

Discordance in Grading Methods of Aortic Stenosis by Pre-Cardiopulmonary Bypass Transesophageal Echocardiography

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BACKGROUND: Current guidelines define severe aortic valve stenosis (AS) as an aortic valve area (AVA) ≤ 1.0 cm² by the continuity equation and mean gradient (ΔP_m) ≥ 40 mm Hg. However, these measurements can be discordant when classifying AS severity. Approximately one-third of patients with normal ejection fraction and severe AS by AVA have nonsevere AS by ΔP_m when measured by preoperative transthoracic echocardiography (TTE). Given the use of positive pressure ventilation and general anesthesia in the pre-cardiopulmonary bypass (pre-CPB) period, we hypothesized that discordance between ΔP_m and AVA during pre-CPB transesophageal echocardiography (TEE) would be higher than previously reported by TTE.

METHODS: We retrospectively examined pre-CPB TEE data for patients who had aortic valve replacement, with or without coronary artery bypass grafting, from 2000 to 2012. Patients were excluded if they had ejection fraction $< 55\%$, emergency surgery, repeat sternotomy, moderate or severe mitral regurgitation, or severe aortic regurgitation. Only patients with both pre-CPB AVA and ΔP_m measurements were included. Patients were grouped according to severity (mild, moderate, and severe) by AVA or ΔP_m . Discordance was defined as disagreement between severities based on either parameter.

RESULTS: A total of 277 patients met inclusion criteria. There were 227 patients with AVA ≤ 1.0 cm². The proportion of these patients with a $\Delta P_m < 40$ mm Hg was 54% (95% confidence interval, 47%–61%). The rate of discordance was significantly higher than the rate (37%; $P < 0.001$) found in previously reported analyses using TTE. Of the patients with a $\Delta P_m \geq 40$ mm Hg, only 8% ($n = 9/113$) had a discordant AVA. In contrast, of the patients with $\Delta P_m < 40$ mm Hg, 80% ($n = 131/164$) had a discordant AVA.

CONCLUSIONS: We confirmed our hypothesis that grading AS by ΔP_m and AVA during pre-CPB TEE exhibits higher discordance than reported for TTE by others. It remains unclear whether these discrepancies reflect the effect of general anesthesia, imaging modality (TTE versus TEE) differences, inaccuracies in AS grading cutoffs when applied to pre-CPB TEE, or selection bias of the surgical population. (Anesth Analg 2016;122:953–8)

Grading aortic valve stenosis (AS) can be challenging because of inconsistencies between the methods used to assign severity. For example, during transthoracic echocardiography (TTE), approximately 22% to 37% of patients with normal left ventricular ejection fraction (LVEF) and an aortic valve area (AVA) ≤ 1.0 cm², which represents severe AS, have a mean gradient (ΔP_m) < 40 mm Hg, which represents nonsevere AS.^{1–5} Similarly, cardiac

catheterization data exhibit a discordance rate of 25% when grading AS in similar patients.⁵ These inconsistencies have been attributed to stroke volume variability, despite normally appearing left ventricular (LV) function, small LV size, diastolic dysfunction, chronic afterload changes from hypertension, and underestimation of AVA secondary to the erroneous assumption that the left ventricular outflow tract (LVOT) is a circle rather than an ellipse.^{6–12} Inconsistent AS grading is problematic because misinterpretation of grading parameters may delay surgical intervention and negatively affect patients.^{1–3}

AS severity is defined by the following echocardiographic parameters: peak velocity, ΔP_m , AVA by continuity equation, dimensionless index, and indexed AVA (Table 1).^{13,14} The 2014 American Heart Association/American College of Cardiology guidelines for the management of patients with valvular heart disease present an algorithmic approach for echocardiographic assessment of AS.¹⁴ In a patient with an abnormally appearing aortic valve, peak velocity or ΔP_m is used initially to determine whether the valve meets criteria for aortic valve replacement (AVR). Subsequently, the presence of symptoms, LVEF, and AVA stratify valves appropriate for AVR.¹⁴ Of note, peak velocity and ΔP_m are primary measurements obtained directly by Doppler echocardiography. Meanwhile, the AVA continuity equation calculation depends on accurate measurement of the LVOT diameter, as well as velocity measurements through the LVOT and

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Accepted for publication October 4, 2015.

Funding: None.

The authors report no conflicts of interest.

The abstract for this research report was previously presented, in part, at the 2014 Society of Cardiovascular Anesthesiology National Meeting in New Orleans, LA (Abstract was selected for oral presentation).

Reprints will not be available from the authors.

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DOI: 10.1213/ANE.0000000000001099

Table 1. Aortic Stenosis Grading Limits

Measurement	Mild	Moderate	Severe
Peak velocity (m/s)	<3.0	3.0–4.0	>4.0
Mean gradient (mm Hg)	<20	20–40	≥40
Aortic valve area (cm ²)	>1.5	1.0–1.5	≤1.0
Indexed valve area (cm ² /m ²)	>0.85	0.60–0.85	<0.6
Dimensionless index	>0.50	0.25–0.50	<0.25

Adapted from Baumgartner et al.¹³ and Nishimura et al.¹⁴

aortic valve. For this reason, AVA calculation is prone to error compared with a ΔP_m measurement.

Although inconsistencies for grading AS with AVA and ΔP_m are well known for preoperative TTE, they are routinely used for grading AS in the pre-cardiopulmonary bypass (pre-CPB) context. In this study, we investigate the frequency of discordance between grading AS with ΔP_m measurements and AVA calculations during pre-CPB transesophageal echocardiography (TEE) to provide insight into their reliability for pre-CPB assessment of AS severity. Conventional AS severity cutoffs were derived from TTE studies performed in awake, spontaneously breathing patients.^{14–18} However, cardiac anesthesiologists perform pre-CPB TEE in anesthetized patients receiving positive pressure ventilation. Because general anesthesia and positive pressure ventilation may influence cardiac loading conditions, we hypothesized that grading discordance by pre-CPB TEE would be higher than previously reported for TTE by others.

METHODS

We obtained Duke University IRB approval, which granted waiver of consent to perform a retrospective database study for information collected between January 1, 2000, and December 31, 2012. This study was an investigator-initiated, single-center, retrospective review of the Duke University, Department of Anesthesiology perioperative echocardiography-reporting database. This database includes all adult patients who have undergone cardiac surgery at Duke University Medical Center and had a TEE report generated electronically since January 1, 2000. The Duke Health Information Technologies Solutions (DHITS) Perioperative Development Group (PDG) maintains the reporting system. A cardiothoracic anesthesiology fellow, attending, or both, generated TEE reports as part of a dedicated perioperative echocardiography training program. All imaging and reports were subsequently reviewed offline by an independent cardiothoracic anesthesiologist to confirm the accuracy of the report.

Subject Selection

We reviewed all patients in the database, who underwent AVR with or without coronary artery bypass grafting from January 1, 2000, until December 31, 2012. Patients were included if the echocardiographer reported both a pre-CPB ΔP_m and an AVA. Patients were excluded if they had emergency surgery or repeat sternotomy. Patients were also excluded if they had an ejection fraction <55%, moderate or severe mitral regurgitation (MR), or severe aortic insufficiency (AI).

Definitions of Variables

Two variables, ΔP_m and AVA, were obtained according to standard practice guidelines established by the American Society of Echocardiography.¹³ The ΔP_m was obtained in

either the deep transgastric long-axis or the transgastric long-axis view with the continuous wave Doppler beam aligned as parallel as possible to the direction of blood flow. The AVA was calculated by application of the continuity equation:

$$AVA(\text{cm}^2) = \frac{(0.785(\text{LVOT Diameter})^2) \times (\text{VTI}_{\text{LVOT}})}{(\text{VTI}_{\text{Aortic Valve}})}$$

Individual measurement of the LVOT diameter was done in the mid-esophageal long-axis view. LVOT velocity time integral and aortic valve velocity time integral were each measured via pulsed wave Doppler or continuous wave Doppler, respectively, in the deep transgastric long-axis or transgastric long-axis views. All measured parameters were obtained per protocol, which required measurements in temporal succession and during normotension (systolic blood pressure < 140 mm Hg, >100 mm Hg), postinduction of anesthesia before sternotomy.

The echocardiographer caring for the patient initially determined LVEF, while a reviewing echocardiographer confirmed this assessment offline. Various modes of assessment were used, including visual inspection, the Simpson method of disks, fractional shortening, or 3D echocardiographic full-volume reconstruction.

Statistical Analysis

IRB approval was obtained in early 2013; therefore, we collected retrospective data as far as possible, up through December 31, 2012. Pre-CPB TEE ΔP_m and AVA values were extracted for all patients meeting clinical inclusion criteria. These values were grouped according to AS severity (mild, moderate, and severe) and compared for discordance rates based on current grading guidelines for ΔP_m and AVA. Values were considered “discordant” if there was disagreement between severities based on either parameter. The discordant proportions of ΔP_m and AVA by AS severity were calculated by dividing the number of cases in each cell of a 2-way table by the marginal total of each severity category. Confidence intervals of 95% for each discordance rate were computed using Newcombe-Wilson tests with continuity correction.^{19,20} All statistical analyses were performed using SAS version 9.3 (SAS Institute, Inc., Cary, NC). To specifically test our hypothesis, the discordance rate of low-gradient, severe AS (AVA ≤ 1.0, ΔP_m < 40) was compared with the discordance rate found for a similar population via TTE (37%) by Minners et al.⁵ using the Fisher exact test.

In addition, AVA (y-axis) data points were plotted against ΔP_m (x-axis) and a curve (Fig. 1) was fit to the data based on the relationship:

$$AVA = \frac{C}{\sqrt{\Delta P_m}}$$

This relationship, as well as the derivation of the coefficient, C, has been described in detail elsewhere.⁵ We used nonlinear regression analysis (SAS Proc MODEL, SAS 9.4) to estimate C, accompanied by its standard error value. The distribution of residuals was approximately normal without correlation between the residuals and another predictor.

RESULTS

After applying all patient selection criteria, 277 patients had both AVA and ΔP_m available for analysis (Fig. 2). The demographic data for the study population of 277 patients are summarized in Table 2. In this population, 227 patients had an AVA ≤ 1.0 cm². Of these patients, 54% (95% confidence interval [CI], 47%–61%) had a discordant ΔP_m (Table 3), which is significantly higher than the discordance rate for AVA ≤ 1.0 cm² reported by Minners et al.⁵ (37%; $P < 0.001$) for TTE.

When ΔP_m was ≥ 40 mm Hg, only 8% (95% CI, 4%–15%) of patients had a discordant AVA (AVA > 1.0 cm²). In contrast, when ΔP_m was between 20 and 40 mm Hg ($n = 145$) and consistent with moderate AS, 84% (95% CI, 77%–89%) of patients had an AVA consistent with either severe ($n = 119$) or mild ($n = 3$) AS. When ΔP_m was < 40 mm Hg, the discordance rate was 80% ($n = 131/164$; Table 3). We found an overall discordance rate of 140/277, 51% (95% CI, 45%–57%) in the study population. This rate reflects grouping of all grades (mild, moderate, or severe) of AS by either ΔP_m or AVA. There were expectedly small numbers of patients categorized as mild AS by ΔP_m ($n = 19$) or AVA ($n = 14$) because the study incorporated only patients receiving valve replacement.

AVA was plotted against ΔP_m and a modeling curve was fit ($R^2 = 0.42$) to the data as described in the Methods (Fig. 1). The result for coefficient, C , for modeling the data via the relationship, $AVA = C/\sqrt{(\Delta P_m)}$, was 4.83 (SE, 0.096). Lines of demarcation for currently accepted cutoffs for severe AS were superimposed over the data.

DISCUSSION

We confirmed our hypothesis that discordance between ΔP_m and AVA was higher during pre-CPB TEE compared

with preoperative TTE, as reported in the literature. We obtained a discordance rate of 54% for patients when AVA ≤ 1.0 cm² and an overall discordance rate across all grades of AS of 51%. When ΔP_m was < 40 mm Hg, 80% of patients exhibited a discordant AVA. Conversely, when ΔP_m was ≥ 40 mm Hg, only 8% of patients exhibited a discordant AVA (Table 3). Modeling our data illustrates how pre-CPB values of ΔP_m and AVA diverge from guideline grading cutoffs (Fig. 1).

Substantially increased discordance when $\Delta P_m < 40$ mm Hg during pre-CPB TEE suggests that either pre-CPB TEE ΔP_m is, on average, lower relative to preoperative TTE ΔP_m , or pre-CPB TEE AVA calculations are, on average, lower relative to preoperative TTE AVA calculations or both. General anesthesia is a potential culprit for such alterations in ΔP_m and AVA. For example, grading discrepancies between pre-CPB TEE and preoperative TTE MR grading have been well established; pre-CPB TEE underestimates MR severity, probably because of changes in loading conditions.^{21–24} Likewise, decreased loading may lead to underestimation of ΔP_m across the aortic valve while under general anesthesia. This consequence has practical importance because artificially low-gradient measurements despite normal LVEF could lead to confusion and underestimation of disease. This problem would be especially challenging in the case of incidental AS. Patients who classify as mild AS ($\Delta P_m < 20$) by pre-CPB might classify as moderate AS ($\Delta P_m \geq 20$), if they were undergoing TTE without general endotracheal anesthesia. Moderate AS in the setting of additional cardiac surgery is an indication for AVR.¹⁴

Loading conditions affect AVA calculations as well. In patients with AS, AVA by the continuity equation is inversely related to blood pressure because of changes in transvalvular flow.²⁵ Thus, without controlling for the effects of general anesthesia, one would expect pre-CPB TEE AVA calculations to yield different values than preoperative TTE AVA calculations in the same patients. Although factors such as LVOT diameter underestimation and beat-to-beat variability in blood flow make AVA calculations prone to error, these problems affect both preoperative TTE and pre-CPB TEE and do not explain increased discordance during pre-CPB TEE.^{26,27} A comparison between preoperative TTE and pre-CPB TEE for both AVA and ΔP_m values is warranted to see which parameter drives discordance during pre-CPB TEE. Similarly, the impact of general anesthesia on AVA calculations and ΔP_m measurements during pre-CPB TEE requires further investigation.

Limitations

The strength of our study lies in our quality-assured echocardiography database, including a large patient population over a 12-year period in a high-volume cardiothoracic surgery center. However, the study is limited by its retrospective design and inability to control for cardiac output, transvalvular flow, LV size, blood pressure, heart rate, and arterial compliance. Such data points were not tied to the echocardiographic data and would be impractical to obtain retrospectively. Nevertheless, the sample size is relatively large, which should distribute this unpredictability

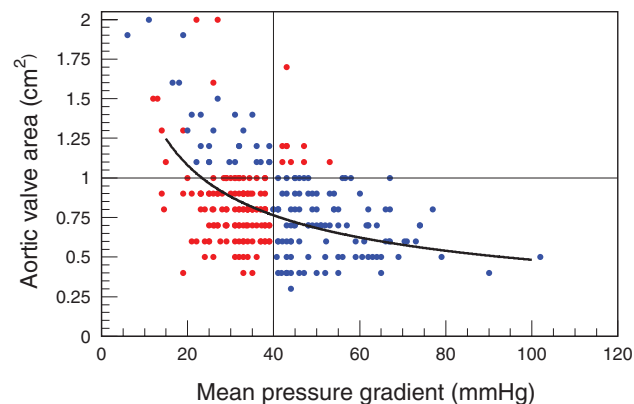


Figure 1. Aortic valve area (AVA) versus mean gradient (ΔP_m) during pre-cardiopulmonary bypass transesophageal echocardiography. A scatter plot of aortic valve stenosis (AS) grading parameters, AVA versus ΔP_m , for study subjects. Red data points represent discordant data, disagreement of AS severity based on either parameter according to current guideline cutoffs for all grades of AS.^{13,14} Blue data points represent concordant data. A nonlinear regression curve (modeled by the equation, $AVA = 4.83/\sqrt{(\Delta P_m)}$) is shown fit ($R = 0.42$) to the data. The plot is divided into quadrants at the demarcation of severe AVA ≤ 1.0 cm² and $\Delta P_m \geq 40$ mm Hg. Cutoff lines highlight areas of high concordance and discordance. Using an AVA = 1.0 cm² in our model gives a ΔP_m of 23.3 mm Hg, whereas using $\Delta P_m = 40$ mm Hg provides an AVA of 0.76 cm². Note that at high ΔP_m s ($\Delta P_m \geq 40$ mm Hg), there is excellent concordance with AVA and at lower ΔP_m s ($\Delta P_m < 40$ mm Hg), there is substantial discordance.

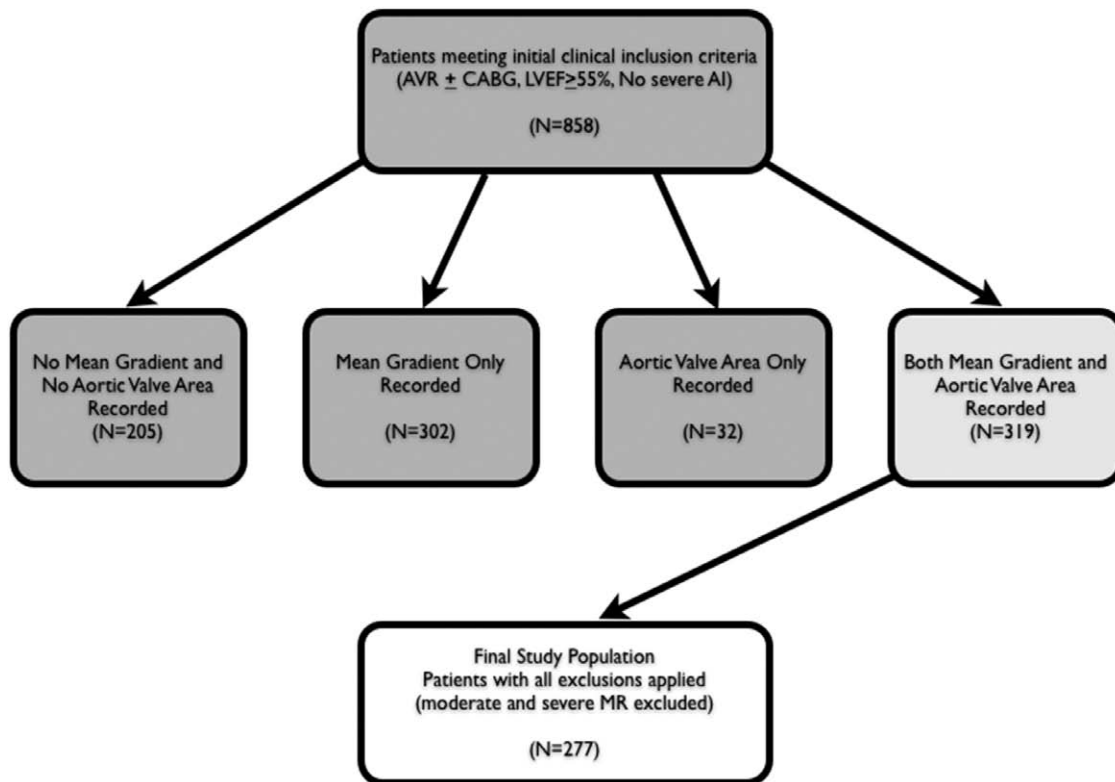


Figure 2. Patient study population. Flow diagram showing breakdown of patients meeting inclusion criteria, as well as availability of mean gradient and aortic valve area values. AI = aortic insufficiency; AVR = aortic valve replacement; CABG = coronary artery bypass grafting; LVEF = left ventricular ejection fraction; MR = mitral regurgitation.

Table 2. Patient Demographics

Characteristic	n = 277
Age at surgery, y ^a	69.1 ± 11
Male sex, n (%) ^b	151 (54.5)
Body mass index, kg/m ^{2a,c}	30.2 ± 6
Surgical procedure, n (%) ^b	
AVR	177 (63.9)
CABG + AVR	100 (36.1)
Aortic insufficiency, n (%) ^b	
None/trace	109 (39.3)
Mild	90 (32.5)
Moderate	78 (28.2)
Mitral insufficiency, n (%) ^b	
None/trace	240 (86.6)
Mild	37 (13.4)

AVR = aortic valve replacement; CABG = coronary artery bypass grafting.

^aData presented as mean ± SD.

^bData presented as frequency in the population.

^cn = 256 for body mass index because of missing data.

randomly across both discordant and concordant patients, thus limiting a systematic error.

In addition, we did not retrieve the reference method for the preoperative AS grade determination. Similarly, we did not include data on the qualitative appearance of the valves. It is unclear whether this information may have affected ΔP_m , AVA, or discordance between the two.

Two notable parts of our methods differ from guideline cutoffs and the preoperative TTE study used for comparison. First, the cutoff for LVEF in the AS grading guideline algorithm is 50%.¹⁴ However, we used 55% as an LVEF

cutoff because our database was constructed with cutoffs in 10% intervals beginning at <15% and ending at >55%. Because individual values were not reported, a group of patients with an LVEF >50% would not have been retrievable. Because we used a stricter estimate of “normal” LVEF (>55% vs 50%), this difference by itself would unlikely select for patients with lower ΔP_m and higher rates of discordance. Second, moderate AI was not excluded in our study. Moderate AI, however, would increase ΔP_m ; therefore, including such patients might underestimate the rate of discordance in pre-CPB TEE.

Finally, the method for determining left ventricular systolic function was not standardized for each study patient. Some of the examinations likely had patients labeled as normal systolic function by visual inspection alone, which leaves the assessments open to the judgment of the reviewing echocardiographer. Further prospective work is necessary to better control for such potential confounders.

CONCLUSIONS

Our study questions the reliability of applying current TTE-derived AS grading cutoffs to pre-CPB TEE ΔP_m measurements and AVA calculations. Given these problems, cardiac anesthesiologists must not overlook qualitative 2D assessment and other parameters for grading AS. Until there is a reliable, validated method for correlating preoperative TTE with pre-CPB TEE values, alternate grading methods that account for differences in loading conditions and LV size should be considered. Further work is necessary to accurately interpret pre-CPB grading values when applying TTE

Table 3. Discordance Between Aortic Valve Area and Mean Pressure Gradient Measurements During Pre-Cardiopulmonary Bypass Transesophageal Echocardiography

AS by mean gradient (ΔP_m ; mm Hg)	Aortic stenosis by aortic valve area (AVA; cm^2)			All	Discordance rate (%)	95% CI
	>1.5 (mild)	1 < AVA < 1.5 (moderate)	<1.0 (severe)			
<20 (mild)	10	5	4	19	9/19 (47%)	25%–70%
20 \leq ΔP_m <40 (moderate)	3	23	119	145	122/145 (84%)	77%–89%
\geq 40 (severe)	1	8	104	113	9/113 (8%)	4%–15%
All	14	36	227	277		
Discordance rate (%)	4/14 (29%)	13/36 (36%)	123/227 (54%)		140/277 (51%)	
95% Confidence Interval	10%–58%	21%–54%	47%–61%*			45%–57%

AS = aortic stenosis; AVA = aortic valve area; CI = confidence interval; ΔP_m = mean gradient.

Bold data show discordance rate in pre-cardiopulmonary bypass TEE for patients with AVA < 1.0 cm^2 . Italicized data highlights numbers of discordant patients in each severity category.

* $P < 0.001$; P value reflects comparison of study patients with the discordance rate for AVA \leq 1.0 cm^2 reported for preoperative transthoracic echocardiography by Minners et al.⁵

grading cutoffs and to determine whether pre-CPB TEE deserves a separate, standardized AS grading schema. ■■

DISCLOSURES

Name: George Whitener, MD.

Contribution: This author helped design the study, conduct the study, analyze the data, and write the manuscript.

Attestation: George Whitener has seen the original study data, reviewed the analysis of the data, approved the final manuscript, and is the author responsible for archiving the study files.

Name: Jeff McKenzie, MD.

Contribution: This author helped design the study, conduct the study, and write the manuscript.

Attestation: Jeff McKenzie has seen the original study data, reviewed the analysis of the data, and approved the final manuscript.

Name: Igor Akushevich, PhD.

Contribution: This author helped analyze the data and write the manuscript.

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