CLINICAL AND ECHOCARDIOGRAPHIC CORRELATES OF VALVULO-ARTERIAL IMPEDANCE IN AORTIC STENOSIS WITH FOCUS ON ASYMPTOMATIC AORTIC STENOSIS

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CERTIFICATE

This is to certify that this dissertation titled "**Clinical and Echocardiographic Correlates of Valvulo-Arterial Impedance in Aortic Stenosis with focus on Asymptomatic Aortic Stenosis"** submitted by **Dr. JEGADEESH . J** to the faculty of Cardiology, The Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfilment of the requirement for the award of DM degree Branch II (Cardiology), is a bonafide research work carried out by him under our direct supervision and guidance. The period of post-graduate study and training was from August 2011 to July 2014.

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DECLARATION

I, **Dr. JEGADEESH . J,** solemnly declare that the dissertation titled "**Clinical and Echocardiographic Correlates of Valvulo-Arterial Impedance in Aortic Stenosis with focus on Asymptomatic Aortic Stenosis"** has been prepared by me under the guidance and supervision of **Prof.M.S.Ravi M.D, D.M,** Professor and Head, Department of Cardiology, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai. This is submitted to The Tamil Nadu Dr. M.G.R. Medical University, Chennai, in partial fulfilment of the rules and regulations for the award of DM degree (Branch II) Cardiology.

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CONTENTS

ABBREVIATIONS

2D	:	2 dimension
AS	:	Aortic Stenosis
AVA	:	Aortic Valve Area
BMI	:	Body Mass Index
BSA	:	Body Surface Area
CMR	:	Cardiac Magnetic Resonance
CSA	:	Cross Sectional Area
CT	:	Computed Tomography
CV	:	Cardiovascular
EF	:	Ejection Fraction
ELCo	:	Energy Loss Coefficient
EOA	:	Effective Orifice Area
LV	:	Left Ventricle
LVEF	:	Left Ventricular Ejection Fraction
LVOT	:	Left Ventricular Outflow Tract
MAPSE	:	Mitral Annular Plane Systolic Excursion
VPC	:	Ventricular Premature Complex
VTI	:	Velocity Time Integral
Zva	:	Valvuloarterial Impedance

INTRODUCTION

Aortic Stenosis is one of the major causes of cardiovascular morbidity and mortality in the elderly. It is the most common causes for valve surgery in the developed countries [(1)].

In recent times aortic stenosis is believed to be due to atherosclerotic process affecting the valves along with the great arteries [(2)] hence aortic valve disease is also considered to be an abnormality of the valve and arterial system together.

In India, the incidence of isolated aortic valve disease has been increasing and many cases of isolated aortic valve disease is being diagnosed due to better utilization of healthcare facilities by people and due to the decline in the incidence of rheumatic heart disease.

Newer therapies have been evolving in the treatment of aortic valve disease like transcatheter replacement of the aortic valve. In this scenario the evaluation of aortic valve pathology has to be precise and it should be helpful in guiding treatment. Traditionally the estimation of severity of aortic valve stenosis has been based on Echocardiographic and Doppler evaluation and these have provided adequate details in most of the cases of aortic stenosis. But in patients with coexisting hypertension and stiffness of the arterial system the conventional methods of estimation of the severity of aortic stenosis may underestimate the magnitude of the severity thereby the ultimate treatment may be delayed, moreover a significant number of patients in whom AS is severe as defined by the valve area criteria show low gradients despite the presence of a good LV function (Paradoxical Low flow low gradient AS[3]) since there is a discrepancy between these values this might lead to postponement of surgical therapy. But in reality these are the subset of patients who are in a more advanced state of disease progression, they have concentric remodeling and a smaller LV cavity a reduced Stroke volume and increased LV after load, the low stroke volume tends to lower the transvalvular gradients. In these conditions the estimation of the severity of aortic valve stenosis can be done by using other methods. The combination load imposed on the left ventricle both by the valve and the arteries in patients with aortic valve stenosis can be calculated by a non invasive method using echo-Doppler and this is known as the valvuloarterial impedance. In many studies it has been shown that high global LV load as quantitated by the increased values of valvuloarterial impedance was associated with poor prognosis and high valvuloarterial impedance patients had more incidence of symptoms , more incidence of cardiovascular mortality and quicker need for aortic valve replacement. [3,4,5,6] So far there has been no medical therapy proven to halt the progression of Aortic Stenosis so surgery becomes the mainstay of treatment, thus the proper evaluation of Aortic Valve stenosis becomes mandatory before subjecting the patient to a procedure that carries a mortality risk of about 2 percent.

In the natural history of Aortic stenosis the patients after development of narrowing of the aortic orifice have a long latent period before the development of symptoms of aortic stenosis like angina, dyspnoea or syncope, but after the development of these symptoms they have a steep downhill course. Severe Aortic stenosis patients who are symptomatic are candidates for surgery and without Aortic valve replacement only 50% survive up to 2 years and 20% survive up to 5 years respectively [8]. But there are subsets of patients who have severe Aortic Stenosis but are asymptomatic, in these patients according to current management guidelines they are subjected to exercise stress testing and if they develop symptoms they are advised surgery, others are advised careful follow up for symptoms or signs of rapid progression of disease. In a study done in 544 patients with asymptomatic Aortic stenosis it has been shown that high valvuloarterial impedance values predicted increase in 4 year mortality and major cardiovascular adverse events independent of traditional indices of severity[6].

In this scenario we thought that it would be prudent to have a study on the valvuloarterial impedance in our south Indian population so as to get information regarding the pattern of global LV load in our subset of patients with Aortic stenosis and to study the relationship of valvuloarterial impedance to patients symptoms and indices of LV function and geometry. Since asymptomatic patients with severe aortic stenosis and high LV global load had a poor prognosis estimation of valvuloarterial impedance in this population would help in risk stratification and direct them towards early surgery thereby reducing adverse event rate.

AIMS AND OBJECTIVES

1. To study the valvuloarterial impedance levels in south Indian population presenting with isolated Aortic valve disease.
2. To study the correlation of symptoms of Aortic stenosis with levels of valvuloarterial impedance
3. To evaluate the relationship between Age, Sex, Body mass index and Hypertension and valvuloarterial impedance in patients with Aortic stenosis.
4. To study the correlation of indices of Left Ventricular geometry and Left Ventricular function (systolic, diastolic and global) with levels of valvuloarterial impedance
5. To evaluate the relationship between mitral annular plane systolic excursion and levels of valvuloarterial impedance in aortic stenosis patients with normal Ejection fraction, and to unmask early Left Ventricular longitudinal dysfunction.
6. To compare the indices of Aortic stenosis severity to levels of valvuloarterial impedance.
7. To evaluate the Doppler echocardiographic characteristics of patients with asymptomatic Aortic stenosis.

REVIEW OF LITERATURE

The earliest descriptions about Aortic stenosis was done by Lazare Riviere, a French physician as early as 1663 AD as autopsy findings in a patient with breathlessness, palpitations and absent pulses in the extremities. In modern day medicine the description of calcific aortic valve disease were first given by Moenckeberg in 1904[(9)].

Aortic stenosis is the commonest valve disease in the developed nations. In patients with asymptomatic aortic stenosis the mortality rate without intervention is 50 % within 4 years of symptom onset [(10)]. Aortic valve disease is not a simple degenerative process but is a complex disease where congenital, genetic, environmental & molecular mechanisms play a role [(2, 11)].

Aortic valve anatomy

The aortic valve is the major valve in the heart operating at high pressure and it is usually tricuspid. The incidence of Bicuspid aortic valve is 1-2% in the general population still lesser numbers of patients have unicuspid aortic valves.

In normal persons the aortic valve opens and shuts about 100,000 times a day and allows 2-20 liters of blood to pass through it per minute depending upon the levels of physical activity [12].

An important function of the aortic valve is to provide streamlined laminar flow from the LV into the aorta and to prevent the backflow of blood into the ventricles during diastole. The effect of aortic valve also helps the LV in maintaining its normal function. The aortic sinuses above the aortic valve is the site where the coronaries originate, since the coronary flow occurs predominantly during diastole the aortic valve the aortic valve mechanism provides a system by which pressure currents are created in the aortic sinuses aiding diastolic coronary flow. [13, 15] In aortic valve disease the processes are in jeopardy leading to deleterious effects on coronary perfusion and Left Ventricular function.

Epidemiology

Aortic valve stenosis is predominantly a disease of the elderly population and it is the most frequent causes of valve disease and valve replacement in the developed world. [1] Aortic valve sclerosis is a condition in which there is thickening of the aortic valve leaflets without significant obstruction to the outflow of increase in gradient across the aortic valve. With progressive increase in age there is a progressive increase in incidence of Aortic Sclerosis and Aortic stenosis. Throughout the world, studies done have shown that of the valvular heart diseases, aortic valve disease is the commonest and it constitutes 43% of cases of valvular heart disease. Aortic valve sclerosis is now thought to be a forerunner of aortic stenosis and the pathology is the same for both the conditions. In studies it has been shown that in elderly individuals of age >65 years the incidence of aortic sclerosis was about 29% and the incidence of Aortic stenosis varied from 2-9%.Of the persons with aortic valve sclerosis 1.7% patients progress to aortic stenosis in a year. Aortic valve sclerosis as thought previously is not a benign entity but is associated with a 50% increased risk of coronary artery disease compared to the general population. [15] Aortic valve disease occurs more commonly in males.

In the Helsinki Ageing study[1] done in elderly patients about 53% had calcification of the aortic valves of these 40% had mild calcification and 13% had severe calcification, in this study 5% of the participants had moderate degrees of Aortic stenosis and 2.9% had severe aortic stenosis.

In another study done in African Americans 18.6% of the participants between the age of 65 to 75 years were found to have aortic valve sclerosis.[16] Of the factors affecting the aortic valve, Rheumatic heart disease affects the aortic valve in about 40-45% and it usually coexists with mitral valve disease. The aortic cusps in RHD are thickened calcified and have a fused commisure. In developed nations the incidence of Rheumatic AS is very less. Other conditions that might lead to aortic valve stenosis are Paget's disease, Familial Hypercholesterolemia, Chronic kidney disease and chest radiotherapy.

Congenital AS is an uncommon cause of Aortic stenosis and the aortic valve may be bicuspid unicuspid or tricuspid. usually congenital bicuspid aortic valve is not associated with stenosis at birth but gradually develops stenosis by early adulthood.

Degenerative calcific aortic stenosis is the commonest cause for aortic stenosis in adults and it is the commonest cause for aortic valve replacement in adults. [2]

Usually the risk factors for developing AS are similar to those of atherosclerotic vascular disease like smoking, high blood pressure male sex, increasing age, high LDL cholesterol levels, and increased BMI. [17]

It is also noted that presentation of bicuspid aortic valve is 2 decades earlier than (40-60 years) tricuspid aortic valve stenosis (60 -70 years). [18]

In a study done by Olsen et al in 2005[19] in 960 hypertensive patients the prevalence of Aortic valve sclerosis was found to be 40.4% and 1.6% of the study population had Significant aortic valve disease, the patients with Aortic valve sclerosis had thicker ventricles , more LV mass and LV mass indexed to body surface area. This study also showed that Aortic valve stenosis and sclerosis was a significant risk factor for CV mortality, Myocardial infarction and stroke.

Pathophysiology

In aortic valve stenosis the obstruction to the ventricular outflow causes left ventricular concentric hypertrophy and increase in thickness of LV and the mass of the LV is also increased, this is a compensatory mechanism and it decreases the Left ventricular wall tension. In a majority of persons with aortic valve stenosis the size of the LV cavity is usually within the normal limits and the Left ventricular systolic function is also normal, in later stages when the compensatory mechanisms fail there is a progressive dilatation of the left ventricle and decrease in LV function.

The altered physiology in aortic valve stenosis is due to three main factors – first is the increase in the load against which the LV has to pump – the after load, second is the decrease in blood supply to the LV myocardium due to decreased coronary flow and increase in LV thickness, and third is the hypertrophy of the left ventricle leading to diastolic and systolic left ventricular dysfunction.

The three classic symptoms of aortic valve stenosis i.e. dyspnoea, angina, and syncope are brought about by the above mechanisms. Patients with AS and normal LV function also have effort induced breathlessness. Diastolic left ventricular function abnormalities are usually the norm in significant aortic valve stenosis and the elevated left ventricular filling pressures are eventually transmitted to the pulmonary circulation leading on to dyspnoea .the reasons for diastolic dysfunction is multiple and it is due to the stiff non compliant ventricle, decreased myocardial blood supply and due to an increase in LV afterload.

Ischemia develops as the coronary blood supply cannot match the needs of the hypertrophied myocardium and hypoxemia of the myocardium ensues the elevated diastolic pressures within the LV cavity also hamper the blood supply worsening the angina. Symptoms of exertional angina may be present in the absence of epicardial coronary artery obstruction.

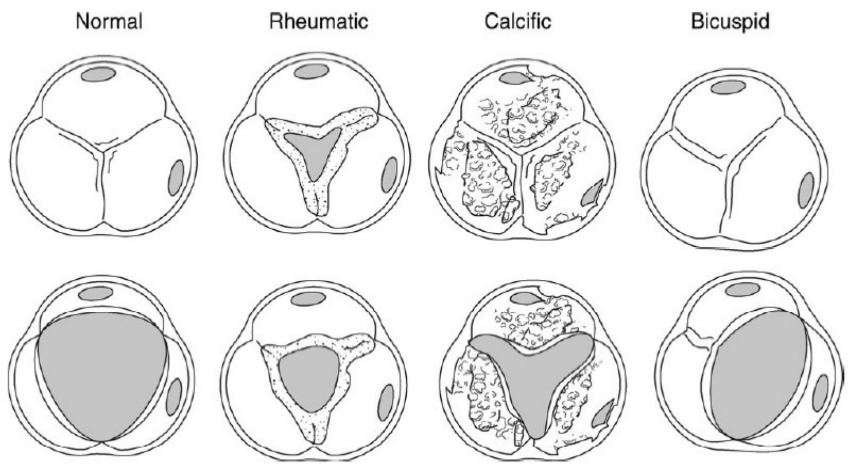
Syncope in Aortic stenosis has varied causes, the reasons for syncope may be due to the onset of Arrhythmias (Brady or Tachy arrhythmias), due to the obstruction to the outflow leading to coronary and cerebral insufficiency or due to activation of various autonomic vasodepressor reflexes triggered by the stress induced activation of the mechanoreceptors in the left ventricle.

When the left ventricle is subjected to chronic pressure overload the afterload mismatch phenomenon results in deterioration of the Left ventricular function and this in turn in due course of time also results in right heart failure .The onset of right heart failure results in systemic hypotension further decreasing the coronary perfusion and worsening ischemia leading to an irreversible downward spiral.

As a progressive, long-standing pressure overload is placed on the left ventricle, systolic decompensation may occur from the afterload mismatch and lead to symptoms of both left-sided and right-sided heart failure. [20, 21]

Echocardiographic evaluation of Aortic stenosis [22]

Doppler and 2 dimensional Echocardiography are the investigations of choice for the diagnosis and to estimate the severity of Aortic stenosis. Echocardiography is useful in studying the anatomy of the valve, gives information about the left ventricular function and evaluates the hydraulic behavior of the aortic valve.



Identification of AS etiology by Echo

Data element	Recording	Measurement
LVOT diameter	• 2D parasternal long-axis view • Zoom mode • Adjust gain to optimize the blood tissue interface	• Inner edge to inner edge • Mid-systole • Parallel and adjacent to the aortic valve or at the site of velocity measurement (see text) • Diameter is used to calculate a circular CSA
LVOT velocity	• Pulsed-wave Doppler • Apical long axis or five-chamber view • Sample volume positioned just on LV side of valve and moved carefully into the LVOT if required to obtain laminar flow curve • Velocity baseline and scale adjusted to maximize size of velocity curve • Time axis (sweep speed) 100 mm/s • Low wall filter setting • Smooth velocity curve with a well-defined peak and a narrow velocity range at peak velocity	• Maximum velocity from peak of dense velocity curve • VTI traced from modal velocity
AS jet velocity	• CW Doppler (dedicated transducer) • Multiple acoustic windows (e.g. apical, suprasternal, right parasternal, etc) • Decrease gains, increase wall filter, adjust baseline, and scale to optimize signal • Gray scale spectral display with expanded time scale • Velocity range and baseline adjusted so velocity signal fits but fills the vertical scale	• Maximum velocity at peak of dense velocity curve • Avoid noise and fine linear signals • VTI traced from outer edge of dense signal curve • Mean gradient calculated from traced velocity curve • Report window where maximum velocity obtained
Valve anatomy	• Parasternal long- and short-axis views • Zoom mode	• Identify number of cusps in systole, raphe if present • Assess cusp mobility and commisural fusion • Assess valve calcification

The above are the recommended measurements to be obtained in patients with aortic stenosis while performing Echocardiography.

Echo criteria for the severity of AS [22] (ACC/AHA guideline values marked *)

	Aortic Sclerosis	Mild AS	Moderate AS	Severe AS
Aortic jet velocity (m/s)	<2.6	2.6–3.0	3–4	>4
Mean gradient (mmHg)	—	<30 (25*)	30–50 (25–40*)	>50 (40*)
AVA (cm^2)	—	>1.5	1.0–1.5	<1.0
Indexed AVA (cm^2/m^2)		>0.9	0.6–0.9	<0.6
Velocity ratio		>0.50	0.25–0.50	<0.25

Measurements for AS severity to be obtained by Doppler Echo

	Units	Formula / Method	Cutoff for Severe	Concept	Advantages	Limitations
AS jet velocity [8-10, 12]	m/s	Direct measurement	4.0	Velocity increases as stenosis severity increase.	Direct measurement of velocity. Strongest predictor of clinical outcome.	Correct measurement requires parallel alignment of ultrasound beam. Flow dependent.
Mean gradient [8-10]	mm Hg	$\Delta P = \sum 4v^2 / N$	40 or 50	Pressure gradient calculated from velocity using the Bernoulli equation	Mean gradient is averaged from the velocity curve. Units comparable to invasive measurements.	Accurate pressure gradients depend on accurate velocity data. Flow dependent
Continuity equation valve area [16, 17, 23]	cm^2	$AVA = (CSA_{LVOT} \times VTI_{LVOT}) / VTI_{AV}$	1.0	Volume flow proximal to and in the stenotic orifice is equal.	Measures effective orifice area. Feasible in nearly all patients. Relatively flow independent.	Requires LVOT diameter and flow velocity data, along with aortic velocity. Measurement error more likely.
Simplified continuity equation [18,23]	cm^2	$AVA = (CSA_{LVOT} \times V_{LVOT}) / V_{AV}$	1.0	The ratio of LVOT to aortic velocity is similar to the ratio of VTIs with native aortic valve stenosis.	Uses more easily measured velocities instead of VTIs.	Less accurate if shape of velocity curves is atypical.
Velocity Ratio [15,18]	none	$VR = \frac{V_{LVOT}}{V_{AV}}$	0.25	Effective aortic valve area expressed as a proportion of the LVOT area.	Doppler-only method. No need to measure LVOT size, less variability than continuity equation.	Limited longitudinal data. Ignores LVOT size variability beyond patient size dependence
Planimetry of Anatomic Valve Area [26, 34]	cm^2	TTE, TEE, 3D-echo	1.0	Anatomic (geometric) cross-sectional area of the aortic valve orifice as measured by 2D or 3D echo.	Useful if Doppler measurements are unavailable.	Contraction coefficient (anatomic / effective valve area) may be variable. Difficult with severe valve calcification.
LV % Stroke Work Loss [27]	%	$\%SWL = \frac{\overline{\Delta P}}{\overline{\Delta P} + SBP} \cdot 100$	25	Work of the LV wasted each systole for flow to cross the aortic valve, expressed as a % of total systolic work	Very easy to measure. Related to outcome in one longitudinal study.	Flow-dependent. Limited longitudinal data
Recovered Pressure Gradient [13, 32]	mm Hg	$P_{distal} - P_{vc} = 4 \cdot v^2 \cdot 2 \cdot \frac{AVA}{AA} \cdot \left(1 - \frac{AVA}{AA}\right)$	-	Pressure difference between the LV and the aorta, slightly distal to the *vena contracta*, where distal pressure has increased.	Closer to the global hemodynamic burden caused by AS in terms of adaptation of the cardiovascular system. Relevant at high flow states and in patients with small ascending aorta.	Introduces complexity and variability related to the measurement of the ascending aorta. No prospective studies showing real advantages over established methods.
Energy Loss Index [35]	cm^2/m^2	$ELI = \frac{AVA \cdot AA}{AA - AVA} / BSA$	0.5	Equivalent to the concept of AVA, but correcting for distal recovered pressure in the ascending aorta	(As above) Most exact measurement of AS in terms of flow-dynamics. Increased prognostic value in one longitudinal study.	Introduces complexity and variability related to the measurement of the ascending aorta.
Valvulo-Arterial Impedance [31]	mm Hg/ml/m^2	$Z_{VA} = \frac{\overline{\Delta P_{net}} + SBP}{SVI}$	5	Global systolic load imposed to the LV, where the numerator represents an accurate estimation of total LV pressure	Integrates information on arterial bead to the hemodynamic burden of AS, and systemic hypertension is a frequent finding in calcific-degenerative disease.	Although named "impedance", only the steady-flow component (i.e. mean resistance) is considered. No longitudinal prospective study available.
Aortic Valve Resistance [28, 29]	dynes/s/cm^5	$AVR = \frac{\overline{\Delta P}}{\overline{Q}} = \frac{\overline{4 \cdot v^2}}{\cdot r^2_{LVOT} \cdot v_{LVOT}} \cdot 1333$	280	Resistance to flow caused by AS, assuming the hydrodynamics of a tubular (non flat) stenosis.	Initially suggested to be less flow-dependent in low-flow AS, but subsequently shown to not be true.	Flow dependence. Limited prognostic value. Unrealistic mathematic modelling of flow-dynamics of AS.
Projected Valve Area at Normal Flow Rate [30]	cm^2	$AVA_{proj} = AVA_{rest} + VC \cdot (250 - Q_{rest})$	1.0	Estimation of AVA at normal flow rate by plotting AVA vs. flow and calculating the slope of regression (DSE)	Accounts for the variable changes in flow during DSE in low flow low gradient AS, provides improved interpretation of AVA changes	Clinical impact still to be shown. Outcome of low-flow AS appears closer related to the presence / absence of LV contractility reserve.

VR, velocity ratio; TVI, time–velocity integral; LVOT, LV outflow tract; AS, AS jet; TTE and TEE, transthoracic and transesophageal echocardiography; SWL, stroke work loss; $\overline{\Delta P}$, mean transvalvular systolic pressure gradient; SBP, systolic blood pressure; P_{distal}, pressure at the ascending aorta; P_{vc}, pressure at the *vena contracta*; AVA, continuity-equation-derived aortic valve area; *v*, velocity of AS jet; AA, size of the ascending aorta; ELI, energy-loss coefficient; BSA, body-surface area; AVR, aortic valve resistance; $\overline{Q}$, mean systolic transvalvular flow-rate; AVA_{proj}, projected aortic valve area; AVA_{rest}, AVA at rest; VC, valve compliance derived as the slope of regression line fitted to the AVA versus Q plot; Q_{rest}, flow at rest; DSE, dobutamine stress echocardiography; N, number of instantaneous measurements.

1 to 3 Essential in all patients with Aortic stenosis (yellow);

4 to 6 Reasonable where additional information is required in selected groups (green); and 7 to 11 routinely not recommended (blue).

Imaging of the Aortic valve

2D Imaging

The 2 dimensional views that are used to evaluate the Aortic valve are the parasternal long axis view, the parasternal short axis view at the level of the aortic valve and the apical long axis view, in some cases the sub- xiphoid short axis view is also useful. These views can identify the number of cusps and the degree of calcification. The aortic valve area may be calculated by planimetry but is does not correlate with the hemodynamically determined effective orifice area.

Echocardiographic assessment of Left Ventricular function

Assessment of left ventricular function is a part and parcel of Echocardiography in Aortic stenosis the minimum information required about the left ventricle is the standard measurement of Left ventricular dimensions, the measurements that are usually made are the dimensions of the interventricular septum , the posterior wall and the left ventricular cavity dimensions the relative wall thickness is calculated. These indices help us to identify the alterations in left ventricular geometry. Many studies have shown that LV geometry is altered in AS and concentric remodeling is common in aortic stenosis and it has also been shown that men with aortic stenosis tend to have dilated LV cavities in later stages of disease. [23]

Next is the assessment of left ventricular ejection fraction and fractional shortening. The left ventricular function assessment should also include long axis function measure using tissue Doppler or using M-mode echocardiography.

Third part of evaluation of the Left ventricle consists of obtaining the time velocity integral of the outflow tract. It is done using pulse wave Doppler with sample volume placed in the LVOT.

The fourth part of assessment of LV consisting of assessing the degree of diastolic dysfunction this is done using pulsed wave Doppler in the mitral inflow or using tissue Doppler techniques.

Doppler measurements in aortic stenosis

The minimum data to be collected are the V max or peak velocity, the mean transvalvular gradient and calculation of Effective orifice area by the continuity equation.

In measuring the V max of peak velocity, the continuous wave Doppler is aligned parallel to the aortic valve in the apical five chamber view so that the spectrum is clear and uniform. The signal with uniform contour and highest peak is chosen for the measurement avoiding the artifacts. Usually post VPC beats are avoided and in patients with atrial fibrillation the average V max of five beats is taken. Using the V max the peak gradient can also be calculated using the Bernoulli equation. ($\Delta P = 4 V^2$, where V is the V max)

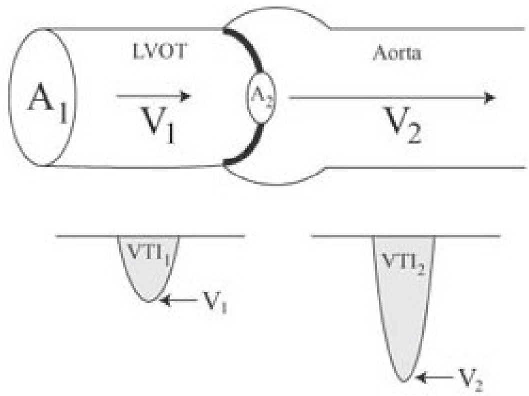
In the continuous wave signal spectrum the morphology of the spectrum helps in identification of the severity of stenosis, a triangular signal indicates severe AS but an early peaking in the signal spectrum indicates mild AS. [(22)]

The mean gradient is a value that is obtained by the integral of all the instantaneous gradients over time so the mean gradient reflects faithfully the stenosis severity than the peak gradient.

The aortic valve area is calculated using the continuity equation

For calculation of the aortic valve area by using the continuity equation the apical three chamber view and the apical five chamber view are used. The cursor is aligned properly parallel to the direction of flow and continuous wave Doppler flow is recorded across the aortic valve and pulse wave Doppler tracings are recorded across the left ventricular outflow tract.

Continuity equation



Here $A_1 \times VTI_1 = A_2 \times VTI_2$

Calculation of Aortic valve area by the continuity equation is the method which is widely accepted. The basis of the continuity equation is that the stroke volume passing through the LV outflow is equal to the stroke volume crossing the stenosed aortic valve:

$$AVA \times VTI_{AS} = CSA_{LVOT} \times VTI_{LVOT}$$

AVA - aortic valve area,

VTI_{AS} and VTI_{LVOT} - velocity time integrals in the effective valve orifice and LVOT, respectively,

CSA *LVOT* - cross-sectional area of the LVOT

This method is prone for error since this assumes that the LVOT is circular in shape also requires the measurement of the LVOT size and the velocity at exactly the same place. The flow velocity in the LVOT is measured in the apical view using pulse Doppler assuming that the flow is laminar, so this method is not so accurate. [22, 23]

Pressure recovery and gradients

Currently the guidelines for the diagnosis for the diagnosis and management of aortic stenosis does not make distinction between Doppler based and cath based measurements. But catheterization derived gradients measure the net gradient between the LV and Aorta but the Doppler estimates the maximal velocity drop through the stenotic valve from the maximum velocity recorded. But as the blood flow decelerates between the valve and the aorta some amount of the kinetic energy is converted back into potential energy in the proximal aorta due to a phenomenon known as the pressure recovery. So the gradients measured by catheterization are always less than the gradients recorded by Doppler echocardiography. Similarly the effective orifice areas which are calculated using Gorlin's formula in cath is based on pressure recovered values and is usually higher than the Effective orifice area calculated by Doppler using the continuity equation.

The ratio between the Effective orifice area and the proximal aorta cross section governs the extent of pressure recovery ,This becomes very important in patients with moderate AS (EOA – 0.8 to1.2 cm2)and small aortas (ST junction <3.0 cm)where the measurement of the gradients might overestimate the severity of Aortic stenosis.

To overcome this some formulas have been proposed and they include the formula proposed by Baumgartner et al [24] and the Energy loss coefficient proposed by Garcia et al [25]

ELCo= (EOA x AA / AA - EOA),

AA is the CSA of the aorta measured at 1 cm distal of the sinotubular junction

Another index called stroke work loss gives indirect information on pressure recovery and it is calculated as the ratio of the mean transvalvular gradient to the estimated LV systolic pressure.

Some studies have shown that including these parameters may be superior to using the gradients or EOA alone to predict adverse outcomes. [26]

Body surface area measurements

For two patients with the same EOA but different Body surface areas the load imposed on the ventricle by the stenotic lesion will be higher in the patient with a higher body surface area and it will be lower in patients with lesser body surface area. So the larger patient has an underestimation of severity and a smaller patient has overestimation of severity. So to overcome this pitfall indexed values are used

The concept of vascular load

Aortic stenosis is a complex disease and it is considered to be a disease affecting the valve as well as the aorta and the pathology in calcific aortic stenosis is similar to atherosclerosis and medial elastocalcinois. Even in young patients with bicuspid aortic valve there are coexisting abnormalities of the aortic media which lead to excessive stiffness of the aorta and patients may also have aortic dilatation. Elderly patients with decreased compliance of the aorta also tend to have systolic hypertension

Briand et al in a study done in 2005 [(4)] reported that in approximately 40% of patients with Aortic stenosis the total systemic arterial compliance was reduced (<0.6ml.m-2.mmHg-1). The systemic arterial compliance was calculated by dividing the Stroke Volume index by pulse pressure. This reduced compliance causes an increase in the LV afterload and this in turn leads to left ventricular dysfunction and culminates in increase in adverse events.

The systemic arterial compliance reflects the pulsatile component of the arterial load but there also exists a steady component in the arterial tree that is estimated by calculation of the Systemic vascular resistance .the systemic vascular resistance is calculated as follows

SVR = (80 x mean arterial pressure)/CO

CO is the cardiac output measured in the LVOT by Doppler

Mean arterial pressure = diastolic pressure + pulse pressure

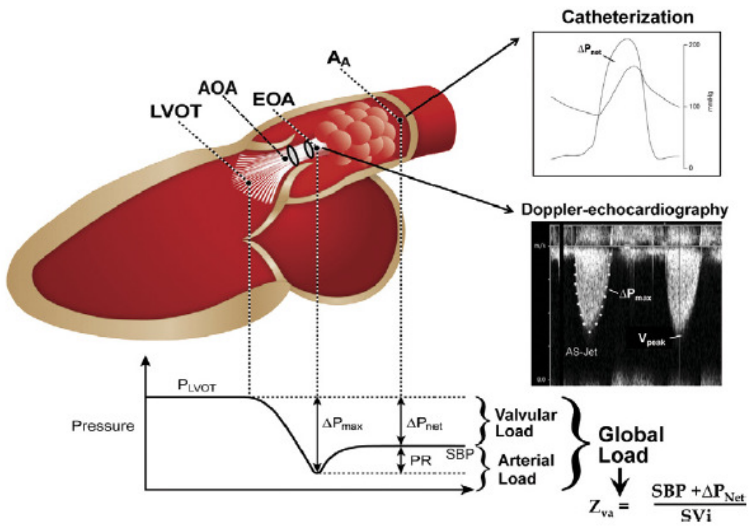
In this context it should be noted that normal BP does not exclude an increased vascular load because the BP may be falsely low in about 30% of patients with decreased compliance, this may be due to a reductio in cardiac output or due to LV systolic dysfuction.

Relationship between aortic stenosis severity and hypertension

Studies have shown that coexisting systemic hypertension was present in 35 to 51% of patiens with aortic stenosis .Increase in pulse pressure and elevation of systolic blood pressure are the features of reduced compliance . So we should be aware that the the parameters of AS severity might be affected the presence of hypertension and the amount of alteration caused by hypertension on AS severity is difficult to measure. In Catheterisation based measrements decreased arterial compliance due to hypertension decreases the peak to peak gradient and it also alters the other indices of AS severity.These changes are brought about by the decrease in transvalvular flow, and the severity of stenosis is underestimated in patients with hypertension.[(28)]

In a study done in animal models (Kadem et al)[(27)]it was demonstrated that the severity of AS may be underestimated in the presence of hypertension. So this gives us a valuable point while clinical examination and while performing echocardiography that blood pressure measurements should be part of the evaluation of AS severity and the severetity of AS should not be based on measurements of gradients alone.

In a paper published by Antonini –Canterin et al [(29)]it has been observed that individuals with AS and systemic hypertension develop symptoms earlier and they do so at larger EOAs when compared to individuals with AS and without hypertension.



The concept of valvuloarterial impedance

The estimation of global hemodynamic load: the concept of valvuloarterial impedance

Global hemodynamic load is the total load faced by the left ventricle. In patients with aortic stenosis the left ventricle has to eject agains a stenotic valve , but in case of patients with aortic stenosis and stiff aortas as in the elderly and the patients with as and coexisting hypertension the Left ventricle faces a double load the load constitutes the valvular plus the vascular load imposed by the aortic valve and the aorta respectively.It is difficult to quantitae this load accurately.

Pibarot et al have proposed a new index for the assesment of global hemodynamic load, known as the valvuloarterial impedance. This is an index that can be measured by Doppler echocardiography.[26]

The Valvuloarterial impedance (ZVa) is defined as the ratio of the estimated LV systolic pressure (the sum of systolic arterial pressure (SAP) and mean pressure gradient (MPG) to the stroke volume indexed (SVi) for body surface area:

$$Zva = (SAP + MPG)/SVi$$

(The value is given in mm Hg/ml m²)

This index represents both the vascular and the valve factors that impede left ventricular ejection by absorbing the kinetic energy (which is transformed to thermal energy) developed by the Left ventricle.

This index gives us the cost in mmHg for every ml of blood pumped by the LV indexed for body area.

Values of Zva are usually <3.5 mm Hg/mL m²

Zva value of 3.5 to 4.5 mm Hg/mL m² is considered to be moderately elevated

Zva value of > 4.5 mm Hg/mL m² is considered to be highly elevated.

Many studies have been performed analyzing the impact of high valvuloarterial impedance in patients with aortic stenosis. (4,6,7) High valves of Valvuloarterial impedance is associated with impaired LV function (both systolic and diastolic) and is also associated with decreased left ventricular longitudinal, circumferential and radial strain patterns , this impairment is observed more frequently in patients with a low flow state with normal Left ventricular function (30)

Patients with moderate degree of aortic stenosis and added hypertension have increased LV global load and this load may sometimes be larger than the load faced by the LV of the patient with Severe Aortic stenosis without hypertension. So the patient might develop myocardial dysfunction earlier and at lesser degrees of stenosis severity (28)

This concept of global load the valvuloarterial impedance may be useful in a clinical point of view and this might be able to explain the discordance between the severity of Aortic stenosis and the patients symptoms (ie moderate AS but with symptoms). In symptomatic patients with low ZVa values the symptoms might be attributed to another condition producing the symptom and in patients with moderate AS and high ZVa the symptoms and LV dysfunction can be explained by the additive effects of moderate Aortic valve stenosis and elevated vascular load of decreased arterial complaince.

In a retrospective study done by Hachica et al [6] in 544 patients with asymptomatic Aortic stenosis of atleast moderate or severe grades,it was shown that elevated ZVa valvues is a marker of excessive LV global load. increased valvuloarterial impedance (values above 3.5 mm Hg/ml) was associated with poor outcomes.It was also found that there was graded relationship between elevated ZVa and reduced overall survival.

In a prospective study done by Lancelloti et al in 163 patients with moderate to severe aortic stenosis it was noted that, elevated valvuloarterial impedance (≥5 mmHg/mL m^2) was a powerful predictor of decreased cardiac event-free survival in patients with asymptomatic Aortic stenosis.[7]

In a retrospective study done by Levy et al in 184 patients with symptomatic severe AS with low gradients and depressed LV function, 48% of the study population had high Zva values (≥5.5 mmHg/ml/m^2). when compared to their counterparts with low Zva values the persons with high values had significantly reduced ejection fraction , had lower LV end diastolic dimensions and had contractile reserve, but the Zva values were not different in patients having severe and pseudo severe AS. [31]

Pitfalls in the measurement of valvuloarterial impedance.

The valvuloarterial impedance is a flow dependent parameter and it is subjected to change due to variations in flow even in the same patient over time and in case of an patient with a low flow AS subtle changes in flow might lead to variations. Two different patients with similar amount of hypertension and similar amount of valve area may have different values of Zva.

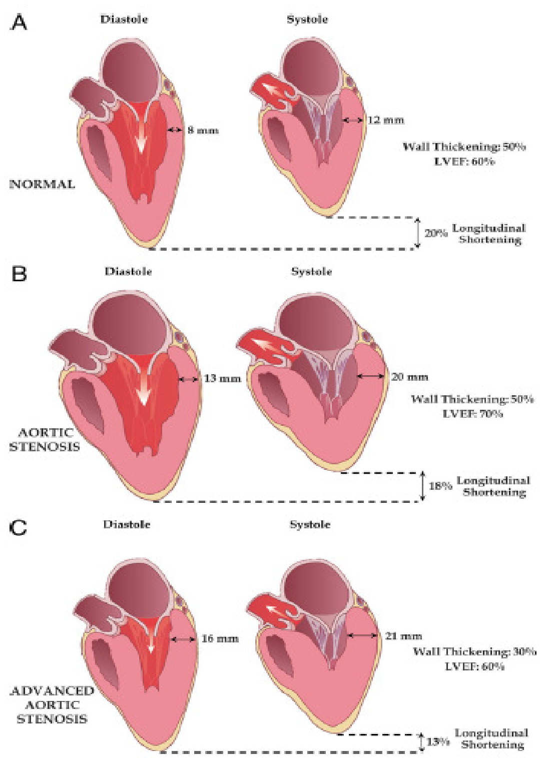
The mean gradient which is a numerator in the calculation of valvuloarterial impedance is a flow dependent parameter hence the flow variability affects Zva values and it is more pronounced in low flow situations than in moderate or high flow states. So, minor variations in heart rate or stroke volume may bring about variations in Zva. Moreover in low flow conditions even a minor error in measurement of stroke volume may alter the Zva values. So calculation of Zva in low flow states might not be so useful. [26]

But the valvuloarterial impedance has been demonstrated to be superior to other indices severity of Aortic stenosis (like the valve area and pressure gradients) in predicting worse clinical outcomes and in predicting LV dysfunction. [4]

Left ventricular dysfunction in aortic stenosis

According to the ACC/AHA and ESC guidelines for the management of valvular heart diseases, irrespective of their symptoms presence of left ventricular systolic dysfunction is a class I indication for valve replacement in aortic valve stenosis. And LVEF is the only index concerned with LV performance that is included in the treatment guidelines. Many studies have observed that in asymptomatic AS patients with normal ejection fraction, about 30% had significant disturbance in their intrinsic myocardial function. It has been noted that the measurement of LV longitudinal kinetics are better than other measures of systolic left ventricular function to identify early myocardial structural deterioration [5,33,34]

The longitudinal contractile function of the left ventricle is governed by the subendocardial myocytes and these myocytes are more prone to ischemic damage due to their location. So In patients with aortic stenosis the left ventricular long axis function gets affected early in the course of the disease and at this stage the patient still has preserved left ventricular ejection fraction Left ventricular longitudinal function can be assessed using pulse wave Doppler imaging. In a study done by Takeda et al [32] using mitral annular plane systolic excursion as a measure of long axis function it was shown that the long axis function was affected in aortic stenosis early even before reduction in ejection fraction or fractional shortening . So assessment of MAPSE in Aortic stenosis will help us to identify myocardial dysfunction before the decrease in ejection fraction. [35]



Picture showing the concept of LV dysfunction in aortic stenosis

Asymptomatic Aortic Stenosis

Since aortic stenosis is common among elder population who restrict their activities, the incidence of asymptomatic aortic stenosis is higher among them.

Identification of true asymptomatic aortic stenosis requires further evaluation. The minimum requirement is that they should be free of symptoms and have an aortic valve area of less than 1 cm^2, they should have normal LV function and should have normal exercise tolerance.

The incidence of sudden death in asymptomatic severe aortic stenosis is approximately less than 2% per year. But the surgical mortality of isolated aortic valve replacement is approximately 4%. So even in patients with asymptomatic severe aortic stenosis, only high risk patients are to be operated. (36)

The progression of in asymptomatic valvular aortic stenosis is usually slow. The mean gradient increases by approximately 7 mm Hg per year and the decrease in orifice area is 0.1 cm^2 per year. So they should be watched for the development of the symptoms or evidence of rapid progression which would direct them towards surgery.

Once the patient becomes symptomatic, life expectancy is very much reduced unless surgery is done. In this situation Exercise testing is useful

Exercise testing in asymptomatic AS helps us to identify the asymptomatic persons with normal LV function who are candidates for surgery. Exercise testing in considered being positive if the patient develops symptoms, if there is a fall in blood pressure, if there is an increase in gradient or if there is development of complex arrhythmias.[37]

The newer classification proposed for aortic stenosis is based on the indexed stroke volume and mean trans aortic gradient (flow and gradient).[38]

Aortic stenosis can be classified into four categories

1. Normal flow - Low gradient

2. Normal flow - High gradient

3. Low flow - High gradient

4. Low flow - Low gradient

Normal flow is indexed stroke volume > 35 ml / m^2 and low flow is < 35 ml / m^2

High gradient is more than 40 mm Hg and low gradient is less than 40 mm Hg.

Comprehensive assessment in aortic stenosis

With present information on the complex nature of aortic stenosis, the assessment of severity of aortic stenosis needs a more elaborate evaluation going beyond normal indices of severity such as gradients and effective orifice areas. The newer modalities that would be useful to risk stratify patients are the Energy loss index, the valvuloarterial impedance, the measurements of BNP levels and measurement of global longitudinal strain. In asymptomatic patients with normal LV function Exercise testing is useful. Recently CT and CMR have been proved to be useful in assessing the severity of aortic stenosis.[(26)]

MATERIALS AND METHODS

Setting:

The study was performed in the Department of Cardiology, Madras Medical College, Chennai.

Design of the study: Prospective analytical study

Period of the Study: Three months

Sample size: 47 patients

Ethical committee approval:

The present project was approved by the Institutional ethics committee.

Inclusion criteria:

Patients attending Cardiology outpatient department and admitted in cardiology wards with moderate and severe aortic stenosis were included in the study.

Exclusion criteria:

01. Presence of mitral valve disease

02. Presence of more than mild aortic regurgitation

03. Previous history of coronary artery disease

04. Presence of moderate or severe LV systolic dysfunction

05. Chronic obstructive lung disease

06. Arrhythmias including atrial fibrillation, supraventricular tachycardia or ventricular ectopics

07. Patients not willing to give consent

Consent:

The study group thus identified by the above criteria (inclusion and exclusion criteria) was first instructed about the nature of the study. Willing participants were taken up after getting a written informed consent from them.

Details of the study subjects:

A total of 47 patients attending cardiology outpatient department and admitted in cardiology ward with moderate to severe degrees of isolated aortic stenosis were enrolled for the study if they fulfilled the inclusion and exclusion criteria. .

Detailed history and physical examination were done. The symptoms of aortic stenosis such as dyspnoea, angina and syncope were recorded in detail.

Physical examination included height, weight; Body Mass Index was calculated using Quetelet's formula and Body Surface Area by Dubois formula.(BSA (m^2) = 0.007184 x Height(cm)$^{0.725}$ x Weight(kg)$^{0.42}$)

Blood Pressure Measurement

Systemic blood pressure was measured in the echo lab during the time of measurement of derived stroke volume in left ventricular outflow tract. A properly calibrated mercury sphygmomanometer was used for this purpose. The arm cuff recordings were taken as standard measurements for all patients. The definition of Hypertension was according to JNC 7 guidelines.

Echocardiography

Echocardiographic examination of the patients was done with Philips HD 7 XE machine. 2.5 mega HZ probe was used for transthoracic echocardiography. A complete trans-thoracic echocardiogram including M -mode, 2 D, Colour Doppler, Pulse and continuous wave Doppler and Tissue Doppler were done for every study participant. The measurements and indices were done according to the American society of Echocardiography guidelines.

Echo Indices studied

Indices of LV geometry

IVS thickness, Left ventricular posterior wall thickness, left ventricular internal dimensions in diastole, relative wall thickness was measured. Using these values the left ventricular mass and mass index were calculated. The LVOT diameter was also carefully measured in the parasternal long axis view with zoom in mode

Mitral Annular Planar Systolic Excursion

Mitral annular motion is measured using M - mode echocardiography. Using apical four chamber view, M - mode cursor is aligned through lateral mitral annulus. M - Mode cursor should be parallel to the mitral annulus. The longitudinal displacement of the annulus from the base to the apex is measured.

Indices of Left ventricular systolic function

Left ventricular ejection fraction was calculated using Simpson's method and Quinone's method and also by visual estimate.

Indices of left ventricular diastolic function

Diastolic function of the left ventricle was assessed using pulse wave Doppler to study the trans-mitral flow velocities and tissue Doppler study of the lateral mitral annulus was done and E/e' was also calculated.

Indices of aortic stenosis severity

The Doppler parameters that where studied included the gradient across the aortic valve using continuous wave Doppler the mean gradient and the peak gradient were and the aortic valve VTI were obtained. Using pulsed wave Doppler in the LVOT the VTI was obtained. Using these values the aortic valve area is calculated by using the continuity equation.

Stroke volume calculation

Stroke Volume = LVOT area x LVOT VTI,

LVOT area was calculated using the LVOT diameter. Stroke volume index was calculated

Myocardial Performance Index

To obtain LV Tei index, pulse wave Doppler recording of the mitral valve inflow and left ventricular outflow is recorded. The duration from the end of A wave of the mitral valve inflow to the starting of the E wave of the mitral inflow is measured. This is taken as total contraction time. The ejection time is measured from the left ventricular outflow tracing. The isovolumic time is calculated by subtracting ejection time from total contraction time. Isovolumic time divided by ejection time gives the myocardial performance index.

Calculation of Valvuloarterial impedance :[26]

Valvuloarterial impedance (Zva) was calculated using the formula

(Zva) = (systolic blood pressure + mean transvalvular gradient)/stroke volume index.

Statistical Analysis:

The collected data was tabulated in Microsoft excel spread sheet and statistical analysis of the data was done using Statistical Package for

Social Sciences software (SPSS version 17.0). Categorical data are presented as absolute values and percentages, whereas continuous data are summarized as mean value ± SD. Independent sample 't' test and Chi - square tests were used for comparison of categorical variables as appropriate. Significance was considered if the 'p' value was below 0.05.Analysis of variance (ANOVA) was used to analyze the difference between group means.

RESULTS AND DATA ANALYSIS

In this study, 47 patients with moderate and severe aortic stenosis without significant aortic regurgitation were studied.

Out of the 47 patients 15 were females (32%), Male gender was the predominant gender that was found to be affected with Aortic Stenosis (68% vs. 32%)

The age group of the study population ranged from 32 to 81 years and the mean age of the study population was 58.55 + 9.760 years. The average age of presentation of Aortic Stenosis in our study population was in the sixth decade and 72% (34 out of 47) patients were in the age group of 50 to 70 years.

The age group distribution of the study population is as follows

Age group (in years)	No of persons
< 40	2
40 to 50	5
50 to 60	19
60 to 70	15
>70	6
Total	47

Chart 1

Age wise distribution of patients

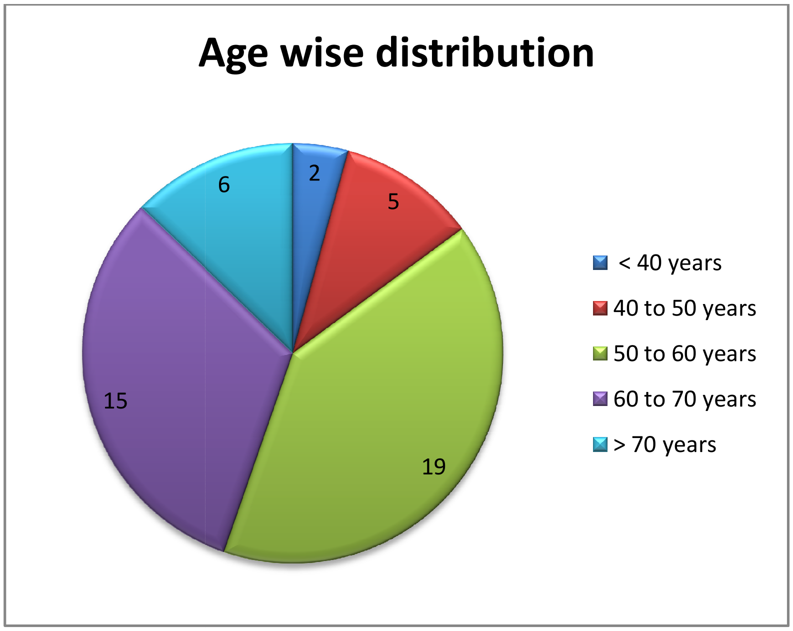
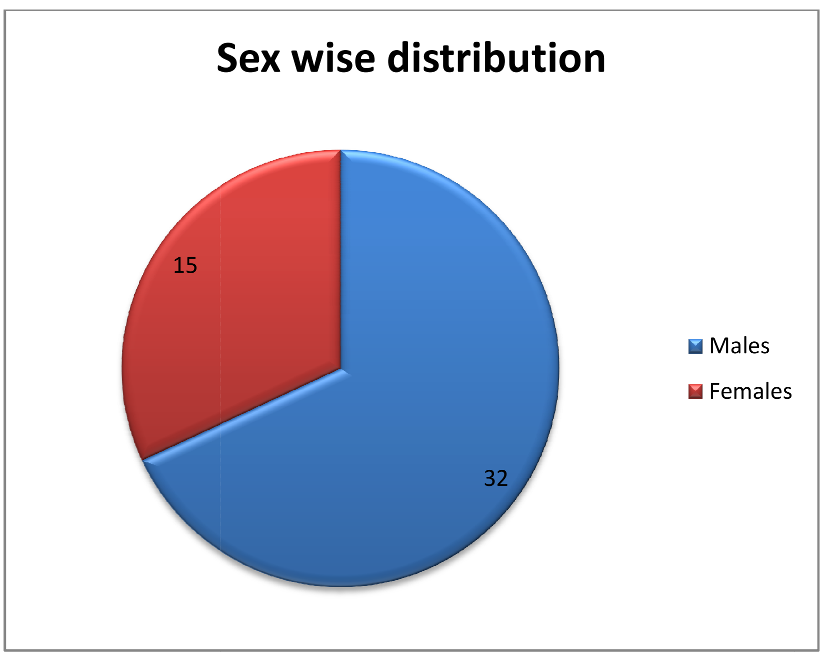


Chart 2



The observations related to patient history are as follows

In the study population 38% of the patients had previous history of hypertension and 40 % of the patients had Diabetes Mellitus and only 4% of the patients had a history of Rheumatic heart disease. 38% of the patients were Smokers.

History	No of patients
Hypertension	18 (38%)
Diabetes mellitus	19 (40%)
Previous RHD	2 (4%)
Smoking	18(38%)

Bicuspid Aortic valve stenosis

Out of the 47 patients studied 4 patients (9%) had Bicuspid Aortic valve, the mean age of the patients in this subgroup was 41±7.07 years when compared to the total population mean age of 58.55 + 9.760 years this group had a significantly lower mean age.

The patients were classified into 3 groups based on the values of valvuloarterial impedance (Zva) for statistical analysis.

Group	Zva (in mmHg/ml/m^2)	No of patients
Low Zva	< 3.5	16 (34%)
Medium Zva	3.5 to 4.4	18(39%)
High Zva	≥4.5	13(27%)

Chart 3

Patient history

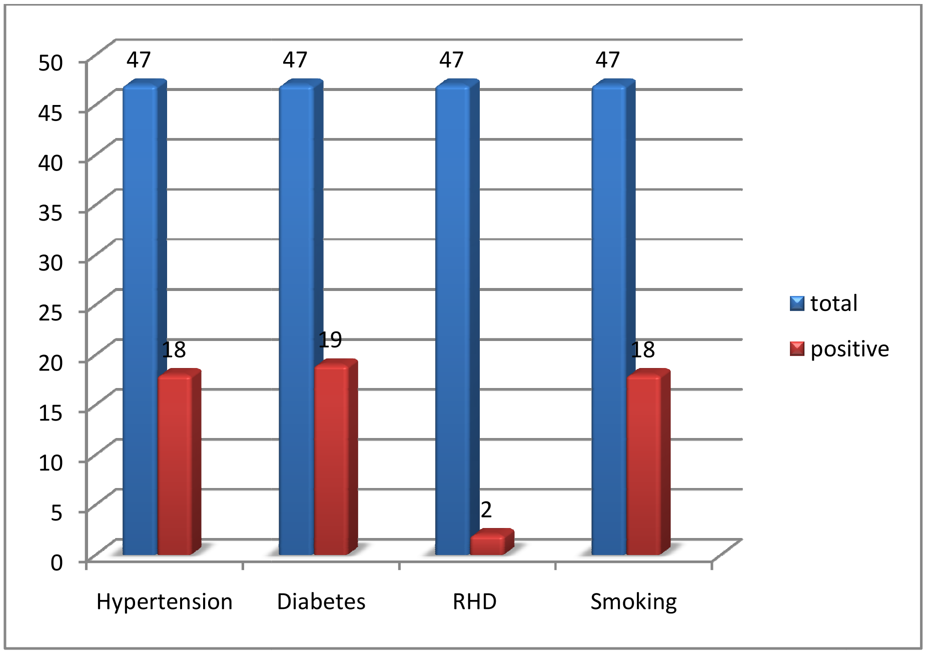
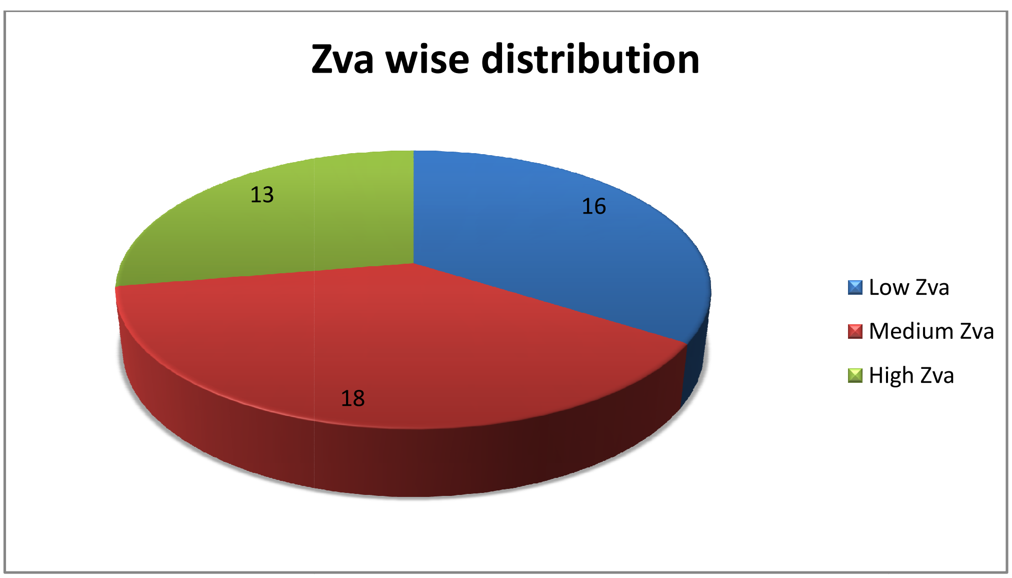


Chart 4

Zva groups



Patients with valvuloarterial impedance levels of < 3.5 mmHg/ml/m^2 were named as the "Low Zva" group they consisted of 34% of the total study population. those with valvuloarterial impedance levels of 3.5 to 4.4 mmHg/ml/m^2 were named as the Medium "Zva group" and they consisted of 39% of the study population , those with Zva levels of ≥4.5 mmHg/ml/m^2 were named as the "High Zva" group and they consisted of 27% of the total study population. The clinical and Echocardiographic variables were compared among these groups using Analysis of Variance.

The baseline characteristics of the study population according to the 3 groups is as follows

Patient Related factors and Zva

Group	Low Zva(n=16)	Medium Zva(n=18)	High Zva(n=13)	P value
Age (in years)	52.81±7.44	57.83±6.71	66.62±10.81	< 0.001
Female gender	4(25%)	5(28%)	4(31%)	0.942
BMI (kg/m^2)	23.04±2.98	24.84±2.93	24.19±2.49	0.187
BSA (m^2)	1.73±0.19	1.77±0.17	1.74±0.16	0.699
Hypertension	3(19%)	8(44%)	7(54%)	0.122
DM	8(50%)	5(28%)	6(46%)	0.371
Smoking	7(44%)	7(39%)	4(30%)	0.773

When comparing the three groups the mean age in the low Zva group was 52.81±7.44 years and the mean age of the high Zva group was 66.62±10.81 years the patients with high Zva were significantly older ($p<0.001$) than the medium and the low Zva groups.

The distribution of females in the three groups was similar and there was no statistically significant difference between the three groups with respect to gender.

The Body mass index and body surface area were comparable between the three groups and there was no statistically significant difference.

The percentage of patients with history of hypertension was 19% in the low Zva group 44% in the medium Zva group and 54% in the high Zva group. When compared to the low Zva group the persons in the medium and high Zva had a higher prevalence of systemic hypertension.

There was no statistically significant difference between the low, medium and high Zva groups with regard to diabetes mellitus and smoking.

Vascular and Valvular factors and Zva

Group	Low Zva(n=16)	Medium Zva(n=18)	High Zva(n=13)	P value
Systolic BP (mm Hg)	123.63±21.20	130.78±12.39	146.77±10.94	0.001
Diastolic BP (mm Hg)	82.38±13.70	80.67±7.39	80.31±6.72	0.826
Pulse pressure	41.25±12.22	50.11±8.44	66.46±9.70	<0.001
AVA (cm^2)	1.26±0.18	1.25±0.19	0.96±0.15	<0.001
Peak gradient (mm Hg)	68.62±18.21	63.67±8.13	79.92±10.72	0.005
Mean gradient (mmHg)	42.64±13.54	43.94±11.03	51.76±12.15	0.114
Zva ($mmHg/ml/m^2$)	2.94±0.41	3.90±0.29	5.68±0.70	<0.001

Blood pressure

The patients with high Zva values had a significantly higher systolic blood pressure when compared to patients with lower Zva values. The mean systolic blood pressure in the high Zva group was 146.77±10.94 as against 130.78±12.39 in the medium Zva group and 123.63±21.20 in the low Zva group and this difference was statistically significant (p=0.001) .There was no statistically significant difference in diastolic blood pressure between the three groups. The pulse pressure as expected was significantly higher in persons with high Zva values (p<0.001) indicating that the patients in the higher Zva group had a higher level of vascular load.

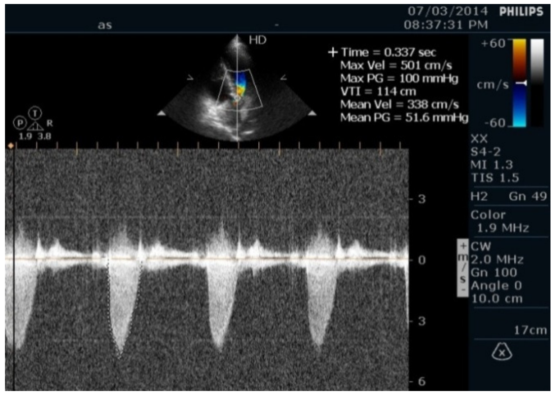
Aortic valve indices

The parameters used to quantify the severity of stenosis are the Aortic valve area, the mean gradient across the stenotic aortic valve and the peak gradients. Patients with high Zva values had a significantly reduced Aortic valve area when compared to the lower Zva value groups. The mean aortic valve area in the high Zva group was 0.96±0.15 compared to 1.26±0.18 in the low Zva group ($p<0.001$).

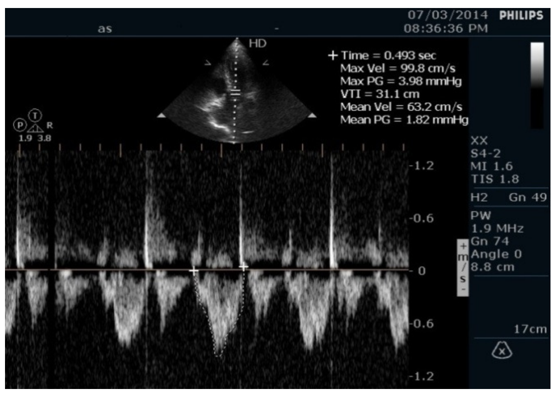
The peak gradients were significantly higher in the High Zva groups. (79.92±10.72 compared to 63.67±8.13, p value 0.005)

The mean gradients were higher in the high Zva group but this difference was not statistically significant. Mean gradient is one of the measures for the classification of Aortic stenosis severity the ACC/AHA and ESC have defined different mean gradient values for classification of severity. The values for mean gradient is 20 to 40 mmHg (ACC/AHA) [30to 50 mmHg for ESC] for moderate severity and above 50mm Hg (ACC/AHA) [>50 mmHg for ESC] for severe aortic stenosis. In this study the mean gradient values suggested by ACC/AHA were adopted, patients in the High Zva group had a mean gradient value of 51.76±12.15 mmHg and the mean gradient of the medium and low Zva groups were 43.94±11.03 mmHg and 42.64±13.54 mmHg respectively.

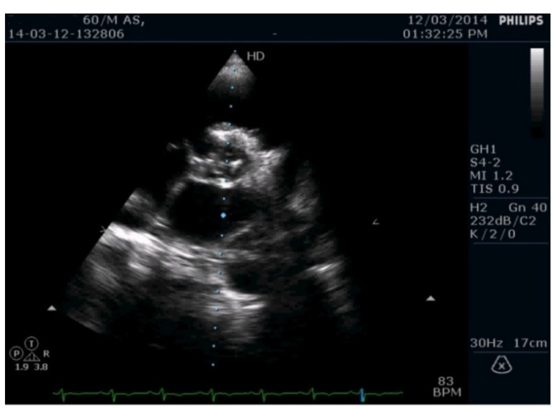
Echo images



Continuous wave Doppler showing mean gradient 51.6mm Hg and peak gradient 100mmHg



Measurement of LVOT VTI



Parasternal short axis view at aortic level showing calcific aortic valve

Based on ACC recommendations all the three groups would classify as severe Aortic Stenosis. Conversely if the ESC guidelines cut off values were used it will come to light that the High Zva group would have gradients which would classify them as severe and the Medium and low Zva patients would be classified as having Moderate Aortic stenosis severity. This shows that even if not statistically significant the patients in high Zva group had a difference in gradient of 8 mmHg.

LV geometry indices and Zva

Group	Low Zva(n=16)	Medium Zva(n=18)	High Zva(n=13)	P value
IVS (cm)	1.67±0.31	1.68±0.23	1.92±0.35	0.046
LVPW(cm)	1.58±0.31	1.56±0.22	1.81±0.35	0.063
LVIDd(cm)	4.26±0.59	4.48±0.78	3.84±0.47	0.033
RWT	0.78±0.19	0.75±0.20	0.98±0.22	0.008

The indices of Left ventricular geometry that were studied were the thickness of the interventricular septum, the left ventricular posterior wall and the relative wall thickness.The Left ventricular internal dimensions in diastole was also studied. The observations showed that there was a statistically significant difference between the three groups in terms of LV geometry. But the patients with High Zva had thicker ventricles (approximately 3mm, p = 0.046), smaller LV cavity (approximately 14mm, p=0.033) and higher relative wall thickness (approximately 0.18, p=0.008) than the medium and low Zva groups.

LV function indices and Zva

Group	Low Zva(n=16)	Medium Zva(n=18)	High Zva(n=13)	P value
LVEF (%)	60.13±8.19	58.39±5.46	63.08±6.37	0.173
Stroke Vol (ml)	100.00±22.45	79.89±10.13	61.57±9.97	<0.001
SVi	57.94±11.46	44.94±3.67	35.31±3.84	<0.001
E/e’	11.48±4.20	11.85±3.31	14.22±4.31	0.145
Tei index	.036	0.39	0.41	0.136

Patients with high Zva values had a statistically significantly lower stroke volume and stroke volume index when compared to the lower Zva groups. There was no significant difference in Left ventricular ejection fraction between the three groups.

LV diastolic dysfunction and Zva

LVDD	Low Zva(n=16)	Medium Zva(n=18)	High Zva(n=13)	P value
Grade 1	6	8	2	0.032
Grade 2	1	15	2	
Grade 3	3	5	5	
Total	10	28	9	47

All the patients in the study population had diastolic dysfunction and the grades of diastolic dysfunction were significantly higher in patients with high Zva values.

Mitral E/e' velocities were above the normal value of 8 in all the three groups implying that all the study patients had mildly elevated filling pressures and moderate degrees of left ventricular diastolic dysfunction.

The left ventricular Tei index was calculated as a measure of global LV function and there was no significant difference in Tei index between the three groups.

Symptoms of AS and Zva

Group	Low Zva(n=16)	Medium Zva(n=18)	High Zva(n=13)	P value
SOB	7(43%)	11(61%)	8(61%)	0.518
Angina	5(31%)	5(28%)	3(23%)	0.887
Syncope	2(12%)	2(11%)	6(46%)	0.036
Giddiness	6(37%)	4(22%)	3(23%)	0.555

Out of the total 47 patients studied 37 patients had one or combination of symptoms, of the symptoms Shortness of breath was the commonest symptom in three groups and the symptoms of SOB, Angina, and giddiness were similar in all the three groups.

Syncope

The incidence of syncope was significantly higher in the High Zva group (46%, p=0.036) showing a positive association between high Zva value and syncope.

MAPSE (longitudinal LV function) and Zva

Group	Low Zva(n=16)	Medium Zva(n=18)	High Zva(n=13)	P value
MAPSE (mm)	10.91±1.51	10.43±0.77	9.26±0.81	0.001

Mitral annular plane systolic excursion of the lateral mitral annulus was studied as a measure of LV longitudinal function our observation showed that in spite of normal LV function in the High Zva group the MAPSE was significantly lower (p=0.001) indicating that LV long axis function was affected.

Chart 5

Symptomatic vs. Asymptomatic

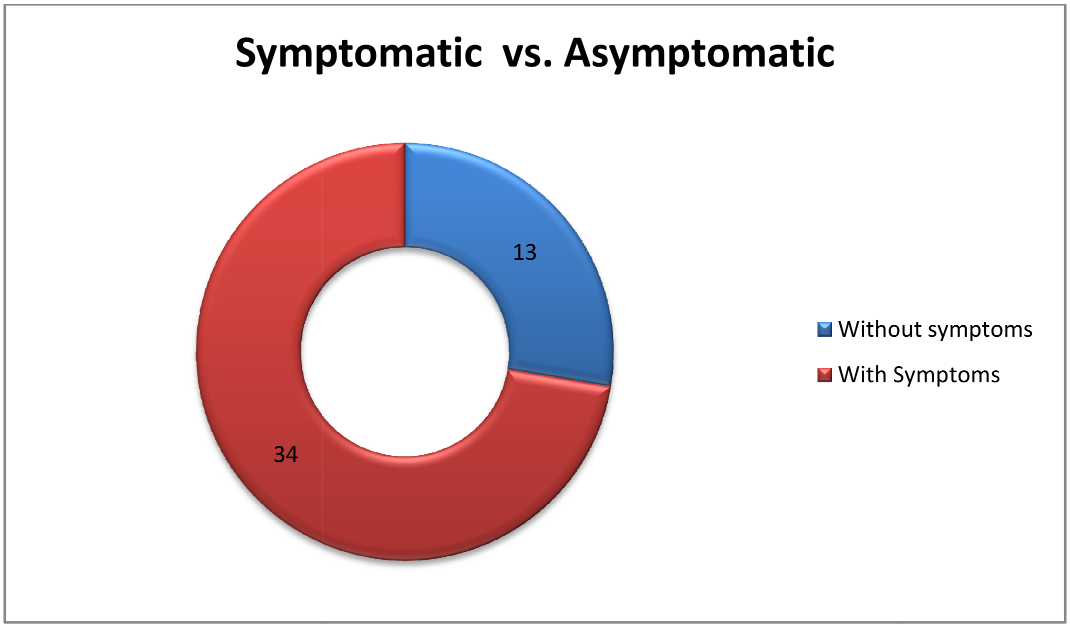
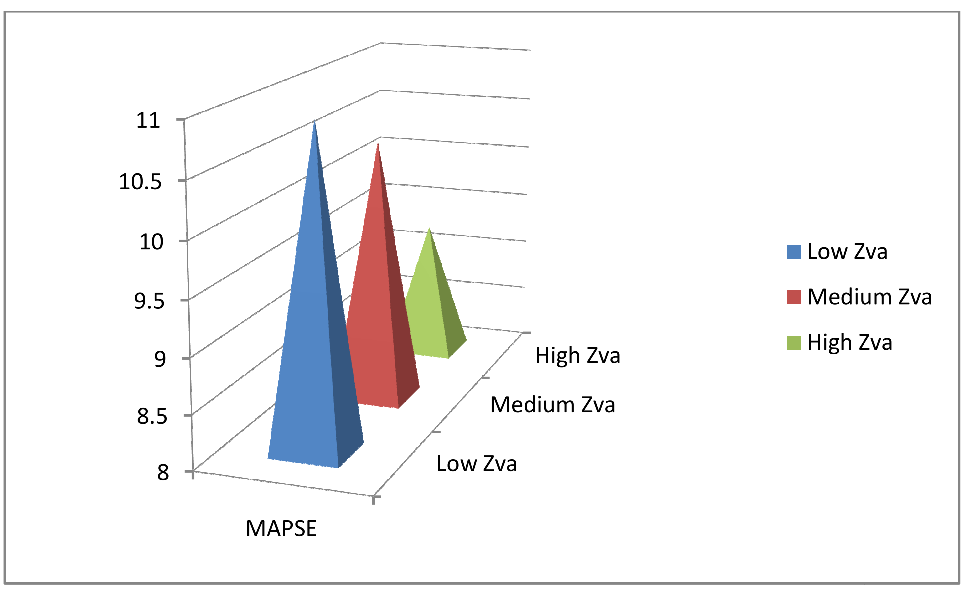


Chart 6

MAPSE and Zva



Asymptomatic AS

Out of the sample population of 47 patients, 34 patients had either or combination of symptoms of SOB, Angina, Syncope or Giddiness.13 patients were asymptomatic.

Symptomatic AS vs Asymptomatic AS

Patient variables

Group	Symptomatic AS	Asymptomatic AS	P Value
Age	58.15±11.18	59.62±4.42	0.650
Female Sex (n=13)	8(61%)	5(39%)	0.304
BMI	23.93±2.78	24.35±3.21	0.662
BSA	1.75±0.17	1.74±0.17	0.910
Hypertension (n=18)	13(72%)	5(28%)	0.989
Diabetes (n=19)	16(84%)	3(16%)	0.134
Smoking(n=18)	16(89%)	2(11%)	0.046

There was no significant difference between Asymptomatic AS patients and symptomatic patients with respect to Age, Gender, Body Mass Index, Body Surface Area, Hypertension or DM.

Smokers had a significantly high incidence of symptoms (p=0.046)

Vascular and Valvular load indices and symptoms

Group	Symptomatic AS	Asymptomatic AS	P Value
Systolic BP	131.47±18.37	136.15±16.82	0.429
Pulse pressure	50.29±13.67	55.08±15.33	0.305
Diastolic BP	81.18±9.71	81.08±10.05	0.975
Aortic valve area	1.17±0.21	1.17±0.24	0.929
Peak gradient	69.64±14.91	70.38±13.42	0.877
Mean gradient	45.16±12.64	47.00±12.82	0.658
Zva	3.90±.12	4.51±1.27	0.117
MAPSE	10.19±1.36	10.50±0.90	0.450

There was no significant difference between the symptomatic patients and asymptomatic patients with respect to vascular factors such as systolic blood pressure, pulse pressure and valvular factors such as aortic valve area and gradients. MAPSE in both groups was comparable.

The values of valvuloarterial impedance (Zva) were higher in asymptomatic patients (mean Zva in asymptomatic patients was 4.51±1.27 $mmHg/ml/m^2$ compared to 3.90±.12 $mmHg/ml/m^2$) but this difference was not statistically significant (p=0.117)

Indices of LV geometry, LV function and symptoms

Group	Symptomatic AS	Asymptomatic AS	P Value
IVS	1.71±0.30	1.83±0.31	0.239
LVPW	1.60±0.32	1.73±0.25	0.175
LVIDd	4.36±0.72	3.88±0.42	0.029
RWT	0.79±0.23	0.92±0.17	0.055
LVEF	58.50±6.96	64.92±3.88	0.003
Stroke Vol	84.36±22.51	74.64±17.24	0.167
SVi	48.15±12.00	42.92±9.68	0.168
E/e'	12.60±4.24	11.80±3.38	0.543
Tei index	0.40±0.07	0.34±0.04	0.010

When comparing the indices of LV geometry and function between the symptomatic patients and asymptomatic patients there was no significant difference between the two groups in terms of Left ventricular wall thickness, stroke volume and stroke volume index, diastolic dysfunction and Tei index.

Asymptomatic patients had significantly lower LV internal diastolic dimensions (3.88±0.42 cm in asymptomatic vs. 4.36±0.72 cm in symptomatic) (p=0.029)

Asymptomatic patients also had significantly higher ejection fraction (64.92±3.88% in asymptomatic vs. 58.50±6.96% in symptomatic) ($p=0.003$)

Paradoxical low flow pattern in which stroke volume index is less than 35ml/min/m^2 and LV ejection fraction ≥50% was found in 6 patients(46%) with high Zva values (Zva >4.5 mmHg/ml/m^2) and none of the patients in the medium or low Zva group had paradoxical low flow pattern.

DISCUSSION

This study was performed with the aim of evaluating the levels of valvuloarterial impedance in aortic stenosis in the south Indian population. The symptoms of aortic stenosis, indices of LV geometry, LV function and Aortic valve stenosis severity were correlated with the levels of valvuloarterial impedance.

Based on the values of valvuloarterial impedance (Zva) the patients were classified into three groups, the group with Zva values below 3.5 mmHg/ml/m^2 were classified as the Low Zva group, the Zva values from 3.5 to 4.5 mmHg/ml/m^2 were classified as Medium Zva group and Zva 4.5 mmHg/ml/m^2 and above were classified as the High Zva group.

Age and valvuloarterial impedance

Aortic stenosis is considered to be disease of the elderly. Since Aortic stenosis and the reduced aortic compliance share the same degenerative and inflammatory etiology it is logical for elderly individuals to have stiffer aortas and hence elevated Zva values. [(1)] In this study the average age in patients participating in the study was 58.55±9.76 years and presenting with high Zva values was 66.62±10.81

years. The individuals in the high Zva group were older than their counterparts.

In a two separate studies done by Hachicha et al[6] and Ashild E Reick et al [39]it has been shown that the mean age of patients with aortic stenosis is high and was around 68 to 70 years, in our study the mean age of the patients was 58 years which shows that the mean age of patients presenting with calcific aortic valve disease is lesser in our population. In the high Zva group the mean age of the patients was higher, it has been proved that older patients have more degenerative changes occurring in the vascular system and have stiffer aortas hence they are prone to have higher systolic BP and stiff arteries.

In our study population the mean age in the high Zva group was significantly higher than in the lower Zva groups and it was comparable to the study done by Hachicha et al and Ashild E Reick et al where the mean age group in patients with high Zva was 73 years

It is known that hypertension is a common association with aortic stenosis and it has been shown in studies that the incidence of hypertension in aortic stenosis varies from 86% in various studies [4, 40, 41] .In our study the history of hypertension was given by 38% of patients and actually 42% of patients were found to be hypertensive. This is comparable observations made in other studies. It has been observed that both systolic and diastolic blood pressure is higher in individuals with high Zva but in our study only the systolic BP had correlation with high Zva levels.

Gatzka et al [42] have observed that women have stiffer blood vessels than males of comparable age and this results in higher impedance values, but in our study female gender did not have elevated Zva values.

The Zva values when compared to indices of LV geometry showed that the persons with high Zva values had a higher incidence of LV hypertrophy and lower cavity dimensions this is consistent with the findings of the observations made by Hachicha et al[6] and observations made in the SEAS trial subset[39] of patients with Aortic stenosis.

Cioffi et al in their study[43] have reported that the adverse outcomes in patients with aortic stenosis are higher if LV hypertrophy indices are >110% of the expected values for sex, body mass and wall stress so the higher incidence of left ventricular hypertrophy in patients with high Zva will pave way for increased incidence of adverse outcomes.

Observations from the study done by Cramariuc D et al [5] show that about 30% of patients with Aortic stenosis have reduced stroke volume but have a normal LV ejection fraction, this leads to a lesser transvalvular pressure gradient and the blood pressure might appear normal even if hypertension is present, sometimes based on gradient levels the severity may be falsely estimated as low and in reality these are the group of patients who are in an advanced state of disease progression.

This low flow state is common in patients with high valvuloarterial impedance levels in our study population 46% of patients in the high Zva group had a low flow state compared to none in other groups.

Syncope

The occurrence of Syncope in Aortic stenosis carries a poor prognosis. Patients with aortic stenosis have a life expectancy of 2 years is the condition is left untreated. Severity of Aortic stenosis was considered to be the predictor of syncope but it was observed that not all patients with severe aortic stenosis had syncope so other factors were also thought to play a role in the development of syncope. In an article published by Harada K et al in 2013[44] in a study done in 451 patients with aortic stenosis, it was shown that even a few patients with moderate aortic stenosis had evidence of syncope and of the total study population 18% had reported syncope. Multivariate analysis it showed that of all the indices only elevated Zva values were predictors of syncope. In that study ROC analysis identified that valvuloarterial impedance values above 4.7mm $Hg/ml/m^2$ had more incidence of syncope.

In our study patients occurrence of syncope had a statistically significant association with high levels of valvuloarterial impedance and 46% of patients with Zva levels $\geq$ 4.5 $mmHg/ml/m^2$ had syncope. It suggests that high levels of valvuloarterial impedance but not stenosis severity, helps in the identification of patients prone to develop syncope.

Mitral Annular Planar Systolic Excursion and Left ventricular Function in Aortic Stenosis

In a study done by Joanna Luszczak et al, it has been shown that mitral annulus planar systolic excursion is a better indicator of longitudinal left ventricular systolic dysfunction and it is comparable to speckle tracking echocardiography. [(35)]

So this modality can be used for the assessment of early left ventricular systolic dysfunction in patients with normal ejection fraction.

Cramaruic et al has shown in his study[5] published in JACC imaging 2009 that one out of three individuals with asymptomatic aortic stenosis and normal LV ejection fraction had significant left ventricular dysfunction as demonstrated by decreased stress corrected shortening of the mid wall.[5]

So in this context, the ejection fraction tends to under estimate the level of myocardial dysfunction in concentric left ventricular hypertrophy which is present in most cases of the aortic stenosis.

So measurement of MAPSE in patients with aortic stenosis and normal LV function can give us an idea of the left ventricular dysfunction which is masked by the alteration in the geometry of the left ventricle.

In our study mitral annular plane systolic excursion levels were found to be significantly lesser (9.26±0.81 mm) in patients with high Zva levels (Zva $\geq$4.5mmHg/ml/m^2) but the LV ejection fraction in the same group patients was within normal limits (63.08±6.37%),this finding is similar to that seen in the previous studies and suggests that patients with Aortic stenosis in spite of having normal LV function have intrinsic myocardial dysfunction as evidenced by the reduction in long axis function of the heart.

Aortic stenosis severity and valvuloarterial impedance

Resistance to LV ejection occurs at two levels in Aortic stenosis, one at the level of the valve and the other above this (at the level of the arteries) since valvuloarterial impedance is a composite of both these values it would be logical to presume that increase in aortic stenosis severity would result in an increase in severity of valvuloarterial impedance. In our study patients with high valvuloarterial impedance had significantly reduced aortic valve areas and higher peak gradients.

Asymptomatic Aortic stenosis

Management of asymptomatic aortic stenosis is a matter of debate, guidelines regarding the management of asymptomatic aortic stenosis recommend that asymptomatic aortic stenosis patients with LV dysfunction benefit from surgical management, in patients who restrict their activity might not have symptoms and if the symptoms are equivocal then exercise testing might help us to risk stratify them and suggest appropriate therapy. Some studies have shown that a subset of patients with severe AS have normal LV function and normal exercise test results management of these patients is challenging. Three recent studies have shown that the surgically treated asymptomatic severe aortic patients had better survival than their medically treated counterparts. In this context assessment of severity of Aortic stenosis needs yet another index which would help in risk stratification, and a study done by Hachicha et at has suggested that in this situation Exercise testing may be useful when combined with elevated levels of Zva to direct patients toward early surgery.[(6)]

CONCLUSIONS

Among the symptoms of Aortic stenosis, only Syncope had significant association with high levels of valvuloarterial impedance.

Older patients with aortic stenosis had significantly higher valvuloarterial impedance values due to a less compliant arterial system.

In patients with Aortic stenosis higher systolic blood pressure and pulse pressure had a significant association with high levels of valvuloarterial impedance

The patients with high levels of valvuloarterial impedance had significantly altered LV geometry as evidenced by thicker ventricles and smaller LV cavity dimensions.

There was no significant difference in LV systolic function indices between the lower and higher valvuloarterial impedance groups.

All the patients in this study group had LV diastolic dysfunction and higher grades of diastolic dysfunction were seen in patients with high valvuloarterial impedance levels.

The Mitral annular plane systolic excursion (MAPSE) was significantly decreased in patients with patients with higher levels of valvuloarterial impedance suggesting the presence of intrinsic myocardial longitudinal dysfunction in spite of preserved LV ejection fraction.

There was a significant correlation between higher valvuloarterial impedance levels and lower aortic valve area and higher aortic valve peak gradients.

There were no significant differences between Doppler characteristics between asymptomatic and symptomatic patients with aortic stenosis except for LV ejection fraction which was higher in the asymptomatic group.

LIMITATIONS OF THE STUDY

Arm cuff pressure recordings were made in all the patients but invasive intra-arterial measurements would have been more accurate, but invasive recordings were not done due to patient and logistic issues. But in a study published in Archives of cardiovascular diseases 2010 has shown that the invasive measurements of blood pressure did not add to the predictive ability of valvuloarterial impedance. [30]

Stroke volume calculation was done using the LVOT diameter and it was subject to variability and the calculation also assumes the LVOT to be circular which in reality is not. But in a study done by Juliane Lauten et al [45] it was reported that echo estimates of stroke volume were only slightly higher than invasive measurements.

In contrast to western countries where isolated degenerative aortic stenosis is common the individuals presenting with isolated aortic stenosis were less in our hospital so the sample size was less limiting statistical accuracy.

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CLINICAL AND ECHOCARDIOGRAPHIC CORRELATES OF VALVULO-ARTERIAL IMPEDANCE IN AORTIC STENOSIS WITH FOCUS ON ASYMPTOMATIC AORTIC STENOSIS.

PROFORMA

NAME : AGE/SEX:

IP / OP NO. ADDRESS :

Mode of referral :

Whether Previously known AS- if yes for how long?:

Hypertension :

Diabetes:

CAD:

RHD/Prev RF:

Smoking/Tobacco use:

Alcohol:

Prev Surgery:

Pulse Rate

Blood Pressure :

Systolic:

Diastolic:

Pulse Pressure:

Height(cm):

Weight(kg):

Body mass Index:

Body Surface Area (Dubois Method):

Symptoms:

Shortness of breath :

Chest Pain :

Syncope:

Giddiness /Presyncope:

Fatigue:

Other Symptoms:

No Symptoms:

Echocardiography

Aortic stenosis

LVOT VTI:

LVOT dia:

LVOT peak velocity:

Aortic valve VTI:

Aortic valve peak velocity:

Aortic valve area:

Peak Gradient:

Mean gradient:

LV geometry

IVSd:

LVPWd:

LVEDV:

LVIDd

LVIDs:

Relative Wall thickness:

LVEF:

FS%:

Stroke Volume:

Stroke volume index:

LV diastolic function

Mitral E:

Mitral A:

E/A:

Tissue doppler

E':

E/E':

MAPSE:

LV Tei Index:

சுய ஒப்புதல் படிவம்

ஆய்வு செய்யப்படும் தலைப்பு

பெருந்தமணி வால்வு சுருக்க நோயில் தமனி எதிர்ப்பு குறித்து மின்-ஒலி வரைவு மற்றும் பிணிசார்ந்த ஆய்வு.

ஆராய்ச்சி நிலையம்: இருதய மருத்துவத் துறை,

இராஜீவ் காந்தி அரசு பொது மருத்துவமன மற்றும் சென்னை மருத்துவக்கல்லூரி,

சென்னை – 600 003.

பங்கு பெறுபவரின் பெயர்: **உறவு முறை:**

பங்கு பெறுபவரின் எண்:

பங்கு பெறுபவர் இதனை (√) குறிக்கவும்

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களைக் கேட்கவும், அதற்கான தகுந்த விளக்கங்களைப் பெறவும் வாய்ப்பளிக்கப்பட்டது. ☐

நான் இவ்வாய்வில் தன்னிச்சையாகத்தான் பங்கேற்கிறேன். எந்தக் காரணத்தினாலோ எந்தக் கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகிக் கொள்ளலாம் என்றும் அறிந்து கொண்டேன். ☐

இந்த ஆய்வு சம்மந்தமாகவும், மேலும் இது சார்ந்தஆய்வு மேற்கொள்ளும்போதும், இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளைப் பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்துகொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன். ☐

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக் கொள்ளவும், அதைப் பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கிறேன். ☐

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். எனக்குக் கொடுக்கப்பட்ட அறிவுரைகளின் படி நடந்துகொள்வதுடன், இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன். என் உடல் நலம் பாதிக்கப்பட்டாலோ அல்லது எதிர்பாராத வழக்கத்திற்கு மாறாக நோய்க்குறி தென்பட்டாலோ உடனே அதை மருத்துவ அணியிடம் தெரிவிப்பேன் என உறுதி அளிக்கிறேன். ☐

இந்த ஆய்வில் எனக்கு மருத்துவப் பரிசோதனை, இரத்தப் பரிசோதனை மற்றும் இதய உத்புகுத்து சிகிச்சை பரிசோதனை செய்து கொள்ள நான் முழு மனதுடன் சம்மதிக்கிறேன். ☐

பங்கேற்பவரின் கையொப்பம் .... இடம் .... தேதி ....

கட்டைவிரல் ரேகை:

பங்கேற்பவரின் பெயர் மற்றும் விலாசம் ....

ஆய்வாளரின் கையொப்பம் .... இடம் ....தேதி ....

ஆய்வாளரின் பெயர் ....

ஆராய்ச்சி தகவல் தாள்

சென்னை அரசு பொது மருத்துவமனையில் பெருந்தமணி வால்வு சுருக்க நோயில் தமனி எதிர்ப்பு குறித்து மின்-ஒலி வரைவு ஆராய்ச்சி செய்ய உள்ளோம்.

நீங்கள் இந்த ஆராய்ச்சியில் பங்கேற்க நாங்கள் விரும்புகிறோம். இந்த ஆராய்ச்சியில் பங்கேற்பதால் தங்களது நோயின் ஆய்வறிக்கையோ அல்லது சிகிச்சையோ பாதிக்கப்படாது என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த ஆராய்ச்சியின் முடிவுகளை அல்லது கருத்துகளை வெளியிடும் போதோ அல்லது ஆராய்ச்சியின் போதோ தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிடமாட்டோம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

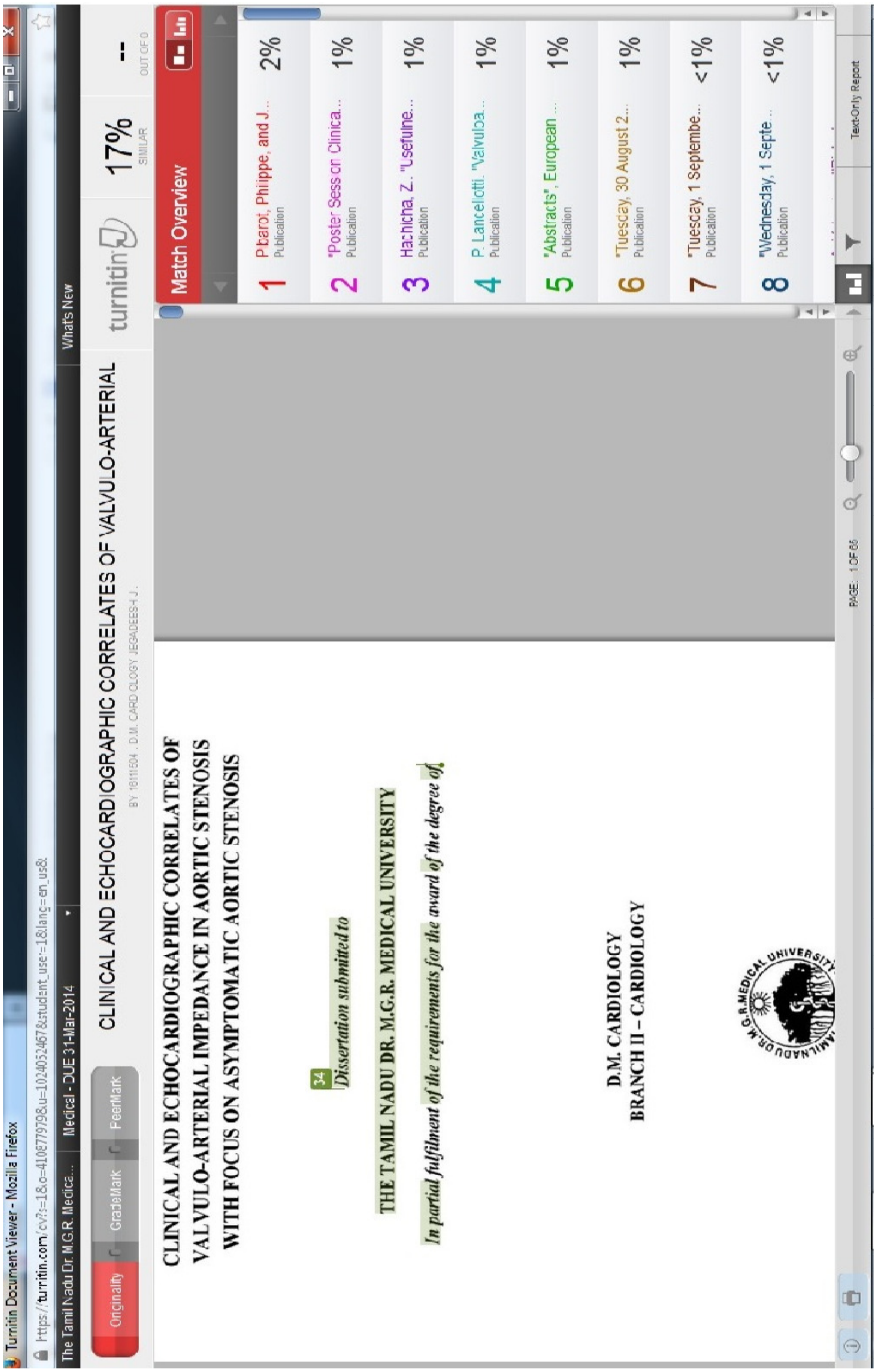
இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆராய்ச்சியில் இருந்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக்கொள்கிறோம்.

இந்த சிறப்புப் பரிசோதனைகளின் முடிவுகளை ஆராய்ச்சியின் போதோ அல்லது ஆராய்ச்சியின் முடிவின் போதோ தங்களுக்கு அறிவிப்போம் என்பதையும் தெரிவித்துக்கோள்கிறோம்.

ஆராய்ச்சியாளர் கையொப்பம் பங்கேற்பாளர் கையொப்பம்

தேதி:

ANTIPLAGIARISM CERTIFICATE



MASTER CHART

S.No	Age	Sex	HT	DM	RHD	Smoking/ tobacco use	Pulse rate	SBP	DBP	Pulse pressure	Height	Weight	BMI	BSA	SOB	Angina	Syncope	Gidiness	LVOT VTI	BCAV
1	72	M	1	0	0	0	72	140	80	60	156	70	24.8	1.79	1	1	1	0	13	0
2	64	M	0	1	0	1	66	126	72	54	163	78	29.4	1.84	1	1	1	0	25	0
3	58	M	0	1	0	1	64	84	60	24	160	70	27.3	1.73	1	0	0	0	15	0
4	58	M	0	0	0	1	81	140	70	70	184	75	24.5	1.90	0	0	0	0	22	0
5	60	M	0	1	0	1	68	142	80	62	168	80	28.3	1.90	1	0	0	0	22	0
6	64	F	0	0	0	0	66	138	84	54	155	62	25.8	1.61	0	1	0	1	27	0
7	67	F	0	1	0	0	88	130	76	54	156	48	20.2	1.43	1	1	1	0	10	0
8	59	M	1	0	0	0	82	144	90	54	170	82	28.4	1.94	0	0	0	0	37	0
9	63	M	1	0	0	0	58	124	80	44	167	65	23.3	1.73	0	0	0	0	27	0
10	61	F	0	1	0	0	82	142	80	62	161	61	24.4	1.62	0	0	0	0	23	0
11	59	M	0	0	0	1	74	136	98	38	159	46	18.2	1.44	1	0	0	0	26	0
12	73	M	0	0	0	1	56	152	90	62	179	76	23.2	1.96	1	1	0	0	17	0
13	48	M	1	1	1	1	68	162	104	58	178	80	25.2	1.98	1	0	0	0	34	0
14	60	M	0	1	0	1	88	134	82	52	180	83	25.6	2.03	1	1	1	0	22	0
15	58	F	0	1	0	0	66	150	76	74	150	58	26.1	1.52	0	0	0	0	14	0
16	51	F	0	0	0	1	70	114	78	36	162	56	21.3	1.59	0	1	0	1	18	0
17	32	M	0	0	0	1	76	130	82	48	167	64	22.9	1.72	0	0	0	1	21	1
18	61	F	1	0	0	0	78	130	74	56	150	66	29.3	1.61	1	0	0	0	21	0
19	68	M	1	0	0	1	74	144	82	62	187	76	24.5	1.92	0	0	0	0	11	0
20	45	M	0	0	0	1	72	116	70	46	180	78	24.1	1.98	0	1	0	0	36	1
21	60	M	0	1	0	0	60	114	90	24	173	60	20.0	1.72	1	0	0	0	29	0
22	74	M	1	1	0	0	70	156	78	78	172	64	23.2	1.71	1	0	1	0	27	0
23	58	M	0	0	0	0	60	148	100	48	178	59	18.6	1.74	0	0	0	0	30	0
24	52	M	0	1	0	0	74	130	100	30	173	70	23.4	1.83	0	1	0	1	43	0
25	61	M	0	0	0	0	72	124	76	48	168	54	19.1	1.61	1	0	0	0	16	0
26	48	M	0	0	0	1	74	110	70	40	165	63	23.1	1.69	1	0	0	0	21	1
27	40	M	1	0	0	1	64	128	82	46	173	62	21.7	1.71	1	0	1	1	16	0

S.No	Age	Sex	HT	DM	RHD	Smoking/ tobacco use	Pulse rate	SBP	DBP	Pulse pressure	Height	Weight	BMI	BSA	SOB	Angina	Syncope	Gidiness	LVOT VTI	BCAV
28	56	M	0	0	0	0	76	120	82	38	170	66	22.8	1.77	0	0	0	0	21	0
29	48	M	1	0	0	1	80	140	80	60	163	63	23.7	1.68	0	1	1	1	25	0
30	56	F	0	0	0	0	90	132	84	48	154	55	23.2	1.52	1	1	0	1	13	0
31	61	F	1	0	0	0	70	162	94	68	154	50	21.1	1.46	0	0	0	0	25	0
32	51	F	0	0	1	0	66	100	72	28	156	50	20.5	1.47	0	0	0	0	24	0
33	53	M	0	1	0	0	58	96	64	32	159	52	20.6	1.52	1	1	0	1	15	0
34	54	F	0	1	0	0	82	100	72	28	167	72	25.8	1.81	0	0	1	0	20	0
35	39	M	0	0	0	1	81	136	78	58	182	83	25.1	2.04	1	1	0	1	25	1
36	58	M	1	1	0	1	68	144	92	52	167	75	26.9	1.84	1	0	0	0	17	0
37	60	M	0	0	0	0	68	118	68	50	173	80	26.7	1.94	0	0	0	0	18	0
38	81	M	1	0	0	0	78	164	90	74	176	65	22.0	1.77	1	0	1	1	14	0
39	56	M	1	0	0	0	60	130	90	40	172	74	25.0	1.87	0	0	0	0	23	0
40	80	M	1	0	0	0	61	152	80	72	164	60	23.7	1.61	1	0	0	0	14	0
41	66	F	0	1	0	0	78	148	70	78	167	78	30.5	1.81	0	0	0	0	15	0
42	55	M	0	1	0	1	69	118	70	48	179	80	25.0	1.99	0	0	0	1	28	0
43	58	M	1	0	0	0	76	130	82	48	172	70	23.7	1.83	1	0	0	0	20	0
44	52	F	1	1	0	0	74	142	90	52	154	48	20.2	1.43	1	0	0	0	17	0
45	70	F	1	1	0	0	82	134	80	54	168	70	24.8	1.79	1	0	0	1	24	0
46	56	M	0	0	0	0	68	124	82	42	176	84	27.1	2.01	1	0	0	0	38	0
47	68	M	1	1	0	0	68	162	90	72	172	73	25.6	1.83	1	0	1	1	28	0

MASTER CHART

S. No	LVOT dia	AV peak velocity	AV VTI	AV area	Peak gradient	Mean gradient	IVS	LVPW	LVIDd	RWT	LVEF	Stroke Vol	SVI	Mitral E	Mitral A	Mitral E/A DD	TDI E'	E/E'	MAPSE	LV Tei index	Zva
1	2.5	4.9	64	0.98	98	64	2.1	1.9	3.6	1.1	58	63	35	142	70	3	7.0	17	8.2	0.48	5.8
2	2.0	4.2	64	1.23	69	57	1.6	1.4	5.0	0.6	56	79	43	116	78	2	7.8	15	10.2	0.50	4.3
3	2.3	4.1	64	1.00	68	42	1.8	1.6	5.0	0.7	58	64	37	122	68	2	12.4	9.8	10.6	0.34	3.4
4	1.9	4.2	68	0.93	72	57	2.0	1.9	4.0	1.0	72	63	33	75	102	1	10.5	7.1	9.8	0.30	6.0
5	2.3	3.6	76	1.20	52	29	1.6	1.6	4.6	0.7	58	91	48	78	104	2	10.3	7.6	10.8	0.38	3.6
6	2.2	4.0	83	1.24	63	45	1.4	1.3	3.9	0.7	60	103	64	128	100	2	11.9	11	10.2	0.38	2.9
7	2.4	5.0	56	0.82	100	72	2.4	2.3	3.2	1.5	70	46	32	80	108	1	10.4	7.6	9.6	0.32	6.3
8	1.8	3.5	103	0.92	50	27	1.8	1.6	3.8	0.9	66	95	49	118	83	2	9.8	12	10.9	0.36	3.5
9	1.9	4.5	53	1.45	80	52	2.1	1.9	3.4	1.2	70	76	44	116	83	2	9.6	12	12.4	0.30	4.0
10	1.8	4.5	55	1.06	80	51	2.0	1.9	3.4	1.1	64	58	36	136	90	2	7.7	18	9.8	0.36	5.4
11	2.3	3.5	73	1.46	48	30	1.6	1.6	4.1	0.8	50	107	74	132	74	2	7.0	11	9.2	0.47	2.2
12	2.4	4.2	93	0.82	72	39	1.6	1.2	3.2	0.9	54	76	39	158	70	3	7.4	19	8.8	0.50	4.9
13	2.4	3.5	104	1.48	49	25	1.5	1.4	5.0	0.6	59	154	78	86	98	1	12.1	7.1	12.4	0.40	2.4
14	2.3	4.0	72	1.27	63	42	1.3	1.2	5.4	0.5	50	91	45	146	72	3	7.4	16	8.9	0.44	3.9
15	2.1	4.3	53	0.95	74	45	1.8	1.9	3.8	1.0	66	50	33	128	88	2	7.9	16	9.6	0.38	5.9
16	2.1	4.1	65	0.98	66	54	1.4	1.2	3.8	0.7	60	64	40	132	90	2	10.9	12	11.5	0.38	4.2
17	2.5	5.0	80	1.27	100	52	1.9	1.6	3.7	0.9	70	101	59	110	86	2	10.4	11	12.8	0.24	3.1
18	2.1	3.8	60	1.24	58	39	1.5	1.4	4.9	0.6	53	74	46	70	94	2	9.3	7.5	9.8	0.38	3.7
19	2.6	4.7	78	0.76	90	67	1.5	1.4	4.2	0.7	68	60	31	146	76	3	9.2	14	9.6	0.36	6.8
20	1.9	4.6	82	1.26	86	51	2.5	2.5	4.0	1.2	70	103	52	126	74	2	7.8	16	12.4	0.32	3.2
21	2.1	5.0	129	0.80	99	67	1.8	1.8	5.4	0.7	40	103	60	124	76	3	6.9	18	7.4	0.50	3.0
22	1.8	4.1	53	1.30	68	37	2.5	2.4	3.9	1.3	68	68	40	150	72	3	8.3	13	10.3	0.41	4.8
23	2.2	3.5	82	1.38	49	28	1.1	1.2	3.6	0.6	61	113	65	77	117	1	11.0	7	10.8	0.32	2.7
24	1.9	3.5	86	1.42	48	26	2.0	2.0	3.9	1.0	68	123	67	78	104	1	10.3	7.6	12.2	0.28	2.3
25	2.3	4.2	48	1.40	72	52	1.8	1.8	5.1	0.7	55	67	42	116	76	2	10.9	11	9.8	0.44	4.2
26	2.0	4.2	72	0.92	72	63	1.5	1.6	4.0	0.8	62	66	39	128	72	2	9.6	13	10.6	0.36	4.4
27	2.1	4.3	65	0.84	73	46	2.0	1.8	4.1	0.9	63	55	32	82	106	1	10.3	7.9	10	0.42	5.4
28	2.1	4.1	62	1.20	68	53	2.1	1.9	3.8	1.1	60	74	42	136	68	2	9.6	14	10.7	0.38	4.1
29	2.4	3.6	79	1.43	52	26	1.8	1.6	3.4	1.0	70	112	67	110	72	2	9.3	12	13	0.38	2.5

S. No	LVOT dia	AV peak velocity	AV VTI	AV area	Peak gradient	Mean gradient	IVS	LVPW	LVIDd	RWT	LVEF	Stroke Vol	SVI	Mitral E	Mitral A	Mitral E/A DD	TDI E'	E/E'	MAPSE	LV Tei index	Zva
30	2.6	4.2	48	1.43	70	48	1.4	1.5	5.6	0.5	54	68	45	128	72	2	12.5	10	10.2	0.47	4.0
31	2.0	3.7	53	1.48	54	26	2.0	1.9	4.0	1.0	63	79	54	110	68	2	11.7	9.4	10.5	0.32	3.5
32	1.9	4.6	52	1.30	84	56	1.6	1.6	3.8	0.8	69	68	46	124	70	2	11.5	11	12	0.36	3.4
33	2.4	4.2	57	1.23	72	60	1.7	1.5	5.1	0.6	56	70	46	90	108	1	4.8	19	10.5	0.44	3.4
34	2.3	4.2	67	1.24	72	53	1.5	1.4	4.7	0.6	60	83	46	82	100	1	11.4	7.2	10.2	0.28	3.3
35	2.2	4.0	67	1.43	64	32	1.7	1.7	3.8	0.9	58	96	47	78	106	1	10.0	7.8	9.9	0.39	3.6
36	2.6	3.8	65	1.36	58	34	1.8	1.4	5.9	0.5	48	88	48	134	90	2	9.3	14	9.6	0.46	3.7
37	2.4	4.2	63	1.32	72	54	1.7	1.6	4.7	0.7	62	83	43	118	72	2	9.4	13	10	0.32	4.0
38	2.4	4.4	70	0.93	76	42	1.4	1.4	4.6	0.6	50	65	37	144	78	3	6.9	19	7.5	0.49	5.6
39	2.2	3.9	61	1.45	60	42	1.8	1.7	3.4	1.0	62	88	47	86	110	2	11.6	7.4	10.8	0.32	3.7
40	2.2	4.6	59	0.87	86	64	1.6	1.5	3.4	0.9	60	52	32	138	92	2	7.9	17	8.4	0.48	6.8
41	2.3	4.5	62	1.02	82	53	2.3	2.1	4.6	1.0	61	63	35	118	86	2	9.3	13	9.7	0.42	5.7
42	2.1	4.2	71	1.35	70	40	1.6	1.5	4.2	0.7	59	95	48	74	104	1	10.1	7.3	11.4	0.28	3.3
43	2.2	3.9	81	0.92	62	43	1.5	1.3	4.2	0.7	58	75	41	146	68	3	7.3	20	10.6	0.42	4.2
44	2.6	3.6	68	1.36	52	32	1.3	1.2	4.5	0.6	54	92	64	147	77	3	7.9	19	9.5	0.40	2.7
45	2.1	3.7	63	1.32	56	44	1.6	1.5	5.3	0.6	56	83	46	134	88	2	11.6	12	10.6	0.36	3.9
46	1.9	4.6	106	1.02	86	50	1.8	1.6	4.0	0.9	58	108	54	124	84	2	10.7	12	10.1	0.41	3.2
47	1.9	4.1	67	1.21	68	36	1.8	1.8	4.0	0.9	66	81	44	128	102	2	8.3	15	9.4	0.44	4.5