, left ventricular volumes, ejection fraction, and stroke volume between BAV patients and controls. As expected, patients with BAV had a larger AAo when compared with control patients. The aortic valve area of BAV patients ranged between 0.5 and 5.8 cm^2. However, only two had a severe aortic stenosis (i.e. <1 cm^2). All other BAV patients did not have aortic valve stenosis (all ≥ 2.7 cm^2).

Table 1 Baseline characteristics

	Bicuspid aortic valve (*N* = 22)	Controls (*N* = 20)	*P*-value
Age, years	43 ± 14	40 ± 15	0.50
Male gender (%)	16 (73)	16 (80)	0.72
BSA (m^2)	1.88 ± 0.19	1.90 ± 0.21	0.65
Heart rate (bpm)	68 ± 13	71 ± 16	0.49
LVEDVi (mL/m^2)	97 ± 35	80 ± 20	0.06
LVEF (%)	57 ± 10	58 ± 7	0.75
LVSV (mL)	101 ± 35	91 ± 24	0.29
Dimensions of the ascending aorta			
Cross-sectional surface (cm^2)	13.9 (8.2–17.8)	8.8 (7.4–10.6)	0.01
Antero-posterior diameter (mm)	42 (31–45)	32 (29–35)	<0.01
Systolic longitudinal excursion of the aortic valve (mm)	9 ± 2	9 ± 2	0.55
Type of fusion			
LC–RC (%)	10 (45)		
NC–RC (%)	12 (55)		

Values are provided as mean ± standard deviation, median (inter-quartile range), or numbers and percentages, as appropriate.
P-value refers to the difference between patients with BAV and controls.
BSA, body surface area; bpm, beats per minute; m, meters; mL, milliliters; LVEDVi, indexed left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVSV, left ventricular stroke volume; LC, left coronary aortic cusp; RC, right coronary aortic cusp; NC, non-coronary aortic cusp.

Flow measurements and correlation with the left ventricular volumetric stroke volume

Figure 2 represents the correlation between the LVSV and the systolic forward flow measured at different locations as assessed with linear regression analyses, showing that the correlation between the LVSV and the systolic forward flow measured in the LVOT, the aortic valve, and the AAo was good in both BAV patients and controls. The Bland–Altman plots confirmed the good agreement between the LVSV and the flow measurement in the LVOT and the aortic valve for controls and BAV patients (*Figure 3A*, *B*, *D*, and *E*, respectively). However, if the LVSV was related with the flow measured in the AAo, the Bland–Altman plots revealed that the systolic aortic forward flow was mildly underestimated in controls and much more in BAV patients, who also showed a much wider range of values, particularly for large stroke volumes (*Figure 3C* and *F*, respectively). Indeed, the relative difference between the LVSV and the systolic forward flow in the AAo differed significantly between control and BAV patients [median (inter-quartile range): 9% (4%/15%) vs. 22% (8%/30%); $P < 0.01$]. This was not the case for the flow measurement in the LVOT [5% (0%/8%) vs. 5% (−3%/11%); $P = 0.94$] and the aortic valve [0% (−5%/8%) vs. 1% (−4%/6%); $P = 0.77$], where the differences were mild, and did not differ significantly between groups (*Figure 4*). Notably, there was no relation between the aortic

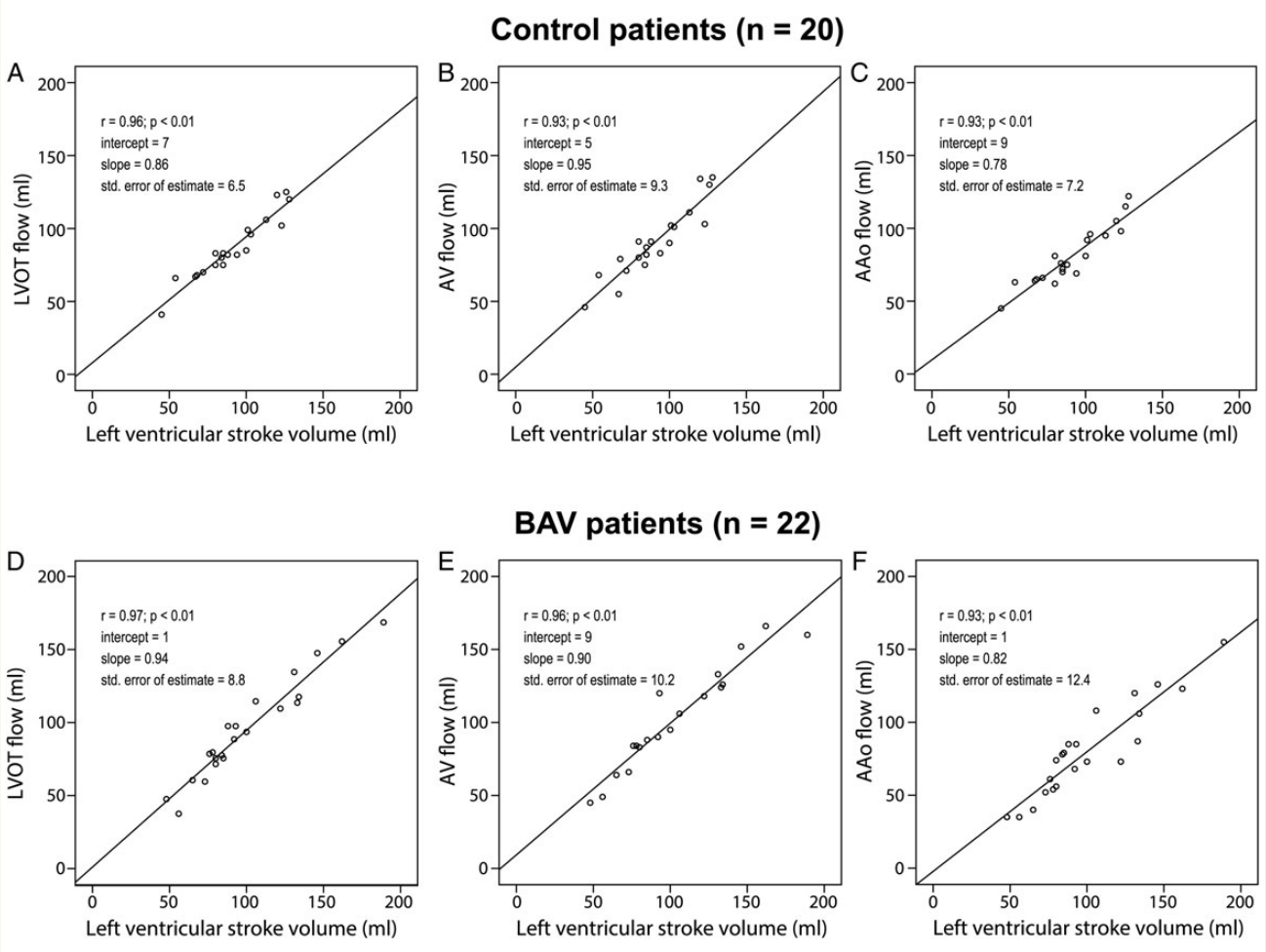

Figure 2: Linear regression analyses showing the correlation between the systolic forward flow measurement and the LVSV in control and BAV patients. LVOT, left ventricular outflow tract; AV, aortic valve; AAo, ascending aorta.

valve area and the flow error in the AAo ($r = 0.04$; $P = 0.9$), and the type of BAV fusion did not impact flow accuracy in the AAo.

Evaluation of potential causative factors influencing the accuracy of flow measurement in the ascending aorta

Complexity of aortic flow pattern and intravoxel dephasing

To explore the inter-relation between the complexity of the flow patterns and the accuracy of flow measurement in the AAo, the systolic flow eccentricity and the relative mean signal intensity in the AAo were measured. As expected, normalized systolic flow displacement in the AAo, as a marker of flow eccentricity, was more pronounced in BAV patients when competed with controls (0.53 vs. 0.26; $P < 0.01$). Notably, even though the correlation between the extent of flow eccentricity and underestimation in the systolic forward flow was, *per se*, modest ($r = 0.48$; $P < 0.01$, *Figure 5A*), eccentric flow pattern was clearly associated with larger underestimation in flow measurement. In addition, in the AAo, the relative mean signal intensity was found to be lower in BAV patients than in controls (1.34 ± 0.15 vs. 1.58 ± 0.26; $P < 0.01$). Conversely, no evidence of a significant difference in the average relative mean signal intensity between controls and BAV patients was found in the LVOT (1.71 ± 0.30 vs. 1.58 ± 0.31; $P = 0.18$) and the aortic valve (1.64 ± 0.28 vs. 1.50 ± 0.34; $P = 0.19$), suggesting a more pronounced intravoxel dephasing in the AAo of BAV patients, but not at the level of the LVOT and the AV.

Longitudinal excursion of the aortic valve annulus

Concerning the longitudinal excursion of the aortic valve annulus and the consequent change in aortic luminal volumes between the fixed imaging plane and the aortic valve during the cardiac cycle, we found no significant difference between BAV patients and controls neither for the systolic increase in aortic cross-sectional surface area (1.97 ± 0.87 vs. 1.96 ± 0.55 cm^2), nor for the estimated magnitude of aortic luminal volume change during the cardiac cycle (1.71 ± 0.99 vs. 1.68 ± 0.45 cm^3; $P = 0.95$). Here too, as opposed to the aortic flow eccentricity, there was no correlation between the estimated

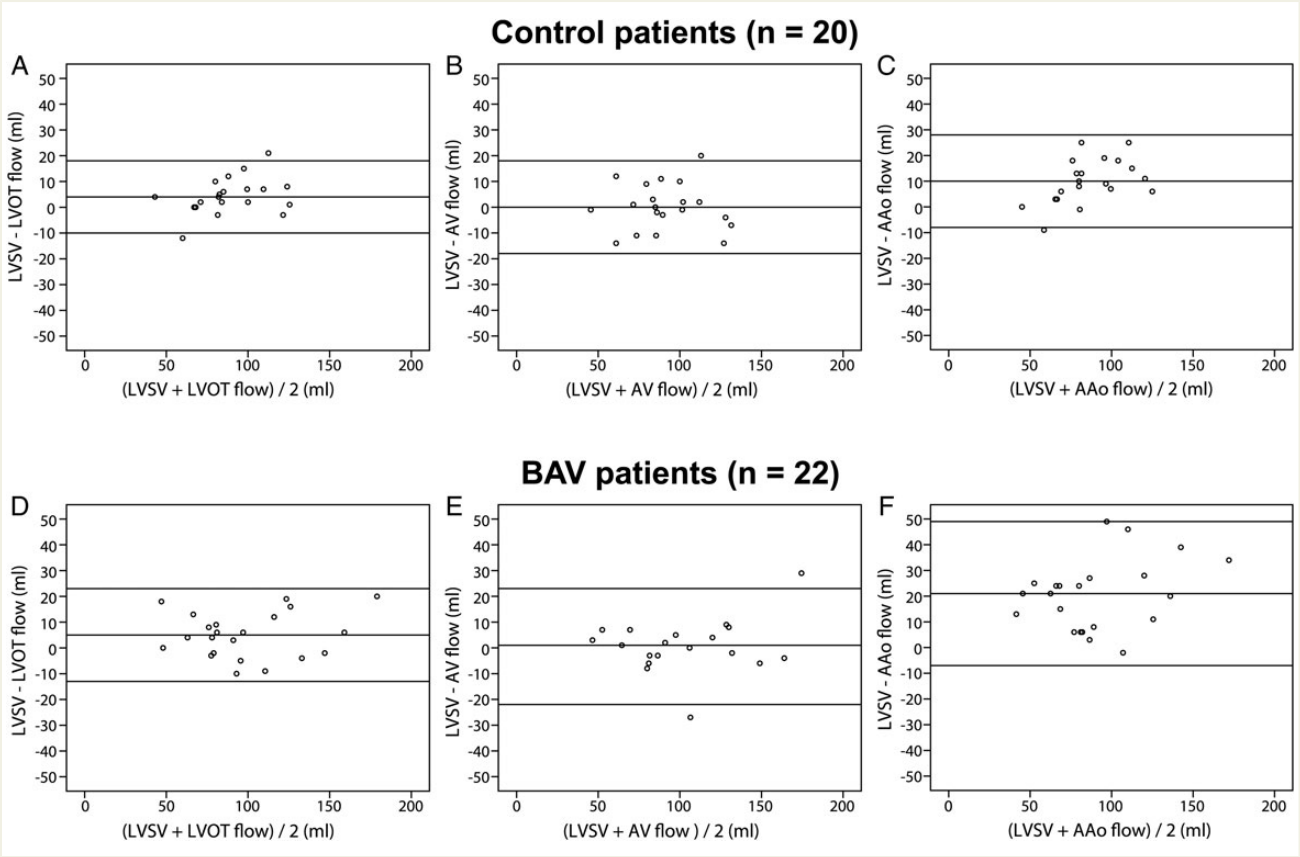

Figure 3: Bland–Altman plots showing the level of agreement between the systolic forward flow measurement and the LVSV in controls and BAV patients. Note that the agreement between the LVSV and the forward flow measurement was quite good at the level of the LVOT and the aortic valve. Conversely, in the AAo, we observe an underestimation in forward flow measurement, that was much more significant and characterized by a wider range of discrepancy in BAV patients. LVOT, left ventricular outflow tract; AV, aortic valve; AAo, ascending aorta.

magnitude of aortic luminal volume change and the extent of underestimation in the aortic systolic forward flow ($r = 0.08$; $P = 0.61$, *Figure 5B*).

Phase-offsets

At each location, no correlation was found between the mean diastolic velocity and the difference in stroke volumes for either the controls ($R^2 < 0.17$) or BAV patients ($R^2 < 0.25$), or for a correlation between the relative mean signal intensity and the difference in stroke volumes in either the controls ($R^2 < 0.1$) or BAV patients ($R^2 < 0.15$), suggesting the absence of major phase-offset.

Discussion

The results of the current study show that the flow measurement at the level of the AAo leads to a significant underestimation of the forward aortic flow in patients with BAV. Notably, the forward flow measured at the level of the aortic valve and the LVOT correlated tightly with the LVSV in BAV patients and controls, and the relative difference between the flow measurement and the stroke volume was mild in both groups, without any significant difference. Conversely, if the forward flow measured in the AAo was compared with the LVSV, we found a relative underestimation of 9% in controls and a significantly greater underestimation of 22% in BAV patients.

Considering that the myocardial perfusion is predominantly diastolic, this difference is not explainable with coronary flow that quits the aorta before the imaging plane in the AAo. Multiple mechanisms, including the complexity of the flow pattern with flow turbulence, helical flow, and consequent intravoxel dephasing,[12,13,19] but also the longitudinal excursion of the aortic annulus with consequent systolic change in the aortic luminal volume between the fixed plane of velocity acquisition and the moving plane of the aortic valve annulus,[11,14] and phase-offsets may compromise the accuracy of flow measurement.[15] Phase-offsets are due to concomitant field effects, which are related with the distance to the isocentre, and to eddy current effects, which are independent of off-centre effect. Correction of the first was performed online during the image reconstruction in all scanners. Though the phase-offsets were not quantified, the mean diastolic velocity can be assumed to be a fair approximation of any baseline shift due to background eddy currents. In volunteers, where no retrograde flow is expected and the mean diastolic velocity should tend to zero, no correlation was found between the mean diastolic velocity and the differences between the LVSV and the flow volumes. Similarly, no correlation was found in the BAV patients. Furthermore, considering that phase-offsets, if any, should be similar in

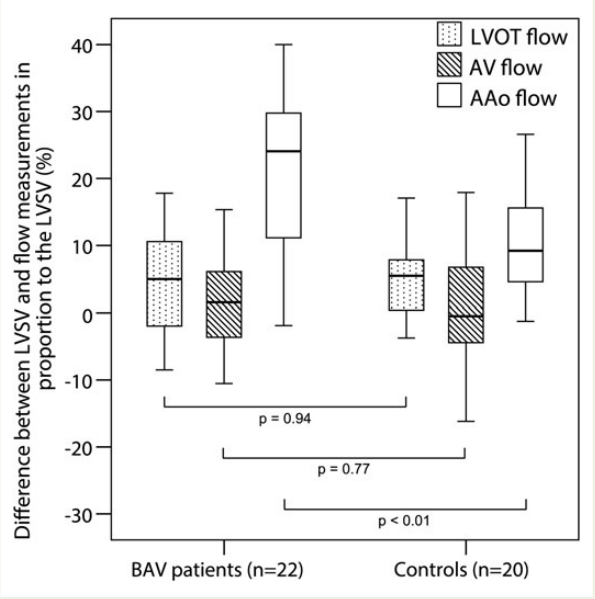

Figure 4: Box-plots showing the relative difference (%) between the LVSV and the flow measurement performed in the different locations [(LVSV – forward flow)/LVSV] × 100. Notably, there was a mild difference between the LVSV and systolic forward flow in the LVOT and the AV, which did not differ between normal BAV patients and controls. Conversely, in the AAo, there was a slight underestimation in systolic forward flow among controls, which was much more pronounced and significant in BAV patients. LVOT, left ventricular outflow tract; AV, aortic valve; AAo, ascending aorta.

patients and controls, the presence and the extent of phase-offsets are not likely to be responsible for the underestimation in flow measurement in the AAo, and for the significant difference between BAV patients and controls. Here too, neither the systolic increase in the aortic cross-sectional surface area, nor the estimated magnitude of aortic luminal volume change, differed between BAV patients and controls. Furthermore, no correlation was found between the estimated magnitude of aortic luminal volume change and the degree of underestimation of aortic forward flow. Therefore, even though the longitudinal excursion of the aortic valve annulus is known to cause underestimation in the aortic forward flow by PC-MR, this mechanism may lead to a systematic offset, but it is unlikely to represent the cause explaining the larger underestimation in aortic forward flow in BAV patients when compared with controls. On the other hand, our data showed a positive correlation between flow eccentricity in the AAo and underestimation in flow measurement, meaning that exaggerated flow eccentricity, as a marker of complex flow pattern, was associated this larger underestimation in aortic forward flow measurement. Unfortunately, due to the utilization on a 2D flow sequence, other aspects of complex flow patterns in the AAo, such as the extent of helical flow, could not be quantified in the current study. However, helical flow is known to be very pronounced in BAV patients and also associated with aortic flow eccentricity. In case of helical flow, the flow direction is no longer orthogonal to the imaging plane of a typical 2D through-plane PC-MR sequence, which is acquired in an orthogonal direction to the aorta. As a consequence, the velocity distribution across a voxel would be larger in BAV patients, causing increased intravoxel dephasing and inaccuracy in flow measurement. This was shown in a phantom study addressing the impact of flow jet orientation relative to the velocity encoding imaging plane by using a 2D PC-MR

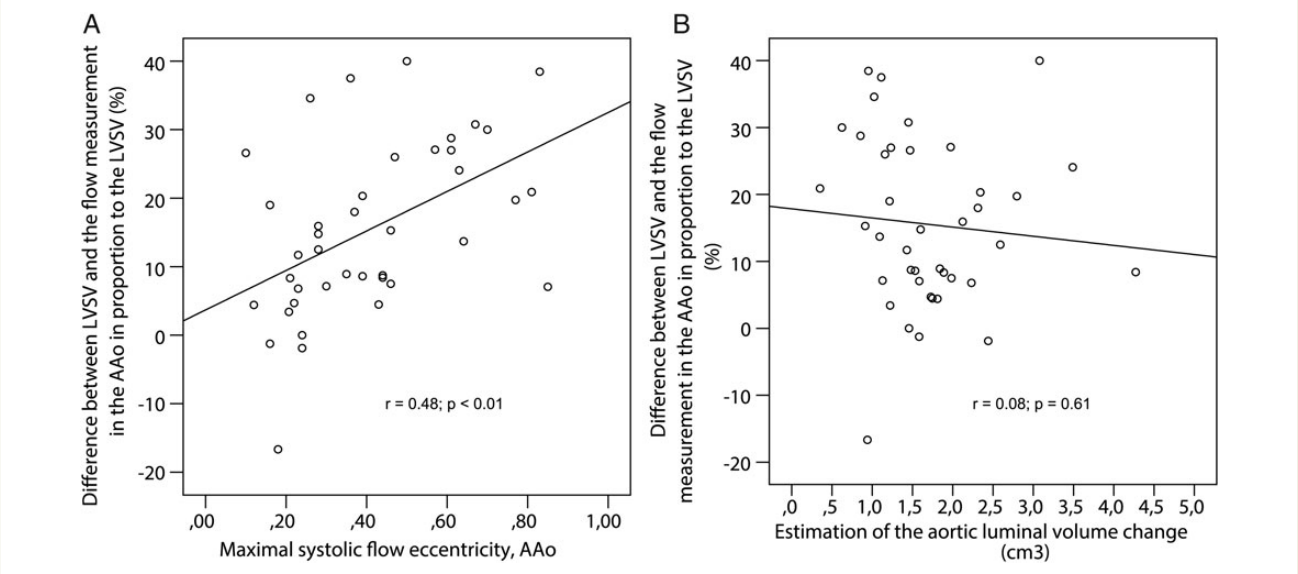

Figure 5: Linear regression analyses showing the inter-relation between (*A*) the extent of flow eccentricity in the AAo and (*B*) the estimated magnitude of aortic luminal volume change with the underestimation of the systolic forward flow measurement in the AAo in relation with the LVSV. Note that patients with eccentric aortic flow were more likely to have larger underestimation in the aortic forward flow measurement. This was not the case for the estimated magnitude of aortic luminal volume change.

sequence. Both intravoxel dephasing and underestimation in flow measurement occurred if the imaging plane was not orthogonal to the flow jet direction. Importantly, both effects were more pronounced at higher angulations between the direction of the velocity encoding gradient and the flow jet, but also at higher TE (results are shown in Appendix). In line with this phantom study, our data suggested larger underestimation in aortic forward flow and intavoxel dephasing in BAV patients with more pronounced flow eccentricity.

Taken together, the results of the current study indicate that complexity of the flow patterns in the AAo may be the major factor contributing to inaccuracy of aortic flow measurement in BAV patients. These findings are also in line with very recently published data by Nordmeyer *et al.*,[12] data showing significant differences in forward flow measurement at different anatomical levels in the AAo in patients with complex aortic flow, whereas such differences were negligible in healthy volunteers with laminar aortic flow pattern.

Notably, the degree of underestimation of forward aortic flow among patients with BAV was very variable and showed a wide range, meaning that utilization of simple correction factors seems unsuitable for solving this issue. However, we observed that the flow measurement at the level of the LVOT and the AV, where abnormal secondary flow patterns are less relevant, correlated well with the stroke volume in BAV patients and controls, indicating that flow measurement in these locations is more accurate and could be use as a more reliable means for assessing LVSV based on flow measurement. This could have important consequences for the calculation of regurgitation fraction and the severity of aortic valve insufficiency in BAV patients. Notably, the results of the present study also may apply to pathological conditions, other that BAV, which are related with complex flow patterns. Here too, utilization of a flow sequence with ultra-short echo time to reduce the impact of intravoxel dephasing[19] could be another strategy to limit the inaccuracy in flow measurement. However, we did not test this hypothesis, and further studies are therefore needed to address the impact of scanning parameters on the accuracy of flow measurement in the presence of complex flow patterns.

Limitations

Three types of CMR systems with different magnetic field strength and slightly different flow sequences and echo times were used. Furthermore, no evaluation or correction for phase-offsets by using static phantoms was performed. Therefore, we cannot rule out with absolute certainty that confounding factors related with scan parameters and/or phase-offsets may have altered the results. However, in this study, the main results are based on 'intra-individual' comparison of flow and LVSV measurements, meaning that in every single patient the same sequence and scanning parameters were used, putting into another perspective the importance of this potential bias. Secondly, the mean relative signal intensity in the aorta was used as an indicator for intravoxel dephasing. These signal intensity measurements were limited to the flow compensated magnitude images, which are most commonly available on clinical scanners. If the flow encoded magnitude images, which are known to be more sensitive to signal loss, were made available, then this would allow a more thorough investigation of intravoxel dephasing effects and intravoxel velocity dispersion by using the generalized phase-contrast CMR principle.[20] Finally, a larger prevalence of significant aortic stenosis could potentially have altered the results, because aortic stenosis may further increase the complexity of aortic flow. However, our data are insufficient to address this point.

Conclusions

Flow measurement in the AAo by PC-MR, as it is typically performed in clinical practice, leads to a significant underestimation of the aortic forward flow in BAV patients. Results of this study suggest that complex flow patterns in the AAo may be an important factor leading to inaccuracy of flow measurements by 2D PC-MR. Flow measurement in the LVOT or the AV better correlates with the LVSV, indicating an alternative and more reliable means for quantifying LVSV based on flow measurement. This could have important implication for the assessment of regurgitation fraction and the severity of aortic valve insufficiency in BAV patients.

Conflict of interest: none declared.

Funding

This study was performed without financial support.

Appendix

It is well known that, under normal flow conditions, the alignment of the slice perpendicular to the forward flow is not essential to accurately quantify flow. The reduced estimate of the mean velocity due to a misalignment with the forward flow is compensated by a corresponding increase in the vessel area. When measuring under complex flow conditions, such as downstream of a bicuspid valve, accurate quantification relies on a good alignment of the velocity encoding direction to the forward flow[11] in order to avoid excessive mixing of fast and slowly moving spins.

To illustrate the importance of the alignment, the steady flow phantom of a stenotic jet described in O'Brien *et al.*[13] was used to rotate the slice relative to the forward flow. The phantom was operated at a constant flow rate of 300 mL/s. The slice was positioned 35 mm downstream of a 12-mm orifice plate in the turbulent separation region of the jet. The slice was orientated at 1.0, 2.0, 3.5, 5.0, 7.0, and 10.0° relative to the phantom. Typical image parameters were TR/TE of 52.0 (45.7)/3.6 (2.8) ms, encoding velocity 550 cm/s, FOV 300 mm, matrix 192 × 132, phases/cardiac cycle = 20.

Background phase correction was applied by subtracting a linear plane fitted to stationary fluid placed around the phantom. The flow rate was quantified by multiplying the mean velocity across the vessel with the phantom's known area, corrected for the area increase due to the slice's alignment with the phantom. The relative signal intensity was calculated by taking the ratio of averaging the signal intensity in the vessel over the average signal intensity in the stationary fluid surrounding the phantom. The ratios were then normalized by the ratio obtained at a rotation of 1°.

Figure A1A shows that, despite the compensatory increase in area, there is a trend to begin underestimating the gold standard flowmeter at large slice rotations. A corresponding trend showing a decrease in the normalized relative signal intensity with larger slice rotations was also present. *Figure A1B* shows that, with a shorter TE, no trend to underestimate the flowmeter at larger slice rotations was present.

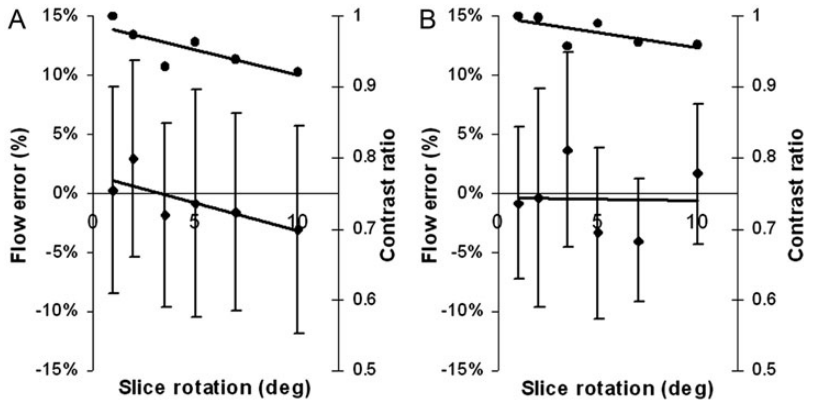

Figure A1: Comparison in a stenotic-jet phantom of the phase-contrast estimate of flow vs. a flowmeter at different slice rotations with a TE of 3.6 ms (*A*) and 2.8 ms (*B*). With a TE of 3.6 ms, large slice rotations that cause the forward flow to become eccentric relative to the slice results in an underestimation of flow and a decrease in the relative signal intensity. At the longer TE, a smaller decrease in the relative signal intensity was observed that coincides with an improved agreement with the flowmeter. Flow measurements = rhombus; contrast ratio = dots.

Moreover, there is still a tendency of the normalized relative signal intensity to decrease with larger slice rotations. The decrease in the normalized relative signal intensity at larger slice rotations is due to an increased level of intravoxel dephasing due to the forward flow being eccentric to the velocity encoding. The shorter TE allows less time for the mixing of spins to occur and is why we see less intravoxel dephasing and an improvement in the flow estimate at large slice rotations. These observations agree with what we saw in the bicuspid valve patients. In cases when the flow estimate was poor it was found that forward flow was eccentric relative to the slice, which was orientated perpendicular to the vessel. No corresponding increase in the vessel area was present to compensate the flow's eccentricity. Furthermore, in cases where the forward flow is very eccentric to the slice, there is an increased likelihood that a significant level of intravoxel dephasing will occur that reduces the reliability of the velocity estimate.[21]

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