

A clinical and echocardiographic model to identify LVOT-related overestimation of aortic stenosis severity in transcatheter aortic valve replacement candidates

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Abstract

Introduction

Echocardiography significantly underestimates left ventricular outflow tract (LVOT) area resulting in the underestimation of aortic valve area (AVA). Our aim was to identify predictors of measurement error between echocardiography and CT-based LVOT area and develop a model to predict CT-based AVA values (hybrid AVA: using CT-based LVOT) using only clinical and echocardiographic parameters.

Methods and results

Consecutive severe AS patients between 1 January 2020 and 1 September 2024 were analysed to identify predictors of relative measurement inaccuracy using linear regression. We developed a model using only clinical and echocardiographic parameters to estimate CT-based hybrid AVA and validated it on consecutive patients between 2 September 2024 and 1 September 2025. Overall, 1367 patients were analysed (mean age 79.3 ± 6.3 years, 725 female). The mean difference between echocardiography- and CT-based LVOT area was $-162 \text{ mm}^2 \pm 98.2 \text{ mm}^2$, resulting in an AVA mean difference of $-0.29 \pm 0.18 \text{ cm}^2$, which led to reclassification of 31% of patients using a hybrid AVA cut-off of $\geq 1 \text{ cm}^2$. Older age, female sex, increased LVOT diameter, aortic valve V_{max} , and Doppler index were associated with reduced relative measurement error, whereas height, end-systolic, and end-diastolic volumes were associated with an increased relative measurement error. Our predicted AVA model had a strong correlation ($r = 0.82$; $P < 0.001$) with CT-based hybrid AVA values which was validated in 448 patients showing similar accuracy ($r = 0.85$; $P < 0.001$).

Conclusion

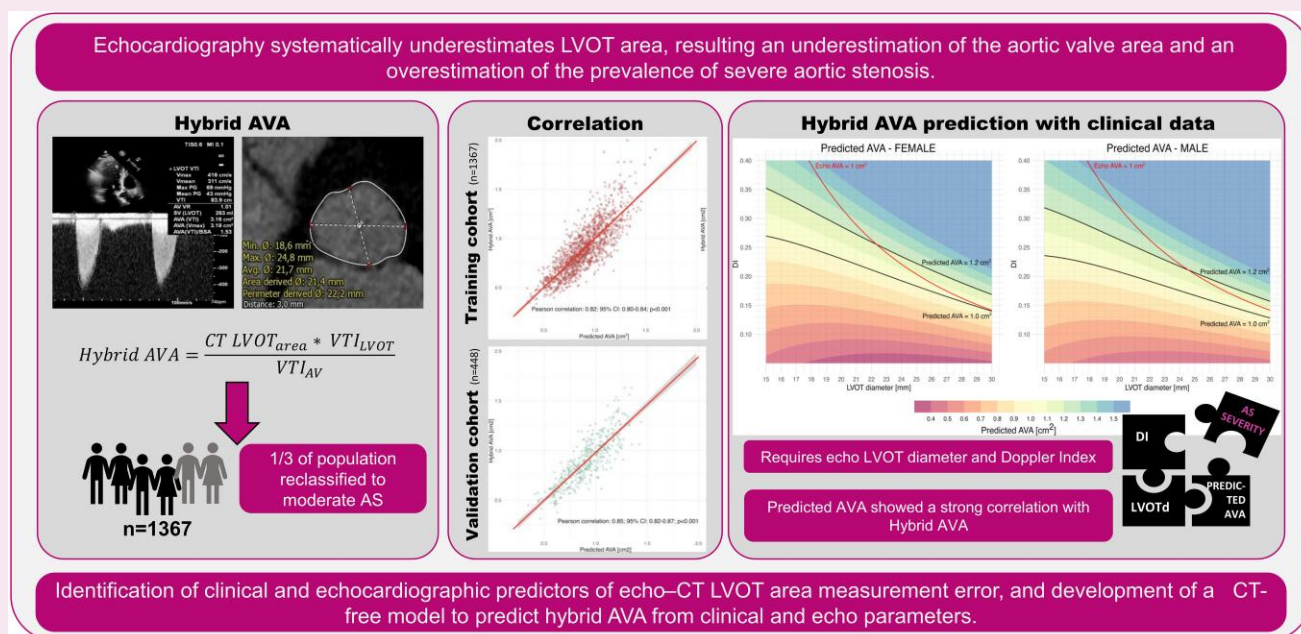
Echocardiography significantly underestimates the LVOT area compared to CT, leading to the reclassification of nearly one-third of patients. Our provided model using clinical and echocardiography-based parameters may support CT-free estimation of hybrid AVA values.

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Graphical abstract



Keywords

aortic stenosis • aortic valve area • LVOT area • echocardiography • cardiac CT

Introduction

Diagnosis of aortic valve stenosis (AS) is based on echocardiographic estimation of aortic valve area (AVA) using the continuity equation.¹ Echocardiographic flow measurements and the diameter of the left ventricular outflow tract (LVOT) are used within the equation to calculate AVA.² Since LVOT diameter is squared, any measurement errors in the diameter leads to substantial changes in the estimated AVA values. Further, the LVOT tends to be elliptical rather than circular, which may lead to underestimation of the AVA, as LVOT diameter on 2D echocardiographic images typically correlates with the short axis diameter of the ellipsoid.^{3,4}

Smaller studies have attempted to predict the LVOT diameter using measurements obtained via transoesophageal or 3D echocardiography, or by applying correction factors derived from CT imaging.⁵⁻⁷ Recently, cardiac MRI- or CT-derived LVOT area has been used in the continuity equation resulting in the hybrid AVA value, which has demonstrated prognostic significance in small-sample sized studies using a cut-off value of 1.2 cm².^{8,9} However, to the best of our knowledge, no study has directly addressed the elimination of measurement bias introduced by echocardiographic LVOT assessment by predicting hybrid AVA values using only patient characteristics and echocardiographic parameters.

Therefore, our primary aim was to identify predictors of measurement error between echocardiography- and CT-based LVOT area measurements. Next, we sought to develop a model to predict AVA in patients with severe aortic stenosis who were evaluated for transcatheter aortic valve implantation (TAVI) at our tertiary care centre, using only clinical and echocardiographic

parameters. Furthermore, we aimed to validate our model in a validation cohort of consecutive patients who were not used to derive the model. Finally, we wished to create classification charts which use echocardiographic parameters to estimate predicted hybrid AVA values to help identify individuals in whom further analyses may be needed to determine aortic stenosis severity.

Methods

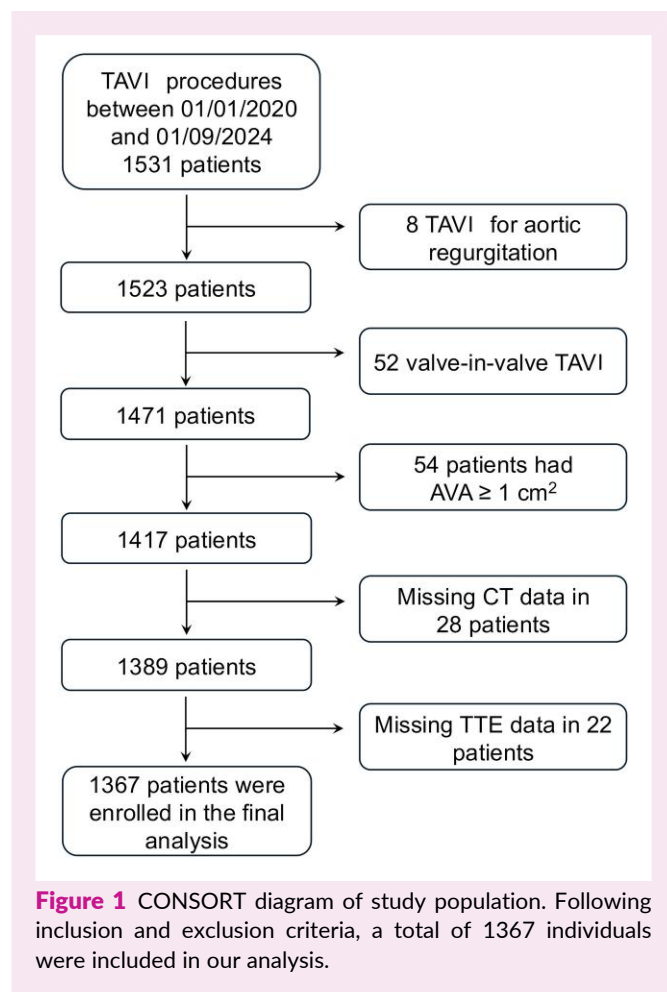
Patient population

We included patients who were being evaluated for TAVI at our tertiary care centre between 1 January 2020 and 1 September 2024. Exclusion criteria were the following: patients under 18 years of age, TAVI for other indications (e.g. aortic regurgitation), valve-in-valve procedures, patients with echo-based AVA ≥ 1 cm², patients with incomplete CT or echocardiographic data. CONSORT diagram of patient selection for our study can be found in [Figure 1](#). Using the same inclusion and exclusion criteria, our validation cohort consisted of consecutive patients scheduled for TAVI between 2 September 2024 and 1 September 2025.

The study was in accordance with local and federal regulations and the Declaration of Helsinki. The study was approved by the medical research council of Hungary (BM/13306-1/2023). Due to the retrospective nature of the study, written informed patient consent was waived.

Transthoracic echocardiography

Before TAVI a comprehensive transthoracic echocardiographic evaluation was performed with a commercially available ultrasound systems (Epiq5, EpiQ CVx, Philips Medical Systems, Best, The



Netherlands) in our EACVI accredited echocardiographic laboratory. The aortic valve area was calculated using the continuity equation according to current guidelines.² From the left ventricular (LV) apical long-axis, five-chamber or right parasternal views, continuous-wave Doppler spectral recordings through the aortic valve were obtained and the mean pressure gradient was estimated with the modified Bernoulli equation. Low-gradient AS was defined as mean gradient <40 mmHg. The highest aortic valve velocity was obtained in all patients. In case of atrial fibrillation, a minimum of five beats was recorded, and a mean value was calculated. The LVOT area was derived from the measured LVOT diameter on a zoomed parasternal long-axis view, 1–2 mm below the aortic annulus, minimizing the underestimation due to the heterogeneous shape (funnel, hourglass, sigmoid septum) of the LVOT. The velocity time integral was measured on the spectral pulsed Doppler recordings of the LVOT obtained from the LV apical long-axis or five-chamber views with the sample volume located just proximal to the aortic annulus and moved towards the apex until a smooth velocity curve is obtained. Stroke volume (SV) was calculated and then indexed (SVi) to body surface area (BSA). Low-flow state was defined as SVi <35 mL/m². For the calculation of LV ejection fraction (EF), the endocardial border of the LV was manually traced in the apical four-chamber and two-chamber views in end-diastole and end-systole and calculated by using the biplane Simpson's method.

Cardiac CT angiography and TAVI sizing

Prior to TAVI, all patients underwent cardiac and aortic CT angiography for assessment of aortic valve dimensions and evaluation of the vascular access routes. All images were acquired using a

16 cm coverage CT scanner (Revolution, GE Healthcare, Chicago, Illinois, United States). A three-phasic contrast injection protocol was used with 80 mL contrast agent at a flow rate of 4.5 mL/s. Cardiac data acquisition was performed during a mid-inspiratory breath-hold in a craniocaudal direction. Images were acquired from the top of the left atrial appendage to the base of the heart using ECG-gated dose modulated scans of the whole heart cycle. Image acquisition was done using 120 kVp and automatic tube current modulation. Images were reconstructed using 0.625 mm slice thickness and increment using iterative reconstruction. Cardiac acquisition was followed by a non-gated helical scan from the aortic arch to the femur head to evaluate the vascular access routes. Three-dimensional aortic root reconstruction was performed using commercially available software (3Mensio Structural Heart, Pie Medical Imaging BV, Maastricht, the Netherlands). The LVOT area was measured by planimetry, 3 mm below the predefined aortic annulus level during systole, at the phase providing the optimal contour for freehand tracing.¹⁰

Hybrid AVA calculation

Hybrid AVA was calculated using the continuity equation formula, combining Doppler echocardiographic data with the LVOT area measured on contrast-enhanced CT:

$$\text{Hybrid AVA} = \frac{\text{CT LVOT}_{\text{area}} * \text{VTI}_{\text{LVOT}}}{\text{VTI}_{\text{AV}}}$$

Where VTI_{LVOT} is the velocity-time integral in the LVOT measured by pulsed Doppler, and VTI_{AV} is the velocity-time integral through the aortic valve measured by continuous-wave Doppler.

Based on echocardiography-derived AVA, hybrid AVA and predicted AVA estimates from our statistical models, patients were classified into three groups:

- (1) *true severe AS*: echo AVA <1 cm² and hybrid/predicted AVA < 1 cm²
- (2) *indeterminate AS*: echo AVA <1 cm² and hybrid/predicted AVA 1.0–1.2 cm²
- (3) *reclassified to moderate AS*: echo AVA <1 cm² and hybrid/predicted AVA >1.2 cm².

Statistical analysis

Continuous variables are presented as means ± standard deviations or medians and interquartile ranges, while categorical parameters are presented as numbers and percentages. Continuous variables were compared using the ANOVA or t-test, while categorical variables were compared using the chi-square test between groups. Bland-Altman analysis was performed to evaluate the absolute measurement error between echocardiographic LVOT area and CT LVOT area, as well as between echocardiographic AVA and hybrid AVA. To identify predictors of measurement error between echo-derived and hybrid AVA, we defined the relative error of LVOT measurements as:

$$\begin{aligned} \text{Relative error of LVOT measurement} \\ = \frac{\text{CT LVOT}_{\text{area}} - \text{echo LVOT}_{\text{area}}}{\text{echo LVOT}_{\text{area}}} * 100\% \end{aligned}$$

Given that CT-derived LVOT area values are systematically larger than echocardiography derived LVOT area values, the echocardiographic LVOT area was used as the reference for the calculation of relative LVOT area error, thereby avoiding negative values and improving interpretability.

Due to the retrospective nature of our study, missing data were observed for heart rate and rhythm during echocardiography, end-diastolic and end-systolic volumes, as well as aortic valve peak velocity. All missing value frequencies were below 5%. The multiple imputation by chained equation (mice R package,

Table 1 Baseline clinical, echocardiographic, and CT data

Clinical characteristics	N = 1367
Age (years)	79.3 ± 6.3
Female (%)	725 (53%)
Height (cm)	165.1 ± 9.3
Weight (kg)	76.1 ± 15.8
Body mass index (kg/m ²)	27.9 ± 5.1
Body surface area (m ²)	1.83 ± 0.21
Bicuspid aortic valve (%)	120 (9%)
Hypertension (%)	1198 (88%)
Diabetes mellitus (%)	511 (37%)
Atrial fibrillation in medical history (%)	547 (40%)
Coronary artery disease (%)	706 (52%)
Chronic kidney disease (%)	206 (15%)
Chronic obstructive pulmonary disease (%)	132 (10%)
Time difference echocardiography-CT (days)	13 [IQR: 3–52]
Time difference echocardiography-procedure (days)	29 [IQR: 7–109]
Echocardiography	
Heart rate during echo (bpm)	76.2 ± 13.8
Sinus rhythm during echo (%)	971 (76%)
Echo-LVOT (mm)	20.3 ± 1.9
Echo-LVOT area (mm ²)	325.2 ± 60.7
Echo-LVOT area index (mm ² /m ²)	178.6 ± 31.4
LV diastolic diameter (mm)	50.6 ± 8.1
LV systolic diameter (mm)	31.2 ± 10.0
Intraventricular septum thickness (mm)	13.4 ± 3.0
Posterior wall thickness (mm)	12.2 ± 2.1
Left ventricular mass index (g/m ²)	142.6 ± 46.1
Relative wall thickness	0.52 ± 0.13
LV end-diastolic volume (ml)	106.5 ± 45.5
LV end-systolic volume (ml)	53.6 ± 39.2
Ejection fraction (%)	53.9 ± 16.4
Ejection fraction <50% (%)	453 (33%)
LVOT velocity-time integral (cm)	19.3 ± 5.4
Stroke volume (mL)	61.6 ± 17.9
Stroke volume index (mL/m ²)	33.9 ± 9.9
Stroke volume index <35 mL/m ² (%)	775 (57%)
Aortic valve peak velocity (m/s)	4.3 ± 0.7
Aortic valve peak gradient (mmHg)	76.5 ± 24.5
Aortic valve mean gradient (mmHg)	47.8 ± 16.2
Aortic valve velocity-time integral (cm)	104.9 ± 23.9
Doppler velocity index	0.19 ± 0.05
Echo-AVA (cm ²)	0.60 ± 0.16
Echo-AVA index (cm ² /m ²)	0.33 ± 0.09
CT findings	
LVOT minimum diameter (mm)	21.5 ± 2.9
LVOT maximum diameter (mm)	28.6 ± 3.3
LVOT mean diameter (mm)	25.1 ± 2.9
LVOT maximum-minimum diameter (mm)	7.1 ± 2.1
LVOT maximum/minimum diameter	1.34 ± 0.12
CT-LVOT area (mm ²)	487.1 ± 117.0
CT-LVOT area index (mm ² /m ²)	266.8 ± 58.8

Continued

Table 1 Continued

Clinical characteristics	N = 1367
Hybrid AVA, (cm ²)	0.89 ± 0.25
Hybrid AVAi, (cm ² /m ²)	0.49 ± 0.13

Values presented are frequency (percentage) for categorical variables or mean ± SD for continuous variables, or median and interquartile ranges (IQR) for time-based variables.

v.3.17.0) framework was used for handling missing data and utilized all patients' data for regression analyses. Overall, 1000 imputed datasets were created with a maximum iteration of 50. Univariable and multivariable linear regression analyses were used to identify predictors of relative LVOT measurement error. Parameters with $P < 0.05$ during univariable regression analysis were included in the multivariable model. Rubin's rule was used to combine the estimates from the repeated complete datasets.¹¹ To estimate a more parsimonious model, backward elimination was used until all parameters had a $P < 0.05$ (R package miceafter, v.0.5.0.). The D1 method was used to compare the fit of the parsimonious model to the multivariable model. Using the final parsimonious model, predicted AVA was calculated using patient- and ultrasound parameters. Pearson correlation was used to evaluate the fit between predicted AVA and hybrid AVA values in both the derivation and the validation cohorts.

Predicted AVA values were simulated using our fitted parsimonious model for a range of possible LVOT diameter and Doppler index values, while holding other covariates at their average or most frequently observed levels. We also predicted the probability of reclassification as a function of echocardiographic AVA values based on our previously defined reclassification groups using logistic regression.

All-cause mortality rates were estimated for reclassification groups and illustrated using Kaplan-Meier survival curves, and group differences were assessed using the log-rank test.

All calculations were done in the R environment (v.4.3.3). A two-sided P value < 0.05 was considered statistically significant.

Results

Patient characteristics

Out of the 1531 patients who underwent TAVI during the study period, 1367 patients were eligible (see consort diagram on [Figure 1](#)). The mean age was 79.3 ± 6.3 years and 53% (725/1367) of the patients were female. Atrial fibrillation was present in 40% (547/1367) of the patients. [Table 1](#) summarizes the baseline clinical, echocardiographic and CT findings. Sex-stratified data are detailed in [Supplementary Data \(Supplementary data online, Table S1\)](#).

Echocardiographic and CT findings

The mean EF was $53.8 \pm 16.4\%$, and echo-derived AVA was 0.60 ± 0.16 cm². The mean transvalvular gradient was 47.8 ± 16.2 mmHg. Low-gradient AS (mean gradient < 40 mmHg) was present in 352 patients (26%). Based on SVi, 775 patients (57%) were classified as having low flow state. Further echocardiographic parameters can be found in [Table 1](#).

Baseline CT data are shown in [Table 1](#). All measured LVOT diameters: minimum (21.5 ± 2.9 mm), average (25.1 ± 2.9 mm), and maximum (28.7 ± 3.3 mm) were significantly larger when assessed by CT compared to the LVOT diameter measured by echocardiography (20.3 ± 1.9 mm; $P < 0.001$, respectively for all). Consequently, the LVOT area calculated from echocardiographic measurements was significantly smaller than the

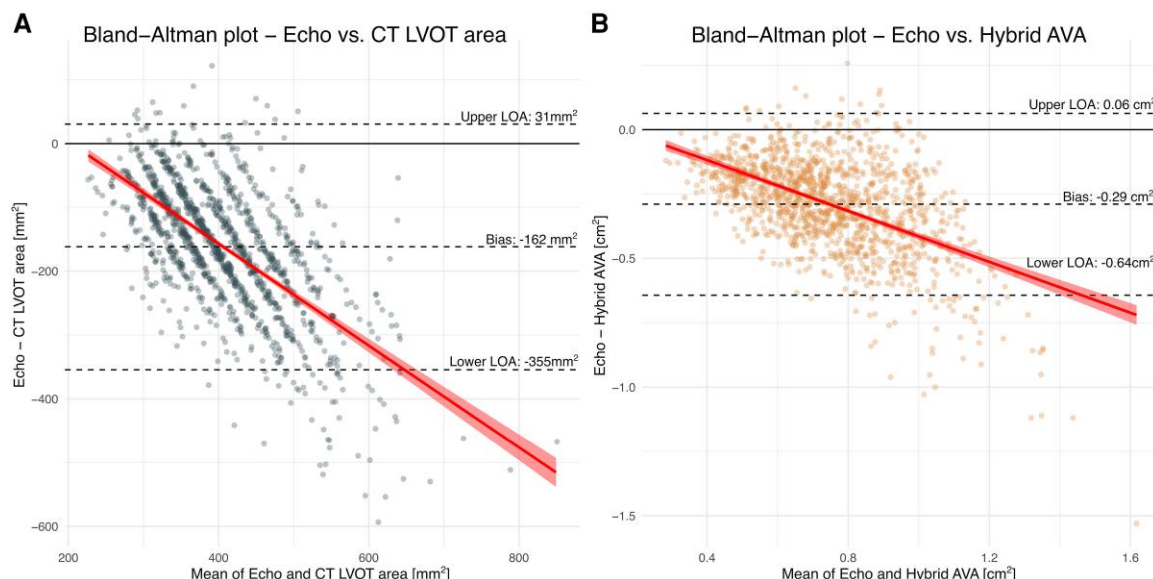


Figure 2 Bland–Altman plots comparing CT- and echocardiographic measurements of LVOT area and resulting AVA. (A) The left panel displays the Bland–Altman plot comparing LVOT area measured by echocardiography and by CT. The plot reveals a systematic underestimation of LVOT area by echocardiography compared to CT derived direct measurement, with increasing bias at larger mean values. (B) The right panel shows the Bland–Altman plot comparing echo-derived AVA and hybrid AVA. A proportional trend is observed, with decreasing agreement at higher AVA values. The red line indicates the regression of the differences against the means with 95% confidence intervals; dashed lines represent the bias, and the limits of agreement (bias $\pm$ 1.96 SD).

directly measured CT-derived LVOT area ($325.2 \pm 60.7 \text{ mm}^2$ vs. $487.1 \pm 117.0 \text{ mm}^2$; $P < 0.001$), resulting in significantly smaller echo-derived AVA compared to the hybrid AVA ($0.6 \pm 0.16 \text{ cm}^2$ vs. $0.89 \pm 0.25 \text{ cm}^2$; $P < 0.001$).

Agreement between echocardiographic and CT measurements

Bland–Altman analysis was used to assess the absolute measurement error between echocardiography and CT. According to LVOT area measurements, the mean difference was $-162 \text{ mm}^2 \pm 98.2 \text{ mm}^2$ (limits of agreement: -354.5 to 30.5 mm^2) between echocardiography and CT, with a clear trend indicating that the absolute error between the two modalities increased with larger LVOT diameters (Figure 2A). Correspondingly, for AVA measurements, the mean difference between echo-derived AVA and hybrid AVA was $-0.29 \pm 0.18 \text{ cm}^2$ (limits of agreement: -0.64 to 0.06 cm^2), with a similarly larger bias towards higher AVA values (Figure 2B).

Overall, 951 patients (69%) had a hybrid AVA $< 1.0 \text{ cm}^2$ (true severe AS); 269 (20%) patients had a hybrid AVA value between 1.0 cm^2 and 1.2 cm^2 (indeterminate AS) and 147 (11%) patients had a hybrid AVA $> 1.2 \text{ cm}^2$ (moderate AS). Reclassification of patients using hybrid AVA across echocardiographic AVA categories is shown in Supplementary data online, Figure S1. The closer the echocardiographic AVA is to the 1.0 cm^2 cut-off, the higher the proportion of patients who were reclassified.

Predictors of LVOT area discrepancy

Univariable, multivariable, and parsimonious logistic regression analyses were used to identify independent predictors of relative LVOT area error (Table 2). The error was expressed as a

relative percentage compared to echocardiographic LVOT area measurements. A positive association indicates that the factor increases the relative error by a given percentage, while a negative association indicates a reduction in the relative error. In univariable analyses, all predictors had a significant association with the relative error of LVOT area measurement and were entered into the multivariable model. In multivariable regression, age, female sex, LVOT diameter, end-diastolic volume, aortic valve V_{max} , and Doppler index were significantly associated with our outcome. Using backward elimination, the same parameters and height and end-systolic volumes were significant in the parsimonious model. Older age, female sex, increases in LVOT diameter, aortic valve V_{max} , and Doppler index were associated with reduced relative measurement error, whereas height, end-systolic, and end-diastolic volumes were associated with increased relative measurement error. Notably, ejection fraction, flow status, and mean transaortic gradient showed no significant association with the degree of discrepancy. A detailed summary of the variables included in each regression model is presented in Table 2.

The parsimonious model had a similar fit to our data as the multivariable model (D1 test statistic: 0.85, degrees of freedom: 1351, $P = 0.53$), suggesting that the reduced model preserved a comparable fit while requiring fewer variables.

Predicted AVA

Using the parsimonious regression model, a predicted AVA was calculated for the patients. A strong correlation ($r = 0.82$; $P < 0.001$) was observed between the predicted- and the hybrid AVA values (Figure 3A). The strength of this correlation remained consistent in sex stratified analyses (females: $r = 0.80$, $P < 0.001$; males: $r = 0.78$, $P < 0.001$), or when stratified into

Table 2 Uni- and multivariable linear regression, and parsimonious multiple regression model to predict relative LVOT measurement error

Variable	Univariable regression			Multivariable regression			Parsimonious regression		
	β (%)	CI	P	β	CI	P	β	CI	P
Age [per 1 year]	-0.65	-0.92; -0.38	<0.001	-0.26	-0.48; -0.04	0.023	-0.24	-0.45; -0.03	0.028
Female sex [y/n]	-15.06	-18.38; -11.74	<0.001	-14.79	-18.57; -11.02	<0.001	-15.11	-18.85; -11.37	<0.001
Height [per 1 cm]	0.67	0.49; 0.85	<0.001	0.24	-0.35; 0.83	0.421	0.47	0.28; 0.66	<0.001
Body mass index [per 1 kg/m ²]	-0.41	-0.74; -0.08	0.015	-0.31	-1.22; 0.59	0.494			
Body surface area [per 0.1 m ²]	0.15	0.07; 0.23	<0.001	0.11	-0.22; 0.43	0.511			
Sinus rhythm during echocardiography	-8.90	-12.96; -4.85	<0.001	-2.07	-5.58; 1.45	0.249			
Heart rate [per 1 bpm]	0.20	0.03; 0.38	0.023	-0.07	-0.21; 0.08	0.384			
LVOT diameter [per 1 mm]	-4.90	-5.77; -4.03	<0.001	-10.70	-11.65; -9.74	<0.001	-11.10	-11.91; -10.29	<0.001
End-diastolic volume [per 1 mL]	0.19	0.15; 0.23	<0.001	0.11	0.02; 0.20	0.015	0.08	0.01; 0.16	0.029
End-systolic volume [per 1 mL]	0.28	0.23; 0.32	<0.001	0.10	-0.02; 0.22	0.107	0.14	0.05; 0.24	0.002
Aortic valve V _{max} [per 0.1 m/s]	-0.96	-1.20; -0.71	<0.001	-0.72	-1.29; -0.15	0.013	-0.75	-0.98; -0.52	<0.001
Aortic valve mean gradient [per 1 mmHg]	-0.33	-0.43; -0.22	<0.001	0.05	-0.19; 0.30	0.673			
Doppler index [per 0.01]	-1.27	-1.62; -0.91	<0.001	-1.58	-1.99; -1.16	<0.001	-1.86	-2.18; -1.53	<0.001
Stroke volume index [<35 mL/m ² y/n]	27.19	24.07; 30.31	<0.001	3.46	-0.43; 7.34	0.081			
Ejection fraction [$\geq$ 50% y/n]	-21.62	-25.05; -18.18	<0.001	-2.81	-7.50; 1.87	0.238			

Relative measurement error was defined as the difference between CT-derived and echocardiographic LVOT area, divided by echocardiographic LVOT area and multiplied by 100%. All parameters that were significant ($P < 0.05$) in univariable models were included into the multivariable model. Parsimonious model was calculated using backward elimination until all parameters had a P value < 0.05 .

low- and high-gradient groups (low-gradient: $r = 0.80$, $P < 0.001$; high-gradient: $r = 0.81$, $P < 0.001$) or low- and normal-flow groups (low-flow: $r = 0.77$, $P < 0.001$; normal-flow: $r = 0.85$, $P < 0.001$).

Validation cohort

The cohort of 448 consecutive patients between 2 September 2024 and 1 September 2025 (44% males, 199/44; mean age: 79.8 ± 5.5 years) with identical inclusion and exclusion criteria were used to validate our model. Baseline characteristics are detailed in [Supplementary Data \(Supplementary data online, Table S2\)](#). The validation cohort was not used in any means to build the predicted AVA model. Similarly, a strong correlation was observed between the predicted and hybrid AVA values ($r = 0.85$; $P < 0.001$) ([Figure 3B](#)).

Reclassification rate according to predicted AVA

According to predicted AVA, 961 (70%) patients had true severe AS (predicted AVA < 1.0 cm²), 309 (23%) patients had indeterminate AS (predicted AVA 1.0 cm² to 1.2 cm²) and 97 (7%) patients had moderate AS (predicted AVA > 1.2 cm²), respectively.

The probability of reclassification to AVA > 1 cm² using hybrid and predicted AVA values—as a function of echocardiographic AVA—was comparable. This further indicates a good fit of our predictive model which only uses patient and echocardiographic

data, to hybrid AVA measurements requiring CT imaging ([Figure 4](#)). For echocardiographic AVA values larger than 0.72 cm², the probability of reclassification to AVA > 1 cm² based on hybrid or predicted AVA is more than 50%.

Survival according to reclassification

[Figure 5](#) illustrates the survival of the three groups stratified by hybrid AVA (true severe AS, indeterminate AS, and reclassified to moderate AS). The reclassified-to-moderate AS group showed the poorest outcome with borderline statistical significance ($P = 0.051$). Baseline characteristics of the three groups are provided in the [Supplementary Data \(Supplementary data online, Table S3\)](#).

Clinical utility

[Figure 6](#) enables the visual estimation of predicted AVA from echocardiographic measurements of LVOT diameter and DI, stratified by sex. By locating a given combination of LVOT and DI on the plot, the corresponding predicted AVA value can be directly derived from the colour-coded contour levels, where the red contour line corresponds to the 1.0 cm² threshold of echo-derived AVA, while black lines represent 1.0 and 1.2 cm² levels of the predicted AVA. [Figure 7](#) illustrates the application of our clinical chart in daily practice through two representative cases.

As shown in [Figure 4](#) and [Supplementary data online, Figure S1](#), the larger the echocardiographic AVA, the higher the likelihood that the patient will be classified into the

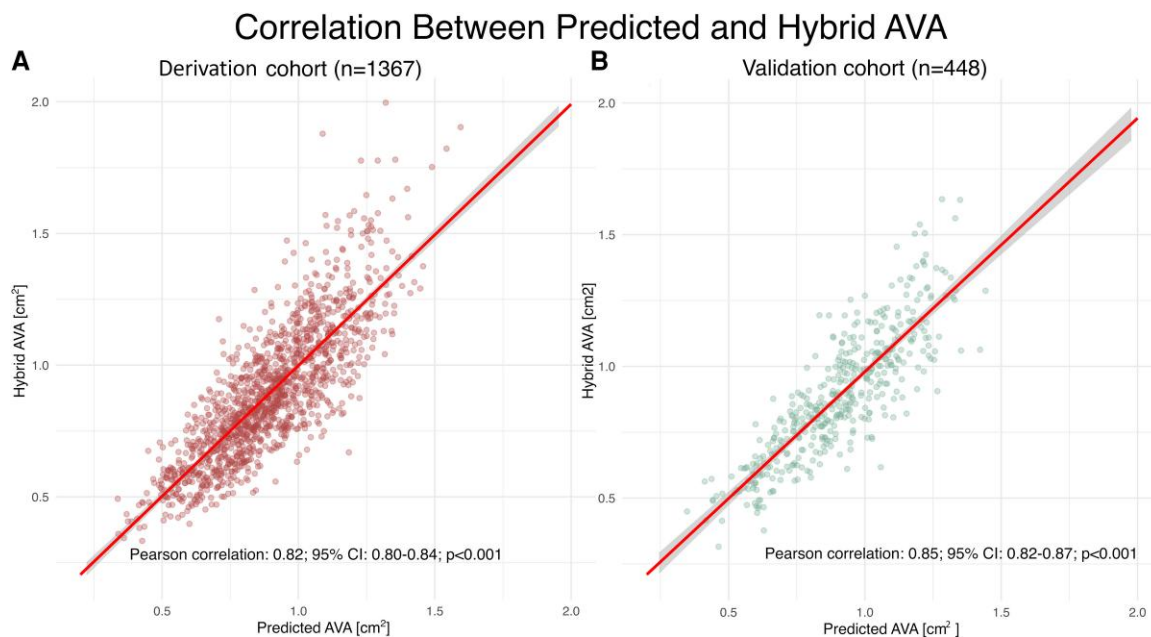


Figure 3 Correlation between hybrid and predicted AVA in the derivation and validation cohorts. Scatter plot and regression line with 95% confidence interval for AVA values predicted by the parsimonious model using only echocardiographic and patient characteristics vs. hybrid AVA values. (A) derivation cohort on which the parsimonious model was developed. (B) validation cohort which was not used in any way to derive the parsimonious model.

indeterminate or moderate AS category based on hybrid AVA. Based on our data, detailed clinical assessment and additional imaging warranted in patients with predicted AVA >1.2 cm², as they tend to be a more vulnerable population. A comprehensive clinical evaluation may be needed in patients within the grey zone (predicted AVA between 1–1.2 cm²) to ensure the diagnosis of severe AS.

Discussion

We demonstrate that echocardiography significantly underestimates the LVOT area compared to CT, resulting in the reclassification of nearly one-third of patients as having an AVA >1 cm² when using a hybrid approach. We identified older age, female sex, increased LVOT diameter, aortic valve $V_{\max}$, and Doppler index as factors associated with reduced measurement error between CT and echo-derived LVOT area assessments. In contrast, greater height, as well as larger end-systolic and end-diastolic volumes were linked to increased error. Notably, our model may be applicable across different AS subtypes since it is not affected by systolic function, flow status, or mean transvalvular gradient. Our model, based on demographic and echocardiographic parameters, showed a strong correlation with hybrid AVA values, which require CT measurements. These findings were further confirmed by the similarly strong correlation observed in the validation cohort. To facilitate clinical application, we provide a chart to predict hybrid AVA from echocardiographic LVOT diameter and Doppler index, offering a practical tool for routine use.

Besides peak transvalvular velocity and mean gradient assessment, the calculation of AVA is the cornerstone of AS diagnosis.^{1,2} In clinical practice, the continuity equation is used to

calculate the functional aortic orifice. However, the calculation relies on the accurate measurement of the LVOT area, which is frequently underestimated by echocardiography. Data show that the shape of the LVOT is often elliptical rather than circular.^{3,4} Moreover, geometrical configurations such as the funnel or hourglass type of LVOT further increase the difficulty to accurately measure the diameter of the LVOT.^{6,8,12}

Various methods have been proposed to address these limitations mentioned above. One of the earliest is the DI which eliminates LVOT area measurement and relies on LVOT and aortic valve velocities. A DI <0.25 has been proposed as a marker of severe AS.^{13,14} Rusinaru *et al.* confirmed the prognostic value of the DI in a larger cohort of patients with preserved ejection fraction.¹⁵ However, limited data are available for its use in low-flow- or low-gradient AS.

A more accurate assessment of the LVOT diameter may be achieved by utilizing 3D transthoracic or transoesophageal echocardiography. Liu *et al.* demonstrated that biplane imaging of the LVOT provides superior concordance with cardiac CT compared to the conventional circular method, resulting in improved concordance between AVA and mean gradient.⁴ Similarly, 3D transoesophageal echocardiography yields larger LVOT area and AVA values compared to both 2D transoesophageal and 2D transthoracic measurements,⁶ however, the routine use of transoesophageal echocardiography in elderly, frail patients is often not feasible.

To overcome these limitations Alsakaf *et al.*⁵ proposed a CT-derived correction factor to improve the correlation between the LVOT area calculated by 2D echocardiography and the direct measurement by CT. In our study, however, we demonstrated that the discrepancy between the calculated and the directly measured LVOT area is influenced by multiple factors, not only by anatomical characteristics.

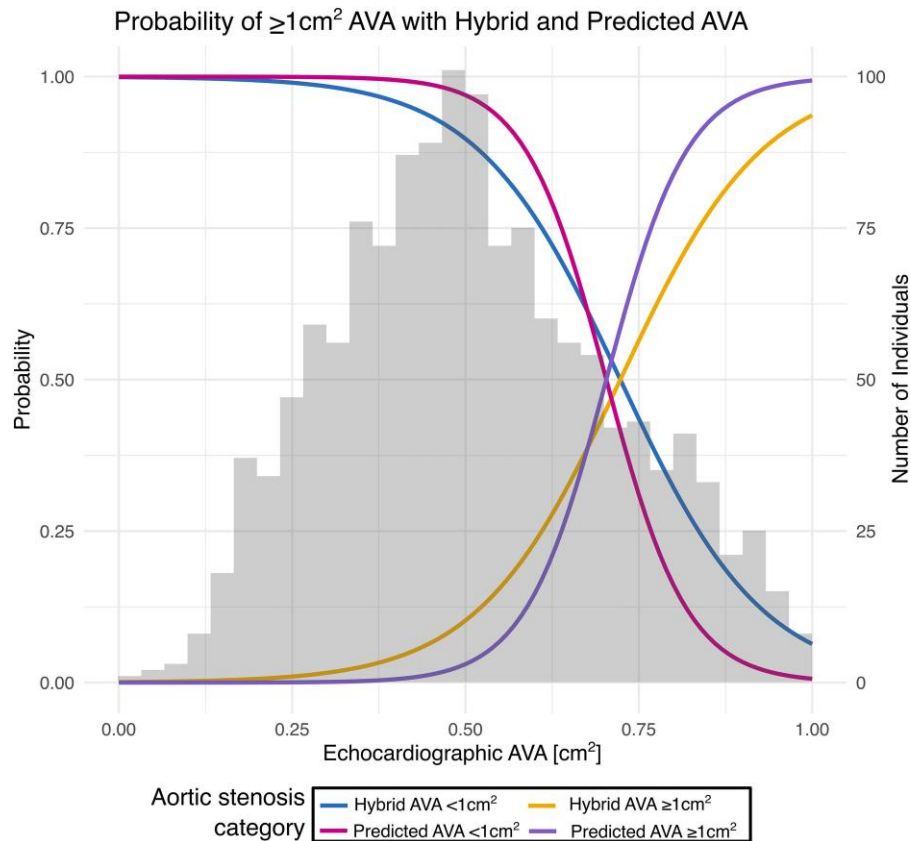


Figure 4 Probability of severe and non-severe AS based on hybrid and predicted AVA across the range of echo-derived AVA values, along with the distribution of echo-derived AVA values within the study population. Yellow line shows the probability of non-severe AS by hybrid AVA and lilac line corresponds to the probability of non-severe AS by predicted AVA across the echo AVA ranges. The grey histogram in the background shows the distribution of echo AVA values in our population of 1367 individuals.

The geometric orifice area can also be calculated using CT. However, it tends to overestimate the effective aortic valve orifice area,^{16,17} and is less reproducible, especially in the presence of heavy calcification.¹⁸ In addition, planimetry lacks outcome validation and may not reliably exclude pseudo-severe AS in low-flow, low-gradient conditions.

Additionally, in discordant cases where the AVA is <1.0 cm² but the mean transaortic gradient remains <40 mmHg, current guidelines recommend an integrative approach, including the assessment of the aortic valve calcium score (CaS) using non-contrast CT.¹ Although established cut-off values for aortic valve CaS (≥1200 AU for women and ≥2000 AU for men) were originally derived from high-gradient aortic stenosis population,¹⁹ recent studies suggest that these thresholds may have limited diagnostic accuracy in low-gradient settings.^{20,21}

While these methods may help to make clinical decisions, they require additional testing. The optimal solution would be to use information available at the time of echocardiography to identify individuals in whom clinical diagnosis of severe AS is less certain. To the best of our knowledge, we present the first study specifically designed to identify predictors of measurement error between echo- and CT-based LVOT area measurements. Our findings may assist clinicians in recognizing patients for whom conventional continuity estimations may be insufficient. Based on our results, male sex, taller height, as well as increased

end-diastolic and systolic volumes should be signs of possible measurement inaccuracies. Furthermore, we show that measurement error increases with LVOT diameter therefore, AVA values closer to 1 cm² are more prone to possible reclassification using the hybrid AVA technique. This leads to the reclassification of a substantial proportion of patients from severe to moderate AS, though this effect varies across AS subtypes. In the study by Kamperidis *et al.*,²² 12% of patients with low-flow, low-gradient AS and 52% of those with normal-flow, low-gradient AS were reclassified as having moderate AS based on an AVAi threshold of 0.6 cm²/m². Similarly, Weber *et al.* found that nearly half of patients with low-gradient AS were reclassified, compared to only 13% in the high-gradient group.²³ However, in both studies, the mean echo-derived AVA in low-gradient groups was closer to the reclassification threshold, potentially explaining the higher rates of reclassification as demonstrated in our study. Therefore, in our cohort, rather than emphasizing the extent of reclassification or its distribution among AS subtypes, we focused on identifying predictors associated with larger discrepancies between echocardiographic- and CT-based LVOT measurements, which may lead to greater measurement error in certain patients.

Only limited and conflicting data are available regarding the impact of reclassification on survival.^{9,23,24} In our study, patients who were reclassified to moderate AS based on hybrid AVA

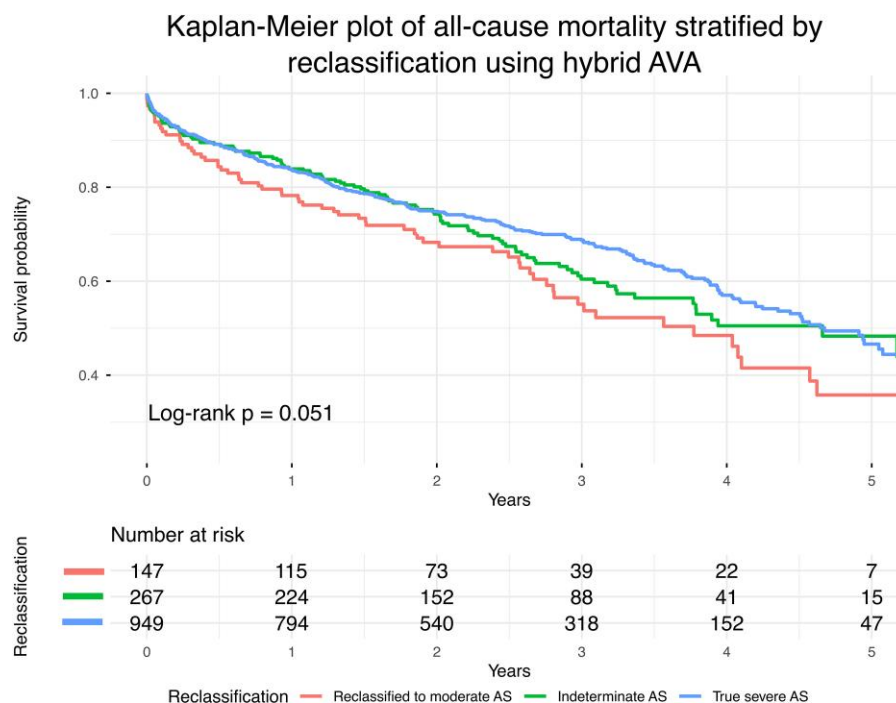


Figure 5 Kaplan-Meier survival analysis in the derivation cohort with comparison between groups stratified by hybrid AVA. Red line shows patients reclassified to moderate AS (hybrid AVA $>1.2 \text{ cm}^2$), green line indicates patients with indeterminate AS (hybrid AVA $1.0\text{--}1.2 \text{ cm}^2$), and blue line presents patients with true severe AS (hybrid AVA $<1.0 \text{ cm}^2$).

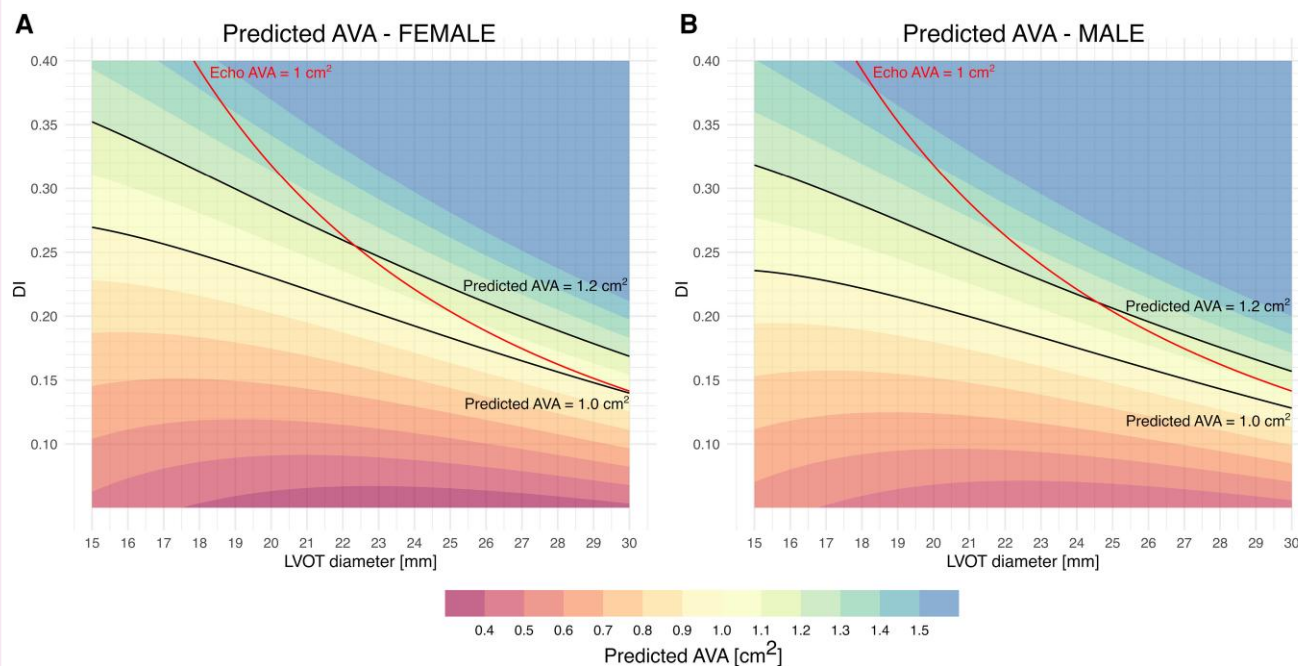


Figure 6 Predicted AVA values for different echocardiographic LVOT diameter and Doppler index values in females and males. (A) Represents predicted AVA values for female patients. (B) Predicted AVA values for male patients. The red contour line indicates the 1.0 cm^2 threshold of echo-derived AVA, while the black lines represent 1.0 and 1.2 cm^2 levels of the predicted AVA.

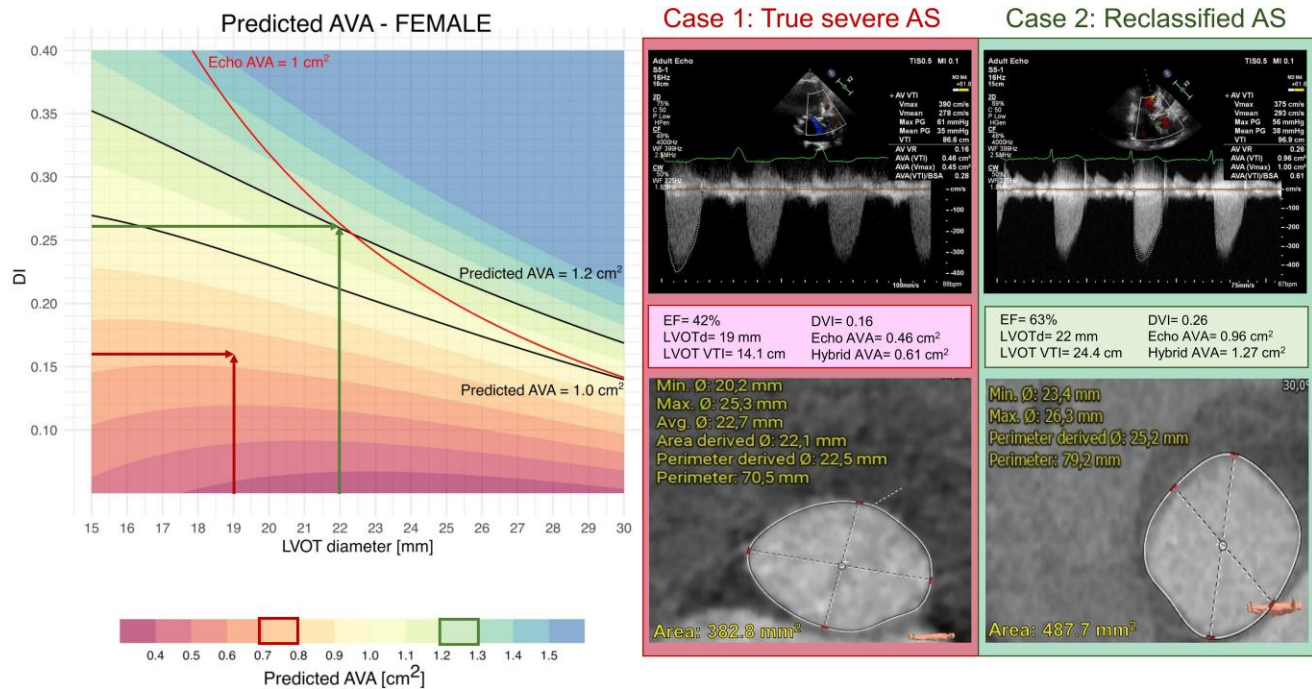


Figure 7 Application of the clinical chart illustrated by two representative cases. Case 1: A 77-year-old female with low-flow, low-gradient AS (AVA 0.46 cm²). Based on an LVOT diameter of 19 mm and a DI of 0.19, the clinical chart predicted a hybrid AVA of 0.7–0.8 cm². The value derived from direct CT LVOT measurement was 0.61 cm², indicating true severe AS. Case 2: A 90-year-old female with normal-flow, low-gradient AS (AVA 0.96 cm²). With an LVOT diameter of 22 mm and a DI of 0.26, the chart estimated a hybrid AVA of 1.2–1.3 cm². The CT-derived value was 1.27 cm², suggesting moderate AS.

calculation (hybrid AVA >1.2 cm²) showed a trend towards worse prognosis compared to those with true severe AS (hybrid AVA < 1 cm²) or those with indeterminate AS (hybrid AVA 1.0–1.2 cm²). Although the results were of borderline statistical significance, this group characterized by a high prevalence of reduced ejection fraction (46%) and low stroke volume index (54%) may represent a vulnerable population, and these findings warrant further investigation.

The optimal cut-off value for hybrid AVA is still controversial. Although previous retrospective studies used an AVAi threshold of 0.6 cm²/m² and observed no significant differences in mortality, these cohorts primarily consisted of patients who eventually underwent TAVI, which potentially influenced outcomes.^{22–24} In contrast, Clavel et al. studied 269 conservatively managed patients with severe AS and proposed a cut-off of 1.2 cm² for hybrid AVA, which provided a similarly strong prediction on mortality as the echo-derived AVA,⁹ and was recently confirmed by Zeb et al.²⁵ Considering that the hybrid AVA method has been shown to carry comparable prognostic value as the conventional echocardiographic AVA, our aim was to develop a model that can accurately predict the hybrid AVA already after the initial echocardiographic examination. This approach may help identify patients who require further testing, while also sparing others from unnecessary investigations and reducing healthcare costs.

Our study has several limitations. As a retrospective analysis of prospectively collected observational data, the findings may be influenced by residual confounding and may not be fully generalizable to broader populations. In the present study, we did not index the LVOT area to BSA, instead, BSA was evaluated

as an independent predictor in the regression analyses. As BSA did not emerge as a significant predictor in the multivariable regression model, neither the LVOT area nor the AVA was indexed to BSA in further analyses. The prognostic value of our predicted AVA is substantially influenced by the fact that all patients in our cohort underwent TAVI; therefore, optimal cut-off values cannot be established. The clinical utility and prognostic significance of our predicted AVA model need to be validated in large prospective, multicentre studies.

Conclusion

Our study demonstrated that echocardiographic assessment significantly underestimates the LVOT area compared to CT, leading to the reclassification of nearly one-third of patients to a non-severe AS category when applying a hybrid approach. We identified key patient characteristics and echocardiographic predictors of measurement error, irrespective of ejection fraction, flow state, or mean transvalvular gradient. These factors may assist clinicians in identifying those in whom continuity equation-based AVA calculations may be inaccurate. Our predicted AVA model demonstrated strong agreement with hybrid AVA values in a separate validation cohort. To support clinical implementation, we created a tool which provides predicted AVA values based on echocardiographic LVOT diameter and Doppler index, offering a practical alternative to CT-scan in the routine evaluation of AS severity in elderly patients undergoing TAVI assessment.

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Supplementary data

Supplementary data are available at [European Heart Journal - Imaging Methods and Practice](#) online.

Conflict of interest: M.K. receives consultation fees from Elucid Bioimaging Inc.

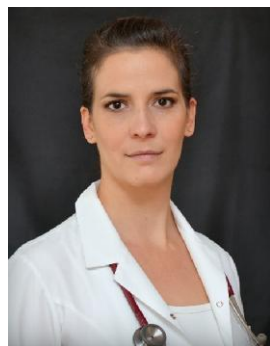
Data availability

The data and statistical code underlying this article will be shared on reasonable request to the corresponding author.

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