Estimation of Stroke Volume and Aortic Valve Area in Patients with Aortic Stenosis: A Comparison of Echocardiography versus Cardiovascular Magnetic Resonance

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Background: In aortic stenosis, accurate measurement of left ventricular stroke volume (SV) is essential for the calculation of aortic valve area (AVA) and the assessment of flow status. Current American Society of Echocardiography and European Association of Cardiovascular Imaging guidelines suggest that measurements of left ventricular outflow tract diameter (LVOTd) at different levels (at the annulus vs 5 or 10 mm below) yield similar measures of SV and AVA. The aim of this study was to assess the effect of the location of LVOTd measurement on the accuracy of SV and AVA measured on transthoracic echocardiography (TTE) compared with cardiovascular magnetic resonance (CMR).

Methods: One hundred six patients with aortic stenosis underwent both TTE and CMR. SV was estimated on TTE using the continuity equation with LVOTd measurements at four locations: at the annulus and 2, 5, and 10 mm below annulus. SV was also determined on CMR using phase contrast acquired in the aorta ($SV_{CMR\text{-}PC}$), and a hybrid $AVA_{CMR\text{-}PC}$ was calculated by dividing $SV_{CMR\text{-}PC}$ by the transthoracic echocardiographic Doppler aortic velocity-time integral. Comparison between methods was made using Bland-Altman analysis.

Results: Compared with the referent method of phase-contrast CMR for the estimation of $SV_{CMR\text{-}PC}$ and $AVA_{CMR\text{-}PC}$ ($SV_{CMR\text{-}PC}$ 83 $\pm$ 16 mL, $AVA_{CMR\text{-}PC}$ 1.27 $\pm$ 0.35 cm^2), the best agreement was obtained by measuring LVOTd at the annulus or 2 mm below (P = NS), whereas measuring 5 and 10 mm below the annulus resulted in significant underestimation of SV and AVA by up to 15.9 $\pm$ 17.3 mL and 0.24 $\pm$ 0.28 cm^2, respectively ($P < .01$ for all). Accuracy for classification of low flow was best at the annulus (86%) and 2 mm below (82%), whereas measuring 5 and 10 mm below the annulus significantly underperformed (69% and 61%, respectively, $P < .001$).

Conclusions: Measuring LVOTd at the annulus or very close to it provides the most accurate measures of SV and AVA, whereas measuring LVOTd 5 or 10 mm below significantly underestimates these parameters and leads to significant overestimation of the severity of aortic stenosis and prevalence of low-flow status. (J Am Soc Echocardiogr 2020;33:953-63.)

Keywords: Aortic stenosis, Stroke volume, Aortic valve area, Doppler echocardiography, Cardiovascular magnetic resonance, Left ventricular outflow tract

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Conflicts of Interest: None.

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Abbreviations

2D = Two-dimensional

3D = Three-dimensional

AS = Aortic stenosis

AVA = Aortic valve area

AVA_{CMR-PC} = Aortic valve area calculated with stroke volume estimated using phase contrast (cardiovascular magnetic resonance/echocardiography hybrid method)

AVA_{CMR-VM} = Aortic valve area calculated with stroke volume estimated by volumetric analysis (cardiovascular magnetic resonance/echocardiography hybrid method)

$AVA_{Doppler-2}$ = Aortic valve area calculated with the left ventricular outflow tract measured 2 mm below the annulus (echocardiography)

$AVA_{Doppler-5}$ = Aortic valve area calculated with the left ventricular outflow tract measured 5 mm below the annulus (echocardiography)

$AVA_{Doppler-10}$ = Aortic valve area calculated with the left ventricular outflow tract measured 10 mm below the annulus (echocardiography)

$AVA_{Doppler-A}$ = Aortic valve area calculated with the left ventricular outflow tract measured at the annular level (echocardiography)

$AVA_{Simpson}$ = Aortic valve area calculated with stroke volume estimated using the biplane Simpson method (echocardiography)

CMR = Cardiovascular magnetic resonance

ICC = Intraclass correlation coefficient

LV = Left ventricular

LVEDV = Left ventricular end-diastolic volume

LVESV = Left ventricular end-systolic volume

LVOT = Left ventricular outflow tract

SV = Stroke volume

SV_{CMR-PC} = Stroke volume estimated using phase contrast (cardiovascular magnetic resonance)

SV_{CMR-VM} = Stroke volume estimated using the volumetric method (cardiovascular magnetic resonance)

$SV_{Doppler-2}$ = Stroke volume estimated with the left ventricular outflow tract measured 2 mm below the annulus (echocardiography)

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$SV_{Doppler-10}$ = Stroke volume estimated with the left ventricular outflow tract measured 10 mm below the annulus (echocardiography)

$SV_{Doppler-A}$ = Stroke volume estimated with the left ventricular outflow tract measured at the annular level (echocardiography)

$SV_{Simpson}$ = Stroke volume estimated using the biplane Simpson method (echocardiography)

TTE = Transthoracic echocardiography

VTI = Velocity-time integral

In aortic stenosis (AS), accurate measurement of left ventricular (LV) stroke volume (SV) is essential for the calculation of aortic valve area (AVA) by the continuity equation and assessment of LV flow status. A low flow state, defined as an SV index $\leq$ 35 mL/m^2, has been shown to be a powerful predictor of adverse outcomes.[1-3] Transthoracic echocardiography (TTE) is the primary imaging modality for this purpose.[1] Effective AVA is calculated using the continuity equation method by dividing SV measured in the LV outflow tract (LVOT) by the transaortic flow velocity-time integral (VTI) measured using continuous-wave Doppler. SV is calculated as the product of the cross-sectional area of the LVOT and the LVOT VTI by pulsed-wave Doppler.[1,4] The greatest potential for error in the measurement of SV and AVA is LVOT diameter, because it is squared in the continuity equation. Hence, a small error in LVOT diameter measurement may result in important errors in the calculation of SV and AVA.[5]

There is currently uncertainty as to which is the best location to measure LVOT diameter on TTE to obtain accurate estimates of SV and AVA using the continuity equation. Furthermore, several studies have demonstrated that TTE underestimates SV and AVA,[6-8] whereas others have suggested that it provides accurate estimates of these parameters[9-14] compared with other techniques. These discordances may be related to differences in the methods used to measure LVOT diameter. Current American Society of Echocardiography and European Association of Cardiovascular Imaging guidelines for assessment of AS severity on TTE suggest measurements of LVOT diameter at different levels (i.e., at the annulus vs 5 or 10 mm below the annulus) often yield similar measures of SV and AVA[1,15] because the shape of the LVOT is cylindrical in most patients.

The primary objective of this study was to evaluate which location of LVOT diameter measurement yields the best agreement for SV and AVA between Doppler TTE and phase-contrast cardiovascular magnetic resonance (CMR) imaging (the referent method). Secondary objectives were (1) to compare transthoracic echocardiographic measurements of SV and AVA using the biplane Simpson method and volumetric CMR measurements with the reference method and (2) to evaluate the repercussions of these different measurements on AS grading and flow status classification.

METHODS

Patient Population

In a subanalysis of the Metabolic Determinants of the Progression of Aortic Stenosis study (ClinicalTrials.gov identifier NCT01679431), we analyzed echocardiographic and CMR studies from 106 patients with AS and preserved LV ejection fraction who were prospectively recruited between 2005 and 2015. Details of inclusion criteria and methods of this study are provided elsewhere.[16] Briefly, inclusion criteria were age > 21 years and a peak aortic jet velocity > 2.0 m/sec. Patients were excluded if they had symptomatic AS, more than mild aortic regurgitation, significant mitral valve disease (mitral stenosis or more than mild mitral regurgitation), LV ejection fraction < 50%, rheumatic valve disease or endocarditis, previous aortic or mitral valve repair or replacement, or previous ascending aorta repair or replacement; if they were pregnant or lactating; or if

HIGHLIGHTS

- LVOT diameter measurement is a critical step in TTE assessment of AS.
- EACVI/ASE guidelines recommend measuring LVOT diameter 5-10 mm below annulus.
- However, this underestimates SV/AVA and overestimates AS severity and LF status vs PC-CMR.
- Measuring LVOT diameter at the annulus agrees best with PC-CMR SV and AVA measurements.

they had contraindications to gadolinium-enhanced CMR. Patients underwent comprehensive TTE and CMR within 3 months. The study was approved by the ethics committee of the Quebec Heart and Lung Institute, and patients provided written informed consent at the time of inclusion.

Doppler Echocardiographic Measurements

All Doppler echocardiographic examinations were acquired using a commercially available ultrasound machine according to the current recommendations of the American Society of Echocardiography.[1,15,17] Images were analyzed offline in a core laboratory. LVOT flow velocity and VTI were acquired using pulsed-wave Doppler in the apical five- or three-chamber view. Sample volume was positioned at valve level and then moved apically until valve noise or “clicks” were no longer detected. Pulsed-wave Doppler signals of LVOT systolic flow were manually traced on the modal curve. Aortic valve flows were obtained using continuous-wave Doppler multiwindow interrogation (including the right parasternal window) to ensure recording of maximal transaortic velocity. LVOT diameter was measured in a zoomed longitudinal parasternal long-axis view, in a midsystolic frame, using the inner edge–to–inner edge technique. Measurements were made at four different locations: (1) at the hinge points of the aortic valve leaflets (i.e., aortic annulus), (2) very close to the annulus (i.e., ≤2 mm below), (3) about 5 mm below the annulus, and (4) about 10 mm below the annulus (Figure 1A). Assuming a circular shape as recommended,[1] we calculated four different LVOT areas and their corresponding Doppler-derived SVs: $SV_{Doppler\text{-}A}$ (annular level), $SV_{Doppler\text{-}2}$ (2 mm below the annulus), $SV_{Doppler\text{-}5}$ (5 mm below the annulus), and $SV_{Doppler\text{-}10}$ (10 mm below the annulus).

Morphology of the LVOT was classified as hourglass shaped (LVOT diameter at the annular level larger than at 10 mm below), funnel shaped (annular diameter smaller than at 10 mm below), or cylindrical (or rectangular) shaped when diameters at the annulus and 10 mm below were similar (i.e., relative difference <5%).

LV end-diastolic volume (LVEDV) and LV end-systolic volume (LVESV) volumes were also measured in apical four-chamber and two-chamber views using the biplane method of disks (modified Simpson rule) according to guidelines[17] (Figure 1B). Special care was taken during the acquisition to avoid apical foreshortening. SV by the Simpson method ($SV_{Simpson}$) was calculated as the difference between LVEDV and LVESV. In summary, we calculated five TTE-derived SVs: four Doppler-derived values ($SV_{Doppler\text{-}A}$, $SV_{Doppler\text{-}2}$, $SV_{Doppler\text{-}5}$, and $SV_{Doppler\text{-}10}$) and one 2D-derived value ($SV_{Simpson}$). Using these SVs, five different AVAs were calculated according to the continuity equation: $AVA = SV/VTI_{aortic}$.

CMR Measures

CMR imaging was performed using a 1.5-T system (Achieva; Philips Healthcare, Best, the Netherlands) as described in detail in the Appendix. Through-plane phase-contrast imaging was performed during a breath-hold in the ascending aorta 10 mm downstream of the aortic annulus, as previously described.[10] The total forward flow during systole was computed using cvi42 version 5.6.4 (Circle Cardiovascular Imaging, Calgary, AB, Canada; Figure 1C).

LV volumes and ejection fraction were measured using contour analysis of end-diastolic and end-systolic phases of complete short-axis stacks. Papillary muscles and trabeculations were included when measuring mass (equivalent to weighting the left ventricle) and excluded when measuring volumes (equivalent to blood-pool techniques), in line with recommendations[18] (Figure 1D). Volumetrically derived LV SV was calculated as the difference between LVEDV and LVESV.

Using both phase-contrast ($SV_{CMR\text{-}PC}$) and volumetric ($SV_{CMR\text{-}VM}$) SVs, two hybrid AVAs ($AVA_{CMR\text{-}PC}$ and $AVA_{CMR\text{-}VM}$, respectively) were calculated using aortic VTI measurements obtained using continuous-wave Doppler echocardiography.

Statistical Analysis

Normal distribution of continuous variables was assessed visually and using the Shapiro-Wilk test. Continuous data are expressed as mean ± SD and categorical variables as percentages. Correlation and agreement (95% CIs) between all measurements compared with the referent method (phase-contrast CMR) were assessed using Spearman correlations and Bland-Altman[19] comparisons, respectively. A paired Student's t test was used to test for the significance of any overestimation or underestimation.

Comparisons of the prevalence of severe AS and low flow according to measurement methods was made using symmetry and marginal homogeneity tests with Bonferroni adjustment for multiple comparisons.

Intraobserver and interobserver variability was evaluated by two blinded observers in a subset of 15 random patients using a two-way mixed-effects model with intraclass correlation coefficients (ICCs). Statistical analyses were performed using Stata version 15.0 (StataCorp, College Station, TX). A two-sided P value < .05 was considered to indicate statistical significance.

RESULTS

Study Population

One hundred and six patients with mild to severe AS (peak velocity 2.9 ± 0.53 m/sec, mean gradient 19 ± 8.5 mm Hg) were included in the analysis. Demographic, echocardiographic, and CMR characteristics are depicted in Table 1. Aortic peak velocity was 2 to 2.99 m/sec in 66%, 3 to 3.99 m/sec in 31%, and ≥4 m/sec in 3% of patients. Bicuspid aortic valve was present in 29 patients (27%). Mitral regurgitation was none or trace in 90% of patients and mild in the remaining 10%. No patients had moderate or greater mitral regurgitation.

Echocardiographic and CMR LV Volumes and Function

LV volumes, ejection fraction, and mass are shown in Table 1. LVEDV was significantly underestimated by the Simpson method compared

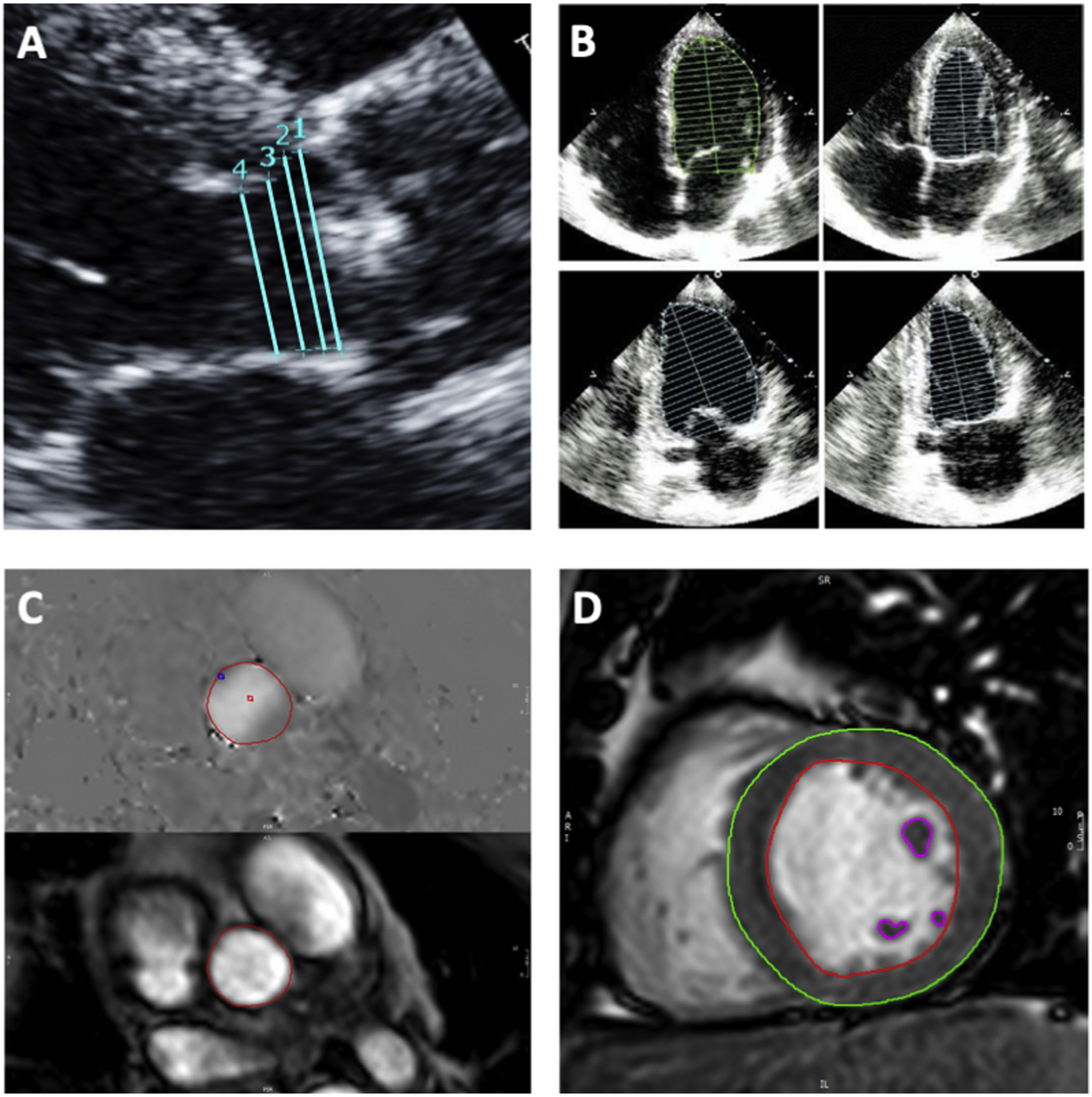

Figure 1 Transthoracic echocardiographic and CMR methods for SV estimation. **(A)** This figure shows the four different measurements made of the left ventricular outflow tract diameter: (1) at the hinge points of the aortic valve leaflets (annular level); (2) 2 mm below the annular level; (3) 5 mm below the annular level; and (4) 10 mm below the annular level. **(B)** Biplane Simpson method. Apical four-chamber LVEDV (upper left) and LVESV (upper right). Apical two-chamber LVEDV (lower left) and LVESV (lower right). **(C)** CMR phase-contrast method. Phase (upper) and magnitude (lower) images of the ascending aorta 10 mm above the annular level. The *red line* represents the region of interest (ROI) where velocity and flow are measured. **(D)** CMR volumetric method. The *red line* shows the endocardial contour, the *green line* the epicardial contour, and the *purple line* the papillary muscle contour.

with CMR (bias, -18 ± 21 mL; $P < .01$). LVESVs, however, were comparable (bias, -1 ± 14 mL; $P = .39$). LV ejection fraction was slightly underestimated by Simpson TTE versus CMR (bias, -4 ± 7%; $P < .01$).

Diameter, Area, and Shape of the LVOT

Mean LVOT diameter by TTE was largest at the annular level and progressively decreased for positions more distant from the annulus (annulus, 22.4 ± 2.1 mm; 2 mm below, 22.2 ± 2.2 mm; 5 mm below, 21.1 ± 2.4 mm; 10 mm below, 20.2 ± 2.8 mm; $P < .01$), as did LVOT area (3.99 ± 0.8, 3.89 ± 0.8, 3.54 ± 0.86, and 3.28 ± 0.93 cm^2, respectively; $P < .01$; Table 2).

Figure 2 shows the distribution of LVOT shapes in the study population. An hourglass shape (i.e., largest LVOT at the annulus) was present in 73% of patients, and 22% of patients had a cylindrical LVOT shape (i.e., <5% difference). Finally, the funnel shape (i.e., smallest

Table 1 Baseline characteristics

Variable	Value
Clinical data	
Age, y	63 ± 15
Sex, male	72 (68)
Weight, kg	78 ± 15
Height, cm	167 ± 8
Body surface area, m^2	1.86 ± 0.20
Hypertension	60 (57)
Dyslipidemia	66 (62)
Diabetes mellitus	17 (16)
Coronary artery disease	37 (35)
Bicuspid aortic valve	29 (27)
Echocardiography	
Interventricular septal thickness, mm	12.2 ± 2.0
LV posterior wall thickness, mm	9.5 ± 1.3
LV end-diastolic diameter, mm	45.4 ± 4.4
LV end-systolic diameter, mm	27.3 ± 5.0
LVEDV, biplane Simpson, mL	124 ± 30
LVESV, biplane Simpson, mL	43 ± 15
LVEF, %	66 ± 6
Peak velocity, mean, m/sec	2.90 ± 0.53
Peak velocity, range	
2–2.99 m/sec	70 (66)
3–3.99 m/sec	33 (31)
≥4 m/sec	3 (3)
Peak gradient, mm Hg	34 ± 13
Mean transvalvular pressure gradient, mm Hg	19 ± 9
Aortic valve VTI, cm	68 ± 15
CMR imaging	
LVEDV, mL	142 ± 32
LVESV, mL	44 ± 19
LVEF, %	70 ± 8
LV mass indexed, g/m^2	56 ± 11
Peak gradient, mm Hg	25 ± 11
Aortic valve VTI, cm	55 ± 13

Data are expressed as mean ± SD or as number (percentage).

diameter at the annulus) was the least frequent type, observed in 5% of the cohort. Prevalence of LVOT shapes was comparable in patients with tricuspid versus bicuspid morphologies (P = .88; Supplemental Figure 2A) and in those with mild versus moderate or severe AS (P = .12; Supplemental Figure 2B).

Echocardiographic and CMR-Derived SV

SV and bias using each method are shown in Table 2, and Bland-Altman plots of agreement are displayed in Figure 3. SV by phase-contrast CMR (the referent method) was 83 ± 16 mL. Within transthoracic echocardiographic Doppler methods, the best agreement with the referent method was achieved at the annular level. Good agreement was also obtained with LVOT measured very close (≤2 mm) to the annulus. On the other hand, calculations using LVOT diameter measured at 5 or 10 mm below the annulus systematically underestimated SV (P < .01 for both). For the transthoracic echocardiographic volumetric method, SV calculated using biplane Simpson showed good agreement with phase-contrast CMR. CMR volumetric analysis systematically overestimated SV (P < .001). Correlations of SV by each method versus phase-contrast CMR are shown in Supplemental Figure 3.

Echocardiographic and CMR-Derived AVA

Results of the five TTE-derived and two hybrid CMR/TTE-derived AVAs and their respective biases are displayed in Table 3 and Figure 4. AVA by phase-contrast CMR (the referent method) was 1.27 ± 0.35 cm^2. Among Doppler methods, AVA measured at the annular level showed the best agreement. Agreement was also good for AVA at 2 mm below the annulus, whereas measurements at 5 or 10 mm below the annulus significantly underestimated AVA (P < .01 for both). AVA calculated using biplane Simpson SV showed good agreement with phase-contrast CMR AVA. A "CMR-only" (i.e., both SV and aortic valve VTI derived from phase-contrast CMR) method lead to significant overestimation of AVA, mostly due to underestimation of aortic valve VTI (Supplementary Appendix).

Prevalence of Low-Flow Status and Severe AS

Prevalence of low flow (i.e., SV ≤ 35 mL/m^2) according to different measurement methods is shown in Figure 5A. Using SV calculated by the referent method (phase-contrast CMR), eight patients (8%) were classified as having low flow (i.e., SV < 35 mL/m^2; Table 2). Prevalence of low flow was similar using $SV_{Doppler\text{-}A}$, $SV_{Doppler\text{-}2}$, and $SV_{Simpson}$ (9%, 13%, and 13%, respectively; P > .05 for all). Prevalence of low flow was significantly higher using $SV_{Doppler\text{-}5}$ and $SV_{Doppler\text{-}10}$ (26% and 42%, respectively; P < .01 for all) and significantly lower using $SV_{CMR\text{-}VM}$ (1%; P = .02). Figure 5B shows the percentage of correctly classified low-flow status according to different measurement methods.

Prevalence of severe AS (as defined by AVA < 1 cm^2) according to different methods is shown in Table 3 and Figure 6A. Using the referent method, 25% of patients were diagnosed with severe AS. Prevalence using $AVA_{Doppler\text{-}A}$, $AVA_{Doppler\text{-}2}$, and $AVA_{Simpson}$ was comparable (20%, 24%, and 31%, respectively; P > .13 for all), whereas $AVA_{Doppler\text{-}5}$ and $AVA_{Doppler\text{-}10}$ significantly overestimated the prevalence of severe AS (35% and 48%, respectively; P < .01 for all), and $AVA_{CMR\text{-}VM}$ underestimated its prevalence (10%; P < .01). Correlations of AVA by each method versus phase-contrast CMR are shown in Supplemental Figure 4. Figure 6B shows the percentage of correctly classified severe AS according to different measurement methods.

Intraobserver and Interobserver Variability

The ICCs of CMR are shown in Supplemental Table 1. Intraobserver and interobserver reproducibility were excellent for both $SV_{CMR\text{-}PC}$ (ICCs of 0.93 [95% CI, 0.75–0.98] and 0.89 [95% CI, 0.64–0.97], respectively) and $SV_{CMR\text{-}VM}$ (ICCs of 0.94 [95% CI, 0.77–0.98] and 0.91 [95% CI, 0.68–0.97], respectively). Regarding transthoracic echocardiographic Doppler measurements of SV, both intraobserver and interobserver reproducibility were best when LVOT diameter was measured at the annular level (0.99 [95% CI, 0.96–1.00] and 0.98 [95% CI, 0.91–0.99], respectively) and worst at 10 mm below (0.93 [95% CI, 0.73–0.98] and 0.83 [95% CI, 0.41–0.96]).

Table 2 LVOT dimensions and SV according to different methods

Variable	$SV_{CMR\text{-}PC}$	$SV_{CMR\text{-}VM}$	$SV_{Doppler\text{-}A}$	$SV_{Doppler\text{-}2}$	$SV_{Doppler\text{-}5}$	$SV_{Doppler\text{-}10}$	$SV_{Simpson}$
LVOTd, mm	—	—	22.4 ± 2.1	22.2 ± 2.2	21.1 ± 2.4	20.2 ± 2.8	—
LVOT area, cm^2	—	—	3.99 ± 0.80	3.89 ± 0.83	3.54 ± 0.86	3.28 ± 0.93	—
SV, mL	83 ± 16	98 ± 19	83 ± 15	81 ± 15	73 ± 15	67 ± 15	81 ± 19
Bias, mL	—	+14.6 ± 11.5	−0.3 ± 17.3	−2.4 ± 17.8	−10.0 ± 17.7	−15.9 ± 17.3	−2.1 ± 15.7
P value	—	<.01	.86	.17	<.01	<.01	.18
Indexed SV, mL/m^2	45 ± 8	53 ± 9	45 ± 8	44 ± 8	39 ± 7	36 ± 7	44 ± 8
Low-flow state (SVi ≤ 35 mL/m^2)	8 (8)	1 (1)	9 (9)	14 (13)	30 (28)	47 (44)	14 (13)

LVOTd, LVOT diameter; *SVi*, SV index.

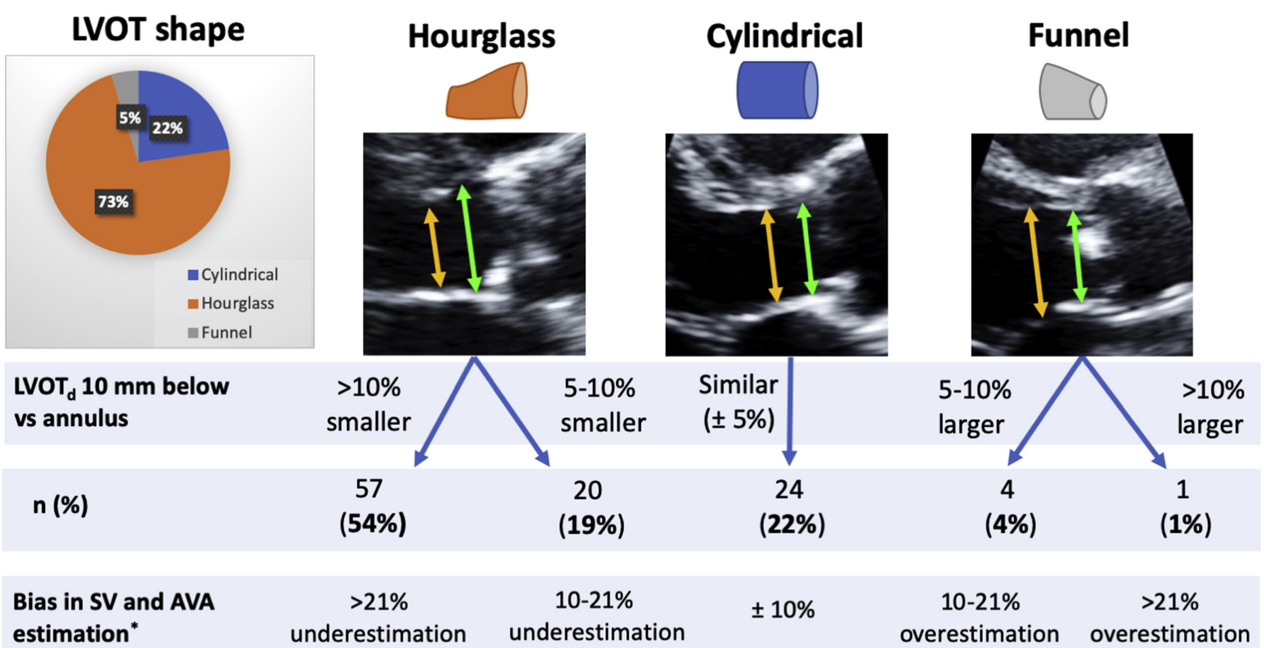

Figure 2 Prevalence of different LVOT shapes and their effect on SV estimation. This figure shows the prevalence of different LVOT shapes in our population along with examples (zoomed parasternal long-axis transthoracic echocardiographic images). *Bias examples: assuming a theoretical LVOT VTI of 20 cm and an aortic valve VTI of 80 cm, a 5% error in diameter (e.g., LVOT diameter [$LVOT_d$] 20 mm corresponding to $LVOT_{area}$ 3.14 cm^2 vs $LVOT_d$ 21 mm and $LVOT_{area}$ 3.46 cm^2) would yield a 10% error in SV (63 vs 69 mL) and AVA (0.79 vs 0.87 cm^2). A 10% error in diameter (e.g., $LVOT_d$ 20 mm corresponding to $LVOT_{area}$ 3.14 cm^2 vs $LVOT_d$ 22 mm and $LVOT_{area}$ 3.80 cm^2) would yield a 21% error in SV (63 vs 76 mL) and AVA (0.79 vs 0.95 cm^2).

DISCUSSION

The main findings of this study are as follows. First, the LVOT shape from LV cavity to aortic valve is not cylindrical (or rectangular), as suggested in the guidelines, but hourglass in the majority of the patients. Hence, the anteroposterior LVOT diameter measured on TTE is generally larger at the annular level than at 5 to 10 mm below the annulus. SV and AVA calculated at 5 to 10 mm below the annulus overestimate the prevalence of low-flow state and the severity of AS, respectively. Second, the transthoracic echocardiographic Doppler method using LVOT diameter measured at or very close to the annulus provides the most accurate and reproducible estimates of SV and AVA compared with phase-contrast CMR. Third, the transthoracic echocardiographic volumetric method (biplane Simpson) provides reasonably accurate estimates of SV and AVA and can be used as an alternative method when Doppler TTE is not feasible.

LVOT Morphology and Effect of Location of LVOT Diameter Measurements on Transthoracic Echocardiographic Estimation of SV and AVA

The exact location at which to measure LVOT diameter has been a subject of debate.[5]

As opposed to what is suggested in the guidelines,[1] our study shows that the estimation of SV and AVA significantly differs depending on the location of the LVOT diameter measurement. Indeed, our results showed that LVOT measurements 5 or 10 mm below the annulus systematically underestimate SV by as much as 16 mL and

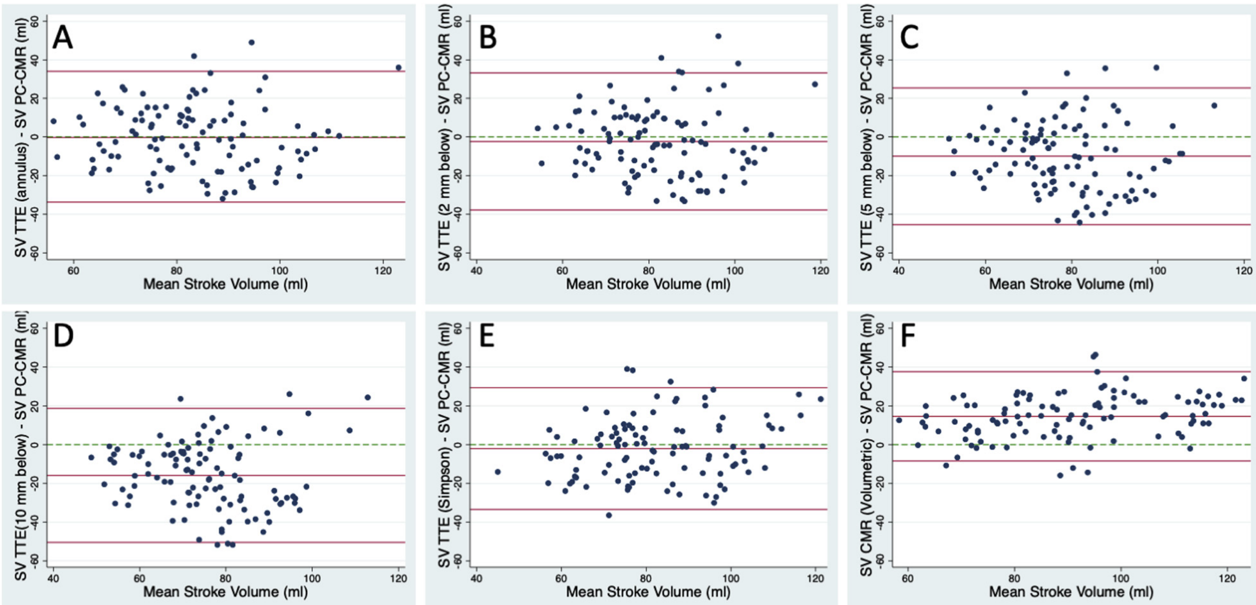

Figure 3 Agreement between measures of SV by different transthoracic echocardiographic or CMR methods versus CMR phase-contrast (PC) imaging. This figure shows Bland-Altman plots comparing different methods of measuring SV with the referent method (CMR PC imaging at the aorta). The *solid red lines* are the mean bias ± 2 SDs. The *dashed green line* is the level of zero bias. **(A)** Doppler SV with LVOT measured at the annulus. **(B)** Doppler SV with LVOT measured 2 mm below the annulus. **(C)** Doppler SV with LVOT measured 5 mm below the annulus. **(D)** Doppler SV with LVOT measured 10 mm below the annulus. **(E)** Simpson-derived SV. **(F)** CMR volumetric method–derived SV.

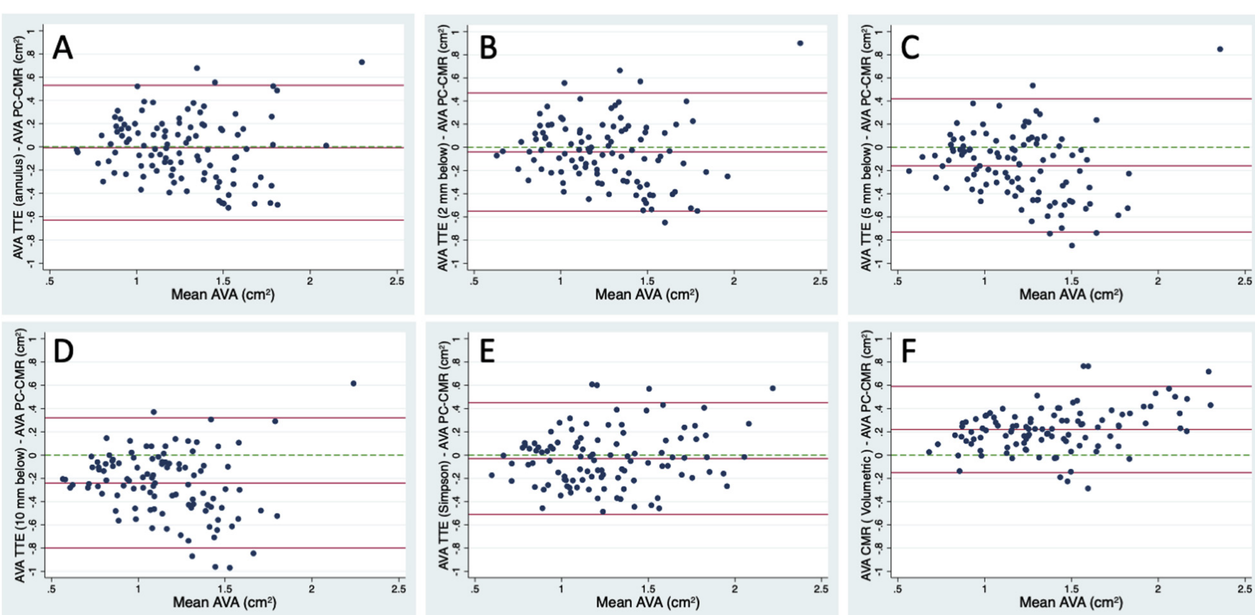

Figure 4 Agreement between measures of AVA by different transthoracic echocardiographic or CMR methods versus CMR phase-contrast (PC) imaging. This figure shows Bland-Altman plots between different methods of measuring SV and the referent method (CMR PC imaging at the aorta). The *solid red lines* are the mean bias ± 2 SDs. The *dashed green line* is the level of zero bias. **(A)** Doppler AVA with LVOT measured at the annulus. **(B)** Doppler AVA with LVOT measured 2 mm below the annulus. **(C)** Doppler AVA with LVOT measured 5 mm below the annulus. **(D)** Doppler AVA with LVOT measured 10 mm below the annulus. **(E)** Simpson-derived AVA. **(F)** CMR volumetric method–derived AVA.

AVA by 0.23 cm^2 (both about 20%) and markedly overestimate the prevalence of low flow (from 8% to 44%) and of severe AS (from 20-25% to as much as 48%).

Regarding LVOT inflow shape, we found that only 23% of our cohort of patients with AS showed a relatively cylindrical shape, whereas the guidelines suggest that vast majority of patients harbor

Table 3 AVA measured by different methods

Parameter	AVA_{CMR-PC}	AVA_{CMR-VM}	$AVA_{Doppler-A}$	$AVA_{Doppler-2}$	$AVA_{Doppler-5}$	$AVA_{Doppler-10}$	$AVA_{Simpson}$
AVA, cm^2	1.27 ± 0.35	1.49 ± 0.41	1.26 ± 0.33	1.23 ± 0.32	1.11 ± 0.31	1.03 ± 0.31	1.24 ± 0.39
Bias, cm^2	—	+0.22 ± 0.19	−0.01 ± 0.27	−0.04 ± 0.28	−0.16 ± 0.29	−0.24 ± 0.28	−0.03 ± 0.24
P value	—	<.01	.76	.12	<.01	<.01	.20
Severe AS (AVA < 1 cm^2)	26 (25)	11 (10)	21 (20)	25 (24)	37 (35)	51 (48)	33 (31)

AVA, Aortic valve area, *CMR*, cardiovascular magnetic resonance, *PC*, phase-contrast.

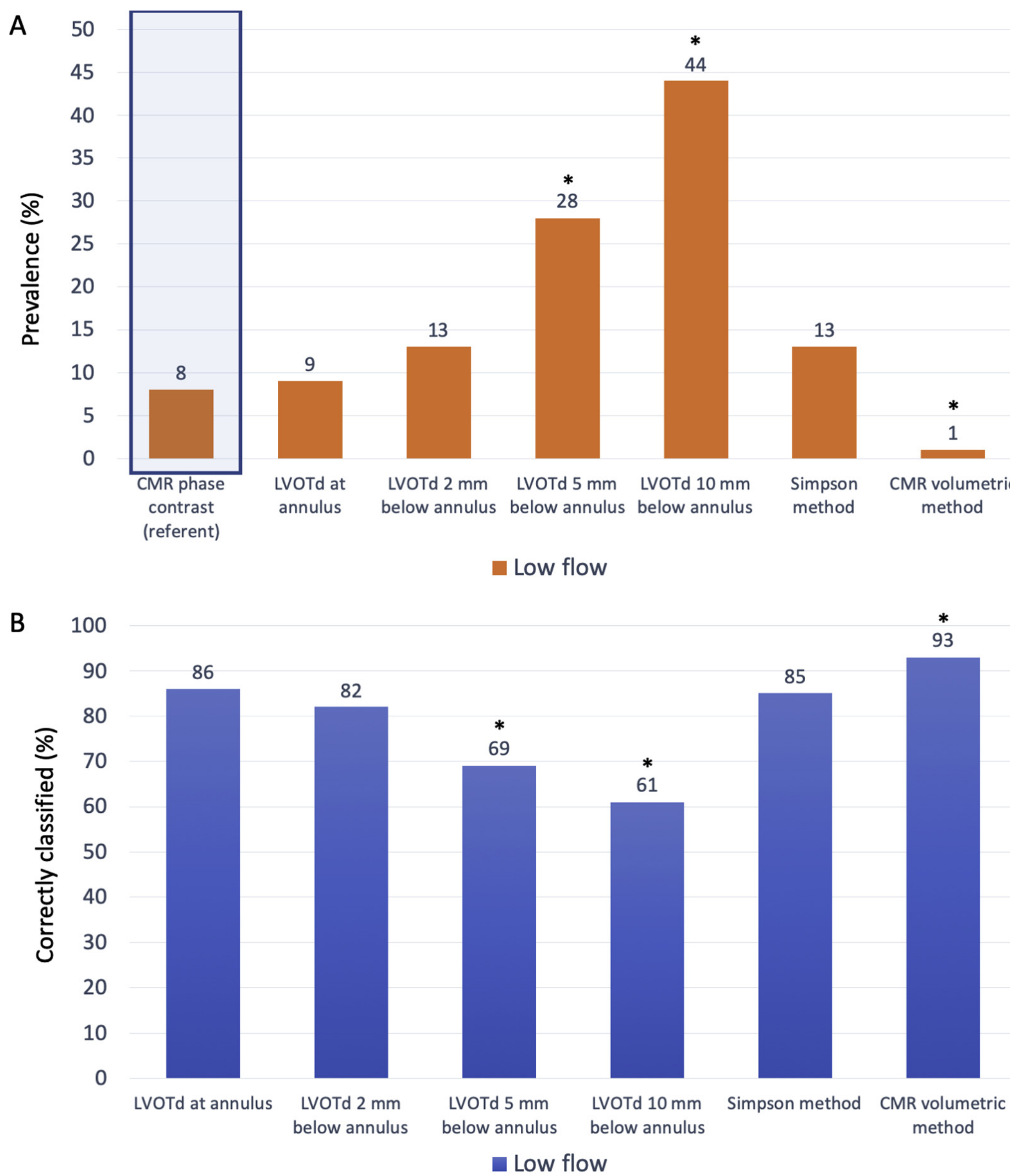

Figure 5 Prevalence of low flow and accuracy according to different measurement methods. **(A)** The prevalence of low-flow state (SV index ≤ 35 mL/m^2) according to different measurement methods. **(B)** The percentage of correctly classified patients according to different measuring methods compared with the referent method (phase-contrast CMR). *LVOTd*, LVOT diameter. **P* < .01 versus phase-contrast CMR (referent method).

this shape.[1] In fact, 73% of patients had a difference of >5% between LVOT diameter at the annulus and 10 mm below, and in more than half this difference was >10%. As shown in the examples in Figure 2, this represents underestimations of SV and AVA of 10% and 21%, respectively, which in many cases may be of clinical significance. Our results further confirm and expand those of LaBounty et al.,[9] who reported that the majority of patients with AS have an hourglass-shaped LVOT compared with funnel type (59% vs 41%).

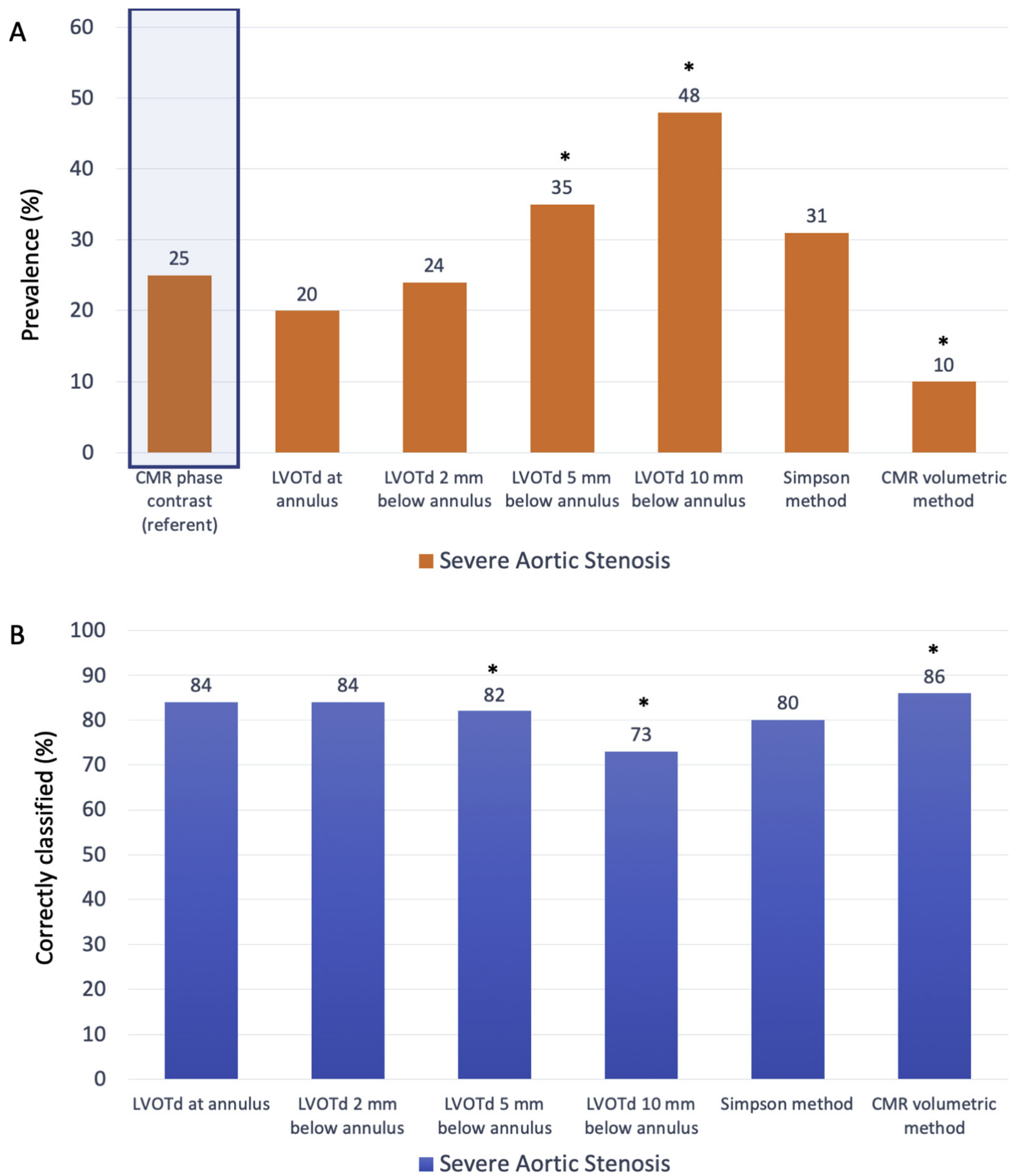

Figure 6 Prevalence of severe AS and accuracy according to different measurement methods. **(A)** The prevalence of severe AS (AVA 1 cm^2) according to different measurement methods. **(B)** The percentage of correctly classified patients according to different measuring techniques compared with the referent method (phase-contrast CMR). *LVOTd*, LVOT diameter. *$P < .01$ versus phase-contrast CMR (referent method).

They also reported better agreement between TTE and invasive (cardiac catheterization) AVA when LVOT was measured at the annulus versus at 5 mm below. Another study by Caballero et al.[20] using three-dimensional (3D) echocardiography to measure LVOT area at the level of annulus and 4 and 8 mm below in 58 patients with severe AS demonstrated better agreement between 2D and 3D transthoracic echocardiographic Doppler AVA when measured at the annular level. Furthermore, besides showing better accuracy, measurement of LVOT diameter at the annulus was also more reproducible than when measured at 5 or 10 mm below, as previously suggested.[5,20]

The recommendation to measure LVOT diameter at 5 to 10 mm below the annulus was based on the rationale that the diameter should be measured at the exact same location where the pulsed-wave Doppler sample is positioned. However, the LVOT cross-section at 5 to 10 mm below the annulus is more likely to be elliptical and/or bean shaped (because of the septal bulge often present in patients with AS).[1,10,20-22] Hence, the anteroposterior diameter measured by 2D TTE in the lower portion of the LVOT is more likely to be smaller than the sagittal diameter and therefore to yield to a substantial underestimation of the actual LVOT area (calculated assuming a circular shape) and thus of SV and AVA. On the other hand, at the level of the annulus, the LVOT cross-section at the level of the aortic annulus is likely more circular and less irregular than 5 to 10 mm below, and this measure may thus provide a more accurate and reproducible estimation of SV and AVA.[1,10,20-22]

The continuity equation assumes a relatively flat flow velocity profile (i.e., mean velocity equals peak velocity), with homogeneous distribution of velocities through the LVOT area. However, there is evidence that the flow velocity profile along the LVOT is indeed not flat but often skewed, with higher velocities along the anterior and right aspects.[10] Thus, the aforementioned LVOT area underestimation by TTE might be somewhat counterbalanced by a Doppler overestimation of LVOT VTI. Furthermore, this provides a theoretical framework to explain the overestimation of AVA and SV using hybrid methods, which should be approached cautiously so as not to underestimate the severity of AS.[23]

Use of Hybrid Methods to Determine SV and AVA

The fact that LVOT cross-section often has an elliptical shape and TTE systematically underestimates its area has been the reason several investigators proposed using "hybrid" methods to calculate SV and AVA. By combining the advantages of Doppler for measurement of LVOT and transaortic flow velocity and 3D imaging such as computed tomography, CMR, or 3D echocardiography for measurement of LVOT area, it has been hypothesized that SV and AVA obtained by hybrid methods (flow velocities measured by Doppler and LVOT area by 3D imaging) could overcome the limitations of 2D TTE and thus improve the classification of flow status and AS severity and prognostication. Several studies demonstrated that these hybrid methods provide systematically larger SVs and AVAs than TTE.[7,8,22] A recent study using a computed tomography/Doppler hybrid method reported larger hybrid effective AVAs versus anatomic orifice areas measured by planimetry,[24] which is impossible from a fluid mechanics standpoint.[25] The effective AVA (cross-sectional area of the flow vena contracta) is indeed always smaller than the anatomic AVA. Also, several studies found that the hybrid AVA would reclassify AS severity from severe to nonsevere even though the patient has a very high transvalvular gradient and aortic valve calcium score.[26,27] These findings suggest that the hybrid methods may overestimate SV and AVA and therefore underestimate the actual severity of AS and low-flow state. Accordingly, it has been shown that a larger cut point value of AVA (1.2 cm^2) should be used to define severe AS when using the computed tomography/Doppler hybrid method compared with the standard transthoracic echocardiographic method threshold (1 cm^2).[22]

Clinical Implications

The present study provides a strong argument for a measurement of LVOT diameter at or very close to the aortic annulus by 2D TTE to calculate SV and AVA and therefore estimate the presence of a low-flow state and the severity of AS. The biplane Simpson method may also provide a useful corroborative or alternative method if Doppler TTE is not feasible (e.g., flow acceleration in the LVOT) to estimate SV and then AVA (by dividing total SV by transaortic flow VTI), provided there is no greater than mild mitral regurgitation. In fact, this method performed as well as the transthoracic echocardiographic Doppler method with LVOT diameter measured at the annular level in terms of accuracy and reproducibility.

Limitations

The main limitation of this study was the absence of an established gold-standard method. Phase-contrast imaging, however, allows accurate measurement of aortic blood velocity and flow and is often considered a noninvasive gold standard for forward LV SV measurement.[10,28-30] Our results also showed that SV and AVA obtained using the CMR volumetric method were systematically higher than those using phase-contrast CMR. It is unlikely that overestimation of SV and AVA by the volumetric method was caused exclusively by mitral regurgitation, as <10% of our cohort had more than trace mitral regurgitation. Analyses excluding those patients provided similar results. The CMR volumetric method may overestimate SV and thus AVA in part because of the inclusion of papillary muscles and trabeculae in the ventricular cavity and also because of partial-volume effects and through-plane motion of basal slices.[28,31]

Finally, there were no outcome data in the present study. Further studies are necessary to determine which method and cutoff values of AVA and SV measurements show the best associations with clinical outcomes in patients with AS. Studies addressing the assessment of the prognostic value of SV and AVA evaluated by phase-contrast CMR versus Doppler TTE are required to assess this matter.

CONCLUSION

The results of this study strongly support the measurement of LVOT diameter at or close to the aortic annulus to estimate SV and AVA. Indeed, this method provided the most accurate and reproducible measurements of SV and AVA. On the other hand, measurements of LVOT diameter 5 or 10 mm below the annulus yield significant underestimations of SV and AVA and therefore overestimations of the prevalence of low-flow status and severe AS. The biplane Simpson method also showed good agreement with Doppler and phase-contrast CMR SV and AVA and may thus be used as an "internal control" to corroborate flow status and AS severity.

SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.echo.2020.03.020.

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APPENDIX

CMR Detailed Protocol

CMR studies were performed using a 1.5-T Philips Achieva scanner operating release 2.6, level 3, dedicated 32-channel phased-array cardiac coil, and vectorcardiographic gating during successive end-expiratory breath-holds (Philips Healthcare). Volumetric and flow analyses were performed using cvi42 version 5.6.4 (Circle Cardiovascular Imaging).

Cine imaging of cardiac morphology and function was performed using a balanced steady-state free precession technique at 30 phases per cardiac cycle in held end-expiration; eight to 14 contiguous parallel short-axis (8-mm thickness, 0-mm gap) and two-chamber, four-chamber, and two orthogonal LVOT planes were acquired using a cine steady-state free precession sequence covering the entire cardiac volume. Typical parameters at 1.5 T were repetition time of 3.2 msec, echo time of 1.6 msec, flip angle of 60°, and number of signals acquired of 1, with in-plane spatial resolution of 1.6 × 2 mm. Equivalent acquisition parameters at 3 T were repetition time of 2.8 msec, echo time of 1.3 msec, flip angle of 45°, and number of signals acquired of 1, with in-plane spatial resolution of 1.7 × 2 mm, 7-mm slice thickness, and 0-mm gap.

LV volume and function measurements were performed using a contiguous short-axis multislice acquisition with delineation of atria and ventricles confirmed in matched long-axis planes.[1] For LV volume analysis, the endocardial border was semiautomatically determined on the left ventricle for all 30 phases of the cardiac cycle, and the cardiac phases that demonstrated the largest and smallest ventricular cavity volumes were defined as end-diastole and end-systole, respectively. The endocardial border was defined as the boundary between myocardium and ventricular blood pool, from the most apical to the most basal slice. Manual correction of automated LV endocardial border and papillary muscles tracing was performed when necessary. Papillary muscles and trabeculations were included when measuring mass (equivalent to weighting the left ventricle) and excluded when measuring volumes (equivalent to blood pool techniques), in line with recommendations. At the base of the heart, careful differentiation of ventricle from atrium and aorta or pulmonary artery relied on examination of matching long-axis planes. For LV mass measurement, the epicardial border was semiautomatically traced, followed by manual correction when necessary. Epicardial fat was excluded from the epicardial border. The LVEDV, LVESV, SV, ejection fraction, and LV mass were computed using the Simpson rule. LVEDV, LVESV, and LV mass were adjusted to body surface area calculated using the Dubois formula.

Through-plane phase-contrast imaging was performed during breath-hold in the ascending aorta at 10 mm downstream of the aortic annulus as previously described,[2] parallel to the aortic valve annular plane. Flow imaging parameters consisted of repetition time of 4.60 to 4.92 msec, echo time of 2.76 to 3.05 msec, flip angle of 15°, 24 phases, pixel spacing of 1.32 to 2.07 mm, slice thickness of 10 mm, and acquisition matrix 256 × 208, scan time of 10 to 25 sec without sensitivity encoding. For each patient, peak aortic jet velocity measured by TTE was used to define CMR encoding velocity (CMR encoding velocity = [1.25 to 1.5] × peak jet velocity; range, 1.5–5.5 m/sec) to optimally define resolution and avoid signal wrap. The total forward flow during systole was computed using cvi42 version 5.6.4. The peak flow velocity within the region of interest was used to determine changes in instantaneous peak aortic velocity. The VTI was calculated using Simpson's rule as previously described[2] to calculate the CMR-only derived AVA.

CMR-Only Derived AVA

Integrating flow and velocity from the phase-contrast CMR images at the aorta, we calculated both SV and peak aortic velocity VTI to calculate an AVA derived from CMR data only. As previously shown, SV was not different between phase-contrast CMR and Doppler at the annular level ($SV_{CMR\text{-}PC}$ 83 ± 16 mL vs $SV_{Doppler\text{-}A}$ 83 ± 15 mL, $P = .86$). However, aortic VTI was significantly lower with phase-contrast CMR than with continuous-wave Doppler echocardiography (55 ± 13 vs 68 ± 15 cm, respectively, $P < .01$). Hence, AVA derived from CMR data only significantly overestimated AVA compared with the referent method ($AVA_{CMR\text{-}PC}$, using hybrid CMR and Doppler data; bias +0.30 ± 0.24 cm^2; $P < .01$; Supplemental Figure 1), leading to a marked underestimation of the prevalence of severe AS (i.e., AVA < 1 cm^2): 8% versus 25%, respectively ($P < .01$). Underestimation of VTI by CMR might have been caused by its lower temporal resolution in relation to Doppler, difficulties in finding the exact perpendicular through plane (position and angle) of the vena contracta, and voxel averaging of flow velocity.[3] Thus, even though some studies have shown the feasibility of AVA calculation by MRI-only methods,[2,4] although using a slightly different method, we believe that considering the current state of the art of CMR technology, VTI underestimation undermines the possibility of using CMR-only methods to assess AVA in AS in clinical practice.

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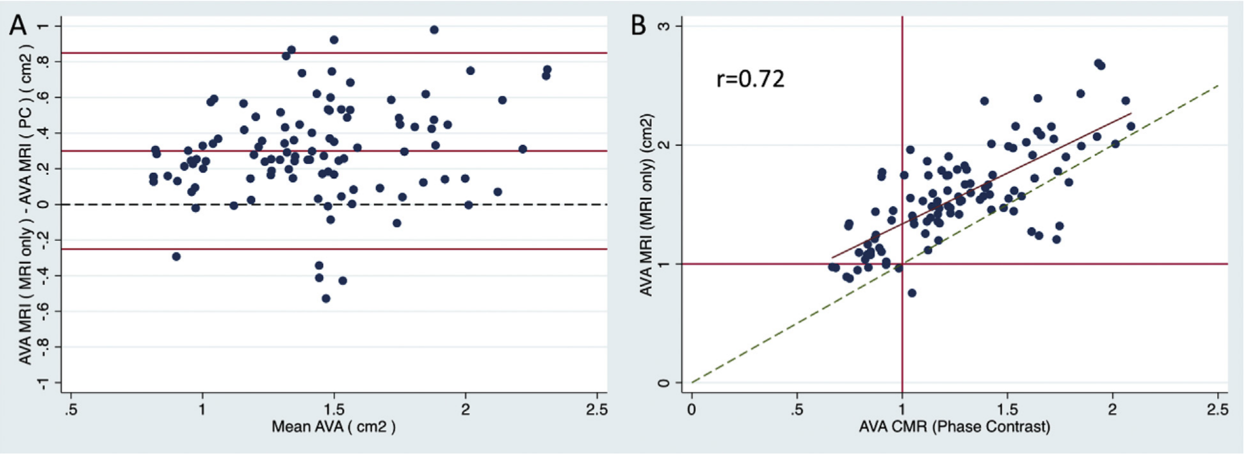
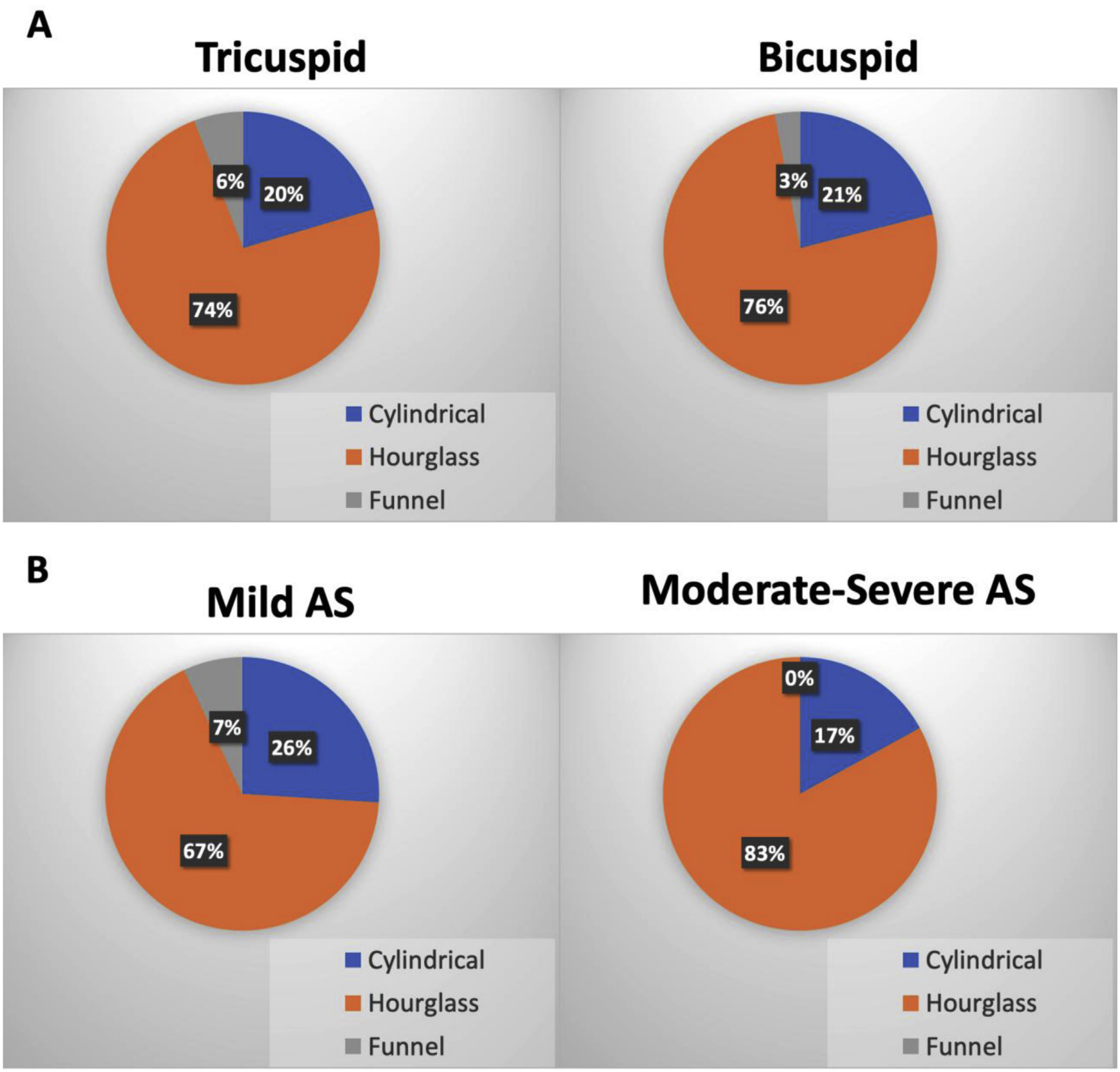
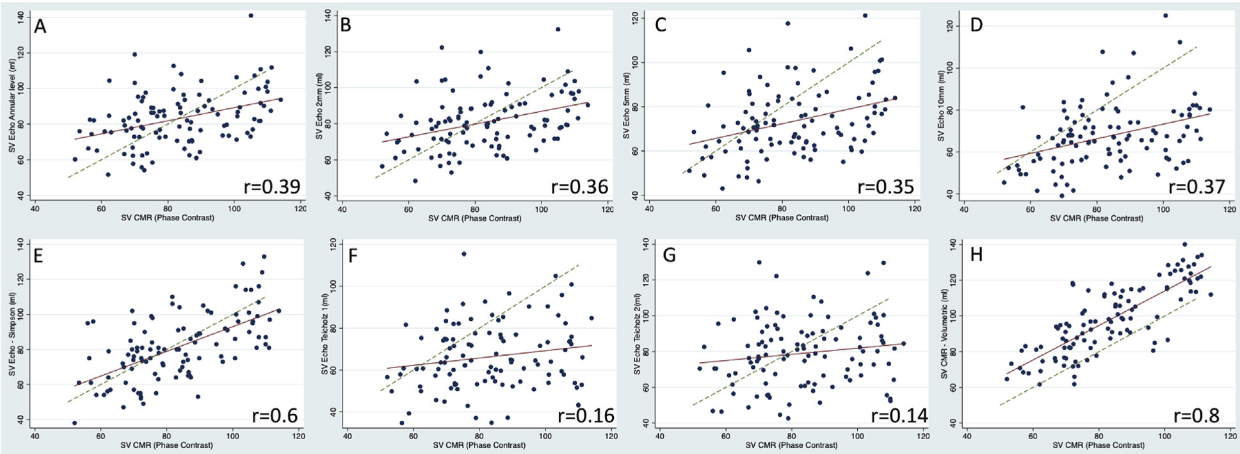


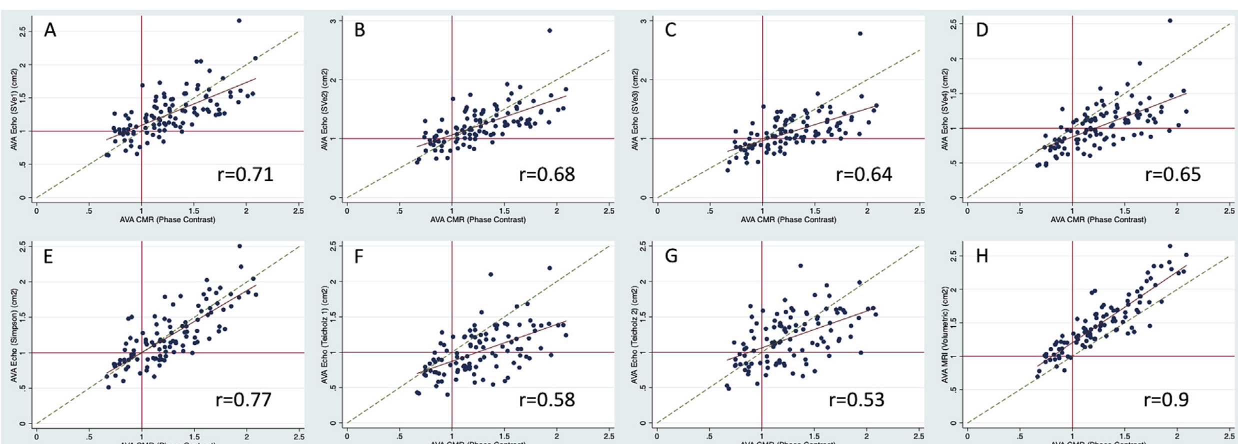
Supplemental Figure 1 Agreement and correlation of CMR-only derived AVA. **(A)** Bland-Altman plot comparing CMR-only AVA with the referent method (CMR phase-contrast hybrid method). The *solid red lines* are the mean bias ± 2 SDs. The *dashed black line* is the level of zero bias. **(B)** Correlation between CMR-only AVA and the referent method. The *red solid line* represents the regression line, and the *green dashed line* represents the identity line. *R* is the Spearman correlation.



Supplemental Figure 2 Prevalence of different LVOT shapes in tricuspid versus bicuspid **(A)** and mild versus moderate or severe AS **(B)**.



Supplemental Figure 3 Correlation of SVs estimated using different methods with phase-contrast (PC) CMR (referent method). The *red solid line* represents the regression line, and the *green dashed line* represents the identity line. *R* is the Spearman correlation. **(A)** Doppler method with LVOT measured at the annulus. **(B)** Doppler method with LVOT measured 2 mm below the annulus. **(C)** Doppler method with LVOT measured 5 mm below the annulus. **(D)** Doppler method with LVOT measured 10 mm below the annulus. **(E)** Simpson method. **(F)** Teichholz method (basal). **(G)** Teichholz method (below septal bulge). **(H)** CMR volumetric method.



Supplemental Figure 4 Correlation of AVAs estimated by different methods and phase-contrast (PC) CMR (referent method). The *red solid line* represents the regression line, and the *green dashed line* represents the identity line. *R* is the Spearman correlation. **(A)** Doppler method with LVOT measured at the annulus. **(B)** Doppler method with LVOT measured 2 mm below the annulus. **(C)** Doppler method with LVOT measured 5 mm below the annulus. **(D)** Doppler method with LVOT measured 10 mm below the annulus. **(E)** Simpson method. **(F)** Teichholz method (basal). **(G)** Teichholz method (below septal bulge). **(H)** CMR volumetric method.

Supplemental Table 1 Intraobserver and interobserver reproducibility

Measurement	Intraobserver ICC (95% CI)	Interobserver ICC (95% CI)
CMR		
SV (phase contrast)	0.93 (0.75–0.98)	0.89 (0.64–0.97)
SV (volumetric)	0.94 (0.77–0.98)	0.91 (0.68–0.97)
LVEDV	0.99 (0.95–1.00)	0.95 (0.80–0.98)
LVESV	0.93 (0.73–0.98)	0.83 (0.41–0.96)
Echocardiography		
LVOT diameter (annulus)	0.99 (0.96–1.00)	0.98 (0.91–0.99)
LVOT diameter (2 mm below)	0.98 (0.92–0.99)	0.96 (0.84–0.99)
LVOT diameter (5 mm below)	0.96 (0.86–0.99)	0.89 (0.62–0.97)
LVOT diameter (10 mm below)	0.94 (0.51–0.99)	0.80 (0.39–0.95)
LVEDV (Simpson biplane)	0.89 (0.61–0.97)	0.87 (0.56–0.97)
LVESV (Simpson biplane)	0.83 (0.48–0.95)	0.92 (0.72–0.98)