JACC: CARDIOVASCULAR IMAGING VOL. 8, NO. 3, 2015

ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER INC. http://dx.doi.org/10.1016/j.jcmg.2015.01.009

Aortic Valve Area Calculation in Aortic Stenosis by CT and Doppler Echocardiography

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ABSTRACT

OBJECTIVES The aim of this study was to verify the hypothesis that multidetector computed tomography (MDCT) is superior to echocardiography for measuring the left ventricular outflow tract (LVOT) and calculating the aortic valve area (AVA) with regard to hemodynamic correlations and survival outcome prediction after a diagnosis of aortic stenosis (AS).

BACKGROUND MDCT demonstrated that the LVOT is noncircular, casting doubt on the AVA measurement by 2-dimensional (2D) echocardiography.

METHODS A total of 269 patients (76 ± 11 years of age, 61% men) with isolated calcific AS (mean gradient 44 ± 18 mm Hg; ejection fraction 58 ± 15%) underwent Doppler echocardiography and MDCT within the same episode of care. AVA was calculated by echocardiography (AVA_{Echo}) and by MDCT (AVA_{CT}) using each technique measurement of LVOT area. In the subset of patients undergoing dynamic 4-dimensional MDCT (n = 135), AVA was calculated with the LVOT measured at 70% and 20% of the R-R interval and measured by planimetry (AVA_{Plani}).

RESULTS Phasic measurements of the LVOT by MDCT yielded slight differences in eccentricity and size (all $p < 0.001$) but with excellent AVA correlation ($r = 0.92$, $p < 0.0001$) and minimal bias (0.05 cm^2), whereas the AVA_{Plani} showed poor correlations with all other methods (all r values <0.58). AVA_{CT} was larger than AVA_{Echo} (difference 0.12 ± 0.16 cm^2; $p < 0.0001$) but did not improve outcome prediction. Correlation gradient-AVA was slightly better with AVA_{Echo} than AVA_{CT} ($r = -0.65$ with AVA_{Echo} vs. −0.61 with AVA_{CT}; $p = 0.01$), and discordant gradient-AVA was not reduced. For long-term survival, after multivariable adjustment, AVA_{Echo} or AVA_{CT} were independently predictive (hazard ratio [HR]: 1.26, 95% confidence interval [CI]: 1.13 to 1.42; $p < 0.0001$ or HR: 1.18, 95% CI: 1.09 to 1.29 per 0.10 cm^2 decrease; $p < 0.0001$) with a similar prognostic value ($p \geq 0.80$). Thresholds for excess mortality differed between methods: $AVA_{Echo} \leq 1.0$ cm^2 (HR: 4.67, 95% CI: 2.22 to 10.50; $p < 0.0001$) versus $AVA_{CT} \leq 1.2$ cm^2 (HR: 3.16, 95% CI: 1.64 to 6.43; $p = 0.005$), with simple translation of spline-curve analysis.

CONCLUSIONS Head-to-head comparison of MDCT and Doppler echocardiography refutes the hypothesis of MDCT superiority for AVA calculation. AVA_{CT} is larger than AVA_{Echo} but does not improve the correlation with transvalvular gradient, the concordance gradient-AVA, or mortality prediction compared with AVA_{Echo}. Larger cut-point values should be used for severe AS if AVA_{CT} (<1.2 cm^2) is measured versus AVA_{Echo} (<1.0 cm^2). (J Am Coll Cardiol Img 2015;8:248–57)

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Manuscript received October 26, 2014; revised manuscript received January 23, 2015, accepted January 26, 2015.

Aortic stenosis (AS) is a frequent valvular disease (1) treatable only by valve replacement, surgical or percutaneous (transcatheter aortic valve replacement [TAVR]) (2,3). Because TAVR does not allow intraprocedural valve sizing, evaluation of the ventriculoaortic transition zone has become an essential goal of aortic valvular imaging to avoid complications of TAVR such as prosthesis embolization, aortic annulus rupture, and paravalvular leak (4–6). This new requirement of thorough preprocedural aortic apparatus evaluation has led to 3-dimensional (3D) imaging studies using 3D echocardiography (7) or multidetector computed tomography (MDCT) (8), which suggested that the "aortic annulus" was complex, often noncircular (9,10) and concluded that MDCT provided superior annular measurement compared with standard 2D echocardiography (11,12).

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However, "aortic annulus" measurements, if improper, would have wide-ranging implications regarding AS hemodynamic assessment. Noninvasive aortic valve area (AVA) calculation requires aortic annular (or left ventricular outflow tract [LVOT]) cross-sectional area (LVOTArea) (13), which for Doppler echocardiography uses a disputed single-diameter measurement. AVA measured by Doppler echocardiography (AVA_{Echo}) has long been regarded as validated and as part of routine clinical practice but recently has been criticized as underestimating AVA calculated with the more anatomically sound LVOTArea measured by MDCT (AVA_{CT}) (7,11,12). The possibility that a faulty AVA_{Echo} may bear responsibility for "discordant" AS cases, with low gradient despite tight AVA, resonates with other challenges to the authenticity of this syndrome (14). The contrast between AVA_{Echo} being revered as fully validated and as the major independent predictor of outcome in AS and being reviled as anatomically illogical and underestimated versus AVA measured by computed tomography (AVA_{CT}) has not been resolved and is crucial to the management of patients with AS.

Thus, the aims of our study were as follows: 1) to verify whether the discordant hemodynamic pattern in AS is associated with aortic "annulus" asymmetry and resolved by use of AVA_{CT} versus AVA_{Echo}; 2) to assess whether the association between gradient and AVA is improved by the use of AVA_{CT} versus AVA_{Echo}; and 3) to assess whether the association between AVA and survival after a diagnosis of AS is improved by use of AVA_{CT} versus AVA_{Echo}. Our main hypothesis is that AVA_{CT} will be superior to AVA_{Echo} with regard to discordant AS severity grading, hemodynamic correlations, and clinical outcome impact. However, our secondary hypothesis is that thresholds to define severe AS will be higher by AVA_{CT} than by AVA_{Echo}.

ABBREVIATIONS AND ACRONYMS

AS = aortic stenosis

AVA = aortic valve area

AVA_{Echo} = aortic valve area measured by Doppler echocardiography

AVA_{CT} = aortic valve area measured by computed tomography

AVR = aortic valve replacement

ΔP = mean gradient

HR = hazard ratio

LVOT = left ventricular outflow tract

MDCT = multidetector computed tomography

TAVR = transcatheter aortic valve replacement

METHODS

We analyzed data for 269 adult AS patients who underwent comprehensive Doppler echocardiography and contrast-enhanced MDCT within the same episode of care (<3 months between evaluations). We excluded children younger than 18 years of age, patients with identified rheumatic disease or endocarditis, and those with moderate or severe mitral valve disease and/or previous valve repair or replacement.

Patients were enrolled in a prospective clinical research study initiated by the Valvular Heart Disease Clinic. Informed consent was obtained according to institutional review board approval. The CT angiography (with contrast) was performed to address clinical questions: 1) uncertainty regarding AS severity; 2) questions regarding LVOT in known AS; 3) in known AS, vascular indications regarding the status of the aorta or peripheral vessels; and 4) questions regarding the presence or severity of coronary artery disease.

DOPPLER ECHOCARDIOGRAPHY MEASUREMENTS. Left ventricular dimensions, peak aortic jet velocity, mean gradient (ΔP), and left ventricular ejection fraction were measured according to recommendations of the American Society of Echocardiography (13). Doppler echocardiographic LVOT diameter was measured at the base of the valve leaflets (**Figure 1**) and used to calculate LVOTArea using echocardiography:

$$LVOTArea_{Echo} = \pi \times \left(\frac{LVOTdiameter}{2}\right)^2$$

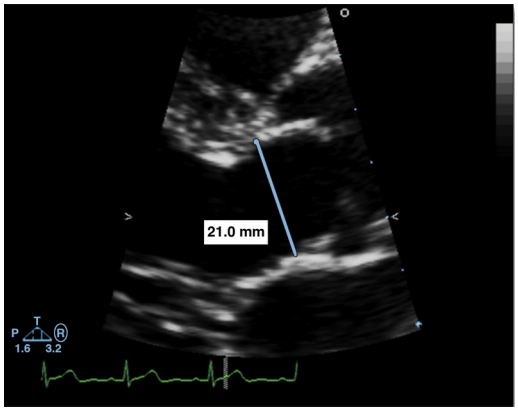
AVA_{Echo} was then calculated by the continuity equation:

$$AVA_{Echo} = LVOTArea_{Echo} \times \frac{VTI_{LVOT}}{VTI_{Ao}}$$

where VTI_{LVOT} and VTI_{Ao} are the velocity time integrals of the LVOT and transaortic flow, respectively.

MDCT IMAGING AND MEASUREMENTS. The contrast-enhanced electrocardiography-gated MDCT examinations were performed with a 64-detector scanner (Sensation 64, Siemens Medical Systems, Forchheim, Germany), without the routine use of β-blocker medications (Online Appendix). Dynamic LVOT assessment was performed in patients in whom the

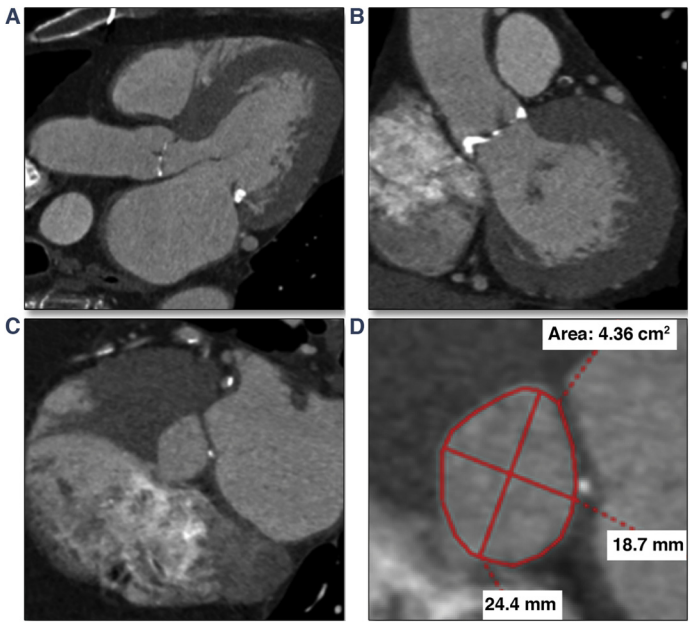
FIGURE 1 Method for Measurement of LVOT Dimensions by Echocardiography



From a zoomed parasternal long-axis view, the left ventricular outflow tract (LVOT) diameter is measured during systole. The **blue line** is drawn from the insertion of the aortic cusp at the level of ventricular septum to the insertion of the aortic cusp at the level of the anterior mitral leaflet.

entire 4-dimensional MDCT dataset of aortic valve and LVOT was recorded and available for quantitative analysis during all phases of the cardiac cycle (n = 135). Dynamic LVOT measurement involved tracing the LVOT contour at 70% and 20% of the R-R interval, allowing the calculation of AVA_{CT} in diastole ($AVA_{CT\text{-}D}$) and AVA_{CT} in systole ($AVA_{CT\text{-}S}$), respectively. Cardiac MDCT was performed using between 80 and 105 ml of isomolar contrast medium.

FIGURE 2 Method for Measurement of LVOT Dimensions by Computed Tomography



(A, B) Two orthogonal plans used to define LVOT plan. **(C)** LVOT plan. **(D)** Zoomed LVOT and measurements. LVOT = left ventricular outflow tract.

All LVOT imaging was performed using the same process with dedicated software (Aquarius iNtuition, TeraRecon, Inc., Foster City, California), involving orientation of a cross-sectional plane of LVOT by using 3 orthogonal planes from multiplanar reconstruction (Figures 2A to 2C) and located at or immediately under the lowest implantation base of aortic cusps (Figure 2C). Once this plane was secured, the LVOT contour was traced, 2 orthogonal diameters were directly measured, and the area of LVOT ($LVOTArea_{CT}$) was planimetered (Figure 2D). The eccentricity index of the aortic valve annulus was calculated by dividing the smaller diameter by the larger one.

AVA_{CT} was calculated by using the measured $LVOTArea_{CT}$ in the continuity equation:

$$AVA_{CT} = LVOTArea_{CT} \times \frac{VTI_{LVOT}}{VTI_{Ao}}$$

In patients with dynamic imaging and full 4-dimensional MDCT volumes, the imaging plane was translated to the tips of the aortic cusps in systole, and planimetry of the aortic valve opening (AVA_{Plani}) was measured.

STUDY ENDPOINT. To assess the respective value of AVA measurements obtained by Doppler echocardiography and MDCT, we examined several endpoints, including the relationship between ΔP and AVAs and the prevalence of discordant AS severity grading. The primary endpoint of this study was the overall survival under medical treatment. Hence, the end of follow-up was marked by aortic valve replacement (AVR) for patients operated on or by death or last known follow-up for patients not operated on. Patients were thus censored (follow-up stopped) at AVR. The secondary endpoint was total mortality during the entire follow-up (i.e., medical and post-AVR) (Online Table 1). Therapeutic decisions in our study were made by the patients' personal physicians based on all the information available. The decision to not operate immediately after the first evaluation was in this cohort mostly linked to nonsevere AS but also to asymptomatic AS or to symptoms interpreted as unrelated to AS. Only 10% of our patients were considered potentially high operative risk.

Outcome data were obtained from the annual visit of the patient or the patient's charts, mailed questionnaires or scripted telephone interviews with the patients or physicians, and death certificates.

We obtained complete follow-up up to AVR, to death, or to the year preceding freezing of the dataset in 96% of patients (258 of 269), and the 11 patients with incomplete follow-up contributed to outcome information for the duration of known follow-up.

STATISTICAL ANALYSIS. Results are expressed as mean ± SD or percentage. Differences between the 4 methods of AVA measurements were analyzed using 1-way repeated-measures analysis of variance followed by the Tukey test. Correlation and agreement between the different LVOTs and AVAs were determined with the use of the Pearson correlation and Bland-Altman methods, respectively. Relationships between AVAs and ΔP were assessed with multiple regression models, and the equation providing the best fit was retained. Comparison between correlation coefficients used the Wolfe test. The comparison of patient's classification between AVA_{Echo} and AVA_{CT} was done with the McNemar test.

To analyze the effect of AVA_{Echo} and AVA_{CT} on mortality, we used spline curve graphs where the x-axis represents AVA and the y-axis the relative risk of mortality. The effect of the clinical, Doppler echocardiographic, and MDCT variables on survival under medical treatment was assessed using Cox proportional hazard models adjusted for age-adjusted Charlson score index (15), sex, symptoms, ΔP, and left ventricular ejection fraction. Analysis of overall mortality during the entire follow-up was done with adjustment for age, sex, symptoms, coronary artery disease, chronic obstructive pulmonary disease, diabetes, hypertension, ΔP, left ventricular ejection fraction, and AVR as a time-dependent variable. All variables in the Cox models verified the proportional hazards assumption on the basis of inspection of trends in the Schoenfeld residuals (all $p > 0.32$). The results of the Cox proportional hazards were presented with hazard ratio and 95% confidence interval. The accuracy of the Cox model was assessed by the Harrell C index and compared by bootstrapping. A p value <0.05 was considered statistically significant.

RESULTS

BASELINE CHARACTERISTICS. Overall, at baseline, patient age was 76 ± 11 years, and 163 patients (61%) were male (Table 1). In terms of comorbidity, prevalence of hypertension (79%), diabetes (29%), coronary artery disease (49%), and chronic pulmonary disease (26%) were as expected in a population of that age. Doppler characteristics were ΔP 44 ± 18 mm Hg and peak velocity 4.2 ± 0.9 m/s.

Evaluation by static MDCT showed that LVOTArea was generally elliptical (93% patients had more than 10% difference between LVOT diameters), with an eccentricity index of 0.79 ± 0.08 in the entire cohort (Table 1). Categorized in the entire cohort using the median LVOT static eccentricity index (i.e., 0.8), patients with the most elliptical annulus (eccentricity index <0.8) had few differences (Table 1) with slightly more severe AS with higher peak velocity ($p = 0.03$) and ΔP ($p = 0.009$) and smaller AVA calculated by Doppler echocardiography, and reduced ejection fraction ($p = 0.002$) compared with patients with more circular annulus.

TABLE 1 Baseline Characteristics of the Population

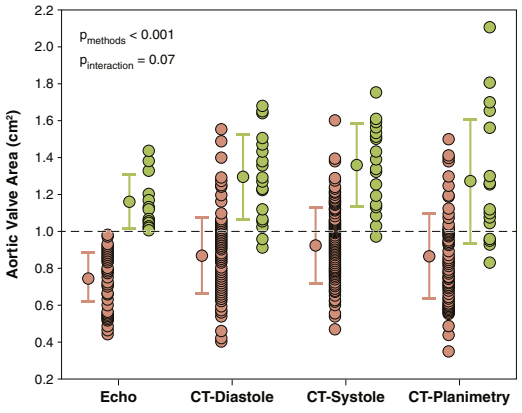
	Whole Cohort (N = 269)	LVOT Eccentricity <0.8 (n = 134)	LVOT Eccentricity ≥0.8 (n = 135)	p Value
Clinical data				
Age, yrs	76 ± 11	77 ± 11	75 ± 9	0.09
Male	163 (61)	80 (60)	83 (61)	0.77
Body mass index, kg/m²	28.9 ± 6.8	28.3 ± 0.5	29.4 ± 7.2	0.17
Body surface area, m²	1.91 ± 0.25	1.89 ± 0.26	1.92 ± 0.23	0.25
Diastolic blood pressure, mm Hg	69 ± 11	70 ± 11	69 ± 11	0.79
Systolic blood pressure, mm Hg	127 ± 18	126 ± 18	128 ± 18	0.35
Heart rate, beats/min	69 ± 13	70 ± 13	68 ± 13	0.49
NYHA functional class ≥III	122 (45)	68 (51)	54 (40)	0.08
Diabetes	77 (29)	35 (26)	42 (31)	0.39
Hypertension	185 (69)	92 (69)	93 (69)	0.97
Coronary artery disease	131 (49)	67 (50)	64 (47)	0.67
Chronic pulmonary disease	69 (26)	37 (28)	32 (23)	0.31
Echocardiographic data				
LVOT diameter, mm	2.21 ± 0.20	2.20 ± 0.20	2.22 ± 0.20	0.42
LVOT area, cm²	3.86 ± 0.71	3.82 ± 0.71	3.89 ± 0.72	0.42
LV end-diastolic diameter, cm	4.96 ± 0.73	5.02 ± 0.78	4.90 ± 0.66	0.20
LV end-systolic diameter, cm	3.31 ± 0.89	3.42 ± 0.94	3.20 ± 0.83	0.06
Stroke volume (LVOT), ml	87 ± 21	87 ± 22	90 ± 19	0.21
Peak aortic jet velocity, m/s	4.2 ± 0.9	4.3 ± 0.9	4.1 ± 0.8	0.03
Mean gradient, mm Hg	44 ± 18	47 ± 20	41 ± 15	0.009
AVA, cm²	0.94 ± 0.32	0.90 ± 0.31	0.98 ± 0.33	0.05
AVAi, cm²/m²	0.50 ± 0.17	0.48 ± 0.16	0.51 ± 0.17	0.14
LV ejection fraction, %	58 ± 15	55 ± 15	60 ± 12	0.002
AVA ≤1 cm² and mean gradient <40 mm Hg	66 (25)	34 (25)	32 (24)	0.75
Static MDCT data				
Large LVOT diameter, cm	2.76 ± 0.34	2.91 ± 0.31	2.61 ± 0.29	<0.0001
Small LVOT diameter, cm	2.17 ± 0.23	2.12 ± 0.22	2.22 ± 0.23	0.0001
LVOT eccentricity index	0.79 ± 0.08	0.73 ± 0.04	0.85 ± 0.05	<0.0001
LVOT area, cm²	4.68 ± 1.02	4.80 ± 1.06	4.55 ± 0.97	0.04
Stroke volume, ml	108 ± 29	109 ± 31	106 ± 26	0.27
AVA, cm²	1.13 ± 0.44	1.12 ± 0.44	1.15 ± 0.45	0.67
AVAi, cm²/m²	0.60 ± 0.23	0.60 ± 0.23	0.60 ± 0.23	0.98

Values are mean ± SD or n (%).

AVA = aortic valve area; AVAi = indexed aortic valve area; LV = left ventricular; LVOT = left ventricular outflow tract; MDCT = multidetector computed tomography; NYHA = New York Heart Association.

ECHOCARDIOGRAPHIC AND DYNAMIC MDCT MEASUREMENTS OF AVA. As LVOTArea (Online Appendix), AVA was different in all methods, with echocardiography measuring the smallest values and with considerable

FIGURE 3 4 Methods of AVA Measurement in Patients With 4-Dimensional MDCT Available According to Echocardiographic AVA



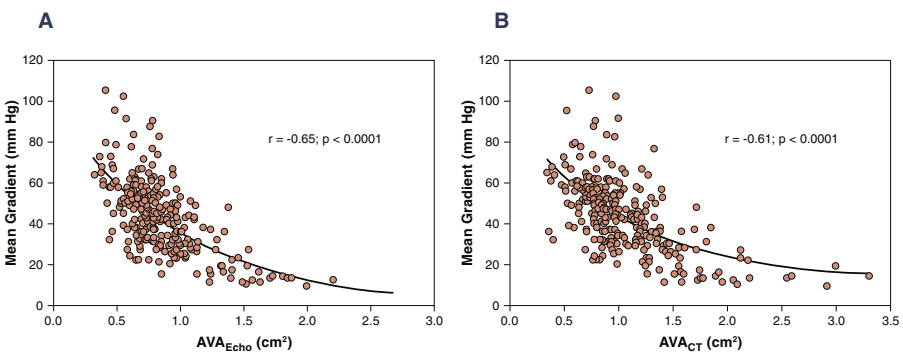
Echocardiographic AVA ≤ 1 cm^2 are reported in **pink** and AVA >1 cm^2 in **green**. Note the similar distribution of aortic valve area with MDCT in systole and diastole, whereas direct aortic valve planimetry in systole is associated with marked widening of distribution. AVA = aortic valve area; CT = computed tomography; Echo = echocardiography; MDCT = multidetector computed tomography.

dispersion of values for AVA_{Plani} compared with other methods (**Figure 3**). The correlations between AVA_{Echo} and either $AVA_{CT\text{-}D}$ or $AVA_{CT\text{-}S}$ (at 70% and 20% of R-R, respectively) were good and equivalent (both r values = 0.78, $p < 0.0001$) (Online Figure 1) with modest dispersion. The correlations obtained with AVA_{Plani} and any other method were significant but much poorer (all r values <0.58) (Online Figure 1). Conversely, the correlation between phasic calculations of AVA by MDCT was excellent (r = 0.92, $p < 0.0001$), with significant but minimal differences (mean 0.05 cm^2) (Online Figures 1E and 1F). In view of these excellent dynamic-static LVOT/AVA measurement correlations, static measurements were used in the entire population with regard to grading consistency and survival. Accordingly, in the whole cohort, the correlation between AVA_{Echo} and AVA_{CT} was good and with modest dispersion (Online Figure 2).

RELATIONSHIP BETWEEN ΔP AND AVA_{CT} OR AVA_{ECHO}. First, regression between ΔP and AVA, AVA_{Echo}, or AVA_{CT} was analyzed. The correlation between ΔP and AVA was better (Wolfe test, $p = 0.01$) for AVA_{Echo} ($r = -0.65$, $p < 0.0001$) than static AVA_{CT} ($r = -0.61$, $p < 0.0001$) (**Figure 4**). The use of indexed AVA provided the same results (see the Online Appendix, Online Figure 3). Thus, AVA_{CT} compared with AVA_{Echo}, despite its accounting for LVOT eccentricity, does not improve hemodynamic correlation of AVA-ΔP. When stratified by eccentricity index, the correlation AVA-ΔP tended to be weaker in patients with a more oval LVOT (i.e., eccentricity index <0.8), irrespective of the method used to measure AVA, but regression slopes were not affected, and use of MDCT to assess AVA did not improve AVA-gradient correlations and regressions in any subset (**Figure 5**). For purposes of completeness, we verified that dynamic MDCT ($AVA_{CT\text{-}S}$) did not improve the AVA-gradient relationship (all p values >0.25) over static MDCT, whereas measuring AVA by planimetry worsened the AVA-gradient correlations (all comparisons, $p \leq 0.04$).

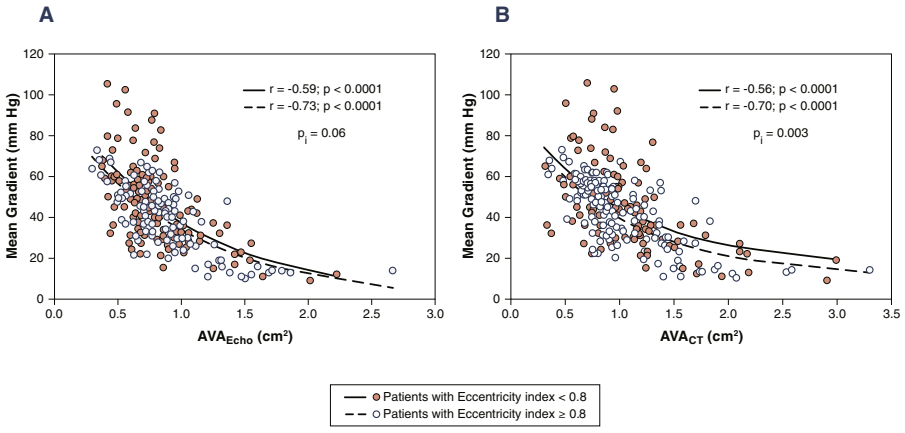
Second, the usefulness of AVA_{CT} to resolve discordant AS severity grading was analyzed. Of our 269 patients, 66 (25%) had a low gradient (<40 mm Hg) despite a tight AVA_{Echo}. This prevalence

FIGURE 4 Correlations Between Mean Gradient and AVA in the Whole Cohort



The AVA was calculated by Doppler echocardiography (AVA_{Echo}) **(A)** or calculated by multidetector computed tomography with direct left ventricular outflow tract measurement (AVA_{CT}) **(B)**. AVA = aortic valve area.

FIGURE 5 Correlations Between Mean Gradient and AVA According to LVOT Eccentricity



AVA_{Echo} **(A)** and AVA_{CT} **(B)** in the whole cohort. p is the p value of the correlation between the mean gradient and AVA. p_i is the p value of the interaction of AVA and LVOT eccentricity with regard to mean gradient. Abbreviations as in Figures 2 and 4.

was not different among patients with a high or low LVOT eccentricity index ($p = 0.75$) (Table 1). Patients classified as concordant AS assessment (either AVA ≤1.0 cm^2 combined with ΔP ≥40 mm Hg or AVA more than 1.0 cm^2 with ΔP <40 mm Hg) represented 74% by AVA_{Echo} and 70% by AVA_{CT} ($p = 0.15$), showing that AVA_{CT} did not improve the concordance of AS severity grading.

Using specific thresholds for each method did not show improvement of grading by AVA_{CT} (Online Appendix).

IMPACT OF AVA_{ECHO} AND AVA_{CT} ON SURVIVAL IN AS.

During a mean follow-up of 2.0 ± 1.4 years under medical treatment, there were 55 deaths (Online Table 1). On univariable and multivariable analyses, AVA calculated by echocardiography ($p < 0.0001$) or by MDCT ($p < 0.0001$) were independent predictors of mortality under medical treatment (Table 2). However, the negative impact on survival under medical treatment occurred for different thresholds for AVA_{Echo} and AVA_{CT}, as shown by the spline curves linking relative risk mortality under medical management and the 2 AVA types as continuous variables (Figure 6, Online Appendix). As dichotomized variables, AVA_{Echo} ≤1.0 cm^2 ($p < 0.0001$) and AVA_{CT} ≤1.2 cm^2 ($p = 0.005$) were independent predictors of mortality under medical treatment (Table 2, Figure 7). Importantly, as continuous or dichotomized variables, AVA_{Echo} and AVA_{CT} showed equivalent power to predict mortality under medical treatment using Harrell C index and net reclassification index (Table 2, Online Appendix).

Interestingly, AVA_{Echo} ≤0.8 cm^2 and AVA_{CT} ≤1.0 cm^2 were not independent predictors of mortality (Table 2, Figure 7).

These results were confirmed in the entire follow-up (3.2 ± 2.5 years) (Online Table 1), with further adjustment for AVR as a time-dependent variable. AVA_{Echo} and AVA_{CT} were independent predictors of total mortality as continuous variables (all p values = 0.02) as well as dichotomized variables (all p values ≤0.03).

DISCUSSION

Our study compares for the first time AVA by using Doppler echocardiography and MDCT obtained during the same episode of care in the same patients with AS with regard to hemodynamic correlations, discordance in AS severity grading, and clinical outcome impact. We first confirm that using static or dynamic MDCT for AVA calculation is equivalent with a minimum bias between phasic measurements. However, the measurement of AVA by planimetry should be avoided given that this measure provides the lowest correlation with the other methods and worsens the association AVA-gradient. Although the larger AVA by planimetry may not be surprising as it measures anatomic (vs. effective) orifice area, the dispersion of values and poor correlations with gradient reflect inconsistent measurements. The most important result of our study addresses the hypothesis that AVA_{CT} is superior to AVA_{Echo}, which is not verified by any of the measured endpoints. Indeed, although AVA_{CT} is larger than AVA_{Echo}, the AVA-gradient

TABLE 2 Univariable and Multivariable Analysis of Impact of AVA Calculated by Echocardiography or Computed Tomography on Mortality Under Medical Treatment in the Whole Cohort

		AVA_{Echo}			AVA_{CT}			p Value for Harrell C Index Comparison
	Increment	HR (95%CI)	p Value	Harrell C Index	HR (95% CI)	p Value	Harrell C Index	
Univariable	−0.10 cm^2	1.33 (1.20–1.49)	<0.0001	0.824	1.23 (1.14–1.33)	<0.0001	0.825	0.98
Multivariable		1.26 (1.13–1.42)	<0.0001	0.802	1.18 (1.09–1.29)	<0.0001	0.799	0.96
Univariable	Specific threshold	6.90 (3.53–14.64)	<0.0001	0.842	5.32 (2.88–10.52)	<0.0001	0.845	0.94
Multivariable	(1.0 and 1.2 cm^2)*	4.67 (2.22–10.50)	<0.0001	0.793	3.16 (1.64–6.43)	0.005	0.803	0.93
Univariable	Specific threshold	3.79 (2.20–6.58)	<0.0001	0.774	3.17 (1.82–5.56)	<0.0001	0.782	0.81
Multivariable	(0.8 and 1.0 cm^2)†	1.28 (0.78–2.45)	0.31	–	1.43 (0.77–2.64)	0.25	–	–

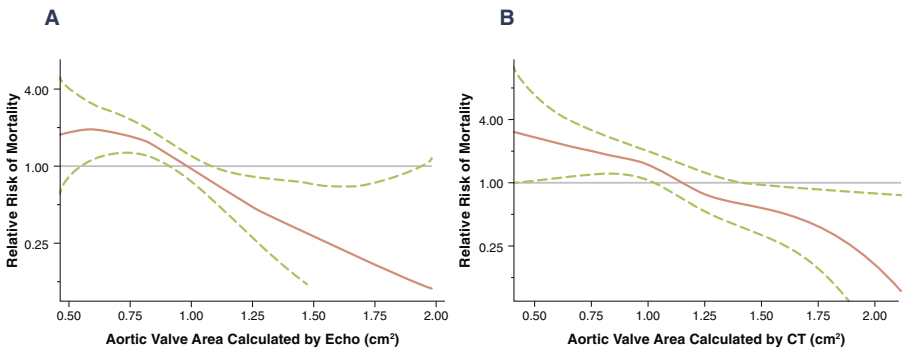
Multivariable analyses are adjusted for age-adjusted Charlson score index, sex, symptoms, mean gradient, and left ventricular ejection fraction. *AVA_{Echo} ≤1.0 cm^2 and AVA_{CT} ≤1.2 cm^2. †AVA_{Echo} ≤0.8 cm^2 and AVA_{CT} ≤1.0 cm^2.

AVA = aortic valve area; AVA_{CT} = aortic valve area calculated by computed tomography; AVA_{Echo} = aortic valve area calculated by echocardiography; HR = hazard ratio; CI = confidence interval.

relationship is not improved, and the frequency of discordant AS grading is unaffected, showing that, as a rule, the use of MDCT results in a translation of the correlation curves. Although our study shows for the first time that AVA_{CT} independently determines subsequent survival, this method did not improve outcome prediction compared with AVA_{Echo}. However, thresholds affecting mortality were different for AVA_{CT} and AVA_{Echo}, with spline curves demonstrating a simple translation of mortality prediction to higher values for AVA_{CT}.

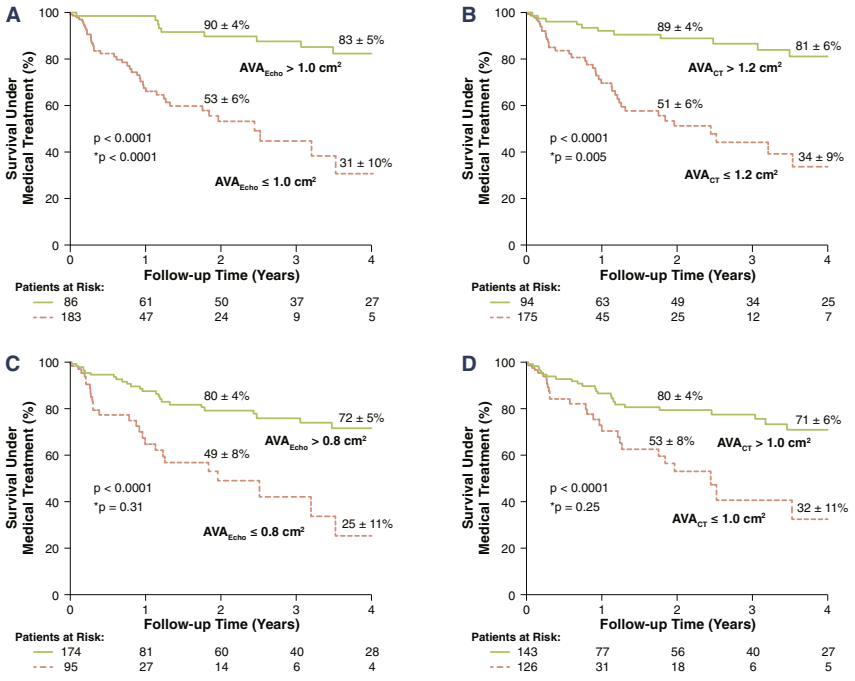
THE COMPLEX ANATOMY OF THE VENTRICULOAORTIC COMPLEX. The aortic valve has a complex structure (16). Until recently, little attention has been paid to this anatomic complexity, but recent work showed that the LVOTArea imaged by 3D imaging techniques does not have the previously presumed circular shape (9,10), and our data confirms a generally elliptical shape of the LVOT. The previous rule by 2D Doppler echocardiography, using the parasternal long-axis view, was to measure the diameter, alternatively called aortic annulus and LVOT, at the level of presumed lowest implantation of leaflets (17). 3D imaging techniques directly measuring of the entire area of the LVOT/annulus with orthogonal positioning ascertained by locating the bottom of all aortic cusps suggested that 2D Doppler echocardiography underestimated (8,11,12,18) this measurement. This issue of smaller LVOTArea calculated by 2D than measured by MDCT, which we undeniably confirm, has been labeled as "underestimation of the LVOT area" and has led to calls for the replacement of 2D annular measurement by 3D measurements in the calculation of the AVA (11,12,18). Such appeals are troubling because 2D measurements of AVA have been widely validated (17,19,20). Hence, it is essential to examine from physiological and outcome points of view whether Doppler echocardiography calculation of the AVA is superseded by the "superior" MDCT measurements.

FIGURE 6 Spline Curves of Relative Risk of Mortality According to the Aortic Valve Area



The curves show the impact of aortic valve area measured by Doppler echocardiography **(A)** and static computed tomography **(B)** on mortality under medical treatment in the whole cohort. **Dashed lines** are 95% confidence intervals. Abbreviations as in Figure 3.

FIGURE 7 Kaplan-Meier Curves of Survival Under Medical Treatment



Kaplan-Meier curves are presented according to AVA_{Echo} ≤1.0 cm² **(A)**, AVA_{CT} ≤1.2 cm² **(B)**, AVA_{Echo} ≤0.8 cm² **(C)**, and AVA_{CT} ≤1.0 cm² **(D)** in the whole cohort. Note: Follow-up was complete, up to aortic valve replacement, death, or the year preceding freezing of the dataset in 96% of patients (258 of 269), and the 11 patients with incomplete follow-up contributed outcome information for the duration of known follow-up. Abbreviations as in Figure 4.

PHYSIOLOGICAL COMPARISONS OF MDCT VERSUS DOPPLER ECHOCARDIOGRAPHY MEASUREMENTS. MDCT and Doppler echocardiography measurements of LVOTArea provide different AVAs so that AVA_{Echo} is generally 0.1 to 0.2 cm² smaller than AVA_{CT} (7,11,12). This different AVA calculation obtained by different methods increases the confusion regarding the best threshold of AVA identifying severe AS. Indeed, there is a purported inconsistency between echocardiographic criteria for grading AS, whereby an AVA of 1 cm² is touted as corresponding to a ΔP of 30 mm Hg, whereas a ΔP of 40 mm Hg would instead correspond to an AVA of 0.8 cm² (21). Hence, although guidelines indicate 1.0 cm² as the threshold for severe AS (2,22), it has been proposed (21) that this threshold for AVA_{Echo} should be decreased to 0.8 cm². This drastic change would conflict with outcome studies showing excess mortality (23) in AS with an AVA ≤1.0 cm², whereas no study has shown a superiority of AVA ≤0.8 cm² in predicting mortality. In that regard, our study provides important information. First, it shows that AVA_{CT}, despite accounting for the LVOT elliptical shape, provides no superior prediction of survival compared with AVA_{Echo}. Second, our spline analysis shows that the threshold of excess mortality is indeed an AVA ≤1.0 cm² for AVA_{Echo}, whereas it is an AVA ≤1.2 cm² for AVA_{CT} with spline curves showing a simple translation between these 2 methods. Third, AVA_{Echo} ≤0.8 cm² and AVA_{CT} ≤1.0 cm² are not independent predictors of mortality. Thus, despite the elliptical shape of the LVOT (9,10), discrepancies between MDCT measurements and direct annular sizing (24) suggest that MDCT and 2D echocardiography do not measure exactly the same structure. An alternate explanation of echocardiography-computed tomography discrepancies may reside with fluid dynamics, as blood velocity is null at the wall level, so that the effective flow area may be more circular than the anatomic elliptical LVOTArea, potentially leading to overestimation of the flow surface and stroke volume by computed tomography. Furthermore, stroke volume and AVA measured by Doppler echocardiography has been validated in studies comparing AVA_{Echo} and AVA calculated by catheterization (19,20,25) or magnetic resonance (26).

Hence, with the hypothesis that MDCT provides superior measurement not verified, measuring LVOT Area by MDCT is not required in clinical routine, unless poor imaging windows preclude aortic annular measurement or TAVR is planned. Indeed, measurement of the mean LVOT diameter and perimeter by MDCT has been linked to better sizing of transcatheter prostheses and to lower post-procedural paravalvular regurgitation (27,28).

STUDY LIMITATIONS. For image stability, static acquisitions were done in the whole cohort at 70% of the R-R interval, and a large number of patients had only static acquisition for minimizing radiation exposure. In patients with dynamic MDCT, we were able to assess phasic variations of LVOTArea. The impact of phasic variations on AVA calculation is significant but minimal. The fact that these phasic changes did not influence the regression between the AVA and ΔP is reassuring. There is no clinically available method yet to coregister images from 2D echocardiography and MDCT to prove beyond a doubt that measurements provided by these 2 techniques are not of the exact same anatomic structure, but imaging progress will soon allow such overlay and allow verification of this hypothesis. For now, our data showing the equivalent hemodynamic and outcome value of these techniques suggest that the history accumulated with Doppler echocardiography should not be discarded and that guidelines need not be revised for the management and severity assessment of AS. The combined endpoint of AVR or death was not used in the study due to potential bias (AVA_{Echo} guided decision making for AVR) and the lack of increased power with this frequent event (Online Table 1). This study should be confirmed by larger studies with longer follow-up.

CONCLUSIONS

This study showed that the hypothesis that AVA calculated using LVOTArea measured by MDCT is superior to AVA assessed by Doppler echocardiography is not verified with regard to hemodynamic correlations, to discordant AS severity grading, and to clinical outcome impact. Indeed, although AVA_{CT} is larger than AVA_{Echo}, the AVA-gradient relationship is not improved and the use of MDCT results in a simple translation of mortality spline curves. Furthermore, our study shows that AVA_{Echo} is an independent predictor of survival under medical treatment with a threshold affecting mortality of AVA_{Echo} ≤1.0 cm^2. Thus, LVOT measurement by MDCT should not replace Doppler echocardiography for hemodynamic assessment of AS severity. Despite suggestions to the contrary, our study finds no rationale in altering current guidelines in terms of use of Doppler echocardiography and threshold-guiding AS management, but conversely suggests that MDCT may be useful in patients with poor annular imaging by echocardiography.

CLINICAL IMPLICATIONS. Doppler echocardiography is the first-line examination for evaluation of AS severity. Asymmetrical LVOT by 3D imaging raised concerns about 2D echocardiographic AVA calculation accuracy but AVA calculation by MDCT does not improve grading concordance or outcome prediction. There are differences between echocardiography and computed tomography measurements, but echocardiography-measured AVA is not inferior to that calculated using LVOT by MDCT. Moreover, based on survival after diagnosis, thresholds defining severe AS should be different: 1.2 cm^2 for AVA by MDCT instead of 1.0 cm^2 for AVA by 2D echocardiography. Thus, measurement of LVOT diameter by MDCT is a valuable method to calculate AVA to assess AS severity. However, the use of MDCT is not mandatory in clinical routine for evaluation of AS severity, and echocardiography should remain the first-line of evaluation. Nevertheless, MDCT may be helpful in patients in whom there is a doubt about the aortic annulus diameter measurements by echocardiography for any reasons.

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KEY WORDS aortic valve stenosis, diagnostic method echocardiography, multidetector CT, survival

APPENDIX For an expanded Methods section as well as supplemental tables and figures, please see the online version of this article.