

Grading Aortic Stenosis With Mean Gradient and Aortic Valve Area: A Comparison Between Preoperative Transthoracic and Precardiopulmonary Bypass Transesophageal Echocardiography



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Objective: The authors hypothesized that average precardiopulmonary bypass (pre-CPB) transesophageal echocardiographic (TEE) mean gradient (PG_m) and aortic valve area (AVA) values would be significantly different from preoperative transthoracic (TTE) values in the same patients and that these changes would affect pre-CPB TEE grading of aortic stenosis (AS).

Design: Retrospective, observational design.

Setting: Single university hospital.

Participants: The study comprised 92 patients who underwent aortic valve replacement with or without coronary artery bypass grafting between 2000 and 2012 at Duke University Hospital and who had PG_m and AVA values recorded in both pre-CPB TEE and preoperative TTE reporting databases.

Interventions: None.

Measurements and Main Results: PG_m with pre-CPB TEE was lower by 6.6 mmHg (95% confidence interval, -4.0 to -9.3 mmHg; $p < 0.001$), whereas AVA was higher by 0.10 cm² (95% confidence interval, 0.04 to 0.15 cm²; $p < 0.001$), compared with preoperative TTE values. When using PG_m, pre-CPB TEE generated an AS severity 1 grade lower 39.1%

of the time and revealed no difference 55.4% of the time compared to preoperative TTE. When using AVA by continuity, pre-CPB TEE generated an AS severity 1 grade lower 14.1% of the time and revealed no difference 81.5% of the time compared to preoperative TTE. When using either PG_m or AVA, preoperative TTE exhibited moderate or severe AS for all study patients, whereas, pre-CPB TEE demonstrated mild AS in 5.4% ($n = 92$) of patients.

Conclusions: The authors confirmed their hypothesis that pre-CPB TEE generates different PG_m and AVA values compared with preoperative TTE. These differences often underestimate AS severity. Hemodynamic standardizations or adjustments of pre-CPB TEE PG_m and AVA values may be necessary in anesthetized patients before assigning an AS grade using these parameters.

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KEY WORDS: aortic stenosis, aortic valve area, discordance, mean gradient, precardiopulmonary bypass (intraoperative) transesophageal echocardiography

PRECARDIOPULMONARY BYPASS (pre-CPB) transesophageal echocardiography (TEE) is essential for intraoperative assessment and surgical guidance during cardiac surgery. Although many patients come to the operating room with an extensive cardiac workup, pre-CPB TEE aortic valve assessment can affect surgical decision-making based on new findings during planned or emergency surgeries. According to a large retrospective review of 3,835 patients undergoing isolated coronary artery bypass grafting (CABG), 3.3% of patients had an unplanned aortic or mitral valve procedure added to the surgery based on pre-CPB TEE findings.¹ Of 1,823 patients

undergoing mitral valve surgery, 1.0% of patients underwent an unplanned aortic valve procedure based on incidental findings during pre-CPB TEE.¹ Given that surgical decisions can be based on pre-CPB TEE findings, accurate interpretation of grading parameters during the pre-CPB period is imperative.

The validated mean gradient (PG_m) and aortic valve area (AVA) grading cutoffs for aortic stenosis (AS) originate from studies that used transthoracic echocardiography (TTE) in spontaneously ventilating patients without the influence of general endotracheal anesthesia.²⁻⁶ Thus, anesthesiologists working with pre-CPB TEE must apply cutoffs derived from a different physiologic setting. The misapplication of TTE AS grading cutoffs during pre-CPB TEE could negatively affect patient care if the surgical plan is changed or erroneously unchanged based on pre-CPB TEE findings.

Given these concerns, the authors conducted a retrospective observational study comparing preoperative TTE PG_m and AVA values with pre-CPB TEE PG_m and AVA values for patients undergoing aortic valve replacement (AVR) with or without CABG. The authors hypothesized that average pre-CPB TEE PG_m measurements and AVA calculations would be significantly different from preoperative TTE values and that these differences would affect the grading of AS during pre-CPB TEE.

METHODS

After obtaining Duke University Institutional Review Board approval, which included a waiver of consent for a retrospective review, the authors obtained data for patients who underwent AVR for AS with or without CABG from January 1, 2000

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through December 31, 2012. Initial patients were identified from the Duke University Department of Anesthesiology perioperative echocardiography database, which includes pre-CPB TEE reports on all patients undergoing cardiac surgery at Duke University Medical Center during the specified time period.

Comparison reports for the same patients were obtained from the Duke Echocardiography Lab Database, which is a prospectively maintained digital archive of all echocardiograms performed at Duke University Hospital and satellite clinics since 1995. This is linked to a corresponding searchable reporting database populated with the information from the clinical interpretation for each study.

Patient Selection Criteria

The authors reviewed all reports in the pre-CPB TEE database of patients who underwent AVR for AS with or without CABG from January 1, 2000 to December 31, 2012. Patients were excluded if they underwent emergency surgery or repeat sternotomy. Patients with a reported left ventricular ejection fraction (LVEF) <55%, severe aortic insufficiency or moderate or severe mitral regurgitation also were excluded. The remaining patients were cross-referenced to the preoperative TTE database to compare PG_m and AVA values. Patients were included only if a TTE was performed within 6 months before surgery and the PG_m and AVA values were recorded for both TTE and TEE. If multiple TTE reports were available for the same patient within the 6-month window, the report nearest the date of surgery was used.

Variable Definitions and Echocardiographic Analysis

PG_m and AVA values were obtained retrospectively from the clinical reports for each echocardiography examination. At the authors' institution, these values are obtained regularly according to practice guidelines proposed by the American Society of Echocardiography.⁷ PG_m was obtained by integrating a continuous-wave Doppler tracing of flow across the aortic valve. For pre-CPB TEE, either the deep transgastric aortic valve long-axis view or the transgastric long-axis view was used to align the sample volume as parallel to blood flow as possible. For preoperative TTE, the flow across the aortic valve was examined from multiple windows including apical, suprasternal notch, and right parasternal views, with the highest gradient recorded. Standard, commercially available ultrasound machines recorded mean gradients after manual tracing of the continuous-wave Doppler waveform.

AVA was calculated via the continuity equation^{3,8} for both imaging modalities:

$$AVA(\text{cm}^2) = \frac{(CSA_{LVOT}) \times (VTI_{LVOT})}{VTI_{AV}}$$

where VTI is the velocity time integral.

To determine the cross-sectional area (CSA) of the left ventricular outflow tract (LVOT), the LVOT diameter was obtained using the midesophageal aortic valve long-axis view in pre-CPB TEE and using the parasternal long-axis view in preoperative TTE. LVOT diameters were obtained within 0.5 to 1.0 cm of the valve orifice at the location of the LVOT VTI measurement, as recommended by European Association of

Echocardiography/American Society of Echocardiography guidelines.⁹ CSA was estimated using the following formula: $CSA = \pi(d/2)^2$, where d is the LVOT diameter. VTIs of the LVOT and AVA were measured via pulsed-wave Doppler and continuous-wave Doppler, respectively. Parameters recorded during pre-CPB TEE were obtained according to institutional protocol during normotension (systolic blood pressure <140 mmHg to >100 mmHg) after induction of general anesthesia and before sternotomy. Parameters recorded during preoperative TTE were obtained during the patient's baseline hemodynamics at the time of the study.

All preoperative TTE examinations were performed and reviewed by cardiologists with level III training. All pre-CPB TEE examinations were obtained by or under the supervision of a cardiothoracic anesthesiologist certified by the National Board of Echocardiography (NBE) for special competence in advanced perioperative TEE. Pre-CPB examinations were performed in the context of a robust cardiothoracic anesthesiology fellowship program, which performs more than 1,500 examinations annually. In addition, all images and reports from pre-CPB examinations were read a second time by a separate, NBE-certified echocardiographer offline to ensure the accuracy of the report.

Statistical Analysis

After obtaining PG_m and AVA values for all patients meeting inclusion/exclusion criteria, the differences between PG_m and AVA during pre-CPB TEE versus preoperative TTE were calculated for each patient. Continuous data are represented as mean \pm standard deviation. Mean values for PG_m and AVA were compared using a paired t test. A p value <0.05 was considered significant. Standard deviations were calculated for the overall means of PG_m and AVA for TTE and pre-CPB TEE, and 95% confidence intervals (CI) were calculated for the mean differences of PG_m and AVA between the imaging modalities.

In addition, the authors constructed a table illustrating the number of patients whose AS grade changed between preoperative TTE and pre-CPB TEE when using either PG_m or AVA. Grading demarcations were taken from American College of Cardiology/American Heart Association and American Society of Echocardiography guideline recommendations.^{2,9} Grading cutoffs used for PG_m were ≥ 40 mmHg, 40 mmHg to ≥ 20 mmHg, and <20 mmHg for severe, moderate, and mild AS, respectively. Meanwhile, grading cutoffs for AVA were ≤ 1.0 cm², 1.0 to ≤ 1.5 cm², and <1.5 cm² for severe, moderate, and mild AS, respectively; p values for comparing the percentage of patients with a grade change in either direction compared with no change were calculated using 2-sided exact tests for binomial proportions.

RESULTS

A total of 277 patients met surgical inclusion criteria. Of those patients, 92 met inclusion criteria for this study, with an available preoperative TTE report for comparison (Fig 1). Patient characteristics for the final study population are summarized in Table 1. The comparative echocardiography results are summarized in Table 2. The mean PG_m using

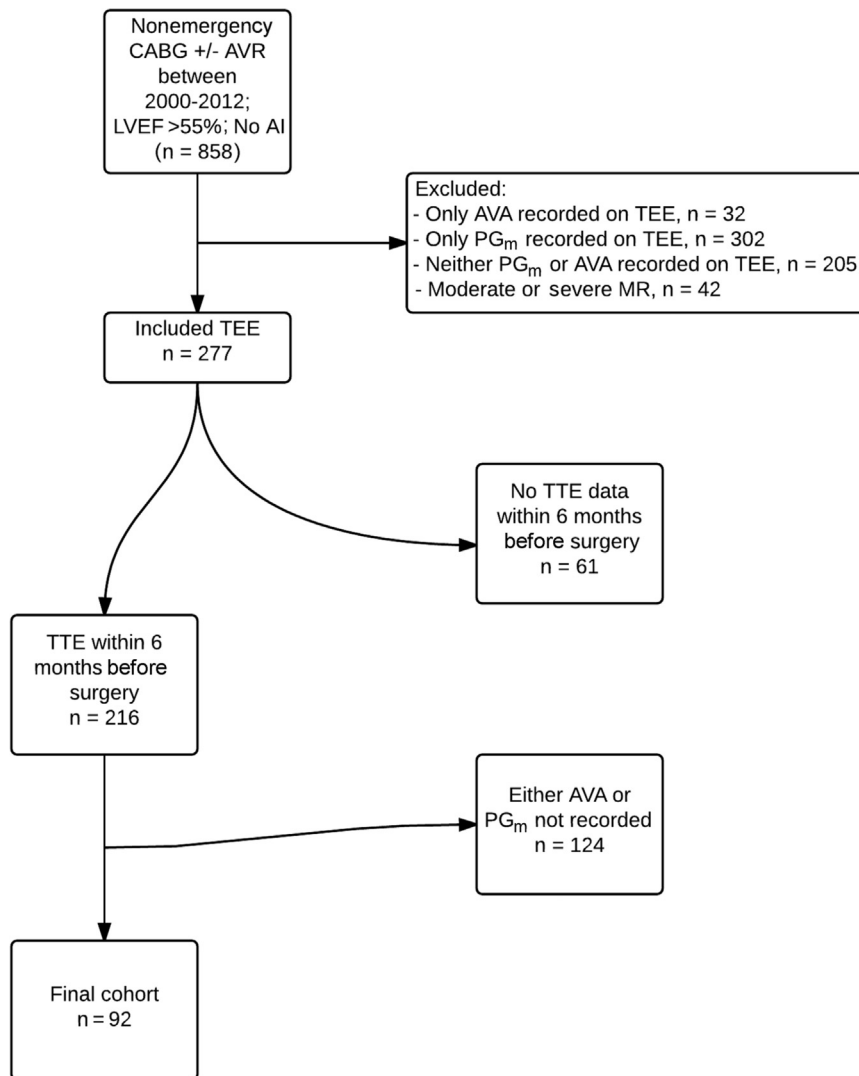


Fig 1. Flow diagram illustrating selection of the study population. AI, aortic insufficiency; AVA, aortic valve area; AVR, aortic valve replacement; CABG, coronary artery bypass grafting; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; PG_m, mean pressure gradient; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography.

preoperative TTE was 46.0 ± 14.3 mmHg, whereas the mean PG_m using pre-CPB TTE was 39.4 ± 14.1 mmHg. Thus, the average PG_m using pre-CPB TTE was significantly lower, by 6.6 mm Hg (95% CI, -4.0 to -9.3 mm Hg; $p < 0.001$), compared with the preoperative TTE value. Meanwhile, the average AVA during preoperative TTE was 0.73 ± 0.24 cm², whereas the average AVA during pre-CPB TTE was 0.83 ± 0.31 . Therefore, the average AVA using pre-CPB TTE was significantly higher, by 0.10 cm² (95% CI, 0.04 - 0.15 cm²; $p < 0.001$), compared with the preoperative TTE value.

Table 3 summarizes how these differences affected AS severity grading between preoperative TTE and pre-CPB TTE. When using PG_m, pre-CPB TTE generated an AS severity 1 grade lower than preoperative TTE 39.1% of the time, no difference 55.4% of the time, and 1 grade higher 5.4% of the time. Any change in severity was noted 44.5% of the time for PG_m. Alternatively, when using AVA, pre-CPB TTE generated

an AS severity 2 grades lower than preoperative TTE 1.1% of the time, 1 grade lower 14.1% of the time, no difference 81.5% of the time, and 1 grade higher 4.3% of the time. Any change in severity was noted 18.5% of the time for AVA. Finally, 5.4% ($n = 5/92$) of patients who experienced mild AS as classified by at least 1 grading parameter during pre-CPB TTE (2 patients were classified as experiencing mild AS using PG_m, 2 patients were classified as experiencing mild AS using AVA, and 1 patient was classified as experiencing mild AS using both parameters) experienced at least moderate AS or greater using both grading parameters during preoperative TTE.

DISCUSSION

The main findings of this study can be summarized as follows: (1) PG_m during pre-CPB TTE was 4.0 to 9.3 mmHg (95% CI; $p < 0.001$) lower compared with preoperative TTE; (2) AVA during pre-CPB TTE was 0.04 to 0.15 cm² (95% CI; $p < 0.001$) higher compared to preoperative TTE; (3) these

Table 1. Patient Demographics

Characteristic	n = 92
Age at surgery, years*	71.2 ± 11.9
Male sex, n (%)†	44 (48)
Body mass index, kg/m ² *	29.9 ± 6.2
Time from TTE to pre-CPB TEE, days‡	38.1 ± 37.8
Surgical procedure, n (%)†	
AVR	60 (65)
CABG + AVR	32 (35)
Aortic insufficiency, n (%)†	
None/trace	21 (23)
Mild	34 (37)
Moderate	28 (30)
Mitral regurgitation, n (%)†	
None/trace	74 (80)
Mild	18 (20)

Abbreviations: AVR, aortic valve replacement; CABG, coronary artery bypass grafting.

*Data are presented as mean ± standard deviation.

†Data are presented as frequency in the population.

‡n = 78 for body mass index, due to missing data.

differences imparted an underestimation of AS severity by 1 grade during pre-CPB TEE 39.1% and 15.2% of the time, when using PG_m and AVA, respectively; (4) 5.4% (n = 5/92) of patients were classified as experiencing mild AS by at least 1 grading parameter during pre-CPB TEE, even though the preoperative TTE exhibited moderate AS or greater for both grading parameters.

Recent American College of Cardiology/American Heart Association guidelines for management of patients with valvular heart disease provide an algorithm for AVR decision making.² This algorithm uses measurements to grade severity and provides recommendations for AVR for AS. The Doppler-derived PG_m or peak velocity are primary determinants of severity, whereas presence of symptoms, LVEF, and AVA by continuity equation are critical branch points along the decision tree. Also, patients undergoing cardiac surgery for another reason, who also experience moderate AS, have a class IIa indication for AVR.²

Grading AS accurately using PG_m and AVA, however, can be confusing due to the issue of grading discordance, defined as a difference in grading assignment between parameters.

Table 2. Mean Values of Aortic Stenosis Grading Parameters in Patients Undergoing AVR ± CABG

	Preoperative TTE (n = 92)	Pre-CPB TEE (n = 92)	Difference (n = 92)
Average mean gradient (mmHg ± SD)	46.0 ± 14.3	39.4 ± 14.1	-6.6* (p < 0.001)
Average aortic valve area (cm ² ± SD)	0.73 ± 0.24	0.83 ± 0.31	0.10† (p < 0.001)

Abbreviations: AVR, aortic valve replacement; CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; SD, standard deviation; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography.

*95% CI, -4.0 to -9.3 mmHg; p < 0.001.

†95% CI, 0.04-0.15 cm²; p < 0.001.

Table 3. Change in AS Severity Based on Imaging Context and Grading Parameter

	AS Grading Parameter Using Preoperative TTE (n = 92)	
	Mean Gradient (PG _m)	Aortic Valve Area (AVA)
Impact of pre-CPB TEE on AS grade		
1 grade higher	5 (5.4)*	4 (4.3)†
No change	51 (55.4)	75 (81.5)
1 grade lower	36 (39.1)‡	13 (14.1)‡
2 grades lower	0 (0.0)	1 (1.1)§
Any change	41 (44.5)‡	17 (18.5)‡

NOTE. Data are expressed as number (percentage).

p values for comparison of grade change to no change using 2-sided exact tests for binomial proportions:

Abbreviations: AS, aortic stenosis; AVA, aortic valve area; CPB, cardiopulmonary bypass; PG_m, mean pressure gradient.

*p = 0.02

†p = 0.04

‡p < 0.0001

§p = 0.3.

Grading discordance may occur even in the setting of normal LVEF because of reductions in left ventricular (LV) stroke volume unrelated to LV systolic function.¹⁰⁻¹⁴ A significant reason for grading discordance has been attributed to the existence of a distinct subtype of aortic valve disease, low-flow AS with preserved EF, also known as “paradoxical AS,” which can occur in patients with LV hypertrophy in the context of small LV size, right heart dysfunction, diastolic dysfunction, or moderate or severe mitral regurgitation.^{13,15-18}

Likewise, grading discordance is greater during pre-CPB TEE compared with preoperative TTE, even when controlling for LVEF and mitral regurgitation.¹⁹ Approximately 51% of patients undergoing AVR or AVR with CABG exhibit discordance between PG_m and AVA grading across all grades (mild, moderate, and severe) of AS during pre-CPB TEE.¹⁹ Therefore, general anesthesia with positive-pressure ventilation may predictably decrease LV stroke volume, thereby affecting AS assessment in a similar fashion to the other characteristics that lead to “paradoxical AS.” The gradient drop quantified in this study when comparing pre-CPB TEE with preoperative TTE was consistent with such reasoning. Further prospective work is necessary to confirm the effect of general anesthesia on AS grading parameters and to standardize pre-CPB TEE assessment to accurately grade AS, should incidental AS arise.

Because quantification of AS with mean gradient is highly dependent on beam alignment, suboptimal probe alignment or differences in alignment between TTE and pre-CPB TEE in the same patient could lead to discrepancies. For example, discrepancies based on apical versus nonapical views using TTE affect the highest velocity or gradient obtained.²⁰ Although the authors routinely used measurements from all viewing windows and recorded the highest value, it is unclear to what extent beam alignment, when transitioning from TTE to pre-CPB TEE, affected the values obtained.

There was a small, albeit statistically significant, difference between preoperative TTE and pre-CPB TEE AVA. AVA calculations notoriously are fraught with error and are

dependent on accurate LVOT diameter measurements.²¹⁻²³ Two-dimensional TTE LVOT measurements underestimate the true LVOT area, especially in patients with AS, who demonstrate less circular LVOTs.²² In addition, LVOT diameter measurements differ slightly between imaging modalities based on the different viewing windows, parasternal long axis and midesophageal long axis, for TTE and TEE, respectively. Shiran et al, for example, demonstrated that TTE underestimated LVOT diameter compared with TEE, which subsequently translated to a smaller AVA for TTE versus TEE.²⁴

As with mean gradient measurement, AVA calculation is highly dependent on accurate beam alignment with the direction of blood flow. The smaller impact on grading between TTE and TEE when using AVA calculations versus PG_m may be due to its integration of LV stroke volume, which could mitigate the hemodynamic changes imparted by anesthesia. Further work is necessary to delineate the impact of simultaneously moving from one clinical context and imaging modality to the next and to determine what is the best way to grade incidental AS, given the current practice of applying TTE-derived guideline cutoffs to pre-CPB TEE.

Limitations

The retrospective nature of this study limited the conclusions due to possible selection bias. However, the database search was large, spanning more than 1 decade, in a high-volume cardiothoracic surgical center, and was part of a dedicated perioperative echocardiography and cardiology fellowship-training program. Both preoperative TTE and pre-CPB TEE acquisition have standard protocols for image acquisition and accuracy enhancement through offline reviews by echocardiographers performing secondary assessments. All performing and reviewing echocardiographers for pre-CPB TEE received NBE special competence certification for advanced perioperative TEE.

Although an exclusion criterion of 6 months between TTE and pre-CPB TEE was used for study inclusion, the mean time from TTE to pre-CPB TEE was only 38.1 days (median time = 28 days) (see Table 1). Ideally, TTE would be performed simultaneously or as closely as possible to the time of pre-CPB TEE. However, the primary finding of this study showed that the mean gradient obtained during pre-CPB was lower than the mean gradient recorded during preoperative TTE. AS disease progression over the time span between imaging techniques would cause the mean gradient to increase in the absence of a decrease in ventricular systolic function.

The largest limitation in this study was the inability to control for cardiac output, arterial compliance, blood pressure, and other hemodynamic parameters. The echocardiographic data were not linked to real-time hemodynamics in a fashion that could be practically gleaned from intraoperative anesthetic records. Nevertheless, the sample size was large enough to distribute this unpredictability randomly across the population. The discrepancies seen in this study might be remedied if hemodynamics were normalized to values obtained at the time of preoperative TTE. Such a possibility, however, highlights

the fact that no current guidelines suggest that pre-CPB echocardiographers perform such a maneuver to grade AS intraoperatively. If changes in PG_m and AVA between preoperative TTE and pre-CPB TEE are the result of easily predictable and modifiable hemodynamic changes brought about by general anesthesia, these findings illustrate the need for further work to quantify such changes to standardize pre-CPB TEE for accurate AS assessment.

Clinical Relevance

Finding modest changes in grading assessment during pre-CPB TEE should not prompt a change in surgical planning if an echocardiographer discovers that such differences conflict with known, quality preoperative TTE (or TEE)-based grading. However, some patients present to cardiac anesthesiologists with incomplete, lost, poor quality, or old cardiac evaluations. Therefore, comparing pre-CPB TEE with preoperative TTE grading parameters provides an important framework for echocardiographers who identify incidental or previously unrecognized AS during pre-CPB TEE.

In this study, patients undergoing AVR demonstrated moderate or greater AS by both parameters during preoperative TTE; meanwhile, 5.4% ($n = 5/92$) of patients exhibited mild AS based on at least 1 grading parameter during pre-CPB TEE. In a patient undergoing CABG or mitral valve surgery, moderate AS is an indication of AVR.² Therefore, artificial underestimation of AS severity using pre-CPB TEE can be problematic for a perioperative echocardiographer tasked with providing useful information to the surgical team in cases of incidental AS. These findings suggested that the effects of general anesthesia and positive-pressure ventilation during the pre-CPB period cannot be ignored during such conditions. These findings also called into question the commonly accepted superiority of PG_m measurements versus AVA calculations for AS assessment during pre-CPB TEE because PG_m differences between modalities affected a grade change more often than did AVA calculations.²⁵

CONCLUSIONS

Rigid application of current guidelines and TTE-based AS grading cutoffs to pre-CPB TEE PG_m and AVA values should be performed with caution in the setting of incidental AS. Alternatively, once precise mechanisms for discrepancies of PG_m and AVA between preoperative TTE and pre-CPB TEE are clarified, hemodynamic alterations or mathematical conversions may be possible to accurately grade AS using AVA or PG_m during pre-CPB TEE. Meanwhile, 2-dimensional qualitative examination and other grading parameters, such as indexed AVA or dimensionless index, should not be overlooked in the setting of low PG_m during pre-CPB TEE AS assessment, given the potential confounding effects of general anesthesia. Further work is necessary to determine the best way to assign an AS grade during pre-CPB TEE should incidental AS arise.

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