Grading Aortic Stenosis with mean gradient and aortic valve area: A comparison between preoperative Transthoracic Echocardiography and Pre-Cardiopulmonary Bypass Echocardiography

Thesis submitted for the partial fulfilment for the requirement of the Degree of DM (Cardiothoracic and Vascular Anaesthesia)

BY

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DECLARATION

I hereby declare that this thesis entitled, **"Grading Aortic Stenosis with mean gradient and aortic valve area: A comparison between preoperative Transthoracic Echocardiography and Pre-Cardiopulmonary Bypass Echocardiography"** has been prepared by me under the capable supervision and guidance of **Dr. Suneel P R**, Professor, Division of Cardiothoracic and Vascular Anaesthesiology, Sree Chitra Tirunal Institute for Medical Sciences & Technology (SCTIMST), Thiruvananthapuram, Kerala.

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Abstract:

1. **Background:** Intraoperative trans esophageal echocardiography (TEE) has been shown to underestimate the severity of aortic stenosis (AS) compared to preoperative trans thoracic echocardiography (TTE) leading to discordance in grading of AS.
2. **Objective:** To compare the mean gradient (PGm) and aortic valve area (AVA) obtained during preoperative TTE and intraoperative TEE. The continuity equation based aortic valve area is compared using the left ventricular outflow tract (LVOT) area obtained during both 2D and 3D echocardiography in both TTE and TEE
3. **Study design:** Prospective observational study
4. **Setting:** Tertiary referral centre, a university - level hospital (SCTIMST), performing more than 600 cardiac surgeries annually.
5. **Participants:** Sixty adult cardiac surgical patients, who will undergo AVR with or without coronary artery bypass grafting (CABG).
6. **Interventions:** None
7. **Materials and methods:** Baseline TTE was done before induction of anaesthesia. After induction of anaesthesia, TEE was done. The hemodynamics were maintained within 20% of baseline during the TEE evaluation. Aortic valve (AV) anatomy, ejection fraction (EF), left ventricular (LV) dimensions, aortic annulus, LVOT CSA (2D, 3D), PG_m,

peak velocity (V_{max}), CE based AVA (2D, 3D), dimensionless velocity index (DVI) were assessed in both.

8. **Results:** The LV dimensions, aortic annulus measured by preoperative TTE and pre-CPB TEE was comparable and statistically not significant. The average of mean gradient significantly decreased from 58.9 ± 16.39 mmHg in preoperative TTE to 42.02 ± 11.84 mmHg in intraoperative TEE ($p < 0.001$) leading to underestimation of AS in 48.3% of patients ($p < 0.001$). The average of peak velocity significantly decreased from 4.85 ± 0.57 m/s in TTE to 4.13 ± 0.47 m/s in TEE ($p < 0.001$) leading to underestimation of AS in 35% of patients ($p < 0.001$). DVI measured by TTE and TEE was comparable and the difference was statistically not significant ($p = 0.159$). DVI caused underestimation of AS in 3.3% of patients which was statistically not significant ($p = 0.15$). The LVOT CSA measured by 2D TTE (3.42 ± 0.79 cm^2), 2D TEE (3.45 ± 0.81 cm^2) and 3D TTE (4.36 ± 0.72 cm^2) were significantly lesser than that measured by 3D TEE (4.44 ± 0.74 cm^2) ($p < 0.001$). The CE based 2D AVA measured by preoperative TTE (0.77 ± 0.11 cm^2) was comparable with that measured by pre-CPB TEE (0.8 ± 0.12 cm^2) and was found to be statistically not significant ($p = 0.034$). The CE based 3D AVA calculated by incorporating 3D LVOT CSA during the preoperative TTE (0.87 ± 0.15 cm^2) was comparable with that measured by pre-CPB 3D

TEE (0.9 ± 0.18 cm^2) and was found to be statistically not significant (p= 0.024). The CE based 2D AVA measured by pre-CPB TEE downgraded severity of AS only in 3.3% patients which was statistically not significant ($p = 0.12$). The CE based 3D AVA measured by pre-CPB TEE downgraded the AS severity in only 1.6% of patients which was statistically not significant ($p = 0.17$). So out of 60 patients, 31 patients (51.6%) exhibited discordance in grading of AS during pre-CPB TEE considering all the grading parameters (PG_m, V_{max}, AVA, DVI).

9. **Conclusion:** The application of flow dependent variables (PG_m and V_{max}) leads to significant discordance in grading of AS due to the influence of positive pressure ventilation and anaesthesia. The application of DVI and continuity equation based AVA measured using 2D or 3D LVOT area, will minimize the disparity in the grading of AS between preoperative TTE and intraoperative TEE.

ABBREVIATIONS

2D : Two dimensional

3D : Three dimensional

AS : Aortic Stenosis

AR : Aortic Regurgitation

AV : Aortic Valve

AVA : Aortic Valve Area

AVR : Aortic Valve Replacement

CE : Continuity Equation

CPB : Cardiopulmonary Bypass

CSA : Cross sectional area

DVI : Dimensionless Velocity Index

EF : Ejection Fraction

LV : Left Ventricle

LVOT: Left Ventricular Outflow Tract

LAX : Long Axis

ME : Mid Esophageal

MR : Mitral Regurgitation

PG_m : Mean Gradient

TEE : Trans Esophageal Echocardiography

TTE : Trans thoracic Echocardiography

VTI : Velocity Time Integral

V_{max} : Peak Velocity

TABLE OF CONTENTS

INTRODUCTION

INTRODUCTION

Severe Aortic Stenosis (AS) is defined as a mean gradient (PG_m) > 40mmHg or Aortic valve area (AVA) < $1cm^2$ or Peak velocity (V_{max}) > 4m/sec.[1] However, there are often discrepancies between grading of AS by the preoperative Trans Thoracic Echocardiography (TTE) and the intraoperative pre-Cardiopulmonary Bypass (pre-CPB) Trans Esophageal Echocardiography (TEE).[2] Usually intraoperative TEE underestimates the severity of AS with respect to flow dependent variables because of the influence of anaesthesia.[3]

The accuracy of AVA measured by continuity equation (CE) depends primarily on the precise measurement of left ventricular outflow tract (LVOT) area. The shape of LVOT is presumed to be circular for the estimation of cross-sectional area (CSA). LVOT CSA has been calculated as π (LVOT diameter/2)^2. Many recent studies based on 3D echocardiography[4], CT[5], MRI[6] have demonstrated that LVOT shape may be elliptical.

Because of the differences in LVOT area observed on two dimensional (2D) and three dimensional (3D) echocardiography, continuity equation derived AVA may differ based on the method used to calculate the LVOT area.[7] In cases of patients with moderate or severe AS and coronary artery disease (CAD), these differences may affect intraoperative clinical decision making. Aortic valve replacement (AVR) is reasonable for patients with moderate AS who are undergoing other cardiac surgery (Class IIa Recommendation)[1].

The purpose of this study is to compare the grading of AS by preoperative TTE and intraoperative pre-CPB TEE done after induction of anesthesia and its impact on grading the severity of AS. The study also aims to calculate and compare aortic valve area obtained by continuity equation using LVOT dimensions derived from 2D and 3D echocardiography during preoperative TTE and intraoperative TEE.

REVIEW OF LITERATURE

Review of Literature

Accurate grading of Aortic Stenosis - Importance

Aortic stenosis is one of the most common valvular heart disease in elderly age group requiring valve replacement.[8] The most common etiology being degenerative AS followed by bicuspid aortic valve.[9] Indication for surgery depends on the symptoms and severity of AS.[1] Preoperatively TTE is used as the standard tool for grading of AS depending on the flow dependent variables such as the peak velocity (Vmax) and mean gradient (PGm) across the stenotic aortic valve and the aortic valve area

Intraoperative TEE is valuable for assessment of aortic valve and surgical guidance in cardiac surgery intraoperatively. Intraoperative TEE aortic valve assessment may affect the surgical decision based on the new findings during elective or emergency surgeries. In a large retrospective review of 3835 patients planned for isolated CABG, Eltzschig et al found that intraoperative TEE influenced surgical decision in 3.3% of patients leading to unplanned aortic or mitral valve surgeries. Also out of 1823 patients planned for mitral valve surgery, based on the incidental findings in pre-CPB TEE, 1% of patients underwent unplanned aortic valve procedure.[10] Hence it is imperative for accurate interpretation of the grading parameters based on intraoperative pre-CPB TEE findings.

In a retrospective study conducted by Whitener et al, they concluded that grading Aortic stenosis by AVA and PG_m during pre-CPB TEE is discordant from the preoperative TTE report.[2] Whitener et al in his another retrospective study concluded that pre-CPB TEE underestimates the severity of AS with respect to PG_m and AVA.[3]

Uda et al in his study found that TEE grading of AS severity was at least one grade lower than TTE grading by peak velocity and mean gradient in 45.1% and 42.7% of patients respectively. Dimensionless Index is considered reliable in assessing severity of AS intraoperatively.[11]

The evaluation of left ventricular outflow tract (LVOT) area with 3D-TEE is of great importance in AS patients due to the discrepancy between the severity assessed by different methods- PG_m, V_{max}, AVA.[12] The patients classified as severe AS using 2D LVOT area could be reclassified into moderate AS when 3D LVOT area is being used in continuity equation. Hence correct assessment of severity of AS using 3D-TEE might result in fewer patients being erroneously diagnosed as having severe AS and thus avoids unnecessary operations or procedures.[7]

HISTORICAL PERSPECTIVE

The severity of AS was originally assessed by measurements obtained from cardiac catheterization and clinical outcomes based on these measurements.[13,14,15] AVA was calculated using Gorlin's equation[16,17] as follows

$$AVA = (CO) \div (HR \times SEP \times 44.3\sqrt{PGm})$$

where CO- Cardiac output, HR- Heart rate, SEP- Systolic ejection period. Braunwald et al in his study found that, AS patients with a PG_m >50mmHg had poor outcomes.[18] Rapaport et al concluded that outcomes were poor when AVA < 1cm^2.[19]

There have been discrepancies between echocardiographic and catheterization derived pressure gradient in AS. The peak gradient measured by echocardiography measures the peak instantaneous gradient between the left ventricle and aorta. This is generally higher than the peak to peak gradient (between peak LV pressure and peak aortic pressure) measured by cardiac catheterization.[22]. In general, there is a good correlation between AVA measured simultaneously by cardiac catheterization and echocardiography.[20-22] AVA measured by Doppler tends to be slightly smaller than that measured by catheterization.[23-26]

ECHOCARDIOGRAPHIC ASSESSMENT OF AS SEVERITY

Echocardiography identifies aortic valve (AV) anatomy including degenerative/ calcified AV, rheumatic disease, bicuspid AV. The degree of calcification and restricted valve mobility correlates with the severity of AS. The valve area can be directly measured by planimetry of the cross-sectional

area (CSA) using TTE in parasternal short-axis view (or) TEE in mid esophageal aortic valve short-axis view.

However, planimetry methods has its own limitations. In most cases, because of heavy calcification, the valve orifice may not be easily measurable. So the degree of AS is most commonly assessed by Doppler-based techniques (PG_m and V_{max}).

Compared to TTE, TEE provides improved image quality due to close proximity of esophagus and cardiac structures including aortic valve. Also, unlike TTE there is no hindrance due to lungs or bony interface between probe and cardiac structures.

In TTE, PG_m and V_{max} are obtained by integrating a continuous-wave Doppler (CWD) tracing of flow across the aortic valve. The views used to align the sample volume parallel to blood flow are apical (5-chamber view), suprasternal or right parasternal view. The values are achieved by directly tracing the CWD signal. In the same views LVOT VTI was assessed by pulse-wave Doppler (PWD) by placing the sample volume 0.5-1cm within the aortic valve. LVOT diameter is also measured at the same location in parasternal long-axis view.

In TEE, PG_m and V_{max} are measured by CWD across aortic valve in deep transgastric long-axis view or transgastric long-axis view. LVOT diameter is measured in mid esophageal aortic valve long-axis view.

Continuity equation (CE) is a physiological method for valve area estimation based on the law of conservation in hydrodynamics. It is valid in a pulsatile chamber like heart where the flow is equal proximal and distal to a stenotic valve. **(Figure 1)** demonstrates the concept of parallel Doppler beam alignment and the concept of "what goes in has to come out".[27] Hence $AVA = (LVOT\ VTI \times LVOT\ CSA) \div AV\ VTI$. This method was initially used by Skjaerpe et al[20] in 1985 to quantify AVA in cohorts with combined AS and Aortic regurgitation (AR). They tested its reliability in comparison with Gorlin's formula.

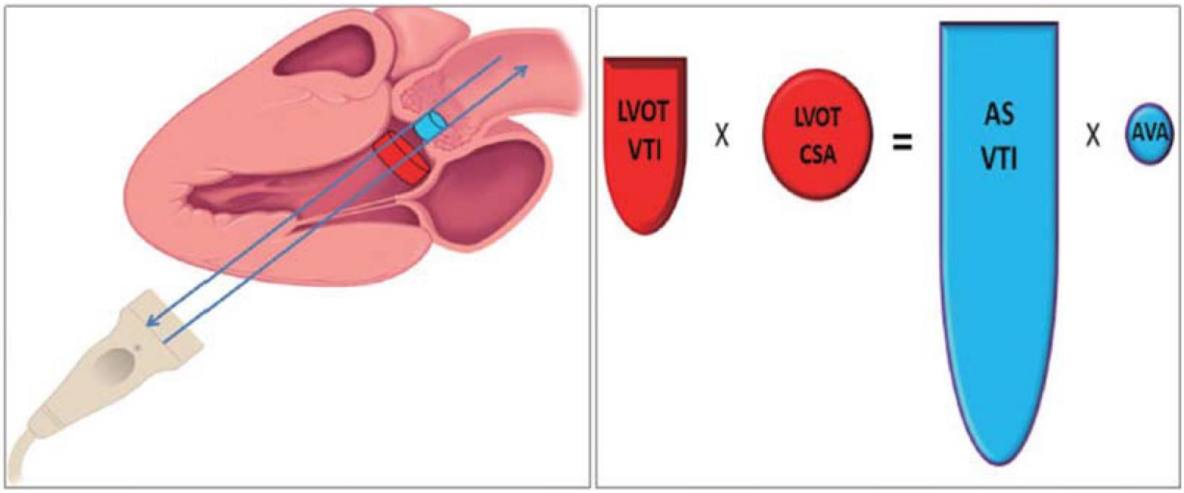

Figure 1: Demonstrates the concept of parallel Doppler beam alignment and the concept of "what goes in has to come out"[27]

POTENTIAL LIMITATIONS IN GRADING SEVERITY OF AS BY ECHOCARDIOGRAPHY

The major potential sources of errors in Echo (or) Doppler techniques include errors in measurement of LVOT diameter, LVOT VTI, peak velocity across AV. The accurate measurement of LVOT VTI should be performed by placing the sample volume at the level of LVOT where its diameter was measured. If the sample volume is too close to the aortic cusps, calculated stroke volume may be overestimated due to flow acceleration. To obtain maximum peak instantaneous velocity across the aortic valve, the Doppler beam needs to be parallel to the aortic jet. Any increase in angulation between the Doppler beam and the aortic jet will result in an underestimation of the jet velocity. When using TTE, velocity measurements obtained from at least three different views (apical, suprasternal, right parasternal) are recommended to obtain highest peak velocity for AS. Contamination of CWD signal from mitral regurgitation jet may overestimate the severity of AS.

The AVA measured by continuity equation requires accurate measurement of LVOT. Any error in the measurement of LVOT will be squared in the continuity equation. So, underestimation of LVOT CSA will result in a smaller AVA.

AHA/ACC guidelines provide the methods for the resolution of apparent discrepancies in AS severity **(Table 1)**[1]

AS velocity >4 m/s and AVA >1.0 cm^2
1. Check LVOT diameter measurement and compare with previous studies[a]
2. Check LVOT velocity signal for flow acceleration
3. Calculate indexed AVA when
a. Height is <135 cm (5′5″)
b. BSA <1.5 m^2
c. BMI <22 (equivalent to 55 kg or 120 lb at this height).
4. Evaluate AR severity
5. Evaluate for high cardiac output
a. LVOT stroke volume
b. 2D LV EF and stroke volume
Likely causes: high output state, moderate–severe AR, large body size
AS velocity ≤4 m/s and AVA ≤1.0 cm^2
1. Check LVOT diameter measurement and compare with previous studies[a]
2. Check LVOT velocity signal for distance from valve
3. Calculate indexed AVA when
a. Height is <135 cm (5′5″)
b. BSA <1.5 m^2
c. BMI <22 (equivalent to 55 kg or 120 lb at this height).
4. Evaluate for low transaortic flow volume
a. LVOT stroke volume
b. 2D LV EF and stroke volume
c. MR severity
d. Mitral stenosis
5. When EF <55%
a. Assess degree of valve calcification
b. Consider dobutamine stress echocardiography
Likely causes: low cardiac output, small body size, severe MR

Table 1- Resolution of apparent discrepancies in severity of AS[1]

GUIDELINES IN DEFINING SEVERITY OF AS

The guidelines defining severity of AS has evolved over time. In the initial guidelines by American College of Cardiology (ACC) and the American Heart Association (AHA), severe AS was defined primarily as AVA < 1cm^2.[28] Later, the revised 2006 guidelines defined severe AS as PG mean >40mmHg, peak velocity >4m/sec, AVA <1cm^2. The European Association of Echocardiography (EAE) and American Society of Echocardiography (ASE) agreed with these measures of severity.[29] Subsequently the European Society of Cardiology (ESC) added aortic valve area index (AVAI) < 0.6cm^2/m^2, and Dimensionless Velocity Index (DVI) < 0.25 to indicate severe AS.[30] DVI is measured as LVOT VTI/ AV VTI. The 2008 AHA/ACC guidelines suggested three hemodynamic parameters in grading severity of AS. **(TABLE 2)**

1) AS jet velocity > 4m/sec[31-33]
2) PG mean > 40mmHg[32,33]
3) AVA <1cm^2 derived by Gorlin's formula/ CE/ planimetry[16,34-36]

	Aortic sclerosis	Mild	Moderate	Severe
Peak velocity (m/s)	≤2.5 m/s	2.6–2.9	3.0–4.0	≥4.0
Mean gradient (mmHg)	–	<20	20–40	≥40
AVA (cm^2)	–	> 1.5	1.0–1.5	<1.0
Indexed AVA (cm^2/m^2)	–	>0.85	0.60–0.85	<0.6
Velocity ratio	–	> 0.50	0.25–0.50	<0.25

Table 2: ASE guidelines for grading of AS severity[1]

These echocardiographic measurements have been validated in the outcome data in several studies.[21,24,37,38,39] In 2015, the guidelines were updated further to provide the framework for staging AS based on the integration of hemodynamic status with symptoms[57] **(Table 3).**

Stage	Symptoms and severity	Aortic valve anatomy and hemodynamics
A	At risk of AS	Examples: aortic sclerosis or congenital bicuspid valve
B	Progressive AS (mild-moderate)	Mild AS: abnormal valve with V_{max} 2–2.9 m/s, mean ΔP < 20 mm Hg
		Moderate AS: abnormal valve with reduced leaflet motion and V_{max} 3–3.9 m/s, mean ΔP < 20–40 mm Hg
C	Asymptomatic severe AS	Calcified and thickened leaflets with limited mobility and $V_{max} \geq 4.0$ m/s or mean $\Delta P \geq 40$ mm Hg (AVA usually < 1.0 cm^2)
		C1: normal LV systolic function
		C2: LV EF < 50%
		Very severe $V_{max} \geq 5.0$ m/s, mean $\Delta P \geq 60$ mm Hg
D	Symptomatic severe AS	Severely thickened and calcified aortic valve leaflets with reduced systolic opening with:
		D1: high gradient severe AS: $V_{max} \geq 4.0$ m/s or mean $\Delta P \geq 40$ mm Hg (AVA usually < 1.0 cm^2 but not needed for diagnosis)
		D2: low-flow low-gradient severe AS (low EF): LV EF < 50% with a resting AVA < 1.0 cm^2 and V_{max} 3 to 4 m/s. On low dose DSE there is a $V_{max} \geq 4.0$ m/s with an AVA < 1.0 cm^2 at any flow rate
		D3: low-flow low-gradient severe AS (normal EF): V_{max} 3 to 4 m/s, AVA < 1.0 cm^2, indexed AVA < 0.6 cm^2/m^2, and indexed SV < 35 mL/m^2, all measured when patient is normotensive

ΔP: mean gradient, AS: aortic stenosis, AVA: aortic valve area, DSE: dobutamine stress echocardiography (maximum dose 20 mcg/mg/min), EF: ejection fraction, LV: left ventricular, SV: stroke volume, V_{max}: maximum aortic velocity

Table 3 – AHA/ACC Staging of AS[57]

THREE-DIMENSIONAL ECHOCARDIOGRAPHY IN AORTIC STENOSIS

Three-dimensional echocardiography can be performed by either transthoracic (3D-TTE) or transoesophageal approach (3D-TEE) and is valuable in the assessment of patients with AS.[40-44] 3D echocardiography visualises AV surface both from aortic and ventricular aspects. It can assess valve morphology, thickness and calcification accurately. 3D-TEE correctly identifies morphology that is consistent with surgical or pathological findings.[42]

3D echocardiography plays an important role in accurately measuring LVOT. 2D-TTE and 2D-TEE measures only the minor axis of the LVOT. But LVOT is now regarded as a non-circular structure. This results in underestimation of LVOT area.[45,46] Inaccurate assessment of LVOT by 2D echocardiography may also result from annular calcification and poor visualisation.[46] These limitations can be overcome by 3D echocardiography

Perez de Isla et al demonstrated that LVOT assessed by 2D-TTE is underestimated when compared to real time 3D-TTE.[46] AVA assessment can also be obtained by CE using LVOT measurement from 3D techniques. Saitoh et al demonstrated that AVA derived from the CE as well as LVOT area measured using 2D-TTE were smaller when compared to those measured using 2D-TEE, which in turn were smaller than those obtained from 3D-TEE. In their

results, AVA measured by continuity equation by 3D-TEE correlated well with that obtained using planimetry by 3D-TEE.[49]

Similarly, Jainandunsing et al demonstrated that AVA calculated from major and minor axes using 3D-TEE agreed well with that obtained using 3D planimetry. 18% of patients who had been classified as having severe AS by 2D method and had undergone AVR, were reclassified to have moderate AS by 3D-TEE methods.[50] 3D derived stroke volume is less angle dependent and is particularly useful when LVOT geometry is irregular secondary to septal hypertrophy or prominent calcification.[51]

Khaw et al demonstrated that planimetric assessment of LVOT and AVA by real-time 3D echocardiography correlated well with the assessment done by invasive methods. It also provided improved accuracy when compared with 2D-TTE. 3D echocardiography may be especially helpful in accurately measuring LVOT and in planimetric assessment in heavily calcified valves.[52]

Utsunomiya et al, using multidetector CT found that the LVOT diameter measured by 2D echocardiography corresponded to the minor diameter of the ellipse. Hence, the LVOT CSA measured by 2D echocardiography significantly underestimated the area when compared to that measured using multidetector CT planimetry.[53]

DISCORDANCE IN GRADING SEVERITY OF AS

In the retrospective study by Whitener et al, they found that out of 227 patients with AVA < 1cm^2, 54% of patients had PGm < 40mmHg when measured by pre-CPB TEE. They confirmed that pre-CPB TEE exhibits higher discordance than that reported by TTE.[2] Usually pre-CPB TEE underestimates the severity of AS with respect to flow dependent variable because of the influence of anaesthesia.[3]

Uda et al in his retrospective study, concluded that intraoperative TEE peak velocity and mean gradients are often significantly lower than preoperative TTE measurements. This leads to underestimation of severity of AS in more than 50% of patients. DVI is a more reliable measurement of severity of AS in intraoperative setting.[11]

In a study conducted by Nanditha et al, they found that mean gradient and peak velocity are significantly reduced during pre-CPB TEE compared with preoperative TTE. They concluded that AVA measured by continuity equation and dimensionless index are reliable in grading AS during pre-CPB TEE.[54]

Michelena et al attributed that the discrepancies in grading of AS is due to LVOT diameter assessment. They concluded that the current guideline of severe AS is most consistent for patients with large LVOT diameter, but not so for patients with average or smaller LVOT diameter in whom AVA cut-off should be studied further.[55]

Mehrotra et al found that, with severe AS, LVOT undergoes remodelling and it becomes less distensible. This leads to greater peak systolic ellipticity and underestimation of LVOT CSA which in turn affects the assessment of AS severity.[56]

AIMS AND OBJECTIVES

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Hypothesis:

We hypothesised that intraoperative pre-CPB TEE PGm measurements and AVA calculations would be significantly different from preoperative TTE values and that these differences would affect the grading of AS during intraoperative pre-CPB TEE**.**

Primary Objective:

To compare preoperative Trans Thoracic Echocardiography derived mean gradient and aortic valve area with pre-Cardiopulmonary bypass Trans oesophageal Echocardiography in patients planned for Aortic Valve Replacement with or without CABG.

Secondary Objective:

To compare continuity equation based aortic valve area using 3D LVOT cross sectional area in both Trans thoracic echocardiography and Trans oesophageal echocardiography.

MATERIALS AND METHODS

MATERIALS AND METHODS

Study design:

This is a prospective observational study. Our study was approved by the Technical Advisory Committee (TAC) and Institutional Ethics Committee (IEC)

TAC registration No- SCT-/S/2018/754

IEC registration No- SCT/IEC/1234/AUGUST-2018

Sample Size:

Based on a retrospective study conducted by George Whitener et al[3], to detect an average mean gradient in preoperative TTE of 46mmHg with a standard deviation of 14.3 and to detect and average mean gradient in pre CPB TEE of 39.4mmHg with a standard deviation of 14.1, 60 patients needed to be studied for a power of 80% and an alpha error of 5%.

Setting:

Tertiary referral centre, a university - level hospital (SCTIMST), performing more than 600 cardiac surgeries annually

Participants:

Adult cardiac surgical patients, who will undergo Aortic valve replacement (AVR) with or without coronary artery bypass grafting (CABG)

Inclusion criteria:

Adult cardiac surgical patients, who will undergo AVR with or without CABG in whom TTE was performed within 1 month before surgery and the PG_m, V_{max}, LV dimensions and AVA values were recorded.

Exclusion criteria:

1. Patients not willing to participate in the study
2. Patients operated for re-do cardiac surgery
3. Patients with moderate or severe Aortic Insufficiency
4. Patients with associated moderate or severe Mitral Regurgitation
5. Patients with LVEF < 55%

Study duration:

18 months

STUDY PROTOCOL

1) After obtaining IEC approval, patients were enrolled in the study during the pre-anaesthetic evaluation.
2) Patients were educated about the study in the presence of a witness. The witness could question the patient as to whether he/she had really understood details of the proposed study. An informed consent form was signed by the patient or his/her relative as per the institutional protocol.

3) On the day prior to the surgery, comprehensive cardiac examination was done using a RT-3D-TTE probe and ultrasound machine. (S5-1, Philips iE33, Philips Ultrasound, Bothell, USA)
4) After induction of anaesthesia an adult sized TEE probe (X7-2t, Philips iE33, Philips ultrasound, Bothell, USA) was inserted and comprehensive cardiac examination was done
5) Comprehensive cardiac examination included the necessary views required for management of the patient.
6) All views necessary for measurement of AVA and LVOT area were acquired as a part of comprehensive examination. 3D analysis was performed using off-line 3DQ software

Preoperative Trans thoracic Echocardiography protocol: (S5-1 probe)

On the day before surgery, the patients underwent a comprehensive 2D and 3D TTE examination. Baseline blood pressure and heart rate were recorded. Echocardiographic measurements were obtained in compliance with the guidelines published by the ASE[47] and are detailed below.

AVA (2D) derived from Continuity Equation using TTE

Step 1: Measuring CSA of LVOT (LVOT-CSA)

Using parasternal long axis view (LAX), LVOT was focused using zoom mode. LVOT diameter was measured 0.5cm from AV, taken from inner edge to inner edge during mid-systole **(Figure 2)**. CSA was automatically calculated using the formula[27],

$LVOT\ CSA = \pi \times (\frac{D}{2})^2$, where D- LVOT diameter.

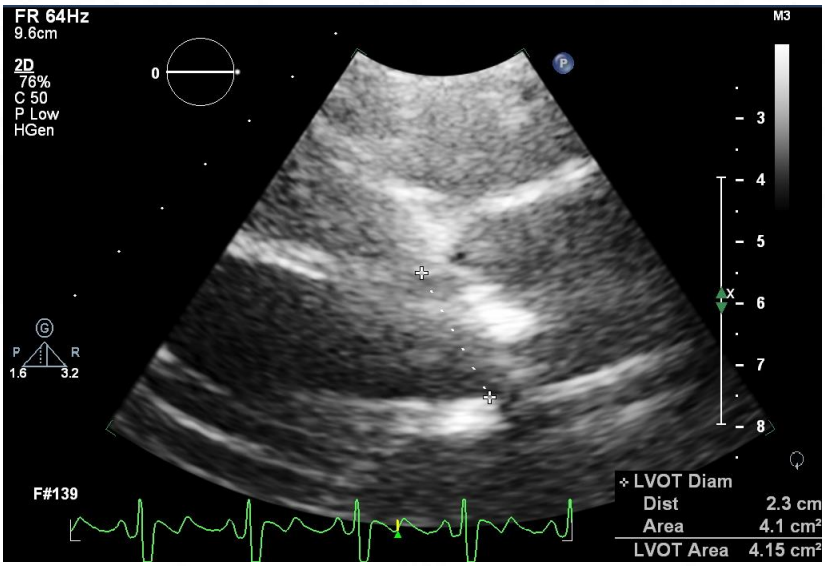

Figure 2 : LVOT diameter calculation in parasternal LAX view

Step 2: Measuring the Velocity Time Integral (VTI) of the LVOT (LVOT-VTI)

In the apical 5-chamber view, the Pulse Wave Doppler (PWD) was aligned parallel to the LVOT. Sample volume was placed approximately 0.5cm

proximal to the aortic valve. PWD envelope was traced to obtain the LVOT-VTI

Step 3: Measuring the VTI of the Aortic valve (AV-VTI)

In the apical 5-chamber view, Continuous Wave Doppler (CWD) beam was aligned parallel to the LVOT. CWD envelope was traced to obtain the AV-VTI. **(Figure 3)**

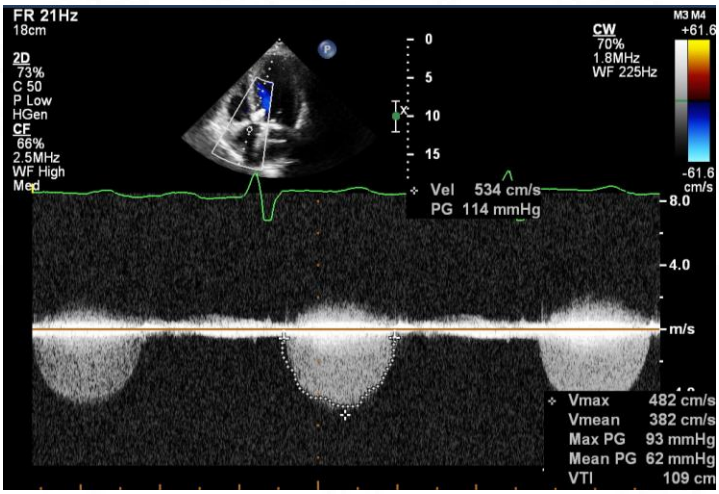

Figure 3: AV VTI calculation by CWD across AV in apical 5-chamber view

2D AVA was estimated using continuity equation method as follows[21,39]

$$AVA = (LVOT\ VTI \times LVOT\ CSA) \div AV\ VTI$$

Measuring Mean gradient and Peak velocity across the AV

In the apical 5-chamber view, Continuous Wave Doppler (CWD) beam was aligned parallel to the LVOT. CWD envelope was traced to obtain the mean gradient and peak velocity. **(Figure 4)**

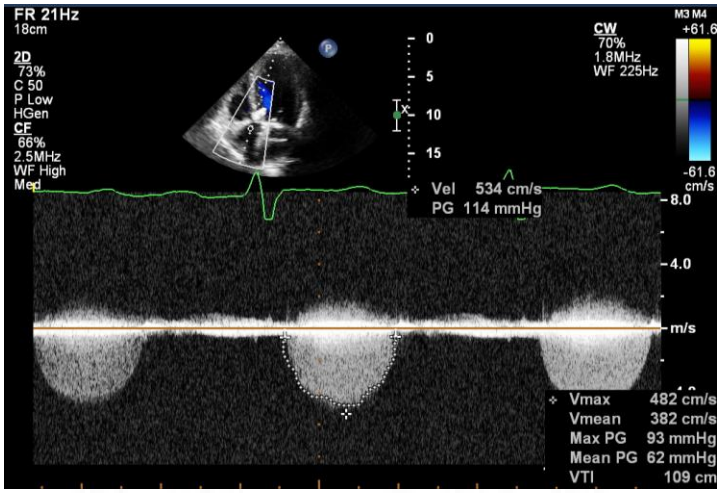

Figure 4 : Calculation of peak velocity and mean gradient by tracing the CWD signal across the AV

Measurement of Dimensionless Velocity Index (DVI) across Aortic valve

Once the Velocity-Time Integral of LVOT and Aortic valve(AV) is obtained, DVI is calculated by[27]

$$DVI = LVOT\ VTI \div AV\ VTI$$

Measurement of 3D LVOT CSA by TTE:

A full volume dataset of LVOT was acquired after optimising gain, compression controls and time-gain compensation over four consecutive heart beats during breath holding. Reference planes for full volume acquisition were para sternal AV-SAX and para sternal AV-LAX views. The full volume analysis was digitally recorded for offline analysis. 3DQ software (Q LAB, Philips medical system) was used for Multi Planar Reconstruction (MPR) of

aortic valve and LVOT. In off-line analysis, LVOT CSA was assessed by planimetry of LVOT in short axis. **(Figure 5)**

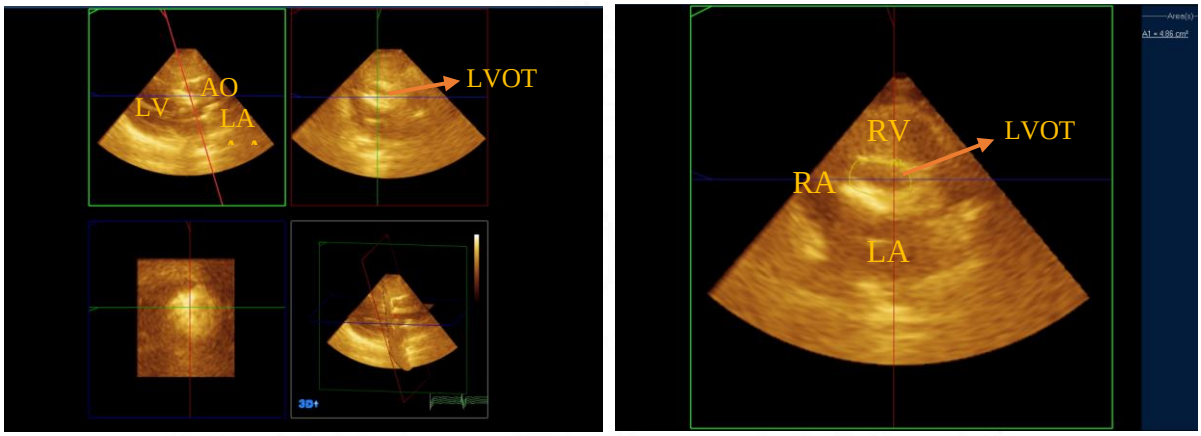

Figure 5: Planimetric assessment of 3D LVOT Cross sectional Area (LV- Left ventricle; Ao- Aorta; LA- Left atrium; RA- Right atrium; LVOT- Left ventricular outflow tract)

Measurement of CE based 3D AVA by TTE:

3D AVA was estimated using continuity equation method by integrating the 3D LVOT CSA measured by TTE as follows[21,39]

$$AVA = (LVOT\ VTI \times 3D\ LVOT\ CSA) \div AV\ VTI$$

INDUCTION

- Premedication - Tab Diazepam 0.1mg/kg (Previous night, day of surgery)
- Standard anaesthesia Induction - Inj. Midazolam 0.05 to 0.1mg/kg, Fentanyl 5 to10mcg/kg, Propofol 2mg/kg, Pancuronium 0.1mg/kg
- Maintenance - Oxygen Air mixture (FiO2 50%), Sevoflurane (MAC - 0.8 to 1), Fentanyl boluses, morphine infusion (20-60mcg/kg/hr)
- Ventilation - Tv 8ml/kg, RR - 12/min, PEEP - 5cm H_20

Pre Cardiopulmonary Bypass (CPB) Trans Esophageal Echocardiography Protocol: (X7-2t probe)

After induction, an adult sized TEE probe was inserted. The patients underwent comprehensive TEE imaging. All parameters are measured when the blood pressure and heart rate were within 20% of baseline. Echocardiographic measurements were obtained in compliance with the guidelines published by the ASE[48].

AVA (2D) derived from Continuity Equation

Step 1: Measuring CSA of LVOT (LVOT-CSA)

Using Mid-esophageal AV Long axis view (LAX), LVOT was focused using zoom mode. LVOT diameter was measured 0.5cm from AV, taken from inner edge to inner edge during mid-systole **(Figure 6)**. CSA was automatically calculated using the formula[27], $LVOT\ CSA = \pi \times (\frac{D}{2})^2$,

where D- LVOT diameter.

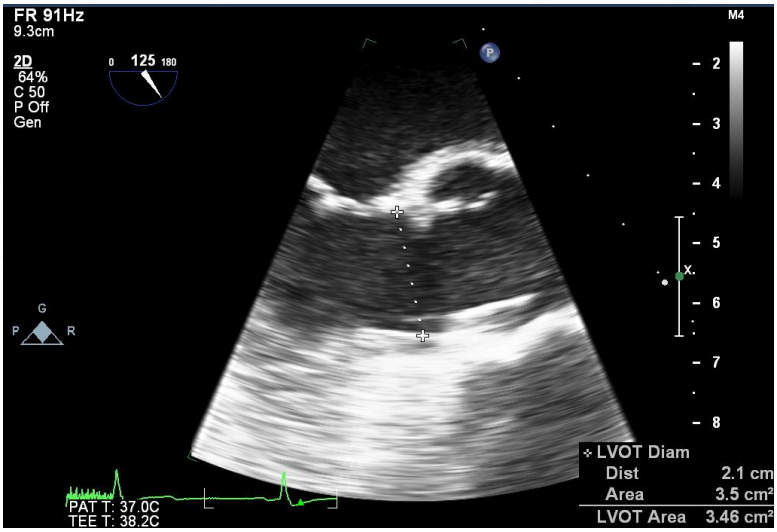

Figure 6: Calculation of LVOT diameter in mid esophageal LAX view

Step 2: Measuring the Velocity Time Integral (VTI) of the LVOT (LVOT-VTI)

In the deep trans-gastric LAX view or trans-gastric LAX view, the Pulse Wave Doppler (PWD) was aligned parallel to the LVOT. Sample volume was placed approximately 0.5cm proximal to the aortic valve. PWD envelope was traced to obtain the LVOT-VTI. **(Figure 7)**

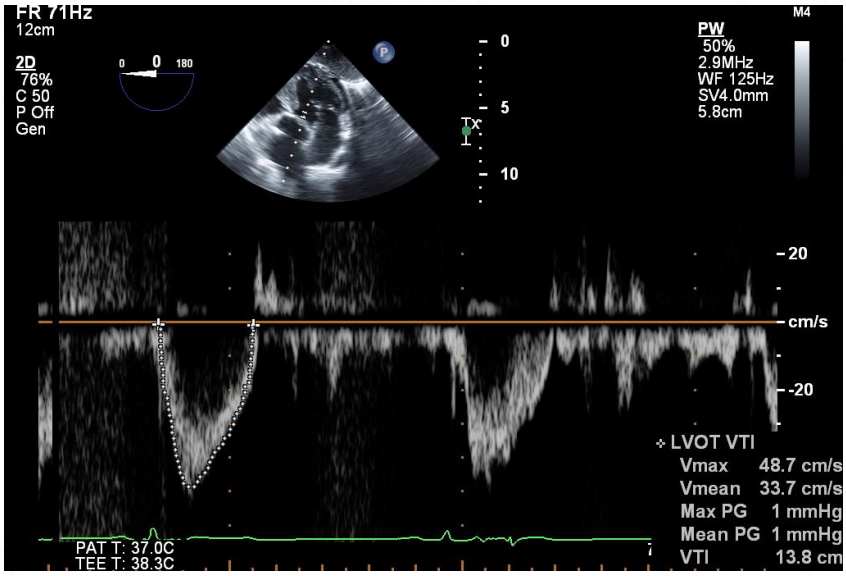

Figure 7 : Calculation of LVOT VTI by deep trans-gastric LAX view

Step 3: Measuring the VTI of the Aortic valve (AV-VTI)

In the deep trans-gastric LAX view and trans-gastric LAX view, Continuous Wave Doppler (CWD) beam was aligned parallel to the LVOT. CWD envelope was traced to obtain the AV-VTI. **(Figure 8)**

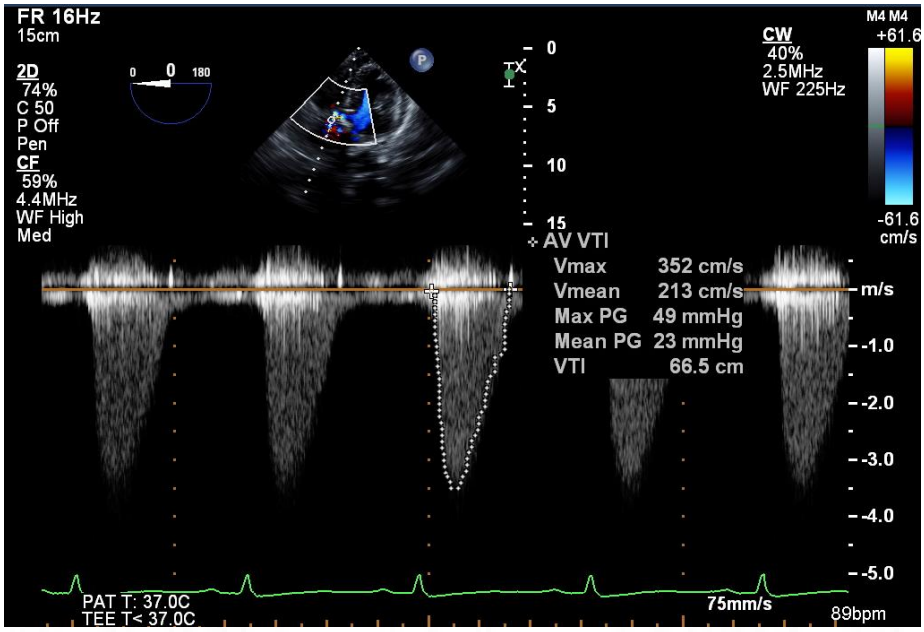

Figure 8: Calculation of AV VTI by CWD in Deep trans-gastric LAX view

2D AVA was estimated using continuity equation method as follows[21,39]

$$AVA = (LVOT\ VTI \times LVOT\ CSA) \div AV\ VTI$$

Measuring Mean gradient and Peak velocity across the AV

In the deep trans-gastric LAX view and trans-gastric LAX view, Continuous Wave Doppler (CWD) beam was aligned parallel to the LVOT. CWD envelope was traced to obtain the Mean gradient and peak velocity. **(Figure 9)**

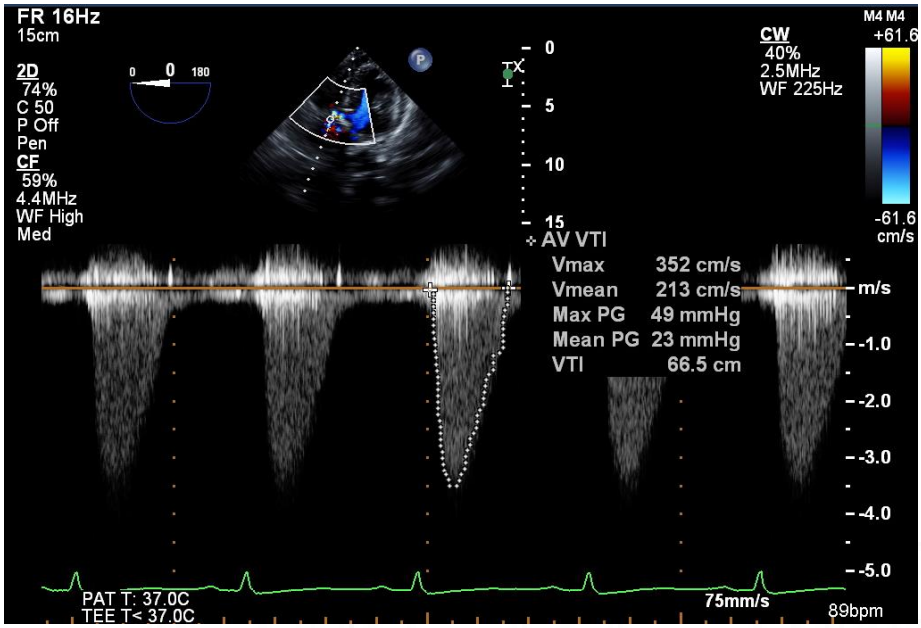

Figure 9: Tracing the CWD Doppler signal of AV for calculation of peak velocity and mean gradient

Measurement of Dimensionless Velocity Index (DVI) across Aortic valve

Once the Velocity-Time Integral of LVOT and Aortic valve (AV) is obtained, DVI is calculated by[27]

$$DVI = LVOT\ VTI \div AV\ VTI$$

Measurement of 3D LVOT CSA:

A full volume dataset of LVOT was acquired after optimising gain, compression controls and time gain compensation over four consecutive heart beats under apnoea. Reference planes for full volume acquisition were mid-oesophageal AV-SAX and mid-oesophageal AV-LAX views. The full volume

analysis was digitally recorded for offline analysis 3DQ software (Q LAB, Philips medical system) was used for Multi Planar Reconstruction (MPR) of aortic valve and LVOT. In off-line analysis, LVOT CSA, geometry of LVOT were assessed. **(Figure 10)**

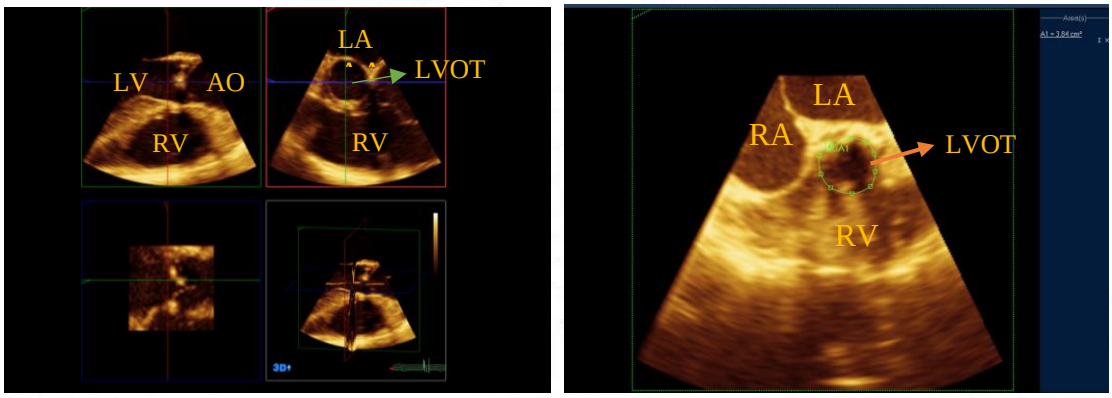

Figure 10: Calculation of 3D LVOT Cross sectional Area (LV-Left ventricle; AO- Aorta; LA- Left atrium; RV- Right ventricle; LVOT- Left ventricular outflow tract)

Measurement of CE based 3D AVA by TEE:

3D AVA was estimated using continuity equation method by integrating the 3D LVOT CSA measured by TEE as follows[21,39]

$$AVA = (LVOT\ VTI \times 3D\ LVOT\ CSA) \div AV\ VTI$$

Study Groups:

Single group in which all the parameters were evaluated by TTE and TEE.

Observations:

The observations will be noted by the principal investigator and confidentiality will be maintained regarding patient identification. Data will be stored by the principal investigator in his personal computer for three years.

Observation chart- Please refer to Annexure page

Interventions:

No interventions were done. The study is observational in nature.

Outcome parameters:

We obtained AVA using continuity equation by employing 2D and 3D derived LVOT area, mean gradient and peak velocity across AV, LVOT CSA (2D and 3D). All these values were obtained both in TTE and TEE which were compared among each other. Also the impact of intraoperative pre-CPB TEE on grading the severity of AS when compared to preoperative TTE with respect to each grading parameter was also observed.

STATISTICAL ANALYSIS

STATISTICAL ANALYSIS

Quantitative Variables were expressed as mean and standard deviation. Qualitative variables were expressed as proportion. Comparison of quantitative data between two group were analysed by independent sample t test or Mann-Whitney U test according to the nature of the data. Comparison of quantitative data among more than two group were done by ANOVA. Between group comparison of qualitative variables were analysed by chi-square test. Association between quantitative variable were analysed by Pearson correlation or Spearmann rank correlation. A p-value <0.05 was considered statistically significant. Data analysis was performed using SPSS software version 22.0. Bland-Altmann analysis was performed to assess agreement between the two methods, and the limits of agreement were defined as mean $\pm$ 1.96 SD of the average differences between the methods.

RESULTS

RESULTS

Feasibility of the study

67 consecutive patients fulfilling the inclusive criteria were enrolled in the study. Among that, in 5 patients satisfactory TTE imaging could not be done due to poor ECHO window and therefore were excluded from the study. Another 2 patients were excluded from the study because of inadequate 3D imaging.

Demography:

Our study population included 60 patients with AS. Mean age of the study population was 55.7 ± 11.2 years. Among them, 42 were males and 18 were females. Mean weight of the patients was 65.08 ± 10.9 kg. Mean height of the study population was 160.3 ± 8.5 cm. Mean BMI of the study population was 25.4 ± 4.4 kg/m^2. Among the 60 patients, 26 (43%) patients presented with New York Heart Association (NYHA) class II symptoms while rest of the patients presented with NYHA class III symptoms (57%). All the patients were in sinus rhythm. Demographic parameters are summarized in Table 4.

Demographic Parameters	
Male	42 (70%)
Female	18 (30%)
Age (years)	55.72 ± 11.26
Weight (kg)	65.08 ± 10.91
Height (cm)	160.3 ± 8.55
BMI (kg/m^2)	25.4 ± 4.4
NYHA Class II Class III	 26 (43%) 34 (57%)

Table 4 : Demographic parameters [Data expressed as mean ± SD or as n (%)]

Echocardiographic parameters:

In preoperative TTE, 40 patients had grade I left ventricular diastolic dysfunction (LV-DD), 6 patients had grade II LV-DD, 4 patients had grade III LV-DD. Right ventricle (RV) function was normal in all patients. Also 13 patients had mild aortic regurgitation (AR), 12 patients had mild mitral regurgitation (MR) and 4 patients had mild tricuspid regurgitation (TR) on preoperative TTE. The echocardiographic parameters are summarized in Table 5.

Preoperative TTE	No. of patients (%)
LV diastolic dysfunction	
Normal	10 (17%)
Grade I	40 (67%)
Grade II	6 (10%)
Grade III	4 (6%)
Mild AR	13 (21.6%)
Mild MR	12 (20%)
Mild TR	4 (6.6%)

Table 5: Echocardiographic parameters recorded from preoperative TTE

Comorbidity:

Hypertension (57%) and diabetes mellitus (50%) were the most common comorbidities in our study population. 14 out of 60 patients (24%) had associated CAD which required coronary artery bypass grafting (CABG) along with AVR. The associated comorbidities in our study population are summarized in Figure 11.

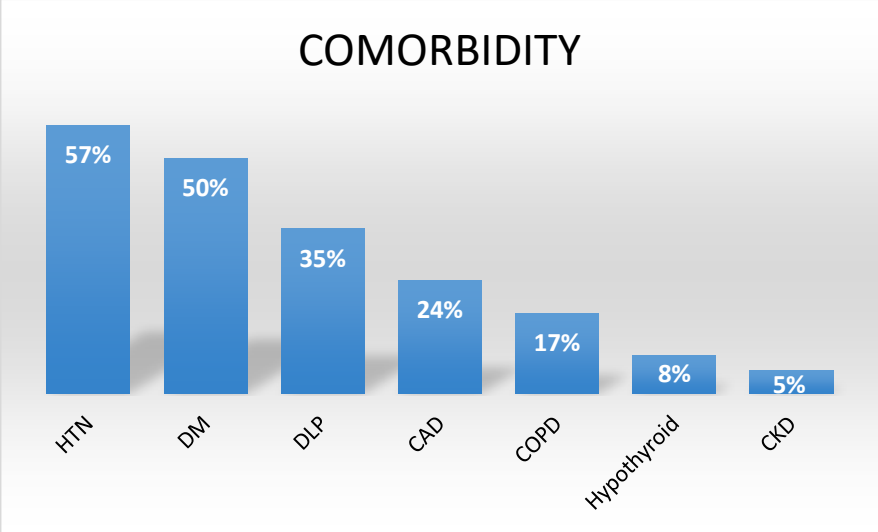

Figure 11: Percentage of comorbidities in study population (HTN- Hypertension, DM- Diabetes Mellitus, DLP- Dyslipidemia, CAD- Coronary artery disease, COPD- Chronic obstructive pulmonary disease, CKD- Chronic kidney disease)

Aetiology of AS:

Among the study population, 31 patients (52%) were diagnosed as degenerative AS. The other causes of AS were Bicuspid aortic valve (BAV) in 26 patients (43%) and rheumatic in 3 patients (5%). The aetiology of AS in our study population is summarized in Figure 12.

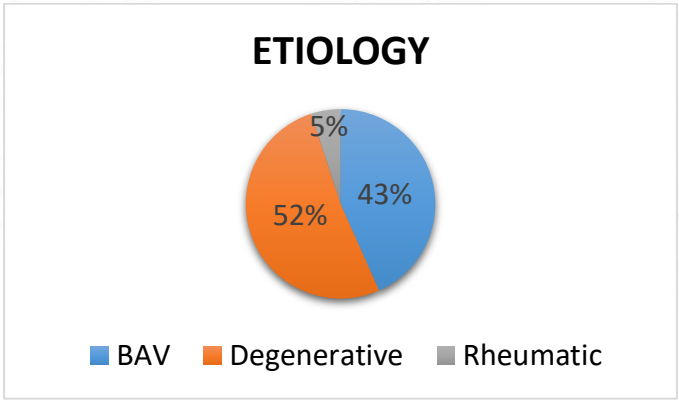

Figure 12: Aetiology of Aortic stenosis (BAV- Bicuspid Aortic Valve)

Surgical procedure:

Among the 60 patients, 46 patients (76.7%) had undergone Aortic valve replacement (AVR) while 14 patients (23.3%) had undergone CABG along with AVR. The procedure performed in our study population is summarized in Table 6.

Surgery	**Frequency**	**Percent**
AVR	46	76.7
CABG + AVR	14	23.3
Total	60	100

Table 6: Surgery done in study population (CABG- Coronary artery bypass grafting, AVR- Aortic valve replacement)

Surgical details:

The mean cardiopulmonary bypass (CPB) and aortic cross-clamp (Acx) time during surgery was 102.7 ± 26.8 mins and 71.8 ± 18.2 mins respectively. The median valve size used for surgery was 21 ± 2 mm. The type of valve used for surgery was mechanical valve (CHVP- Chitra valve prosthesis) in 38 patients and bioprosthetic valve in 22 patients. The surgical details are summarized in Table 7.

Surgical Details	
CPB time (mins)	102.7 ± 26.8
Acx time (mins)	71.8 ± 18.2
Valve size (mm)	21 ± 2
Type of valve Mechanical Bioprosthetic	 38 (63.3 %) 22 (36.7 %)

Table 7: Surgical details of study population [Data expressed as mean ± SD or as n (%)]

Morphology of Aortic valve:

In preoperative TTE, 22 patients were found to have bicuspid aortic valve (BAV), while in intraoperative pre-CPB TEE 26 patients were found to have BAV. The AV was diagnosed tricuspid in 38 patients in preoperative TTE while in pre-CPB TEE 34 patients were found to have tricuspid AV. The difference is statistically not significant ($p = 0.16$). The morphology of AV is summarized in Table 8.

AORTIC VALVE (Bi/Tri)	**TTE**		**TEE**	
	n	**%**	**n**	**%**
Bicuspid	22	36.7	26	43.3
Tricuspid	38	63.3	34	56.7

Table 8: Morphology of Aortic valve

Comparison of LV dimensions:

The LV dimension (systole) measured by preoperative TTE was 30.72 ± 7.35 mm, while by pre-CPB TEE it was 31.43 ± 6.87 mm. The measurements were comparable and statistically not significant (p = 0.139). The LV dimension (diastole) measured by preoperative TTE was 47.72 ± 7.16 mm, while by pre-CPB TEE it was 46.68 ± 6.84 mm. The measurements were comparable and statistically not significant (p = 0.039). The results are summarized in Table 9.

LV Dimension	**TTE (n=60)**		**TEE (n=60)**		**p**
	mean	**SD**	**mean**	**SD**	
LV Dimension (Diastole) (mm)	47.72	7.164	46.68	6.841	0.039
LV Dimension (Systole) (mm)	30.72	7.356	31.43	6.873	0.139

Table 9: **Comparison of LV dimension measured by TTE and pre-CPB TEE** (Statistically not significant)

Comparison of Ejection fraction :

Comparison of Ejection fraction (EF) measured by preoperative TTE and pre-CPB TEE showed that, EF measured by pre-CPB TEE (60.05 ± 5.05%) was significantly lower than that measured by preoperative TTE (68.17 ± 7.06%). The results were statistically significant ($p < 0.001$). The results are summarized in Table 10 and Figure 13.

	Ejection Fraction (%)					
	Mean	**SD**	**Median**	**1st Quartile**	**3rd Quartile**	**P**
TTE	68.17	7.06	69.5	62.25	73.75	<0.001
TEE	60.05	5.05	61	56	64	

Table 10: Comparison of Ejection fraction (EF) measured by preoperative TTE and pre-CPB TEE. (Statistically significant, $p < 0.001$)

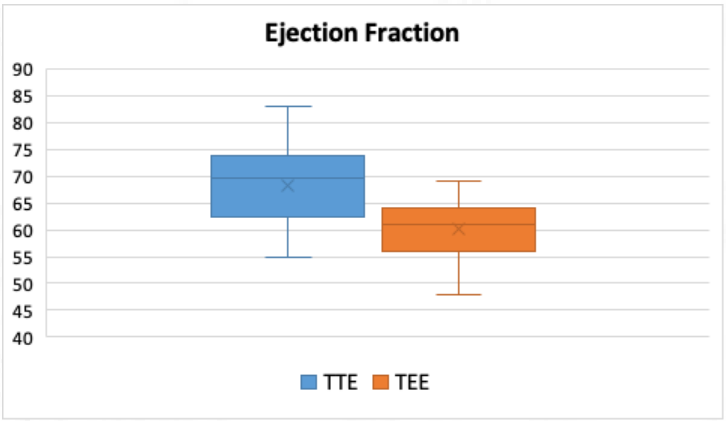

Figure 13: Box and Whisker plot comparing ejection fraction measured by preoperative TTE and pre-CPB TEE (Y axis- EF in %)

Comparison of aortic annulus:

Comparison of aortic annulus measurement by preoperative TTE and pre-CPB TEE was statistically not significant (p= 0.846). The aortic annulus size measured by preoperative TTE (22.25 ± 2.64 mm) was comparable with that measured by pre-CPB TEE (22.2 ± 2.35 mm). The results are summarized in Table 11 and Figure 14.

	Aortic Annulus (mm)					
	Mean	**SD**	**Median**	**1st Quartile**	**3rd Quartile**	**P**
TTE	22.25	2.64	22	21	24	0.846
TEE	22.2	2.35	22	21	23.75	

Table 11: Comparison of aortic annulus measured by preoperative TTE and pre-CPB TEE. (Statistically not significant, p = 0.846)

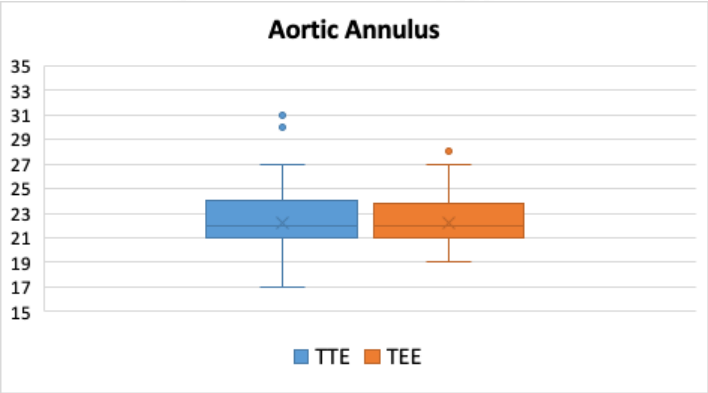

Figure 14: Box and Whisker plot comparing aortic annulus measured by preoperative TTE and pre-CPB TEE (Y axis- Aortic annulus size in mm)

Comparison of 2D LVOT CSA (TTE vs TEE):

The LVOT cross sectional area (CSA) measured by 2D TTE (3.42 ± 0.79 cm^2) was comparable with that measured by pre-CPB 2D TEE (3.45 ± 0.81 cm^2) and was found to be statistically not significant (p = 0.627). The correlation between the two methods was good (R = 0.8). The results are summarized in Table 12, Figure 15.

	2D LVOT CSA (cm^2)					
	Mean	**SD**	**Median**	**1st Quartile**	**3rd Quartile**	**P**
TTE	3.42	0.79	3.46	3.14	3.8	0.627
TEE	3.45	0.81	3.3	2.91	3.8	

Table 12: Comparison of 2D LVOT CSA measured by preoperative TTE and pre-CPB TEE [Statistically not significant (p= 0.627), Good correlation (R = 0.8)] (2D- 2 Dimensional, CSA- Cross Sectional Area)

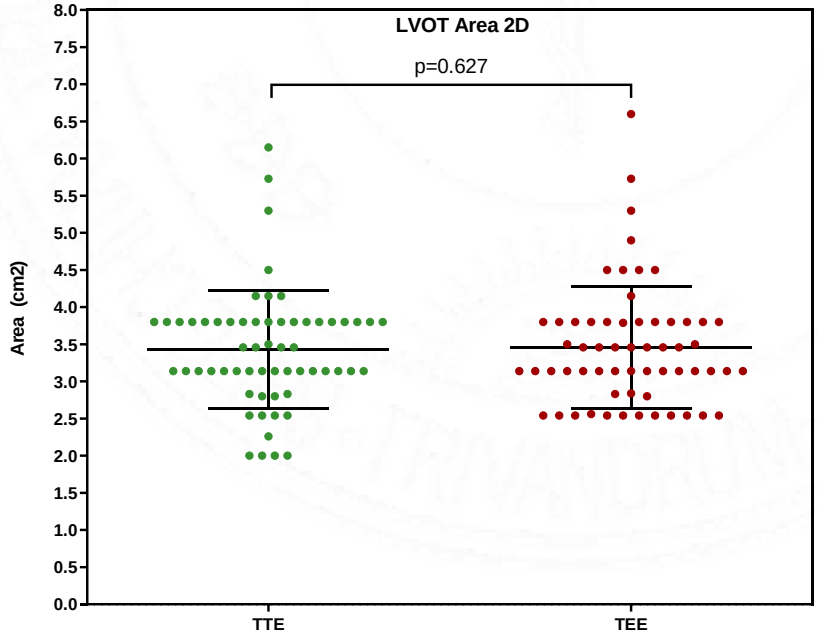

Figure 15: Scatter plot comparing 2D LVOT CSA measured by preoperative TTE and pre-CPB TEE. (2D- 2 Dimensional, CSA- Cross sectional Area)

Comparison of 3D LVOT CSA (TTE vs TEE):

The LVOT cross sectional area (CSA) measured by 3D TTE (4.36 ± 0.72 cm^2) was lower than that measured by pre-CPB 3D TEE (4.44 ± 0.74 cm^2) and was found to be statistically significant ($p < 0.001$). The correlation between the two methods was excellent (R = 0.98). The results are summarized in Table 13, Figure 16.

	3D LVOT CSA (cm^2)					
	Mean	**SD**	**Median**	**1st Quartile**	**3rd Quartile**	**P**
TTE	4.36	0.72	4.28	3.86	4.83	< 0.001
TEE	4.44	0.74	4.45	3.84	4.89	

Table 13: **Comparison of 3D LVOT CSA measured by preoperative TTE and pre-CPB TEE** [Statistically significant ($p < 0.001$), Excellent correlation (R = 0.98)] (3D- 3 Dimensional, CSA- Cross Sectional Area)

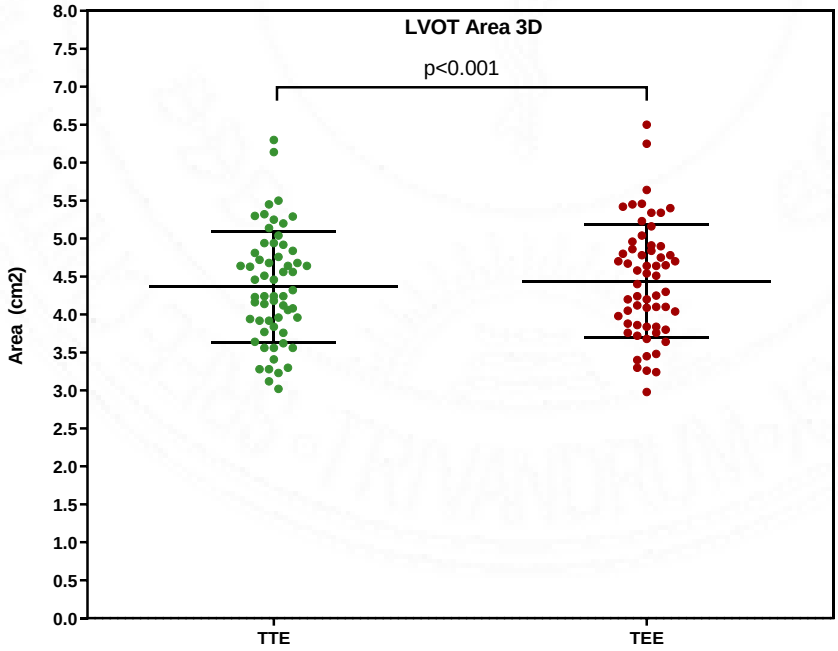

Figure 16: Scatter plot comparing 3D LVOT CSA measured by preoperative TTE and pre-CPB TEE. (3D- 3 Dimensional, CSA- Cross sectional Area)

Figure 17 shows the Box and Whisker plot comparing preoperative TTE LVOT CSA (2D, 3D) and pre-CPB TEE LVOT CSA (2D, 3D). The 2D LVOT CSA measured by TTE and TEE was comparable and statistically not significant ($p = 0.627$), while the 3D LVOT CSA measured by TTE was lower than TEE and found to be statistically significant ($p < 0.001$).

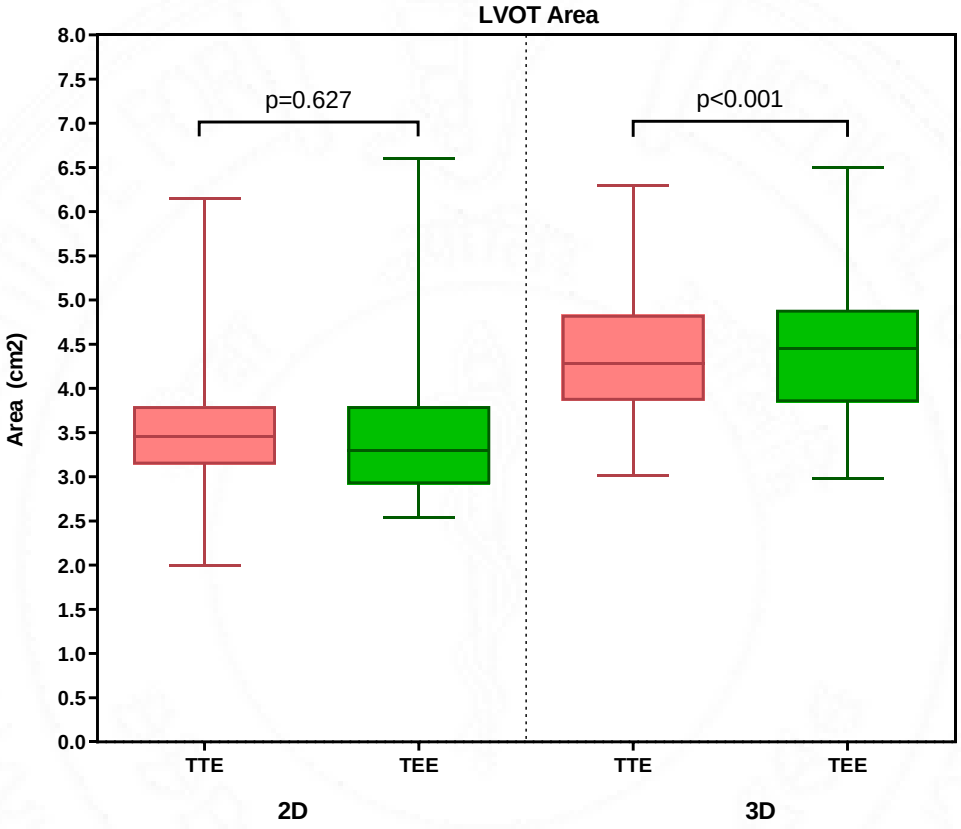

Figure 17: Box and Whisker plot comparing LVOT CSA measured by 2D TTE vs 2D TEE and 3D TTE vs 3D TEE

Comparsion of LVOT CSA (2D TTE vs 3D TTE) :

The LVOT cross sectional area (CSA) measured by 2D TTE (3.42 ± 0.79 cm^2) was significantly lower than that measured by 3D TTE (4.36 ± 0.72 cm^2) and was found to be statistically significant ($p < 0.001$). The results are summarized in Table 14, Figure 18.

TTE	LVOT CSA (cm^2)					
	Mean	**SD**	**Median**	**1st Quartile**	**3rd Quartile**	**P**
2D	3.42	0.79	3.46	3.14	3.8	< 0.001
3D	4.36	0.72	4.28	3.86	4.83	

Table 14: **Comparison of LVOT CSA measured by 2D TTE and 3D TTE** [Statistically significant ($p < 0.001$)]

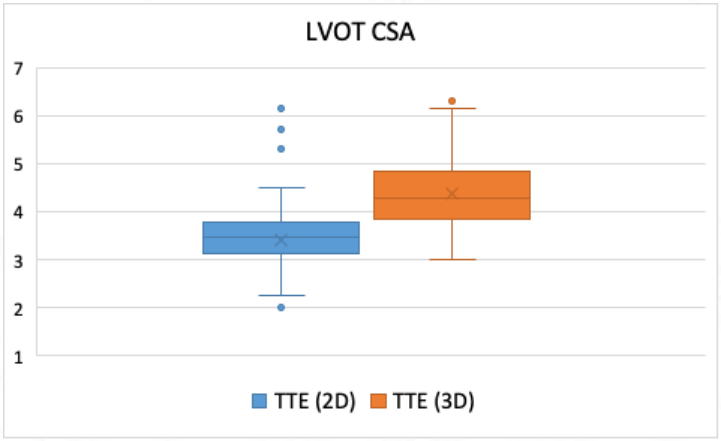

Figure 18: Box and Whisker plot comparing LVOT CSA measured by 2D TTE vs 3D TTE (Y axis- LVOT CSA in cm^2)

The Bland-Altmann analysis revealed that the difference in LVOT CSA between 2D and 3D TTE was -0.939 ± 0.6 cm^2 (95% confidence interval-0.246 to -2.12) (Figure 19). By Bland-Altmann analysis the limits of agreement is superior when the range is less and it should be centred around the mean.

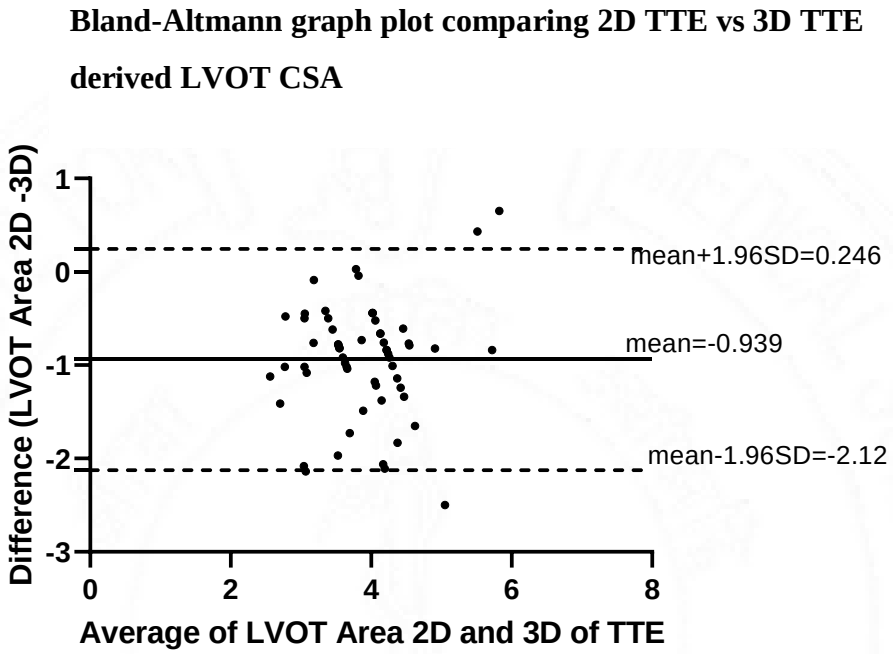

Figure 19: Bland-Altmann plot showing differences in LVOT CSA using 2D TTE vs 3D TTE. Solid lines represent mean difference (-0.939), broken lines represent ± 1.96 SD. Range of 95% confidence interval as shown by broken lines in the plot are over a wider range from the baseline (-2.12 to 0.246). This implies poor agreement between 2D and 3D TTE measurement of LVOT CSA and they cannot be used interchangeably. (Statistically significant, $p < 0.001$)

Comparison of LVOT CSA (2D TEE vs 3D TEE)

The LVOT cross sectional area (CSA) measured by 2D TEE (3.45 ± 0.81 cm^2) was significantly lower than that measured by 3D TEE (4.44 ± 0.74 cm^2) and was found to be statistically significant ($p < 0.001$). The results are summarized in Table 15, Figure 20.

TEE	LVOT CSA (cm^2)					
	Mean	**SD**	**Median**	**1st Quartile**	**3rd Quartile**	**P**
2D	3.45	0.81	3.3	2.91	3.8	< 0.001
3D	4.44	0.74	4.45	3.84	4.89	

Table 15: **Comparison of LVOT CSA measured by 2D TEE and 3D TEE**

[Statistically significant ($p < 0.001$)]

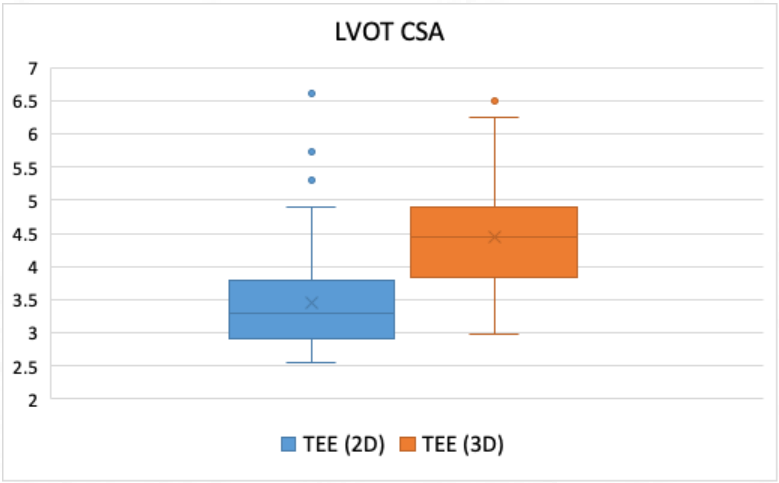

Figure 20: Box and Whisker plot comparing LVOT CSA measured by 2D TEE vs 3D TEE (Y axis- LVOT CSA in cm^2)

The Bland-Altmann analysis revealed that the difference in LVOT CSA between 2D and 3D TEE was -0.987 ± 0.56 cm^2 (95% confidence interval-0.151 to -2.11) (Figure 21).

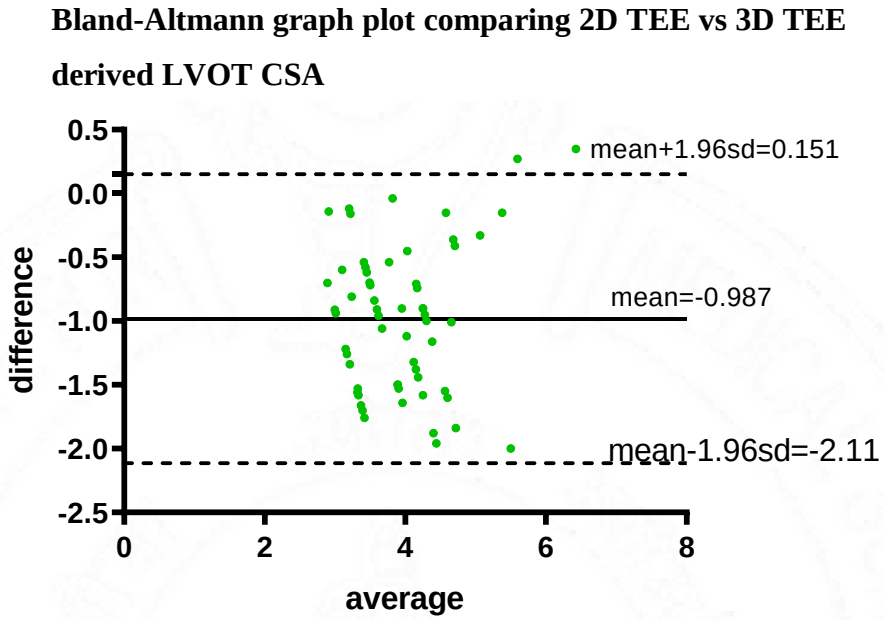

Figure 21: Bland-Altmann plot showing differences in LVOT CSA using 2D TEE vs 3D TEE. Solid lines represent mean difference (-0.987), broken lines represent ± 1.96 SD. Range of 95% confidence interval as shown by broken lines in the plot are over a wider range from the baseline (-2.11 to 0.151). This implies poor agreement between 2D and 3D TEE measurement of LVOT CSA and they cannot be used interchangeably. (Statistically significant, $p < 0.001$)

Comparison of peak gradient (TTE vs TEE):

The peak gradient measured by pre-CPB TEE (69.85 ± 16.4 mmHg) is significantly lower than that measured by preoperative TTE (96.45 ± 23.7 mmHg) and was found to be statistically significant ($p < 0.001$). The results are summarized in Table 16.

	Peak gradient (mmHg)					
	Mean	**SD**	**Median**	**1st Quartile**	**3rd Quartile**	**P**
TTE	96.5	23.7	92	78.25	106.5	< 0.001
TEE	69.85	16.4	67.5	58.5	79.75	

Table 16: Comparison of peak gradient measured by preoperative TTE and pre-CPB TEE [Statistically significant ($p < 0.001$)]

Comparison of mean gradient (TTE vs TEE):

The mean gradient measured by pre-CPB TEE (42.02 ± 11.84 mmHg) is significantly lower than that measured by preoperative TTE (58.9 ± 16.39 mmHg) and was found to be statistically significant ($p < 0.001$). The results are summarized in Table 17 and Figure 22.

	Mean gradient (mmHg)					
	Mean	**SD**	**Median**	**1st Quartile**	**3rd Quartile**	**P**
TTE	58.9	16.39	55	48	67.5	< 0.001
TEE	42.02	11.84	39	34.25	49	

Table 17: Comparison of mean gradient measured by preoperative TTE and pre-CPB TEE [Statistically significant ($p < 0.001$)]

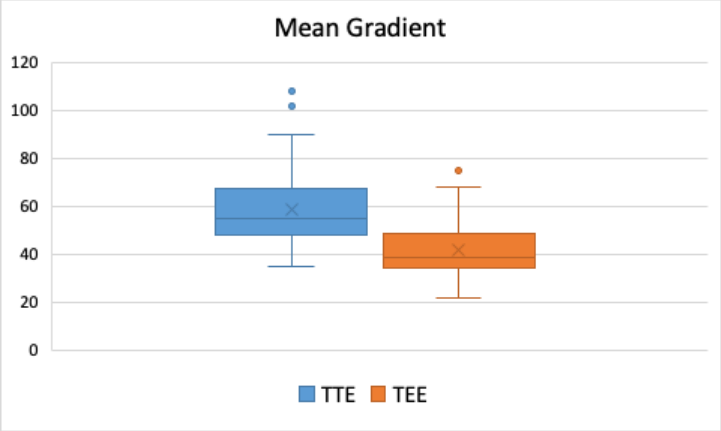

Figure 22: Box and Whisker plot showing statistically significant difference between mean gradient measured by TTE and TEE (Y axis- Mean gradient in mmHg)

Comparison of peak velocity (TTE vs TEE):

The peak velocity measured by pre-CPB TEE (4.13 ± 0.47 m/s) is significantly lower than that measured by preoperative TTE (4.85 ± 0.57 m/s) and was found to be statistically significant ($p < 0.001$). The results are summarized in Table 18 and Figure 23.

	Peak Velocity (m/sec)					
	Mean	**SD**	**Median**	**1st Quartile**	**3rd Quartile**	**P**
TTE	4.85	0.57	4.8	4.4	5.15	< 0.001
TEE	4.13	0.47	4.09	3.81	4.45	

Table 18: Comparison of peak velocity measured by preoperative TTE and pre-CPB TEE [Statistically significant ($p < 0.001$)]

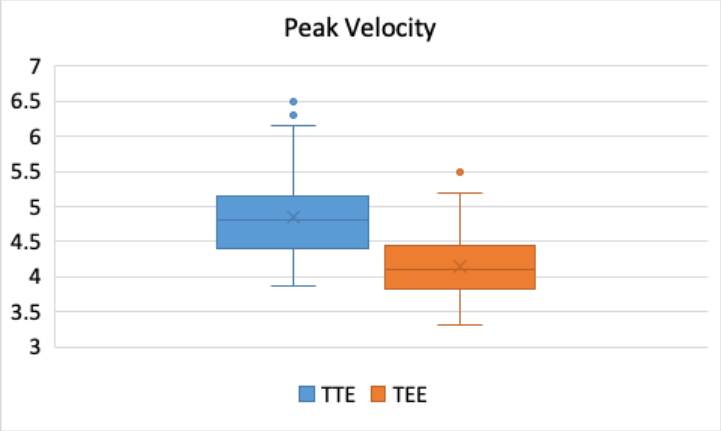

Figure 23: Box and Whisker plot showing statistically significant difference between peak velocity measured by TTE and TEE (Y axis- Peak velocity in m/sec)

Comparison of Dimensionless velocity index (TTE vs TEE):

The Dimensionless Velocity Index (DVI) measured by preoperative TTE (0.2) was comparable with that measured by pre-CPB TEE (0.203 ± 0.018) and was found to be statistically not significant (p = 0.159). The results are summarized in Table 19.

	Dimensionless Velocity Index (DVI)					
	Mean	**SD**	**Median**	**1st Quartile**	**3rd Quartile**	**P**
TTE	0.2	0	0.2	0.2	0.2	0.159
TEE	0.203	0.018	0.2	0.2	0.2	

Table 19: Comparison of Dimensionless velocity index measured by preoperative TTE and pre-CPB TEE [Statistically not significant (p= 0.159)]

Comparison of continuity equation (CE) based 2D aortic valve area (AVA) (TTE vs TEE):

The continuity equation (CE) based 2D Aortic valve area (AVA) measured by preoperative TTE (0.77 ± 0.11 cm^2) was comparable with that measured by pre-CPB TEE (0.8 ± 0.12 cm^2) and was found to be statistically not significant ($p = 0.034$). The results are summarized in Table 20.

	CE - 2D AVA (cm^2)					
	Mean	**SD**	**Median**	**1st Quartile**	**3rd Quartile**	**P**
TTE	0.77	0.11	0.78	0.7	0.87	0.034
TEE	0.8	0.12	0.82	0.7	0.9	

Table 20: Comparison of Continuity equation (CE) based 2D Aortic valve area (AVA) measured by preoperative TTE and pre-CPB TEE [Statistically not significant ($p= 0.034$)]

Figure 24 (Scatter plot) and **Figure 25** (Box and whisker plot) shows the difference between CE based 2D AVA measurement by preoperative TTE and pre-CPB TEE which was statistically not significant.

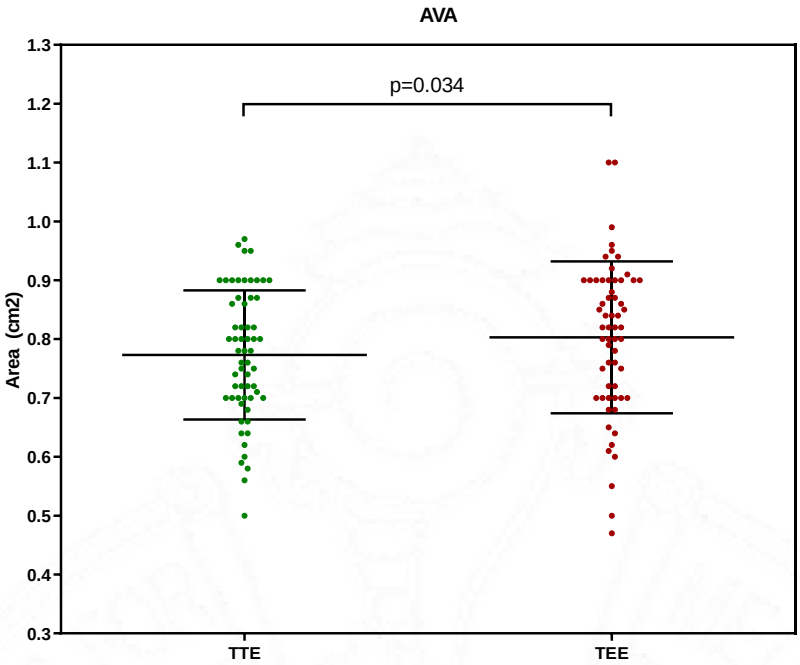

Figure 24: Scatter plot comparing Continuity equation based 2D AVA measured by preoperative TTE and pre-CPB TEE. (AVA- Aortic valve area)

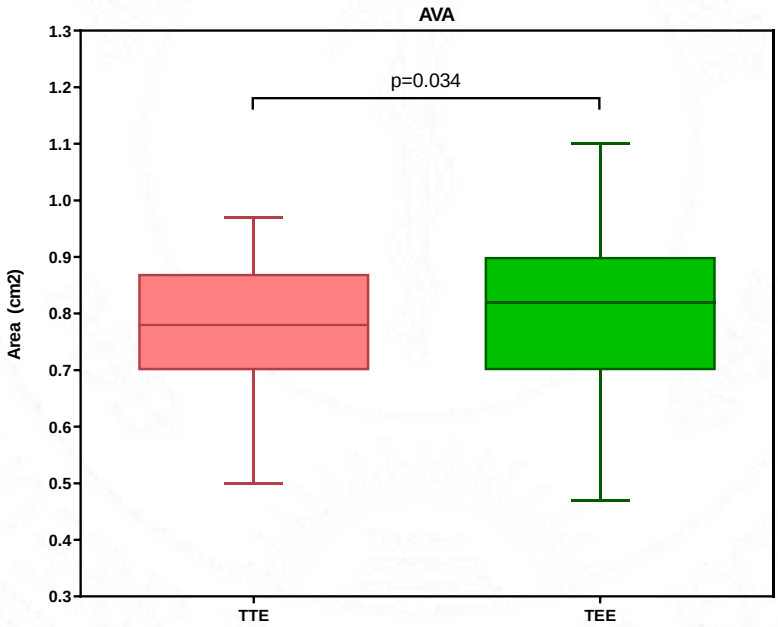

Figure 25: Box and Whisker plot comparing Continuity equation based 2D AVA measured by preoperative TTE and pre-CPB TEE. (AVA- Aortic valve area)

Comparison of CE based 3D aortic valve area (AVA) (TTE vs TEE):

The aortic valve area obtained by continuity equation by using LVOT area obtained by 3D during the preoperative TTE (0.87 ± 0.15 cm^2) was comparable with that measured by pre-CPB 3D TEE (0.9 ± 0.18 cm^2) and was found to be statistically not significant (p= 0.024). The results are summarized in Table 21 and Figure 26.

	CE – 3D AVA (cm^2)					
	Mean	**SD**	**Median**	**1st Quartile**	**3rd Quartile**	**P**
TTE	0.87	0.15	0.86	0.77	0.96	0.024
TEE	0.90	0.18	0.89	0.77	0.97	

Table 21: Comparison of CE based 3D AVA measured by preoperative TTE and pre-CPB TEE [Statistically not significant (p= 0.024)]

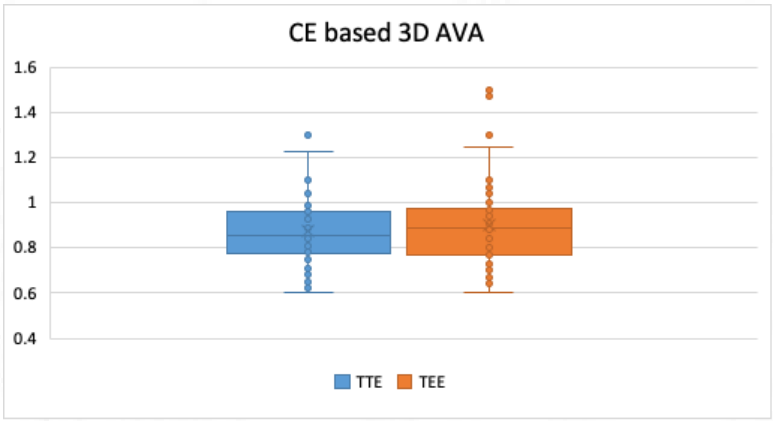

Figure 26: Box and Whisker plot comparing CE based 3D AVA measured by preoperative TTE and pre-CPB TEE. (Y axis- AVA in cm^2)

Comparison of CE based AVA measured by preoperative TTE (2D vs 3D):

The continuity equation (CE) based Aortic valve area (AVA) measured by preoperative 2D TTE (0.77 ± 0.11 cm^2) was significantly lower than that measured by preoperative 3D TTE (0.87 ± 0.15 cm^2) and was found to be statistically significant ($p < 0.001$). The results are summarized in Table 22 and Figure 27.

TTE	CE – AVA (cm^2)					
	Mean	**SD**	**Median**	**1st Quartile**	**3rd Quartile**	**P**
2D	0.77	0.11	0.78	0.7	0.87	<0.001
3D	0.87	0.15	0.86	0.77	0.96	

Table 22: Comparison of CE based AVA measured by preoperative TTE (2D vs 3D) [Statistically significant ($p < 0.001$)]

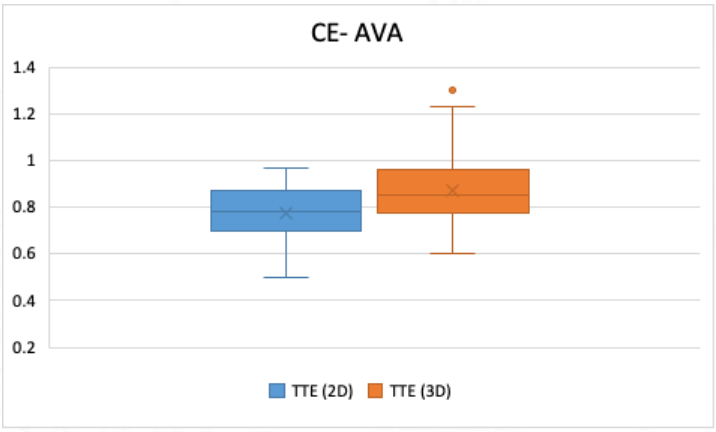

Figure 27: Box and Whisker plot comparing CE based AVA measured by 2D TTE vs 3D TTE (Y axis- AVA in cm^2)

Comparison of CE based AVA measured by pre-CPB TEE (2D vs 3D):

The continuity equation (CE) based Aortic valve area (AVA) measured by pre-CPB 2D TEE (0.87 ± 0.15 cm^2) was significantly lower than that measured by pre-CPB 3D TEE (0.9 ± 0.18 cm^2) and was found to be statistically significant ($p < 0.001$). The results are summarized in Table 23 and Figure 28.

TEE	CE – AVA (cm^2)					
	Mean	**SD**	**Median**	**1st Quartile**	**3rd Quartile**	**P**
2D	0.87	0.12	0.82	0.70	0.90	<0.001
3D	0.90	0.18	0.89	0.77	0.97	

Table 23: Comparison of CE based AVA measured by preoperative TTE (2D vs 3D) [Statistically significant ($p < 0.001$)]

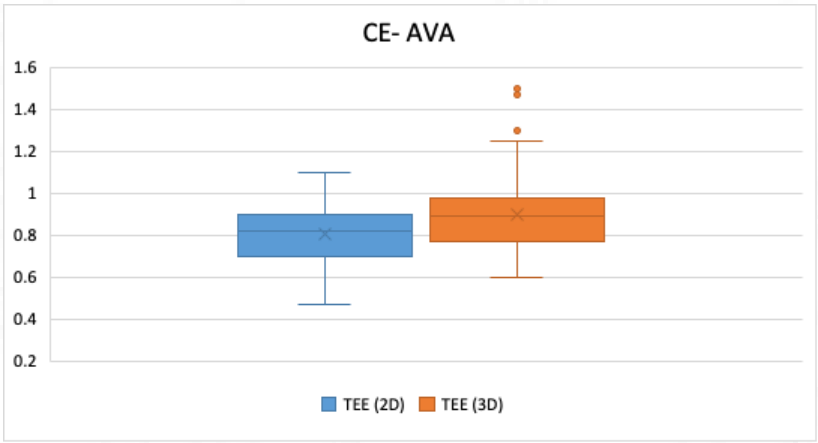

Figure 28: Box and Whisker plot comparing CE based AVA measured by 2D TEE vs 3D TEE (Y axis- AVA in cm^2)

Impact of pre-CPB TEE on grading the severity of AS with respect to each grading parameter:

Table 24 summarizes how these differences in measurement of AVA, Peak velocity (V_{max}), mean gradient (PG_m), Dimensionless velocity index (DVI) affected the grading of AS between preoperative TTE and pre-CPB TEE. When using PG_m, pre-CPB TEE graded the AS severity one grade lower than TTE in 29 patients (48.3%) which was statistically significant ($p < 0.001$). While using V_{max} as grading parameter, pre-CPB TEE graded the AS severity one grade lower than TTE in 21 patients (35%) which was statistically significant ($p < 0.001$). While using DVI as grading parameter, only 2 patients (3.3%) were graded one grade lower by pre-CPB TEE which was statistically not significant ($p= 0.15$). When using CE based 2D AVA, pre-CPB TEE generated an AS severity one grade lower than TTE only in 2 patients (3.3%) which was statistically not significant ($p = 0.12$). While using CE based 3D AVA, pre-CPB TEE graded the AS severity one grade lower than TTE in only 1 patient (1.6%) which was statistically not significant ($p = 0.17$). So out of 60 patients, 31 patients (51.6%) exhibited discordance in grading of AS during pre-CPB TEE considering all the grading parameters (PG_m, peak velocity, AVA, DVI). The results are summarized in Table 24 and Figure 29.

Impact of pre-CPB TEE on grading AS	Mean Gradient	Peak Velocity	DVI	AVA (2D)	AVA (3D)
	n (%)	n (%)	n (%)	n (%)	n (%)
Same Grade	31 (51.7)	39 (65)	58 (96.7)	58 (96.7)	59 (98.4)
1 Grade Lower	29 (48.3)	21 (35)	2 (3.3)	2 (3.3)	1 (1.6)
p value	< 0.001	< 0.001	0.15	0.12	0.17

Table 24: Change in grading of AS based on the grading parameter (p values are calculated by the comparison between change in grading to no change with respect to the grading parameter)

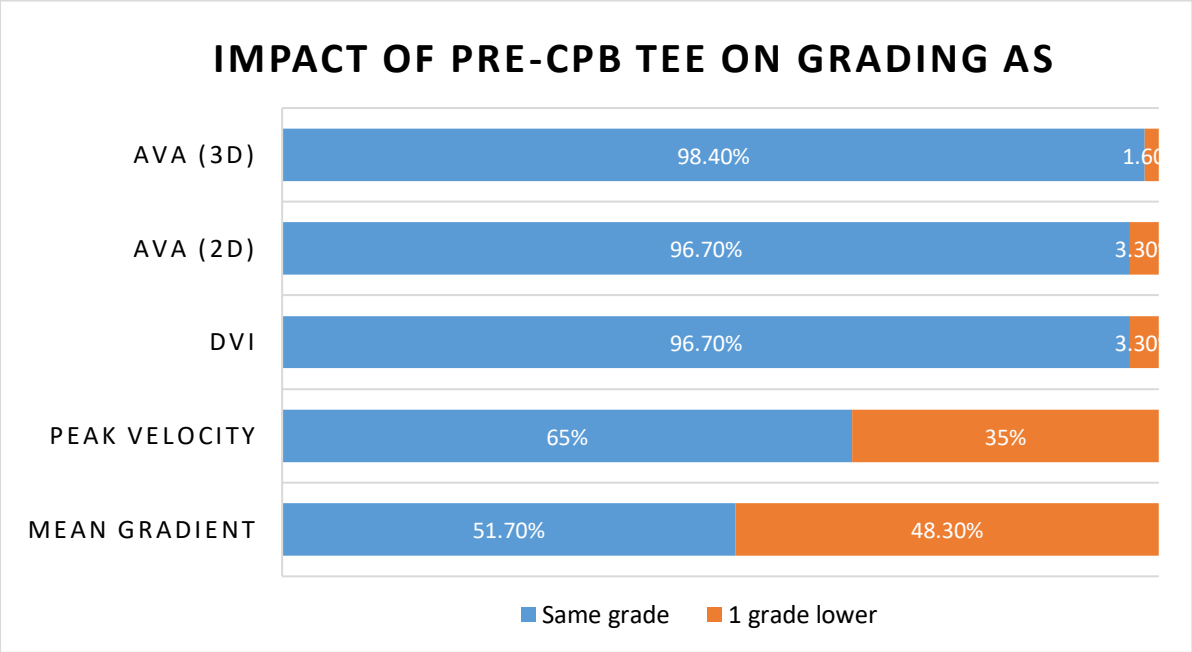

Figure 29: Impact of pre-CPB TEE on grading AS with respect to each grading parameter (AVA- Aortic valve area, DVI- Dimensionless velocity index)

DISCUSSION

DISCUSSION

This is a prospective study which compared the grading of AS by preoperative TTE and intraoperative pre-CPB TEE based on grading parameters such as AVA, PG_m and V_{max}. This study was conducted on 60 patients who had severe AS. Among them, 46 patients underwent AVR while 14 patients underwent CABG with AVR. The mean age in our cohort was 56 years. The most common cause of AS was degenerative (52%) followed by bicuspid aortic valve (43%). Gamaza-Chulián et al in his study, reported that the mean age of patients with AS was 77 years and the most common cause was degenerative (92%).[76] Our study group was younger in comparison with western literature.

The LV dimensions and aortic annulus diameter measurements in our cohort were comparable between TTE and TEE and the difference was statistically not significant . This is in accordance with the results of Stoddard et al, in which LV dimensions, aortic root diameter were comparable between TTE and TEE.[80]

In our cohort, we found that there was a statistically significant decrease in ejection fraction (EF) calculated during pre-CPB TEE compared to preoperative TTE. Even though statistically significant, the difference was clinically not significant as in both TTE and TEE all the patients were classified under good LV function (EF > 55%). This difference in EF may have been due to the difference in the method of EF calculation between TTE and TEE. Measurement of EF using TTE was done by Teichholz method (cubed formula)

in the parasternal short axis view at the level of papillary muscle using M-mode by measuring the LV internal diameter (LVID) at end systole and end diastole. During pre-CPB TEE, EF was calculated using biplane planimetry (area calculated using simultaneous ME four and two chamber views) with modified Simpson's rule. Teichholz method (M-mode) is used during TTE because it is less time consuming and it only needs adequate visualisation of the endocardium in mid-ventricle. However, it only measures circumferential contraction of LV in a single plane. Hence significant assumptions about the LV geometry is made for the LV volume calculation leading to errors in EF calculation. On the other hand, biplane planimetry with modified Simpson's rule directly measures the contribution of longitudinal contraction.[84] Hence it corrects for the shape distortion and minimizes mathematical assumption.[27] So the biplane method of disks (modified Simpson's method) is the method recommended by the ASE for measuring LVEF.[85] However we used Teichholz method (M-mode) in TTE because, TTE requires good acoustic windows to visualise the endocardial border to allow accurate tracing when using modified Simpson's method. Obese patients, patients with chronic obstructive pulmonary disease, patients with limited space between ribs, respiratory movement of patients will often lead to poor image quality. Studies have reported that LVEF calculation could not be done accurately using modified Simpson's method due to poor image quality in 31-38% of patients while using TTE.[84]

The significant reduction in EF during pre-CPB TEE may also have been due to the myocardial depressant effect of the anaesthetic agents used in general anaesthesia. We routinely used propofol-fentanyl combination for induction followed by sevoflurane for maintenance of anaesthesia. Propofol-fentanyl combination has been associated with negative inotropic effect leading to decrease in heart rate, blood pressure, stroke volume and EF. While the decrease in blood pressure may be due to the vasodilatory effect of propofol, the decrease in LV function is predominantly due to its myocardial depressant effect.[81,82,83] Sevoflurane also causes myocardial depression as evidenced by significant dose-dependent decrease in fractional shortening, stroke volume and EF.[84]

In our study, we found that there was a statistically significant difference between the PG_m and V_{max} measured by preoperative TTE and intraoperative pre-CPB TEE. ACC/AHA guidelines for management of patients with valvular heart disease provides an algorithm for decision making in patients with AS.[57] According to this algorithm, Doppler derived peak velocity or PG_m are the primary determinants of severity of AS. The presence of symptoms, CE based AVA and LV ejection fraction (LVEF) are the critical branch points in the decision tree for AVR. Further, patients with moderate AS planned for other cardiac surgery is a class IIa indication for AVR.[57] Hence the accurate grading of AS is of prime importance for surgical decision of AVR.

However, accurate grading of AS can be difficult due to the grading discordance. Grading discordance is defined as a difference in grading assignment between the parameters. This usually occurs in patients with depressed LV function termed as low-flow, low-gradient AS.[58] But grading discordance may occur even in patients with normal LVEF due to reduction in LV stroke volume with preserved LV systolic function.[59-63] "Paradoxical AS", a subtype of aortic valve disease describes low-flow AS with preserved LVEF. This entity can occur in patients with diastolic dysfunction, right ventricle (RV) dysfunction, LV hypertrophy, moderate to severe mitral regurgitation (MR).[58,62,64-66] In this study we have focused on patients with normal LVEF who have been diagnosed with severe AS. All our patients had normal RV function.

Studies have noted discordance in grading AS is greater during pre-CPB TEE compared with preoperative TTE even when controlling for LVEF and MR.[2] This holds true in our study, as we excluded patients with LV dysfunction and more than mild MR. Approximately 51% of patients in our cohort had discordance in grading of AS with respect to anyone of the grading parameter during pre-CPB TEE. We found a significant decrease in V_{max} and PG_m during pre-CPB TEE compared to preoperative TTE. This finding is similar to the results reported by Uda et al.[11] The influence of positive pressure ventilation (PPV) during general anaesthesia produces predictable decreases in the LV stroke volume affecting the grading of AS in a similar fashion to the

characteristics that lead to “paradoxical AS”.[2] The transvalvular flow depends on the preload, afterload, heart rate (HR), LV systolic function and diastolic compliance. The influence of general anaesthesia, positive pressure ventilation, hemodynamic changes and surgical manipulation affects the transvalvular flow which leads to significant decrease in PG_m and $V_{max.}$ [54]

The grading of AS based on V_{max} and PG_m is highly dependent on the alignment of the Doppler beam to the flow across the stenotic aortic valve. Any suboptimal probe alignment or differences in probe alignment between preoperative TTE and pre-CPB TEE can also lead to discordance in grading in the same patient. During TTE, there have been discrepancies in PG_m and V_{max} in same patient based on apical or non-apical views used for measurement of the grading parameter. This is due to the aortic root angulation with respect to LV which varies with individuals.[67] But in our study, we routinely used measurements from all the possible windows and recorded the highest value. Anyhow, it is not clear to what extent the alignment of Doppler beam influences the values obtained during transition from TTE to intraoperative pre-CPB TEE. Since the same operator performed the TTE and TEE and relied on optimal alignment and reliance of the highest velocity, we have been able to minimise any discordance based on inter-observer variability.

In our cohort, there was a marginal increase in CE based AVA, when the LVOT area was measured by 2D in the intraoperative pre-CPB TEE when compared to preoperative TTE but it was statistically not significant. This is in

contrary to the report published by Whitener et al[3] in which AVA measured by pre-CPB TEE was significantly higher than that measured by preoperative TTE. The calculation of CE based AVA depends on the accurate LVOT diameter assessment.[12,56,68] Two dimensional TTE measurement of LVOT diameter underestimates the true LVOT CSA, especially in patients with AS who demonstrate elliptical or less circular LVOT.[12] Also, assessment of LVOT diameter varies slightly between the imaging modalities based on the viewing windows like parasternal long axis view in TTE and midesophageal long axis view in TEE. Shiran et al demonstrated that TTE underestimates the LVOT diameter when compared with TEE. This leads to a smaller CE based AVA for TTE when compared with TEE.[69] But in our cohort, LVOT CSA measured by 2D TTE and 2D TEE were comparable and statistically not significant. This may be the reason for the comparable CE based 2D AVA in our study. The accurate reproducibility of LVOT diameter using TTE and TEE have been reported.[78] In our study the LVOT area measured by 2D was similar both by TTE and TEE and there was no difference in the AVA measured between TTE and TEE. We hypothesise that anaesthetic induced changes in the LV stroke volume produces similar decreases in the peak velocity and VTI of both LVOT and aortic valve, leading to similar AVA between preoperative TTE and intraoperative TEE. Our finding of similar AVA on TTE and TEE is thus different from study published by Whitener et al[3] The study by Whitener et al

was retrospective and relied on chart assessments of cases done by different clinicians who were not specifically addressing the study question.

In our study, Dimensionless velocity index (DVI) was found to be comparable between TTE and TEE with a mean of 0.2. This is in concordance with the results reported by Uda et al.[11] DVI is a flow independent grading parameter and is less influenced by the loading conditions of heart. Also LVOT diameter is not taken into account for DVI calculation making it less prone for errors. DVI is considered reliable in assessing severity of AS intraoperatively.[79] The finding of similar DVI between the preoperative TTE and intraoperative TEE also supports our contention that the anaesthetic induced reduction in the stroke volume produces similar changes in the VTI at the level of LVOT and the aortic valve.

The European Association of Echocardiography and American Society of Echocardiography guidelines advocate LVOT diameter derived from 2-dimensional echocardiography to be used to estimate CE based AVA.[29] The accuracy of CE based AVA is important, especially when severe calcification of the aortic valve makes it difficult to measure the planimetric AVA. This calculation is based on the assumption that LVOT has circular geometry. But several studies have reported elliptical geometry of LVOT, casting a doubt on the CE derived AVA which is based on 2D LVOT cross sectional area.[5,70,71]

As already discussed, studies have found that 2D TTE underestimates the assessment of LVOT diameter when compared to TEE.[12,56,68,69] Therefore,

we decided to incorporate 3D derived LVOT area in the CE equation to derive the AVA. LVOT diameter was measured both using 3D TTE preoperatively and 3D TEE intraoperatively. The LVOT area assessed by 3D was incorporated to the CE to derive the AVA, with a view to assess whether an increase in LVOT area would affect the grading of the severity of the AS. In our cohort, 2D TTE underestimated the LVOT CSA when compared to 2D TEE but it did not reach statistical significance. But when compared to 3D-TEE, LVOT CSA was significantly underestimated both by 2D TTE and 2D TEE. 2D TTE and 2D TEE considers LVOT as circular leading to underestimation of 2D LVOT CSA when compared to 3D TEE derived LVOT CSA. This observation is in accordance with the results of Saitoh et al, which also reported that 2D-TTE and 2D-TEE significantly underestimated the LVOT area compared to 3D-TEE.[7]

In our study, 3D derived LVOT area was significantly higher than the 2D derived LVOT area by both TTE and TEE. However, the 3D TTE derived LVOT CSA was significantly lower than that measured by 3D TEE. This may have been due to the insufficient image quality in 3D TTE which led to inaccurate LVOT CSA. The reduced spatial and temporal resolution of TTE compared to TEE may account for this. Gaspar et al in his study found similar limitation with 3D TTE and reported that LVOT CSA derived from 3D TTE is not good as that of 2D TTE and CT derived LVOT CSA.[72] However, 3D TEE has superior image quality and can be used for accurate assessment of LVOT CSA.[71] TEE has better imaging windows by which good quality 2D images can

be acquired which in turn improves the quality of 3D images. Therefore, 3D TEE overcomes the problem associated with 3D TTE.[72] Using high quality 3D TEE acquisitions, LVOT CSA can be calculated by lining up two orthogonal planes and then tracing the LVOT CSA in the short axis using quantification software.[73] Koto et al reported similar findings to our study as 3D TEE provides precise assessment of LVOT in AS patients than 2D and 3D TTE and it is comparable to values obtained from multi-detector CT (MDCT).[74]

In our cohort, we calculated the AVA using continuity equation, based on LVOT area measured by 3D. We found that when AVA was calculated using continuity equation based on 3D LVOT area, the AVA was marginally higher with TEE when compared with preoperative TTE, but the difference was statistically not significant. But when compared to 3D TEE, 2D TTE and TEE significantly underestimated the AVA. But the valve area derived from 3D LVOT area was still less than 1.0cm^2 and therefore the grading of the severity of AS was not affected. This is in concordance with the results of Teixeira et al, which also reported that CE based 2D AVA measured by TTE is significantly less than that measured by 3D TEE when 3D LVOT CSA is integrated in the CE.[86] Poh et al also used real time 3D color doppler derived LVOT stroke volume in the CE for AVA calculation and found it to be more accurate than 2D CE derived AVA.[87] The CE based AVA using 2D echocardiography significantly underestimates the AVA owing to the elliptical shape of the LVOT.[86] Saitoh et al also demonstrated that patients classified as severe AS

using 2D LVOT area could be reclassified into moderate AS when 3D LVOT area is being used in continuity equation.[7] The accuracy of CE based AVA is of prime importance, especially when the aortic valve is heavily calcified making it difficult to measure the planimetric AVA. Therefore, evaluation of LVOT CSA with 3D TEE would be of great importance in accurate assessment of AVA, especially in patients with discrepancy regarding grading of AS with respect to other parameters and thus avoids unnecessary procedures.[7]

Brien et al reported that incorporation of multi-detector CT (MDCT) derived LVOT CSA in the CE provides accurate assessment of AVA.[88] Koto et al reported comparable values of LVOT CSA measured by 3D TEE and MDCT.[74] MDCT and magnetic resonance imaging (MRI) provides accurate assessment of LVOT CSA. However, MDCT with contrast study is contraindicated in patients with renal failure and hypersensitivity to iodine contrast. MRI cannot be used in patients with a pacemaker or implanted cardioverter defibrillator. 3D TEE helps in simultaneous evaluation of LVOT and aortic valve using orthogonal plane in AS patients. Also, unlike MDCT or MRI, real time (RT) 3D TEE allows on-site or live evaluation of LVOT and aortic valve geometry during transcatheter aortic valve implantation (TAVI). Measurement of annular diameter in both anteroposterior and medial-lateral planes is of prime importance during TAVI where the annular geometry and LVOT geometry are the key factors deciding the seating of valve and thereby preventing paravalvular regurgitation after the procedure.[75]

To summarize, with supportive evidence from the available literature we made the following interpretations.

1. LV dimensions and aortic annulus diameter measurements were comparable between preoperative TTE and intraoperative TEE.
2. Ejection fraction measured by intraoperative TEE is significantly less than that measured by preoperative TTE probably due to the difference in method of EF calculation and due to the myocardial depressant effect of anesthetic agents.
3. TEE underestimates mean gradient and peak velocity when compared to TTE and this leads to downgrading of AS (statistically significant).
4. Continuity equation based 2D AVA measured by TTE and TEE were comparable, and the difference was statistically not significant. The grading of AS was not affected when AVA was used as the criteria for grading AS intraoperatively
5. Dimensionless velocity index measured by TTE and TEE were similar and the difference was statistically not significant. This suggests the influence of positive pressure ventilation and anaesthetic agents affect the LVOT VTI and aortic valve VTI to a similar extent in patients with severe AS. Using DVI will not affect the grading of AS intraoperatively.

6. TTE (2D, 3D) and 2D TEE significantly underestimated the LVOT cross sectional area when compared with 3D TEE which is considered as the reference method.
7. AVA measured by continuity equation using 3D derived LVOT area by 3D TTE and 3D TEE were comparable and the difference was statistically not significant.
8. 2D TTE and 2D TEE significantly underestimated the CE based AVA when compared to 3D TTE and 3D TEE. The difference reached statistical significance. The AVA measured by 3D derived LVOT area by continuity equation does not affect the grading of AS.

Limitations

1. Although 3D TEE is considered as the reference method, there is no gold standard reference technique to determine the LVOT CSA. The essential message from our study is that TTE (2D, 3D) and 2D TEE derived LVOT CSA may not be consistent with the 3D TEE derived LVOT CSA.
2. The comparison of LVOT area between 3D TTE and 3D TEE showed a statistically significant difference between the two even though the difference in the mean area between the two is only 0.08 cm^2. This is because more patients in our study had a greater increase in 3D TEE derived LVOT area compared to 3D TTE. This is reflected in the difference in the median shown in the Box-Whisker plot in figure 17. More patients have to be studied to bring this difference into greater prominence.
3. Our study group includes only patients with severe AS who presented for surgery. In this group of severe AS, the AVA may not increase with flow due to extensive calcification of aortic valve leaflets. This may not hold true in patients with moderate/ mild AS where the LVOT area and thickened aortic valve leaflets may increase in size with increased flow across the aortic valve.
4. Also we have excluded patients with LV dysfunction, which is an important confounding factor. Our results cannot be extended to patients with LV dysfunction.

CONCLUSION

Conclusion

The use of peak velocity and mean gradient across the aortic valve as a grading parameter of AS significantly underestimated the severity of AS during pre-CPB TEE despite maintaining hemodynamics within 20% of baseline. However, when the aortic valve area is calculated by means of continuity equation, there is no discordance in grading of severity of AS between preoperative TTE and intraoperative TEE. This is irrespective of whether the LVOT area has been calculated by 2D or 3D echocardiography. This finding is explained by the fact that anesthesia and positive pressure ventilation produces similar decreases in the LVOT and aortic valve velocities and VTI. Therefore, assessing the aortic valve area will be useful in patients with discordance in grading of AS severity due to the use of flow dependent variable like mean gradient and peak velocity. 3D TEE provides better assessment of LVOT geometry and cross-sectional area compared to TTE and 2D TEE. The use of 3D TEE derived LVOT area in AVA does not influence the grading of the severity of the AS.

In conclusion, the application of dimensionless velocity index and calculating the aortic valve area using continuity equation based on 2D or 3D LVOT area, will minimize the disparity in the grading of AS between preoperative TTE and intraoperative TEE.

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ANNEXURES

Observation Chart

Preoperative assessment:

Name of patient: Hospital number:

Age: Gender:

Weight : Height:

Diagnosis: Surgical procedure:

Comorbidities: NYHA:

Heart Rate: Rhythm:

SpO_2 : Blood pressure:

Table 1:

	LV Dimension (mm)	**Aortic Valve (Bi/Tri)**	**Aortic Annulus (mm)**	**Ejection Fraction (%)**	**LVOT CSA 2D (cm^2)**	**LVOT CSA 3D (cm^2)**
Preoperative TTE						
Pre-CPB TEE						

Table 2:

	Mean Gradient (mmHg)	Peak Gradient (mmHg)	AVA 2D (cm^2)	AVA 3D (cm^2)	Peak Velocity (m/s)	DVI	Grading of AS
Preop TTE							
Pre-CPB TEE							

Outcome parameters:

Impact of pre-CPB TEE on AS grade	Mean Gradient	Peak Velocity	Dimensionless velocity index	AVA 2D	AVA 3D
1 Grade Higher					
No Change					
1 Grade Lower					
2 Grades Lower					
Any Change					

Patient Information form

Title of the study:

Grading Aortic Stenosis with mean gradient and aortic valve area: A comparison between preoperative Transthoracic Echocardiography and precardiopulmonary bypass Echocardiography

Why are we doing this study?

The purpose of this study is to assess the role of Transesophageal echocardiography in assessment of aortic stenosis in comparison to preoperative transthoracic Echocardiography. It will also help to explore further the management of aortic stenosis during cardiac surgery.

Study numbers: We request you to participate in the study wherein we are planning to evaluate intraoperative echocardiographic characteristics of aortic stenosis using Trans-esophageal echocardiography and verify the preoperative transthoracic echocardiography findings. We hope to include 60 people from this hospital in this study.

What is aortic stenosis?

Heart valves lie at the exit of each of your four heart chambers and maintain one-way blood flow through your heart. The four heart valves make sure that blood always flows freely without obstruction in a forward direction and that there is no backward leakage. Aortic valve is one of the heart valves lying between left ventricle and aorta. The aortic valve normally opens and closes to let the blood pass away from the left ventricle to aorta. Aortic Stenosis means obstruction passage of blood from left ventricle to aorta. It occurs due to various reasons.

What is Trans-esophageal echocardiography?

Trans-esophageal echocardiography or TEE is a test that uses sound waves to create high-quality moving pictures of the heart and its blood vessels. This can pin point the problematic areas of the heart and helpful in assessing function of heart valves before and after valve replacement surgery. Usually echocardiography is performed via chest (transthoracic echocardiography). However, under anesthesia, transthoracic echocardiography cannot be performed during cardiac surgery as the surgeon will be operating in that area. Hence echocardiography probe is inserted via esophagus (food pipe). TEE involves a flexible tube (probe) with a transducer at its tip. The Anesthesiologist will guide the probe down your throat and into your esophagus (the passage leading from your mouth to your stomach). This will be done when you will be unconscious under anesthesia and it will not cause any discomfort to you. This approach allows your doctor to get more detailed pictures of your heart because the esophagus is directly behind the heart.

What is the role of Trans-esophageal echocardiography in Aortic Stenosis?

Trans-esophageal echocardiography (TEE) is a useful monitoring tool during cardiac surgery. American society of Anesthesiology and Society of cardiovascular Anesthesiologists have

strongly recommended the use of intraoperative TEE in adult patients having aortic stenosis(AS). It helps to determine the cause of AS, to know how severe it is and plan the surgical procedure. Based on the TEE findings about AS, the anesthetic plan and course of surgery may be changed. This is of great help in assessing the heart function during the operation.

How is Transesophageal echocardiography performed?
This will be done when you are under anesthesia and will not cause any discomfort to you. Your Anesthesiologist will insert the lubricated probe into your mouth. He or she will then gently guide it down your throat into your esophagus. Your esophagus lies directly behind your heart. During this process, Anesthesiologist will take care to protect your teeth and mouth from injury.

What are the risks and side-effects?
We do not expect that our study will cause any injury to you because our study protocol is a part of routine intraoperative TEE examination. You will be under the effect of anesthesia while the test is being performed, thus you are unlikely to experience any discomfort.

Can you withdraw from this study after it starts?
Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way.

What will happen if you develop any study related injury?
We do not expect any injury to happen to you because of our study as it is a part of routine examination during the surgery. If any injury occurs it will be managed either conservatively or surgically at free of cost.

Will you have to pay for the study? No.

Will your personal details be kept confidential?
Your personal details will be kept confidential. The result of this study will be published in a medical journal but you will not be identified by name in any publication or presentation of results.

If you have any further questions, please ask:
Dr.K.Vasanth, Senior Resident, Department of Cardiothoracic and Vascular Anaesthesia (Ph No: 7708311090) Email : vasanthdr20@gmail.com
Dr.Suneel P.R, Professor of Department of Cardiothoracic and Vascular Anaesthesia.
Dr Mala Ramanathan, Member Secretary IEC,SCTIMST (Ph No-0471-2524234)
Email: iec.mem.sec@sctimst.ac.in

CONSENT FORM

I, _____,[**Participant's name: Date of Birth / Age (in years)**] declare that I have read the patient information sheet provided to me regarding the study titled

Grading Aortic Stenosis with mean gradient and aortic valve area: A comparison between preoperative Transthoracic Echocardiography and precardiopulmonary bypass Echocardiography

- I have clarified any doubts that I had. [ ]
- I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my usual treatment or my legal rights [ ]
- I understand that the study staff and institutional ethics committee members will not need my permission to look at my health records even if I withdraw from the trial. I agree to this access [ ]
- I understand that my identity will not be revealed in any information released to third parties or published [ ]
- I understand that I have to undergo Transthoracic and Transesophageal echocardiography which is routinely done for all open heart surgery patients [ ]
- I voluntarily agree to take part in this study [ ]
- I received a copy of this signed consent form [ ]

Name: Name of witness :

Signature: Relation to participant :

Date:

Study Independent contact person- Dr.Mala Ramanathan, AMCHSS & IEC Member Secretary, SCTIMST (0471-2446234) Email: iec.mem.sec@sctimst.ac.in

<u>Declaration by Person Obtaining Consent</u>

I attest that the requirements for informed consent for the medical research project described in this form have been satisfied. I have discussed the research project with the participant and explained to him or her in nontechnical terms all of the information contained in this informed consent form, including any risks and adverse reactions that may reasonably be expected to occur. I further certify that I encouraged the participant to ask questions and that all questions asked were answered.

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രോഗിക്കുള്ള കാര്യവിവരണപത്രം

പഠന ശീർഷകം:

അയോർട്ടിക് സ്റ്റെനോസിന്റെ മീൻ ഗ്രേഡിയന്റിന്റെയും അയോർട്ടിക് വാൽവ് മേഖലയുടെയും ഗ്രേഡിംഗ്. ശസ്ത്രക്രിയക്ക്മുൻപുള്ള ട്രാൻസ് തൊറാസിക് എക്കോകാർഡിയോഗ്രഫിയുടെയും കാർഡിയോപൾമനറി ബൈപ്പാസിനു മുൻപുള്ള ട്രാൻസ്ഈസോഫേജിയൽ എക്കോകാർഡിയോ ഗ്രഫിയുടെയും താരതമ്യം

പഠന നമ്പർ

ശസ്ത്രക്രിയക്കിടയിൽ ട്രാൻസ് ഈസോഫേജിയൽ എക്കോകാർഡിയോഗ്രഫി ഉപയോഗിച്ചുള്ള അയോർട്ടിക് സ്റ്റെനോസിസിന്റെ എക്കോകാർഡിയോഗ്രഫി സ്വഭാവങ്ങൾ അപഗ്രഥിക്കാനും ശ്സ്ത്രക്രിയക്കുമുൻപുള്ള ട്രാൻസ് തൊറാസിക് എക്കോകാർഡിയോഗ്രഫി കണ്ടെത്തലുകൾ പരിശോധിക്കാനും ഞങ്ങൾ ആസൂത്രണം ചെയ്യുന്ന പഠനത്തിൽ പങ്കെടുക്കാൻ താങ്കളോട് ആഭ്യർത്ഥിക്കുന്നു.

ഈ ആശുപത്രിയിൽ നിന്നും 60 പേരെ പങ്കെടുപ്പിക്കാമെന്ന് ഞങ്ങൾ പ്രതീക്ഷിക്കുന്നു.

അയോർട്ടിക് സ്റ്റെനോസിസ് എന്നാലെന്ത്?

താങ്കളുടെ ഹൃദയത്തിന്റെ നാല് അറകളുടെയും പുറത്തേക്കുള്ള വഴിയൽ ഹൃദയ വാൽവുകൾ രക്ത പ്രവാഹം ഒരുദിശയിലേക്ക് നിലനിർത്തി സ്ഥിതിചെയ്യുന്നു. രക്തം മുന്നോട്ടുള്ള ദിശയിൽ തടസ്സമൊന്നുംകൂടാതെ സ്വതന്ത്രമായി പ്രവാഹിക്കുന്നു എന്നും പുറകിലേക്ക് ഒരു ചോർച്ചയും ഉണ്ടാകുന്നില്ലെന്ന് നാല് ഹൃദയ വാൽവുകളും ഉറപ്പാക്കുകയും ചെയ്യുന്നു. അയോർട്ടക്കും ഇടതു വെൻട്രിക്കിളിനുമിടയിലാണ് അയോർട്ടിക് വാൽവ് സ്ഥിതിചെയ്യുന്നത്. ഇടതുവെൻട്രിക്കിളിൽ നിന്നും അയോർട്ടയിലേക്ക് രക്തം ഒഴുകുന്നതിനാണ് സാധാരണയായി അയോർട്ടിക് വാൽവ് തുറക്കുകയും അടയ്ക്കുകയും ചെയ്യുന്നത്. ഇടതു വെൻട്രിക്കിളിൽനിന്നും അയോർട്ടയിലേക്ക് രക്തം പ്രവഹിക്കുന്നതിന് തടസ്സമുണ്ടാകുന്നതിനെയാണ് അയോർട്ടിക് സ്റ്റെനോസിസ് എന്നു പറയുന്നത്. വിവിധകാരണങ്ങളാൽ അതുണ്ടാകുന്നു.

ട്രാൻസ്സ് ഈസോഫേജിയൽ എക്കോകാർഡിയോഗ്രഫി(റ്റിഇഇ) എന്നാൽ എന്താണ്?

ഹൃദയത്തിന്റെയും അതിന്റെ രക്തക്കുഴലുകളുടെയും, ചലിക്കുന്നതും ഉയർന്ന ഗുണനിലവാര മുള്ളതുമായ ചിത്രങ്ങൾ സൃഷ്ടിക്കുന്നതിന് ശബ്ദതരംഗങ്ങളുപയോഗിക്കുന്ന ഒരു പരിശോധന യാണ് എക്കോ കാർഡിയോഗ്രഫി (റ്റിഇഇ). ഹൃദയത്തിലെ പ്രശ്നമുള്ള മേഖലകൾ ഇതിന് ചൂണ്ടി ക്കാണിക്കുവാനാകും, ആയത് വാൽവ് മാറ്റശസ്ത്രക്രിയക്കുമുൻപും ശേഷവുമുള്ള ഹൃദയ വാൽവിന്റെ പ്രവർത്തനം വിലയിരുത്താൻ സഹായകമാണ്. സാധാരണ എക്കോകാഡിയോഗ്രഫി ചെയ്യുന്നത് നെഞ്ചുവഴിയാണ്. എന്നിരുന്നാലും മയക്കലിന് വിധേയമായിരിക്കുമ്പോൾ കാർഡിയാക് സർജൻ ശസ്ത്രക്രിയനടത്തുന്നത് അതേ മേഖലയിലായതിനാൽ റ്റിറ്റിഇ ചെയ്യാനാകില്ല. അതിനാൽ എക്കോ കാർഡിയോഗ്രഫിയുടെ നിരീക്ഷണ ഉപകരണം ഈസോഫാഗസിലൂടെ (അന്നനാളം) കട ത്തുന്നു. റ്റിഇഇയിൽ അറ്റത്ത് ട്രാൻസ്ഡ്യൂസർഘടിപ്പിച്ച വഴക്കമുള്ള ഒരു കുഴലുണ്ട് (പ്രോബ്). അനസ്തീഷ്യോളജിസ്റ്റ് താങ്കളുടെ തൊണ്ടയിലൂടെ ഈസോഫാഗസിൽ പ്രോബ് എത്തിക്കു ന്നു(താങ്കളുടെ വായിൽനിന്നും ആമാശയത്തിലേക്കുള്ള വഴി). ഇത് ചെയ്യുന്നത് താങ്കൾ മയക്കലിന് വിധേയമായി ബോധരഹിതമായിരിക്കുമ്പോഴാണെന്നതിനാൽ താങ്കൾക്ക് അസ്വസ്ഥതയുണ്ടാക്കില്ല. ഈസോഫാഗസ് ഹൃദയത്തിന്റെ നേരെ പുറകിലാണെന്നതിനാൽ താങ്കളുടെ ഡോക്ടർക്ക് താങ്ക ളുടെ ഹൃദയത്തിന്റെ കൂടുതൽ വിശദമായ ചിത്രങ്ങൾ ലഭിക്കാൻ ഈ സമീപനം സഹായിക്കും.

അയോർട്ടിക് സ്റ്റെനോസിസിൽ ട്രാൻസ്സ് ഈസോഫേജിയൽ എക്കോകാർഡിയോഗ്രഫി യുടെ പങ്കെന്ത്?

ഹൃദയശസ്ത്രക്രിയയിൽ നിരീക്ഷണത്തിന് പ്രയോജനപ്രദമായ ഒരു ഉപകരണമാണ് ട്രാൻസ്സ് ഈസോഫേജിയൽ എക്കോകാഡിയോഗ്രഫി (റ്റിഇഇ). അയോർട്ടിക് സ്റ്റെനോസിസ് (എഎസ്) രോഗികളുടെ ശസ്ത്രക്രിയക്കിടയിൽ അമെരിക്കൻ സൊസൈറ്റി ഓഫ് അനസ്തീഷ്യോളജിയും സൊസൈറ്റി ഓഫ് കാർഡിയോളജിയും ട്രാൻസ്സ് ഈസോഫേജിയൽ എക്കോകാർഡിയോഗ്രഫിയുടെ ഉപയോഗം ശക്തമായി നിർദ്ദേശിക്കുന്നു. അത് അയോർട്ടിക് സ്റ്റെനോസിസിന്റെ കാരണം കണ്ടെത്താനും ഗുരുതരാവസ്ഥ മനസ്സിലാക്കാനും ശസ്ത്രക്രിയാനടപടി ആസൂത്രണം ചെയ്യാനും സഹായിക്കുന്നു. അയോർട്ടിക് സ്റ്റെനോസിസ്സിന്റെ റ്റിഇഇ കണ്ടെത്തലുകളുടെ അടിസ്ഥാനത്തിൽ മയക്കൽ ആസൂത്രണം ചെയ്യുന്നതിലും ശസ്ത്രക്രിയയുടെ നടപടികളിലും മാറ്റമുണ്ടായേക്കാം. ശസ്ത്രക്രിയക്കിടയിൽ ഹൃദയത്തിന്റെ പ്രവർത്തനം വിലയിരുത്തുന്നതിന് ഇത് വളരെ സഹായകമാണ്.

റ്റിഇഇ എങ്ങിനെയാണ് ചെയ്യുന്നത്?

ഇത് ചെയ്യുന്നത് താങ്കൾ മയക്കലിന് വിധേയമായിരിക്കുമ്പോഴാണെന്നതിനാൽ താങ്കൾക്ക് ഒരു അസ്വസ്ഥതയുമുണ്ടാക്കില്ല. താങ്കളുടെ അനസ്തീഷ്യോളജിസ്റ്റ്, മയപ്പെടുത്തിയ പ്രോബ് താങ്കളുടെ വായിൽ കടത്തും. എന്നിട്ട് സാവകാശം തൊണ്ടയിലൂടെ അത് താങ്കളുടെ ഈസോഫാഗസിലേക്ക് നയിക്കും. ഹൃദയത്തിന് നേരേ പുറകിലാണ് താങ്കളുടെ ഈസോഫാഗസ് സ്ഥിതിചെയ്യുന്നത്. ഈ പ്രക്രിയക്കിടയിർ താങ്കളുടെ പല്ലുകൾക്കും വായ്ക്കും പരുക്കുണ്ടാകാതെ സംരക്ഷിക്കാൻ അനസ്തീഷ്യോളജിസ്സ് ശ്രദ്ധിക്കും.

അപായങ്ങളും പാർശ്വഫലങ്ങളും എന്തെല്ലാം ?

ശസ്ത്രിക്രിയക്കിടയിലുള്ള പതിവ് റ്റിഇഇ പരിശോധനയുടെ ഭാഗമാണ് ഞങ്ങളുടെ പഠന പദ്ധതി എന്നതിനാൽ ഞങ്ങളുടെ പഠനംകൊണ്ട് താങ്കൾക്ക് പരുക്കുണ്ടാകുമെന്ന് ഞങ്ങൾ പ്രതീക്ഷിക്കുന്നില്ല. ഇത് ചെയ്യുന്നത് താങ്കൾ മയക്കലിന് വിധേയമായിരിക്കുമ്പോഴാണെന്നതിനാൽ താങ്കൾക്ക് ഒരു അസ്വസ്ഥതയും അനുഭവപ്പെടാൻ സാദ്ധ്യതയില്ല.

ഞങ്ങൾ എന്തിന് ഈ പഠനം നടത്തുന്നു?

അയോർട്ടിക് സ്റ്റെനോസിസ്സിന്റെ അപ്ഗ്രഥനത്തിൽ വിലയിരുത്തലിൽ ട്രാൻസ്സ് ഈസോഫേജിയൽ എക്കോകാഡിയോഗ്രഫിയുടെ പങ്ക് ശസ്ത്രക്രിയക്കുമുൻപുള്ല ടാൻസ്സ് ഈസോഫേജിയൽ എക്കോകാഡിയോഗ്രഫിയുമായി താരതമ്യം ചെയ്യുക എന്നതാണ് ഈ പഠനത്തിന്റെ ഉദ്ദേശം. ഹൃദയശസ്ത്രക്രിയക്കിടയിൽ റ്റിഇഇയുടെ ഉപയോഗം കൂടുതൽ അന്വേഷിക്കാൻ ഇത് സഹായകമാകും.

പഠനമാരംഭിച്ചശേഷം താങ്കൾക്ക് പിൻമാറാമോ?

താങ്കളുടെ പഠനത്തിലുള്ള പങ്കാളിത്തം തികച്ചും സ്വമേധയായാണ്, പഠനത്തിലെ പങ്കാളിത്തത്തിൽ നിന്നും പിൻമാറാൻ തീരുമാനമെടുക്കാൻ താങ്കൾക്ക് സ്വാതന്ത്ര്യമുണ്ട്. താങ്കളങ്ങിനെ ചെയ്താലും താങ്കളുടെ ഈ ആശുപത്രിയിലെ പതിവ് ചികിത്സയെ ഒരുവിധത്തിലും ബാധിക്കില്ല.

പഠനവുമായി ബന്ധപ്പെട്ട് താങ്കൾക്ക് എന്തെങ്കിലും പരുക്കുണ്ടായാലെന്ത് സംഭവിക്കും ?

ശസ്ത്രിക്രിയക്കിടയിലുള്ള പതിവ് റ്റിഇഇ പരിശോധനയുടെ ഭാഗമാണ് ഞങ്ങളുടെ പഠന പദ്ധതി എന്നതിനാൽ ഞങ്ങളുടെ പഠനംകൊണ്ട് താങ്കൾക്ക് പരുക്കുണ്ടാകുമെന്ന് ഞങ്ങൾ പ്രതീക്ഷിക്കുന്നില്ല.

പഠനത്തിനായി താങ്കൾ പണം ചിലവാക്കണോ?
വേണ്ട

താങ്കളുടെ വ്യക്തിവിവരങ്ങൾ രഹസ്യമായിരിക്കുമോ?
പഠനഫലങ്ങൾ ഒരു വൈദ്യശാസ്ത്ര ജേർണലിൽ പ്രസിദ്ധീകരിക്കുമെങ്കിലും താങ്കളെ വ്യക്തിപരമായി തിരിച്ചറിയാനിടയാക്കുന്നതൊന്നും പ്രസിദ്ധീകരണത്തിലോ, പഠനഫലങ്ങളുടെ പ്രദർശനത്തിലോ ഉണ്ടാവില്ല.
താങ്കൾക്ക് കൂടുതൽ എന്തെങ്കിലും ചോദ്യങ്ങൾ ഉണ്ടെങ്കിൽ ദയവായി ഡോ. കെ. വസന്ത് , കാർഡിയോതൊറാസിക് ആന്റ് വാസ്ക്കുലാർ അനസ്തീഷ്യേ സീനിയർ റസിഡന്റിനോട് ചോദിക്കുക (ഫോൺ: 7708311090). ഇമെയിൽ. vasanthdr20@gmail.com
പ്രധാന ഗവേഷകന്റെ പേര്. ഡോ. കെ. വസന്ത്
ഡോ. സുനീൽ പിആർ, പ്രൊഫസർ കാർഡിയോതൊറാസിക് ആന്റ് വാസ്ക്കുലാർ അനസ്തീഷ്യേ

പഠനവുമായി ബന്ധമില്ലാത്ത വ്യക്തിയെ ബന്ധപ്പെടുന്നതിന് ദയവായി സ്ഥാപനത്തിലെ നൈതീക കമ്മിറ്റി മെംമ്പർ സെക്രട്ടറി ഡോ. മാല രാമനാഥനെ ബന്ധപ്പെടാം. ഫോൺ 04712524234, email: iec.mem.sec@sctimst.ac.in

കാര്യബോധത്തോടെയുള്ള സമ്മതപത്രം

പ്രഖ്യാപനം

ഞാൻ, _____, **പങ്കാളിയുടെ പേര്, ജനനതിയതി, വയസ്സ് (വർഷത്തിൽ)** പഠനസംബന്ധമായി എനിക്ക് നൽകിയ വിവരങ്ങൾ വായിച്ചു എന്ന് പ്രസ്താവിക്കുന്നു.
അയോർട്ടിക് സ്റ്റെനോസിന്റെ മീൻ ഗ്രേഡിയന്റിന്റെയും അയോർട്ടിക് വാൽവ് മേഖലയുടെയും ഗ്രേഡിംഗ്. ശസ്ത്രക്രിയക്ക്മുൻപുള്ള ട്രാൻസ് തൊറാസിക് എക്കോകാർഡിയോഗ്രഫിയുടെയും കാർഡിയോപൾമനറി ബൈപ്പാസിനു മുൻപുള്ള ട്രാൻസ്ഈസോഫേജിയൽ എക്കോകാർഡിയോഗ്രഫിയുടെയും താരതമ്യം

ദയവായി പ്രസക്തമായ കോളങ്ങൾ അടയാളപ്പെടുത്തുക.

- എനിക്കുണ്ടായ സംശയങ്ങൾ പരിഹരിച്ചു [ ]
- എന്റെ ഈ പഠനത്തിലുള്ള പങ്കാളിത്തം സ്വമേധയായുള്ളതാണെന്നും, എനിക്ക് ഒരു കാരണവും കൂടാതെ ഏതുസമയത്തും, എനിക്കുള്ള വൈദ്യശുശ്രൂഷയെയോ നിയമപരമായ അവകാശങ്ങളെയോ ബാധിക്കാതെ പിൻവാങ്ങാമെന്നും ഞാൻ മനസ്സിലാക്കുന്നു. [ ]
- ഈ പഠനത്തിന്റെ ഗവേഷകർ, നൈതീക കമ്മിറ്റി, നിയന്ത്രണാധികാരികൾ എന്നിവർക്ക് എന്റെ ആരോഗ്യവിവരങ്ങൾ ഞാൻ പഠനത്തിൽനിന്നും പിൻവാങ്ങിയാലും പരിശോധിക്കാൻ എന്റെ സമ്മതം അവശ്യമില്ലെന്ന് ഞാൻ മനസ്സിലാക്കുന്നു. ഇതിനു ഞാൻ സമ്മതിക്കുന്നു, [ ]
- എല്ലാ ഹൃദയം തുറന്നുള്ള ശസ്ത്രക്രിയയിലും പതിവായി ചെയ്യുന്ന ട്രാൻസ് തൊറാസിക്കും ട്രാൻസ് ഈസോഫേജിയലും എക്കോകാർഡിയോഗ്രഫിക്ക് വിധേയനാകണമെന്ന് ഞാൻ മനസ്സിലാക്കുന്നു. [ ]
- ഭാവിയിൽ മൂന്നാം കക്ഷികൾക്കോ പ്രസിദ്ധീകരണത്തിനോ നൽകുമ്പോൾ എന്റെ വ്യക്തിവിവരങ്ങൾ വെളിപ്പെടുത്തുകയില്ലെന്നും ഞാൻ മനസ്സിലാക്കുന്നു. [ ]

- സ്വമേധയാ പഠനത്തിൽ പങ്കെടുക്കാൻ ഞാൻ സമ്മതിക്കുന്നു. [ ]
- സമ്മതപത്രത്തിന്റെ ഒപ്പിട്ട ഒരു പ്രതി എനിക്ക് കിട്ടി. [ ]

പേര്	സാക്ഷിയുടെ പേര്
ഒപ്പ്	ഒപ്പ്
തീയതി	തീയതി

(സമ്മതം വാങ്ങുന്നയാൾ)

മെഡിക്കൽ റിസർച്ച് പ്രോജക്ടിനാവശ്യമായ സമ്മതപത്രത്തിനു വേണ്ടുന്ന എല്ലാ ഘടകങ്ങളും തൃപ്തികരമായി നിർവഹിച്ചിരിക്കുന്നുവെന്ന് ഞാൻ ബോധ്യപ്പെടുത്തുന്നു. പഠനപങ്കാളിയുമായി ഗവേഷണപദ്ധതിയെപ്പറ്റി സാങ്കേതികേതര പദങ്ങളുപയോഗിച്ച് എല്ലാ വിവരങ്ങളെപ്പറ്റിയും ചർച്ച നടത്തുകയും പ്രതീക്ഷിക്കാവുന്ന അപകടസാധ്യതകളും പാർശ്വഫലങ്ങളും വിശദീകരിക്കുകയും ചെയ്തു. പങ്കാളിയെ ചോദ്യങ്ങൾ ചോദിക്കാൻ പ്രേരിപ്പിക്കുകയും എല്ലാ ചോദ്യങ്ങൾക്കും ഉത്തരം നൽകുകയും ചെയ്തു എന്നും ഞാൻ സാക്ഷ്യപ്പെടുത്തുന്നു.

സമ്മതപത്രം വാങ്ങുന്ന ആളുടെ പേരും ഒപ്പും
ഡോ കെ വസന്ത് (ഫോൺ. 7094013291)
സീനിയർ റസിഡന്റ്.

കാർഡിയോതൊറാസിക് ആന്റ് വാസ്ക്കുലാർ അനസ്തീഷ്യ

പഠനവുമായി ബന്ധമില്ലാത്ത വ്യക്തിയെ ബന്ധപ്പെടുന്നതിന് ദയവായി സ്ഥാപനത്തിലെ നൈതീക കമ്മിറ്റി മെംമ്പർ സെക്രട്ടറി ഡോ. മാല രാമനാഥനെ ബന്ധപ്പെടാം. ഫോൺ 04712524234, email: iec.mem.sec@sctimst.ac.in

Technical Advisory Committee (Clinical Studies)

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES & TECHNOLOGY
THIRUVANANTHAPURAM – 695011, INDIA

TAC Registration No: SCT-/S/2018/754 **Date:09.07.2018**

Project title: GRADING AORTIC STENOSIS WITH MEAN GRADIENT AND AORTIC VALVE AREA: A COMPARISON BETWEEN PREOPERATIVE TRANSTHORACIC ECHOCARDIOGRAPHY AND PRECARDIOPULMONARY BYPASS ECHOCARDIOGRAPHY

Principal Investigator:
Dr. K.Vasanth, Senior Resident, Department of Cardiac Anaesthesiology, SCTIMST Degree: M.D. (Anaesthesiology), M.B.B.S.
Co-Principal Investigator(s)
Dr. Suneel, Professor, Department of Cardiac Anaesthesiology , SCTIMST
Dr. Thomas Koshy, Professor, Department of Cardiac Anaesthesiology, SCTIMST
Dr. Bineesh, Assistant Professor, Department of Cardiovascular & Thoracic Surgery, SCTIMST

Members who participated in the TAC meeting on 16/06/2018
Dr. Rupa Sreedhar (Chairperson)
Dr. Prasantakumar Dash
Dr. Krishna Kumar K
Dr. Sankara Sarma P
Dr. Bijulal S
Dr. Jayadevan ER
Dr. Syam K
Dr. Varghese T. Panicker
Dr. K. Shivakumar (Member Secretary)

Dr. Varghese T Panicker, Dr. Rupa Sreedhar, Dr. Jayadevan ER, Dr. Syam K, Dr. Krishna Kumar K, and Dr. Bijulal S stayed away from the proceedings when the projects in which they are involved as investigator were discussed (#762, 768, 769, 772, 775, 776, 778, 782, 784, 785).

Risk Classification of the project (Minimum/ Moderate/ High): Minimum

Requirement of DSMB: No

Recommended members of DSMB: Not applicable

Recommendations of TAC:
Recommended for consideration of IEC in the light of the responses received from the investigator

The PI may note that there can be no additions / alterations in the documents approved by TAC when they are submitted to the IEC.

Signature of the Member Secretary, TAC (Clinical Studies)

Note for IEC
Copy of the investigator's responses to questions/suggestions from TAC is attached (Appendix-1).

श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेन्द्रम
तिरुवनन्तपुरम - ६९५०११, केरल, इंडिया
SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM
Thiruvananthapuram - 695 011, Kerala, India
(An Institute of National Importance under Govt. of India)
Grams : Chitramet, Phone : +91-471-2443152, Fax : +91-471-2550728 / 2446433, E-mail : sct@sctimst.ac.in, Website : www.sctimst.ac.in

Institutional Ethics Committee

(IEC Regn No. ECR/189/Inst/KL/2013/RR-16)

SCT/IEC/1234/AUGUST-2018

28.08.2018

Dr. K. Vasanth
Senior Resident
Department of Anaesthesiology
SCTIMST, Thiruvananthapuram

Dear Dr.Vasanth,

The Institutional Ethics Committee reviewed and discussed your application to conduct the study entitled "GRADING AORTIC STENOSIS WITH MEAN GRADIENT AND AORTIC VALVE AREA: A COMPARISON BETWEEN PREOPERATIVE TRANSTHORACIC ECHOCARDIOGRAPHY AND PRECARDIOPULMONARY BYPASS ECHOCARDIOGRAPHY (IEC/1234)" on 17th August, 2018.

The following documents were reviewed:

Original submission

1. *Covering letter addressed to the Chairman, IEC, SCTIMST with checklist*
2. *TAC Approval Letter*
3. *IEC Application Form*
4. *Project Proposal*
5. *Forwarding Letter from the HOD*
6. *Proforma*
7. *Patient Information Sheet and Informed Consent Form in English and Malayalam*
8. *CV of Principal Investigator and Co- Principal Investigators*

Revised submission

1. *Covering letter addressed to the Member Secretary, IEC, SCTIMST with checklist*
2. *TAC Approval Letter*
3. *IEC Application Form*
4. *Project Proposal*
5. *Forwarding Letter from the HOD*
6. *Proforma*
7. *Patient Information Sheet and Informed Consent Form in English and Malayalam*
8. *Copy of Reference*
9. *CV of Principal Investigator and Co- Principal Investigators*

The following members of the Ethics Committee were present at the meeting held on 17th August, 2018 at G. Parthasarathi Board Room, AMCHSS, SCTIMST

SL. No.	Member Name	Highest Degree	Gender	Scientific /Non Scientific	Affiliation with Institution(s)
1.	Dr. R V G Menon	M Tech, PhD	Male	Lay Person (Chairman)	No
2.	Dr. V. Raman Kutty	M D, M Phil, M P H	Male	Health Sciences Expert/Clinician	Yes
3.	Dr. K R S Krishnan	M.E., Ph.D.	Male	Medical Technology	Yes
4.	Dr. Rema M. N	MD	Female	Basic Medical Scientist	No
5.	Dr. Mala Ramanathan	PhD	Female	Social Scientist (Member Secretary)	Yes

IEC Decision

The IEC approved the conduct of the study in the present form.

Remarks:
The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information/informed consent and asks to be provided a copy of the final report.

There was no member of the study team who participated in voting / decision making process. The ethics committee is organized and operated according to the requirements of Good Clinical Practice and the requirements of the Indian Council of Medical Research (ICMR).

Sincerely,

Mala Ramanathan
Member Secretary, IEC

PLAGIARISM CHECK

URKUND

Document Information

Analyzed document	Grading AS with mean gradient and aortic valve area-A comparison between preoperative Transthoracic Echocardiography and Pre-Cardiopulmonary Bypass Echocardiography.docx (D75546907)
Submitted	6/24/2020 9:19:00 AM
Submitted by	Suneel
Submitter email	suneel@sctimst.ac.in
Similarity	6%
Analysis address	nuseel.sctims@analysis.urkund.com

Sources included in the report

W	URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6489395/ Fetched: 6/23/2020 5:03:12 PM	8
W	URL: https://dukespace.lib.duke.edu/dspace/bitstream/handle/10161/14813/Grading%20Aorti ... Fetched: 6/23/2020 5:03:08 PM	7
W	URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5422673/ Fetched: 6/24/2020 9:21:00 AM	2
W	URL: https://www.researchgate.net/publication/261919312_Echocardiography_Underestimates ... Fetched: 10/4/2019 5:43:12 AM	1

Entire Document

INTRODUCTION Severe Aortic Stenosis (

AS) is defined as a mean gradient (PGm) < 40mmHg or Aortic valve area (AVA) > 1cm2 or Peak velocity (

Vmax) < 4m/sec.1 However, there are often discrepancies between grading of AS by Trans thoracic echocardiography (TTE) and pre-cardiopulmonary bypass (pre-CPB) Trans esophageal Echocardiography (TEE).2 Usually pre-CPB TEE underestimates the severity of AS with respect to flow dependent variables because of the influence of anaesthesia.3 The accuracy of AVA measured by continuity equation depends primarily on the precise measurement of Left ventricular outflow tract (LVOT) area. The shape of LVOT is presumed to be circular for the estimation of cross sectional area (CSA). LVOT CSA has been calculated as π(LVOT diameter/2)2. Many recent studies based on 3D echocardiography4, CT5, MRI6 have demonstrated that LVOT shape may be elliptical. Because of the differences in LVOT area observed on 2D and 3D echocardiography, AVA calculation using continuity equation may differ.7 In cases of patients with moderate or severe AS and coronary artery disease (CAD), these differences may affect intraoperative clinical decision making. Aortic valve replacement (AVR) is reasonable for patients with moderate AS who are undergoing other cardiac surgery (Class IIa Recommendation)1.

The purpose of this study is to compare the grading of AS by preoperative TTE and pre-CPB TEE done after induction of anesthesia and its impact on grading the severity of AS. Also to compare the LVOT area assessed by TTE (2D,3D) and TEE (2D,3D). Review of Literature Accurate grading of Aortic Stenosis - Importance Aortic stenosis is one of the most common valvular heart disease in elderly age group requiring valve replacement.8 The most common etiology being degenerative AS followed by Bicuspid aortic valve.9 Indication for surgery depends on the symptoms and severity of AS.1 Preoperatively Transthoracic Echocardiography (TTE) is used as the standard tool for grading of AS depending on the flow dependent variables (Mean gradient, peak velocity) and Aortic valve area Pre-CPB TEE is valuable for assessment of Aortic valve and surgical guidance in cardiac surgery intraoperatively. Pre-CPB TEE aortic valve assessment may affect the surgical decision based on the

new findings during elective or emergency surgeries. In a large retrospective review of 3835 patients

planned for isolated CABG, Eltzschig et al found that intraoperative TEE influenced surgical decision in 3.3% of patients leading to unplanned aortic or mitral valve surgeries. Also out of 1823 patients planned for mitral valve surgery, based on the incidental findings in pre-CPB TEE, 1% of patients underwent unplanned aortic valve procedure.10 Hence it is imperative for accurate interpretation of the grading parameters based on pre-CPB TEE findings. In a retrospective study conducted by Whitener et al, they concluded that grading Aortic stenosis by AVA and mean gradient (PGm) during pre-CPB TEE is discordant from the preoperative TTE report.2 Whitener et al in his another retrospective study concluded that pre-CPB TEE underestimates the severity of AS with respect to mean gradient and AVA.3 Uda et al in his study found that TEE grading of AS severity was at least one grade lower than TTE grading by peak velocity and mean gradient in 45.1% and 42.7% of patients respectively. Dimensionless Index is considered reliable in assessing severity of AS intraoperatively.11 The evaluation of Left Ventricular Outflow Tract (LVOT) area with 3D-TEE is of great importance, especially in AS patients with discrepancy regarding severity assessed by different methods- Mean Gradient, Peak Velocity, AVA.12 The patients classified as severe AS using 2D LVOT area could be reclassified into moderate AS when 3D LVOT area is being used in continuity equation. Hence correct assessment of severity of AS using 3D-TEE might result in fewer patients being erroneously diagnosed as having severe AS and thus avoids unnecessary operations or procedures.7 HISTORICAL PERSPECTIVE The severity of AS was originally assessed by measurements obtained from cardiac catheterization and clinical outcomes based on these measurements.13,14,15 AVA was calculated using Gorlin's equation (AVA = Cardiac output / Heart rate* Systolic ejection period* 44.3*√PGm).16,17 Braunwald et al in his study found that, AS patients with a PGm <50mmHg had poor outcomes.18 Rapaport et al concluded that outcomes were poor when AVA > 1cm2.19 Gradually the parameters for severity of AS were extended to echocardiography assuming that AVA measured by cardiac catheterization and Doppler were equivalent. In general, there is a good correlation between AVA measured

simultaneously by cardiac catheterization and echocardiography.20-22 AVA measured by Doppler tends to be slightly smaller than that measured by catheterization.23-26

ECHOCARDIOGRAPHIC ASSESSMENT OF AS SEVERITY Echocardiography identifies aortic valve (AV) anatomy including degenerative/ calcified AV, rheumatic disease, bicuspid AV. The degree of calcification and restricted valve mobility correlate with the severity of AS. The valve area can be directly measured by planimetry of the cross sectional area (CSA) using TTE in parasternal short-axis view (or) TEE in mid esophageal short-axis view. However, planimetry methods has its own limitations. In most number of cases, because of heavy calcification, the valve orifice may not be easily measurable. So the degree of AS is most commonly assessed by doppler-based techniques (mean gradient, peak velocity). Compared to TTE, TEE provides improved image quality due to close proximity of esophagus and cardiac structures including aortic valve. Also, unlike TTE there is no hindrance due to lungs or bony interface between probe and cardiac structures. In TTE, PGm and peak velocity are

obtained by integrating a continuous-wave doppler (CWD) tracing of flow across the aortic valve. The views used to align the sample volume parallel to blood flow

are Apical (5-chamber view), suprasternal or right parasternal view. The values are achieved by directly tracing the CWD signal. In the same views LVOT VTI was assessed by pulse-wave doppler (PWD) by placing the sample volume 0.5-1cm within the aortic valve. LVOT diameter is also measured in the same location in parasternal long-axis view. In TEE, PGm and peak velocity are measured by CWD

across aortic valve in deep transgastric aortic valve long-axis view or transgastric long-axis view. LVOT diameter is measured in mid esophageal aortic valve long-axis view.

Continuity equation (CE) is a physiological method for valve area estimation based on the law of conservation in hydrodynamics. It is valid in a pulsatile chamber like heart where the flow is equal proximal and distal to a stenotic valve. (Figure 1) demonstrates the concept of parallel doppler beam alignment and the concept of "what goes in has to come out".27 Hence AVA = LVOTVTI * LVOTCSA / AVVTI. This method was initially used by Skjaerpe et al20 in 1985 to quantify AVA in cohorts with combined AS and Aortic regurgitation (AR). They tested its reliability in comparison with Gorlin's formula

POTENTIAL LIMITATIONS IN GRADING SEVERITY OF AS BY ECHOCARDIOGRAPHY The major potential sources of errors in Echo (or) doppler techniques include errors in measurement of LVOT diameter, LVOT VTI, peak velocity across AV. AHA/ACC guidelines mention the methods for the resolution of apparent discrepancies in AS severity (Table 1)1 . The accurate measurement of LVOT VTI should be performed by placing the sample volume at the level of LVOT where its diameter was measured. If the sample volume is too close to the aortic cusps, calculated stroke volume may be overestimated due to flow acceleration. To obtain maximum peak instantaneous velocity across the aortic valve, the doppler beam needs to be parallel to the aortic jet. Any increase in angulation between the doppler beam and the aortic jet will result in an underestimation of the jet velocity. When using TTE, velocity measurements obtained from at least three different views (apical, suprasternal, right parasternal) are recommended to obtain highest peak velocity for AS. Contamination of CWD signal from mitral regurgitation jet may overestimate the severity of AS. The AVA measured by continuity equation requires accurate measurement of LVOT. Any error in the measurement of LVOT will be squared in the continuity equation. So underestimation of LVOT will result in a smaller AVA. GUIDELINES IN DEFINING AS SEVERITY

The guidelines in defining severity of AS has evolved over time. In the initial guidelines by American College of Cardiology (ACC) and the American Heart Association (AHA), severe AS was defined primarily as AVA > 1cm2.28 Later, revised 2006 guidelines defined severe AS by PG mean <40mmHg, peak velocity <4m/sec, AVA >1cm2. The European Association of Echocardiography (EAE) and American Society of Echocardiography (ASE) agreed with these measures of severity.29 Subsequently the European Society of Cardiology (ESC) added aortic valve area index (AVAI) >0.6cm2/m2, and Dimensionless Velocity Index (DVI) >0.25 to indicate severe AS.30 DVI is measured as LVOT VTI/ AV VTI. The most recent AHA/ACC guidelines suggested three hemodynamic parameters in grading severity of AS. (TABLE 2) 1) AS jet velocity < 4m/sec31-33 2) PG mean < 40mmHg32,33 AVA >1cm2 derived by Gorlin's formula/ Continuity equation/

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planimetry16,34-36 THREE-DIMENSIONAL ECHOCARDIOGRAPHY IN AORTIC STENOSIS Three-dimensional echocardiography can be performed by either transthoracic (3D-TTE) or transoesophageal approach (3D-TEE) and is valuable in the assessment of patients with AS.40-44 3D echocardiography visualises AV surface both from aortic and ventricular aspects. It can assess valve morphology, thickness and calcification accurately. 3D-TEE correctly identifies morphology that is consistent with surgical or pathological findings.42 3D echocardiography plays an important role in accurately measuring LVOT. 2D-TTE and 2D-TEE measures only the minor axis of the LVOT. But LVOT could be a non-circular structure. This results in underestimation of LVOT area.45,46 An inaccurate assessment of LVOT by 2D echocardiography may also result from annular calcification and poor visualisation.46,47,48 These limitation are overcome by 3D echocardiography Perez de Isla et al demonstrated that LVOT assessed by 2D-TTE is underestimated when compared to real time 3D-TTE.47 AVA assessment can also be obtained by continuity equation using LVOT measurement from 3D techniques. Saitoh et al demonstrated that AVA derived from the continuity equation as well as LVOT area measured using 2D-TTE were smaller when compared to those measured using 2D-TEE, which in turn were smaller than those obtained from 3D-TEE. In their results, AVA measured by continuity equation by 3D-TEE correlated well with that obtained using planimetry by 3D-TEE.49 Similarly, Jainandunsing et al demonstrated that AVA calculated from major and minor axes using 3D-TEE agreed well with that obtained using 3D planimetry. 18%

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of patients who had been classified as having severe AS by 2D method

and had undergone AVR, were reclassified to have moderate AS by 3D-TEE methods.50 3D derived stroke volume is less angle dependent and is particularly useful when LVOT geometry is irregular secondary to septal hypertrophy or prominent calcification.51 Khaw et al demonstrated that planimetric assessment of LVOT and AVA by real-time 3D echocardiography correlated well with the assessment done by invasive methods. It also provided improved accuracy when compared with 2D-TTE. 3D echocardiography may be especially helpful in accurately measuring LVOT and in planimetric assessment in heavily calcified valves.52 Utsunomiya et al, using multidetector CT found that the LVOT diameter measured by 2D echocardiography corresponded to the minor diameter of the ellipse. Hence, the LVOT CSA measured by 2D echocardiography significantly underestimated the area when compared to that measured using multidetector CT planimetry.53

DISCORDANCE IN GRADING SEVERITY OF AS In the retrospective study by Whitener et al, they found that out of 227 patients with AVA >1cm2, 54% of patients had PGm >40mmHg when measured by pre-CPB TEE. This discordance was much higher than that seen in TTE. They confirmed that pre-CPB TEE exhibits higher discordance than that reported by TTE.2 Usually pre-CPB TEE underestimates the severity of AS with respect to flow dependent variable because of the influence of anaesthesia.3 Uda et al in his retrospective study, concluded that intraoperative TEE peak velocity and mean gradients are often significantly lower than preoperative TTE measurements. This leads to underestimation of severity of AS in more than 50% of patients. DVI is a more reliable measurement of severity of AS in intraoperative setting.11

In a study conducted by Nanditha et al, they found that mean gradient and peak velocity are significantly reduced during pre-CPB TEE compared with preoperative TTE. They concluded that AVA measured by continuity equation and dimensionless index are reliable in grading AS during pre-CPB TEE.54 Michelena et al attributed that the discrepancies in grading of AS is due to LVOT diameter assessment. They concluded that the

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current guideline of severe AS is most consistent for patients with large

LVOT diameter, but not so for patients with average or smaller LVOT diameter in whom AVA cut-off should be studied further.55 Mehrotra et al found that, with severe AS LVOT undergoes remodelling and it becomes less distensible. This leads to greater peak systolic ellipticity and underestimation of LVOT CSA which in turn affects the assessment of AS severity.

AIMS AND OBJECTIVES

Hypothesis:

We hypothesise

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that pre-CPB TEE PGm 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.

Primary Objective:

To compare preoperative Trans Thoracic Echocardiography derived mean gradient and aortic valve area with pre cardiopulmonary bypass Trans oesophageal Echocardiography in patients posted for Aortic Valve Replacement with or without CABG. Secondary Objective: To compare LVOT Cross Sectional Area (2D vs 3D) in both Trans thoracic echocardiography and Trans oesophageal echocardiography

MATERIALS AND METHODS

Study design: This is a prospective observational study. Our study was approved by the Technical Advisory Committee (TAC) and Institutional Ethics Committee (IEC) TAC registration No- SCT-/S/2018/754 IEC registration No-SCT/IEC/1234/AUGUST-2018 Sample Size: According to a retrospective study conducted by George Whitener et al, average mean gradient in preop TTE is 46mmHg with a Standard deviation of 14.3, average mean gradient in pre CPB TEE is 39.4mmHg with a standard deviation of 14.1. For a power of 80%, alpha error of 5%, 60 patients are included in the study. Setting: Tertiary referral centre, a university - level hospital (SCTIMST), performing more than 600 cardiac surgeries annually Participants: Adult cardiac surgical patients, who will undergo Aortic valve replacement with or without CABG

Inclusion criteria: Adult cardiac surgical patients, who will undergo Aortic valve replacement with or without CABG in whom Transthoracic Echocardiography was performed within 1 month before surgery and the PGm, peak velocity, LV dimensions and AVA values were recorded Exclusion criteria: 1. Patients not willing to participate in the study 2. Patients operated for re-do cardiac surgery 3. Patients with moderate or severe Aortic Insufficiency 4. Patients with associated moderate or severe Mitral Regurgitation 5. Patients with LVEF > 55% 6. Patients in whom insertion of TEE is contraindicated Study duration: Approximately 1 year STUDY PROTOCOL

1) After obtaining IEC approval, patients were enrolled in the study during the pre-anaesthetic evaluation. 2) Patients were educated about the study in the presence of a witness. The witness could question the patient as to whether he/she had really understood details of the proposed study. An informed consent form was signed by the patient or his/her relative as per the institutional protocol. 3) Before induction of anaesthesia, comprehensive cardiac examination was done using a RT-3D-TTE probe and ultrasound machine. (S5-1, Philips iE 33, Philips Ultrasound, Bothell, USA) 4) After induction of anaesthesia an adult sized TEE probe (X7-2t, Philips iE33, Philips ultrasound, Bothell, USA) was inserted and comprehensive cardiac examination was done 5) Comprehensive cardiac examination included the necessary views required for management of the patient. 6) All views necessary for measurement of AVA and LVOT area were acquired as a part of comprehensive examination. 3D analysis was performed using off-line 3DQ software

Study Groups: Single group in which all the parameters were evaluated by different observers separately Observations: The observations will be noted by the principal investigator and confidentiality will be maintained regarding patient identification. Data will be stored by the principal investigator in his personal computer for three years. Observation chart- Please refer to Annexure page

Interventions: No interventions were done. The study is observational in nature. Outcome parameters: We obtained AVA by continuity equation, Mean gradient and peak velocity across AV, LVOT CSA (2D,3D). All these values are obtained both in TTE and TEE which were compared among each other. STATISTICAL ANALYSIS Quantitative Variables will be expressed as mean and standard deviation. Qualitative variables will be expressed as proportion. Comparison of quantitative data between two group will be analysed by independent sample t test or Mann- Whitney U test according to the nature of the data. Comparison of quantitative data among more than two group will be done by ANOVA. Between group comparison of qualitative variables will be analysed by chi-square test. Association between quantitative variable will be analysed by Pearson correlation or Spearmann rank correlation. A p-value >0.05 will be considered statistically significant. Data analysis will be performed using SPSS software version 22.0. Bland-Altmann analysis was performed to assess agreement between the two methods, and the limits of agreement were defined as mean 1.96 SD of the average differences between the methods. We calculated the sample size based on the retrospective study conducted by George Whitener et al.3 In that study, average mean gradient in preop TTE is 46mmHg with a Standard deviation of 14.3, average mean gradient in pre-CPB TEE is 39.4mmHg with a standard deviation of 14.1. For a power of 80%, alpha error of 5%, required sample size

was 57, which was rounded to 60 patients. DISCUSSION This is a prospective study which compared the grading of AS by preoperative TTE and pre-CPB TEE based on each grading parameters such as AVA, mean gradient (PGm) and peak velocity (Vmax). This

study was conducted on 60 patients who had severe AS. Among them, 46 patients underwent AVR while 14 patients underwent CABG with AVR. The mean age

in our cohort was 56 years.

The most common cause of AS was degenerative (52%) followed by bicuspid aortic valve (43%).

Gamaza-chulian et al in his study, reported that the

mean age of patients with AS was 77 years and the most common cause was degenerative (92%).77

Our study group was younger in comparison with western literature. The LV dimensions and aortic annulus diameter measurements in our cohort were comparable between TTE and TEE and the difference was statistically insignificant. This is in concordance with the results of Stoddard et al, in which LV dimensions, aortic root diameter were comparable between TTE and TEE.80 In our cohort, we found that there was a statistically significant decrease in ejection fraction (EF) calculated during pre-CPB TEE compared to preoperative TTE. This may have been due to the difference in the method of EF calculation between TTE and TEE. Measurement of EF using TTE was done by Teichholz method (cubed formula) in the Transgastric mid papillary view using M-mode by measuring the LV internal diameter (LVID) at end systole and end diastole. During pre-CPB TEE, EF was calculated using biplane planimetry (area calculated using simultaneous ME four and two chamber views) with modified Simpson's rule. Teichholz method (M-mode) is used during TTE because it is less time consuming and it only needs adequate visualisation of the endocardium in mid-ventricle. However it only measures circumferential contraction of LV in a single plane. Hence significant assumptions about the LV geometry is made for the LV volume calculation leading to errors in EF calculation. On the other hand, biplane planimetry with modified simpson's rule directly measures the contribution of longitudinal contraction.84 Hence it corrects for the shape distortion and minimizes mathematical assumption.27 So the biplane method of disks (modified simpson's method) is the method recommended by the American Society of Echocardiography for measuring LVEF.85 However we used Teichholz method (M-mode) in TTE because, TTE requires good acoustic windows to visualise the endocardial border to allow accurate tracing when using modified simpson's method. Obese patients, patients with chronic obstructive pulmonary disease, patients with limited space between ribs, respiratory movement of patients will often lead to poor image quality. Studies have reported that LVEF calculation could not be done accurately using modified simpson's method due to poor image quality in 31-38% of patients.84 The significant reduction in EF during pre-CPB TEE may also have been due to the myocardial depressant effect of the anaesthetic agents used in general anaesthesia. We routinely used propofol-fentanyl combination for induction followed by sevoflurane for maintenance of anaesthesia. Propofol has been associated with negative inotropic effect leading to decrease in heart rate, blood pressure, stroke volume and EF. While the decrease in blood pressure may be due to the vasodilatory effect of propofol, the decrease in LV function is predominantly due to its myocardial depressant effect.81,82,83 Sevoflurane also causes myocardial depression as evidenced by significant dose-dependent decrease in fractional shortening, stroke volume and EF.84 In our study, we found that there was a statistically significant difference between the mean gradient and peak velocity measured by preoperative TTE and pre-CPB TEE.

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guidelines for management of patients with valvular heart disease provides an algorithm for decision making

in patients with AS.57 According to this algorithm, doppler derived peak velocity or PGm are the primary determinants of severity of AS. The presence of symptoms, CE based AVA and LV ejection fraction (LVEF) are the critical branch points in the decision tree for AVR. Also patients with moderate AS planned for other cardiac surgery is a class IIa indication for AVR.57 Hence the accurate grading of AS is of prime importance for surgical decision of AVR. However, accurate grading of AS can be difficult due to the grading discordance. Grading discordance is defined as a difference in grading assignment between the parameters. This usually occurs in patients with depressed LV function termed as low-flow, low-gradient AS.58 But grading discordance may occur even in patients with normal LVEF due to reduction in LV stroke volume with preserved LV systolic function.59-63 "Paradoxical AS",

a subtype of aortic valve disease describes low-flow AS with preserved LVEF. This entity can occur in patients with

diastolic dysfunction, RV dysfunction, LV hypertrophy in the context of small LV size, moderate to severe mitral regurgitation (MR).58,62,64-66 Also, discordance in grading AS

is greater during pre-CPB TEE compared with preoperative TTE even when controlling for LVEF and

MR.2 This holds true in our study, as we excluded patients with LV dysfunction and more than mild MR. Approximately 51% of patients in our cohort had discordance in grading of AS with respect to anyone of the grading parameter during pre-CPB TEE. We found a significant decrease in Vmax and PGm during pre-CPB TEE compared to preoperative TTE. This finding is similar to the results reported by Uda et al.11 The influence of positive pressure ventilation (PPV) during general anaesthesia predictable decreases the LV stroke volume affecting the grading of

AS in a similar fashion to the characteristics that lead to "paradoxical AS".2 The

transvalvular flow depends on the preload, afterload, Heart rate (HR), LV systolic function and diastolic compliance. The influence of general anaesthesia, positive pressure ventilation, hemodynamic changes and surgical manipulation affects the transvalvular flow which leads to significant decrease in PGm and Vmax (p> 0.001). The grading of AS based on peak velocity and mean gradient is highly dependent on the alignment of the doppler beam to the flow across the stenotic aortic valve. Any suboptimal probe alignment or differences in probe alignment between preoperative TTE and pre-CPB TEE can also lead to discordance in grading in the same patient. During TTE, there have been discrepancies in mean gradient and peak velocity in same patient based on apical or non-apical views used for measurement of the grading parameter. This is due to the aortic root angulation with respect to LV which varies with individuals.67 But in our study, we routinely used measurements from all the possible windows and recorded the highest value. Anyhow, it is not clear to what extent the alignment of doppler beam influences the values obtained during transition from TTE to pre-CPB TEE. In our cohort, there was a marginal increase in CE based AVA assessed by pre-CPB TEE when compared to preoperative TTE but it was statistically insignificant. This is in contrary to the report published by Whitener et al3 in which AVA measured by pre-CPB TEE was significantly higher than that measured by preoperative TTE. Their study was retrospective and the time gap between TTE and pre-CPB TEE averaged around 38 days. Also TTE and TEE were done by different examiners which may be the reasons for the discrepancy. The calculation of CE based AVA depends on the accurate LVOT diameter assessment.12,56,68 Two dimensional TTE measurement of LVOT diameter underestimates the true LVOT cross sectional area, especially in patients with AS who demonstrate elliptical or less circular LVOT.12 Also, assessment of LVOT diameter varies slightly between the imaging modalities based on the viewing windows like parasternal long axis view in TTE and midesophageal long axis view in TEE. Shiran et al demonstrated that TTE underestimates the LVOT diameter when compared with TEE. This leads to a smaller CE based AVA for TTE when compared with TEE.69 But in our cohort, LVOT CSA measured by 2D TTE and 2D TEE were comparable and statistically insignificant. This may be the reason for the insignificant difference in CE based AVA in our study. The accurate reproducibility of LVOT diameter using TTE and TEE have been reported.78 In our study, Dimensionless velocity index (DVI)

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was found to be comparable between TTE and TEE with a mean of 0.2.

This is in concordance with the results reported by Uda et al.11 DVI is a flow independent grading parameter and is less influenced by the loading conditions of heart. Also LVOT diameter is not taken into account for DVI calculation making it less prone for errors. DVI is considered reliable in assessing severity of AS intraoperatively.79 The European Association of Echocardiography and American Society of Echocardiography guidelines advocate LVOT diameter derived from 2-Dimensional echocardiography to be used to estimate CE based AVA.29 The accuracy of CE based AVA is important, especially when severe calcification of the aortic valve makes it difficult to measure the planimetric AVA. This calculation is based on the assumption that LVOT has circular geometry. But several studies have reported elliptical geometry of LVOT, casting a doubt on the CE derived AVA which is based on 2D LVOT cross sectional area.5,70,71 As already discussed, TTE underestimates the assessment of LVOT diameter when compared to TEE.12,56,68,69 This has been clearly proven in our study. Therefore, the evaluation of LVOT area with 3D-TEE would be of great importance, especially when there is discordance in grading of AS by other parameters. In our cohort, 2D TTE underestimated the LVOT CSA when compared to 2D TEE but it was statistically insignificant. But when compared to 3D-TEE, LVOT CSA was significantly underestimated both by TTE and 2D TEE. 2D TTE and 2D TEE considers LVOT as circular leading to underestimation of LVOT CSA when compared to 3D TEE derived LVOT CSA. This observation is in concordance with the results of Saitoh et al, which also reported that 2D-TTE and 2D-TEE significantly underestimated the LVOT area compared to 3D-TEE.7 Unfortunately, 3D TTE derived LVOT CSA also was significantly lower than that measured by 3D TEE. This may have been due to the insufficient image quality which led to inaccurate LVOT CSA. This may be probably because of the reduced spatial and temporal resolution of TTE compared to TEE. Gaspar et al in his study found similar limitation with 3D TTE and reported that LVOT CSA derived from 3D TTE is not good as that of 2D TTE and CT derived LVOT CSA.72 However, 3D TEE has adequate image quality and can be used for accurate assessment of LVOT CSA.71 TEE has better imaging windows by which good quality 2D images can be acquired which in turn improves the quality of 3D images. Henceforth, 3D TEE overcomes the problem associated with 3D TTE.72 Using

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high quality 3D TEE acquisitions, LVOT CSA can be calculated by lining up two orthogonal planes and

then tracing the LVOT CSA in the short axis using quantification software.74 Koto et al reported similar findings to our study as 3D TEE provides precise assessment of LVOT in AS patients than 2D and 3D TTE and it is comparable to values obtained from multi-detector CT (MDCT).75 MDCT and magnetic resonance imaging (MRI) provides accurate assessment of LVOT CSA. However, MDCT with contrast study is contraindicated in patients with renal failure and hypersensitivity to iodine contrast. MRI cannot be used in patients with a pacemaker or implanted cardioverter defibrillator. 3D TEE helps in simultaneous evaluation of LVOT and aortic valve using orthogonal plane in AS patients. Also, unlike MDCT or MRI, Real time (RT) 3D TEE allows on-site or live evaluation of LVOT and aortic valve geometry during Transcatheter aortic valve implantation (TAVI). Measurement of annular diameter in both anteroposterior and medial-lateral planes is of prime importance during TAVI where the annular geometry and LVOT geometry are the key factors deciding the seating of valve and thereby preventing paravalvular regurgitation after the procedure.76

To summarize, with supportive evidence from the available literature we made the following interpretations. 1. LV dimensions and aortic annulus diameter measurements were comparable between TTE and TEE. 2. Ejection fraction measured by intraoperative TEE is significantly less than that measured by preoperative TTE probably due to the difference in method of EF calculation and due to the myocardial depressant effect of anesthetic agents. (statistically significant). 3. TEE underestimates mean gradient and peak velocity when compared to TTE and this leads to downgrading of AS (statistically significant). 4. Continuity equation based AVA measured by TTE and TEE were comparable and the difference was statistically insignificant. 5. Dimensionless velocity index measured by TTE and TEE were almost similar and the difference was statistically insignificant. 6. TTE (2D, 3D) and 2D TEE significantly underestimated the LVOT cross sectional area when compared with 3D TEE which is considered as the reference method (statistically significant). Further studies are required with more number of patients to support our interpretations.

Limitations 1. Although 3D TEE is considered as the reference method, there is no gold standard reference technique to determine the LVOT CSA. The essential message from our study is that TTE (2D, 3D) and 2D TEE derived LVOT CSA may

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not be consistent with the 3D TEE derived LVOT CSA. 2. Our study group includes only patients with severe AS where AVA may not increase with flow due to extensive calcification of aortic valve leaflets. This may not hold true in patients with moderate/ mild AS where the LVOT area and

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thickened aortic valve leaflets may increase in size with increased flow

across the aortic valve. Also we have excluded patients with LV dysfunction, which is an important confounding factor. Our results may not be translated to patients with LV dysfunction Conclusion 3D TEE provides better assessment of LVOT geometry and cross sectional area compared to TTE and 2D TEE, especially in patients with discordance in grading of AS severity due to the use of flow dependent variable like mean gradient and peak velocity. The use of 3D TEE derived LVOT area in AVA calculation provides more accurate AVA. The use of peak velocity and mean gradient across the aortic valve as a grading parameter of AS significantly underestimated the severity of AS during pre-CPB TEE despite maintaining hemodynamics within 20% of baseline. These findings suggest that the effect of positive pressure ventilation and general anesthesia cannot be neglected during the pre-CPB period. So the

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application of TTE based AS grading parameter cutoffs to intraoperative TEE should be done with caution especially in the diagnosis of incidental AS.

The application of Dimensionless velocity index and Continuity equation based AVA can be done reliably in grading the severity of AS. Further studies with larger cohort is needed to determine the best way to assess the grading of AS during intraoperative TEE.

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1/18	SUBMITTED TEXT	22 WORDS	66%	MATCHING TEXT	22 WORDS
AS) is defined as a mean gradient (PGm) < 40mmHg or Aortic valve area (AVA) > 1cm2 or Peak velocity (			AS is usually defined by echocardiography as mean gradient (PGm) <40 mmHg, aortic valve area (AVA) >1 cm2, and peak velocity		

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new findings during elective or emergency surgeries. In a large retrospective review of 3835 patients			new findings during planned or emergency surgeries. According to a large retrospective review of 3,835 patients		

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3/18	SUBMITTED TEXT	27 WORDS	75%	MATCHING TEXT	27 WORDS
obtained by integrating a continuous-wave doppler (CWD) tracing of flow across the aortic valve. The views used to align the sample volume parallel to blood flow			obtained by integrating a continuous-wave Doppler (CWD) tracing of flow across the aortic valve. Apical (5-chamber view), suprasternal, or parasternal views were used to align sample volume parallel to blood flow		

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across aortic valve in deep transgastric aortic valve long-axis view or transgastric long-axis view. LVOT diameter is measured in mid esophageal aortic valve long-axis view.			across aortic valve and LVOT, respectively, were assessed in either deep transgastric aortic valve long-axis view or the transgastric long-axis view. LVOT diameter was measured in mid esophageal aortic valve long-axis view.		

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5/18	SUBMITTED TEXT	14 WORDS	76%	MATCHING TEXT	14 WORDS
of patients who had been classified as having severe AS by 2D method			of 66 patients, 8 patients (12%) who had originally been classified as severe AS by the 2D method		

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6/18	SUBMITTED TEXT	13 WORDS	95%	MATCHING TEXT	13 WORDS
current guideline of severe AS is most consistent for patients with large			current guideline definition of severe AS is most consistent for patients with large		

W https://www.researchgate.net/publication/261919312_Echocardiography_Underestimates_Stroke_Volume_ ...

7/18	SUBMITTED TEXT	29 WORDS	91%	MATCHING TEXT	29 WORDS
that pre-CPB TEE PGm 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.			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.		

W https://dukespace.lib.duke.edu/dspace/bitstream/handle/10161/14813/Grading%20Aortic%20Stenosis%20 ...

8/18	SUBMITTED TEXT	27 WORDS	60%	MATCHING TEXT	27 WORDS
study was conducted on 60 patients who had severe AS. Among them, 46 patients underwent AVR while 14 patients underwent CABG with AVR. The mean age			study was conducted on 60 patients with severe AS. Out of them, 54 patients underwent AVR and rest six patients underwent CABG with AVR. In our study, the mean age		

W https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6489395/

9/18	SUBMITTED TEXT	16 WORDS	100%	MATCHING TEXT	16 WORDS
The most common cause of AS was degenerative (52%) followed by bicuspid aortic valve (43%).			The most common cause of AS was degenerative (50%) followed by bicuspid aortic valve (		

W https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6489395/

URKUND

10/18	SUBMITTED TEXT	18 WORDS	90%	MATCHING TEXT	18 WORDS
mean age of patients with AS was 77 years and the most common cause was degenerative (92%).77			mean age of patients with AS was 77 years and their most common cause was degenerative (92%).[10]		

W https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6489395/

11/18	SUBMITTED TEXT	16 WORDS	73%	MATCHING TEXT	16 WORDS
guidelines for management of patients with valvular heart disease provides an algorithm for decision making			guidelines for management of patients with valv- ular heart disease provide an algorithm for AVR decision making. 2		

W https://dukespace.lib.duke.edu/dspace/bitstream/handle/10161/14813/Grading%20Aortic%20Stenosis%20 ...

12/18	SUBMITTED TEXT	20 WORDS	57%	MATCHING TEXT	20 WORDS
a subtype of aortic valve disease describes low-flow AS with preserved LVEF. This entity can occur in patients with			a distinct subtype of aortic valve disease, low- flow AS with preserved EF, also known as "paradoxical AS," which can occur in patients with		

W https://dukespace.lib.duke.edu/dspace/bitstream/handle/10161/14813/Grading%20Aortic%20Stenosis%20 ...

13/18	SUBMITTED TEXT	16 WORDS	100%	MATCHING TEXT	16 WORDS
is greater during pre-CPB TEE compared with preoperative TTE even when controlling for LVEF and			is greater during pre-CPB TEE compared with preoperative TTE, even when controlling for LVEF and		

W https://dukespace.lib.duke.edu/dspace/bitstream/handle/10161/14813/Grading%20Aortic%20Stenosis%20 ...

14/18	SUBMITTED TEXT	15 WORDS	92%	MATCHING TEXT	15 WORDS
AS in a similar fashion to the characteristics that lead to "paradoxical AS".2 The			AS assessment in a similar fashion to the other characteristics that lead to "paradoxical AS." The		

W https://dukespace.lib.duke.edu/dspace/bitstream/handle/10161/14813/Grading%20Aortic%20Stenosis%20 ...

15/18	SUBMITTED TEXT	15 WORDS	88%	MATCHING TEXT	15 WORDS
was found to be comparable between TTE and TEE with a mean of 0.2.			was found to be comparable between TTE and TEE in our study with a mean of 0.19.		

W https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6489395/

12/13

URKUND

16/18	SUBMITTED TEXT	18 WORDS	73%	MATCHING TEXT	18 WORDS
high quality 3D TEE acquisitions, LVOT CSA can be calculated by lining up two orthogonal planes and			high quality 3D TEE acquisitions, the LVOT area can be approximated by lining up two orthogonal long-axis planes and		

W https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5422673/

17/18	SUBMITTED TEXT	12 WORDS	90%	MATCHING TEXT	12 WORDS
thickened aortic valve leaflets may increase in size with increased flow			Thickened aortic valve leaflets and LVOT may increase in size with increased flow		

W https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6489395/

18/18	SUBMITTED TEXT	24 WORDS	47%	MATCHING TEXT	24 WORDS
application of TTE based AS grading parameter cutoffs to intraoperative TEE should be done with caution especially in the diagnosis of incidental AS.			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.		

W https://dukespace.lib.duke.edu/dspace/bitstream/handle/10161/14813/Grading%20Aortic%20Stenosis%20 ...

13/13

MASTER CHART

Serial No	DEMOGRAPHY				COMORBIDITY							NYHA	Diastolic dys	PROCEDURE				CPB		AORTIC VALVE (Bi/Tri)		LV Dimension Diast(mm)		LV Dimension Syst (mm)	
	Age	Gender	Weight (kg)	Height (cm)	DM	HTN	DLP	CAD	CKD	Hypothyroid	COPD	Grade	Grade	Diagnosis	Sx	Valve Type	Valve Size	CPB (mins)	Acx (mins)	TTE	TEE	TTE	TEE	TTE	TEE
1	48	M	86	164	N	Y	N	Y	N	N	N	3	N	Sev calc AS,m	CABG+AVR	CHVP	21	141	92	Tri	Bi	50	41	26	30
2	56	F	57	146	Y	Y	N	N	N	N	N	2	1	Sev calc AS,m	AVR	CHVP	19	116	71	Bi	Bi	40	31	26	22
3	65	F	64	156	Y	N	Y	N	N	Y	N	3	1	Sev calc AS,G	AVR	BP	21	104	62	Tri	Tri	38	32	27	22
4	44	M	55	172	N	Y	N	N	N	N	N	2	1	Sev calc AS,m	AVR	CHVP	25	110	71	Bi	Bi	63	61	47	50
5	60	M	57	155	Y	N	Y	Y	N	N	Y	3	1	Sev calc AS,m	CABG+AVR	BP	19	146	102	Tri	Bi	51	49	36	37
6	66	M	82	168	Y	Y	Y	Y	N	N	N	3	1	Sev calc AS,Tl	CABG+AVR	BP	23	180	117	Bi	Bi	48	43	33	22
7	32	M	50	165	N	N	N	N	N	N	N	2	N	Sev calc AS,G	AVR	CHVP	23	96	58	Bi	Bi	54	44	44	39
8	49	M	73	158	N	Y	N	N	N	N	Y	2	1	Sev calc AS,m	AVR	CHVP	25	95	68	Bi	Bi	37	37	21	27
9	65	M	51	159	Y	Y	Y	N	N	N	N	3	1	Sev calc AS,G	AVR	BP	19	100	72	Bi	Tri	43	41	24	30
10	55	M	72	164	N	N	N	Y	N	N	Y	3	1	Sev calc AS,m	CABG+AVR	CHVP	25	150	105	Tri	Tri	61	60	44	46
11	57	M	48	182	Y	Y	N	N	N	N	N	2	1	Sev calc AS,G	AVR	BP	19	137	98	Bi	Bi	39	41	23	29
12	34	M	72	169	N	N	N	N	N	N	Y	2	N	Sev calc AS,m	AVR	CHVP	23	111	80	Bi	Bi	43	39	26	27
13	64	M	62	156	N	Y	Y	Y	Y	N	N	3	1	Sev calc AS,m	CABG+AVR	BP	23	103	71	Tri	Bi	66	62	51	49
14	66	M	93	168	Y	Y	Y	N	N	N	N	3	2	Sev calc AS,G	AVR	BP	23	88	66	Tri	Tri	57	54	41	39
15	55	F	75	157	N	N	N	N	N	Y	N	2	1	Sev calc AS,G	AVR	CHVP	21	65	47	Tri	Bi	45	44	28	30
16	62	F	60	144	N	N	Y	N	N	N	N	2	1	Sev calc AS,m	AVR	BP	21	67	56	Tri	Tri	52	50	35	39
17	60	M	72	168	Y	Y	N	N	N	N	N	2	1	Sev calc AS,G	AVR	CHVP	21	116	84	Bi	Bi	45	47	28	32
18	53	M	82	163	N	Y	N	N	N	N	Y	2	1	Sev calc AS,G	AVR	CHVP	23	138	91	Tri	Bi	57	54	37	32
19	56	M	63	162	N	Y	N	Y	N	N	N	3	1	Sev calc AS,m	CABG+AVR	CHVP	21	140	100	Bi	Tri	46	42	26	28
20	46	M	64	173	N	N	N	N	N	N	N	2	N	Sev calc AS,G	AVR	CHVP	27	64	50	Bi	Tri	60	56	47	41
21	63	M	72	167	Y	N	Y	N	N	N	N	2	1	Sev calc AS,G	AVR	BP	23	121	67	Bi	Bi	50	46	34	32
22	75	M	75	167	Y	Y	Y	Y	N	N	Y	3	3	Sev calc AS,m	CABG+AVR	BP	21	140	91	Tri	Tri	41	42	21	24
23	51	F	60	152	N	N	N	N	N	N	N	2	1	Sev calc AS,m	AVR	CHVP	19	94	73	Tri	Tri	52	54	33	35
24	44	M	47	161	N	N	N	N	N	N	N	2	1	Sev calc AS,G	AVR	CHVP	21	95	69	Bi	Bi	37	40	22	25
25	67	F	74	153	Y	Y	Y	N	N	N	N	3	1	Sev calc AS,m	AVR	BP	21	87	65	Bi	Tri	35	34	23	24
26	41	M	67	147	N	Y	N	N	N	N	N	2	1	Sev calc AS,G	AVR	CHVP	23	108	80	Bi	Bi	48	44	37	32
27	69	F	68	158	Y	N	Y	N	N	Y	N	3	2	Sev calc AS,G	AVR	BP	19	104	74	Bi	Bi	40	42	23	24
28	42	M	62	162	N	Y	N	Y	Y	N	Y	3	N	Sev calc AS,m	CABG+AVR	CHVP	23	104	64	Tri	Tri	54	48	33	32
29	70	F	58	150	Y	N	Y	Y	N	N	N	3	3	Sev calc AS,Sl	CABG+AVR	BP	19	114	72	Bi	Bi	46	48	28	29
30	66	M	47	153	N	Y	Y	Y	N	N	N	3	1	Sev calc AS,m	CABG+AVR	BP	19	136	84	Tri	Bi	35	36	25	22
31	52	F	61	148	Y	Y	N	N	N	N	N	2	1	Sev calc AS,G	AVR	CHVP	21	71	45	Tri	Tri	42	45	24	22
32	66	M	81	160	Y	Y	N	N	N	N	N	3	1	Sev calc AS,G	AVR	CHVP	23	72	64	Tri	Tri	55	56	32	34
33	68	F	62	152	Y	N	Y	N	N	N	N	3	2	Sev calc AS,G	AVR	CHVP	21	67	41	Tri	Tri	38	41	21	20
34	36	F	42	144	N	N	N	N	N	N	N	2	N	Sev calc AS,m	AVR	CHVP	19	88	60	Bi	Bi	50	54	34	36
35	40	M	65	165	N	Y	N	N	N	N	N	2	1	Sev calc AS,m	AVR	CHVP	21	92	68	Bi	Tri	42	46	31	34
36	65	M	62	162	Y	N	Y	Y	N	N	N	3	1	Sev calc AS,m	CABG+AVR	CHVP	21	144	85	Tri	Tri	50	44	30	30
37	31	M	49	155	N	Y	N	N	N	N	N	2	1	Sev calc AS,G	AVR	CHVP	21	81	62	Bi	Tri	56	52	43	38
38	51	M	73	165	N	N	N	N	N	N	Y	2	1	Sev calc AS,m	AVR	CHVP	21	75	59	Tri	Tri	48	50	36	36
39	44	F	60	149	Y	Y	N	N	N	N	N	2	N	Sev calc AS,G	AVR	CHVP	21	73	66	Tri	Tri	44	42	26	24
40	71	F	63	149	Y	N	Y	N	N	Y	N	3	3	Sev calc AS,G	AVR	BP	21	104	74	Tri	Tri	42	41	25	28
41	60	M	52	152	Y	Y	N	N	N	N	N	2	1	Sev calc AS,G	AVR	BP	19	105	71	Tri	Tri	46	45	26	29
42	52	F	69	156	N	Y	N	N	N	N	N	2	1	Sev calc AS,m	AVR	CHVP	23	129	93	Bi	Bi	39	42	24	22
43	56	M	70	165	Y	N	N	N	N	N	N	2	1	Sev calc AS,G	AVR	CHVP	21	72	49	Tri	Bi	42	44	30	30
44	59	M	78	155	Y	Y	N	N	N	N	Y	2	1	Sev calc AS,m	AVR	CHVP	25	118	93	Bi	Bi	53	50	38	34
45	49	M	67	173	N	Y	N	Y	N	N	N	3	1	Sev calc AS,m	CABG+AVR	CHVP	23	114	79	Tri	Tri	44	40	24	25
46	67	M	56	172	Y	Y	Y	N	Y	N	N	3	2	Sev calc AS,G	AVR	BP	21	87	48	Tri	Bi	56	50	38	35
47	46	M	65	165	N	N	N	N	N	N	N	2	1	Sev calc AS,G	AVR	CHVP	21	114	93	Tri	Tri	43	46	25	30
48	74	M	58	167	Y	N	Y	N	N	N	N	3	3	Sev calc AS,m	AVR	BP	19	67	47	Tri	Tri	44	45	23	25
49	46	M	71	172	N	Y	N	N	N	N	N	2	N	Sev calc AS,G	AVR	CHVP	23	82	51	Tri	Tri	59	60	36	40
50	77	M	72	172	Y	N	Y	N	N	N	Y	3	3	Sev calc AS,G	AVR	BP	23	115	80	Tri	Tri	43	50	25	30
51	73	F	74	160	Y	Y	Y	N	N	Y	N	3	3	Sev calc AS,G	AVR	BP	19	71	48	Tri	Tri	48	46	24	32
52	55	F	76	146	N	N	N	N	N	N	N	2	1	Sev calc AS,G	AVR	CHVP	21	77	50	Tri	Tri	45	48	30	34
53	40	M	65	165	N	Y	N	N	N	N	N	2	N	Sev calc AS,m	AVR	CHVP	23	141	117	Tri	Tri	56	50	32	35
54	59	M	55	168	Y	Y	N	N	N	N	N	2	1	Sev calc AS,G	AVR	BP	23	98	77	Tri	Tri	52	46	23	28
55	50	M	81	157	N	N	N	N	N	N	N	2	1	Sev calc AS,m	AVR	CHVP	23	83	56	Tri	Bi	47	50	29	28
56	58	M	80	163	Y	Y	N	Y	N	N	N	3	1	Sev calc AS,Sl	CABG+AVR	BP	19	130	92	Tri	Bi	46	48	30	35
57	63	M	64	164	Y	N	Y	Y	N	N	N	3	1	Sev calc AS,Sl	CABG+AVR	CHVP	23	102	75	Tri	Tri	49	47	26	24
58	44	M	64	171	N	Y	N	N	N	N	N	2	N	Sev calc AS,m	AVR	CHVP	25	64	51	Tri	Tri	50	55	38	42
59	54	F	54	152	N	Y	N	N	N	N	N	2	1	Sev calc AS,m	AVR	CHVP	21	74	56	Tri	Tri	52	54	37	40
60	56	F	48	155	Y	N	N	N	N	N	N	2	1	Sev calc AS,G	AVR	CHVP	21	82	58	Tri	Tri	49	52	34	36

Serial No	EF (%)		Aortic Annulus (mm)		LVOT Area 2D (cm2)		LVOT Area 3D (cm2)		Peak Gradient (mmHg)		Mean Gradient (mmHg)		Peak Velocity (m/s)		DVI		2D AVA (cm2)		3D AVA (cm2)		Grade		Impact of TEE on grading AS		
	TTE	TEE	TTE	TEE	TTE	TEE	TTE	TEE	TTE	TEE	TTE	TEE	TTE	TEE	TTE	TEE	TTE	TEE	TTE	TEE	TTE	TEE	Mean Gradi	AVA	Peak Vel
1	77	58	22	21	3.14	3.14	3.96	4.1	107	60	61	38	5.17	3.87	0.2	0.2	0.8	0.84	0.79	0.82	Sev	Mod	1 Lower	Same	1 Lower
2	72	64	21	19	3.14	2.54	3.92	3.88	101	90	52	64	5	4.74	0.2	0.2	0.96	0.84	0.78	0.77	Sev	Sev	Same	Same	Same
3	76	64	23	21	3.8	3.14	4.56	4.64	152	84	104	52	6.16	4.58	0.2	0.2	0.8	0.9	0.91	0.92	Sev	Sev	Same	Same	Same
4	60	55	23	25	3.8	4.5	4.72	4.86	102	83	62	54	5.04	4.55	0.2	0.2	0.76	0.9	0.94	0.97	Sev	Sev	Same	Same	Same
5	56	50	17	19	2	2.54	3.41	3.48	92	60	49	25	4.8	3.9	0.2	0.2	0.87	0.68	0.68	0.69	Sev	Mod	1 Lower	Same	1 Lower
6	66	55	25	23	4.15	3.46	4.92	4.84	93	52	47	32	4.8	3.6	0.2	0.2	0.9	0.8	0.98	0.96	Sev	Mod	1 Lower	Same	1 Lower
7	58	48	25	23	3.8	3.8	4.68	4.8	68	57	54	37	4.1	3.8	0.2	0.2	0.5	0.47	0.93	0.96	Sev	Mod	1 Lower	Same	1 Lower
8	73	62	24	27	3.8	4.15	5.04	5.16	60	67	35	38	3.87	4.09	0.2	0.2	0.9	0.5	1	1	Sev	Sev	Same	Same	Same
9	75	66	24	19	3.8	2.54	4.24	4.1	78	55	42	30	4.4	3.7	0.2	0.2	0.7	0.61	0.84	0.82	Sev	Mod	1 Lower	Same	1 Lower
10	55	53	26	22	4.15	3.46	4.76	4.58	171	68	102	34	6.5	4.12	0.2	0.2	0.8	0.82	0.95	0.91	Sev	Mod	1 Lower	Same	Same
11	73	64	22	19	3.14	2.54	4.06	4.12	100	98	60	65	5	4.94	0.2	0.2	0.9	1.1	0.81	0.82	Sev	Mod	Same	1 Lower	Same
12	76	64	24	23	3.8	3.8	5.14	4.96	127	72	78	44	5.6	4.2	0.2	0.2	0.9	0.7	1	0.99	Sev	Sev	Same	Same	Same
13	62	55	25	25	3.46	3.46	4.84	4.9	119	68	80	45	5.45	4.12	0.2	0.2	0.8	0.9	0.96	0.98	Sev	Sev	Same	Same	Same
14	63	56	24	23	3.8	3.46	4.94	5.04	70	47	40	24	4.18	3.42	0.2	0.3	0.8	0.9	1.02	1.5	Sev	Mod	1 Lower	Same	1 Lower
15	67	65	23	22	3.46	3.14	4.68	4.78	92	64	65	43	4.8	4	0.2	0.2	0.9	0.64	0.94	0.95	Sev	Sev	Same	Same	Same
16	59	60	20	24	3.8	4.5	6.3	6.5	77	55	51	35	4.4	3.4	0.2	0.2	0.7	0.68	1.3	1.3	Sev	Mod	1 Lower	Same	1 Lower
17	75	65	22	21	3.14	3.8	5.2	5.4	90	64	55	42	4.7	4	0.2	0.2	0.86	0.94	1.04	1.08	Sev	Sev	Same	Same	Same
18	62	56	25	23	4.5	3.8	5.32	5.64	80	56	40	38	4.5	3.74	0.2	0.2	0.64	0.7	1.06	1.12	Sev	Mod	1 Lower	Same	1 Lower
19	75	69	23	23	3.46	3.46	5.29	5.42	95	68	52	42	4.87	4.12	0.2	0.2	0.7	0.75	1.05	1.08	Sev	Sev	Same	Same	Same
20	64	55	31	28	6.15	5.3	5.5	5.45	71	44	40	22	4.2	3.3	0.2	0.2	0.95	0.9	1.1	1.1	Sev	Mod	1 Lower	Same	1 Lower
21	65	58	30	28	5.3	6.6	6.14	6.25	71	76	44	49	4.21	4.36	0.2	0.2	0.82	0.9	1.23	1.25	Sev	Sev	Same	Same	Same
22	82	62	20	21	2.83	3.14	4.56	4.67	78	55	44	30	4.4	3.7	0.2	0.2	0.6	0.7	0.91	0.93	Sev	Mod	1 Lower	Same	1 Lower
23	65	59	17	19	2	2.54	4.08	4.2	71	64	44	36	4.2	4	0.2	0.2	0.78	0.84	0.82	0.84	Sev	Mod	1 Lower	Same	Same
24	70	62	18	20	2	2.54	3.12	3.24	88	92	60	53	4.7	4.7	0.2	0.2	0.64	0.6	0.62	0.64	Sev	Sev	Same	Same	Same
25	65	60	20	20	2.54	2.54	3.62	3.8	160	106	108	68	6.3	5.2	0.2	0.2	0.59	0.65	0.72	0.65	Sev	Sev	Same	Same	Same
26	62	58	21	22	2.8	3.14	3.56	3.72	89	64	53	36	4.7	4	0.2	0.2	0.75	0.82	0.71	0.74	Sev	Mod	1 Lower	Same	Same
27	73	66	22	19	3.14	2.54	4.12	4.3	130	74	70	44	5.7	4.3	0.2	0.2	0.62	0.7	0.82	0.86	Sev	Sev	Same	Same	Same
28	58	52	24	23	3.8	3.46	5.45	5.34	71	44	42	28	4.2	3.3	0.2	0.2	0.58	0.62	1.1	1.07	Sev	Mod	1 Lower	Same	1 Lower
29	70	62	20	21	2.54	3.14	4.51	4.64	86	70	48	41	4.6	4.2	0.2	0.2	0.69	0.72	0.9	0.92	Sev	Sev	Same	Same	Same
30	56	50	23	21	3.8	3.14	4.24	3.86	82	44	51	28	4.5	3.4	0.2	0.2	0.7	0.9	0.85	0.78	Sev	Mod	1 Lower	Same	1 Lower
31	73	62	18	19	2	2.54	4.14	4.24	79	54	40	25	4.4	3.67	0.2	0.2	0.7	0.8	0.82	0.85	Sev	Mod	1 Lower	Same	1 Lower
32	72	64	21	22	3.14	3.79	5.25	5.34	111	106	68	65	5.2	5.1	0.2	0.2	0.78	0.76	1.05	1.07	Sev	Sev	Same	Same	Same
33	75	62	19	20	2.54	2.83	3.56	3.64	97	44	48	24	4.9	3.3	0.2	0.2	0.66	0.7	0.7	0.72	Sev	Mod	1 Lower	Same	1 Lower
34	60	54	18	19	2.26	2.54	3.28	3.45	78	79	41	49	4.4	4.4	0.2	0.2	0.76	0.8	0.66	0.7	Sev	Sev	Same	Same	Same
35	55	50	21	21	3.14	3.14	3.56	3.68	109	64	60	36	5.2	4	0.2	0.2	0.86	0.9	0.7	0.73	Sev	Mod	1 Lower	Same	Same
36	68	58	21	21	3.14	3.14	3.96	4.05	84	60	56	38	4.58	3.88	0.2	0.2	0.9	0.95	0.8	0.81	Sev	Mod	1 Lower	Same	1 Lower
37	66	60	21	22	3.8	3.8	3.77	3.84	102	124	61	75	4.5	5.5	0.2	0.2	0.97	0.87	0.75	0.77	Sev	Sev	Same	Same	Same
38	60	53	23	21	3.8	3.14	3.84	3.76	141	90	90	58	5.9	4.7	0.2	0.2	0.87	0.99	0.77	0.75	Sev	Sev	Same	Same	Same
39	73	66	20	21	2.8	2.8	3.3	3.4	92	55	55	31	4.8	3.5	0.2	0.2	0.87	0.88	0.67	0.67	Sev	Mod	1 Lower	Same	1 Lower
40	71	62	22	21	3.14	3.14	3.76	3.84	104	64	56	31	5	4	0.2	0.2	0.9	0.96	0.75	0.77	Sev	Mod	1 Lower	Same	Same
41	75	64	21	19	3.14	2.54	3.64	3.76	129	68	76	46	5.6	4.1	0.2	0.2	0.74	0.82	0.73	0.75	Sev	Sev	Same	Same	Same
42	64	59	27	26	5.73	5.73	5.3	5.46	100	85	66	50	5	4.6	0.2	0.2	0.8	0.91	1.06	1.09	Sev	Sev	Same	Same	Same
43	60	57	21	20	3.14	2.84	3.23	2.98	74	73	48	43	4.3	4.28	0.2	0.2	0.95	0.94	0.65	0.6	Sev	Mod	Same	Same	1 Lower
44	58	54	24	27	4.15	4.9	4.94	5.23	66	58	40	36	4.1	3.8	0.2	0.2	0.78	0.86	0.99	1.04	Sev	Mod	1 Lower	Same	1 Lower
45	77	68	23	24	3.8	3.8	4.64	4.75	78	66	50	36	4.4	4.06	0.2	0.2	0.9	0.92	0.93	0.95	Sev	Mod	1 Lower	Same	Same
46	63	57	19	23	2.54	3.14	3.02	3.26	90	61	57	30	4.7	3.9	0.2	0.2	0.7	0.8	0.6	0.65	Sev	Mod	1 Lower	Same	1 Lower
47	68	63	21	21	2.83	3.14	3.28	3.3	120	84	72	57	5.4	4.6	0.2	0.2	0.71	0.82	0.66	0.66	Sev	Sev	Same	Same	Same
48	76	66	23	23	3.8	3.8	4.46	4.54	109	83	74	49	5.2	4.5	0.2	0.2	0.68	0.75	0.89	0.9	Sev	Sev	Same	Same	Same
49	69	60	24	25	3.8	4.5	4.81	4.91	73	58	41	34	4.2	3.7	0.2	0.3	0.9	1.1	0.96	1.47	Sev	Mod	1 Lower	1 Lower	1 Lower
50	74	67	20	24	3.14	3.8	4.16	4.25	80	79	51	38	4.5	4.4	0.2	0.2	0.72	0.9	0.83	0.85	Sev	Mod	1 Lower	Same	Same
51	73	60	21	20	3.14	2.56	4.18	4.09	86	64	52	42	4.6	4	0.2	0.2	0.56	0.55	0.83	0.82	Sev	Sev	Same	Same	Same
52	63	56	22	23	3.46	3.46	4.64	4.78	98	77	64	40	4.9	4.38	0.2	0.2	0.75	0.86	0.93	0.95	Sev	Sev	Same	Same	Same
53	72	60	24	24	3.8	3.8	4.64	4.7	93	68	68	38	4.8	4.12	0.2	0.2	0.72	0.76	0.93	0.94	Sev	Mod	1 Lower	Same	Same
54	70	64	21	24	3.14	3.8	4.63	4.7	112	82	65	55	5.3	4.5	0.2	0.2	0.66	0.72	0.93	0.94	Sev	Sev	Same	Same	Same
55	68	62	22	23	3.14	3.5	3.92	4.04	82	64	53	36	4.52	4	0.2	0.2	0.82	0.87	0.78	0.8	Sev	Mod	1 Lower	Same	Same
56	83	65	23	22	3.5	3.14	4.23	4.2	105	90	88	57	5.1	4.7	0.2	0.2	0.72	0.79	0.85	0.84	Sev	Sev	Same	Same	Same
57	78	64	23	24	3.8	3.8	4.46	4.51	140	76	75	47	5.9	4.35	0.2	0.2	0.82	0.85	0.89	0.9	Sev	Sev	Same	Same	Same
58	74	66	23	26	3.8	4.5	4.24	4.65	96	72	64	48	4.9	4.24	0.2	0.2	0.72	0.78	0.85	0.93	Sev	Sev	Same	Same	Same
59	72	65	23	21	3.8	3.5	4.32	4.4	84	62	54	38	4.58	3.93	0.2	0.2	0.82	0.85	0.86	0.88	Sev	Mod	1 Lower	Same	1 Lower
60	70	62	22	22	3.14	3.14	3.94	3.98	104	80	68	52	5.1	4.47	0.2	0.2	0.74	0.7	0.78	0.8	Sev	Sev	Same	Same	Same