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Clinical Assessment of Aortic Valve Stenosis: Comparison Between 4D Flow MRI and Transthoracic Echocardiography

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Background: The prevalence of valvular aortic stenosis (AS) increases as the population ages. Echocardiographic measurements of peak jet velocity (V_{peak}), mean pressure gradient (P_{mean}), and aortic valve area (AVA) determine AS severity and play a pivotal role in the stratification towards valvular replacement. A multimodality imaging approach might be needed in cases of uncertainty about the actual severity of the stenosis.
Purpose: To compare four-dimensional phase-contrast magnetic resonance (4D PC-MR), two-dimensional (2D) PC-MR, and transthoracic echocardiography (TTE) for quantification of AS.
Study Type: Prospective.
Population: Twenty patients with various degrees of AS (69.3 ± 5.0 years).
Field Strength/Sequences: 4D PC-MR and 2D PC-MR at 3T.
Assessment: We compared V_{peak}, P_{mean}, and AVA between TTE, 4D PC-MR, and 2D PC-MR. Flow eccentricity was quantified by means of normalized flow displacement, and its influence on the accuracy of TTE measurements was investigated.
Statistical Tests: Pearson's correlation, Bland–Altman analysis, paired *t*-test, and intraclass correlation coefficient.
Results: 4D PC-MR measured higher V_{peak} ($r = 0.95$, mean difference + 16.4 ± 10.7%, $P < 0.001$), and P_{mean} ($r = 0.92$, mean difference + 14.9 ± 16.0%, $P = 0.013$), but a less critical AVA ($r = 0.80$, mean difference + 19.9 ± 20.6%, $P = 0.002$) than TTE. In contrast, unidirectional 2D PC-MR substantially underestimated AS severity when compared with TTE. Differences in V_{peak} between 4D PC-MR and TTE showed to be strongly correlated with the eccentricity of the flow jet ($r = 0.89$, $P < 0.001$). Use of 4D PC-MR improved the concordance between V_{peak} and AVA (from 0.68 to 0.87), and between PG_{mean} and AVA (from 0.68 to 0.86).
Data Conclusion: 4D PC-MR improves the concordance between the different AS parameters and could serve as an additional imaging technique next to TTE. Future studies should address the potential value of 4D PC-MR in patients with discordant echocardiographic parameters.
Level of Evidence: 2
Technical Efficacy Stage: 2

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CALCIFIC AORTIC STENOSIS (AS) is the most common valvular heart disease in developed countries, affecting up to 12.4% of elderly patients.[1,2] Since the Western population grows progressively older, AS will put an increasing burden on public health and health resources over the coming decades. Transthoracic echocardiography (TTE) is

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the key diagnostic tool for evaluation of stenosis severity, and the main parameters recommended to be recorded include peak jet velocity (V_{peak}), mean transvalvular pressure gradient (P_{mean}), and aortic valve area (AVA).[3] However, certain pitfalls apply to the echocardiographic assessment of AS, which should be avoided in order to ascertain the accuracy of measurements.[4] First, image quality is operator-dependent and can be hampered by poor acoustic windows. Second, Doppler measurements rely on a parallel alignment between the ultrasound beam and the direction of blood flow, and violation of this condition results in underestimation of flow velocities and pressure gradients.[5] Third, AVA is calculated using the continuity equation, a formula that includes the cross-sectional area of the left ventricular outflow tract (LVOT). This area is typically computed from the LVOT diameter, implicating the outflow tract to have a circular shape. In fact, the LVOT is elliptical in the majority of patients, and this approach has been reported to result in a considerable underestimation of AVA.[6,7] In a subgroup of patients, in whom image quality is insufficient or there is discordance between the TTE-derived AS parameters, clinical decision-making may benefit from alternative noninvasive imaging techniques.

Phase-contrast magnetic resonance imaging (PC-MRI) has evolved as a reliable tool for noninvasive flow and velocity measurements and has been validated in vitro and multiple patient groups.[8–10] The technique is usually performed using a prospectively planned 2D acquisition with a unidirectional through-plane velocity-encoding. However, this method is only capable of quantifying flow velocities in the direction oriented perpendicular to the imaging slice. Moreover, the exact location of peak jet velocity (the so-called vena contracta) cannot be visualized prior to planning of the acquisition plane, which further reduces the accuracy of measurements. For these reasons, 2D PC-MR has shown significant underestimation of flow rates and velocities when compared with TTE.[11–13] Over recent years, three-directional 3D PC-MR (better known as 4D flow MR or 4D PC-MR) has emerged as a promising in vivo flow imaging technique that enables visualization and quantification of complex flow patterns in the heart and large vessels.[14–16] In contrast to unidirectional 2D PC-MR, 4D PC-MR provides for velocity-encoding in all three spatial directions. Furthermore, the entire acquired volume can be analyzed in a search for the highest flow jet velocity. In healthy volunteers and patients with normally functioning valves, 4D PC-MR has shown improved flow quantification relative to echo.[17,18] We hypothesized that in AS patients, who often exhibit eccentric and dynamic flow jets, the technical features of 4D PC-MR could be even more advantageous.[19] Hence, the purpose of the current study was to assess the performance of TTE and PC-MR in a cohort of AS patients, and to investigate the influence of flow eccentricity on the accuracy of measurements.

Materials and Methods

Study Population

Consecutive adult patients who visited our outpatient clinic for the echocardiographic follow-up of AS between June 2017 and December 2018 were invited for participation in this prospective single-center study. Exclusion criteria comprised prior aortic valve replacement, heart failure (NYHA class ≥3), renal failure (estimated glomerular filtration rate <30 ml/min/1.73 m^2), and the regular exclusion criteria for MR (such as metallic implants and claustrophobia). Furthermore, patients with atrial fibrillation were excluded, since beat-to-beat flow variability caused by irregular heart rhythms might limit the accuracy of PC-MR measurements. Eventually, a total of 20 patients were included. Our local Ethical Review Board approved the study protocol, and all participants provided written informed consent.

Transthoracic Echocardiography

Echocardiograms were performed according to clinical guidelines using a Philips iE33 ultrasound system (Philips Medical Systems, Andover, MA).[3,20] Recordings were made from the subcostal, parasternal, and apical windows with patients lying in supine or left lateral decubitus position. All images were obtained by experienced echocardiographers and reviewed by a single certified cardiologist with >15 years of experience in cardiac ultrasound (S.S.). Aortic V_{peak} was measured using continuous-wave Doppler ultrasound; the highest velocity recorded from any acoustic window was used for analyses. Transvalvular pressure gradients were calculated from velocity information through the modified Bernoulli equation ($P = 4{*}v^2$), with P_{mean} being the average gradient over the cardiac systole. AVA was computed using the continuity-equation as $AVA = \frac{Area^{LVOT} * VTI^{LVOT}}{VTI^{Aorta}}$. In this equation, VTI_{LVOT} and VTI_{Aorta} are the velocity-time integrals of the LVOT and aorta as obtained by pulsed-wave Doppler and continuous-wave Doppler, respectively. The area of the LVOT was computed using the LVOT diameter as measured on a parasternal long-axis view: $Area^{LVOT} = \pi * \left(\frac{\text{Diameter LVOT}}{2}\right)^2$.

MR Acquisition

All scans were performed with a 3T scanner (Ingenia CX, Philips Healthcare, the Netherlands) equipped with a 32-channel torso coil for signal reception. A steady-state free precession sequence was used to obtain ECG-gated cine images in 2- and 4-chamber long-axis views and in two orthogonal LVOT planes. Unidirectional 2D PC-MR was performed in end-expiratory breath-hold at the level of the LVOT and in two adjacent slices ranging from the aortic valve tips towards the sinotubular junction (Fig. 1a). Typical PC-MR acquisition parameters are summarized in Table 1. Cine LVOT views were used to position imaging planes perpendicular to the aortic valve and aorta. Velocity-encoding (VENC) was individually adapted by repetition of acquisitions with decreasing VENC until the lowest value, at which no aliasing occurred, was reached. 4D PC-MR acquisition was initiated immediately after manual administration of a low-dose (0.1 mmol/kg body weight) bolus of gadobutrol (Gadovist, Bayer Healthcare, Berlin, Germany). A 3D volume with full coverage of the thoracic aorta was acquired in a sagittal oblique orientation, using a retrospectively ECG-gated and respiratory navigated spoiled turbo-field echo sequence (Fig. 1b). VENC for the three spatial

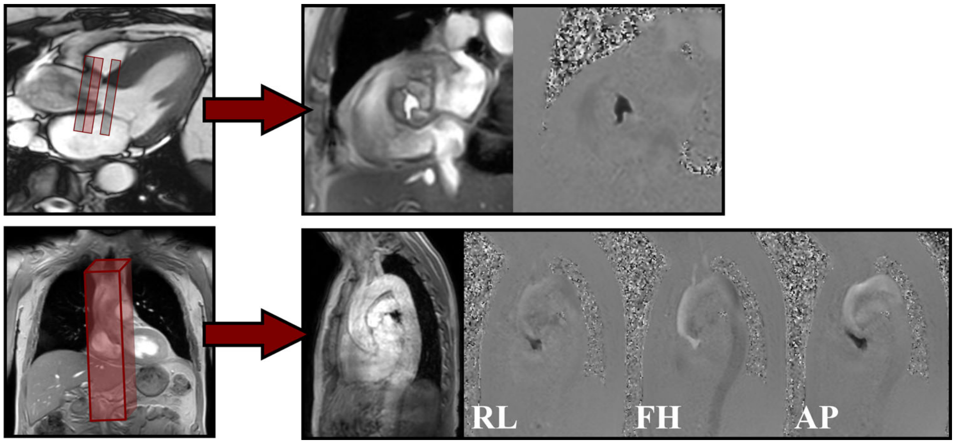

FIGURE 1: Methodology for 2D and 4D PC-MR acquisition. (a) Through-plane 2D PC-MR was performed at the level of the LVOT and in two adjacent planes covering the aortic valve and aortic root. Magnitude and velocity images are provided for the imaging slice depicted in red. (b) In 4D PC-MR, a 3D volume covering the thoracic aorta was acquired. Velocity maps for the three spatial directions are shown bottom right. LVOT: left ventricular outflow tract; PC-MR: phase contrast magnetic resonance.

directions was set to the same values as in 2D PC-MR. Gradient correction and local phase correction were performed from standard available scanner software. Acquisition lasted 17.2 ± 5.5 minutes, depending on heart and respiratory rate.

MR Analysis

MR datasets were reviewed by a single observer (B.A., 5 years of experience in cardiac MR), who was blinded for echocardiographic findings. 2D PC-MR was analyzed semiautomatically (CAAS MR Flow 2.1, PieMedical Imaging, Maastricht, The Netherlands). Regions of interest drawn by the software were checked for their adequacy across all time frames and manually corrected if deemed necessary. Flow rates and velocities were exported for each phase, and the aortic imaging slice that yielded the highest V_{peak} was used for analyses. Planimetric LVOT area was obtained from magnitude images at peak systole. Velocity–time integrals were manually calculated by the observer as the area under the velocity–time curve and used for calculation of AVA using the continuity equation.

4D PC-MR data were imported into a commercially available software package (CAAS 4D Flow 2.0, PieMedical Imaging), and additional phase offset correction and antialiasing was performed. Delimiter points were manually placed in the LVOT and descending aorta on a weighted speed image and marked the borders of the volume of interest (ie, the thoracic aorta). This volume was then automatically segmented for the peak systolic phase. The adaptation tool provided by the software was used for manual correction of vessel lumen delineation in case of incorrectness of the automatic segmentation. After completion of the segmentation, analysis planes were placed just below the lowest insertion point of the aortic valve cusps (LVOT), and in the aortic region in which V_{peak} was identified. Calculations of pressure gradients and AVA were performed similarly as in 2D PC-MR. LVOT area was obtained by planimetry on magnitude images. Peak systolic flow displacement in the aortic plane was computed as the linear distance between the luminal center and the center of velocity, which represents the average position of pixels weighted by velocity information (see also Fig. 4a).[21] Analysis of 4D PC-MR data of 10 randomly selected patients was repeated by the primary observer and also carried out by a second observer (Y.C., 4 years of experience) in order to assess intra- and interobserver variability.

TABLE 1. CMR Acquisition Parameters

	2D PC-MR	4D PC-MR
FOV (mm × mm × mm)	350 × 300	350 × 280 × 75
Acquired voxel size (mm × mm)	2.5 × 2.5	2.5 × 2.5 × 2.5
Slice thickness (mm)	8.0	—
Reconstructed voxel size (mm)	1.22 × 1.22	1.46 × 1.46 × 2.5
Flip angle (°)	10	10
TE (ms)	2.4	2.3
TR (ms)	4.0	4.2
TFE factor	6	2
SENSE factor	2	2.5 (P) × 1.5 (S)
VENC (cm/s)	210–600	210–600
Shot duration (msec)	48	33
(Reconstructed) cardiac phases	40	29–42*

*Depending on cardiac frequency.
FOV: field-of-view; P: phase-encoding direction; S: slice direction; TE: echo time; TR: repetition time; VENC: velocity-encoding.

Statistical Analysis

Statistical analysis was performed using dedicated software (IBM SPSS Statistics, v. 24, Armonk, NY). Continuous data were tested for normality using the Shapiro–Wilk test. Baseline characteristics are presented as mean ± standard deviation or as frequency and percentages. Pearson's correlation and Bland–Altman analysis were

TABLE 2. Baseline Characteristics of the Study Population

	N = 19	Range
Male	13 (68,4%)	
Age (years)	69.3 ± 5.0	57–77
Height (cm)	168.9 ± 7.3	150–181
Weight (kg)	75.7 ± 9.4	61–93
BMI (kg/m^2)	26.5 ± 2.4	21.1–29.8
BSA (m^2)	1.9 ± 0.14	1.6–2.1
Hypertension	16 (84.2%)	
Dyslipidemia	11 (57.9%)	
Diabetes	1 (5.3%)	
Smoker	3 (15.8%)	
eGFR	70.7 ± 14.9	44–90
NYHA classification		
I	15 (78.9%)	
II	4 (21.1%)	
Valve morphology		
Bicuspid	4 (21.1%)	
Tricuspid	15 (78.9%)	
TTE findings		
LVEF (%)	63.0 ± 5.5	50–70
LV mass (g)	162.3 ± 49.0	91–247
LVEDD (mm)	47.1 ± 5.1	39–59
LVESD (mm)	31.1 ± 4.7	24–41

BMI: body mass index; BSA: body surface area; eGFR: estimated glomerular filtration rate; LV: left ventricle; LVEF: left ventricular ejection fraction; LVEDD: left ventricular end-diastolic diameter; LVESD: left ventricular end-systolic diameter; NYHA: New York Heart Association.

performed to assess the agreement between the TTE- and PC-MR-derived AS parameters, while the paired samples *t*-test was used to determine whether there was a significant mean difference between both modalities. Intra- and interobserver variability for 4D PC-MR measurements were calculated using the intraclass correlation coefficient (ICC). P <0.05 was considered significant.

Results

Study Population

Twenty patients were included and underwent consecutive TTE and MR. The mean time interval between both examinations was 17.2 ± 7.2 days. Pronounced respiratory motion artifacts were encountered in the 4D PC-MR dataset of one patient, who was therefore excluded from further analysis. Baseline characteristics are summarized in Table 2. Based on an echocardiographic AVA <1.0 cm^2, five patients were diagnosed with severe AS. The others suffered from moderate (AVA between 1.0 and 1.5 cm^2, n = 8) or mild (AVA >1.5 cm^2, n = 6) valvular stenosis. The aortic valve was bicuspid in four patients (one severe and three moderate AS, all with raphes between the left- and right-coronary cusps). Of the five subjects with severe aortic stenosis, four underwent aortic valve replacement and experienced improvement of echocardiographic peak velocities (from mean 4.75 ± 0.43 m/s to 2.49 ± 0.25 m/s) and mean pressure gradients (from mean 50.8 ± 8.0 mmHg to 13.3 ± 2.5 mmHg).

Peak Jet Velocity, Mean Pressure Gradient, and Aortic Valve Area

Measurements of V_{peak} obtained by 2D PC-MR and 4D PC-MR were strongly correlated with those derived from TTE (Table 3, and Figs. 2 and 3). However, there was a notable systematic difference between the three imaging techniques. Compared with TTE, 2D PC-MR underestimated V_{peak} by a mean difference of –11.2 ± 10.2% (P <0.001), whereas 4D PC-MR yielded a significantly higher peak jet velocity (mean difference from TTE: +16.6 ± 10.5%, P <0.001). A similar pattern was found for P_{mean}: correlations between modalities were excellent, with pressure gradients from 4D PC-MR being significantly larger than those obtained by TTE or 2D

TABLE 3. Mean and Percentage Differences Between TTE and PC-MR

	4D PC-MR vs. TTE				2D PC-MR vs. TTE			
	r	Δ (mean)	Δ (perc.)	*P*	*r*	Δ (mean)	Δ (perc.)	*P*
V_{peak} (m/s)	0.95	+0.5 ± 0.4	+16.6 ± 10.5	<0.001	0.95	–0.4 ± 0.4	–11.2 ± 10.2	<0.001
P_{mean} (mmHg)	0.92	+4.3 ± 7.2	+13.8 ± 16.3	0.017	0.92	–8.9 ± 7.7	–30.2 ± 17.6	<0.001
AVA (cm^2)	0.80	+0.3 ± 0.3	+19.5 ± 20.1	0.001	0.80	+0.6 ± 0.4	+38.2 ± 25.4	<0.001

AVA: aortic valve area; P_{mean}: mean transvalvular pressure gradient; PC-MR: phase contrast magnetic resonance; perc: percentage; V_{peak}: peak jet velocity.

PC-MR (4D PC-MR vs. TTE: +13.8 ± 16.3%, P = 0.017, and 2D PC-MR vs. TTE: –30.2 ± 17.6%, P <0.001). Scatter diagrams revealed larger underestimation of peak velocities and pressure gradients by 2D PC-MR in more severe cases of AS, whereas 4D PC-MR and TTE maintained relatively good agreement (Figs. 2 and 3).

Although higher V_{peak} and P_{mean} would suggest more critical stenosis, AVA was larger when calculated from 4D PC-MR (mean difference from TTE: +19.5 ± 20.1%, P = 0.001). Since the dimensionless index (ie, the ratio between VTI_{LVOT} and VTI_{Aorta}) was comparable between techniques (P = 0.76), the higher AVA obtained by 4D PC-MR can be explained only by differences in LVOT area measurements. Indeed, planimetric LVOT area (4D PC-MR) was significantly larger than the same area that was computed from the echocardiographically obtained LVOT diameter (4.7 ± 0.57 cm^2 vs. 3.9 ± 0.54 cm^2, P <0.001).

Flow Displacement

Flow displacement in the ascending aorta differed highly between individuals (range 0.02–0.15 for patients with tricuspid valves, range 0.07–0.15 for those with bicuspid valves). There was no significant relationship between the severity of AS and the eccentricity of the flow jet (r = 0.23 for the association between flow displacement and V_{peak}, P = 0.35). However, a strong correlation (r = 0.89, P <0.001) was found between flow displacement and the extent to which V_{peak} differed between 4D PC-MR and TTE, indicating the influence of flow eccentricity on the accuracy of ultrasound measurements (Fig. 4b).

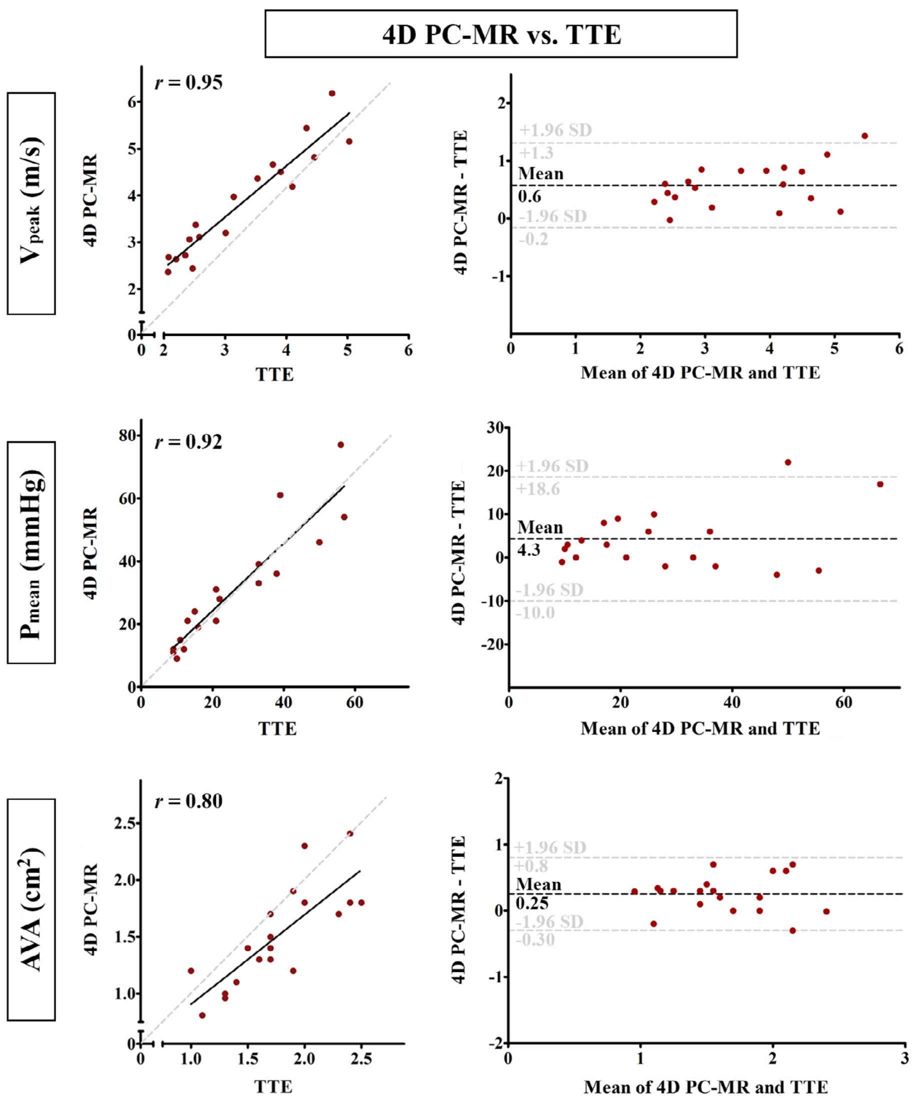

FIGURE 2: Agreement between 4D PC-MR and TTE. Regression lines and Bland–Altman plots showing the agreement between TTE and 4D PC-MR for measurements of V_{peak}, P_{mean}, and AVA. Despite strong correlations between both techniques, 4D PC-MR systematically yielded higher velocities and pressure gradients when compared with TTE. AVA: aortic valve area; P_{mean}: mean transvalvular pressure gradient; PC-MR: phase-contrast magnetic resonance; TTE: transthoracic echocardiography; V_{peak}: peak jet velocity.

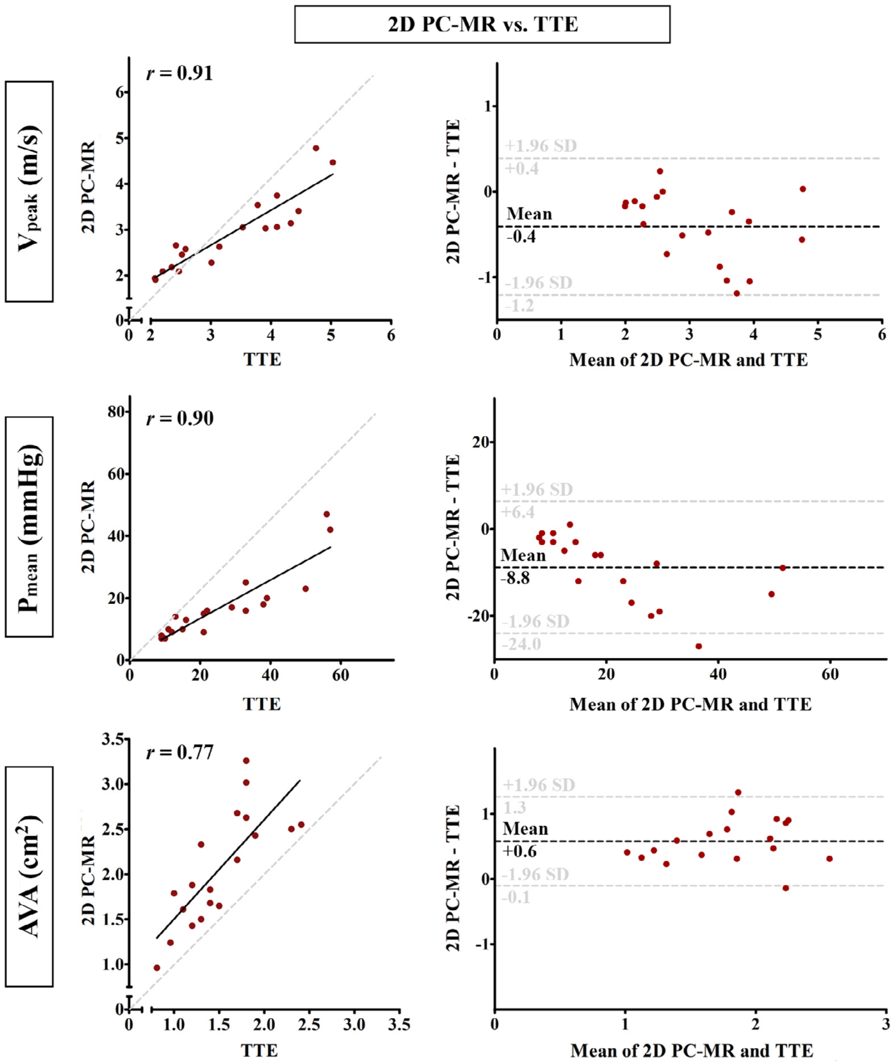

FIGURE 3: Agreement between 2D PC-MR and TTE. Regression lines and Bland–Altman plots showing agreement between TTE and 2D PC-MR for measurements of V_{peak}, P_{mean}, and AVA. As shown, the underestimation of velocities and pressure gradients by 2D PC-MR becomes more pronounced in more critical cases of AS. AVA: aortic valve area; P_{mean}: mean transvalvular pressure gradient; PC-MR: phase-contrast magnetic resonance; TTE: transthoracic echocardiography; V_{peak}: peak jet velocity

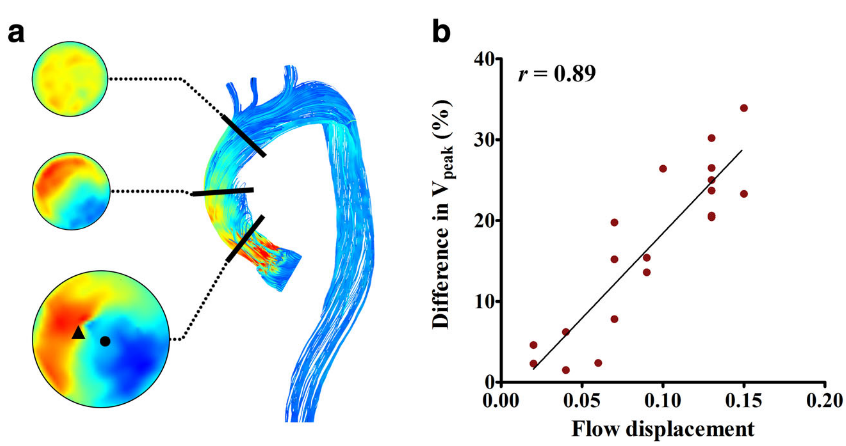

FIGURE 4: Influence of flow eccentricity on peak jet velocity measurements. (a) 4D PC-MR streamline visualization of the thoracic aorta in a patient with severe aortic stenosis. Velocity profiles (left panel) show marked eccentric flow from the aortic valve into the ascending aorta. Flow displacement (bottom left) is defined as the linear distance between the center of the vessel lumen (marked by the black dot) and the center of velocity (triangle), normalized for vessel lumen diameter. (b) Association between flow displacement and the extent to which peak jet velocity is underestimated by TTE. PC-MR: phase-contrast magnetic resonance; TTE: transthoracic echocardiography.

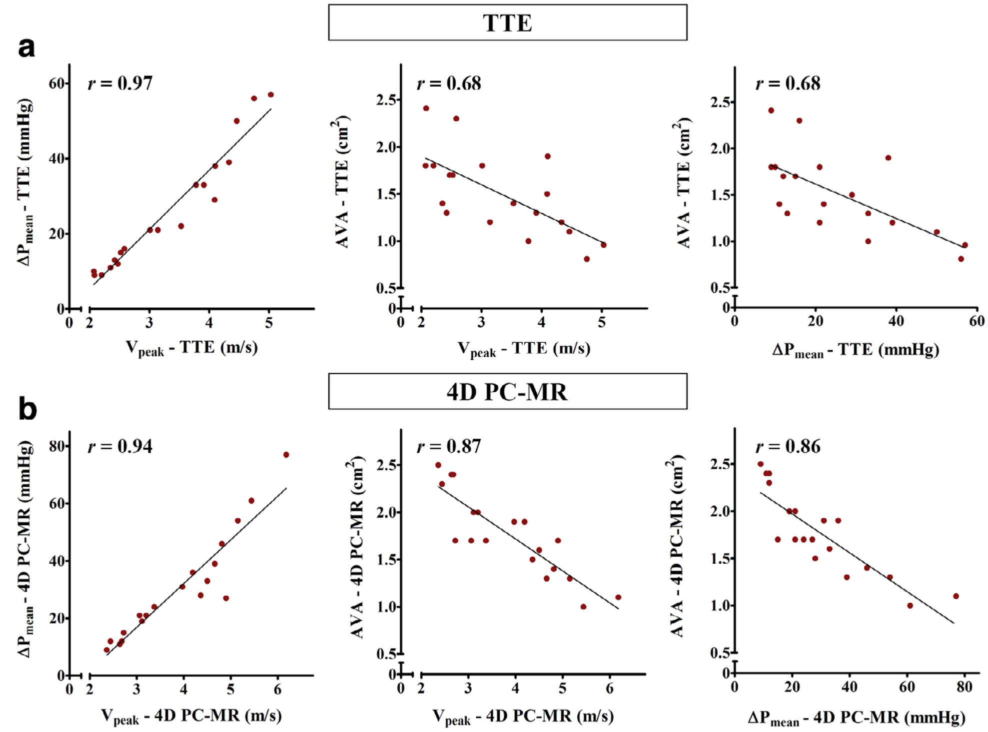

FIGURE 5: Concordance between the different parameters used for AS grading. Regression lines showing concordance between V_{peak}, P_{mean}, and AVA from (a) transthoracic echocardiography and (b) 4D PC-MR. As depicted, the correlation coefficients between V_{peak} and AVA, and between P_{mean} and AVA improved through the use of 4D PC-MR (from r = 0.68 to r = 0.87 and from r = 0.68 to r = 0.86, respectively). AS: aortic stenosis; AVA: aortic valve area; P_{mean}: mean transvalvular pressure gradient; PC-MR: phase-contrast magnetic resonance; TTE: transthoracic echocardiography; V_{peak}: peak jet velocity.

Concordance Between AS Parameters

Regression analysis showed excellent correlation between TTE-derived V_{peak} and P_{mean} (r = 0.97, Fig. 5a). In contrast, correlations between V_{peak} and AVA and between P_{mean} and AVA were only moderate (r = 0.68 for both). Use of 4D PC-MR markedly improved these correlations, to r = 0.87 and r = 0.86, respectively (Fig. 5b).

Intra- and Interobserver Variability

Intraobserver agreement was excellent for 4D PC-MR measurements of V_{peak} (ICC 1.00), P_{mean} (ICC 0.99), and AVA (ICC 0.94). Also, interobserver agreement was excellent (ICC 0.97 for V_{peak}, ICC 0.96 for P_{mean}, and ICC 0.90 for AVA).

Discussion

Transthoracic echocardiography is the imaging modality of first choice for the evaluation of AS, given its practicality, portability, and cost-effectiveness. Furthermore, current thresholds for valve replacement are based on echocardiographic studies that investigated the association between various AS parameters and adverse outcomes.[22–24] However, TTE should be performed with care, as its potential pitfalls may result in either under- or overestimation of stenosis severity.[3,4] In the current study, we investigated whether 4D PC-MR can overcome certain limitations that apply to TTE. Our main findings are: 1) 4D PC-MR measures higher V_{peak} and P_{mean} in AS patients when compared with TTE; 2) 2D PC-MR substantially underestimates AS severity when compared with TTE; 3) pronounced flow eccentricity is associated with greater differences in V_{peak} between TTE and 4D PC-MR; and 4) 4D PC-MR improves concordance between the parameters that define AS severity. To date, logistic constraints (such as long acquisition times and the need for advanced MR hardware and postprocessing tools) have impeded the widespread use of 4D PC-MR. Nevertheless, it affords a uniquely detailed assessment of flow patterns in the heart and aorta. Validation studies have compared 4D PC-MR with echocardiography in healthy volunteers and in patients without valvular disease (ie, subjects with laminar flow patterns), and found good agreement between both modalities.[17,18] However, as previously reported by others, we found that systolic flow jets in AS patients are often eccentric.[19,25] 4D PC-MR is not hindered by flow eccentricity, since its multidirectional velocity-encoding provides for quantification of velocities regardless of the spatial orientation of the flow jet. In TTE, however, abnormal flow patterns confer a risk for misalignment of the ultrasound beam with the AS jet. Therefore, it is conceivable that TTE underestimates V_{peak} and P_{mean} in AS patients, which is in line with the findings of the current study. The excellent correlation that was found between flow displacement and the extent to which TTE underestimated V_{peak} serves as internal validation for this hypothesis.

Of note, use of unidirectional 2D PC-MR led to substantial underestimation of velocities and pressure gradients, especially in patients with more critical valvular stenosis. Recently, Da Silveira et al evaluated a 2D PC-MR sequence with three-directional velocity-encoding and demonstrated the importance of multidirectional flow imaging in AS patients.[12] Their sequence, which they were able to acquire within one breath-hold, showed improved correlations with TTE for most AS parameters. Rose et al performed 4D PC-MR in a pediatric cohort of nonstenotic bicuspid aortic valve patients and calculated the underestimation of peak velocities by unidirectional methods to be 6.6%.[26] Our study adds to this knowledge by showing that the benefits of 4D PC-MR are more pronounced in AS patients with higher peak velocities and in those with highly eccentric flows. Furthermore, and in contrast to 2D PC-MR, 4D PC-MR facilitates visualization of aortic flow patterns and estimation of secondary flow-related metrics (such as wall shear stress), which is of potential interest in the pathophysiology of valve-related aortopathy.[15,27,28]

AVA is, in theory, the ideal parameter to reflect AS severity, albeit the most challenging one to assess. It has been well-described that AVA shows considerable variability depending on measurement method (anatomical vs. functional) and imaging modality.[29] 2D echocardiography usually underestimates AVA in comparison with other imaging techniques, because it measures the anteroposterior (ie, minor) axis of the LVOT for calculation of its cross-sectional area.[6,7] Our results confirm that the TTE-derived LVOT area is ~20% smaller than its planimetric equivalent from 4D PC-MR.[30] Hence, AVA differs to the same extent. Since current thresholds for valve replacement are based on echocardiographic studies that showed AVA ≤1.0 cm^2 to be associated with increased mortality risk, the higher AVA from 4D PC-MR would require definition of new, modality-specific, cutoffs for AS grading. Nevertheless, the technique has potential to develop into a useful tool for the hemodynamic assessment of stenosis severity, as it is the first imaging modality that showed the ability to improve correlations between different AS parameters.[7] Whereas this might not be of added value for patients with symptomatic high-gradient AS (since these already qualify for valve intervention), it can be particularly useful for the assessment of patients with discordant echocardiographic grading patterns. Such patterns are observed in up to 35% of patients with severe AS and typically involve cases of low-gradient AS (ie, presence of a small valve orifice [AVA ≤1.0 cm^2] accompanied by a relatively low transvalvular pressure gradient [P_{mean} <40 mmHg]).[31,32] Although, depending on flow status and left ventricular (LV) ejection fraction, several subtypes of low-gradient AS have been acknowledged; the first step in their encountering should be to exclude any measurement errors from TTE. Future studies should investigate whether 4D PC-MR has the potential to distinguish between actual low-gradient severe AS and overestimated moderate AS, and if the technique can play a role in determining the need and timing of aortic valve replacement in this specific patient group.

Several limitations of the current study and the 4D PC-MR imaging technique should be addressed. First, there exists no gold standard for velocity measurements in AS patients against which our findings could be compared.

Second, in vitro studies have demonstrated that phase-contrast techniques tend to underestimate flow rates in stenotic flows, and that measurement errors increase with higher velocities and longer TE.[33] Although 4D PC-MR revealed higher flow velocities than TTE in the current study, patients with severe AS were relatively underrepresented. Future studies that include a larger number of patients with highly accelerated flows are required to investigate the potential impact of the limited temporal resolution of 4D PC-MR on the accuracy of flow and velocity measurements in more detail.

Third, even though our results indicate that 4D PC-MR is a feasible imaging modality that can be performed using clinically available hardware and software platforms, shortening of scan duration is a prerequisite in order for the technique to find its way into clinical practice guidelines. Several technical advances (such as compressed SENSE, parallel imaging, and novel reconstruction algorithms) hold promise to significantly reduce the long scan time of 4D PC-MR.

Finally, based on our results on improved concordance between V_{peak}, P_{mean}, and AVA using 4D PC-MR, future studies should address the potential value of 4D PC-MR for the assessment of AS patients with discordant echocardiographic parameters.

In conclusion, 4D PC-MR can be performed with high intra- and interobserver accuracy in patients with AS. Pronounced flow eccentricity is associated with greater differences in V_{peak} between TTE and 4D PC-MR. Use of 4D PC-MR increases concordance between V_{peak}, P_{mean}, and AVA. Based on these findings, future studies should address the potential value of 4D PC-MR for the assessment of patients with discordant echocardiographic AS grading.

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