Complete Transesophageal Assessment of the Aortic Valve Using the Continuity Equation in Equivocal Cases of Aortic Stenosis

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ABSTRACT **Background:** The continuity equation (CE) used for evaluating aortic stenosis (AS) is based on values obtained from transthoracic echocardiography (TTE) with the assumption that the left ventricular outflow tract (LVOT) has a circular shape. Transesophageal echocardiography (TEE) may be used for accurate measurement of the LVOT cross-sectional area (CSA). Previous studies have focused on fusion from TEE for LVOT-CSA measurement and TTE for velocity time integrals (VTI) calculations.

Objectives: To assess aortic valve area (AVA) using parameters obtained exclusively from TEE as an alternative approach.

Methods: Thirty patients with equivocal AS based on TTE were evaluated using TEE for further assessment.

Results: The mean pressure gradient across the aortic valve (AV) was 38 ± 5.9 and 37.9 ± 7.6 mmHg in TTE and TEE, respectively, $P = 0.42$. LVOT-CSA was larger in TEE (3.6 ± 0.3 vs. 3.4 ± 0.3 cm^2, $P = 0.049$). VTI over the AVA was similar (98.54 ± 22.8 and 99.52 ± 24.52 cm in TTE and TEE, respectively, $P = 0.608$), while VTI across the LVOT was higher when measured by TTE (24.06 ± 5.8 vs. 22.03 ± 4.3 cm, $P < 0.009$). Using the CE, AVA was 0.82 ± 0.3 vs. 0.83 ± 0.17 cm^2 in TEE vs. TTE, respectively, $P = 0.608$. Definitive grading was achieved in all patients (26 patients defined with severe AS and 4 with moderate).

Conclusions: In equivocal cases of AS, full assessment using TEE may be a reliable modality for decision making.

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KEY WORDS: aortic stenosis (AS), continuity equation (CE), echocardiography, pressure, velocity

Determining the grade of aortic stenosis (AS) as mild, moderate, or severe is critical for decision-making and may be challenging in some cases. Calculating aortic valve area (AVA) is based on measuring velocity time integrals (VTI) across the aortic valve (AV) and the left ventricular outflow tract (LVOT), in addition to estimating LVOT cross sectional area (CSA) and using the continuity equation (CE): AVA = (CSALVOT) × (VTILVOT) / VTIAV [1]. One of the major pitfalls of the CE is assuming that the LVOT has a circular shape, which is not correct in many cases [2]. Common modalities used for direct measurement of LVOT-CSA are transesophageal echocardiography (TEE), multidetector computed tomography (MDCT), and cardiac magnetic resonance imaging (CMR) [3-6]. In one study, LVOT-CSA measured by TTE was underestimated by 13%, resulting in 26.3% reduction in AVA compared to TEE in candidates for transcatheter aortic valve replacement (TAVR) [7]. Moreover, several studies showed underestimation of LVOT-CSA in 2-dimensional compared to 3-dimensional echocardiography, translated into reclassification of AS grade [8-10]. During TEE, the visualization of the LVOT may be optimized in the mid-esophageal long axis view. In addition, continuous-wave doppler and pulse-wave doppler in the deep transgastric view enable accurate measurements of the VTI across the AV and the LVOT respectively [11]. Previous studies focused on fusion data using TEE for accurate LVOT-CSA measurements and TTE for VTI calculation and subsequent use of the CE. In the current study, we assessed the severity of AS in equivocal cases using parameters obtained exclusively from TEE, including LVOT-CSA and VTI across the AV and LVOT, as an alternative approach to other modalities such as MDCT and CMR.

PATIENTS AND METHODS

STUDY POPULATION

In this retrospective study, 38 consecutive patients with equivocal AS (in which the severity of AS was not clear due to poor image quality) between 2016 and 2018, were evaluated in the cardiology unit at the Galilee Medical Center using TTE and TEE. The TTE and TEE were performed within one week of each other. Four patients with other significant valvular disease such as severe aortic regurgitation and severe mitral regurgitation, one patient in whom the aortic valve disease was demonstrated during an acute infective endocarditis, one patient with reduced ejection fraction (EF < 40%), and two patients with poor quality of the echocardiographic parameters were all excluded from the analysis. Thirty patients were included in the final analysis. All echocardiographic parameters were conducted in accordance with current guideline of valvular heart disease [12]. Informed consent was obtained from all patients or their legal guardians. The study was approved by the institutional review board of Galilee Medical Center.

Table 1. Patient characteristics

Characteristic	Value
Age in years	76 ± 11
Male	15 (50%)
Weight (kg)	70.5 ± 13.2
Height (m)	162.3 ± 10
Body mass index (kg/m^2)	27 ± 6
Body surface area (m^2)	1.75 ± 0.2
Ischemic heart disease	14 (46.7%)
Diabetes mellitus	8 (26.7%)
Hypertension	18 (60%)
Hyperlipidemia	18 (60%)
Atrial fibrillation	2 (6.7%)
Chronic kidney disease*	14 (46.7%)
Tobacco smoking	8 (26.7%)
Prior stroke	4 (13.3%)

*defined as eGFR < 90 ml/min

ECHOCARDIOGRAPHIC MEASUREMENTS

All patients underwent TTE and TEE by the same cardiologist (echocardiography specialist, AS) using Philips Epiq-7 machine and EPIQ X8-2t transducer (Phillips, Adnover, MA, USA). Measurements during TTE were obtained as follows: VTI over the AV and the LVOT in the 5-chamber view using continuous and pulsed wave Doppler, respectively. The LVOT-CSA was calculated with the assumption of a circular shape using the formula: CSA = π (D/2)2, D = diameter measured 0.5–1.0 cm from AV orifice in the parasternal long axis view). In addition, EF and pressure gradient (mean and maximal) across the AV (using continuous wave Doppler) were also obtained. During TEE, the LVOT-CSA was measured using 3-dimensional zoom in the mid-esophageal long axis view. The VTI (across the AV and LVOT) was obtained in the deep transgastric long axis view while the probe was positioned 50–60 cm in the stomach adjacent to the left ventricular apex followed by probe anteflexion toward the heart base and slow withdrawal. In the later view, both doppler continuous wave across the AV and pulse doppler wave across the LVOT were performed. The AVA was calculated us-

Figure 1. Velocity time integrals calculation and LVOT-CSA measurement during TEE

LVOT = left ventricular outflow tract, CSA = cross sectional area, TEE = transesophageal echocardiography, TTE = transthoracic echocardiography, VTI = velocity time integral

[A] Evaluation of the VTI across the LVOT using pulse wave Doppler in the deep transgastric or transgastric long axis view

[B] Evaluation of the VTI across the aortic valve using continuous wave Doppler in the deep transgastric or transgastric long axis view

[C] Measurement of LVOT-CSA during TEE using 3D zoom in the mid-esophageal long axis view. Direct visualization enables accurate assessment compared to TTE

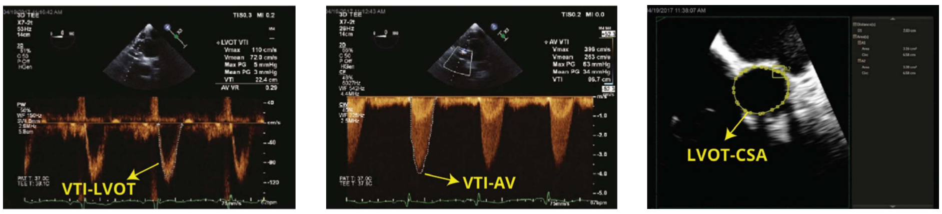

Figure 2. Study flow chart

AS = aortic stenosis, EF = ejection fraction, TEE = transesophageal echocardiography, TTE = transthoracic echocardiography

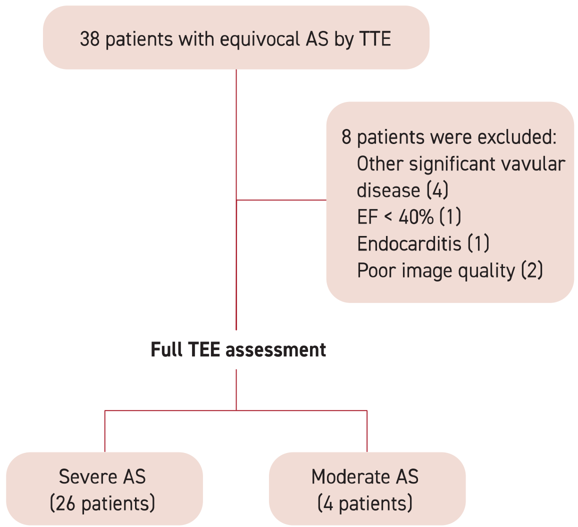

Table 2. Echocardiographic parameters obtained by TTE and TEE

	TTE	TEE	*P*-value
LVOT area (cm^2)	3.4 ± 0.3	3.6 ± 0.3	0.049
VTI (LVOT)	24.06 ± 5.8	22.03 ± 4.3	0.009
VTI (AV)	98.54 ± 22.8	99.52 ± 24.5	0.608
Mean AV pressure gradient (mmHg)	38 ± 5.9	37.9 ± 7.6	0.421
Ejection fraction (%)	49.1 ± 3	48.3 ± 3	0.6
Heart rate (beats/minute)	82.3 ± 7	80.2 ± 5	0.45
Systolic blood pressure (mmHg)	126.4 ± 12	124.1 ± 12	0.12

AV = aortic valve, LVOT = left ventricular outflow tract, TEE = transesophageal echocardiography, TTE = transthoracic echocardiography, VTI = velocity time integral

ing the CE: AVA (cm2) = (CSALVOT) X (VTILVOT) / VTIAV. Mild sedation was obtained during TEE using low doses of midazolam and propofol, with systolic blood pressure kept around 100–120 mmHg. Severe AS was defined as AVA < 1 cm2 whereas moderate AS was AVA of 1–1.4 cm2. Representative images of VTI (across the AV and LVOT) and LVOT-CSA measurement by TEE are shown in Figure 1.

STATISTICAL ANALYSIS

Categorical variables are expressed as percentages, and continuous parameters as means with standard deviation. Wilcoxon signed ranks test and paired sample t-test were used in results analysis. Pearson test was used to test the correlation between parameters when measured in the two modalities (TTE and TEE). We consider *P*-value < 0.05 significant for statistical analysis. All the statistical tests were performed using IBM SPSS Statistics, version 25. No local ethical approval was needed for the study.

RESULTS

After excluding 8 patients (4 with other significant valvular disease, 1 with EF < 40%, 1 with endocarditis, and 2 with poor image quality), we included a total number of 30 patients (15 males, 15 females) in the final analysis. Demographic and basic characteristics of the patients are shown in Table 1.

The LVOT-CSA was larger when measured in TEE than in TTE (3.6 ± 0.3 vs. 3.4 ± 0.3 cm2, *P* = 0.049), with spearman's rank correlation coefficient r = 0.68, *P* < 0.001) for the two modalities. The VTI over the LVOT was significantly higher in TTE compared to TEE (24.06 ± 5.8 vs. 22.03 ± 4.3 cm2/second, *P* = 0.009), with r = 0.68, *P* < 0.001, while VTI over the aortic valve did not differ between the two modalities (99.52 ± 24.52 vs. 98.54 ± 22.8 cm2/second, *P* = 0.608). Mean pressure gradient across the AV was similar in the two modalities (38 ± 5.9 and 37.9 ± 7.6 mmHg in TTE and TEE, respectively, *P* = 0.42). When applying values in the CE, the calculated AVA was 0.82 ± 0.3 and 0.83 ± 0.17 cm2 (based on TEE and TTE, respectively, *P* = 0.799). There was no correlation between the two methods for measuring AVA when using Pearson and Bland-Altman tests (r = 0.231, *P* = 0.219). Table 2 summarizes the echocardiographic measurements obtained in TTE and TEE.

In the final assessment of AS grade, 26 results were defined as severe and 4 as moderate. Figure 2 summarizes the study flow chart.

DISCUSSION

Accurate assessment of AS severity is a common clinical challenge in cardiology; thus, mandating a comprehensive approach for appropriate decision making. The most accepted way to assess AVA relies on the CE by applying the required parameters obtained from TTE. The following factors may limit the accuracy of this method: assumption of a circular shape of the LVOT (which was found to be incorrect in many cases), measurement of VTI across the LVOT not always accurate in TTE [13,14], and quality of the image not optimal in obese patients and in those with chronic pulmonary disease. It is well established that imaging modalities such as TEE, MDCT, and CMR are superior in measuring LVOT-CSA compared to TTE [3-6,15]. The fusion approach combining TEE or MDCT for measuring LVOT-CSA with TTE for calculating VTI across the AV and the LVOT is an acceptable approach to eliminate some of these limitations [16,17]. In this study, we assumed that obtaining all parameters during the same imaging modality would be more accurate than the fusion approach. This alternative strategy may be useful in equivocal cases of AS when accurate grading cannot be obtained due to poor echocardiographic windows, particularly in centers where MDCT and CMR are not available. Nanditha and colleagues [18] demonstrated a reduction in the mean pressure gradient and peak jet velocity across the AVA without change in AVA during intraoperative TEE compared to TTE in patients scheduled for elective AV replacement [18]. To determine the quality of this strategy in assessing AS, the accuracy and the feasibility of this method should be considered. These results may reflect acceptable accuracy and safety profile of the modality in classifying AS before decision making in equivocal cases. When performed by experts, full assessment of the AV based on the CE by TEE does not take longer than the standard TEE examination. In only two of our patients the measurements were unreliable for an accurate diagnosis needed to make a final decision, and therefore excluded.

LIMITATIONS

Although the small number of patients in our cohort may limit our conclusions, the idea of using TEE parameters in the CE is reasonable. The results may not be extrapolated to patients with active infection (endocarditis) and patients with other severe valvular disease or reduced LV function (EF < 40%), so they were excluded from our study. In two patients, the quality of the images was not adequate to obtain accurate alignment and subsequently they were excluded from the study. Last, the hemodynamic and the echocardiographic measurements are altered during TEE due to the effects of the sedative drugs. Although the patients were not connected to invasive continuous blood pressure monitor, blood pressure was kept at a narrow range of 110/70–120/80 mmHg in non-invasive measurements obtained every 3 minutes.

CONCLUSIONS

The use of the CE with parameters derived exclusively from TEE may be a reliable method for grading equivocal cases of AS, particularly when MDCT is not available.

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For me, words are a form of action, capable of influencing change.

Ingrid Bengis (1944–2017), writer and teacher

We allow our ignorance to prevail upon us and make us think we can survive alone, alone in patches, alone in groups, alone in races, even alone in genders.

Maya Angelou (1928–2014), American poet, memoirist, and civil rights activist

Capsule

A series of unfortunate events

The severe acute respiratory syndrome coronavirus 2 (SARSCoV- 2) pandemic was marked by waves of new strains of virus differing in virulence and immune reactivity. The advent of each new variant of concern brought more human casualties and waves of onerous quarantine measures. To map the evolutionary trajectory of the variants, **Wilks** and colleagues obtained sera from people who had been vaccinated or infected with a range of variants of concern and applied antigenic cartography to visualize structural changes in the virus. The authors observed changes in immunodominance and immune escape depending on the variant that had infected the patient or after vaccination. Such analysis has implications for variant risk assessment and for selecting the next candidate vaccine strains that will confer the highest protection.

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Eitan Israeli

Capsule

Clonal eviction is key to tolerance

During their development, thymocytes with potentially autoreactive T cell receptors (TCRs) engage self-ligands presented by thymic epithelial cells with high affinity and are eliminated in a process called negative selection. Although TCR signaling is sustained during CD4 T cell selection in the thymus, this is not the case for CD8 T cells so autoreactive CD8 T cells must be managed differently. **Badr** and co-authors reported that immature autoreactive CD8 thymocytes in mice are prematurely evicted from the thymus when strong TCR signaling down-regulates the transcriptional repressor Gfi1 and induces the expression of S1P1. Thymocytes then travel to the periphery, where they develop into mature but self-tolerant clones.

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Eitan Israeli