Semiautomated Analysis of Aortic Stenosis Parameters on Velocity-Encoded Phase-Contrast MR Images in Patients with Severe Aortic Stenosis: A Comparison with Echocardiography

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Objective: The aim of the study was to determine the reliability of semiautomated analysis of aortic stenosis (AS) parameters on velocity-encoded (VENC) phase-contrast (PC) MR images in patients with severe AS.

Materials and Methods: This study included 55 patients with severe AS and normal left ventricular ejection fraction who underwent transthoracic echocardiography (TTE) and VENC PC sequencing. Aortic valve area (AVA) and transvalvular velocity were measured semiautomatically with commercial software at three aortic valve levels [the level of the aortic leaflet tips (0 mm) and 6 mm upstream and downstream of the leaflet tips]. The AVA was drawn on VENC PC images, and the maximum, minimum, and average were calculated. The peak and mean transaortic pressure gradient (PG) were calculated with a modified Bernoulli equation. All estimates were compared with TTE values by using the concordance correlation coefficient (CCC).

Results: Estimates at the 0 mm level were more highly correlated with TTE values (parameter, CCC): peak velocity, 0.394; average AVA, 0.735; maximum AVA, 0.538; peak PG, 0.539; and mean PG, 0.048. Among these parameters, average AVA_{0 mm} had the highest reliability.

Conclusion: If AS parameters are measured on VENC PC sequences, average AVA_{0 mm} should be considered as a parameter for diagnosing severe AS.

Key words Aortic stenosis · Valvular heart disease ·
Magnetic resonance imaging · Transthoracic echocardiography.

INTRODUCTION

Aortic valve stenosis (AS) is the most prevalent valvular heart

disease, and its incidence increases with age [1]. According to the 2014 American Heart Association/American College of Cardiology (AHA/ACC) guidelines for the management of patients with valvular heart disease, the severity of AS is defined by valve anatomy and valve hemodynamics, such as aortic valve area (AVA), peak velocity, and mean transaortic pressure gradi-

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ent (PG) [2].

Transthoracic echocardiography (TTE) is the standard tool used to evaluate AS severity [3]. However, TTE is limited in some patients by poor acoustic windows and can be affected by the experience of the sonographer, particularly in assessing PG and AVA [4]. Cardiac catheterization is the gold standard for hemodynamic assessment, but it is invasive and requires exposure to ionizing radiation [5]. Cardiovascular magnetic resonance (CMR) has emerged as an alternative non-invasive modality to evaluate AS severity without exposure to ionizing radiation [3,5]. Accurately measuring velocity requires velocity-encoded (VENC) phase-contrast (PC) pulse sequences based on the accumulated phases of moving protons, but this technique tends to underestimate the actual velocity in severe AS [4,5].

AVA is commonly used to evaluate AS severity, as proposed by standard guidelines [2]. Previous CMR studies have reported that direct planimetry of the aortic opening area correlates with AS morphology [6,7]. However, the planimetry of AVA on CMR is prone to measurement errors, especially in severe or heavily calcified AS, because calcifications and turbulence have a low signal close to the borders of the aortic leaflets [8]. VENC PC images provide direct visualization of the transplanar flow. We tested the ability of magnetic resonance imaging (MRI) to quantify the orifice area by using planimetry of VENC PC images. Another CMR study using VENC PC images showed that systolic variability of the vena contracta could also be used as a quantitative parameter [9]. However, the reliability of semiautomated measurements of AS parameters, including peak velocity, PG, and AVA during ejection, on VENC PC images by using commercial software has not yet been described.

The aim of this study was to determine the reliability of semi-automated analysis of AS parameters from VENC PC images acquired at three different aortic valve levels in patients with severe AS.

MATERIALS AND METHODS

Patients

The Institutional Review Board approved this prospective single-center study, and all patients gave written informed consent. Between January 2012 and December 2014, patients with severe AS on TTE (defined as AVA <1 cm² and peak aortic velocity (AV) ≥ 4 m/s or mean transaortic PG (AV mean PG) ≥ 40 mm Hg) underwent VENC PC sequencing before valve surgery. Both tricuspid and bicuspid AS patients were included. The exclusion criteria were as follows: left ventricular ejection fraction (LVEF) $<50\%$, more severe than mild mitral disease or aortic regurgitation, and poor TTE image quality. Ultimately, 55 patients with severe AS were included in this study.

Cardiovascular magnetic resonance

CMR images were obtained with a 1.5-T MR system (Magnetom Avanto; Syngo MR B17 version; Siemens Medical Solutions, Erlangen, Germany) equipped with a maximum strength gradient of 45 mT/m, a 200 mT/m/msec slew rate, and a 32-channel body array coil. CMR image scans consisted of localizing images (axial, coronal, and sagittal), cine scans (2-chamber view, 3-chamber view, 4-chamber view, and short-axis view), and a VENC PC pulse sequence. All examinations were carried out by experienced technicians and supervised by an experienced radiologist.

Image acquisition parameters are described focusing on PC pulse sequences. On cine images, the balanced steady-state free precession was used to visualize the systolic jet flow from the stenotic aortic valve and to optimize plane positioning for the VENC PC pulse sequence. VENC PC images were acquired on cross-sectional planes perpendicular to the jet at three aortic valve levels: 0 mm, +6 mm and -6 mm, with 0 mm corresponding to the level of the tips of the opened aortic leaflets, and +6 mm and -6 mm located upstream and downstream of the leaflet tips, respectively (Fig. 1). Acquisition parameters for the VENC PC image were repetition time/echo time=4.60–4.92/2.76–3.05 ms, flip angle=30, 30 phases, pixel spacing=1.32–2.07 mm, slice thickness=4.5 mm, acquisition matrix=192 $\times$ 106, and scan time=8–15 s without a parallel acquisition technique. A VENC scout sequence with a VENC of 3.5 m/sec, 4.0 m/sec, or 4.5 m/sec was used to choose the appropriate VENC. When aliasing occurred at 4.5 m/sec, the flow was acquired at higher VENCs in 0.5 m/s steps.

Fig. 1. To quantify velocity, three aortic valve levels were analyzed on VENC PC images. VENC PC images were obtained in an imaging plane perpendicular to the jet. Transvalvular velocity was measured at 0 mm, +6 mm, and -6 mm, with 0 mm corresponding to the reference plane at the level of opened aortic leaflet tips. VENC: velocity-encoded, PC: phase-contrast.

Cardiovascular magnetic resonance analysis

CMR images analyses were independently performed by two experienced investigators (S.H.B and S.M.K., with 6 and 10 years of experience, respectively) blinded to the clinical and TTE results. The VENC PC sequences display both a magnitude and phase image. The proximal vena contracta was contoured semi-automatically on the systolic images by commercial software (Argus; Siemens Healthcare, Erlangen, Germany) (Fig. 2). The largest AVA during systole was defined as the maximum AVA (AVA_{max}). The mean AVA was acquired by averaging all planimetered areas during systole. The smallest AVA was defined as the minimum AVA (AVA_{min}). Peak and average velocities were calculated automatically and were used to calculate PG. PG was calculated with a simplified Bernoulli equation ($\Delta p = 4 \times \text{velocity}^2$). Peak and mean PG were calculated from peak and mean velocity at the three different levels. The means of values measured by both investigators were used for the analysis.

Transthoracic echocardiography

Comprehensive TTE was performed on each patient with commercially available equipment (Vivid 7, GE Medical System, Milwaukee, WI; Acuson 512, Siemens Medical Solutions, Mountain View, CA; or Sonos 5500, Philips Medical System, Andover, MA, USA). Standard M-mode, two-dimensional, and Doppler images were collected for all standard views. End diastole was defined as the frame with the largest cavity area closest to the QRS onset, and end systole was defined as the frame with the smallest cavity area. LV end-diastolic volume, LV end-systolic volume, and LVEF were calculated from two-dimensional recordings with the modified biplane Simpson's method [10].

Continuous wave Doppler was used to assess peak AV (AVV_{max}) and mean transaortic PG (AV mean PG) with a simplified Bernoulli equation according to the guidelines of the American Society of Echocardiography [11,12]. The time-velocity integral at the aortic valve and LV outflow tract level were acquired with continuous wave and pulse wave Doppler echocardiography, respectively, and AVA was calculated by using the continuity equation with the parameters mentioned previously. The aver-

age of three consecutive Doppler signals was used.

Statistical analysis

Quantitative variables are expressed as the mean $\pm$ standard deviation. To estimate the difference between the VENC PC sequence and TTE, a t test was used for normally distributed data, whereas Wilcoxon's signed rank test was used for data that were not normally distributed. Parameter agreement of the two techniques was assessed with the Bland-Altman method and the concordance correlation coefficient (CCC) [13]. CCC values were categorized as follows: low <0.4 , $0.4 \leq$ moderate ≤ 0.75 , and high >0.75 . Interobserver agreement for velocity and AVA was assessed with a two-way random, single-measure interclass correlation coefficient (ICC). All analyses were performed with SPSS for Windows Version 21.0 (IBM, Chicago, IL, USA).

RESULTS

Patient characteristics and CMR and TTE estimates

Patient characteristics and TTE and VENC PC sequence estimates are summarized in Table 1. The mean interval between TTE and CMR was 14.6 ± 18.3 days. Fifty-five patients (mean age, 67.8 ± 9.0 years; range, 39 to 84 years) with severe AS were included in this study. Of these 55 patients, 36 (65.5%) had a tricuspid aortic valve, and 19 (34.5%) had a bicuspid aortic valve. All patients had a normal LVEF ($66.9 \pm 7.1\%$).

Correlation of peak velocity, pressure, and aortic valve area gradient between CMR and TTE

Correlation analyses for peak velocity obtained from VENC PC images at the three different valve levels are presented in Table 2 and Fig. 3. On CMR, the peak velocities at all levels were significantly different and underestimated when compared with TTE. Estimates at the 0 mm level showed the highest correlation with the peak velocity from echocardiography (0.394, 0.250–0.522). The maximum peak velocity from all three valve levels had a higher correlation (0.549, 0.388–0.677) than did the 0 mm level.

Fig. 2. From VENC PC images, both magnitude (upper row) and phase (bottom row) images can be reconstructed. The region of interest of the proximal vena contracta was determined manually on systolic images. VENC: velocity-encoded, PC: phase-contrast.

Table 1. Patient characteristics and estimates of TTE and CMR

Patients (n=55)	
Patient demographics	
Age	67.8±9.0
Sex*	26:29
Estimates of TTE	
Peak aortic velocity (m/sec)	5.1±0.7
Mean transaortic PG (mm Hg)	63.1±18.9
AVA (cm ²)	0.7±0.2
Estimates of CMR	
Peak velocity (m/sec)	
Level 0 mm	4.1±1.0
Level +6 mm	4.2±0.7
Level -6 mm	2.9±1.2
Pressure gradient (mm Hg)	
Peak-PG, Level 0 mm	72.3±34.4
Peak-PG, Level +6 mm	72.7±25.2
Peak-PG, Level -6 mm	39.5±33.3
Mean-PG, Level 0 mm	19.3±8.3
Mean-PG, Level +6 mm	18.0±7.3
Mean-PG, Level -6 mm	10.4±7.4
AVA of vena contracta (cm ²)	
Max AVA, Level 0 mm	0.7±0.2
Max AVA, Level +6 mm	0.7±0.2
Max AVA, Level -6 mm	0.9±0.4
Ave AVA, Level 0 mm	0.5±0.2
Ave AVA, Level +6 mm	0.5±0.2
Ave AVA, Level -6 mm	0.7±0.3
Min AVA, Level 0 mm	0.9±0.2
Min AVA, Level +6 mm	0.9±0.5
Min AVA, Level -6 mm	1.1±0.4

All data are expressed as mean±SD. *data are M:F. AVA: aortic valve area, Ave: average, CMR: cardiac magnetic resonance, Max: maximum, Min: minimum, PG: pressure gradient, TTE: transthoracic echocardiography

For the PG, the peak and mean PG from the VENC PC images were compared with the mean PG from TTE (Table 3 and Fig. 4). On CMR, the peak and mean PGs at all levels were significantly different from the mean PG from TTE. The peak PG0 mm and PG+6 mm were overestimated, and the other values were underestimated. Of all peak and mean PG values, the peak PG0 mm had the highest correlation with mean PG from TTE (0.539, 0.384–0.665).

The AVA determined from the vena contracta on VENC PC images was compared with the AVA from TTE calculated with the continuity equation (Table 4 and Fig. 5). The average AVA0 mm did not differ significantly from the TTE AVA and showed the highest correlation (0.735, 0.588–0.835) with the TTE AVA. The average AVA+6 mm was underestimated, and the other values were overestimated. With the exception of average AVA0

mm, all AVA estimates on the VENC PC images differed significantly from the TTE AVA.

Of all the measurements, including peak velocity, PG, and AVA, taken from the VENC PC images, average AVA0 mm had the highest correlation with TTE.

The ICCs of the two observers for peak velocity and AVA were as follows: peak velocity, 0.990, 0.982–0.994; AVA_{max}, 0.865, 0.780–0.919; average AVA, 0.887, 0.814–0.933; and AVA_{min}, 0.815, 0.702–0.888.

DISCUSSION

Comparing imaging parameters to diagnose severe AS illustrated that average AVA0 mm measured from a semiautomated VENC PC sequence by commercial software had the highest correlation value of all VENC PC sequence parameters. The VENC PC sequence is an established and non-invasive tool used to quantify the velocity and blood flow based on the accumulated phase of moving protons [14,15]. Previous studies have manually assessed AVA on cine sequences and used in-house or customized software to assess hemodynamic parameters from a VENC PC sequence in valvular stenosis [3,8,16-18]. We only used VENC PC sequences and commercial software for easy access in daily clinical practice.

Previous studies identified that VENC PC sequences tend to underestimate peak velocity and PG when compared with TTE [4,5]. The tendency to underestimate was apparent in severe AS due to intravoxel dephasing signal loss related in part to acceleration, alignment of the image plane with the jet, flow turbulence, partial volume effect, background noise, and phase wrap [3,5,9,19-22]. Caruthers et al. [14] reported that the VENC PC sequence underestimated velocity-time integral in more than half of patients with an AVA less than 0.8 mm². O'Brien et al. [20] showed that the underestimation was greater in patients with a Doppler jet velocity greater than 4 m/sec. Our peak velocity data were consistent with these studies. However, the peak velocity at the 0 mm level showed a better correlation than did those at +6 mm and -6 mm, and all peak velocities had lower correlations than did peak PG and AVA. If semiautomated measured peak velocities are used to diagnose AS, multi-level data acquisition is recommended given our finding that the combined measurement (0.549) had a higher correlation than that of each individual level (0 mm, 0.394; +6 mm, 0.294; -6 mm, 0.122). To compare the PGs, we calculated the peak and mean PG, despite using only mean PG from TTE as a reference standard. Unfortunately, the mean PG acquired from the VENC PC images was underestimated by more than 40 mm Hg at each level, which resulted in a low correlation coefficient. The peak PG estimates from the VENC PC sequence at the 0 mm and +6 mm levels were overestimated by almost 11 mm

Hg, and the estimate at 0 mm had a higher correlation than did the other PG values. Based on our results, obtaining accurate measurements of mean PG from mean velocity on VENC PC images is difficult with the current commercial software. However, peak PG might be able to replace mean PG on VENC PC images when diagnosing severe AS.

In assessing AVA, previous studies demonstrated that direct planimetric measurement of the anatomic opening area correlated with morphologic AS by gradient-echo and SSFP cine [6,7]. This planimetry of the anatomic opening area was assessed on the cine image, which showed the maximal valve area at a single time point during systole. If the valve area varies sig-

nificantly during ejection in patients with AS, the mean and maximal measurements of the valve area are not expected to be equal [23]. Our study only used the VENC PC sequence instead of a cine sequence. The region of interest for AVA on the phase images was not a planimetric measurement, but instead a drawing of the convergence of aortic blood flow (proximal vena contracta), which is presumed to represent the true functional orifice area [24]. In our study, the commercial software provided the maximal, average, and minimal valve areas from serial measurements of all systolic valve areas. Mean AVA0 mm during ejection did not differ significantly from TTE AVA when using the continuity equation. However, the maximal AVA estimates

Table 2. The differences in peak velocity between CMR and TTE in patients with severe AS

CMR	Mean	SD	p value	CCC	95% CI
Level 0 mm	-0.942	0.773	<0.001	0.394	0.250–0.522
Level +6 mm	-0.866	0.702	<0.001	0.294	0.143–0.432
Level -6 mm	-2.167	1.080	<0.001	0.122	0.050–0.193

Mean and SD were calculated from differences between CMR and TTE. AS: aortic stenosis, CMR: cardiac magnetic resonance, CCC: concordance correlation coefficient, CI: confidence interval, SD: standard deviation, TTE: transthoracic echocardiography

Fig. 3. Peak velocity measured from the VENC PC sequence was compared with that from TTE. Bland-Altman plots (A, B, and C) show the peak velocities at 0 mm (A), +6 mm (B), and -6 mm (C) on VENC PC images compared with that from TTE images, depicting agreement between the difference (vertical axis) and average (horizontal axis) of the two measurements. The blue lines represent the mean $\pm$ SD. Scatter plot (D) showing the relationship between peak velocity measured on VENC PC images at three valve levels and peak velocity according to TTE. AS: aortic stenosis, ECHO: echocardiography, VENC: velocity-encoded, PC: phase-contrast, TTE: transthoracic echocardiography, SD: standard deviation.

at all three valve levels were overestimated and differed significantly from the TTE values. Previous studies have also reported that maximal areas were significantly higher than mean systolic areas, which is one reason for the consistent overestimation of planimetered AVAs compared with invasively and noninvasively determined effective orifice areas [10,17,18,23]. This current study demonstrated that the average AVA0 mm during ejection

on VENC PC images had the best correlation with TTE (0.735, 0.589–0.835).

This study had some limitations. TTE was used as a reference standard, but TTE estimates might be inaccurate in cases of poor acoustic shadow and are affected by the experience of the sonographer [4]. However, TTE is currently used as the clinical standard for assessing AS severity. In addition, the correlation

Table 3. The differences in pressure gradient between CMR and TTE in patients with severe AS

CMR	Median	1st quartile	3rd quartile	p value	CCC	95% CI
PC-PG (peak)						
Level 0 mm	11.636	-5.876	23.450	0.010	0.539	0.384–0.665
Level +6 mm	11.325	3.433	22.262	<0.001	0.462	0.258–0.626
Level -6 mm	-25.793	-43.988	-13.188	<0.001	0.286	0.126–0.432
PC-PG (mean)						
Level 0 mm	-41.147	-55.601	-31.412	<0.001	0.048	0.011–0.085
Level +6 mm	-40.240	-55.929	-30.858	<0.001	0.004	-0.026–0.034
Level -6 mm	-48.671	-60.286	-19.147	<0.001	0.030	0.006–0.055

Median and quartile were calculated from differences between CMR and TTE. AS: aortic stenosis, CMR: cardiac magnetic resonance, CCC: concordance correlation coefficient, CI: confidence interval, PC: phase contrast, PG: pressure gradient

Fig. 4. Peak PG measured from the VENC PC sequence compared with mean PG from TTE. Bland-Altman plots (A, B, and C) show the peak PGs at 0 mm (A), +6 mm (B) and -6 mm (C) on VENC PC images compared with mean PG from TTE, depicting agreement between the difference (vertical axis) and average (horizontal axis) of the two measurements. The blue lines represent the mean $\pm$ SD. Scatter plot (D) showing the relationship between peak PG from VENC PC images at three valve levels and mean PG from TTE. AS: aortic stenosis, ECHO: echocardiography, PG: pressure gradient, VENC: velocity-encoded, PC: phase-contrast, TTE: transthoracic echocardiography, SD: standard deviation.

coefficients were generally low in our study. While previous studies used Pearson correlation analysis, our study used the CCC, which is considered to be more strict and reliable when

comparing two parameters. In the future, more data are needed to verify the reliability of semiautomated analysis in measuring velocity and AVA with commercial software. We included only

Table 4. The differences in aortic valve area between CMR and TTE in patients with severe AS

CMR	Median	1st quartile	3rd quartile	p value	CCC	95% CI
Ave AVA						
Level 0 mm	0	-0.071	0.084	0.940	0.735	0.588–0.835
Level +6 mm	-0.048	-0.115	0.019	0.008	0.599	0.412–0.738
Level -6 mm	0.155	-0.043	0.359	<0.001	0.308	0.128–0.469
Max AVA						
Level 0 mm	0.170	0.069	0.264	<0.001	0.538	0.373–0.671
Level +6 mm	0.113	0.032	0.264	<0.001	0.351	0.189–0.495
Level -6 mm	0.340	0.094	0.500	<0.001	0.197	0.062–0.325
Min AVA						
Level 0 mm	-0.182	-0.339	-0.097	<0.001	0.392	0.237–0.528
Level +6 mm	-0.204	-0.319	-0.168	<0.001	0.445	0.304–0.567
Level -6 mm	-0.131	-0.262	0.099	0.041	0.403	0.186–0.582

Median and quartile were calculated from differences between CMR and TTE. AS: aortic stenosis, AVA: aortic valve area, Ave: average, CMR: cardiac magnetic resonance, CCC: concordance correlation coefficient, CI: confidence interval, TTE: transthoracic echocardiography, Max: maximum, Min: minimum

Fig. 5. Comparison of average AVA measured from the VENC PC sequence versus effective orifice area according to TTE. Bland-Altman plots (A, B, and C) show the average AVA at 0 mm (A), +6 mm (B) and -6 mm (C) on VENC PC images compared with the effective orifice area from TTE, depicting agreement between the difference (vertical axis) and average (horizontal axis) of the two measurements. The blue lines represent the mean $\pm$ SD. Scatter plot (D) showing the relationship between average AVA from VENC PC at three image planes and effective orifice area from TTE. AS: aortic stenosis, AVA: aortic valve area, ECHO: echocardiography, VENC: velocity-encoded, PC: phase-contrast, TTE: transthoracic echocardiography, SD: standard deviation.

patients with normal LVEF. In patients with decreased LVEF, the correlation of peak velocity and AVA between CMR and TTE might differ from our results. Finally, the study population was small. Further studies with larger populations are needed to validate our findings.

Conclusion

The estimation of AS parameters, including peak velocity, PG, and AVA, at three different aortic valve levels by semiautomated analysis with commercial software demonstrated that parameters at the 0-mm level were more highly correlated with TTE parameters. Among these parameters, average AVA0 mm showed the best correlation with TTE. Therefore, if AS parameters are measured on VENC PC sequences with commercial software, average AVA0 mm should be considered as a candidate measure to diagnose severe AS.

Conflicts of Interest

The author declare that they has no conflict of interest.

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