Evaluation of Aortic Valve Stenosis Using Cardiovascular Magnetic Resonance

Comparison of an Original Semiautomated Analysis of Phase-Contrast Cardiovascular Magnetic Resonance With Doppler Echocardiography

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Background—Accurate quantification of aortic valve stenosis (AVS) is needed for relevant management decisions. However, transthoracic Doppler echocardiography (TTE) remains inconclusive in a significant number of patients. Previous studies demonstrated the usefulness of phase-contrast cardiovascular magnetic resonance (PC-CMR) in noninvasive AVS evaluation. We hypothesized that semiautomated analysis of aortic hemodynamics from PC-CMR might provide reproducible and accurate evaluation of aortic valve area (AVA), aortic velocities, and gradients in agreement with TTE.

Methods and Results—We studied 53 AVS patients (AVA_TTE=0.87±0.44 cm²) and 21 controls (AVA_TTE=2.96±0.59 cm²) who had TTE and PC-CMR of aortic valve and left ventricular outflow tract on the same day. PC-CMR data analysis included left ventricular outflow tract and aortic valve segmentation, and extraction of velocities, gradients, and flow rates. Three AVA measures were performed: AVA_CMRI based on Hakki formula, AVA_CMRR based on continuity equation, AVA_CMRRS simplified continuity equation=left ventricular outflow tract peak flow rate/aortic peak velocity. Our analysis was reproducible, as reflected by low interoperator variability (<4.56±4.40%). Comparison of PC-CMR and TTE aortic peak velocities and mean gradients resulted in good agreement (r=0.92 with mean bias=−29±62 cm/s and r=0.86 with mean bias=−12±15 mm Hg, respectively). Although good agreement was found between TTE and continuity equation–based CMR-AVA (r=0.94 and mean bias=−0.01±0.38 cm² for AVA_CMRR, −0.09±0.28 cm² for AVA_CMRRS), AVA_CMRR values were lower than AVA_TTE especially for higher AVA (mean bias=−0.45±0.52 cm²). Besides, ability of PC-CMR to detect severe AVS, defined by TTE, provided the best results for continuity equation–based methods (accuracy >94%).

Conclusions—Our PC-CMR semiautomated AVS evaluation provided reproducible measurements that accurately detected severe AVS and were in good agreement with TTE. (Circ Cardiovasc Imaging. 2012;5:604-612.)

Key Words: aortic stenosis ■ cardiovascular magnetic resonance ■ transthoracic echocardiography ■ phase contrast

Aortic valve stenosis (AVS) has become the most frequent cardiac valvular disease,¹ and its prevalence will continue to increase with the aging population. Aortic valve area (AVA) is commonly used to evaluate AVS severity as proposed by the current American College of Cardiology/American Heart Association/European Society of Cardiology guidelines.²,³ Indeed, a significant reduction in AVA gradually induces hemodynamic changes, which have deleterious effects on left ventricular (LV) function and are associated with adverse cardiovascular outcomes.⁴ Despite some limitations such as poor image quality and inadequate acoustic window as well as inaccuracies in LV outflow tract (LVOT) diameter measurements and potential mismatch between ultrasound beam and flow alignment, transthoracic Doppler echocardiography (TTE) is commonly used, in clinical routine, for the evaluation of AVA and the related hemodynamic changes (transvalvular aortic velocities and pressure gradients). More recently, cardiovascular magnetic resonance (CMR) has emerged as a new complementary tool for a noninvasive evaluation of AVS: several studies have demonstrated its usefulness for the assessment of AVA and aortic hemodynamic parameters either by planimetric analysis of cine anatomical images⁵,⁶ or by analyzing velocity-encoded images using the continuity equation⁷–¹⁰ or Hakki formula.⁷,¹¹ Indeed, most CMR studies performed a direct planimetry of the stenotic aortic valve, which is prone to measurement errors, especially in severe or heavily calcified AVS, because of voxel size relative to the area, low signal in calcifications as well as within turbulences close to the borders of the aortic leaflets, and irregularity of the stenotic orifice shape. In addition to planimetry, a few CMR studies based...
on phase-contrast (PC) imaging demonstrated the ability of velocity-encoded sequences to characterize AVS by evaluating: peak transvalvular velocity,\textsuperscript{12} AVA using the continuity equation,\textsuperscript{5-10} or Hakki formula,\textsuperscript{7,11} derived from the Gorlin equation. The evaluation of AVA and hemodynamic parameters in the aforementioned PC-CMR studies was mostly based on manual delineation\textsuperscript{5-8,10,11} of the aortic valve and the LVOT, which is subjective and time-consuming, rendering the usefulness of CMR in clinical routine for AVS evaluation limited. In addition, among these studies, some used the estimation of LVOT area from its diameter.\textsuperscript{5-8} Although this strategy complies with TTE measurements, it does not take full advantage of PC-CMR data, which when combined with an accurate segmentation enable a direct estimation of the LVOT stroke volume ($SV_{LVOT}$) while taking into account the shape of the outflow tract.

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Accordingly, our first objective was to design a semiautomated analysis of LVOT and aortic valve PC-CMR data, which would enable an accurate evaluation of AVA, mean and maximal aortic velocities, and gradients. This analysis comprised a semiautomated segmentation of blood flow patterns and an automated processing of velocity and flow-rate curves. It has been previously used for the evaluation of diastolic function from PC-CMR\textsuperscript{13} and was adapted in this study for aortic valve analysis. Our second objective was to test the ability of our method to detect AVS and its severity in comparison with TTE while using 3 different estimates of AVA from PC-CMR.

Methods

Study Population
Fifty-three consecutive patients (33 male, age: 75±14 years [23–92 years]) with known moderate-to-severe AVS and 21 healthy asymptomatic subjects (10 male, age: 50±17 years) were studied. Exclusion criteria comprised: significant mitral or aortic regurgitation, poor echocardiographic imaging quality, or contraindications to CMR. Patients who had LV impairment (ejection fraction <50%) or atrial fibrillation were not excluded. All subjects had both TTE and CMR on the same day. A follow-up in terms of surgery, percutaneous valve replacement, and death during this period was performed during 6 months after the examinations. Study protocol was approved by the local institutional review board, and all patients and volunteers were informed and provided signed consent.

Transtracheal Echocardiography
TTE was performed by an experienced echocardiographer blinded to clinical and CMR data using a GEMS Vivid7 system. The optimal velocity envelope and the true maximal transvalvular aortic velocity ($V_{maxAO}$) were obtained using continuous Doppler waves from multiple imaging windows (apical, right parasternal, and suprasternal). LVOT velocity profile was obtained using an apical 5-chamber view by a careful placement of the pulsed wave Doppler sample volume in the LVOT immediately below the aortic valve.

LVOT diameter (D) was measured using the parasternal long axis view providing the LVOT area while assuming a circular shape (LVOT area=π×D$^{2}$/4). Velocity time integrals of blood flow were calculated for the LVOT ($VTI_{LVOT}$) and for the aortic valve ($VTI_{AO}$). Maximum and mean transvalvular aortic pressure gradients were calculated using the modified Bernoulli equation ($ΔP=4V^{2}$). The continuity equation\textsuperscript{14,15} combining systolic velocity time integrals $VTI_{LVOT}$ and $VTI_{AO}$ with LVOT area, was used to assess AVA, AVA$_{TTE}$ as follows:

\[
AVA_{TTE} = \frac{SV_{LVOT} \times V_{maxAO}}{VTI_{AO}}
\]

Indexed LV mass was calculated using the American Society of Echocardiography computation method,\textsuperscript{16} and LV ejection fraction was recorded using the Simpson method.

Cardiac Magnetic Resonance

Image Acquisition
CMR was performed using a 1.5-T GE system with cardiac phased array coil (8 channels). Cine images of the LVOT were acquired, during breath-holding, using the steady-state free precession cine sequence in 2 orthogonal planes (sagittal oblique and oblique coronal) with the following averaged scan parameters: repetition time ($TR$)=3.2 ms, echo time=$1.4$ ms, flip angle=50°, slice thickness=8 mm, pixel spacing=0.74 mm, and interphase duration=33 ms. These steady-state free precession images enabled the visualization of the systolic jet originating from the stenotic aortic valve. They were used to optimize valvular planes positioning for velocity-encoded acquisitions (Figure 1), which were performed with retrospective gating during breath-holding. PC images were acquired on cross-sectional planes perpendicular to the jet, at the level of the LVOT just below the aortic annulus and at 3 aortic valve levels, valve 0 mm, valve 5 mm, and valve 10 mm, with valve 0 mm corresponding to the reference plane at the level of tips of the opened aortic leaflets, valve 5 mm and valve 10 mm, located 5 and 10 mm above this reference, respectively (Figure 1). Averaged acquisition parameters for the velocity-encoded technique were: TR=4.3 ms, echo time=2.1 ms, flip angle=20°, number of excitations=1, slice thickness=8 mm, pixel spacing=1.9 mm, acquisition matrix=256×128, views per segment=2, effective temporal resolution=17 ms. To minimize background offsets so that acquisition duration remained compatible with breath-holding, a 50% rectangular field of view was used. The imaged structure was always at the center of the acquired image and away from PE-wraparound. Encoding velocity was Venc=2 m/s for LVOT acquisition and for aortic valve acquisitions of subjects without AVS, and Venc=5 m/s for aortic valve acquisitions when AVS was suspected. In case of velocity aliasing, PC acquisition was repeated with a higher Venc.

Image Analysis
CMR data analysis was performed by an investigator blinded to clinical and TTE findings using a custom software previously used for the analysis of transmitial flow from PC images.\textsuperscript{13} Similar to our previous method, $\Delta P$ for TTE was estimated from the peak transvalvular velocit, $V_{maxAO}$ using the continuity equation.

Figure 1. Oblique coronal steady-state free precession (SSFP) cine acquisition used for placement of phase-contrast cardiovascular magnetic resonance planes. See text for more details. LVOT indicates left ventricular outflow tract.
study, the segmentation process was performed on velocity images rather than modulus images. Segmentation of velocity images was based on the connectivity in terms of pixels sign, defined by the local direction of blood flow. It was applied to both LVOT and aortic valve transverse PC images. In case of severe AVS, several orifices can be observed in the aortic flow images (Figure 2). Thus, the segmentation algorithm was adapted to this specific application.

Segmented velocity images provided mean and maximal velocity curves as well as flow-rate curves throughout the cardiac cycle. To reduce the effect of noise, maximal velocity was calculated for each phase as the average of velocity values >95% of the maximal velocity within the segmented region of interest while excluding boundary pixels.

Ejection velocity, flow-rate peaks, and end of the systolic phase were automatically estimated using an automated process previously described in detail by Bollache et al. VTIAO was calculated by integrating aortic maximal velocity curves during systole. Of note, the automated analysis was performed on the 3 acquisition planes, and the plane providing the maximal aortic velocity was used to estimate VTIAO as well as the aortic peak velocity, VmaxAO. The SVLVOT was also calculated by integrating LVOT flow-rate curve during systole and was multiplied by heart rate to estimate cardiac output. Finally, transvalvular aortic mean and maximal systolic pressure gradients, ΔPmaxAO, were calculated using the simplified Bernoulli equation.

After estimation of these parameters from LVOT and aortic valve PC images (Figure 3), AVA was estimated using 3 methods:

1. The first method was based on Hakki formula, which is a simplification of Gorlin formula previously applied to PC-CMR data by Puymirat et al. 11 AVACMR1 = cardiac output/√ΔPmaxAO.

2. The second method was based on the continuity equation, commonly used in echocardiography but also in previous CMR studies. AVACMR2 = SVLVOT/VTIAO.

3. The third approach was also based on the continuity equation. This method has been described with echocardiographic data and is commonly used in clinical routine. AVAECMR = QmaxLVOT/VmaxAO. Our hypothesis was that using a single phase would introduce less measurement errors than using time integrals because the velocity-to-noise ratio of the velocity image at peak velocity is higher than during early systole, and also because accuracy in estimating velocities close to the Venc is higher than velocity estimates close to zero.

**Variability Measurements**

Because flow segmentation required a manual initialization on a single phase, interoperator variability of our analysis in terms of functional velocity, flow-rate parameters, and AVA obtained by the 3 techniques was studied: analysis of LVOT and aortic valve PC data was performed by 2 independent operators on a subgroup of 21 subjects including, 16 patients and 5 controls.

**Statistical Analysis**

Values are reported as medians and interquartile ranges. For comparison between controls’ and AVS patients’ TTE and PC-CMR measurements, a nonparametric Mann–Whitney test was used, after testing the normality of continuous variables distribution using the Shapiro–Wilk test. Significance was considered for \( P < 0.05 \). Linear regression was used for comparison between CMR and TTE measurements and Pearson correlation coefficient was provided. In addition, degree of agreement between methods was assessed by Bland–Altman analysis and mean biases±SD were reported. Sensitivity, specificity, positive, and negative predictive values as well as accuracy of CMR detection of severe stenosis defined by TTE (AVA<1 cm² or mean gradient >40 mm Hg) were calculated using the abnormality threshold calculated by the receiver operating characteristic (ROC) analysis while maximizing sensitivity and specificity. Areas under the ROC curve as well as the abnormality threshold were provided. Interoperator variability was calculated for each subject as the absolute difference of the repeated measurements in percentage of their mean. These percentages were averaged on the whole subgroup.

**Results**

Patients’ and controls’ characteristics and LV functional parameters as well as TTE and CMR hemodynamic parameters are summarized in Table 1. TTE indicated that 81% of the AVS patients had a severe stenosis. At month 6 after imaging examinations, 8 patients had died. Among the remaining
patients, 8 patients showed no symptoms, 29 had surgery, and 8 had percutaneous valve replacement.

All developments were integrated in a custom interface developed on Matlab (Mathworks, Natick, MA), which was used to analyze PC data. For each subject, the processing time of the 3 valvular and the LVOT levels was <5 minutes, on a personal computer (CPU 2.67 GHz, 3 Gb RAM). This processing time is equivalent or slightly higher than those of direct planimetry on steady-state free precession images, but much lower than those of manual delineation on the whole cardiac cycle, which was estimated to be ≈20 minutes for each level. Table 2 summarizes the average interoperator variability measurements of the CMR hemodynamic parameters.

Figure 4 shows the comparison of CMR and TTE maximal aortic velocity values, which resulted in a high correlation coefficient (r=0.92, P<0.0001). Bland–Altman analysis indicated a slight underestimation of velocity values with CMR (mean bias=−29.5±62.2 cm/s), which was found to be significant (paired t test P<0.0001). Similar comparison was performed for aortic velocity time integral VTIAO, resulting in a high correlation coefficient (r=0.86, P<0.0001). Bland–Altman analysis indicated an underestimation of VTIAO values with PC-CMR (mean bias=−19±21 cm). Comparison of PC-CMR and TTE resulted in lower percentage of variation for peak aortic velocities (18±15%) than for aortic VTIAO (34±23%). These percentages of variation were calculated as the absolute difference between TTE and PC-CMR measurements in percentage of their mean. Comparisons of maximal aortic velocities estimated from each PC-CMR plane (valve 0 mm, valve 5 mm, valve 10 mm) against TTE are summarized in Table 3, indicating slightly better results in terms of correlation coefficient and mean bias when considering the valve 5 mm plane. Aortic maximal velocity was estimated for the majority of subjects (53%) from the valve 5 mm plane whereas it was estimated from the valve 0 mm plane for 28% of subjects and from the valve 10 mm plane for 19% of subjects.

Although PC-CMR underestimated transvalvular aortic mean gradients when compared with TTE values (bias=−12±15 mm Hg), a high correlation coefficient was found between the 2 measurements (r=0.86, P<0.0001). A slight improvement in these results was found when the 7 patients with atrial fibrillation were excluded from the analysis (r=0.89, P<0.0001, bias=−12±15 mm Hg). Figure 5 summarizes comparisons of CMR and TTE AVA measurements. Although a strong correlation coefficient (r=0.90, P<0.0001) was found for AVA CMR1, derived using the Hakki formula, significant differences were found between the 2 measurements. Indeed, the Bland–Altman diagram indicated a mean bias of −0.45±0.52 cm², which was increased for higher AVA values. AVA CMR2 and AVA CMR3 derived from the continuity equation and from its modified version, respectively, provided higher correlation coefficients (r=0.94, P<0.0001 and r=0.97, P<0.0001, respectively). Bland–Altman diagrams corresponding to these 2 AVA measurements revealed low mean biases (0.01±0.38 cm² and 0.09±0.28 cm², respectively). Although the overall linear regression slopes were close to 1 for both comparisons between AVA TTE and AVA CMR1 (0.90) as well as AVA CMR2 (1.01), a paired t test indicated that the differences between TTE and CMR AVA were significantly different.

ROC analysis was performed on the entire study group that included 58% of patients with severe stenosis as defined by TTE to evaluate the ability of CMR AVA values to detect severe AVS. This analysis resulted in high values of sensitivity, specificity, negative, and positive predictive values, accuracy, and area under ROC curves that are summarized in Table 4.

**Discussion**

Accurate evaluation of the hemodynamic severity of stenosis is crucial for clinical decision making in patients with AVS.23
Several indices such as transvalvular peak velocities and pressure gradients as well as AVA have been proposed to assess AVS severity.\textsuperscript{2,3} In the present study, a semiautomated segmentation of LVOT and aortic flow patterns from PC-CMR data was combined with an automated analysis of velocity and flow-rate curves, and was tested on consecutive subjects, including patients with moderate-to-severe AVS, providing the aforementioned aortic valve indices that were (1) reproducible, (2) highly correlated with those provided by TTE, and (3) able to detect severe AVS as defined by TTE.

An original feature of our method relies on the segmentation process and its ability to detect various flow patterns regardless of their size, shape, and temporal variation in geometry. Indeed, thanks to the local connectivity of pixels in terms of velocity sign property, our segmentation\textsuperscript{13} was successfully used in the present study to detect LVOT and transvalvular aortic flow. Of note, for transvalvular aortic flows, a modified version of the segmentation algorithm was designed to take into account multiple orifices (Figure 2). This situation occurred in our cohort because of the high prevalence of patients with severe AVS. Furthermore, our method was reproducible, as reflected by low interoperator variability. Indeed, coefficients of variability obtained for our 3 AVA evaluation techniques were <7\% reported by Garcia et al.\textsuperscript{9} Moreover, a larger proportion of patients with severe AVS, and thus with a complex aortic valve morphology, were included in our study, highlighting the robustness of our method. Finally, semiautomated segmentation of LVOT enabled a direct estimation of its stroke volume converse to most of the PC-CMR studies, which estimated LVOT area from its diameter\textsuperscript{5–8} while using the erroneous assumption\textsuperscript{9} of circular shape.

### Table 1. Left Ventricular and Hemodynamic Population’s Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Whole Group (n=74)</th>
<th>AVS (n=53)</th>
<th>Controls (n=21)</th>
<th>P Value Between AVS and Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>73 (55–82)</td>
<td>79 (68–84)</td>
<td>52 (35–60)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>64 (57–69)</td>
<td>63 (55–68)</td>
<td>65 (63–69)</td>
<td>0.07</td>
</tr>
<tr>
<td>LVMi, g/m(^2)</td>
<td>100 (78–122)</td>
<td>110 (87–128)</td>
<td>71 (64–91)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Bicuspid aortic valve, n</td>
<td>14</td>
<td>14</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>LVEF ≤50%, n</td>
<td>12</td>
<td>12</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Atrial fibrillation, n</td>
<td>7</td>
<td>7</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Asymptomatic, n</td>
<td>16</td>
<td>16</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>TTE hemodynamic parameters</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vmax(_{LVOT}), cm/s</td>
<td>94 (81–110)</td>
<td>93 (80–107)</td>
<td>96 (89–121)</td>
<td>0.15</td>
</tr>
<tr>
<td>Max gradient, mm Hg</td>
<td>69 (9.6–82)</td>
<td>77 (65–93)</td>
<td>6.5 (4.4–8.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mean gradient, mm Hg</td>
<td>39 (4.8–51)</td>
<td>45 (36–58)</td>
<td>3.4 (2.4–4.0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>VT(_{LVOT}), cm</td>
<td>22 (18–25)</td>
<td>22 (18–26)</td>
<td>22 (18–24)</td>
<td>0.62</td>
</tr>
<tr>
<td>VT(_{AO}), cm</td>
<td>86 (35–108)</td>
<td>100 (74–115)</td>
<td>25 (22–30)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>AVA, cm(^2)</td>
<td>0.93 (0.68–2.42)</td>
<td>0.76 (0.58–0.95)</td>
<td>2.97 (2.46–3.21)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CMR hemodynamic parameters</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vmax(_{LVOT}), cm/s</td>
<td>293 (142–433)</td>
<td>402 (281–471)</td>
<td>117 (108–137)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Max gradient, mm Hg</td>
<td>34 (8.1–75)</td>
<td>65 (32–89)</td>
<td>5.5 (4.7–7.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mean gradient, mm Hg</td>
<td>14 (3.8–34)</td>
<td>29 (14–38)</td>
<td>2.7 (2.0–3.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>SV(_{LVOT}), mL</td>
<td>66 (48–75)</td>
<td>66 (48–74)</td>
<td>67 (47–75)</td>
<td>0.7</td>
</tr>
<tr>
<td>VT(_{LVOT}), cm</td>
<td>52 (27–79)</td>
<td>70 (49–84)</td>
<td>23 (20–27)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>AVA(_{CMR1}), cm(^2)</td>
<td>0.72 (0.49–1.67)</td>
<td>0.58 (0.42–0.78)</td>
<td>2.06 (1.82–2.33)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>AVA(_{CMR2}), cm(^2)</td>
<td>1.00 (0.80–2.30)</td>
<td>0.84 (0.72–1.06)</td>
<td>2.74 (2.38–3.07)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>AVA(_{CMR3}), cm(^2)</td>
<td>1.00 (0.72–2.54)</td>
<td>0.80 (0.66–1.01)</td>
<td>2.98 (2.71–3.34)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

AVS indicates aortic valve stenosis; LVEF, left ventricular ejection fraction; LVMi, indexed left ventricular mass; TTE, transthoracic echocardiography; Vmax, maximal velocity; LVOT, left ventricular outflow tract; AO, transvalvular aortic; VTI, velocity time integral; AVA, aortic valve area; CMR, cardiovascular magnetic resonance; and SV, stroke volume.

### Table 2. Interoperator Variability of PC-CMR Hemodynamic Parameters

<table>
<thead>
<tr>
<th></th>
<th>Interoperator Variability, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>SV(_{LVOT})</td>
<td>2.79±4.62</td>
</tr>
<tr>
<td>VT(_{LVOT})</td>
<td>2.93±3.38</td>
</tr>
<tr>
<td>Qmax(_{LVOT})</td>
<td>1.26±2.13</td>
</tr>
<tr>
<td>Vmax(_{AO})</td>
<td>0.62±0.87</td>
</tr>
<tr>
<td>AVA(_{CMR1})</td>
<td>2.96±4.56</td>
</tr>
<tr>
<td>AVA(_{CMR2})</td>
<td>4.56±4.40</td>
</tr>
<tr>
<td>AVA(_{CMR3})</td>
<td>1.80±2.27</td>
</tr>
</tbody>
</table>

PC-CMR indicates phase-contrast cardiovascular magnetic resonance; SV, stroke volume; LVOT, left ventricular outflow tract; VTI, velocity time integral; AO, transvalvular aortic; Qmax, maximal flow rate; Vmax, maximal velocity; and AVA, aortic valve area.

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Transvalvular Aortic Maximal Velocities and Gradients

Our semiautomated process for PC-CMR data analysis enabled the estimation of transvalvular aortic peak velocities and mean gradients as well as AVA. For velocity and gradient measurements, high correlations were obtained for comparisons against TTE. However, similar to previous studies, PC-CMR underestimated maximal velocities.

These differences between CMR and TTE values are likely mainly due to a mismatch between orientation of transvalvular flow and acquisition plane, which is particularly challenging to place adequately perpendicular to the flow in patients with severe AVS. Indeed, there are significant spatial and temporal changes in direction of the aortic jet in case of severe AVS, previously highlighted using direct pulsed Doppler on the aortic wall during AVS surgery. Thus, measuring through-plane velocity orthogonal to one of the directions of the aortic jet defined on steady-state free precession imaging can lead to maximal velocity underestimation. In-plane encoding of velocity in x and y directions or 3-dimensional PC-CMR acquisitions can offer an original alternative to overcome this issue. Although other differences such as temporal resolution can be noted between CMR and TTE acquisitions, its effect is reduced for transvalvular peak velocity estimation by the length (>2 × temporal resolution) of the period during which maximal velocity is reached. Moreover, the presence of phase-offset errors can also lead to significant errors in PC-CMR velocity estimation. These offset errors were not corrected in our study but were minimized using a 50% rectangular field of view centered on the LVOT or aortic valve. Alternatively, these errors can be corrected using techniques presented in previous studies.

Also, inclusion of patients with atrial fibrillation can be another potential source of differences between TTE and PC-CMR measurements. Indeed, in such patients with irregular heart rates, a low velocity-to-noise ratio in PC images can occur inherently to CMR acquisitions, which are based on averaging data from several cardiac cycles. However, during reconstruction, cardiac cycles were excluded if their length was 20% different from the mean cardiac cycle length. Moreover, systolic period, which is of interest in this study, is less affected by heart rate irregularity than diastolic period. Although the low number of atrial fibrillation patients does not allow an exhaustive analysis of effect of this condition on our findings, their exclusion from our data resulted in slightly stronger relationships between TTE and PC-CMR. In addition, differences between CMR and TTE measurements might be related to the scanning on a fixed imaging plane, which does not take into account through-plane cardiac motion. These differences can be accounted for using 3-dimensional acquisitions or minimized, as suggested in our study, by acquiring 3 planes and considering the plane providing highest transvalvular velocities. Similar to results reported by Garcia et al and Yap et al, in which maximal transvalvular aortic velocity was obtained 6 mm beyond the aortic orifice, it was obtained on the valve 5 mm plane in 53% of our subjects. Furthermore, comparison of maximal velocity values calculated from the 3 acquisition planes against TTE in our study demonstrated that although results obtained when considering the valve 5 mm plane were slightly better than those obtained for valve 0 mm and valve 10 mm, the best results were obtained when considering the plane providing the highest maximal velocity. These differences might be partially explained by the predominance of flow turbulences–related signal void at the aortic valve 0 mm level.

Table 3. Results of Comparisons Between TTE and PC-CMR Measurements of Maximal Transvalvular Aortic Velocity Calculated From the 3 Valvular Acquisition Planes

<table>
<thead>
<tr>
<th>Valve Location</th>
<th>Correlation Coefficient, r</th>
<th>Bland–Altman Analysis, Mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimal valvular plane*</td>
<td>0.92</td>
<td>-29±62</td>
</tr>
<tr>
<td>P&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valve 0 mm</td>
<td>0.79</td>
<td>-77±98</td>
</tr>
<tr>
<td>P&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valve 5 mm</td>
<td>0.87</td>
<td>-55±80</td>
</tr>
<tr>
<td>P&lt;0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valve 10 mm</td>
<td>0.86</td>
<td>-67±99</td>
</tr>
<tr>
<td>P&lt;0.0001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TTE indicates transthoracic Doppler-echocardiography; PC-CMR, phase-contrast cardiovascular magnetic resonance. Correlation coefficients as well as P values and results of the Bland–Altman analysis are provided for the maximal transvalvular aortic velocity (cm/s).

*Optimal valvular plane is individually defined as the level providing the maximal aortic velocity.

Aortic Valve Area

For AVA measurements, the 3 CMR methods resulted in high correlations when compared against TTE, with a superiority.
of methods based on the continuity equation. This superiority was expected because: (1) as for TTE, AV\textsubscript{CMR1} and AV\textsubscript{CMR2} were also calculated using the continuity equation, and (2) the Hakki formula includes simplifications inducing an underestimation of AV\textsubscript{CMR1}, which was previously described.\textsuperscript{7,11,29} Indeed, A\textsubscript{VA} calculated by the Hakki formula is conversely proportional to maximal transvalvular gradient, estimated using the simplified Bernoulli equation.\textsuperscript{30} As illustrated by our results (Figure 5A), whereas the Hakki formula resulted in only a slight underestimation regarding TTE for severe AVS, its reliability is jeopardized for subjects with less severe stenosis because their subvalvular maximal velocity is not

![Figure 5. Linear regressions (left) and Bland–Altman diagrams (right) of comparisons between transthoracic Doppler echocardiography (TTE) and the 3 cardiovascular magnetic resonance (CMR) techniques for aortic valve area (AVA) estimation: (A) AV\textsubscript{CMR1} (Hakki), (B) AV\textsubscript{CMR2} (SV\textsubscript{LVOT}/VT\textsubscript{IAO}), and (C) AV\textsubscript{CMR3} (Qmax\textsubscript{LVOT}/Vmax\textsubscript{AO}).](610.png)

of methods based on the continuity equation. This superiority was expected because: (1) as for TTE, AV\textsubscript{CMR1} and AV\textsubscript{CMR2} were also calculated using the continuity equation, and (2) the Hakki formula includes simplifications inducing an underestimation of AV\textsubscript{CMR1}, which was previously described.\textsuperscript{7,11,29} Indeed, A\textsubscript{VA} calculated by the Hakki formula is conversely proportional to maximal transvalvular gradient, estimated using the simplified Bernoulli equation.\textsuperscript{30} As illustrated by our results (Figure 5A), whereas the Hakki formula resulted in only a slight underestimation regarding TTE for severe AVS, its reliability is jeopardized for subjects with less severe stenosis because their subvalvular maximal velocity is not

### Table 4. Results of ROC Analysis Performed on the 74 Subjects, Reflecting the Ability of PC-CMR AVA Measurements to Detect AVS Severity, as Defined by TTE

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>PPV, %</th>
<th>NPV, %</th>
<th>Accuracy, %</th>
<th>AUC</th>
<th>Threshold, cm(^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AV\textsubscript{CMR1}</td>
<td>98</td>
<td>84</td>
<td>89</td>
<td>96</td>
<td>92</td>
<td>0.97</td>
<td>0.95</td>
</tr>
<tr>
<td>AV\textsubscript{CMR2}</td>
<td>95</td>
<td>94</td>
<td>95</td>
<td>94</td>
<td>94</td>
<td>0.99</td>
<td>1.13</td>
</tr>
<tr>
<td>AV\textsubscript{CMR3}</td>
<td>98</td>
<td>90</td>
<td>93</td>
<td>97</td>
<td>95</td>
<td>0.98</td>
<td>1.21</td>
</tr>
</tbody>
</table>

PC-CMR indicates phase-contrast cardiovascular magnetic resonance; AVA, aortic valve area; TTE, transthoracic Doppler-echocardiography; PPV, positive predictive value; NPV, negative predictive value; AUC, area under curve; ROC, receiver operating characteristic. Sensitivity, specificity, PPV, and NPV, accuracy and AUC as well as the abnormality threshold of the ability of AV\textsubscript{CMR1}, AV\textsubscript{CMR2} and AV\textsubscript{CMR3} to detect severe aortic valve stenosis, as defined by TTE, are provided.
negligible compared with valvular velocity as assumed in the simplified Bernoulli equation. Estimation of AVA using the continuity equation (AVA_{CMR}) is the most commonly reported in the few previous PC-CMR studies. These studies proposed various formulations of the continuity equation, which can be mainly distinguished by the methodology used for SV_{LVOT} calculation. Indeed, this volume was calculated from a single measurement of LVOT diameter, from the difference between LV end-diastolic and end-systolic volumes, or from PC-CMR flow data that provided the best results.\textsuperscript{5,10} In our study, SV_{LVOT} was semiautomatically calculated from PC-CMR flow data resulting in high correlation and low overall bias, in terms of AVA measurements. Although a direct comparison is not possible because of differences in databases, comparison of our AVA findings with those of Yap and Garcia who used PC-CMR approaches indicated a slight superiority of our results. Indeed, Yap et al\textsuperscript{10} reported a correlation coefficient r=0.86 and bias=0.02±0.23 cm\textsuperscript{2} in 20 AVS patients and Garcia et al\textsuperscript{9} reported a correlation coefficient r=0.92 and bias=0.06±0.29 cm\textsuperscript{2} in 31 AVS patients and 7 controls.

Another continuity equation, AVA_{CMR}\textsuperscript{3} based on a single systolic phase was tested in our study resulting in the highest correlations and also in low bias for AVA comparison against TTE. This approach has been previously used in echocardiography but was used in a single PC-CMR study without comparison against TTE.\textsuperscript{6} The slight superiority of this latter technique might be due to the fact that differences between PC-CMR and TTE in velocity and flow-rate estimations were less significant in a single phase at peak velocity than when calculating time integrals. Indeed, time integrals result in accumulated errors during the systolic phase, especially when velocities are far from Venc. This highlights the importance of an adapted setting of encoding velocity in CMR studies. Indeed, for optimal noise performance, Venc should be selected as close as possible to the velocity to be measured.

ROC analysis used for the evaluation of the ability of CMR techniques to detect severe AVS as defined by TTE resulted in the highest sensitivity, specificity, positive predictive value, negative predictive value, and accuracy values when considering continuity equation–based PC-CMR AVA measurements (Table 4).

Limitations

Our study lacks a reliable gold standard; however, there is no such method for in vivo evaluation of AVA. The invasive evaluation of AVA by applying the Gorlin formula to catheterization data could be used as an alternative to TTE in our study. However, these data were not available for our patients because such invasive examination was not approved by the local institutional review board because of the associated increased risk for patients\textsuperscript{11} especially for those with heavily calcified valves. Moreover, such invasive measurements might be prone to the previously described pressure recovery effects within the aortic valve.\textsuperscript{21} Despite the aforementioned technical limitations, high correlations were found between PC-CMR and TTE parameters and, more importantly, PC-CMR parameters were able to accurately detect severe AVS as defined by TTE.

Following these encouraging findings, large prospective studies are needed to demonstrate the usefulness of PC-CMR AVS evaluation in clinical decision making. However, PC-CMR AVA, maximal velocity, and mean gradient as provided by semiautomated methods could be used to define CMR-specific thresholds for severity of AVS in such prospective studies. The clinical value of CMR may reside in reference myocardial function\textsuperscript{32} and fibrosis evaluation\textsuperscript{33-37} combined with reliable quantification of transvalvular hemodynamics.

Conclusions

Our semiautomated method was fast, reproducible, and successfully used on PC-CMR data of 74 subjects, including patients with moderate-to-severe AVS and controls. Transvalvular aortic peak velocities, mean gradients, and AVA estimated in our study were highly correlated with TTE measurements. In addition, when compared with the approach based on the Hakki formula, CMR methods based on the continuity equation presented a superiority in terms of correlation and mean bias with TTE as well as in terms of AVS severity detection.

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Disclosures

None.

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CLINICAL PERSPECTIVE

Aortic valve stenosis (AVS) is increasingly prevalent as a result of global population aging. Accurate quantification of stenosis severity is crucial for relevant patient management decisions. Although transthoracic Doppler echocardiography remains the clinical workhorse for AVS severity assessment, cardiovascular magnetic resonance is emerging as an appealing noninvasive modality to estimate AVS severity in the context of myocardial assessment with respect to remodeling and fibrosis. This work investigated the agreement and reproducibility of cardiovascular magnetic resonance and transthoracic Doppler echocardiography to evaluate aortic valve area coupled with hemodynamic parameters such as transvalvular aortic velocities and pressure gradients, showing good agreement between modalities and excellent reproducibility of phase-contrast cardiovascular magnetic resonance semiautomated AVS evaluation. The addition of accurate and reproducible estimation of aortic valve area and hemodynamic parameters to myocardial function, geometry, and tissue characterization afforded by comprehensive cardiovascular magnetic resonance examination warrants larger-scale validation as an effective tool for decision making in patients with AVS.
Evaluation of Aortic Valve Stenosis Using Cardiovascular Magnetic Resonance: Comparison of an Original Semiautomated Analysis of Phase-Contrast Cardiovascular Magnetic Resonance With Doppler Echocardiography

Carine Defrance, Emilie Bollache, Nadjia Kachenoura, Ludivine Perdrix, Nataliya Hrunchyshyn, Eric Bruguière, Alban Redheuil, Benoit Diebold and Elie Mousseaux

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